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TOMUS 88

Fasciculus 1: 1976
Fasciculus 2: 1976
Fasciculus 3: 1976
Fasciculus 4: 1976

INDEX

Acta Chimica Academiae Scientiarum Hungaricae, Tomus 88 (1), pp. 1—11 (1976)

LIGAND SUBSTITUTION AND COMPLEX STRUCTURE, XIII

NMR SPECTRA OF DIAMAGNETIC Ni(II)-SCHIFF-BASE COMPLEXES

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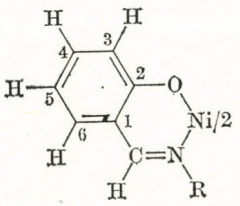
The NMR spectra of the chelate complexes Ni[HSAI-N-n-alkyl]$_2$ have been studied. From the variation of the spectra with the solvent, concentration and temperature, conclusions have been drawn on the nature of the equilibria in inert solvents, under the assumption that, depending on the temperature, a paramagnetic tetrahedral species may also be formed in the solutions of *n*-alkyl compounds.

Compounds of the type bis(N-*n*-alkylsalicylaldiminato) nickel(II) (in the following Ni[HSAI-N-R]$_2$, compound I) are known to have a *trans*-square-planar structure in the solid state with their dipole moments close to zero. The compounds are diamagnetic, thus the central ion has a singlet ground state [1—9]. In non-coordinating solvents, they are slightly paramagnetic [10—12], this fact is attributed to molecular association [13—20]. In the paramagnetic associates the nickel(II) ion of triplet ground state is penta- (square pyramidal) or hexa-coordinate (strongly distorted octahedral). In such solvents the amount of associated species is low, except for the case of the N-methyl derivative. In coordinating solvents, such as pyridine, the compounds are paramagnetic to an extent corresponding to two electrons: bis-pyridine adducts can be isolated from the solution, and all properties of the adducts are the same as those of hexa-coordinate compounds [21—23].

This paper is concerned with the NMR spectra of chelate complexes of the type Ni[HSAI-N-R]$_2$, where R=*n*-alkyl, C_2-C_6 and C_8.



Experimental

The complexes were prepared by reacting the parent compound bis(salicylaldehydato)-nickel(II) · 2H_2O with the appropriate alkylamine, on the basis of literature data [10, 24] or by analogous processes. The crude product was recrystallized from acetone. The Zn_2[HSAI-N-*n*-C_6H_{13}]$_4$ complex was prepared and purified according to Charles [25].

The NMR spectra were recorded on a 60 MHz JEOL C-60 HL spectrometer, by using TMS as external standard. The solvents, temperature range and concentrations will be given in the discussion.

As a typical example, the figures show the results obtained with the *n*-hexyl derivative; the conclusions for the other compounds are more or less analogous.

Results and discussion

The properties of $Ni[HSAI\text{-}N\text{-}CH_3]_2$ in solution are so different from those of the other members of the homologous series, owing to the extensive association, that a separate paper has been devoted to this compound.

In the spectra of compounds containing lower *n*-alkyl groups (C_2 to C_4), relatively sharp signals correspond to the various kinds of protons, with a usually well resolved fine structure (Table I).

Table I

The signals of Ni[HSAI-N-n-alkyl]$_2$ compounds [in δ (ppm)] in carbon disulfide solution at 25°C

R = \ Proton	CH_3	..., γ-CH_3	β-CH_2	α-CH_2	Ring protons		CH=N
$-C_2H_5$	1.22	—	—	3.25	6.24	6.92	8.14
	1.34			3.35	6.37	7.08	
	1.45			3.47	6.51	7.17	
				3.57			
$-C_3H_7$	0.86	—	1.63[a]	3.12	6.24	6.91	7.91
	0.98		1.74	3.24	6.36	7.02	
	1.10		1.88	3.35	6.50	7.12	
			1.99[a]				
$-C_4H_9$	0.87	1.23	1.58	3.19	6.23	6.91	8.05
	1.00	1.34	1.68	3.31	6.36	7.03	
	1.09	1.46	1.79	3.42	6.49	7.13	
$-C_5H_{11}$	0.83	1.34[a]	1.67	3.17	6.23	6.91	7.93
	0.94	1.40	1.79	3.29[a]	6.36	7.03	
	0.98	1.47[a]	1.90		6.49	7.14	
$-C_6H_{13}$	0.90[a]	1.36[a]	1.77[a]	3.13	6.24	6.87	7.82
				3.24	6.34	6.99[a]	
				3.36	6.48		
$-C_8H_{17}$	0.87[a]	1.30[a]	1.69[a]	3.42[a]	6.33[a]	6.93	7.90
					6.47	7.05[a]	

[a] overlapping signals

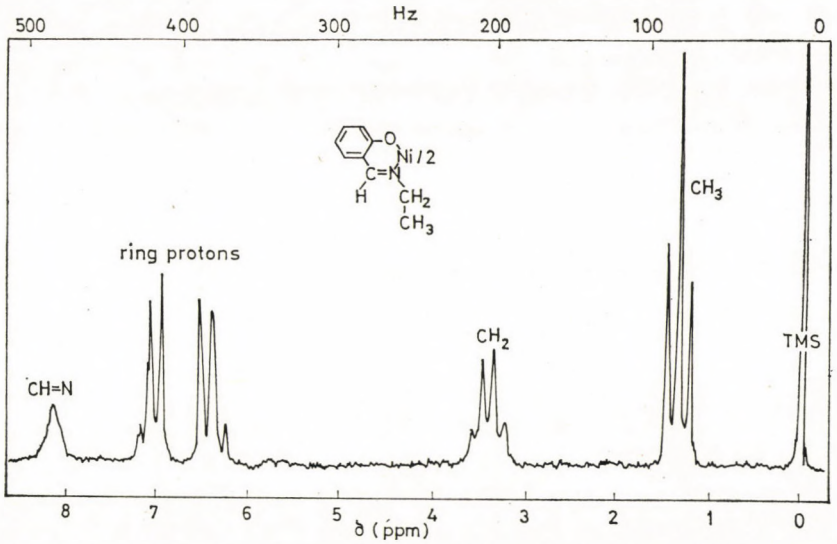


Fig. 1. PMR spectrum of $Ni[HSAI\text{-}N\text{-}C_2H_5]_2$ in CS_2 at 25°C

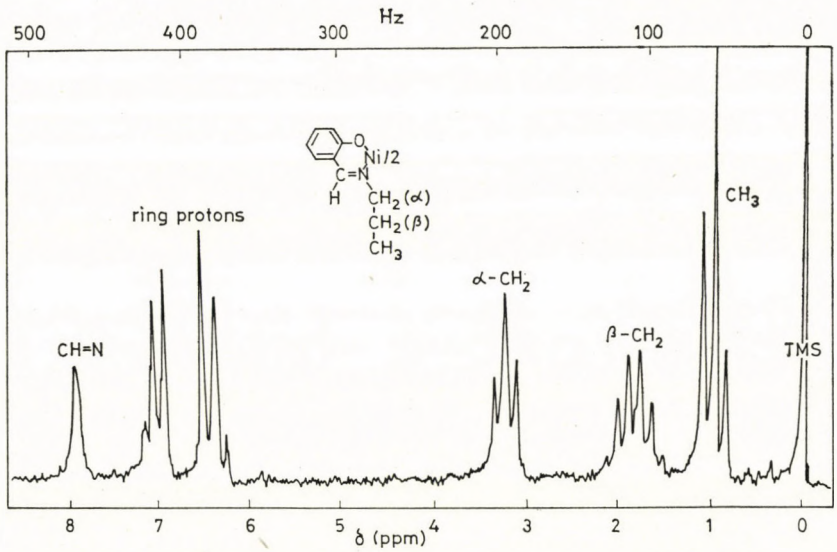


Fig. 2. PMR spectrum of $Ni[HSAI\text{-}N\text{-}n\text{-}C_3H_7]_2$ in CS_2 at 25°C

The signals of the N-alkyl substituent appear in the range of 0.8—3.6 ppm, with an increasing chemical shift in the order of methyl, . . . γ-, β- and α-methylene groups. The different chemical shifts of the protons in different positions with respect to the azomethine nitrogen clearly reflect the decreasing effect of the nitrogen atom along the carbon chain. The signals of alkyl protons are split as expected ($J = 7$ Hz, see Figs 1 and 2); but with higher homologues

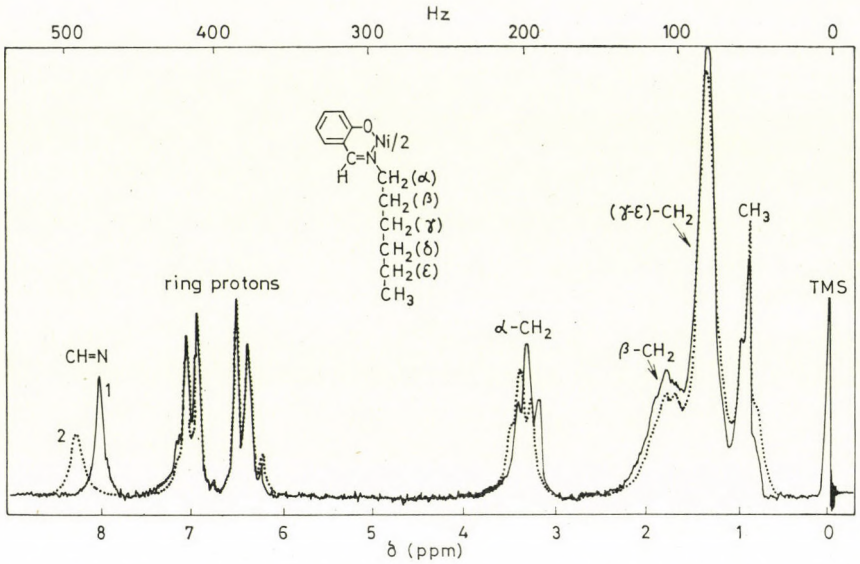


Fig. 3. PMR spectra of Ni[HSAI-N-*n*-C_6H_{13}]$_2$ in CS_2 at 25°C; $c_1 = 0.14\,M$, $c_2 = 0.24\,M$

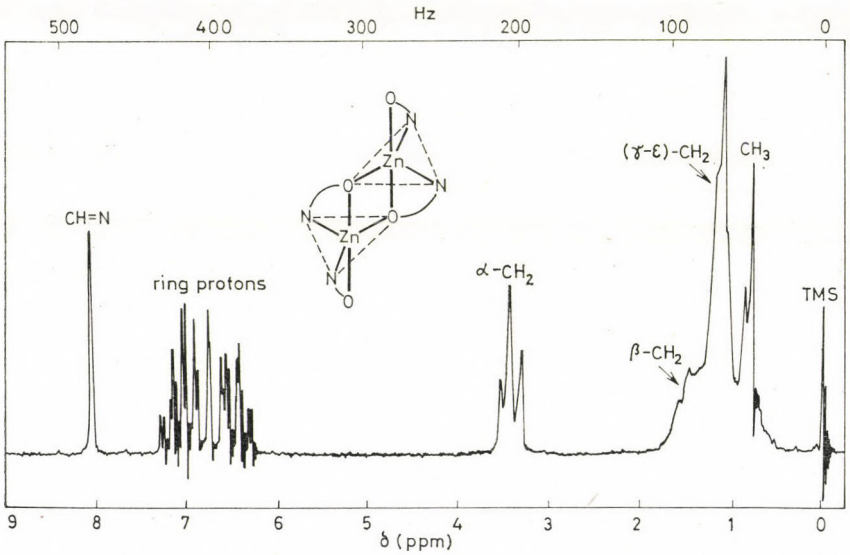


Fig. 4. PMR spectrum of Zn_2[HSAI-N-*n*-C_6H_{13}]$_4$ in CS_2 at 25°C; $c = 0.14\,M$

the signals are broader and blurred, and their fine structure is more difficult to observe (Fig. 3).

The region of aromatic protons contains two groups of signals; this part of the spectrum is, in our opinion, characteristic of an A_2B_2 spin system,

Table II

Concentration dependence of the signals [in δ (ppm)] of various protons of the n-hexyl complex in carbon disulfide at 25°C

Proton / mol/l	CH_3	$(\gamma-\varepsilon)$-CH_2	β-CH_2	α-CH_2	Ring protons		CH=N
a	0.89	1.35	1.60	3.35	6.65—7.35		8.25
				3.48			
				3.60			
0.06	0.90[b]	1.36	1.77	3.13	6.24	6.87	7.82
				3.24	6.34	6.99[b]	
				3.36	6.48		
0.08	0.89[b]	1.37	1.80	3.19	6.23	6.88	8.04
				3.30	6.33	7.02[b]	
				3.40	6.48		
0.12	0.89[b]	1.36	1.78	3.20	6.22	6.89	8.08
				3.31	6.35	7.02[b]	
				3.41	6.47		
0.14	0.89[b]	1.36	1.79	3.18	6.24	6.89	8.00
				3.30	6.36	7.01[b]	
				3.41	6.49		
c	0.8	1.12	1.48	3.31	6.25—7.25		8.02
				3.43			
				3.54			
0.16	0.90[b]	1.37	1.97	3.21	6.23	6.89	8.11
				3.33	6.36	7.02	
				3.44	6.48	7.14	
0.20	0.90[b]	1.36	1.78	3.23	6.22	6.87	8.17
				3.33[b]	6.34	7.01[b]	
					6.46		
0.24	0.89[b]	1.37	1.75	3.27	6.22	6.89	8.28
				3.39[b]	6.35	7.03[b]	
					6.48		
0.30	0.88[b]	1.31	1.73	3.37[b]	6.32[b]	6.88	8.34
					6.46	7.03[b]	

[a] HSAI-N-n-C_6H_{13}
[b] overlapping signals
[c] δ (ppm) values of the diamagnetic zinc complex at a concentration of 0.14 mol/l

which indicates the magnetic equivalence of two pairs of protons. Nevertheless, this conclusion should be supported by theoretical calculations.

The signals of azomethine protons are less sharp, they can be found above 7.8 ppm.

In the spectrum of the $Zn_2[HSAI\text{-}N\text{-}n\text{-}C_6H_{13}]_4$ derivative (Fig. 4, Table II), which is also diamagnetic in solution, one can observe all the resonance

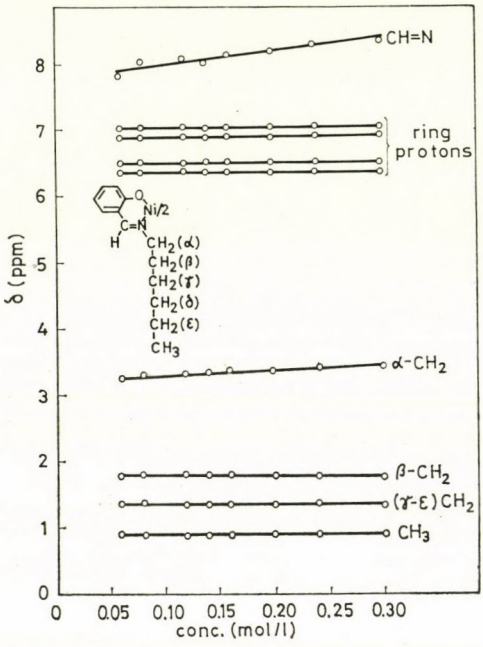


Fig. 5. Concentration dependence of the proton chemical shifts of the *n*-hexyl derivative in CS_2 at 25°C

lines that can be found in the spectrum of the corresponding nickel(II) chelate. The most striking difference between the spectra is in the range of aromatic protons (see Fig. 3). The α-methylene and azomethine signals of the zinc complex are much sharper, and the spectrum, unlike that of the corresponding nickel(II) chelate, is independent of the concentration.

In Table II the chemical shifts of the Schiff-base, $HSAI\text{-}N\text{-}n\text{-}C_6H_{13}$, are also shown. The NMR spectra of the ligand molecule, the diamagnetic zinc complex and of the nickel(II) complex are extremely similar. In the spectrum of the ligand the aromatic proton signals appear in the expected range, furthermore, the signal of the azomethine proton is not split, and the signal of the α-methylene protons is split only into a triplet. These facts suggest that in solution the ligands of the complexes under study are present in the enolimine form, similarly to the Schiff-bases of aniline derivatives [26, 27].

The NMR spectra of the nickel(II) chelates under study are sensitive to the concentration. With increasing concentration the signals of α-methylene, but particularly of azomethine protons are shifted down-fields (Fig. 5). These signals become strongly broadened, and the fine structure of the α-methylene signal is gradually blurred. The small shift of β-methylene signal is opposite in direction.

In inert solvents the Ni[HSAI-N-*n*-alkyl]$_2$ complexes are partially present in associated form. The concentration dependence of the spectrum is a consequence of a contact interaction between the unpaired electrons of the paramagnetic nickel(II) ions of the molecular associates and the nuclei of the

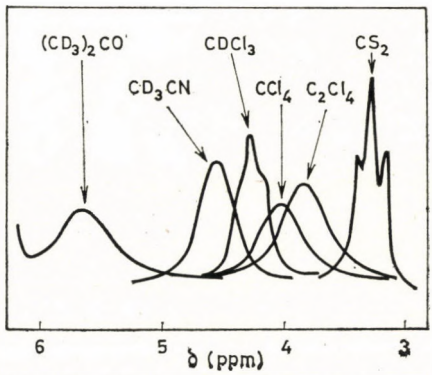


Fig. 6. α- CH_2 signal of Ni[HSAI-N-*n*-C_6H_{13}]$_2$ in different solvents at 25°C; $c = 0.14\ M$

ligands. It has been shown [28, 29] that in Ni[HSAI-N-R]$_2$ chelates the dipolar shifts can be neglected, and that the tetra-coordinate (tetrahedral), penta-coordinate and hexa-coordinate species are characterized by different contact shift patterns [28—31]. With the pyridine adducts of the N-ethyl and N-*n*-propyl derivatives investigated by us, LA MAR [32] has detected the presence of a penta-coordinate, square pyramidal, paramagnetic intermediate form besides the strongly distorted octahedral bispyridine adduct. The difference in contact shift between the two species appears most characteristically in the aromatic 5-H signal, for which even the direction of shift is different. The contact shifts of azomethine and α-methylene protons of the bispyridine adduct and penta-coordinate chelates [31] are negative and by 1—2 orders of magnitude higher than those of the other protons; the shifts of β-CH_2 and β-CH_3 protons are positive.

If the above facts are combined with the observation that the number of paramagnetic species also containing penta-coordinated, or, in the higher associates, hexa-coordinate nickel(II), is very small in comparison with the number of diamagnetic molecules, and that their relative proportion increases only to a minor extent with the concentration, it becomes understandable

why also the azomethine or α-methylene signals are only slightly concentration-dependent in the average spectrum, and why the shifts in the other signal are even smaller.

In various inert solvents different NMR spectra can be obtained (Table III). In these spectra, except for the signals of the terminal methyl protons,

Table III

Signals of the hexyl derivative [in δ (ppm)] measured in various solvents at 25°C; c = 0.14 mol/l

Solvent \ Proton	CH_3	$(\gamma-\varepsilon)$-CH_2	β-CH_2	α-CH_2	Ring protons		CH=N	[b]
CS_2	0.89[a]	1.36	1.79	3.18	6.24	6.89	8.0	2.641
				3.30	6.36	7.01[a]		
				3.41	6.49			
C_2Cl_4	0.83	1.43	1.75	3.88	6.46[a]	7.04	9.7	
	0.95					7.14		
	1.00							
CCl_4	0.91[a]	1.39	1.78	4.06	6.36[a]	7.02	11.6	2.238
					6.48	7.15[a]		
$CDCl_3$	0.90[a]	1.40	1.89	4.32[a]	6.29	7.13	12.2	4.806
					6.45	7.44		
					6.59			
CD_3COCD_3	0.90[a]	1.42	1.7	5.65	6.24	7.32	13.11	20.70
	1.00				6.36	7.45[a]		
					6.48			
CD_3CN	0.91[a]	1.42	—	4.57	6.25	7.19	14.1	37.5
					6.37	7.32[a]		
					6.50			

[a] overlapping signals
[b] dielectric constants (at 20°C) of the corresponding undeuterated solvents

the shapes and chemical shifts of all resonance signals show certain variation with the solvent. The degree of association, *i.e.* the relative proportion of penta- and hexa-coordinate species present beside the diamagnetic square-planar form, varies with the solvent, and this variation has, as discussed above, a significant effect on the spectrum. The solvent effect is most pronounced in the shifts of the azomethine and α-methylene signals (Fig. 6.) It is clear from the data of Table III that an unambiguous correlation can be ob-

Table IV

Temperature dependence of the signals [in δ (ppm)] of the hexyl derivative in C_2Cl_4; $c \approx$ const.

Proton / t(°C)	CH_3	$(\gamma - \varepsilon)$-CH_2	β-CH_2	α-CH_2	Ring protons		CH=N
25	0.95[a]	1.43	1.75	3.88	6.46[a]	7.04[a]	9.7
						7.14	
50	0.94[a]	1.43	1.83	3.91	6.19	7.03[a]	9.7
	1.00				6.30	7.15	
					6.41		
					6.54		
60	0.94[a]	1.46	1.83	3.98	6.15	6.99[a]	9.9
	0.99				6.27	7.11	
					6.37		
					6.51		
70	0.93[a]	1.42	1.85	4.13	6.16	6.99	10.2
	1.00				6.28	7.13	
					6.39	7.21	
					6.53	7.33	
80	0.93[a]	1.42	1.87	4.29	6.13	6.99	10.6
	1.00				6.26	7.11	
					6.37	7.21	
					6.49	7.33	
90	0.91[a]	1.43	1.87	4.48	6.10	6.98	11.1
	1.00				6.23	7.11	
					6.34	7.21	
					6.47	7.34	
100	0.88[a]	1.42	1.89	4.68	6.08	6.99	11.7
	0.99				6.20	7.13	
					6.31	7.24	
					6.44	7.38	
110	0.93[a]	1.46	1.81	4.98	6.05	7.03	12.5
	1.01				6.17	7.15	
					6.28	7.29	
					6.42	7.43	
120	0.94[a]	1.51	1.93	5.26	5.97	7.02	13.1
	1.02				6.11	7.15	
					6.23	7.33	
					6.36	7.44	

[a] overlapping signals

served primarily between the signal of azomethine protons and the dielectric constant of the solvent, but similar tendencies appear in connection with the dipole moment. Presumably, the differences in averaged shielding of the protons are due to the presence of different associates in various solvents, but it cannot be excluded either that there is a variation in the extent of coupling between the azomethine and α-methylene protons.

Since the degree of association decreases with increasing temperature one can expect a decrease in linewidth, and a variation in the chemical shifts similar in sense to the effect of decreasing concentration. The widths of azomethine and α-methylene signals indeed decrease with increasing temperature, and the triplet structure of the latter signal becomes gradually more distinguish-

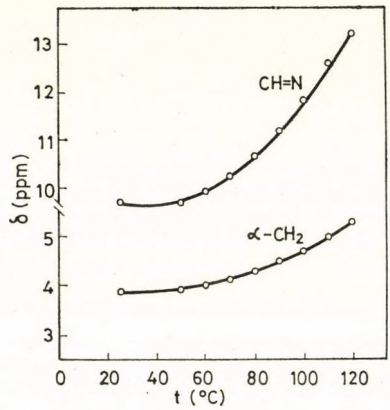


Fig. 7. Chemical shifts of α-CH_2 and CH=N protons of Ni[HSAI-N-*n*-C_6H_{13}]$_2$ as functions of the temperature; c = const.

able. These signals are, however, shifted downfield above ca. 50°C. With the exception of the methyl signal, the chemical shifts of all signals depend more or less on the temperature, and with the ring protons even the fine structure is changed (Table IV, Fig. 7).

It is known that the R=α-branched derivatives, which are, primarily for steric reasons, tetrahedral in the solid state, form, in inert solvents, a ternary equilibrium system involving associated (paramagn.), $\rightleftharpoons$ monomeric square-planar (diamagn.) $\rightleftharpoons$ and tetrahedral (paramagn.) species. At lower temperatures the formation of paramagnetic associates, at higher temperatures that of the paramagnetic tetrahedral species is preferred [3, 28]. On this basis it is assumed that the above changes observed in the NMR spectra can be attributed to the fact that although the amount of paramagnetic associates decreases with temperature, the probability of formation of paramagnetic tetrahedral species increases in parallel. Accordingly, also in the solutions of the complexes of *n*-alkyl derivatives the above mentioned ternary equilibrium system is present above a certain temperature.

REFERENCES

[1] Fox, M. R., Lingafelter, E. C., Orioli, P. L., Sacconi, L.: Acta Cryst., **17,** 1159 (1964)
[2] Frasson, E., Panattoni, C., Sacconi, L.: J. Phys. Chem., **63,** 1908 (1959)
[3] Sacconi, L., Paoletti, P., Ciampolini, M.: J. Amer. Chem. Soc., **85,** 411 (1963)
[4] Holm, R. H.: J. Amer. Chem. Soc., **83,** 4683 (1961)
[5] Clark, H. C., Macvicar, K., O'Brien, R. J.: Can. J. Chem., **40,** 822 (1962)
[6] Ferguson, J.: J. Chem. Phys., **34,** 611 (1961)
[7] Methuen, B., v. Stackelberg, M.: Z. anorg. allg. Chem., **305,** 279 (1960)
[8] Frasson, E., Panattoni, C., Sacconi, L.: Acta Cryst., **17,** 85 (1964)
[9] Frasson, E., Panattoni, C., Sacconi, L.: Gazz. Chim. Ital., **92,** 1470 (1962)
[10] Sacconi, L., Paoletti, P., Del Re, G.: J. Amer. Chem. Soc., **79,** 4062 (1957)
[11] Willis, J. B., Mellor, D. P.: J. Amer. Chem. Soc., **69,** 1237 (1947)
[12] Clark, H. C., Odell, A. L.: J. Chem. Soc., **3431** (1955); **520** (1956)
[13] Ferguson, J.: J. Phys. Chem., **63,** 343 (1959)
[14] Ferguson, J.: Spectrochim. Acta, **17,** 316 (1961)
[15] Holm, R. H., McKinney, I. M.: J. Amer. Chem. Soc., **82,** 5506 (1960)
[16] Holm, R. H.: 6th Int. Conf. on Coord. Chem. Detroit, 1961, p. 341.
[17] Holm, R. H., Swaminathan, K.: Inorg. Chem., **1,** 599 (1962)
[18] Sacconi, L., Paoletti, P., Cini, R.: 4th Int. Conf. on Coord. Chem. Roma, 1957
J. Inorg. Nucl. Chem., **8,** 429 (1958)
J. Amer. Chem. Soc., **80,** 3583 (1958)
[19] Harris, C. H., Lenzer, S. L., Martin, R. L.: Austr. J. Chem., **11,** 331 (1958)
[20] Miller, J. R.: Advances in Inorganic Chemistry and Radiochemistry. Ed.: J. H. Emeleus and A. G. Sharpe, Vol. 4, p. 133, Acad. Press, New York 1962
[21] Maki, G.: J. Chem. Phys. **29,** 1129 (1958)
[22] Yamada S. *et al.:* Coord. Chem. Rev., **3,** 247 (1968)
[23] Sacconi, L.: Coord. Chem. Rev., **1,** 126, 192 (1966), and references therein
[24] Klem, W., Raddatz, K. H.: Z. anorg. allg. Chem., **250,** 207 (1942)
[25] Charles, R. G.: J. Inorg. Nucl. Chem., **9,** 145 (1959)
[26] Percy, G. C., Thornton, D. A.: Chimia, **25,** 194 (1971)
[27] Percy, G. C., Thornton, D. A.: J. Inorg. Nucl. Chem., **34,** 3357 (1972)
[28] Holm, R. H., Chakravorty, A., Dudek, G. O.: J. Amer. Chem. Soc., **86,** 379 (1964)
[29] La Mar, G. N.: Mol. Phys., **12,** 427 (1967)
[30] Chakravorty, A., Fennessey, J. P., Holm, R. H.: Inorg. Chem., **4,** 26 (1965)
[31] La Mar, G. N., Sacconi, L.: J. Amer. Chem. Soc., **89,** 2282 (1967)
[32] La Mar, G. N.: Inorg. Chim. Acta, **3,** 183 (1969)

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INVESTIGATION OF HYDRATION OF MACROMOLECULES, I

MEASUREMENT OF SELF-DIFFUSION OF WATER IN SOLUTIONS OF POLYVINYL ALCOHOL

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Self-diffusion coefficient of water in solutions of polyvinyl alcohol (PVA) has been determined at two temperatures (25 and 35°C) in the concentration range between 0 and 10 w/w%. Determinations were made using open-end capillary method without stirring. Water was labelled with ^{18}O isotope, analysis has been performed by mass spectrometry.

It has been stated that self-diffusion coefficient of water decreases proportionally to increasing PVA concentrations in the given concentration range, at both temperatures. Energy of activation of self-diffusion was found to be 4.5 ± 1.4 kcal/mole. Hydration number of PVA has been calculated; it was found identical at both temperatures, *i.e.* 3.7—4 molecules of H_2O per OH group, depending on the shape factor. The density of solutions grew proportionally to the concentration of the macromolecule. Specific volume of PVA was found to be 0.734_4 cm^3/g at 25°C and 0.762_8 cm^3/g at 35°C. The viscosity of solutions increased markedly with increasing PVA concentration; the energy of activation of viscous flow has been found to be 7.4 ± 0.4 kcal/mole.

Introduction

The more or less exact study of hydration of macromolecules has a past of about forty years. Owing to their vital importance, mainly the study of various proteins and nucleic acids represented particular interest. The interpretation of the results of these investigations is, however, very difficult, as it is obvious *e.g.* from the review monography of LING [1]. One of the main problems is the complexity of the systems to be studied, in particular, that even their structure is not known exactly and, they contained in several cases other components in addition to the macromolecular substance and water. Thus, the supposed amount of combined water could not be ascribed to individual functional groups, and *e.g.* even the hydration of a peptide chain can not be regarded as a problem solved. Additional difficulty of interpretation arises from the fact that different authors applied different single methods of the several possible ones giving each different type of information; and further, that different authors applied different models for calculation of hydration number.* Consequently, if the extent of hydration of given functional groups

* *Hydration number* is the average amount of water per unit weight or structural unit of macromolecule that is bound to the latter and moves together with it in solution.

is to be determined (this seems to be the most important question in this subject) macromolecules with identical structure have to be chosen as model substances containing one type of group to be considered with respect to hydration. In addition, it is advisable to use several methods of measurement sensitive against the extent of hydration, for the investigation of each system.

Polyvinyl alcohol has been selected as the first model substance for our series of investigation. This was justified by the assumption that the study of aqueous solutions of polyvinyl alcohol (abbreviated hereinafter through PVA) by appropriate methods allows to estimate the amount of water bound by one hydroxyl group.

The present paper summarizes our results obtained in the study of self-diffusion coefficient of water. This was studied in PVA solution in the concentration range between 0 and 10 w/w% at 25 and 35°C. Viscosity and density of the solutions have also been measured.

Experimental

Polyvinyl alcohol and its fractionation

A commercial product called Rhodoviol 16/20 has been used as polyvinyl alcohol; it was previously partially fractionated by *n*-propanol in order to remove low molecular weight fractions. The weight average molecular weight after fractionation was determined by light scattering 110, 000 ± 10%. Acetate content: about 2 mole%.

Bidistilled water was used for its dissolving. The concentrations have been determined by measuring their dry substance content. Average error of concentration measurements was ±0.1 rel.%. The salt concentration of the solutions was less than 5×10^{-5} with respect to actual PVA concentration, as determined by flame photometry.

Selection of an isotope label

^{18}O was used for labelling water since — according to our own measurements — in this case exchange reactions between water and alcoholic OH groups should not be taken into account. Any exchange would make impossible to evaluate self-diffusion of the labelled molecules. No isotope effect occurs if ^{18}O is used.

Diffusion method

Self-diffusion coefficient was measured by the open-end capillary method without stirring. The experimental technique and the method of calculation of self-diffusion coefficient was described in the paper of ERDEY-GRÚZ *et al.* [2] and its references. Correction for capillary length (GERGELY *et al.* [3]) was negligible as compared with other sources of experimental error. The accuracy of thermostating was ±0.01°C.

Hydration number was calculated according to WANG's equation [4]:

$$\frac{D'}{D_0} - \Delta_1 = 1 - [\bar{\alpha}\,(V_p + \mathrm{H}/d_0) + \mathrm{H}]\,w + \Delta_2 \qquad (1)$$

where D' denotes self-diffusion coefficient of water measured in the solution; D_0 that of pure water; $\bar{\alpha}$ a constant depending on the shape of the molecule; V_p the apparent specific volume of the given macromolecule in solution; d_0 the density of water; H the hydration number expressed as g of water per g of dissolved substance; w the weight fraction of macromolecule in the solution; Δ_1 and Δ_2 minor correction factors which can be calculated theoretically.

Analysis of labelled solutions

Isotope composition of water obtained by vacuum distillation from solutions has been determined by a mass spectrometer Type MI-1311 by measuring the ratio of ion intensities of $H_2{}^{18}O/H_2{}^{16}O$.

Viscosity measurements

Viscosities of solutions have been measured by Höppler-viscosimeter, at 25, 30 and 35 $\pm$ 0.05°C.

Density measurements

Densities were determined by picnometer method at 25 and 35 $\pm$ 0.01°C.

Results and discussion

Self-diffusion coefficient of water (more exactly, the value of $\frac{D'}{D_0} - \Delta_1$) in solutions of polyvinyl alcohol decreases proportionally to the weight fraction at both temperatures. The energy of activation of self-diffusion of water ($\Delta H_D^{\ddagger}$) in PVA solutions is equal to that of self-diffusion of pure water, within the limits of experimental error. Values of self-diffusion coefficient and energy of activation have been summarized in Table I. Our data indicate that

Table I

Self-diffusion coefficient of water in PVA solutions at 25 and 35°C

PVA concentration (%)	$D^{25} \cdot 10^5$ ($cm^2\ s^{-1}$)	$D^{35} \cdot 10^5$ ($cm^2\ s^{-1}$)	$\Delta H_D^{\ddagger}$ (kcal/mole)
0.00	2.57 $\pm$ 0.024	3.49 $\pm$ 0.15	4.9 $\pm$ 0.8
3.93	1.95 $\pm$ 0.103	2.48 $\pm$ 0.15	4.4 $\pm$ 1.4
6.01	1.69 $\pm$ 0.051	—	—
7.69	1.54 $\pm$ 0.077	1.99 $\pm$ 0.10	4.7 $\pm$ 1.3
9.20	1.25 $\pm$ 0.078	—	—
9.56	1.30 $\pm$ 0.104	—	—

Every data in the Table is the average of 5—9 measurements. Errors given are standard deviations of the mean

the WANG-equation (1) is valid also for PVA-water systems, in agreement with data concerning aqueous solutions of ovalbumin [5] and DNA [6]. It should be noted that in our case, since PVA contains no ionic groups, only obstruction and direct hydration effects should be considered. The condition that the diffusion coefficient of the macromolecule should be much lower than that of water is also fulfilled (the former being approximately 2×10^{-7} cm^2/s at 25 °C [7]).

In order to be able to determine hydration number from Eq. (1), it is necessary to know the specific volume of macromolecules as well as the shape factor $\bar{\alpha}$. According to our measurements, the specific volume of PVA is constant in the concentration range investigated, its value being 0.737_4 cm^3/g at 25°C and 0.762_8 cm^3/g at 35°C. Data on specific volume of solutions have been summarized in Table II.

Table II

Specific volume of aqueous PVA solutions at different temperatures

PVA concentration (%)	V_e^{25} (cm^3/g)	V_e^{35} (cm^3/g)
0.00	1.004	1.006
3.93	0.9932[a]	0.9960[a]
6.01	0.9884	0.9919
7.69	0.9831	0.9878
9.20	0.9795	0.9831
9.56	0.9785	—

[a] The relative error of specific volumes is $\pm 0.6\%$

The greatest problem arises from the correct selection of the shape factor $\bar{\alpha}$. The original derivation was related to rotational ellipsoids being impermeable and large as compared with solvent molecules and having different axis ratios. Since random coils of PVA molecules are probably permeable for water molecules, two extreme $\bar{\alpha}$ values were selected for calculation of hydration number. The value of $\bar{\alpha} = 1.500$ belongs to spherical molecules and $\bar{\alpha} = 1.667$ to rod-like ones. Hydration numbers calculated by both values are to be seen in Table III. In our case, with identical hydration positions and

Table III

Hydration numbers of hydroxyl groups of PVA for different values of $\bar{\alpha}$ at 25 and 35°C

T (°C)	H (mole H_2O per OH group)	
	$\bar{\alpha} = 1.500$	$\bar{\alpha} = 1.667$
25	4.0 ± 0.3	3.7 ± 0.3
35	4.0 ± 0.7	3.7 ± 0.6

Deviations were calculated as the error of the straight line $\frac{D'}{D_0} - A_1$ *vs* w

no hydration at the vinyl chain of the polymer, hydrate water can be assigned to alcoholic OH groups, thus the average number of water molecules bound by one hydroxyl group has been given. It should be noted, however, that this is an average value only, since inter- and intramolecular association of macromolecules through hydroxyl groups has also to be taken into consideration [7, 8]. The extent of association can be regarded as constant in our concentration and temperature range. This is supported by the change of specific volume of the solutions being proportional to concentration, and especially by the fact that although the viscosity of solutions (η) increases very markedly with increasing PVA concentration, the energy of activation of viscous flow ($\Delta H_\eta^\ddagger$) can be regarded as a constant value (*cf.* Table IV). Consequently, if the degree

Table IV

Viscosity of aequous PVA solutions at different temperatures

PVA concentration (%)	η_{15} (cP)	η_{30} (cP)	η_{15} (cP)	$\Delta H_\eta^\ddagger$ (kcal/mole)
0	0.8941	0.8019	0.7250	—
3.93	21.9 ± 0.2	17.9(5) ± 0.2	14.6(6) ± 0.1	7.3 ± 0.3
6.01	82.5 ± 0.8	—	54.8 ± 0.5	7.5 ± 0.3
7.69	223.0 ± 2.2	176.0 ± 2.0	149.(7) ± 1.0	7.3 ± 0.3
9.20	479.(5) ± 5.0	—	316.(2) ± 3.0	7.6 ± 0.4
9.56	—	—	—	—

of association is known, the real amount of water molecules bound by one OH group can be simply calculated.

Since the decrease of self-diffusion coefficient of water is much lower than the increase of viscosity, the product $D\eta$ increases considerably as a function of concentration. Consequently, self-diffusion of water is not related to macroviscosity but to the microviscosity of its surrounding. According to our other results [8], the product of self-diffusion coefficient of water and the microviscosity calculated from the variation of dielectric relaxation time of water will give a constant value with better approximation. The theoretical interpretation of such a microviscosity is, however, not yet clear in all respects.

Hydration numbers determined by us are in good agreement with the qualitative suggestion of M. NAGY on the basis of viscosity measurements [9] according to which PVA is strongly hydrated in aqueous solutions. A similarly good agreements is obtained with quantitative data of SPONSLER *et al.* [10]

suggesting 3 water molecules per OH group as the theoretical hydration number of hydroxyl groups. This was also verified by X-ray diffraction and IR absorption studies of protein–water systems.

*

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REFERENCES

[1] LING, G. N.: Water and Aqueous Solutions, ed. Horne, R. A., Wiley-Interscience, N. Y. 1972. p. 663.
[2] ERDEY-GRÚZ, T., INZELT, GY., FODOR–CSÁNYI, P.: Acta Chim. Acad. Sci. Hung., **77,** 173 (1973)
[3] GERGELY, J., TAMÁS, J., VÉRTES, A., LENGYEL, S.: Acta Chim. Acad. Sci. Hung., **39,** 423 (1963)
[4] WANG, J. H.: J. Amer. Chem. Soc., **76,** 4755 (1954)
[5] WANG, J. H., ANFINSEN, C. B., POLESTRA, F. M.: J. Amer. Chem. Soc., **76,** 4763 (1954)
[6] WANG, J. H.: J. Phys. Chem., **77,** 258 (1955)
[7] DÉKÁNY, I., SIPOS, S., SZÁNTÓ, F.: Kolloid-Z. u. Z. Polymere, **251,** 752 (1973)
[8] INZELT, GY., GRÓF, P.: Proc. Int. Conf. Colloid and Surface Sci., Vol. 1., p. 645. Budapest, 1975.
[9] NAGY, M.: Kémiai Közl., **29,** 1 (1968)
[10] SPONSLER, O. L., BATH, J. D., ELLIS, J. W.: J. Phys. Chem., **44,** 996 (1940)

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KOMPLEXBILDUNGSVERMÖGEN VON NICKEL MIT 1-HYDROXYÄTHAN-1,1-DIPHOSPHONSÄURE

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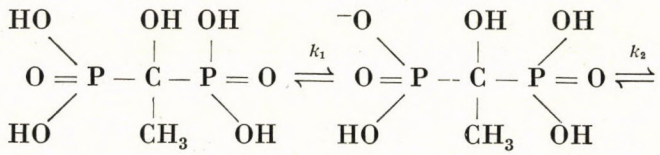
Nickelionen bilden in wäßriger Lösung mit 1-Hydroxyäthan-1,1-diphosphonsäure Komplexe, die in Abhängigkeit vom pH-Wert unterschiedlich protoniert sind. Mit Hilfe spektralphotometrischer Methoden konnten die Gleichgewichtskonstanten sowie die Protonierungskonstanten für NiH_2Y, $NiHY^-$ und NiY^{2-} bestimmt werden.

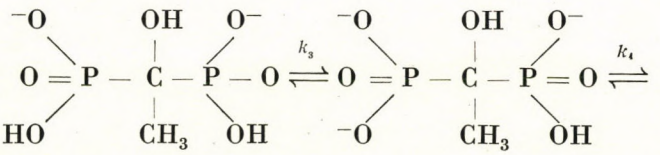
Einleitung

1-Hydroxyäthan-1,1-diphosphonsäure bildet als mehrzähniger Ligand eine Reihe von löslichen Komplexen mit vielen Metallionen [1—9].

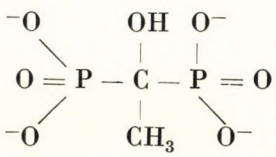
Das Auftreten von Komplexen mit verschiedener Zusammensetzung ist auf die unterschiedliche Beteiligung der Sauerstoffatome der Phosphonsäuregruppen an der Komplexbildung zurückzuführen. Die Komplexliganden sind die Dissoziationsstufen der Säure



(H_4Y) (H_3Y^-)



(H_2Y^{2-}) (HY^{3-})



(Y^{4-})

Mit ihnen bauen sich Einkernkomplexe auf, wenn jeweils nur eine Phosphonsäuregruppe in die Komplexbindung eintritt. Zweikernkomplexe mit viergliedrigen Chelatringen entstehen aus einem Liganden und zwei Metallionen. Weiterhin sind Einkernkomplexe mit sechsgliedrigen Chelatringen bekannt. Die Vielfalt der möglichen Komplexe erhöht sich durch die mehr oder weniger ausgeprägte Protonisierung der genannten Einkern- bzw. Zweikernkomplexe.

Außerdem wird besonders für die Komplexe mit Calcium, Magnesium, einigen Nebengruppenelementen sowie seltenen Erden die Beteiligung der an den Kohlenstoff gebundenen Hydroxylgruppe diskutiert [1 3, 4, 5, 9].

Versuchsbedingungen

Geräte: Registrierendes Spektralphotometer DK-2A (Beckman)
pH-Meßgerät MV 11 (Clamann & Grahnert) mit Glaselektrode und Kalomelelektrode.
Substanzen: 1-Hydroxyäthan-1,1-diphosphonsäure (chemisch rein), $NiSO_4 \cdot 7H_2O$ p. a., $NiCl_2 \cdot 6H_2O$ p. a., NaOH p. a.
Die Probelösungen wurden aus 0,03 molaren wäßrigen Stammlösungen der 1-Hydroxyäthan-1,1-diphosphonsäure (HEDP) bzw. der Nickelsalze hergestellt. Zur Einstellung des jeweiligen pH-Wertes diente 3*n* NaOH.
Die spektralphotometrische Messung erfolgte bei Raumtemperatur (22°C).

Ergebnisse und Auswertung

Das Absorptionsspektrum des $[Ni(H_2O)_6]^{2+}$-Ions weist drei Absorptionsmaxima bei 395, 665 und 725 nm auf. Lösungen, die Nickelionen und den Komplexbildner HEDP im molaren Verhältnis 1 : 1 enthalten, ergeben in Abhängigkeit vom pH-Wert die in Abbildung 1 dargestellten Spektren. Aus dem Auftreten isosbestischer Punkte (Tabelle I) ist auf das Vorhandensein isolierter Gleichgewichtsstufen zu schließen. Den Spektren in Abbildung 1 ist zu entnehmen, daß die Natur der in Lösung vorliegenden Verbindungen über einen großen pH-Bereich von 2,55—11,80 erhalten bleibt. So verschiebt sich bei niederen pH-Werten das Extinktionsmaximum nur geringfügig von 398 nm auf 412 nm, bleibt aber dann im pH-Bereich 6,0—11,8 konstant bei 412 nm. Eine Änderung des Absorptionsverhaltens erfolgt erst oberhalb pH 11,8. Es entsteht ein weiterer Komplex, dessen Auftreten durch zwei isosbestische Punkte bei 401 nm und 728 nm angezeigt wird, jedoch im Rahmen der vorliegenden Untersuchung nicht charakterisiert wurde.

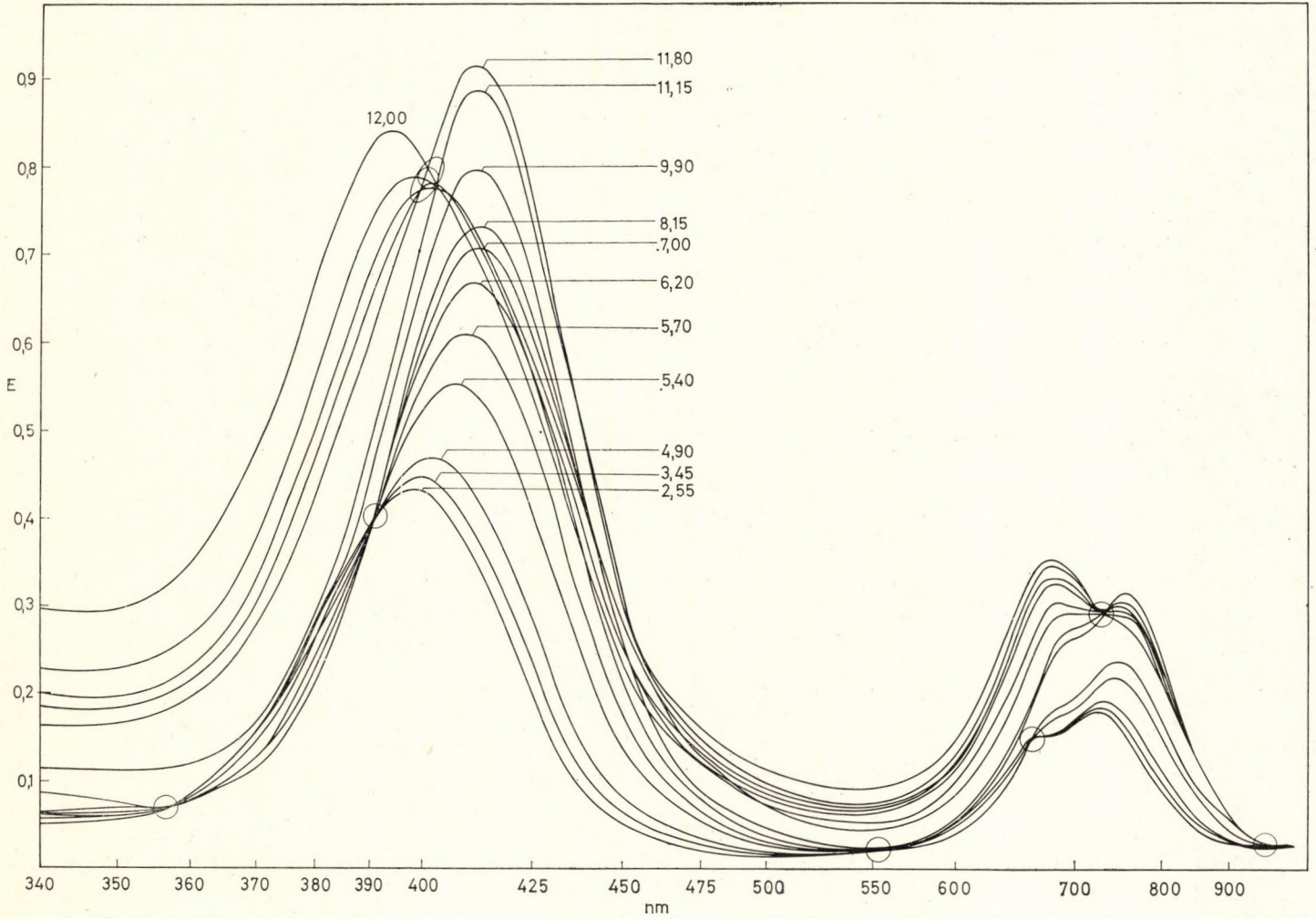


Abb. 1 Absorptionskurven von Mischungen der 0,03 mol Ni^{2+}-Lösung mit 0,03 mol HEDP-Lösung (1 : 1) bei verschiedenen pH-Werten

Tabelle I

Lage der Isosbestischen Punkte für Lösungen von $NiSO_4$/HEDP ($NiSO_4$ 0,015 mol/l, HEDP 0,015 mol/l)

	pH-Bereich	nm
Isosbestische Punkte 1	3,45—8,15	357
	3,45—8.15	391
	4,9 —8,15	554
	3,45—8,15	662
	3,45—8,15	960
Isosbestische Punkte 2	11,8—12,0	401
	11,8—12,0	728

Zur Bestimmung der Zusammensetzung des in der Lösung bei pH-Werten unterhalb pH 11,8 vorliegenden Komplexes diente die Methode der kontinuierlichen Variation [10]. Die Ergebnisse zeigt Abbildung 2, in der die bei drei verschiedenen Wellenlängen ermittelten Extinktionsdifferenzen der komplexhaltigen Lösungen gegenüber einer reinen Nickelsalzlösung gleicher Konzentration in Abhängigkeit vom Molenbruch des Nickels aufgetragen sind. Alle drei Kurven besitzen ihr Maximum beim Molenbruch 0,5, so daß die Existenz eines 1 : 1-Komplexes als bewiesen angesehen werden kann und Komplexzusammensetzungen in anderen molaren Verhältnissen auszuschließen sind.

Nach SCHWARZENBACH [11, 12] können die Kurven durch eine Gleichung der Form

$$\Delta E = \varepsilon_m \left[\frac{c + \frac{1}{K}}{2} - \sqrt{\left(\frac{c + \frac{1}{K}}{2} \right)^2 - c^2 \cdot x(1-x)} \right]$$

beschrieben werden.

Hierin sind

K = Gleichgewichtskonstante

c = Konzentration der Stammlösungen

x = Molenbruch

$\varepsilon_m = \varepsilon_{AB} - \varepsilon_1 - \varepsilon_2$

ε_1, ε_2 = Extinktionskoeffizienten der Lösungen $NiCl_2$ bzw. HEDP

Zusätzlich ermittelt man auf graphischem Wege die Steigung der Kurven im Punkte $x = 0$ bzw. $x = 1$. Dafür gilt

$$\varepsilon_m = \frac{Kc^2}{Kc + 1}.$$

Dieser Ausdruck dient als zweite unabhängige Beziehung. Einsetzen der experimentellen Werte und Lösen der Gleichungen führt auf den Wert lg K = = 3,3 für die Gleichgewichtskonstante der Reaktion

$$Ni^{2+} + H_2Y^{2-} \rightleftarrows NiH_2Y .$$

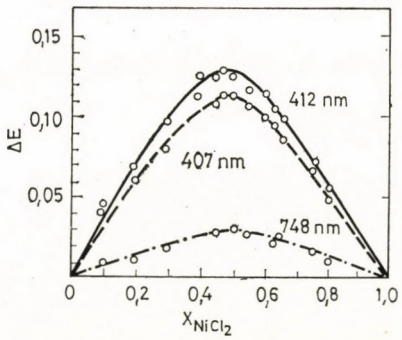


Abb. 2. Extinktionsdifferenzen ΔE für Lösungen verschiedener Zusammensetzung von Ni^{2+} (0,03 mol) und HEDP (0,03 mol) bei λ = 407, 412 und 748 nm

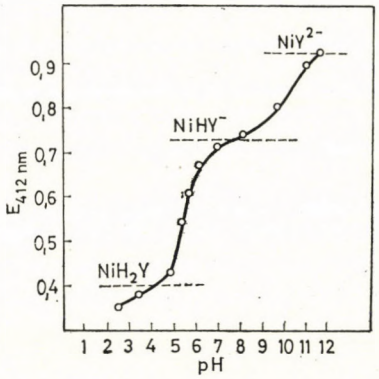


Abb. 3. Absorptionsmaximum bei λ = 412 nm von Mischungen der 0,03 mol Ni^{2+}-Lösungen mit 0,03 mol HEDP-Lösung (1 : 1) in Abhängigkeit vom pH-Wert

Die in der Abbildung 1 diskutierte Konstanz der Lage der Absorptionsmaxima im pH-Bereich von 2,55—11,80 ist jedoch mit einer wesentlichen Erhöhung der Extinktion verbunden (Abbildung 3). Es treten deutlich drei Stufen hervor, die den unterschiedlich protonierten Komplexen NiH_2Y, $NiHY^-$ und NiY^{2-} zuzuordnen sind.

Die Konstanten für die Protonierungsgleichgewichte zwischen den Komplexen NiH_2Y, $NiHY^-$ und NiY^{2-} sind aus der in Abbildung 4 dargestellten pH-Wert-Abhängigkeit der Extinktionen bei den Wellenlängen der

isosbestischen Punkte zu ermitteln. Die Protonierungsgleichgewichte lassen sich durch das Massenwirkungsgesetz beschreiben:

$$K^{H+}_{NiH_2Y} = \frac{[NiH_2Y]}{[NiHY^-][H^+]} \cdot K^{H+}_{NiHY-} = \frac{[NiHY^-]}{[NiY^{2-}][H^+]} .$$

Unter der Voraussetzung gleicher Konzentration der im Gleichgewicht befindlichen Komplexe gilt

$$K^{H+}_{NiH_2Y} = \frac{1}{[H^+]} \text{ und } K^{H+}_{NiHY-} = \frac{1}{[H^+]} ,$$

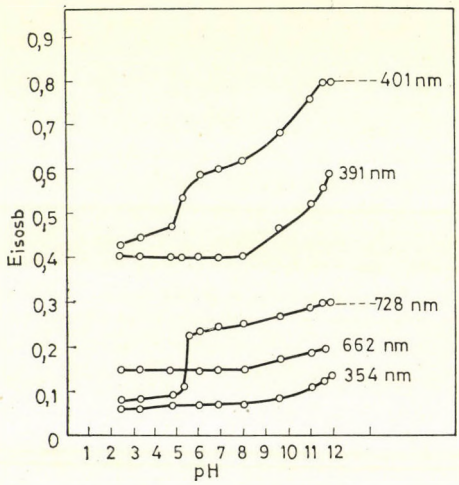


Abb. 4. Abhängigkeit der Extinktion an den isosbestischen Punkten λ = 354, 391, 401, 662 und 728 nm vom pH-Wert

das heißt zur Bestimmung der Konstanten genügt die Kenntnis des pH-Wertes, für den diese Forderung zutrifft. Nach VAREILLE [13] ergeben sich diese pH-Werte aus der folgenden Betrachtung:

$$[NiHY^-] = [NiY^{2-}] = \frac{c}{2}$$

c = Ausgangskonzentration an Metallsalz.
Daraus folgt für die Extinktion beim gesuchten pH-Wert

$$E = (\varepsilon_{NiHY-} + \varepsilon_{NiY^{2-}}) \cdot \frac{c}{2} .$$

Dann ist

$$E = \frac{1}{2}(E_{\mathrm{NiHY}^-} + E_{\mathrm{NiY}^{2-}}),$$

wobei E_{NiHY^-} und $E_{\mathrm{NiY}^{2-}}$ jene Extinktionen sind, bei denen diese Komplexe vollständig vorliegen. Man findet so durch einfache Mittelwertbildung aus den Extinktionskurven bei den Wellenlängen der isosbestischen Punkte die Gleichgewichtskonstante des dem isosbestischen Punkt vor- bzw. nachgelagerten Gleichgewichts.

Aus der Abbildung 4 ergeben sich folgende Werte:

$$\lg K^{\mathrm{H}^+}_{\mathrm{NiH_2Y}} = 5{,}5 \qquad \lg K^{\mathrm{H}^+}_{\mathrm{NiHY}^-} = 10{,}0$$

Diese Werte gestatten die Berechnung von zwei weiteren Komplexbildungskonstanten. Die Beziehungen dafür lauten:

$$K^{\mathrm{H}^+}_{\mathrm{NiH_2Y}} = K^{\mathrm{H_2Y^{2-}}}_{\mathrm{NiH_2Y}} / K^{\mathrm{HY^{3-}}}_{\mathrm{NiHY}^-} \cdot K_3$$
$$K^{\mathrm{H}^+}_{\mathrm{NiHY}^-} = K^{\mathrm{HY^{3-}}}_{\mathrm{NiHY}^-} / K^{\mathrm{Y^{4-}}}_{\mathrm{NiY}^{2-}} \cdot K_4$$

K_3 und K_4 sind die Dissoziationskonstanten der HEDP und wurden der Arbeit von WADA und FERNANDO [8] entnommen. Es ergeben sich

$$\lg K^{\mathrm{HY^{3-}}}_{\mathrm{NiHY}^-} = \lg \frac{[\mathrm{NiHY}^-]}{[\mathrm{Ni}^{2+}]\,[\mathrm{HY}^{3-}]} = 4{,}8$$

und

$$\lg K^{\mathrm{Y^{4-}}}_{\mathrm{NiY}^{2-}} = \lg \frac{[\mathrm{NiHY}^-]}{[\mathrm{Ni}^{2+}]\,[\mathrm{Y}^{4-}]} = 5{,}7$$

Im untersuchten pH-Bereich 2,55—11,80 sind außer den beschriebenen 1 : 1-Komplexen Verbindungen mit anderen molaren Verhältnissen nicht erhalten worden, da beim Erreichen des molaren Ni/HEDP-Verhältnisses von 2 : 1 stets ein Niederschlag ausfiel. Dies steht in Übereinstimmung mit den Ergebnissen von WADA und FERNANDO an Komplexen von HEDP mit Kupfer [9].

LITERATUR

[1] CALLIS, C. F., KERST, A. F., LYONS, I. W.: »Coordination Chemistry« Herausgeber St. Kirschner, Plenum Press NY (1969)
[2] GRABENSTÄTTER, R. J., QUINLEY, O. T., FLAUTT, T. J.: J. physic. Chem. **71,** 4194 (1967)
[3] CARROLL, R. L., IRANI, R. R.: J. inorg. Chem. **6,** 1994 (1967)
[4] CARROLL, R. L., IRANI, R. R.: J. inorg. nucl. Chem. **30,** 2971 (1968)
[5] KABACHNIK, M. I., LASTOVSKI, R. P., MEDVED, T. YA., MEDYNTSEV, V. V., KOLPAKOVA, I. D., DYATIOVA, N. M.: Dokl. Akad. Nauk SSSR **177,** 585 (1967)
[6] GRABENSTÄTTER, R. J., CILLEY, W. A.: J. physic. Chem. **75,** 676 (1971)
[7] PŘIBIL, R., VESELY, V.: Talanta **14,** 591 (1967)
[8] WADA, H., FERNANDO, Q.: Anal. Chem. **43,** 751 (1971)
[9] WADA, H., FERNANDO, Q.: Anal. Chem. **44,** 1640 (1972)
[10] JOB, P.: Ann. Chim. Phys. **9,** 113 (1928)
[11] SCHWARZENBACH, G.: Helv. chim. Acta **32,** 839 (1949)
[12] SCHWARZENBACH, G.: Helv. chim. Acta **34,** 528 (1951)
[13] VAREILLE, L.: Bull. Soc. chim. France 870, 872 (1955)

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CLEAVAGE OF THE HETERO RING OF ISOFLAVONOIDS WITH NUCLEOPHILIC REAGENTS, III

KINETICS OF THE DECOMPOSITION OF α-FORMYL-2-HYDROXYDEOXYBENZOIN TO 2-HYDROXYDEOXYBENZOIN

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Received July 29, 1974

A kinetic study of the decomposition of α-formyl-2-hydroxydeoxybenzoin-enol (**II**) to 2-hydroxydeoxybenzoin has shown that this decomposition is inhibited by hydroxide ions. It is assumed that the inhibition consists essentially in shifting of the dissociation equilibrium **II** ⇌ **III** in the presence of the hydroxide ions towards **III**, and the di-anion thus produced is inactive.

The activation energy and entropy of the decomposition reaction, as well as the equilibrium constant of the above dissociation equilibrium have been determined.

In our preceding communication [1] it has been reported that, under the experimental conditions used by us, the alkaline decomposition of isoflavone can be separated kinetically into two reaction steps: ring opening beginning with nucleophilic A_N2 addition, followed by the much slower decomposition to 2-hydroxydeoxybenzoin. The rate determining step of the decomposition of isoflavone to 2-hydroxydeoxybenzoin is just the decomposition of α-formyl-2-hydroxydeoxybenzoin-enol (**II**) to 2-hydroxydeoxybenzoin; therefore, the kinetical investigation of the said conversion is very important in the elucidation of the whole decomposition process.

Our present work deals with these kinetic investigations.

Experimental

The kinetic measurements were made by the spectrophotometric method [1]. A UNICAM SP 800 B spectrophotometer was used for recording the spectra and effecting the kinetic measurements, using aqueous sodium hydroxide solutions of various concentrations (0.02—1 *M*) and aqueous ethanolic NaOH solutions. The ionic strength of the solutions was adjusted, in aqueous medium with potassium chloride, and in the solutions containing alcohol with $NaClO_4$, to a constant value ($I = 1$).

Twenty minutes after the starting of the reaction, ring cleavage was complete under the given experimental conditions, and the measurement of the decomposition process began only afterwards [1].

Results and discussion

The spectrum of the enol (**II**) or rather the enolate (**III**) of α-formyl-2-hydroxydeoxybenzoin [1], formed during the cleavage of the isoflavone ring, changes slowly in alkaline medium in the direction of the spectrum of

* This paper has been written on the basis of the dissertation of M. ZSUGA.

2-hydroxydeoxybenzoin phenolate (**IV**) (Figs 1, 2), so that the change of the spectrum corresponds to a decomposition process to 2-hydroxydeoxybenzoin phenolate (**IV**). The decomposition reaction has been repeated under preparative conditions. The progress of the reaction and its final state were followed by thin-layer chromatography. The preparative experiments fully supported the results of the spectrophotometric measurements.

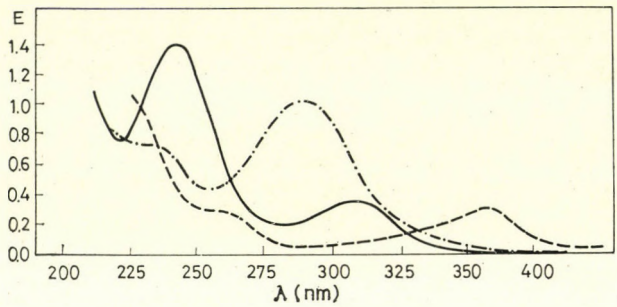


Fig. 1. Spectrum of isoflavone in H_2O ———; spectrum of α-formyl-2-hydroxydeoxybenzoin-enol in 0.1 *N* NaOH -·-·-·-; spectrum of 2-hydroxydeoxybenzoin in 0.1 *N* NaOH - - - - - - -. $C = 5 \cdot 10^{-5}$ *M*

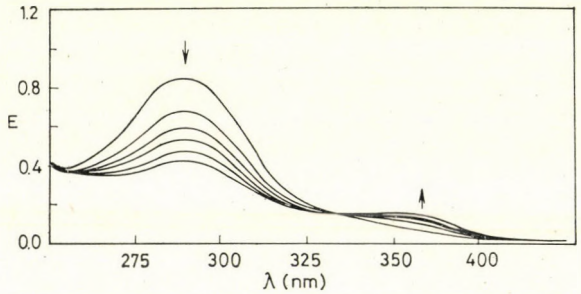


Fig. 2. Changing of the spectrum of α-formyl-2-hydroxydeoxybenzoin in alkaline medium at 35°C
$\Delta t = 1$ hr; $C = 5 \cdot 10^{-5}$ *M*; $[OH^-] = 0.6$ *M*

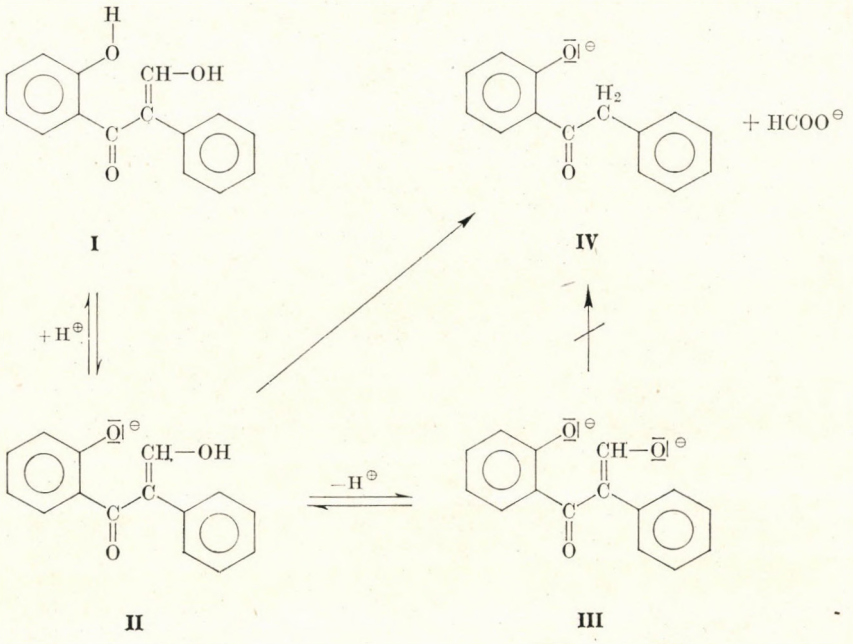
The kinetic study of the decomposition reaction was carried out at the wavelength 290 nm. The apparent reaction rate constant (k_d) was calculated in the same way as described in our earlier paper [1].

With the aid of the apparent reaction rate constants (k_d), the extinction values belonging to the various points of time have been calculated [1]. The good agreement between the measured and calculated extinction values ($\sigma = \pm 2.7 \cdot 10^{-3}$ absorption unit) proves that under the given experimental conditions the decomposition process can be regarded as a pseudo-first order reaction.

The dependence of the apparent reaction rate constants of the decomposition on the hydroxide ion concentration [OH^-], of the medium is shown

in Fig. 3. (The average relative error of the apparent reaction rate constants is $\delta = \pm 3.0\%$.)

Investigations of the ring opening reaction of isoflavone [1], the dehydration reaction of 2-hydroxyisoflavone [2] and the catalytic hydrogenation of isoflavone in alkaline medium [3] have led to the conclusion that in alkaline medium the reactions shown in Scheme 1 are to be expected.



Since the kinetics of the decomposition reaction were studied after the ring opening reaction ($t \geq 20$ min), when equilibrium of the ring cleavage had been attained and since the equilibrium **II** ⇌ **III** is established according to our experiences [2] instantaneously, the reaction system shown in Scheme 1 can be simplified; the dissociation equilibrium **II** ⇌ **III** is to be regarded as the pre-equilibrium of the decomposition to 2-hydroxydeoxybenzoin phenolate (**IV**). Under the conditions of the experiment, the reaction system contains practically only **II**, **III** and **IV** [1], so that the decomposition reaction of α-formyl-2-hydroxydeoxybenzoin-enol (**II**) to 2-hydroxydeoxybenzoin phenolate (**IV**) can be described by the following reaction mechanism:

$$\mathbf{II} + OH^- \overset{K}{\rightleftharpoons} \mathbf{III} + H_2O$$
$$\mathbf{II} \xrightarrow{k} \mathbf{IV} + HCOO^-$$

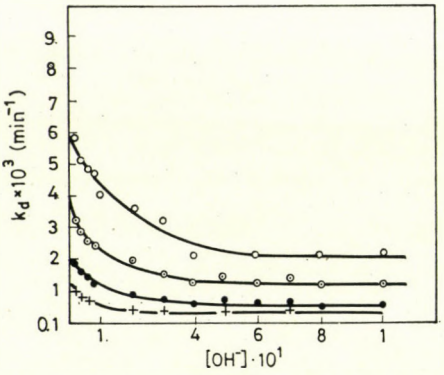


Fig. 3. Dependence of the k_d constants on [OH$^-$] o - o - o - o - o at 35°C; -⊙-⊙-⊙- at 30°C; ..... at 25°C; −+−+−+− at 20°C

Since

$$K = \frac{[\mathbf{III}]\ [H^+]}{[\mathbf{II}]} \quad \text{and} \quad K = \frac{[\mathbf{III}]\ Kw}{[\mathbf{II}]\ [OH^-]} \tag{2}$$

where Kw = ionic product of water,

$$\text{and } C_b = [\mathbf{II}] + [\mathbf{III}] + [\mathbf{IV}], \tag{3}$$

i.e. C_b is the total concentration of the organic component.

Expressing [II] from Eqs (2) and (3):

$$[\mathbf{II}] = C^* \left(1 - \frac{K\,[OH^-]}{K\,[OH^-] + Kw}\right) = \frac{Kw}{K\,[OH^-] + Kw}\, C^* \tag{4}$$

where $C^* = C_b - [\mathbf{IV}]$.

$$\frac{d\,[\mathbf{II}]}{dt} = -\,k\,[\mathbf{II}] = -\,k\,\frac{Kw}{K\,[OH^-] + Kw}\, C^* \tag{5}$$

If $[OH^-]$ = const., then the apparent reaction rate constant is:

$$k_d = \frac{k\,Kw}{K\,[OH^-] + Kw} \tag{6}$$

and

$$\frac{1}{k_d} = \frac{K^*\,[OH^-]}{k} + \frac{1}{k} \tag{7}$$

where

$$K^* = \frac{K}{Kw}.$$

$1/k_d$ plotted as a function of $[OH^-]$ gives a straight line (Fig. 4), which means that the apparent reaction rate constant is, in accordance with Eq. (7), inversely proportional to $[OH^-]$. Thus, hydroxide ions inhibit the decomposition of α-formyl-2-hydroxydeoxybenzoin-enol (**II**) to 2-hydroxydeoxybenzoin phenolate (**IV**); this is the opposite of the effect of hydroxide ions catalyzing the decomposition of β-diketones in alkaline medium [5].

The inhibitive effect of the hydroxide ions has been interpreted similarly as in the catalytic hydrogenation of isoflavone [3] in alkaline medium and in the dehydration reaction of 2-hydroxyisoflavanone [2], by the shifting of the **II** ⇄ **III** dissociation equilibrium in the direction of the upper arrow. This

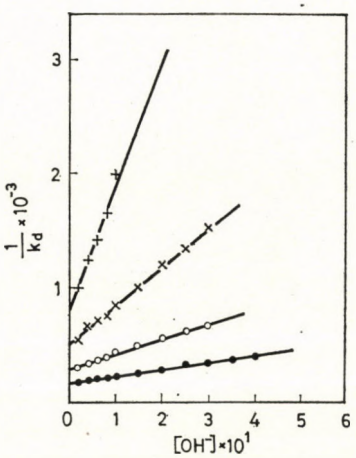


Fig. 4. Dependence of $1/k_d$ on $[OH^-]$
—+—+—+— at 20°C; -x-x-x-x-x- at 25°C; -o-o-o-o-o- at 30°C; ..... at 35°C

inhibitive effect is a further confirmation of our observation made in several chemical reactions [2, 3] that the di-anion-**III** is very stable in alkaline medium; it is not converted either to isoflavone or 2-hydroxydeoxybenzoin phenolate (**IV**), and cannot be reduced even by catalytic reaction.

With the aim to study the hydrolytic character of the decomposition reaction, the change of the decomposition rate was investigated, at constant hydroxide ion concentration and ionic strength, as a function of the alcohol concentration. It has been found that k_d increases in linear proportion with the alcohol concentration (Fig. 5). Since the ionic strength was constant, the increase of k_d can only be interpreted by a decrease in the hydroxide ion activity caused by the change in the activity of water, so that this experimental series affords additional proof for the inhibite effect of hydroxide ions [4, 8].

On the basis of Eq. (7), the rate constants of the decomposition reaction have been determined, at various temperatures, from the axis intersections

of the straight lines shown in Fig. 4, and the equilibrium constants of the dissociation **II** ⇄ **III** from the slope of the lines. From the reaction rate constants determined in aqueous alkaline medium at various temperatures, the activa-

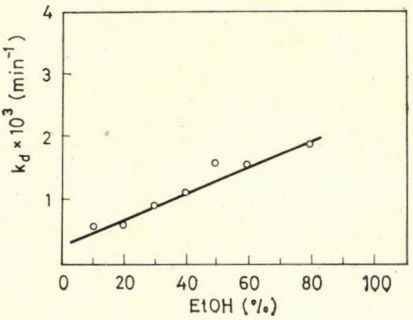


Fig. 5. Dependence of k_d on the alcohol content of the solution at 20°C $C = 5 \cdot 10^{-5}$ *M*; $[OH^-] = 0.05$ *M*

tion parameters of the decomposition reaction have also been calculated. A value of $E^* = (20.00 \pm 0.04$ kcal mole^{-1} has been obtained for the activation energy, and a value of $\Delta S^* = (-11.50 \pm 1.4)$ cal mole^{-1}.degree^{-1} for the entropy of activation. The reaction rate and equilibrium constants are summarized in Table I.

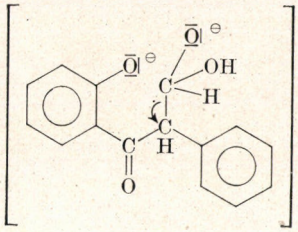
Table I

The reaction rate constants and dissociation constants of the decomposition of α-formyl-2-hydroxydeoxybenzoin-enol to 2-hydroxydeoxybenzoin at various temperatures

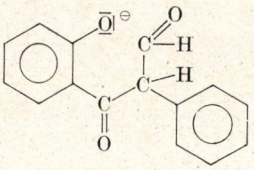
T (°K)	$k \cdot 10^3$	$K^* \cdot 10^{-1}$	$K \cdot 10^{14}$
293	1.078 ± 0.21	1.1448	9.85
298	1.96 ± 0.15	0.6736	8.56
303	3.276 ± 0.17	0.4262	8.06
308	5.89 ± 0.03	0.3751	7.84

The values of the ionic product of water have been taken from the literature [8, 9]

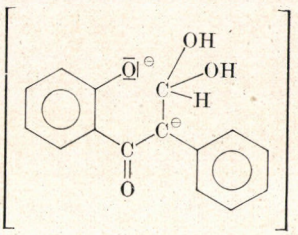
The activation entropy of the decomposition process shows [7] that the transition state of the decomposition from **II** is not much more complicated than **II**. It seems therefore probable that, similarly to the alkaline cleavage of diketones [5], decomposition proceeds through the intermediate products **VI** and **VII**, formed from both **II** and its oxo form **V** [10]; the formation of **VI** and **VII** is instantaneous, while their decomposition to 2-hydroxydeoxybenzoin phenolate (**IV**) is a much slower process (Scheme 2).



VI



V



VII

The presence of the intermediate products **VI** and **VII** is also indicated by the fact that formic acid is formed in the decomposition of isoflavone in alkaline medium [6], and its formation cannot be interpreted neither from **II** nor from the oxo form of **II** (**V**) without a new nucleophilic attack.

REFERENCES

[1] Szabó, V., Zsuga, M.: Acta Chim. (Budapest) **85,** 179 (1975)
[2] Szabó, V., Zsuga, M.: Acta Chim. (Budapest) **85,** 191 (1975)
[3] Szabó, V., Antal, E.: Tetrahedron Letters **1973,** 1659
[4] Bowden, K.: Chem. Rev. **66,** 119 (1966); Paabo, M., Robinson, R. A., Bates, R. G.: J. Am. Chem. Soc. **87,** 415 (1965); Paul, M. A., Long, F. A.: Chem. Rev. **1** (1957)
[5] Pearson, R. G., Mayerle, E. A.: J. Am. Chem. Soc. **73,** 926 (1951)
[6] Geissman, T. A.: The Chemistry of Flavonoid Compounds. Pergamon Press, Oxford 1962
Cheng, E. Yorder L.: Proc. Iowa Acad. Sci. **65,** 220 (1958); Inoue, N.: Sci. Rep. Tohoku Univ. Ser. 1 XLV, 73 (1961)
[7] Szántay, Cs.: Elméleti Szerves Kémia (Theoretical Organic Chemistry). Műszaki Könyvkiadó, Budapest 1971
[8] Fiordiponti, P., Rallo, F., Rodante, F.: Z. phys. Chem. Neue Folge **88,** 149 (1974)
[9] Weast, R. C.: Handbook of Chemistry and Physics. CRC Press, Cleveland, Ohio 1973—74
[10] Hauser, C. R., Swamer, F. W., Ringler, B. J.: J. Am. Chem. Soc. **70,** 4023 (1948)

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STUDY OF THE ISOMERIZATION OF UNSATURATED ALCOHOLS ON METAL CATALYSTS BY AN IMPULSE TECHNIQUE

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The transformations of three isomeric unsaturated alcohols (allylcarbinol, crotyl alcohol and methylvinylcarbinol) were studied by an impulse technique on thermolite-supported platinum, palladium and rhodium, and on Raney-type copper, nickel and zinc catalysts in the presence of hydrogen at 100—400°C. The main reaction directions (isomerization to oxo compound and hydrogenation to saturated alcohol) were followed as functions of the various experimental parameters. Conclusions were drawn from the experimental results about the mechanism of the isomerization.

1. Introduction

Metal catalysts are known to catalyze not only the hydrogenation of unsaturated alcohols, but also their isomerization to oxo compounds [1—6]. A survey of the literature relating to the process reveals that the individual metal catalysts have not been subjected to comparative study under identical experimental conditions, nor has the mechanism of the isomerization process been investigated.* Similarly, no reference was found to the examination of the metal-catalyzed isomerization by an impulse technique method.

Accordingly, we set out to study the isomerization of three isomeric unsaturated alcohols (allylcarbinol, crotyl alcohol and methylvinylcarbinol) on thermolite-supported platinum, palladium and rhodium catalysts (in the following: Pt/T, Pd/T and Rh/T) and on Raney-type nickel, copper and zinc catalysts (in the following: Ni/Al, Cu/Al and Zn/Al). Thermolite is a support employed in gas chromatography; it is a fire-resistant clay, consisting predominantly of calcium magnesium silicate. The examinations were carried out by an impulse technique in the presence of hydrogen as carrier gas, at 100—400°C, at atmospheric pressure. As a consequence of the presence of hydrogen, hydrogenation to saturated alcohols also occurred.

With regard to the study of the mechanism of the isomerization process, examinations were carried out on thermolite, on a carrier-free rhodium catalyst, on a platinum-carbon catalyst, in the absence of hydrogen (with helium

* While the present report was being written, a paper was published by EADON and SHIEKH [7] about an investigation of the mechanism of the copper-catalyzed isomerization of α,β-unsaturated alcohols.

as carrier gas), and on catalysts poisoned with pyridine. An investigation was further made of the transformations of the main products (butyraldehyde, methyl ethyl ketone, 1-butanol and 2-butanol) under the same experimental conditions as used for the unsaturated alcohols.

2. Results

2.1 Transformations of the unsaturated alcohols on thermolite

When the transformations of the three model compounds were studied on thermolite at 100—250°C, it was found that they underwent considerably less conversion than on the catalysts. Allylcarbinol proved to be completely stable; the conversions of methylvinylcarbinol and crotyl alcohol at 250°C were 30% and 50%, respectively, while at 185°C practically no conversion was obtained. In the case of methylvinylcarbinol, fragmentation occurred, whereas part of the crotyl alcohol isomerized at 250°C to allylcarbinol (7%) and methylvinylcarbinol (8%). It should be noted that the formation of the isomeric oxo compounds, butyraldehyde and methyl ethyl ketone, was not observed on a thermolite support. These experimental data thus show that there can be no doubt about the correctness of the suggestion as regards the isomerizing effect of these supported metal catalysts, leading to the formation of oxo compounds.

2.2 Main directions of transformation

The experimental data are presented in Figs 1—16, which show the variation of the product composition with temperature in the transformations of the three model compounds on the six catalysts. The amount of product formed varies as a function of temperature according to a maximum curve; this can be explained by their further conversions. The study of these latter processes was not part of this programme.

The following more important conclusions can be drawn from the experimental data.

In the course of the transformations of the three model compounds, the products shown in the schemes below are formed.

In the cases of allyl carbinol and crotyl alcohol:

$$\begin{array}{lcl} CH_2{=}CH{-}CH_2{-}CH_2{-}OH & & CH_3{-}CH_2{-}CH_2{-}CHO \\ & \xrightarrow{H_2} & \\ CH_3{-}CH{=}CH{-}CH_2{-}OH & & CH_3{-}CH_2{-}CH_2{-}CH_2{-}OH \end{array}$$

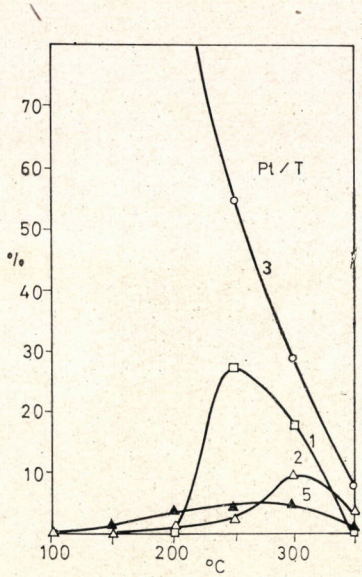


Fig. 1.

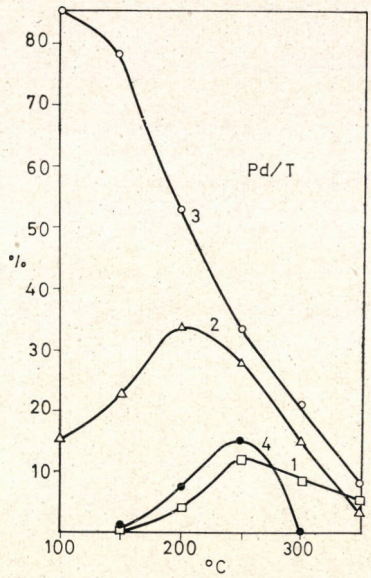


Fig. 2.

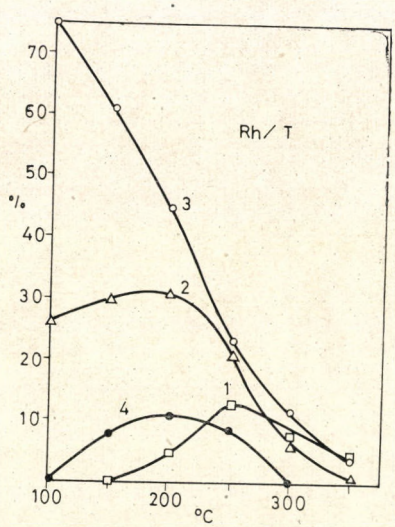


Fig. 3.

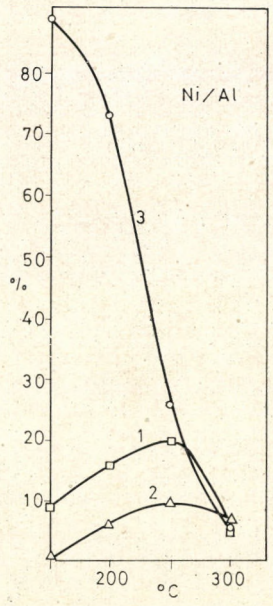


Fig. 4.

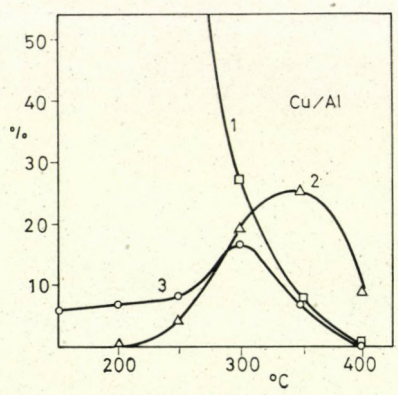


Fig. 5.

Figs 1—5. Variation of the product composition as a function of temperature in the transformation of allylcarbinol (1: allylcarbinol; 2: butyraldehyde; 3: 1-butanol; 4: crotyl alcohol; 5: dibutyl ether)

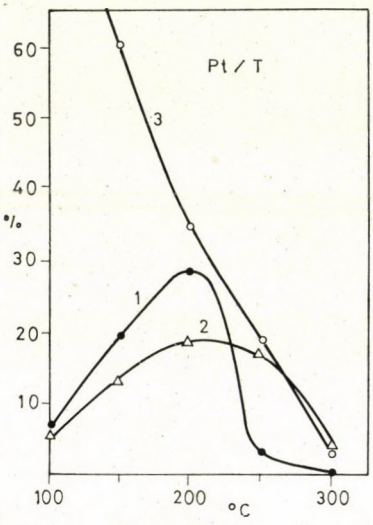


Fig. 6.

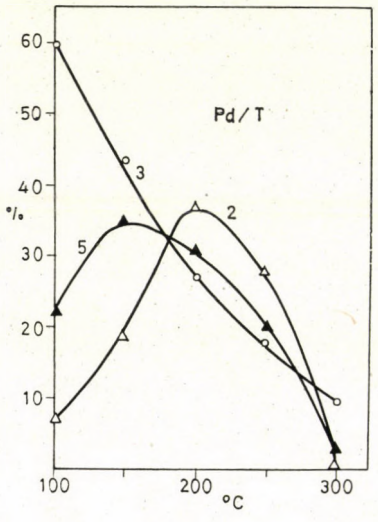


Fig. 7.

In addition to these products, the formation of the following compounds can also be observed: dibutyl ether,* crotonaldehyde, 2-butanol and methyl ethyl ketone.

* The ether-formation process has been reported in an earlier paper [8].

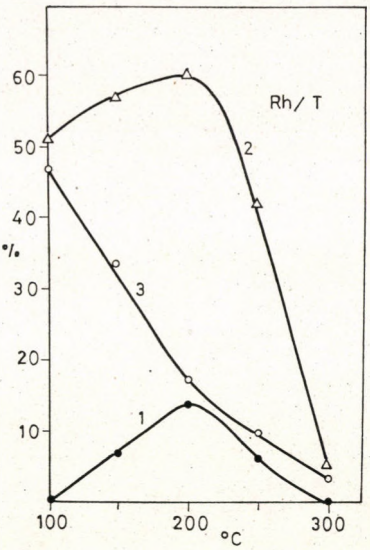


Fig. 8.

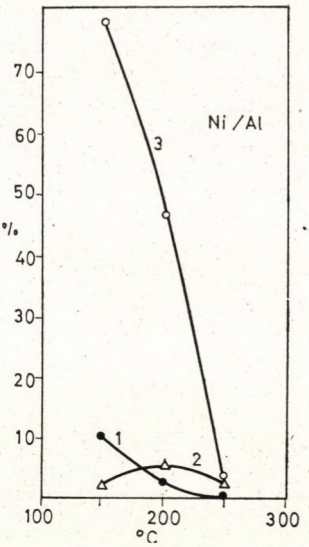


Fig. 9.

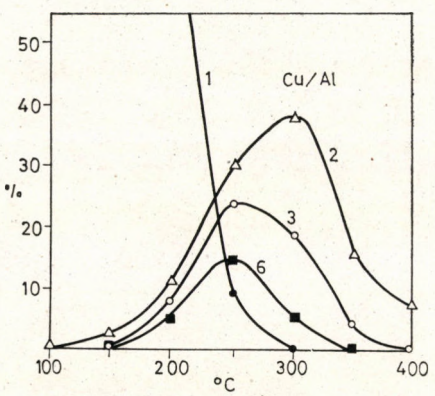
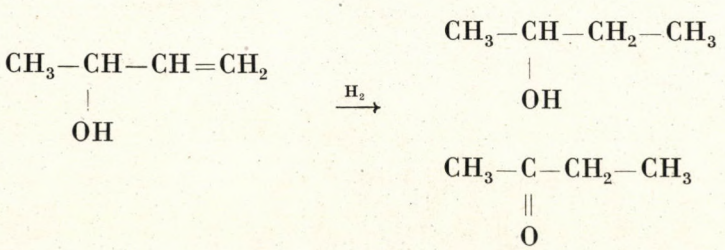


Fig. 10.

Figs 6—10. Variation of the product composition as a function of temperature in the transformation of crotyl alcohol (1: crotyl alcohol; 2: butyraldehyde; 3: 1-butanol; 5: dibutyl ether; 6: crotonaldehyde)

In the case of methyl vinyl carbinol:



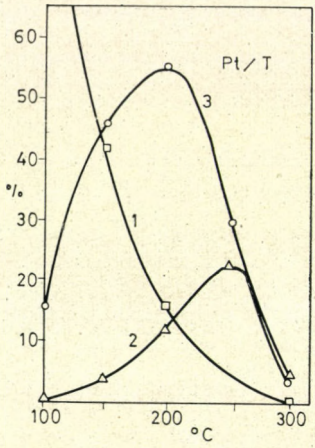


Fig. 11.

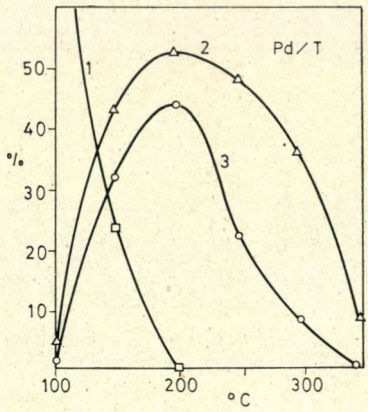


Fig. 12.

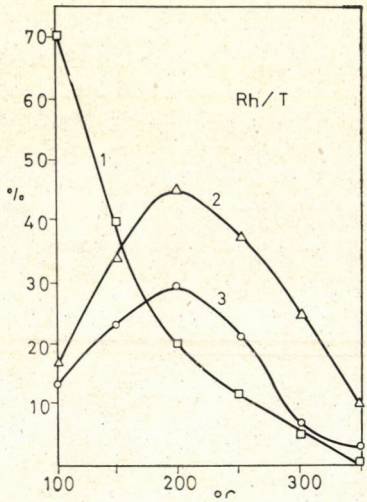


Fig. 13.

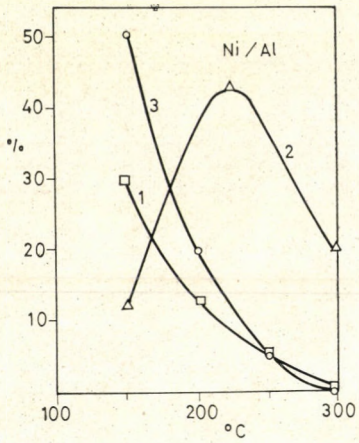


Fig. 14.

The main reactions are thus hydrogenation to saturated alcohols and isomerization to the corresponding oxo compounds. Additionally, isomerization of the unsaturated alcohols from one to another is observed (Figs 2, 3).

2.3 Transformation rate of the unsaturated alcohols

Our experimental data on the rates of transformation of these unsaturated alcohols permit the following conclusions. The transformations of all three unsaturated alcohols are considerably faster on the metals of the eighth

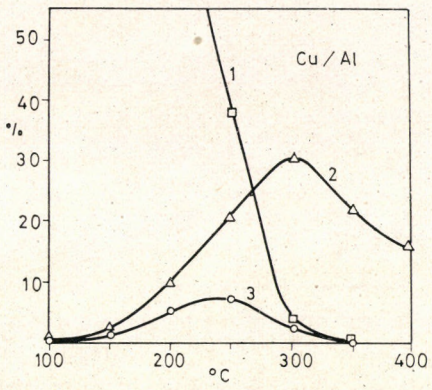


Fig. 15.

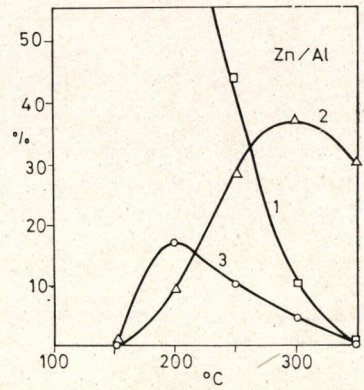


Fig. 16.

Figs 11—16. Variation of the product composition as a function of temperature in the transformation of methylvinylcarbinol (3: 2-butanol; 2: methyl ethyl ketone; 1: methylvinylcarbinol)

column of the periodic system, mainly because of the rapid hydrogenation of the carbon–carbon double bond (*cf.* Figs 5, 10, 15 with the others). An interesting, characteristic change can be observed in the rate of hydrogenation of the compounds on platinum metals. The transformation of methylvinylcarbinol (Figs 11—13) is slower than those of the other two isomers (Figs 1—3, 6—8), probably as a consequence of the shielding effect of the secondary hydroxyl group on the carbon–carbon double bond. On copper the transformation of allyl carbinol is slower (Fig. 5) than those of the two α,β-unsaturated alcohols (Figs 10, 15); this can be well interpreted *via* the mechanism of the isomerization (see later).

2.4 Activity and selectivity of the catalysts

On the basis of literature data, the catalysts employed can be divided into two main groups. The metals belonging to the eighth column of the periodic system are good catalysts of the hydrogenation of the carbon–carbon double bond, while copper and zinc mainly exhibit activity in the hydrogenation of the oxo group.

At low temperature Pt/T, Rh/T, Pd/T and Ni/Al catalyze the hydrogenation of the unsaturated alcohols to butanols with relatively high selectivity (Figs 1—4, 6—9, 11—14). In the cases of Cu/Al and Zn/Al the hydrogenation proceeds with significantly lower selectivity and only at higher temperature (Figs 5, 10, 15, 16). Since these metals do not adsorb hydrogen below 300°C [9], in our view the saturated alcohols are formed by hydrogenation of the oxo compounds resulting from isomerization.

Pd/T (Figs 2, 7, 12), Rh/T (Figs 3, 8, 13) and Cu/Al (Figs 5, 10, 15) proved the most active catalysts in the isomerization of the unsaturated alcohols examined. Zn/Al catalyzed the isomerization of methylvinylcarbinol (Fig. 16) much better than those of the other two alcohols. The selectivity of isomerization was generally higher for the two α,β-unsaturated alcohols than for allylcarbinol.

2.5 Effect of the thermolite support

With regard to the nature of the active centres responsible for the catalytic reactions, a study was made of the transformation of crotyl alcohol on pyridine-poisoned Rh/T, on carrier-free rhodium, and on pyridine-poisoned rhodium. These experiments led to the following conclusions.

The isomerizing selectivity of Rh/T is significantly greater than that of the support-free catalyst. At the same time the hydrogenating selectivity of the rhodium catalyst is higher than that of the Rh/T.

In the presence of pyridine (a 1 : 1 crotyl alcohol + pyridine mixture) the active sites of the Rh/T responsible for the isomerization are appreciably poisoned, the rate of formation of butyraldehyde decreasing to a half.

Pyridine decreased both the isomerizing and the hydrogenating activities of the rhodium catalyst, but to a smaller extent than in the case of Rh/T. The rate of adsorption of pyridine is probably higher than that of crotyl alcohol; by this means the pyridine decreases the active surface accessible to the crotyl alcohol, and accordingly the isomerizing and hydrogenating activities of the catalyst both decrease.

Since isomerization does not occur on the thermolite support itself, and proceeds only at a low rate on the carrier-free rhodium, the Rh/T catalyst must possess active centres which are different from the foregoing. This is shown among others by the fact that the rate of isomerization is lowered by the presence of pyridine, while the isomerization takes place only in the presence of hydrogen.

2.6 Effect of the carrier gas

With the aim of the elucidation of the effect of the hydrogen carrier gas on the isomerization of the unsaturated alcohols, experiments were also performed on Pt/T, Pt/C, Ni/Al and Cu/Al in the presence of helium as carrier gas. The experimental data obtained in the case of crotyl alcohol are given in Fig. 17, which shows the maximum yields of the main products under various experimental conditions. The main conclusions to be drawn from these examinations, apart from the fact that hydrogenation does not proceed in the absence of hydrogen, are as follows.

In a helium atmosphere the Pt/T catalyst actually lost its activity (see Fig. 17). The transformation of crotyl alcohol is slow, while butyraldehyde is

not even formed in traces; thus the presence of hydrogen is a determining factor as regards the occurrence of the isomerization.

In the case of Cu/Al the carrier gas does not exert an effect on the rate of transformation, but the composition of the product does change. It appears that in the presence of this catalyst, too, hydrogen plays a part in the isomerization to butyraldehyde, its role, however, being different from that in the case of Pt/T.

Very little isomerization was observed in the presence of hydrogen on Ni/Al. It was earlier assumed that in the absence of hydrogen (by repressing

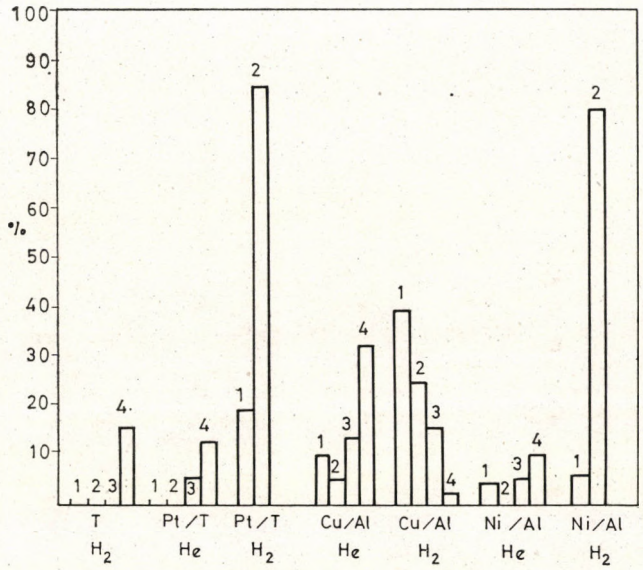


Fig. 17. Maximum yields of the main products from crotyl alcohol at 100—300°C, on various catalysts, in the presence of hydrogen and helium carrier gases (2: butyraldehyde; 3: 1-butanol; 6: crotonaldehyde; 4: allylcarbinol + methylvinylcarbinol)

the hydrogenation) Ni/Al would catalyze the isomerization of the unsaturated alcohols by means of intramolecular hydrogen migration. The experimental data now reveal that this assumption was not confirmed.

In the presence of helium on Pt/T and Pt/C methylvinylcarbinol suffered fragmentation, and isomerization did not occur.

2.7 Dehydrogenation of saturated alcohols

Since the saturated alcohols could presumably be intermediates, the dehydrogenation of 1-butanol and 2-butanol to butyraldehyde and methyl ethyl ketone was studied under the experimental conditions applied in the

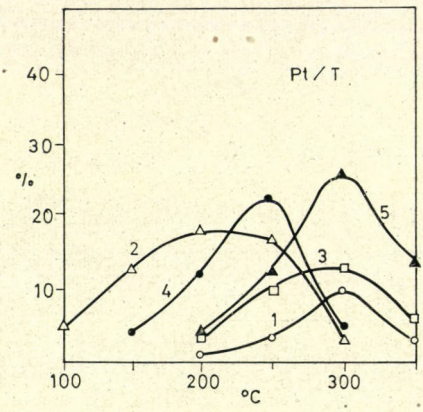


Fig. 18.

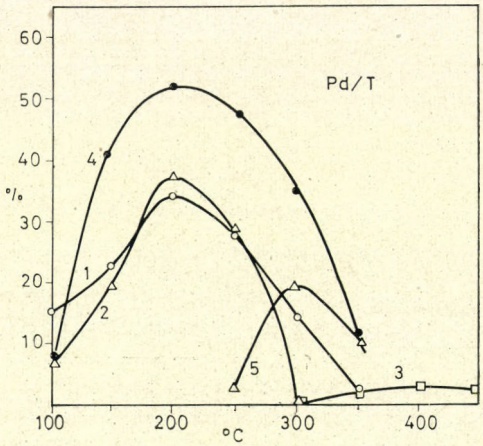


Fig. 19.

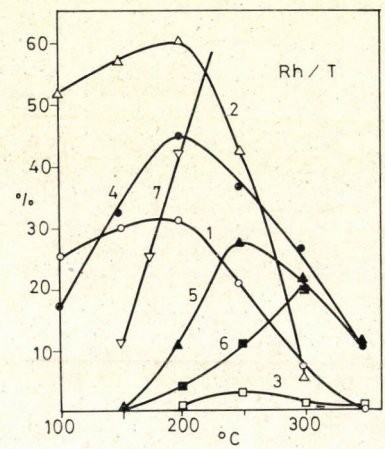


Fig. 20.

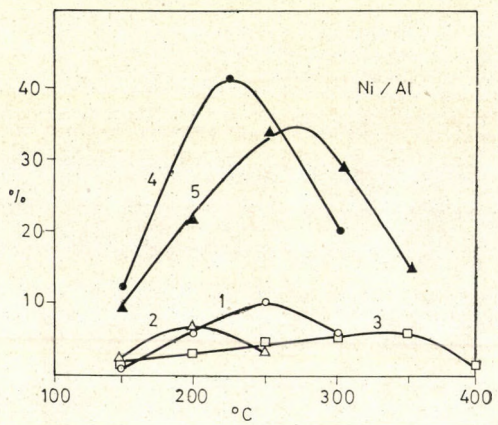


Fig. 21.

case of the model compounds. The experimental data are given in Figs 18—23. For the sake of better comparison, the Figures present the temperature dependence of the yields of the corresponding oxo compounds not only for the two alcohols, but also for the three unsaturated alcohols. It can be seen from the experimental data that the oxo compounds are generally formed at a higher rate by isomerization of the unsaturated alcohols than by dehydrogenation of the corresponding saturated alcohols. The difference in rate is most striking in the case of Rh/T and Pd/T. Based on these experimental data, however, the possibility of the above mechanism cannot be excluded on Pt/T and Ni/Al, particularly since the rates of hydrogenation of the unsaturated alcohols are very high on these catalysts. The possibility of this mechanism is similarly supported by the experimental data presented in Fig. 24. It can

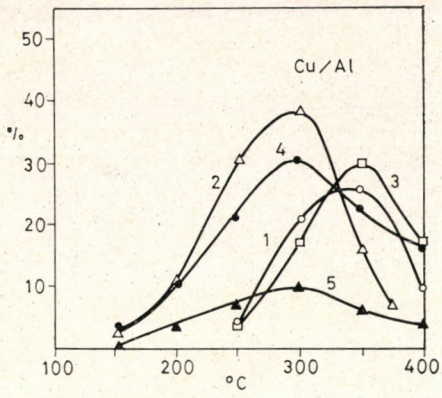


Fig. 22.

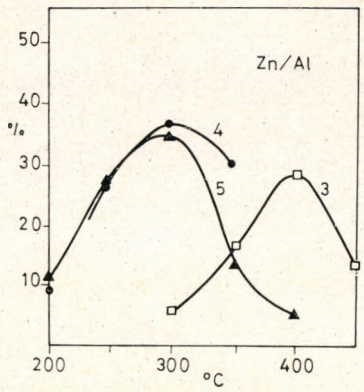


Fig. 23.

Figs 18—23. Variation of the yields of butyraldehyde and methyl ethyl ketone in the isomerization of the corresponding unsaturated alcohols and the dehydrogenation of the saturated alcohols (1: % butyraldehyde from allylcarbinol; 2: % butyraldehyde from crotyl alcohol; 3: % butyraldehyde from 1-butanol; 4: % methyl ethyl ketone from methylvinylcarbinol; 5: % methyl ethyl ketone from 2-butanol; 6: equilibrium conversion curve of the 1-butanol–butyraldehyde process, calculated from thermodynamic data; 7: equilibrium conversion curve of the 2-butanol–methyl ethyl ketone process, calculated from thermodynamic data)

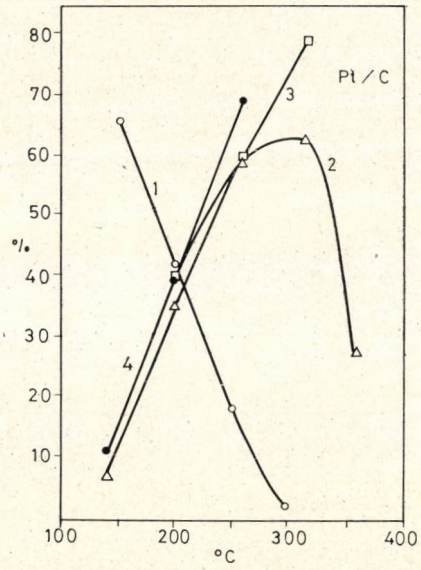


Fig. 24. Variation of the product composition as a function of temperature in the transformations of methylvinylcarbinol and 2-butanol on Pt/C (1: % 2-butanol from methylvinylcarbinol; 2: % methyl ethyl ketone from methylvinylcarbinol; 3: % methyl ethyl ketone from 2-butanol; 4: equilibrium conversion curve calculated for the 2-butanol–methyl ethyl ketone process)

be seen that on Pt/C the rate of dehydrogenation of 2-butanol is higher than the rate of isomerization of methylvinylcarbinol.

On Cu/Al and Zn/Al, too, the rates of isomerization of the unsaturated

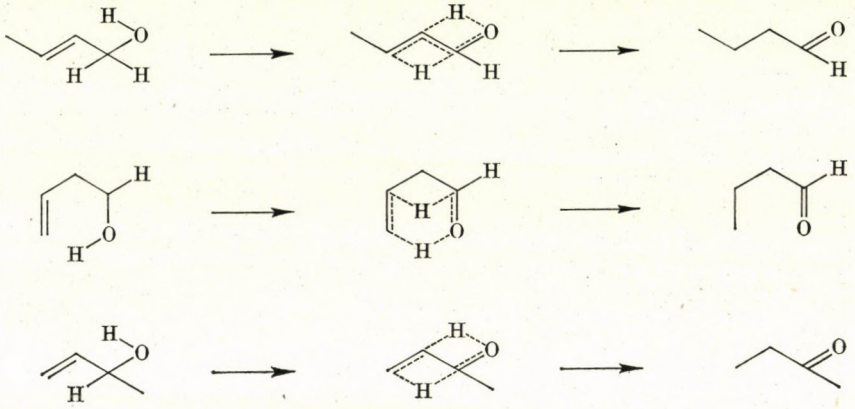
alcohols are in some cases comparable with the rates of dehydrogenation of the saturated alcohols, but since the activities of these catalysts are low in the hydrogenation of the carbon–carbon double bond, the route *via* the intermediate is probable only in the system copper catalyst–allylcarbinol.

3. Discussion

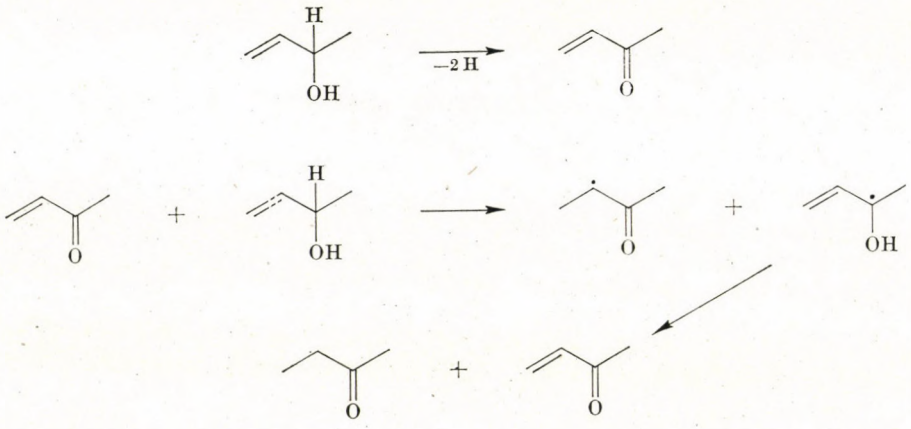
3.1 Reaction mechanisms presumable theoretically

The possible mechanisms of isomerization of the unsaturated alcohols are presented below.

1. Formation of oxo compounds by 1,3 intramolecular migration of hydrogen atoms or ions. These processes are schematically outlined for the three chemisorbed substrate molecules as follows



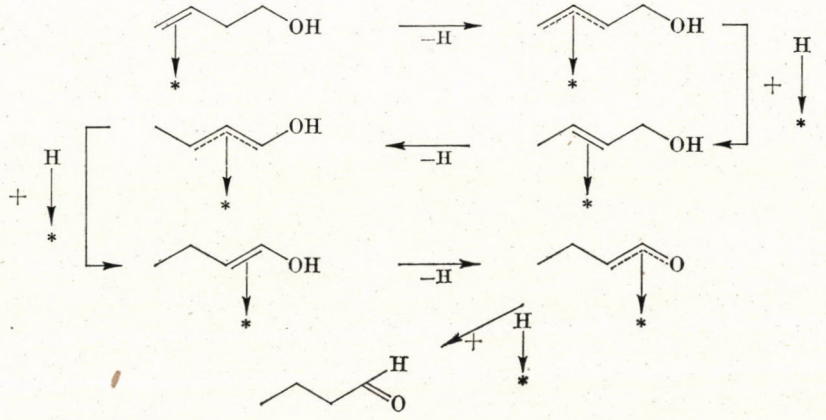
2. The isomerization can be interpreted by means of the following intermolecular mechanism which takes place through some hydrogen transfer processes:



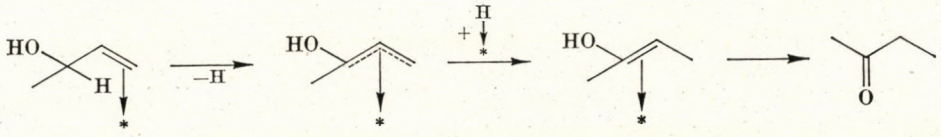
The main point of the isomerization process is the intermolecular dehydro-hydrogenation taking place through an unsaturated oxo compound as intermediate. The presumption of this reaction mechanism is justified convincingly by the experimental results quoted earlier [7].

3. According to this mechanism the isomerization of the unsaturated alcohols to oxo compounds is accomplished with the participation of the chemisorbed hydrogen — *i.e.* with intermolecular mechanism —, with high probability *via* complexes of π-allyl type. These processes are outlined below for the three model compounds.

Isomerization of allylcarbinol and crotyl alcohol:



Isomerization of methylvinylcarbinol:



In these reaction mechanisms use was made of the mechanism proposed by TWIGG [10] to explain the double bond migration in olefins, which is proved experimentally and hereby accepted in the literature. In the case of unsaturated alcohols the final step of the process is the rearrangement of the enol form of the oxo compound to the oxo form. This change can similarly take place with the participation of chemisorbed hydrogen, or *via* a four-membered transition state with intramolecular 1,3 hydrogen migration, depending on the experimental conditions.

4. The formation of the oxo compounds can also be explained by the catalytic dehydrogenation of the saturated alcohols produced in the hydrogenation of the unsaturated alcohols:

$$CH_3-CH=CH-CH_2OH$$

$$\xrightarrow{H_2} CH_3-CH_2-CH_2-CH_2OH \xrightarrow{-H_2} CH_3-CH_2-CH_2CHO$$

$$CH_2=CH-CH_2-CH_2OH$$

$$CH_2=\underset{\displaystyle OH}{\underset{|}{CH}}-CH-CH_3 \xrightarrow{H_2} CH_3-\underset{\displaystyle OH}{\underset{|}{CH}}-CH_2-CH_3 \xrightarrow{-H_2} CH_3-\overset{\displaystyle O}{\overset{\|}{C}}-CH_2-CH_3$$

Based on the experimental results reported in the previous section — utilizing some other observations and statements from the literature — the isomerization of the unsaturated alcohols can be suitably interpreted to a first approximation by one or other of the four reaction mechanisms.

3.2 Mechanism of the isomerization on platinum metals

The majority of the experimental data obtained with the platinum metal suggest *mechanism 3*. In the absence of hydrogen the isomerization process does not take place (Fig. 17), which is clearly in opposition to mechanisms 1 and 2, while confirming the realistic nature of mechanisms 3 and 4. However, the equilibrium conversions of alcohol dehydrogenation (Fig. 20) calculated from the thermodynamic data, and the experimental data referring to the dehydrogenation of the alcohols (Figs 18—20) do not confirm the validity of mechanism 4 in most cases. Mechanism 4 achieves a certain degree of probability only in the platinum-catalyzed isomerizations of allylcarbinol and methylvinylcarbinol (Fig. 18). This latter can be explained by the rapid hydrogenation of methylvinylcarbinol, and by the thermodynamically favoured dehydrogenation of the secondary alcohols. The experimental data found on Pt/C (Fig. 24) confirm this.

3.3 Mechanism of the isomerization on Ni/Al catalyst

Our experimental results indicate that Ni/Al behaves differently from the thermolite-supported platinum metal catalysts in the isomerization of unsaturated alcohols, in spite of the fact that, similarly to the platinum metals, it chemisorbs hydrogen and is very active in the hydrogenation of the carbon–carbon double bond (Figs 4, 9 and 14). Ni/Al displayed very low

activity in the isomerization of crotyl alcohol and allylcarbinol (Fig. 21), in contrast with the platinum metals, while at the same time it had the same activity as the platinum metals in the isomerization of methylvinylcarbinol; it can be concluded from these experimental facts, that the mechanism is different from that of the platinum metal-catalyzed isomerization. Based on the appropriate calculated equilibrium conversion curve (Fig. 20) and the experimental data relating to the dehydrogenation of 2-butanol (Fig. 21), the isomerization of methylvinylcarbinol to methyl ethyl ketone on Ni/Al can be interpreted by *mechanism 4*. From another aspect this same mechanism is supported by the low degree of isomerization of allylcarbinol and crotyl alcohol, which is a consequence of the thermodynamically unfavoured nature of the second part-step of the consecutive process.

3.4 Mechanism of the isomerization on Cu/Al and Zn/Al catalyst

The isomerization of allyl carbinol to butyraldehyde on Cu/Al is explained by *mechanism 4*. Under the experimental conditions applied here this catalyst is capable of hydrogenating the chain-terminating carbon–carbon double bond [11], while the occurrence of the second part-process is supported by both the thermodynamic and the experimental data (Fig. 22).

The majority of our experimental data obtained in the isomerization of crotyl alcohol can be interpreted with *mechanism 2*. Since copper does not chemisorb hydrogen, the possibility of mechanisms 3 and 4 is eliminated, in spite of the fact that certain of our experimental data (Fig. 17) suggest that the presence of hydrogen (in a manner as yet unclarified) exerts an effect on the process. The probability of mechanism 4 is mainly contradicted by the formation of significantly more butyraldehyde than expected on the basis of the equilibrium constant of the second part-process of mechanism 4. (The possibility of the first part-process does exist in principle, since copper catalyzes the isomerization of crotyl alcohol to allyl carbinol.) In addition to the above, mechanism 2 is confirmed by the following data: the investigations of EADON and SHIEKH [7]; the fact that, even though at a lower rate, the isomerization does proceed in the absence of hydrogen; and the big amount of the crotonaldehyde formed (Fig. 10). A mechanism different from that of the isomerization of allylcarbinol is indicated by the rates of isomerization of the two α,β-unsaturated alcohols which are considerably larger than that for allylcarbinol, the reason for this being that the first part-process according to mechanism 2 — dehydrogenation of the α,β-unsaturated alcohols — is significantly more favoured even thermodynamically than that of α,γ-unsaturated alcohols.

Mechanism 2 is similarly applied to explain the isomerization of methylvinylcarbinol to methyl ethyl ketone on Cu/Al and Zn/Al. Mechanism 3 can

obviously be eliminated, while at the same time the occurrence of mechanism 4 is not supported either by theoretical considerations and our experimental data. The dehydrogenation of 2-butanol on Cu/Al is significantly slower (Fig. 22) than the isomerization of methylvinylcarbinol on the same catalyst, while on Zn/Al the occurrence even of the first part-process of mechanism 4 is impossible [12]. It is to be noted that on Cu/Al the dehydration of 2-butanol to butenes is considerably faster than its dehydrogenation (at 300°C the dehydration proceeds with a 60% conversion).

In connection with the reaction mechanism variants outlined above, it should be noted that at the present stage of our experimental work the individual mechanisms can be confirmed only approximatively. The understanding of the detailed mechanisms of these processes is obstructed not only by the lack of various complex experimental data, but also by the fact that even within the main types one can conceive various reasonable variations, with numerous, not too well understood elementary steps, associated further with the problematics and complexity of the mechanisms of considerably simpler catalytic processes on metals.

4. Methods

The compounds examined (allylcarbinol, crotyl alcohol, methylvinylcarbinol, 1-butanol, 2-butanol, butyraldehyde and methyl ethyl ketone) were commercial products. They were purified by fractional distillation, and their purities were checked by GC.

Catalysts. Pt/T, Rh/T, Pd/T and Pt/C (metal content 10%) were prepared as described previously [13, 14]. The Raney-type catalysts were prepared from aluminium alloys (grain size 0.2—0.4 mm) containing 30% active metal [15]. The carrier-free rhodium catalyst was also prepared by a literature method [16] (specific surface: 5.7 $m^2 \cdot g^{-1}$).

Description of the experimental method. The investigations were carried out by an impulse microreactor technique. The measurements were repeated several times; the reproducibility was satisfactory. The technique described previously [13] was modified only in so far as the microreactor was constructed from Rasotherm glass, and its internal diameter was 6 mm. The quantity of thermolite-supported catalyst used was 1 ml, while that of Raney-type and Pt/C catalysts was 0.2 ml. The active metal contents of the catalysts were approximately the same. 60 mg of the carrier-free rhodium catalyst was employed. The microreactor was attached to a Carlo-Erba GV gas chromatograph. The chromatographic conditions were as follows:

Column: Two 1 m glass columns, 4 mm in internal diameter, connected in series. The first contained 15% polyethylene glycol (M.W. 20,000) on thermolite (grain size 0.2—0.3 mm), and the second 15% tris(cyanoethoxy)propane (Fractonitrile III) on the same support.
Carrier gas: 60 ml hydrogen (or helium) per minute.
Temperature of thermostat: 120°C.
Detector current: 140 mA.
Amount of sample injected: 0.005 ml.

The peaks of the chromatograms were identified with the aid of the appropriate authentic substances, and evaluated quantitatively *via* calibration curves. The chromatogram of a mixture containing all the starting compounds and products, obtained under the chromatographic conditions described above, is given in Fig. 25.

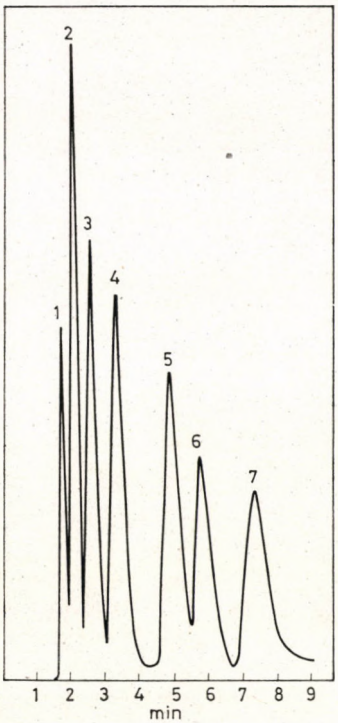


Fig. 25. Chromatograms of the unsaturated alcohols studied, and their isomerization and hydrogenation products (1: butyraldehyde; 2: methyl ethyl ketone; 3: 2-butanol; 4: methylvinylcarbinol; 5: 1-butanol; 6: allylcarbinol; 7: crotyl alcohol)

REFERENCES

[1] DELABY, P.: Compt. rend. **182,** 140 (1926)
[2] HEARNE, G., TAMELE, M., CONVERSE, W.: Ind. Eng. Chem. **33,** 805 (1941)
[3] PAUL, R.: Bull. Soc. Chim. France [5] **8,** 507 (1941)
[4] FREYDLIN, L. H., ABIDOVA, M. F., SULTANOV, A. S.: Izv. Akad. Nauk SSR, Ser. Khim. **1958,** 498
[5] SIMONIK, J., BERANEK, L.: J. Catal. **24,** 348 (1972)
[6] KRAUS, M.: Coll. Czech. Chem. Commun. **37,** 460 (1972)
[7] EADON, G., SHIEKH, M. Y.: J. Am. Chem. Soc. **96,** 2288 (1974)
[8] BARTÓK, M., NOTHEISZ, F., TÖRÖK, I.: Acta Phys. et Chem. Szeged **17,** 101 (1971)
[9] BABKOVA, P. B., AVETISOV, A. K., LYUBARSKII, G. D., GELBSTEIN, A. I.: Kin. i Kataliz. **11,** 1451 (1970)
[10] TWIGG, G. H.: Trans. Faraday Soc. **35,** 934 (1939)
[11] Kataliticheskie svoystva veschestv, p. 1216. Naukova Dumka, Kiev, 1968
[12] FREYDLIN, L. H., GORSKOV, V. I.: Kin. i Kataliz. **1,** 593 (1960)
[13] BARTÓK, M., FÉNYI, SZ.: Acta Phys. et Chem. Szeged **12,** 157 (1966)
[14] BARTÓK, M., APJOK, J., KARAKHANOV, R. A., KOVÁCS, K.: Acta Chim. Acad. Sci. Hung. **61,** 315 (1969)
[15] BARTÓK, M., KOZMA, B.: Acta Phys. et Chem. Szeged **9,** 116 (1963)
[16] TÉTÉNYI, P., SCHACHTER, K.: Acta Chim. Acad. Sci. Hung. **50,** 129 (1966)

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STUDY OF THE SCHIFF-BASES OF SALICYLALDEHYDE AND AMINOPHENOLS

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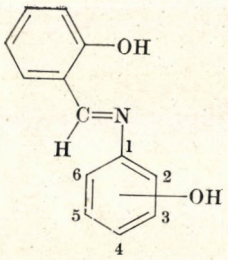
Schiff-bases of salicylaldehyde and 2-, 3- and 4-aminophenol have been studied. A reaction occurring in *n*-butanol is explained by the partial decomposition of the Schiff-base and the formation of quinonamine.

In earlier communications [1, 2] we discussed the absorption spectra of aromatic Schiff-bases and the effect of the solvent on the spectra. In polar solvents an advance band of medium intensity between 400 and 450 nm was interpreted as due to the tautomeric equilibrium [3, 4] of the Schiff-base molecule.

This paper deals with the Schiff-bases obtained from salicylaldehyde and 2, 3- and 4-amino phenol (I).



I

Experimental

The Schiff-bases described here are easily prepared by mixing stoichiometric quantities of salicylaldehyde and an aminophenol, dissolved in methanol. Melting points and analyses are listed in Table I.

Absorption spectra were recorded on a Beckman DU, infrared spectra with a Perkin Elmer 200 spectrophotometer; proton resonance spectra were recorded on a JEOL 60 MHz instrument at 25°C, in CD_3OD, using TMS as external standard.

Results

The pattern of the spectra is similar to those of other aromatic Schiff-bases. In methanol four groups of bands are discernible between 430 and 450, 338 and 350, 267 and 270, 225 and 230 nm, respectively. In a non-polar solvent the advance band between 430 and 450 nm is absent (*cf.* Table I, Fig. 1). The further three groups of bands are due to the excitation processes of the azomethine group and of the aromatic system [5]. The intensity of the advance band in the case of the 4-OH derivative in *n*-alcohols (C_1–C_5) is a function

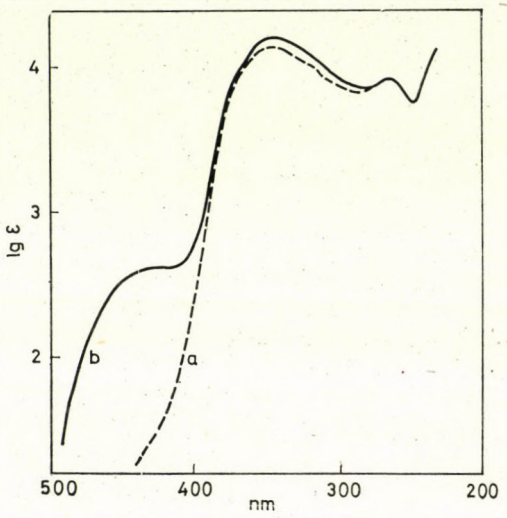


Fig. 1. Spectrum of HSAI-4-OH-aniline in benzene (a) and in methanol (b)

of the dielectric constant of the solvent (Fig. 2a); in a mixture of methanol and benzene this intensity changes according to Fig. 2b. Similar results are obtained with the 2- and the 3-OH derivatives. The constant [6, 7] for the benzenoid/quinonoid equilibrium measured in methanol/benzene mixture at 25°C is K = 2.76, 1.06 and 1.92 for the 2-, 3-, and 4-OH derivative, respectively.

Table I shows the infrared and the PMR data of the compounds. A great number of bands emerge in the infrared spectra; the main frequencies can be identified with certainty. A number of maxima appear in the range between 2500 and 3000 cm^{-1}, these correspond to the vibrations of the aromatic CH-groups and to those of the intramolecularly associated OH-groups.

A complex pattern of bands due to the aromatic protons, in the PMR spectra recorded in CD_3OD, is found between 6.5 and 7.6 ppm; between 8.7 and 8.9 ppm the signal of the azomethine proton can be seen. Owing to rapid exchange, no OH signal is observed in the CD_3OD solution. The position of

Table I

Analyses and spectral data of Schiff-bases

Schiff-base	m.p.[a]	Analysis[b]			Band maxima[c] λ (nm) and lg ε				K[d]	Infrared frequencies[e]		δCH=N[f] (ppm)
		C %	H %	N %						νC=N	νC—O	
HSAI-2-OH-aniline	186.0	73.62	4.75	6.60	~452	347	269	~226	2.76	1634	1278	8.89
		(73.58)	(4.71)	(6.57)	3.28	4.08	4.00					
					—	357	270	—				
						4.03	3.98					
HSAI-3-OH-aniline	128.9	73.62	4.75	6.60	~425	338	267	~225	1.06	1622	1290	8.68
		(73.57)	(4.69)	(6.55)	2.50	3.98	3.98					
					—	342	268	—				
						4.07	4.04					
HSAI-4-OH-aniline	139.0	73.62	4.75	6.60	~430	348	270	~230	1.92	1626	1282	8.71
		(73.60)	(4.71)	(6.51)	2.60	4.20	3.91					
					—	350	268	—				
						4.14	3.93					

[a] uncorrected
[b] the values found are in parentheses
[c] first line in methanol second line in solution
[d] calculated according to the least squares method as described in Ref. [1]
[e] in KBr pellets
in CD_3OD at 25°C

the azomethine proton signal is nearly unaffected by the substituents on the aniline ring. This is due to the fact that the aniline part is turned out of the plane and thus no conjugation with the $C_6H_4(OH)CH=N$ moiety is possible, consequently, the electron donor effect of the substituents is restricted.

The position and intensity of the advance band, the value of the equilibrium constant, the infrared $\nu C=N$ frequencies and the chemical shift of the CH=N proton change in the sequence $2 > 4 > 3$, in accordance with the electron donor effect of the OH-substituent. The $\nu C-O$ frequency changes in the sequence $2 < 4 < 3$, as expected.

The butanol solutions of the Schiff-bases studied change their colour from a light yellow to red-brown when allowed to stand. A similar change

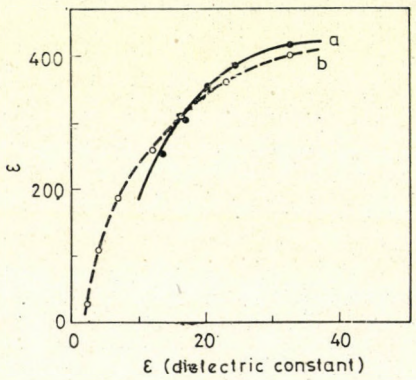


Fig. 2. Variation of the intensity of the advance band of HSAI-4-OH-aniline as a function of the dielectric constant, in alcohol (a) and in methanol (b)

occurs is *n*-propyl- and *n*-amyl-alcohol, but the rapidity of this change decreases in the sequence *n*-butanol $\gg$ *n*-amyl $>$ *n*-propyl alcohol. In diffuse light and in the dark, this conversion takes place in the same way and to the same extent.

The spectra of the 4-OH-derivative in *n*-butanol recorded after 0, 40, 72, 144, 168 and 216 hrs are shown in Fig. 3. From the variation of the absorbance at 338 and 350 nm, a first order rate constant of $k = 2.2 \times 10^{-5}$ sec^{-1} can be calculated [9]; in the case of the 3- and the 2-OH derivatives more complex processes take place.

Of the Schiff-base components, only the butanol solution of aminophenol shows a change similar to that found with the Schiff-base itself. The product thus formed can be isolated. The spectrum (Fig. 4) of the product (m.p. 135°C, not sharp) recovered after leaving the Schiff-base stand for 240 hrs deviates from that of the parent substance only in the domain between 450 and 500 nm, where a medium, additional absorption can be seen. The

Schiff-base molecule is not decomposed, or only to a very low extent. This statement is supported by

a) the infrared spectrum of the product, where the $\nu C{=}N$ frequency of the Schiff-base is sharply in evidence at 1620 cm^{-1};

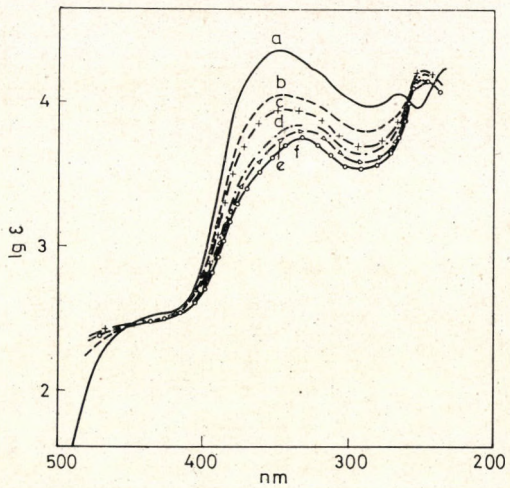


Fig. 3. Spectrum of HSAI-4-OH-aniline dissolved in *n*-butanol after 0 (a), 44 (b), 72 (c), 144 (d), 168 (e), and 216 (f) hrs

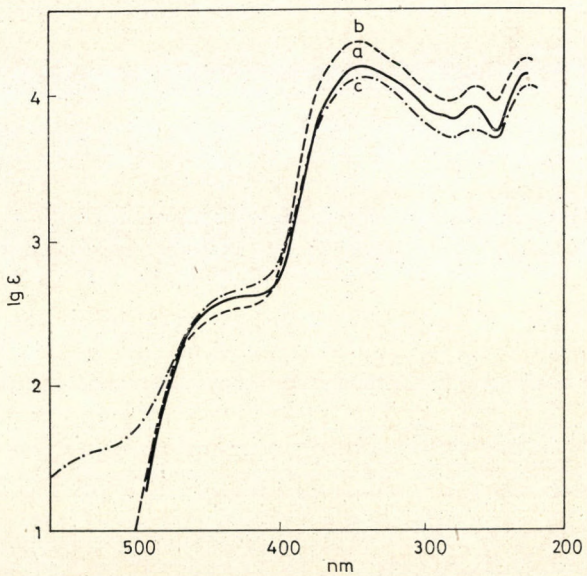


Fig. 4. HSAI-4-OH-aniline. (a) In methanol; (b) in *n*-butanol, fresh solution; (c) spectrum in methanol of the product isolated from the *n*-butanol solution after 7 days

b) the PMR spectra of the parent Schiff-base and its product, which are practically the same (in $CDCl_3$ the CH=N proton signal is at 8.60 ppm in both cases);

c) thin layer chromatography,* which does not unequivocally reveal the presence of on aldehyde or amine.

The change of 4-aminophenol (m.p. 184°C) is very pronounced (the m.p. of the product is 135°C) (Fig. 5). The sharp ultraviolet bands become completely slurred, and in the visible range very intense broad bands appear.

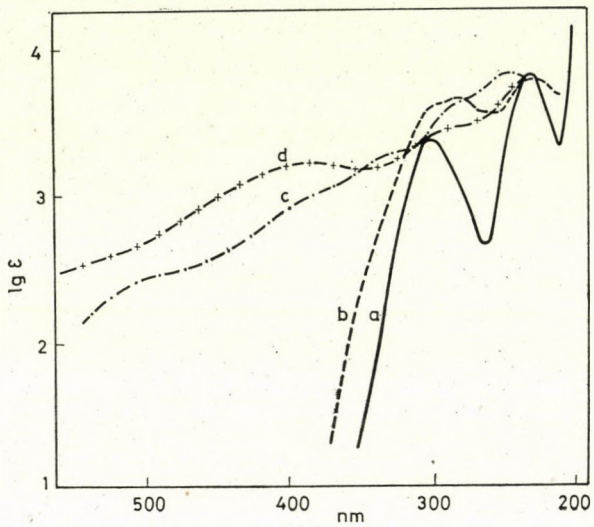


Fig. 5. 4-OH-Aniline. (a) In methanol; (b) in *n*-butanol after about 10 min.; (c) in *n*-butanol after 20 hrs; (d) spectrum in methanol of the product isolated from *n*-butanol solution after 7 days

We suppose that the Schiff-base in solution is decomposed to a smad degree. The amine component thus formed is then converted into a compoun that shows the intensive colour characteristics of aminophenols and pre sumably a quinonoid structure. This is supported by the existence of such a transformation for aminophenols and by the fact that in the case of a Schiff-base molecule there is no possibility for the formation of a quinonoid structure. Further evidence in favour of this supposition is the fact that, among the Schiff-bases of substituted anilines, only the OH-derivatives show this transformation and the rate of the change decreases in the $4 > 2 \gg 3$ order.

Attempts at the separation and identification of this small amount of a supposedly quinonoid product have failed. However, there are two findings

* For the TLC analyses our thanks are due to Dr. J. Weisz, Department of Organic Chemistry József A. University.

that seem to support our assumption. The reaction product of the Schiff-base with $NiAc_2$ yields the well-known chelate $Ni[HSAI\text{-}4\text{-}OH\text{-}aniline]_2$; when this is decomposed by hydrogen sulfide, the original Schiff-base can be recovered from the solution. Also we find that when the end-product of the Schiff-base, sealed in a glass tube under 10^{-6} to 10^{-7} Torr, is slowly heated, the original, orange-red Schiff-base separates and can be identified by its melting point.

REFERENCES

[1] CSÁSZÁR, J., BALOG, J.: Acta Chim. (Budapest), **86,** 101 (1975)
[2] BALOG, J., CSÁSZÁR, J.: Acta Chim. (Budapest). (In press)
[3] LEDBETTER, J. W.: J. Phys. Chem., **70,** 2245 (1966)
[4] DUDEK, G. O., DUDEK, E. P.: J. Amer. Chem. Soc., **86,** 4283 (1964); **88,** 2407 (1966)
[5] MASON, S. F.: J. Chem. Soc., **1253** (1959); JAFFÉ, H. H., YEH, S. Y., GARDNER, R. W.: J. Mol. Spectr., **2,** 120 (1958); EBARA, N.: Bull. Chem. Soc. Japan, **33,** 534 (1960)
[6] NAGY, P.: Magy. Kém. Foly., **72,** 108 (1966)
[7] NAGY, P.: Szegedi Tanárképző Főisk. Közl., 123 (1968)
[8] TABEI, K., SAITU, E.: Bull. Chem. Soc. Japan, **42,** 1440 (1969)
[9] VAN SENDEN, K. G., KONING, H. N.: Recl. Trav. Chim., **81,** 49 (1962)

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SYNTHESIS OF 2,2- AND 2,4-SUBSTITUTED 1,3-BENZTHIAZINES*

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2-Phenyl-4*H*-1,3-benzthiazin-4-one derivatives **(I)** give with Grignard reagents, depending on the organic group of the latter, 4-hydroxy-2,4-substituted-4*H*-1,3-benzthiazines **(III)** and 2,2-substituted-3,4-dihydro-2*H*-1,3-benzthiazin-4-one **(II)** derivatives. The structures of compounds **III** were verified by their hydrolysis products.

Since only derivatives substituted in position 2 of 1,3-benzthiazine are known, the aim of our present work was the synthesis and chemical and pharmacological investigation of 2,4-substituted 1,3-benzthiazine derivatives.

2-Phenyl-4*H*-1,3-benzthiazin-4-one (**Ia**) [1] and 2-phenyl-6,7-dimethoxy-4*H*-1,3-benzthiazin-4-one (**Ib**) [2] were found to be suitable starting materials. The latter compound was synthesized according to SZABÓ and VINKLER in a good yield from 2-phenyl-6,7-dimethoxy-4*H*-1,3-benzthiazine by oxidation with chromium trioxide in anhydrous acetic acid solution.

The oxo-derivatives of **I** were allowed to react with various Grignard reagents. In principle, the formation of both structures **II** and **III** is possible by addition to the conjugated bond —CO—N=C—. Compounds of type **II** by 1,4-addition, and subsequent iminohydrin → amide tautomerization *i.e.* actually by saturation of the —C=N— bond.

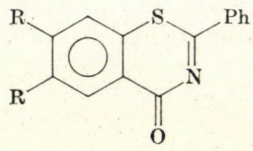
Our experiences are summarized in the scheme on p. 62.

With phenylmagnesium halide, probably owing to the higher space requirement of the phenyl group, only 4-hydroxy-2,4-diphenyl-4*H*-1,3-benzthiazine derivatives of type **III** were obtained.

It is remarkable that **Ib** with benzylmagnesium halide, gave besides compound **IIe**, the benzal derivative **IV**. The latter is probably formed from the non-isolable intermediate product **IIIc** by the elimination of water.

Presumably, the reaction proceeds also with alkylmagnesium halides (Q = Et, *n*-Bu) in both directions, but the compounds of type **III** formed are further converted, and only the corresponding compound of type **II** could be isolated.

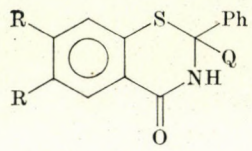
* Parts of this paper were presented at the Conference of the Hungarian Chemical Society, Debrecen, 1971.



I

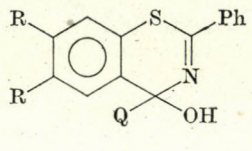
a R = H
b R = OMe

QMgX



II

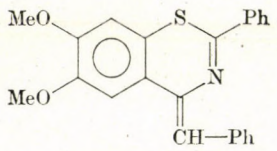
a R = H; Q = Et
b R = H; Q = CH_2Ph
c R = OMe; Q = Et
d R = OMe; Q = *n*-Bu
e R = OMe; Q = CH_2Ph



III

a R = H; Q = Ph
b R = OMe; Q = Ph
[**c** R = OMe; Q = CH_2Ph]

$(-H_2O)$

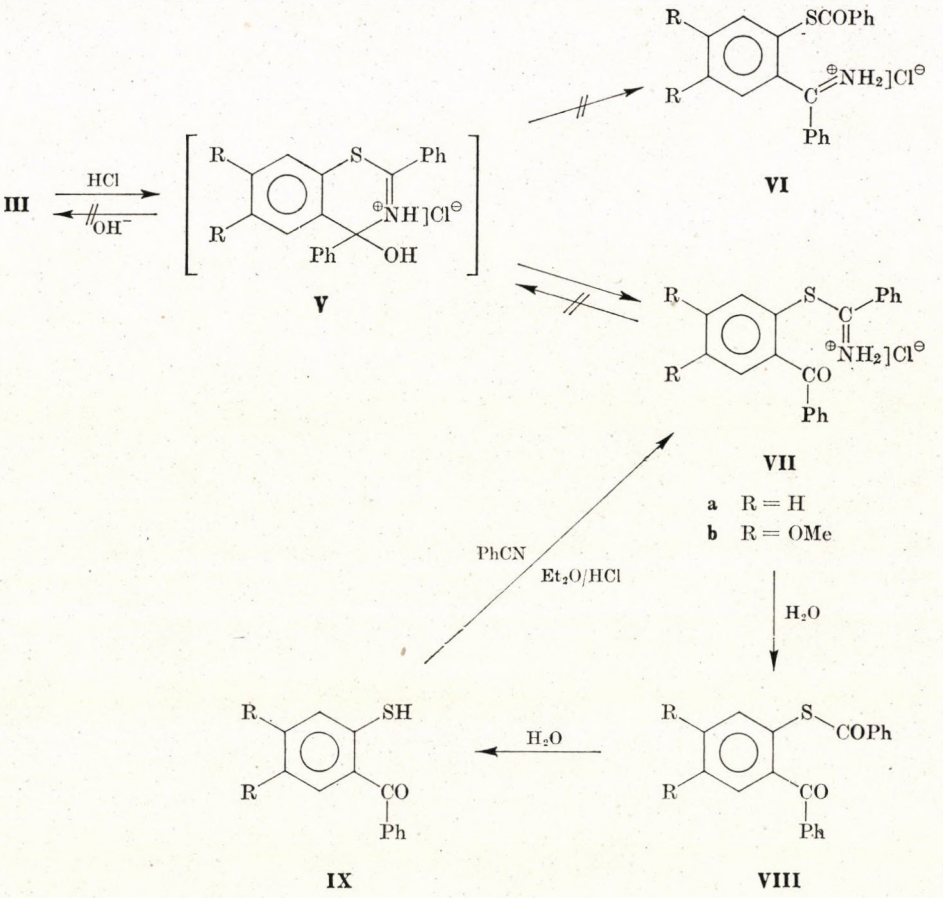


IV

The structures of the compounds **II** and **III** prepared have been verified by IR and NMR investigations [3], supported by elementary analyses.

The structures of compounds **IIIa** and **IIIb** have also been proved by preparative method. In anhydrous benzene solution, compound **IIIb** is converted by dry hydrogen chloride almost quantitatively into an unstable compound of immonium salt structure. The conversion is introduced by the formation of an orange-yellow benzthiazinium salt (**V**), precipitating from the benzene solution when hydrogen chloride is introduced; however, compound **V** cannot be isolated, because it is immediately dissolved with the formation of the immonium salt. For this compound, structures **VI** and **VII** are both

possible, but no decision can be made between them on the basis of the IR spectra. The iminothioether structure **VII**, which is stabilized by mesomerism due to the non bonded electron pairs of the sulfur atom, seems much more probable.



It should be mentioned that compound **IIIb** gave also with aqueous hydrochloric acid the same compound of immonium salt type, but in a lower yield, because this salt is hydrolyzed in aqueous solution, being converted, with the formation of ammonium ion, into S-(benzoyl)-4,5-dimethoxy-2-mercaptobenzophenone (**VIII**).

Similarly, compound **IIIa** was converted into the corresponding immonium salt; its IR spectrum also has the band at 2830 cm^{-1}, characteristic of imino salts.

The formation of compound **VIII** is not conclusive for structure **VI** or **VII** of the immonium salt, because it can be formed from either, but as a hydrol-

ysis product it proves the 2,4-disubstituted-4*H*-1,3-benzthiazine structure of **III**. Therefore, by the debenzoylation of compound **VIII**, 4,5-dimethoxy-2-mercaptobenzophenone (**IX**) has been prepared, and converted with benzonitrile and dry hydrogen chloride in anhydrous ether solution into the authentic compound **VIIb**. On the basis of its chemical and physical properties and IR spectrum, this compound proved to be identical with the immonium salt of structure **VIIb**.

The conversion **III** → **VII** is not reversible, because the reaction in even weakly alkaline solutions does not give the benzthiazine derivative **III** but, due to hydrolysis of compound **VII**, the S-(benzoyl)-2-mercaptobenzophenone derivative is obtained.

Owing to their high instability, 2,4-substituted-4-hydroxy-4*H*-1,3-benzthiazine derivatives (**III**) are unsuitable for pharmacological testing.

Experimental

M.p.'s are uncorrected

1. Modified preparation of 2-phenyl-6,7-dimethoxy-4H-1,3-benzthiazin-4-one (Ib)

28.5 g (0.1 mole) of 2-phenyl-6,7-dimethoxy-4*H*-1,3-benzthiazine [4] was dissolved in 100 ml anhydrous acetic acid and, under continuous stirring, a cold solution of 18 g (0.18 mole) chromium(VI) oxide prepared by dissolution in a warm mixture of 10 ml of water, 110 ml of glacial acetic acid and 25 ml of acetic anhydride, was added at such a rate that the temperature of the reaction mixture remained between 22 and 25°C. Stirring was then continued for another hour, and the mixture was poured into 600 ml of water. The reaction product which separated was filtered off, washed with water and dried in a desiccator. Recrystallization from ethanol gave felty needles (18.2 g; 61%), m.p. 194°C; no melting point depression was found in admixture with an authentic sample [2].

2. 2-Ethyl-2-phenyl-3,4-dihydro-2H-1,3-benzthiazin-4-one (IIa)

1.2 g (0.005 mole) of 2-phenyl-4*H*-1,3-benzthiazin-4-one was suspended in 100 ml anhydrous ether, and 0.025 mole of ethylmagnesium bromide dissolved in 40 ml ether was added. The mixture was allowed to stand for 30 min. It was then shaken with cold, saturated aqueous ammonium chloride solution, and the reaction product was extracted with ether. The solution in ether was dried over anhydrous sodium sulfate, and the solvent was evaporated. Crystallization of the residue gave colourless prisms, m.p. 174—176°C (from ethanol). Yield: 0.26 g (19.5%).

$C_{16}H_{15}NOS$ (269.35). Calcd. C 71.34; H 5.61. Found C 70.90; H 5.88%.

3. 2-Benzyl-2-phenyl-3,4-dihydro-2H-1,3-benzthiazin-4-one (IIb)

1.2 g (0.005 mole) of 2-phenyl-4*H*-1,3-benzthiazin-4-one was suspended in 40 ml of anhydrous tetrahydrofuran, a solution of 0.025 mole benzylmagnesium chloride in 40 ml tetrahydrofuran was added, and the mixture was allowed to stand for 30 min. The volume of the mixture was then reduced in vacuum to 15 ml. From here on, the producere was the same as described in Experiment 2. The yield of product was 0.52 g (38.2%). Crystallization from benzene–petroleum ether gave colourless prisms, m.p. 164—167°C.

$C_{21}H_{17}NOS$ (331.44). Calcd. C 76.10; H 5.17. Found C 76.40; H 4.91%.

4. 2,4-Diphenyl-4-hydroxy-4H-1,3-benzthiazine (IIIa)

1.2 g (0.005 mole) of 2-phenyl-4*H*-1,3-benzthiazin-4-one was suspended in 40 ml of anhydrous tetrahydrofuran, and a solution of 0.025 mole phenylmagnesium bromide in 40 ml tetrahydrofuran was added. From here on, the procedure was the same as described in Experiment 2. The yield was 1.2 g (95%), colourless needles, m.p. 138—140°C from ethanol.

$C_{20}H_{15}NOS$ (317.39). Calcd. C 75.68; H 4.76. Found C 75.65; H 4.81%.

5. 2-Ethyl-2-phenyl-6,7-dimethoxy-3,4-dihydro-2H-1,3-benzthiazin-4-one (IIc)

4.5 g (0.015 mole) of 2-phenyl-6,7-dimethoxy-4*H*-1,3-benzthiazin-4-one was dissolved in 450 ml of anhydrous tetrahydrofuran, and 0.075 mole of ethylmagnesium bromide dissolved in 40 ml of ether was added. Processed as described in Experiment 2, the yield was 1.15 g (23.5%), colourless prisms, m.p. 144—147°C (from ethanol).

$C_{18}H_{19}NO_3S$ (329.40). Calcd. C 65.63; H 5.81. Found C 66.34; H 6.14%.

6. 2-(n-Butyl)-2-phenyl-6,7-dimethoxy-3,4-dihydro-2H-1,3-benzthiazin-4-one (IId)

1.5 g (0.005 mole) of 2-phenyl-6,7-dimethoxy-4*H*-1,3-benzthiazin-4-one was dissolved in 150 ml of anhydrous tetrahydrofuran, and a solution of 0.025 mole *n*-butylmagnesium iodide in 40 ml ether was added. Processed as described in Experiment 2, the yield was 0.35 g (19.5%), colourless plates, m.p. 151—152°C (from ethanol).

$C_{20}H_{23}NO_3S$ (357.48). Calcd. C 66.58; H 6.48; S 8.97. Found C 65.91; H 6.96; S 9.17%.

7. 2-Benzyl-2-phenyl-6,7-dimethoxy-3,4-dihydro-2H-1,3-benzthiazin-4-one (IIe) and 2-phenyl-4-benzal-6,7-dimethoxy-4H-1,3-benzthiazine (IV)

1.2 g (0.004 mole) of 2-phenyl-6,7-dimethoxy-4*H*-1,3-benzthiazin-4-one was dissolved in 120 ml of anhydrous tetrahydrofuran, and a solution of 0.02 mole benzylmagnesium chloride in 30 ml ether was added. Thereafter the procedure as described in Experiment 2 was followed. The reaction product was chromatographed on a silica gel column with benzene–petroleum ether solvent mixture. Two identifiable products were obtained:

0.40 g (27%) of compound **IV**, orange yellow plates, m.p. 111—113°C (from ether).

$C_{23}H_{19}NO_2S$ (373.45). Calcd. C 73.96; H 5.13. Found C 73.68; H 5.28%.

0.46 g (28.6%) of compound **IIe**, colourless prisms, m.p. 234—235°C (from chloroform–ethanol).

$C_{23}H_{21}NO_3S$ (391.47). Calcd. C 70.56; H 5.41; N 3.58. Found C 70.54; H 5.37; N 3.66%.

8. 2,4-Diphenyl-6,7-dimethoxy-4-hydroxy-4H-1,3-benzthiazine (IIIb)

1.5 g (0.005 mole) of 2-phenyl-6,7-dimethoxy-4*H*-1,3-benzthiazin-4-one was dissolved in 150 ml of anhydrous tetrahydrofuran, and 0.025 mole of phenylmagnesium bromide dissolved in 30 ml of ether was added. Processed as described in Experiment 2, a yield of 0.77 g (40.5%) was obtained, colourless plates (from ethanol), m.p. 168—170°C.

$C_{22}H_{19}NO_3S$ (377.44). Calcd. C 70.00; H 5.07. Found C 69.89; H 5.59%.

9. Preparation of S-(benzimido)-4,5-dimethoxy-2-mercaptobenzophenone hydrochloride (VIIb) in anhydrous medium

A solution of 0.75 g (0.0002 mole) 2,4-diphenyl-6,7-dimethoxy-4-hydroxy-4*H*-1,3-benzthiazine in 40 ml dry benzene was saturated with dry hydrogen chloride gas. The orange-yellow crystalline precipitate separating at the beginning of the introduction of hydrogen chloride was quickly dissolved. The orange-yellow solution was evaporated to dryness in vacuum, the residue was dissolved in chloroform and the product precipitated by adding dry ether to the solution; lemon-yellow crystals (0.78 g; 95%), m.p. 158—159°C (d.).

$C_{22}H_{20}ClNO_3S$ (413.93). Calcd. C 63.84; H 4.87; Cl 8.57. Found C 62.92; H 4.46; Cl 9.17%.

10. S-(benzimido)-2-mercaptobenzophenone hydrochloride (VIIa)

0.64 g (0.002 mole) of 2,4-diphenyl-4-hydroxy-4*H*-1,3-benzthiazine was dissolved in 20 ml of 17% hydrochloric acid and the solution boiled for 20 min. After cooling, the crystals which separated were filtered off, washed with 10% HCl, and dried in a desiccator to obtain 0.69 g (95.8%) of the product, pale yellow plates, m.p. 194—195°C (d.) (from ethanol containing 5% HCl).

$C_{20}H_{18}ClNOS$ (355.87). Calcd. C 67.50; H 5.10; N 3.94; Cl 9.96. Found C 66.87; H 4.90; N 3.83; Cl 9.96%.

11. Preparation of S-(benzimido)-4,5-dimethoxy-2-mercaptobenzophenone hydrochloride (VIIb) with aqueous hydrochloric acid

0.38 g (0.001 mole) of 2,4-diphenyl-6,7-dimethoxy-4-hydroxy-4*H*-1,3-benzthiazine was dissolved in 20 ml of 17% hydrochloric acid, and the solution was boiled for 20 min. Processed as described in Experiment 10, the yield was 0.41 g (89.2%), yellow prisms, m.p. 155—157°C (from ethanol containing 5% of hydrochloric acid). With the product of Experiment 9 it gave no m.p. depression.

$C_{22}H_{20}ClNO_3S$ (413.93). Calcd. C 63.84; H 4.87; N 3.38. Found C 63.03; H 5.04; N 3.53%.

12. S-(benzoyl)-4,5-dimethoxy-2-mercaptobenzophenone (VIII)

2.07 g (0.005 mole) of 2-(benzimido)-4,5-dimethoxy-2-mercaptobenzophenone hydrochloride was dissolved in 100 ml of water and the solution was heated to the boiling point. After cooling, it was extracted with ethylacetate to obtain 1.15 g (62%) of colourless prisms, m.p. 129—130°C (from 50% ethanol).

$C_{22}H_{18}O_4S$ (378.42). Calcd. C 69.82; H 4.79. Found C 69.70; H 4.91%.

13. 4,5-dimethoxy-2-mercaptobenzophenone (IX)

0.95 g (0.0025 mole) of S-(benzoyl)-4,5-dimethoxy-2-mercaptobenzophenone was dissolved in nitrogen atmosphere in 5 ml of warm 5% ethanolic sodium hydroxide. After cooling, the solution was acidified with 10% HCl and extracted with ether. The ether extract was washed several times with 5% Na_2CO_3 solution and dried over anhydrous Na_2SO_4, then the ether was evaporated. The residue was a non crystallizing yellow oil. Thin-layer chromatography indicated a homogeneous substance; it gave with lead acetate solution a positive mercaptan reaction. The product was dried over phosphorous(V)oxide in vacuum.

$C_{15}H_{14}O_3S$ (274.32). Calcd. C 65.67; H 5.14. Found C 66.89; H 5.45%.

Its *p*-nitrobenzoate was obtained as yellow crystals, m.p. 131—131.5°C (from ethanol).

$C_{22}H_{17}NO_6S$ (423.43). Calcd. N 3.31. Found N 2.98%.

14. Synthesis of S-(benzimido)-4,5-dimethoxy-2-mercaptobenzophenone hydrochloride (VIIb)

0.22 g of 4,5-dimethoxy-2-mercaptobenzophenone and 0.10 g of benzonitrile were dissolved in 3 ml of dry ether and, under cooling, the solution was saturated with dry gaseous hydrogen chloride. The solution was allowed to stand for 2 days and the solvent evaporated in the vacuum of a water pump. The residue was dissolved in a mixture of ethanol and chloroform, and the product was precipitated by the addition of ether to obtain yellow crystals, m.p. 153—155°C (from ethanol containing 5% HCl). It gave no m.p. depression with **VIIb** prepared in Experiments 9 and 11; the IR spectra of the three products were identical.

$C_{22}H_{20}ClNO_3S$ (413.93). Calcd. C 63.84; H 4.87; Cl 8.57. Found C 62.90; H 5.22; Cl 8.96%.

REFERENCES

[1] Böhme, H., Schmidt, W.: Arch. Pharmaz. Ber. dtsch. pharmaz. Ges. **286/58,** 437 (1953)
[2] Szabó, J., Vinkler, E.: Acta Chim. Acad. Sci. Hung. **17,** 201 (1958)
[3] Varga, I., Szabó, J., Sohár, P.: (In press)
[4] Vinkler, E., Szabó, J.: Acta Chim. Acad. Sci. Hung. **6,** 323 (1955)

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SYNTHESIS OF N-METHYL-OLIGOPEPTIDES OF POTENTIAL ANTIMICROBIAL ACTIVITY

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Cyclic and acyclic N-methyl-oligopeptides, simplified griselimycin analogues of potential antimicrobial activity, were prepared from simple amino acids. For the elucidation of structure-activity relationships, the effect of the number and configuration of amino acids and N-methylamino acids as well as that of cyclization was studied. The most potent molecules: cyclo[L-leucyl-L-prolyl-L-leucyl-L-valyl (or N-methyl--L-valyl)-L-prolyl-N-methyl-D-leucyl-glycyl]; L-threonyl-L-leucyl-L-prolyl-L-leucyl-L--valyl (or N-methyl-L-valyl)-L-prolyl-N-methyl-D-leucyl-glycine and N-acetyl-cyclo[L--threonyl-L-leucyl-L-prolyl-L-leucyl-L-valyl (or N-methyl-L-valyl)-L-prolyl-N-methyl-D--leucyl-glycyl] had minimum inhibitory concentrations in the range of 6—50 μg/ml against *Mycobacterium tuberculosis* $H_{37}R_V$, and 20—50 μg/ml against *Candida albicans*, *in vitro*.

In an earlier communication [1] we reported the synthesis of acyclic N-acyl oligopeptides of potential antimicrobial activity, built up from fatty acids, basic, aromatic amino acids, and valine or leucine. In the present work cyclic and acyclic N-methyl-oligopeptides, simplified griselimycin analogues, were prepared. Griselimycin is a macrocyclic peptide antibiotic, isolated by French scientists [2] (Fig. 1). It exhibits antimicrobial activity according to

N-Acetyl-MeVal-Pro(4-*trans*-Me)-cyclo[MeThr-Leu-Pro(4-*trans*-Me)-Leu-MeVal-Pro-MeLeu-Gly]

neogriselimycin

Fig. 1. Structure of griselimycin

Table I. Instead of aromatic or basic amino acid moieties, it consists of a cumulated number of N-methyl-amino acids and 4-*trans*-methyl-prolines. Selective hydrolysis of the N-terminal N-acyl-N-methyl-L-valine residue of the side chain gave neogriselimycin, which served as starting material in the synthesis of semi-synthetic griselimycins. Besides penicillins and cephalosporins, this was the first time that non-toxic peptide antibiotic derivatives of 100-fold activity as compared with griselimycin itself, could be prepared (Fig. 2) [3].

For the elucidation of structure-activity relationships the effect of the number and configuration of the amino acids and N-methyl-amino acids, as well as that of cyclization was studied. The peptides prepared are listed in Table II, together with their antimicrobial activities.

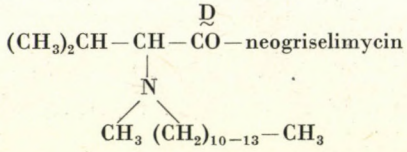

Fig. 2. Structure of the most potent semi-synthetic griselimycin analogues

In the course of their preparation the amino group was protected by carbobenzoxy and benzyl groups, and cleaved by catalytic hydrogenolysis, the carboxyl group by methyl ester formation. The molecules were built up by stepwise synthesis and fragment condensation, applying DCC and the mixed anhydride method. The active ester procedure which led to good yields in the

Table I

Antimicrobial activity of griselimycin (11072 R. P.) [2]

Test organism	Min. inhib. concn., μg/ml
Mycobacterium tuberculosis $H_{37}R_V$	1—5
Mycobacterium tuberculosis Vy	0.5—1
Mycobacterium species ATCC 607	0.25—0.5
Sarcina lutea ATCC 9341	0.36
Streptococcus faecalis ATCC 9790	>250
Bacillus subtilis ATCC 6633	>250
Escherichia coli ATCC 9637	>250
Pseudomonas aeruginosa	>250

preparation of peptides described in the earlier paper [1], did not furnish appreciable yields in this series of peptides. The N-methyl-amino acids were prepared by forming Schiff bases with benzaldehyde, reducing them with sodium borohydride, and methylating the obtained N-benzyl-amino acid [9]. The benzyl group was retained as an N-protective group. Unfortunately, though the N-benzyl group could easily be cleaved by catalytic hydrogenolysis in both peptides, namely N-benzyl-N-methyl-L-valyl-L-proline methyl ester and N-benzyl-N-methyl-L (or D)-leucyl-glycine methyl ester, it could not be removed from the tetrapeptide N-benzyl-N-methyl-L-valyl-L-prolyl-N-methyl-D-leucyl-glycine methyl ester. When carbobenzoxy group was used instead, this group proved to be highly sensitive to acid; in both tetrapeptides **12** and **30** it was cleaved spontaneously in aqueous 1*N* HCl, together with the methyl ester group. In this side reaction the ratio of the free peptide could amount to 80%. Most probably this special sequence of amino acids, as well as the

Table II

	Peptide	Minimal inhibitory concentration against			
		Gram-positive micro-organisms μg/ml	Gram-negative micro-organisms μg/ml	Fungi, μg/ml	*M. tub.* $H_{37}R_V$ μg/ml
6	Pro-Meleu- Gly-OMe	>100	>100	>100	>100
63	MeVal-Pro-Meleu- - - -OMe	>100	>100	>100	>100
31	Val-Pro-Meleu- Gly-OMe	>100	>100	<100	>100
13	MeVal-Pro-Meleu- Gly-OMe	>100	>100	>100	>100
65	Leu-MeVal-Pro-Meleu- - - -OMe	>100	>100	>100	>100
33	Leu- - -Val-Pro-Meleu- Gly-OMe	>100	>100	>100	>100
15	Leu-MeVal-Pro-Meleu- Gly-OMe	>100	>100	>100	>100
67	Leu-Pro-Leu-MeVal-Pro-Meleu- - - -OMe	>100	>100	>100	>100
51	Leu-Pro-Leu- - -Val-Pro-MeLeu-Gly	>100	>100	>100	>100
36	Leu-Pro-Leu- - -Val-Pro-Meleu- Gly	>100	>100	>100	>100
20	Leu-Pro-Leu-MeVal-Pro-Meleu- Gly	>100	>100	>100	>100
52	cyclo(Leu-Pro-Leu- - -Val-Pro-MeLeu-Gly)	>100	>100	>100	>100
37	cyclo(Leu-Pro-Leu- - -Val-Pro-Meleu- Gly)	12	>100	50	12
21	cyclo(Leu-Pro-Leu-MeVal-Pro-Meleu- Gly)	25	>100	20	50
58	Thr-Leu-Pro-Leu- - -Val-Pro-MeLeu-Gly.DCHA	>100	>100	>100	>100
43	Thr-Leu-Pro-Leu- - -Val-Pro-Meleu- Gly.DCHA	12	>100	20	6
27	Thr-Leu-Pro-Leu-MeVal-Pro-Meleu- Gly.DCHA	25	>100	20	6
57	N-acetyl-cyclo(Thr-Leu-Pro-Leu- - -Val-Pro-MeLeu-Gly)	>100	>100	>100	>100
42	N-acetyl-cyclo(Thr-Leu-Pro-Leu- - -Val-Pro-Meleu- Gly)	25	>100	>100	25
26	N-acetyl-cyclo(Thr-Leu-Pro-Leu-MeVal-Pro-Meleu- Gly)	50	>100	>100	10
69	N-palmitoyl-Thr-Leu-Pro-Leu- - -Val-Pro-Meleu- Gly.DCHA	>100	>100	>100	>100
70	N-palmitoyl-cyclo(Thr-Leu-Pro-Leu- - -Val-Pro-Meleu- Gly)	>100	>100	>100	>100
74	lauryl-val-Pro-Thr-Leu-Pro-Leu- - -Val-Pro-Meleu- Gly	>100	>100	>100	>100
75	lauryl-val-Pro-cyclo(Thr-Leu-Pro-Leu- - -Val-Pro-Meleu- Gly)	>100	>100	>100	>100

simultaneous presence of proline and at least one N-methyl-amino acid, resulted in an electron distribution where the carbobenzoxy group behaved like a *p*-methoxycarbobenzoxy group, which could easily be cleaved in acid media [7]. IR measurements confirmed the assumption that the by-product was in a zwitterion form. The characteristic CO frequency of acids did not appear between 1730 and 1760 cm^{-1}, nor did the CO frequency of the ester group at 1720 cm^{-1}. This unusual phenomenon is going to be investigated further.

In the course of the synthesis of peptides containing two N-methyl groups, first the simple tripeptide, carbobenzoxy-L-valyl-L-prolyl-D-leucine methyl ester, was prepared, and subsequently methylated in the presence of NaH with methyl iodide, in dimethylformamide. The completion of methylation was checked by IR and NMR spectroscopy.

In peptides containing a single N-methyl-amino acid moiety, the original strategy utilizing N-benzyl-N-methyl-D-leucine was retained.

Cyclization was effected at concentrations of 1 mole/10 ml dichlormethane, by means of DCC, and its completion was checked by IR spectroscopy, in both the lactone and the peptide bond formation. In the course of the decarbobenzoxylation of the protected cyclo-octapeptides by catalytic hydrogenolysis, however, the lactone ring also suffered cleavage. Consequently, in the following the protected acyclic octapeptide was decarbobenzoxylated, the free amino group acetylated, and finally the lactone was formed, after saponification of the ester group. In a similar way in the cyclo-octa- and cyclo-decapeptides, containing palmitoyl or lauryl-D-valyl-L-prolyl side chain (**70** and **75**) the lactone was formed in the last step.

In the course of the syntheses intermediary substances were rather difficult to handle, mostly owing to their high solubility in organic solvents. In several cases they had to be characterized in the form of their DCHA or HCl salts.

Assessing the structure-activity relationship of the peptides synthesized, it is apparent that up till heptapeptides (**6**, **63**, **31**, **13**, **65**, **33**, **15**, **67**, **51**, **36** and **20**) all acyclic peptides are devoid of antimicrobial activity. If the heptapeptides, smaller by one amino acid residue than the neogriselimycin cycle, are cyclized, both cycloheptapeptides (**37** and **21**) exhibit antibacterial activity against Gram-positive microorganisms (12 and 26 μg/ml) *Candida albicans* (50 and 20 μg/ml) and *Mycobacterium tuberculosis* $H_{37}R_V$ (12 and 50 μg/ml), but only if the N-methyl-leucine moiety is of D-configuration. The molecule containing N-methyl-L-leucine (**52**) is devoid of antimicrobial activity. The potency of **37** is not enhanced if the molecule contains an additional N-methyl-amino acid in the form of N-methyl-L-valine (**21**).

N-terminal chain-elongation by L-threonine led to octapeptides which are effective even in the acyclic form (**43** and **27**). Similarly to the cyclic hepta-

peptides, the N-methyl-L-leucine-containing acyclic octapeptide (**58**) was inactive, and additional N-methyl-amino acid (**27**) did not enhance the potency of **43** either. The antimicrobial activity of the acyclic substances was rather striking, as all macrocyclic peptide antibiotics described in the literature (staphylomycin [4], etamycin [5], etc.), including griselimycin [2], were inactive in the open chain form. In actinomycins the opening of one of the two lactone rings is sufficient to reduce activity to a minimum [6]. In our case even the acyclic octapeptide, containing one single unnatural amino acid, exhibited antimicrobial activity (**43**), while the more sophisticated acyclic form of griselimycin was devoid of any potency. Consequently the mode of action of our molecule is assumed to be different. This hypothesis is supported by the fact that acyclic and cyclic palmitoyl-octapeptides (**69** and **70**), as well as those having an N-lauryl-dipeptide side chain (**74** and **75**) were devoid of antimicrobial activity, although this was the way which had led to the most potent semi-synthetic griselimycins.

The formation of a lactone ring in octapeptides **42** and **26** did not result in molecules of enhanced potency, and the cyclo-octapeptide, built up solely from L-amino acids (**57**), was equally devoid of any potency.

It may be concluded that we succeeded in synthesizing highly simplified griselimycin analogues exhibiting considerable antimicrobial potency (Table III). Seven residues in cyclic, and eight residues in acyclic form are sufficient

Table III

Compound	Min. inhibitory concn.		
	M. tub. $H_{37}R_V$ μg/ml	*B. subtilis* μg/ml	Fungi μg/ml
Griselimycin [2]	1—5	>250	>250
Neogriselimycin [3]	0.005	>250	>250
cyclo(Leu-Pro-Leu- - -Val-Pro-Meleu-Gly) (**37**)	12	50	12
cyclo(Leu-Pro-Leu-MeVal-Pro-Meleu-Gly) (**21**)	25	20	50
Thr-Leu-Pro-Leu- - -Val-Pro-Meleu-Gly.DCHA (**43**)	12	20	6
Thr-Leu-Pro-Leu-MeVal-Pro-Meleu-Gly.DCHA (**27**)	25	20	6
N-Ac-cyclo(Thr-Leu-Pro-Leu- - -Val-Pro-Meleu-Gly) (**42**)	25	>100	25
N-Ac-cyclo(Thr-Leu-Pro-Leu-MeVal-Pro-Meleu-Gly) (**26**)	50	>100	10

for an active molecule. One single unnatural amino acid, N-methyl-D-leucine, is essential for antimicrobial activity; if it has L-configuration, the molecule loses its potency. Introduction of one additional N-methyl-amino acid, N-methyl-L-valine, did not enhance the potency. Formation of a lactone ring did not affect antimicrobial activity, while the addition of an N-acyl- or N-alkyl side chain led to molecules devoid of potency.

Experimental

Thin-layer chromatograms were run on "Silica Gel for TLC According to Stahl" or on "Kieselgel $HF_{254+366}$ nach Stahl für Dünnschicht" plates with chloroform-methanol 9 : 1 (R_{FI}), ethyl acetate-pyridine-acetic acid-water 30 : 20 : 6 : 11 (R_{FII}), chloroform–acetone 8 : 2 (R_{FIII}), and chloroform–acetone 9 : 1 (R_{FIV}). The spots were revealed with ninhydrine, 1% *p*-nitrobenzoylchloride–pyridine (in the case of N-methyl-amino acids), Cl_2-tolidine, or UV light (by incorporating a fluorescent indicator in the thin-layer), and iodide vapor.

Silica gel column chromatography was carried out on "Kieselgel Reanal 1/14 for Chromatography".

Organic extracts were dried over anhydrous sodium sulfate and evaporations were carried out under reduced pressure in a rotary evaporator.

Acid hydrolysates of the peptide derivatives were prepared using 6*N* HCl (110°C/16 hrs.) and the amino acid composition of the hydrolysates was determined either qualitatively or quantitatively with gas chromatography or by means of an amino acid analyser, respectively.

M.p.'s are uncorrected.

Starting materials. Carbobenzoxy amino acids and amino acid methyl esters were prepared according to general procedures, and the N-lauryl- and N-benzyl-N-methyl-amino acids by the method of QUITT *et al.* [9].

Intermediates and end products were purified with chromatography, recrystallization, repeated precipitation, and preparative TLC.

Microbiological assays (Table II) were carried out by serial dilution and the agar diffusion method on the following test organisms: *Mycobacterium tuberculosis* $H_{37}R_V$ (Dubos' medium), apathogenic *Mycobacteria*, *Bendo pyogenes*, *Escherichia coli GR*, *Shigella sonnei*, *Sarcina lutea*, *Staphylococcus Duncan*, *Streptococcus faecalis*, *Bacillus subtilis*, *Haemophylus* group, pathogenic and apathogenic fungi, and *Candida albicans*.

General procedures (Table IV)

Method A: DCC coupling

The appropriate methyl-amino acid- or methyl-peptide hydrochloride (10 mmoles) in dichloromethane (100 ml) and triethylamine (10 mmoles) was coupled at 0°C for 12 hrs with a protected amino acid or a protected peptide, respectively (10 mmoles), in the presence of DCC (10 mmoles). The precipitated DCU was filtered off, and the filtrate diluted with dichloromethane (100 ml).

Up till tripeptides the solution was washed with 1*N* HCl, 5% $NaHCO_3$ solution, water, dried over sodium sulfate and evaporated to dryness under reduced pressure.

From tetrapeptides on, however, the washings were omitted, and the concentrated solution was purified by rapid silica gel chromatography, to avoid the decomposition of the protected peptides.

Method B: Mixed anhydride method

The appropriate protected amino acid (50 mmoles) was suspended in a mixture of THF (80 ml) and triethylamine (50 mmoles) and, at −40°C, ethyl chloroformate (50 mmoles) was added over a period of 30 min. The mixture was stirred at −5°C for min, refrigerated to −20°C, and a suspension of the methyl-amino acid hydrochloride (50 mmoles) in THF (60 ml) and triethylamine (50 mmoles) was added over a period of 15 min. The mixture was stirred at −5°C for 5 hrs, and allowed to stand at room temperature overnight. The THF was evaporated under reduced pressure, the dry residue dissolved in chloroform (400 ml), washed with 0.1*N* HCl (2 × 200 ml), 5% $NaHCO_3$ solution (2 × 200 ml) and water (200 ml) dried over Na_2SO_4 and evaporated to dryness under reduced pressure.

Method C: Hydrogenolysis

A solution of Z-peptide-OMe or Bzl-peptide-OMe (10 mmoles) in MeOH (100 ml) and HCl (10 mmoles) was hydrogenated at room temperature in the presence of 10% palladized charcoal (1.0 g). The filtered solution was evaporated to dryness at reduced pressure.

Table IV

Physicochemical data of the peptides

	Formula	Method	Yield, %	M.p., °C	$[\alpha]_D^{20}$			R_F I	R_F II	R_F III	R_F IV	Analysis: Required, % C	H	N	Cl⁻	Formula	Analysis: Found, % C	H	N	Cl⁻
1	Bzl-Meleu-Gly-OMe	A	55.0	174[a]	−36.6	c = 2	$CHCl_3$	0.8				66.60	8.57	9.13		$C_{17}H_{26}N_2O_3$	66.45	8.70	9.37	
		B	87.5	173[a]	−36.0												66.80	8.75	9.27	
2	Bzl-MeLeu-Gly-OMe	B	87.8	168[a]	+34.5	c = 2.19	$CHCl_3$	0.8				66.60	8.57	9.13		$C_{17}H_{26}N_2O_3$	66.35	8.62	9.57	
3	Meleu-Gly-OMe · HCl	C	91.0					0.0												
4	MeLeu-Gly-OMe · HCl	C	90.0					0.0												
5	Z-Pro-Meleu-Gly-OMe	A	88.8	74[b]				0.8				61.70	7.43	9.40		$C_{23}H_{33}N_3O_6$	61.42	7.55	9.02	
6	Pro-Meleu-Gly-OMe · Hcl	C	19.4					0.01	0.9					12.11	10.2	$C_{15}H_{27}N_2O_4 \cdot HCl$			11.80	9.80
7	Z-Pro- - -leu- - - -OMe	A	80.7	66[c]				0.92		0.8	0.7	63.80	7.52	7.45		$C_{20}H_{28}N_2O_5$	63.70	7.30	7.30	
		B	39.9	65[c]				0.92		0.8							63.70	7.30	7.30	
8	Pro- - -leu- - - -OMe · HCl	C	96.0	245[b]				0.1	0.7	0.0				10.10	12.8	$C_{12}H_{23}N_2O_3 \cdot HCl$			9.55	12.55
9	Z-Val-Pro- - -leu- - - -OMe	B	69.0	138[d]	− 7.9	c = 0.1	MeOH	0.8		0.35		63.00	7.84	8.82		$C_{28}H_{37}N_3O_6$	63.20	7.86	8.64	
10	Z-MeVal-Pro-Meleu- - - -OMe	D						0.82												
11	Z-MeVal-Pro-Meleu · DCHA	E	64.7*	295[e]	− 0.75	c = 4	EtOH		0.9			68.01	9.31	8.35		$C_{26}H_{39}N_3O_6 \cdot DCHA$	67.90	9.42	8.05	
12	Z-MeVal-Pro-Meleu-Gly-OMe	F + A								0.7										
13	MeVal-Pro-Meleu-Gly-OMe · HCl	C	34.4*	129−34[a]	− 7.9	c = 5	$CHCl_3$	0.0	0.86					12.10		$C_{21}H_{38}N_4O_5 \cdot HCl$			11.72	
14	Z-Leu-MeVal-Pro-Meleu-Gly-OMe	A								0.75										
15	Leu-MeVal-Pro-Meleu-Gly-OMe · HCl	C	58.5*	63[a]	−62.4	c = 0.1	MeOH		0.9	0.0				12.15		$C_{27}H_{49}N_5H_6 \cdot HCl$			11.65	
16	Z-Leu-Pro-OMe	A								0.8										
17	Z-Leu-Pro · DCHA	E	28.0*	72[e]	−54.2	c = 0.4	MeOH			0.13				7.74		$C_{19}H_{26}N_2O_5 \cdot DCHA$			7.91	
18	Z-Leu-Pro-Leu-MeVal-Pro-Meleu-Gly-OMe	F + A	81.9							0.8										
19	Leu-Pro-Leu-MeVal-Pro-Meleu-Gly-OMe · HCl	C	96.5	52[b]	−65.2	c = 0.1	MeOH		0.8	0.0				12.47		$C_{38}H_{67}N_7O_8 \cdot HCl$			12.08	
20	Leu-Pro-Leu-MeVal-Pro-Meleu-Gly	E	98.8	90[b]	−60.2	c = 0.1	MeOH		0.9	0.0				13.33		$C_{37}H_{65}N_7O_8$			13.21	
21	Cyclo(Leu-Pro-Leu-MeVal-Pro-Meleu-Gly)	G		oil				0.9		0.8										
22	Z-Thr-Leu-Pro-Leu-MeVal-Pro-Meleu-Gly-OMe	A	48.3*	96−7[b]	− 5.0	c = 5	MeOH	0.83		0.7				11.38		$C_{50}H_{80}N_8O_{12}$			11.25	
23	Thr-Leu-Pro-Leu-MeVal-Pro-Meleu-Gly-OMe · HCl	C								0.1										
24	N-Ac-Thr-Leu-Pro-Leu-MeVal-Pro-Meleu-Gly-OMe	H								0.4										
25	N-Ac-Thr-Leu-Pro-Leu-MeVal-Pro-Meleu-Gly	E								0.1										
26	N-Ac-cyclo(Thr-Leu-Pro-Leu-MeVal-Pro-Meleu-Gly)	G	43.2*	113[b]						0.73				13.00		$C_{43}H_{72}N_8O_{10}$			12.75	
27	Thr-Leu-Pro-Leu-MeVal-Pro-Meleu-Gly · DCHA	E	59.2	207[e]					0.5	0.0				12.40		$C_{41}H_{72}N_8O_{10} \cdot DCHA$			12.19	
28	Z-Val-Pro- - - - - - - -OMe	A	69.4	oil						0.6										
29	Z-Val-Pro DCHA	E	96.2	42[e]	−81.4	c = 0.1	MeOH		0.9	0.3				7.98		$C_{18}H_{24}N_2O_5 \cdot DCHA$			7.81	
30	Z-Val-Pro-Meleu-Gly-OMe	F + A								0.69										
31	Val-Pro-Meleu-Gly-OMe · HCl	C	66.7*	129[b]	− 7.7	c = 0.1	MeOH	0.0	0.76					12.49		$C_{20}H_{36}N_4O_5 \cdot HCl$			12.33	
32	Z-Leu- - -Val-Pro-Meleu-Gly-OMe	A								0.75										
33	Leu- - -Val-Pro-Meleu-Gly-OMe · HCl	C	69.8*	72[a]	−63.6	c = 0.1	MeOH		0.87					12.51		$C_{26}H_{47}N_5O_6 \cdot HCl$			11.91	
34	Z-Leu-Pro-Leu- - -Val-Pro-Meleu-Gly-OMe	F + A	85.2	oil						0.8										
35	Leu-Pro-Leu- - -Val-Pro-Meleu-Gly-OMe · HCl	C	95.1	74[b]	−64.3	c = 0.1	MeOH			0.25				12.72		$C_{37}H_{65}N_7O_8 \cdot HCl$			12.51	
36	Leu-Pro-Leu- - -Val-Pro-Meleu-Gly	E	91.1	95[b]	−63.2	c = 0.1	MeOH		0.9	0.0				13.58		$C_{36}H_{63}N_7O_8$			13.31	
37	Cyclo(Leu-Pro-Leu- - -Val-Pro-Meleu-Gly)	G	69.2	oil				0.9		0.8										
38	Z-Thr-Leu-Pro-Leu- - -Val-Pro-Meleu-Gly-OMe	A	40.7	116−7[b]	− 5.05	c = 5	MeOH	0.85		0.7				11.52		$C_{49}H_{78}N_8O_{12}$			11.52	
39	Thr-Leu-Pro-Leu- - -Val-Pro-Meleu-Gly-OMe · HCl	C								0.12										
40	N-Ac-Thr-Leu-Pro-Leu- - -Val-Pro-Meleu-Gly-OMe	H								0.43										
41	N-Ac-Thr-Leu-Pro-Leu- - -Val-Pro-Meleu-Gly	E								0.1										
42	N-Ac-cyclo(Thr-Leu-Pro-Leu- - -Val-Pro-Meleu-Gly)	G	49.7*	114[b]						0.75				13.23		$C_{42}H_{70}N_8O_{10}$			13.51	
43	Thr-Leu-Pro-Leu- - -Val-Pro-Meleu-Gly · DCHA	E	79.0	209[e]					0.5	0.0				12.12		$C_{46}H_{70}N_8O_{10} \cdot DCHA$			12.41	
44	Z-Thr-Leu-Pro-Leu- - -Val-Pro-Meleu-Gly · DCHA	E	93.1	169[e]	− 5.0	c = 1	MeOH		0.9	0.0				11.01		$C_{48}H_{76}N_8O_{12} \cdot DCHA$			10.07	
45	Z-Val-Pro-MeLeu-Gly-OMe	F + A		72[b]						0.75										
46	Val-Pro-MeLeu-Gly-OMe · HCl	C	64.8*	134[b]	−28.62	c = 5	$CHCl_3$		0.76	0.0		53.40	8.32	12.50		$C_{20}H_{36}N_4O_5 \cdot HCl$	53.78	8.60	11.98	
47	Z-Leu- - -Val-Pro-MeLeu-Gly-OMe	A	66.0	72[b]	−47.20	c = 5	MeOH			0.75				10.62		$C_{34}H_{53}N_5O_8$			11.00	
48	Leu- - -Val-Pro-MeLeu-Gly-OMe · HCl	C	90.1	141[b]	−40.3	c = 1	MeOH		0.87	0.0				12.52		$C_{26}H_{47}N_5O_6 \cdot HCl$			12.85	
49	Z-Leu-Pro-Leu- - -Val-Pro-MeLeu-Gly-OMe	F + A	82.4	oil						0.8										
50	Leu-Pro-Leu- - -Val-Pro-MeLeu-Gly-OMe · HCl	C	96.0	78[b]	−105.8	c = 1	MeOH		0.8	0.0				12.72		$C_{37}H_{65}N_7O_8 \cdot HCl$			12.95	
51	Leu-Pro-Leu- - -Val-Pro-MeLeu-Gly	E	90.0	90[b]	−105.8	c = 1	MeOH		0.9	0.0				13.58		$C_{36}H_{63}N_7O_8$			13.65	
52	Cyclo(Leu-Pro-Leu- - -Val-Pro-MeLeu-Gly)	G	65.0	oil				0.9		0.8										
53	Z-Thr-Leu-Pro-Leu- - -Val-Pro-MeLeu-Gly-OMe	A	66.4	122[b]	−58.9	c = 5	MeOH			0.7				11.52		$C_{49}H_{78}N_8O_{12}$			11.69	
54	Thr-Leu-Pro-Leu- - -Val-Pro-MeLeu-Gly-OMe · HCl	C								0.11										
55	N-Ac-Thr-Leu-Pro-Leu- - -Val-Pro-MeLeu-Gly-OMe	H								0.4										
56	N-Ac-Thr-Leu-Pro-Leu- - -Val-Pro-MeLeu-Gly	E								0.12										
57	N-Ac-cyclo(Thr-Leu-Pro-Leu- - -Val-Pro-MeLeu-Gly)	G	39.3*	105−10[b]	−92.02	c = 5	MeOH			0.75				13.23		$C_{42}H_{70}N_8O_{10}$			13.18	
58	Thr-Leu-Pro-Leu- - -Val-Pro-MeLeu-Gly · DCHA	E	96.0	206[e]	−58.3	c = 5	MeOH		0.5	0.0				12.55		$C_{46}H_{70}N_8O_{10} \cdot DCHA$			12.04	
59	Z-Thr-Leu-Pro-Leu- - -Val-Pro-MeLeu-Gly · DCHA	E	86.4	162[e]	−58.3	c = 5	MeOH	0.0	0.9					11.01		$C_{48}H_{76}N_8O_{12} \cdot DCHA$			11.25	
60	Bzl-MeVal-Pro- - - - - - - -OMe	A		oil				0.8	0.7											
61	Bzl-MeVal-Pro	E								0.0										
62	Bzl-MeVal-Pro-Meleu-Gly-OMe	A								0.7										
63	MeVal-Pro-Meleu- - - -OMe · HCl	C	97.6*					0.1												
64	Z-Leu-MeVal-Pro-Meleu- - - -OMe	A	71.1	oil						0.8										
65	Leu-MeVal-Pro-Meleu- - - -OMe · HCl	C	96.5	71[b]	− 7.9	c = 0.1	MeOH	0.18						10.80		$C_{25}H_{46}N_4O_5 \cdot HCl$			10.20	
66	Z-Leu-Pro-Leu-MeVal-Pro-Meleu- - - -OMe	F + A	79.8							0.83										
67	Leu-Pro-Leu-MeVal-Pro-Meleu- - - -OMe · HCl	C	46.6	112[b]	− 5.0	c = 1	MeOH			0.18				11.55		$C_{36}H_{64}N_6O_7 \cdot HCl$			11.01	
68	N-Palm-Thr-Leu-Pro-Leu- - -Val-Pro-Meleu-Gly-OMe	I								0.75										
69	N-Palm-Thr-Leu-Pro-Leu- - -Val-Pro-Meleu-Gly · DCHA	E	31.8*	148[e]				0.55		0.4				10.13		$C_{56}H_{100}N_8O_{11} \cdot DCHA$			9.80	
70	N-Palm-cyclo(Thr-Leu-Pro-Leu- - -Val-Pro-Meleu-Gly)	G	30.0	68[a]				0.85		0.75				10.73		$C_{36}H_{98}N_8O_{10}$			10.50	
71	Lau-val · DCHA	(9)	60.0	190[e]					0.82	0.0		74.68	12.50	6.03		$C_{17}H_{35}NO_2 \cdot DCHA$	74.30	12.20	5.87	
72	Lau-val-Pro · DCHA	F + A	59.1	183[e]					0.8	0.1				7.46		$C_{22}H_{42}N_2O_3 \cdot DCHA$			7.61	
73	Lau-val-Pro- - - - - - - -Thr-Leu-Pro-Leu- - -Val-Pro-Meleu-Gly-OMe	A								0.7										
74	Lau-val-Pro- - - - - - - -Thr-Leu-Pro-Leu- - -Val-Pro-Meleu-Gly	E	34.8*	134[f]					0.8	0.1				11.80		$C_{62}H_{110}N_{10}O_{12}$			11.50	
75	Lau-val-Pro- - - -cyclo(Thr-Leu-Pro-Leu- - -Val-Pro-Meleu-Gly)	G	25.6							0.7										

Solvents: a MeOH; b treated with petroleum ether; c ethylacetate–petroleum ether; d ethylacetate; e ether; f MeOH–petroleum ether

* Overall yield including former steps where no yield was indicated.

Method D: Methylation of the protected tripeptide **9**

Sodium hydride (90 mmoles) was washed twice with ether (2×30 ml) and added in portions into a solution of the protected tripeptide **9** (20.5 mmoles) in dry methylformamide (150 ml) at 0°C. As the evolution of hydrogen ceased, methyl iodide (90 mmoles) was added dropwise to the stirred solution, which was then allowed to stand for 3 days at room temperature. The semi-solid mixture was poured in portions on crushed ice, and extracted with dichloromethane, washed with 1*N* HCl (2×200 ml) and water (200 ml), dried over Na_2SO_4 and evaporated to dryness at reduced pressure. The oily residue was used without purification in the next step.

According to the IR and NMR spectra, methylation was complete. No NH-signals could be found in the IR (3300 cm^{-1}) or NMR spectrum, only $N-CH_3$ signals were present at $\delta = 3.0$ and 2.9 ppm, corresponding to the N-methyl group of the valine and leucine residues, respectively, as well as OCH_3-signals, due to the methyl glycinate group, at $\delta = 3.8$ ppm.

In TLC the spot of the product failed to appear with Cl_2-tolidine, but could be detected with iodine vapour or in UV light. The chromatogram of its acid hydrolysate gave a single yellow spot upon spraying with ninhydrine reagent, indicating the presence of proline. No spots characteristic of valine or leucine could be visualized with 1% *p*-nitrobenzoylchloride-pyridine reagent.

Method E: Saponification

The appropriate protected peptide methyl ester (40 mmoles) was saponified for 2 hrs at room temperature with 20% methanolic NaOH (20 ml). In more dilute solution the reaction was long drawn-out, and by-products were formed. As the C-terminal was either glycine, proline or N-methyl-leucine, no hydantoin formation or racemization was observed. The end of the reaction was checked by TLC. The reaction mixture was diluted with water (200 ml) and the impurities, having higher R_F values than the product, were removed by extraction with ethyl acetate (2×100 ml). The pH of the aqueous layer was adjusted to pH 3, and extracted with chloroform (2×100 ml). The combined chloroform extracts were dried over Na_2SO_4 and evaporated at reduced pressure.

Formation of DCHA salt. The oily residue was dissolved in ether (150 ml) and DCHA (5.5 ml). The crystals of the DCHA salt were formed upon standing for several days.

Method F: Formation of free C-terminal from the DCH salt

The appropriate protected peptide DCHA salt (10 mmoles) was dissolved in a mixture of water (45 ml) and 1*N* HCl (11 ml). The aqueous solution was extracted with dichloromethane (3×100 ml), the combined extracts dried over Na_2SO_4 and concentrated under reduced pressure to 50 ml. This concentrate was used without purification in the next step.

Method G: Cyclization

The appropriate peptide, having a free amino and carboxyl group, or a free hydroxyl and carboxyl group (1 mmole) was cyclized for 3 days at room temperature in dichloromethane (10 ml) with DCC (1 mmole). The reaction mixture was kept for 24 hrs at 0°C, the DCU removed and the solution evaporated to dryness under reduced pressure. The oily residue solidified after treatment with petroleum ether. The formation of the cycloheptapeptide cycle was confirmed by the NH frequencies at 3270 cm^{-1}, and by the lack of a frequency characteristic of COOH groups in the IR spectrum (1730—1760 cm^{-1}). The formation of the lactone ring in the cyclo-octapeptides was supported by the NH frequencies at 3270 cm^{-1} and the lactone frequency at 1705 cm^{-1} in the IR spectrum. The N-acetyl methyl protons appeared at $\delta =$ = 2.15 ppm in the NMR spectrum.

Method H: Acetylation

Threonyl-peptide methyl ester (0.92 mmoles) was acetylated for 24 hrs at room temperature with acetic anhydride (2 ml) in methanol (5 ml). The mixture was poured on ice-water (100 ml) and extracted with ethyl acetate (3×50 ml). The combined extracts were washed with 5% Na_2CO_3 solution (50 ml) and water (50 ml), dried over Na_2SO_4 and evaporated to dryness in vacuum. The residue was used without purification in the next step.

Method I: Active ester method

Compound **39** (5 mmoles) in the base form was coupled in a mixture of dichloromethane (50 ml) and triethylamine (5 mmoles) at room temperature for 72 hrs with palmitic acid *p*-nitrophenyl ester (5 mmoles). The mixture was evaporated to dryness at reduced pressure, washed with water, dried, washed with ether, and used without purification in the next step.

*

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Symbols

Abbreviations

Ac	acetyl
Bzl	benzyl
DCC	dicyclohexylcarbodiimide
DCU	dicyclohexylurea
DCHA	dicyclohexylamine
Lau	lauryl
Meleu	N-methyl-D-leucine
MeVal	N-methyl-L-valine
palm	palmitoyl
THF	tetrahydrofuran
TLC	thin-layer chromatography
Z	carbobenzoxy

The abbreviations for L-amino acid residues and their derivatives, as well as their mode of use are in accordance with the suggestions of the Committee on Nomenclature adopted by IUPAC (J. Biol. Chem. **247,** 977 (1972)). D-amino acids are abbreviated in small letters (D-Leu = leu, whereas: L-Leu = Leu).

REFERENCES

[1] STVERTECZKY, J., HOLLÓSI, I., BAJUSZ, S.: Acta Chimica (Budapest), **87,** (3) 269 (1975)
[2] TERLAIN, B., THOMAS, J.-P.: Bull. Soc. Chim. France, **1971,** 2349, 2357, 2363; French. Pat. 1 393 208 (1961)
[3] RHONE—POULENC: French Appl. 125 842 (1967), 6878M and 144 421 (1968). Hungarian Appl. 13 732, 13 733 (1968). Belgian Pat. 722 846 (1967). South African Pat. 70 00248 (1970). Belgian Pat. 741 588 (1969)
[4] VANDERHAEGHE, H., PARMENTIER, G.: J. Am. Chem. Soc., **82,** 4414 (1960)
[5] SHEEHAN, J. C., ZACHAU, H. G., LAWSON, W. B.: J. Am., Chem. Soc. **79,** 3933 (1957)
[6] PERLMAN, K. L., WALKER, J., PERLMAN, ;D.: J. Antibiot., **24,** 135 (1971)
[7] WEYGAND, F., HUNGER, K.: Ber. **95,** 1 (1962)
[8] ZAORAL, M., RUDINGER, J.: Coll. Czechoslov. Chem. Commun. **20,** 1183 (1955)
[9] QUITT, P., HELLERBACH, J., VOGLER, K.: Helv. Chim. Acta, **46,** 327 (1963)

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ELECTRON DEFICIENT HETEROAROMATIC AMMONIOAMIDATES, VI*

THE SYNTHESIS AND SOME REACTIONS OF 10-AMINOACRIDINIUM SALTS AND *N*-(10-ACRIDINIO)-AMIDATES

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9-Phenylacridine and acridine were *N*-aminated with *O*-mesitylenesulfonylhydroxylamine. The resulting *N*-(10-acridinio)-amides of type **1** were transformed into pseudobases of type **2**, *N*-(10-acridino)-amidates of type **6**, the related compounds **7** and the hydrochlorides (**5**) of the former. Some reactions of the pseudobases have also been studied.

A brief report by Japanese authors [1] on the anomalous reaction of acridine with hydroxylamine-*O*-sulfonic acid prompts us to describe our amination studies of acridine and 9-phenylacridine with *O*-mesitylenesulfonylhydroxylamine ("MSH") [2] and some reactions of the resulting *N*-amino derivatives.

The key compound for the synthetic studies described in the present paper was 10-amino-9-phenylacridinium mesitylenesulfonate (**1a**) which was obtained by treating 9-phenylacridine with MSH. Acridine and MSH reacted similarly to yield **1b**.

When methanolic or ethanolic solutions of **1a** were treated with 1*N* NaOH or NH_4OH, the corresponding 9-alkoxy derivatives (**2a** and **2b**, respectively) were obtained. The reactivity of the latter is as expected for typical pseudobases. Thus **2a** and **2b**, when refluxed in the presence of alkali with ethanol and methanol, respectively, furnished equilibrium mixtures of **2a** and **2b**, easily detected by NMR. With hydrochloric acid both **2a** and **2b** were transformed into 10-amino-9-phenylacridinium chloride (**1c**). Furthermore, **2a** reacts with the CH acid nitromethane to yield **3**.

Characteristic violet colourations are observed when the pseudobases **2a** and **b** are refluxed with a solvent such as gasoline or toluene. When refluxed with nitromethane, the initial violet colouration disappears at the pace as **2a** is converted into **3**. Prolonged refluxing with chlorobenzene also causes the violet colour to disappear, because **2a** is transformed, probably *via* *N*-(10-acridinio)-amide (**4**), into 9-phenylacridine.

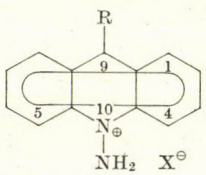
When an aqueous solution of **1a** is treated with alkali, a violet amorphous product is obtained resisting all attempts at crystallization. The pseudo-

* Part V: FETTER, J., LEMPERT, K. MØLLER, J.: Tetrahedron, **31**, 2559 (1975)

base structure **2c** and the ammonioamide structure **4*** are both in agreement with the reactions of this product, *viz.* that it yields **2a** and **3**, when treated with methanol and nitromethane, respectively, and that, when refluxed with chlorobenzene, it is transformed into 9-phenylacridine.

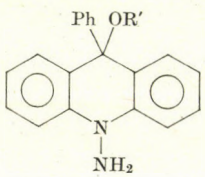
Reduction of **1a** with $NaBH_4$ is analogous to its reaction with alcohols in that it is again the C-9 atom which is attacked by the nucleophile, to yield the product 10-amino-9-phenyl-9,10-dihydroacridine.

The (acylamino)acridinium salts of type **5** are obtained by acylation of the aminoacridinium salts of type **1**, or the corresponding pseudobases **2**. Interestingly, reaction of the pseudobase **2a** with ethyl chloroformate gives **1c** rather than the expected **5d**. Treatment of the type **5** compounds with a base furnishes the acridinioamidates of type **6**. *N*-(9-Phenyl-10-acridinio)--*N*-phenylthiocarbamoylamide **7** has been synthesized by allowing **2a** to react with phenyl isothiocyanate.



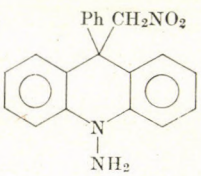
1

a: R = Ph, X = 2,4,6-$Me_3C_6H_2SO_3$
b: R = H, X = 2,4,6-$Me_3C_6H_2SO_3$
c: R = Ph X = Cl

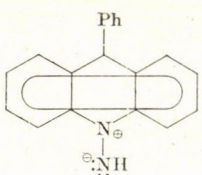


2

a: R′ = Me
b: R′ = Et
c: R′ = H



3



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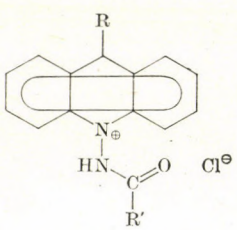
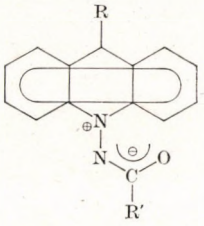


5

a: R = Ph, R′ = Me
b: R = Ph, R′ = Ph
c: R = H, R′ = Ph
d: R = Ph, R′ = OEt

* Heterocyclic ammonioamides are, in general, unstable and furnish 1,2,4,5-tetrazine-type dimers *(cf.* [3]), which are in equilibrium with the monomeric forms. Dimer formation appears unlikely in the case of **4** for steric reasons.



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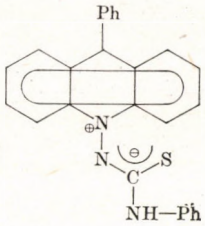

7

a: R = Ph, R′ = Me
b: R = Ph, R′ = Ph
c: R = H, R′ = Ph

Experimental

10-Amino-9-phenylacridinium mesitylenesulfonate (1a)

MSH (~ 4.7 g; 22 mmoles), dissolved in CH_2Cl_2 (30 ml), was poured into a solution of 9-phenylacridine (5.1 g; 20 mmoles) in CH_2Cl_2 (30 ml). Heat was evolved, and the mixture started to boil. After the vigorous reaction had subsided, the mixture was kept for 1 hr at room temperature and evaporated to dryness. The residue was dissolved in ethanol (30 ml), EtOAc (80 ml) was added, the insoluble impurities were removed by filtration, and ether (200 ml) was added to precipitate 5.0 g (55%) of the greenish yellow crystals of **1a**, m.p. 178—180°C (from EtOH–EtOAc–Et_2O).

$C_{19}H_{15}N_2 \cdot C_9H_{11}O_3S$ (470.58). Calcd. N 5.95; S 6.81. Found N 6.16; S 7.05%.

10-Aminoacridinium mesitylenesulfonate (1b)

An ethereal solution (140 ml) of MSH (~ 7.5 g; 35 mmoles) was rapidly mixed with an ethereal solution (100 ml) of acridine (5.4 g; 30 mmoles). The mixture immediately became greenish opaque and crystallization of the product started within a few minutes. The mixture was allowed to stand overnight to yield 8.9 g (75%) of **1b**, greenish yellow crystals, m.p. 233—234°C (from EtOH).

$C_{13}H_{11}N_2 \cdot C_9H_{11}O_3S$ (394.50). Calcd. N 7.10; S 8.13. Found N 7.54; S 8.02%.

10-Amino-9-phenylacridinium chloride (1c)

Methanolic suspensions of the pure pseudobases **2a** or **2b** (see below) were saturated with dry HCl gas. The resulting solutions were evaporated to dryness in vacuum and the residues triturated with ether to furnish **1c** in theoretical yield, m.p. 257—259°C (d.; from MeOH–Et_2O).

$C_{19}H_{15}ClN_2$ (306.79). Calcd. Cl 12.72; N 10.05. Found Cl 12.36, N 9.96%.

10-Amino-9-methoxy-9-phenyl-9,10-dihydroacridine (2a)

1*N* aqueous NaOH (8 ml) was added by drops to a methanolic (15 ml) solution of **1a** (2.35 g; 5.0 mmoles) to yield 1.4 g (93%) of a light-brown crystalline product which was filtered off and washed with water until neutral. M.p. 129°C (d.; from a large amount of MeOH).

$C_{20}H_{18}N_2O$ (302.38). Calcd. C 79.44; H 6.00; N 9.26. Found C 79.63; H 6.07; N 9.40%.

NMR ($CDCl_3$, TMS): δ 7.65—6.9 ppm (m, 13 H, Ar**H**); 3.98 ppm (s, 2H, NH_2); 2.95 ppm (s, 3H, OMe).

When heated to the b.p., a toluene or gasoline solution of **2a** turned violet; the colour disppeared, when the solutions were allowed to cool.

Thermal decomposition

A solution of **2a** (1.0 g; 3.3 mmoles) in PhCl (20 ml) was refluxed for 1.5 hr. The resulting *colourless* solution was evaporated to dryness in vacuum, and the residue was recrystallized from EtOH to yield 0.6 g (73%) of 9-phenylacridine which, by m.p., mixed m.p., IR spectra and TLC, proved identical with an authentic sample.

10-Amino-9-ethoxy-9-phenyl-9,10-dihydroacridine (2b)

This compound was obtained similarly to **2a**. The yield was 85%, m.p. 134°C (from EtOH).

$C_{21}H_{20}N_2O$ (316.41). Calcd. C 79.72; H 6.37; N 8.85. Found C 79.78; H 6.36; N 8.75%.

The colour reactions of **2b** were identical with those of the 9-methoxy analogue (**2a**).

NMR ($CDCl_3$, TMS): δ 7.6—6.75 ppm (m, 13 H, ArH); 3.85 ppm (s, 2 H, NH_2); 3.08 ppm (qu, 2 H) + 1.12 ppm (t, 3H, $J = 7$ Hz, OEt).

Reaction of 1a with aqueous alkali

An aqueous solution (50 ml) of **1a** (2.35 g) was treated with 5% aqueous NaOH (40 ml) to yield a violet amorphous precipitate (1.25 g) which was washed with water until neutral and filtered off. All attempts at purification of the product failed.

When the product was triturated with methanol at room temperature, the violet colour disappeared and cream-coloured crystals were obtained which, according to the IR spectra, m.p.'s and TLC, proved identical with authentic **2a**.

When the amorphous product was boiled up with nitromethane, the violet colour gradually disappeared and, after evaporation of the solvent and recrystallization of the residue from PhCl–light petroleum, pure **3** (IR, mixed m.p., TLC) was obtained.

When the amorphous product was boiled for a few minutes with PhCl, the violet colour gradually disappeared, and crystals of 9-phenylacridine (IR, mixed m.p., TLC) deposited on allowing the solution to cool.

10-Amino-9-nitromethyl-9-phenyl-9,10-dihydroacridine (3)

A mixture of **2a** (1.0 g; 3.3 mmoles) and nitromethane (15 ml) was refluxed for 1 hr. The hot solution turned initially violet and later green. The excess solvent was evaporated in vacuum and the residue recrystallized from PhCl–light petroleum to yield 0.95 g (90%) of **3**; green crystals, m.p. 160°C (d.).

$C_{20}H_{17}N_3O_2$ (331.36). Calcd. 72.49; H 5.06; N 12. 68. Found C 72.65; H 5.19; N 12.71%.

NMR ($CDCl_3$, TMS): δ 7.7—6.8 ppm (m, 13 H, ArH); 5.1 ppm (s, 2 H, CH_2); 3.95 ppm (s, 2 H, NH_2).

Partial conversion of **2a** into **3** took place even on recrystallization of **2a** from nitromethane.

10-Amino-9-phenyl-9,10-dihydroacridine

A methanolic solution (15 ml) of **1a** (2.35 g; 5.0 mmoles) was mixed with an aqueous solution (10 ml) of $NaBH_4$ (0.22 g; 6.0 mmoles). Gas was evolved, the solution became colourless, and the product started to precipitate. Crystallization was completed by the addition of water (80 ml) to yield 1.2 g (88%) of the reduction product, fine colourless crystals, m.p. 182—184°C (from EtOH).

$C_{19}H_{16}N_2$ (272.34). Calcd. C 83.79; H 5.92; N 10.92. Found C 83.52; H 5.98; N 10.85%.

NMR ($CDCl_3$, TMS): δ 7.45—6.75 ppm (m, 13 H, ArH); 5.2 ppm (s, 1 H, 9-H); 3.7 ppm (2 H, NH_2).

10-Acetylamino-9-phenylacridinium chloride (5a) and *N*-(9-phenyl-10-acridinio)-acetamidate (6a)

(a) A mixture of **1a** (4.7 g; 10 mmoles), NaOAc (1.0 g; 12 mmoles) and Ac_2O (10 ml) was stirred for 1 hr at 80°C. The solvent was distilled off and the residue triturated with water (50 ml). The insoluble yellow product was dried and taken up in methanol (15 ml), and dry HCl gas was introduced into the suspension until a clear solution resulted. The solvent was distilled off and the residue recrystallized from EtOH–ether to yield 2.1 g (59%) of **5a**, greenish yellow crystals, m.p. 285—288°C.

$C_{21}H_{17}ClN_2O$ (348.82). Calcd. $Cl^{\ominus}$ 10.17. Found $Cl^{\ominus}$ 10.35%.

IR (KBr): ν NH 3400—3300, $\nu C{=}O$ 1690 cm^{-1}.

NMR ($CDCl_3$, TMS): δ 8.7 ppm (d, $J = 9$ Hz, 2 H, 4-H + 5-H); 8.5—7.4 ppm (m, 11 H, other ArH's); 2.75 ppm (s, 3 H, Ac).

(b) A mixture of **1c** (2.0 g; 6.5 mmoles) and Ac_2O (6 ml) was boiled until a clear solution resulted transiently and, after about 2 min, the product started to crystallize. A thick crystalline paste was obtained when the mixture was allowed to cool. Ether was added and the product (2.25 g; 100%), m.p. 285—288°C, identical according to the IR spectra with the product obtained as described under *(a)*, was filtered off.

(c) An aqueous solution (50 ml) of **5a** (1.75 g; 5 mmoles) was treated with 1 *N* aqueous NaOH (10 ml), and the mixture was extracted with CH_2Cl_2 (50 ml) to yield, after conventional work-up and recrystallization from toluene, 1.24 g (73%) of **6a**, m.p. 222—224°C.

$C_{21}H_{16}N_2O$ (312.36). Calcd. C 80.74; H 5.24; N 8.97. Found C 80.51; H 5.24; N 8.90%.

IR (KBr): *no* νC=O band.

NMR ($CDCl_3$, TMS): δ 8.85 ppm (d, J = 9 Hz, 2 H, 4-H + 5-H); 8.2—7.35 ppm (m, other ArH's); 2.42 ppm (s, 3 H, Ac).

10-Benzoylamino-9-phenylacridinium chloride (5b) and *N*-(9-phenyl-10-acridinio)-benzamidate (6b)

(a) The pseudobase **2a** (0.3 g; 1 mmole) was shaken for 5 min with PhCOCl (2 ml), and the mixture was heated for 5 min at 130—140°C. A thick paste was obtained which, after being allowed to cool, was diluted with ether to yield 0.4 g (97%) of **5b**, greenish yellow crystals, m.p. 252°C (EtOH–ether).

$C_{26}H_{29}ClN_2O$ (410.88). Calcd. Cl 8.63; N 6.82. Found Cl 9.00, N 6.82%.

IR (KBr): νC=O 1675 cm^{-1}.

(b) A mixture of **1c** (0.3 g; 1.0 mmole) and PhCOCl (2 ml) was heated for 5 min at 140°C and worked up as described above to yield 0.4 g (97%) of **5b**, identical, according to the IR spectra, with the product obtained as described under *(a)*.

(c) A solution of **5b** (0.4 g; 9.7 mmoles) in a mixture of MeOH (2 ml) and water (5 ml) was treated with 1 *N* aqueous NaOH (2 ml) to yield 0.25 g (70%) of **6b**, orange coloured crystals, m.p. 248—250°C (from aqueous EtOH).

$C_{26}H_{18}N_2O$ (374.42). Calcd. C 83.40; H 4.85; N 7.48. Found C 83.48; H 4.96; N 7.37%.

IR (KBr): *no* νC=O band.

NMR ($CDCl_3$, TMS): δ 8.85 ppm (d, J = 9 Hz, 2 H, 4-H + 5-H); 8.65—8.45 ppm (m, 2 H, PhCO, *o*-protons); 8.2—7.45 ppm (m, 14 H, other ArH's).

Attempted ethoxycarbonylation of 2a

A mixture of **2a** (0.6 g; 2 mmoles) and ethyl chloroformate (5 ml) was heated for 1 hr at 110°C. The mixture remained heterogeneous throughout. It was allowed to cool, and the greenish yellow crystalline product (0.5 g; 82%) was filtered off and washed with ether. According to its m.p. (256—258°C) and IR spectrum it proved to be identical with an authentic sample (see above) of **1c**.

N-(10-Acridinio)-benzamidate (6c)

A mixture of **1b** (3.95 g; 10 mmoles) and PhCOCl (20 ml) was heated for 5 min at 170°C. Ether (80 ml) was added, after cooling, to the resulting dark solution to precipitate a gummy product. The supernatant was decanted and the residue triturated with two portions (30 ml, each) of ether and dissolved in MeOH (40 ml). The solution was made slightly alkaline (pH 9) with 10% aqueous NaOH. Water (120 ml) was added under ice-cooling to obtain 1.5 g (51%) of **6c**, orange coloured crystals, m.p. 273—275°C (d.; from aqueous MeOH).

$C_{20}H_{14}N_2O$ (298.23). Calcd. C 80.51; H 4.73; N 9.39. Found C 80.04; H 4.87; N 9.25%.

N-(9-Phenyl-10-acridinio)-*N*-phenylthiocarbamoylamide (7)

A solution of **2a** (1.5 g; 5.0 mmoles) in dioxane (20 ml) was treated with PhNCS (1.5 ml; 12 mmoles) for 20 min at 40—45°C. A red solution resulted from which the product soon started to crystallize. The mixture was allowed to stand overnight, and the product (1.7 g; 84%), red needles, m.p. 147°C (from nitromethane or 1-butanol) was filtered off.

$C_{26}H_{19}N_3S$ (405.50). Calcd. C 77.01; H 4.72; N 10.36. Found C 77.46; H 4.44; N 10.57%.

The spectra were obtained with the aid of a MOM (Hungarian Optical Works, Budapest) Type 2000 IR and a Perkin-Elmer Type R12 (60 MHz) NMR spectrometer, respectively.

*

Thanks of the authors are due to Mrs. I. Balogh-Batta and Dr. P. Kolonits and staffs for the microanalyses and spectra, respectively.

REFERENCES

[1] OZAWA, T., IITAKA, Y., HIROBE, M., OKAMOTO, T.: Chem. Pharm. Bull. Tokyo **22,** 2069 (1974)
[2] TAMURA, Y. *et al.*: Tetrahedron Letters **1972** (No. 40) 4133; Tetrahedron **29,** 2359 (1973); J. Org. Chem. **38,** 1239 (1973)
[3] HUISGEN, R., GRASHEY, R., KRISCHKE, R.: Tetrahedron Letters **1962,** 387

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ELECTRON DEFICIENT HETEROAROMATIC AMMONIOAMIDATES, VII*

THE SYNTHESIS AND SOME REACTIONS OF *N*-(2-PHTHALAZINIO)- AND *N*-(1,4-DIPHENYL-2-PHTHALAZINIO)-BENZAMIDATES

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The synthesis, thermo- and photolysis of the title compounds are described.

In continuation of our studies into the chemistry of electron deficient heteroaromatic ammonioamidates, we have synthesized *N*-(2-phthalazinio)--benzamidate (**4a**). Phthalazine was allowed to react with *O*-mesitylenesulfonylhydroxylamine [1] to give 2-aminophthalazinium mesitylenesulfonate (**1a**).** The sulfonate was transformed into the chloride (**1b**) by treatment with hydrochloric acid in hot ethanol. When heated with an excess of hot benzoyl chloride, **1b** gave 2-(benzoylamino)-phthalazinium chloride (**3a**). Alternatively, the latter product was prepared by treating the crude dimer **5a** of (2-phthalazinio)-amide **2a**) — obtained by alkaline treatment of either **1a** or **1b** — with benzoyl chloride. **3a** and **4a** were mutually interconverted by treatment with alkali and aqueous hydrochloric acid, respectively.

The benzamidate **4a** is thermally unstable: when subjected to vacuum sublimation it partly rearranges into 1-(benzoylamino)-phthalazine (**6**) [2], partly suffers elimination of benzoylnitrene to yield phthalazine, and partly decomposes to furnish a product of unknown structure. Attempted photolyses in de-aerated acetonitrile, ethanol and dichloromethane solutions gave untractable tarry mixtures of photodecomposition products.

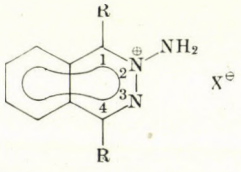
1,4-Diphenylphthalazine was obtained by the adaptation of the method of STAUNTON and TOPHAM [3]. 2,4-Diphenyl-1(2*H*)-phthalazinone (**7**) was treated with phenylmagnesium bromide, and the resulting 1,2,4-triphenyl--2-phthalazinium bromide (**8**) was transformed with the aid of hydrazine into the desired product. This method proved in our hands superior to those reported in the literature [4, 5]. Amination of 1,4-diphenylphthalazine was effected with *O*-mesitylenesulfonylhydroxylamine, and the resulting sulfonate (**1c**) was converted, *via* crude **5b** and **3b** into **4b**, similarly to the procedure described above for the non-phenylated series.

* Part VI: ÁGAI, B., LEMPERT, K., preceding paper.

** A by-product, $C_8H_6N_2$, probably 2-(iminomethylene)-benzonitrile was obtained in the form of its mesitylenesulfonate in this reaction.

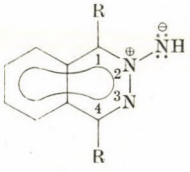
Thermolysis of **4b** furnished 1,4-diphenylphthalazine; the benzoylnitrene thereby eliminated rearranged partly into phenyl isocyanate, which was detected in the form of ethyl *N*-phenylcarbamate. Part of the isocyanate was hydrolyzed to aniline, and small amounts of benzonitrile were also detected among the volatile thermolysis products.

Photolyses of **4b** in de-aerated benzene, EtOH and dichloromethane furnished mixtures of tarry products which, in some cases, contained small amounts of diphenylphthalazine, according to TLC. Photolysis of **4b** in dichloromethane in the presence of oxygen furnished 40% of 1,2-dibenzoylbenzene; this behaviour parallels that of 1,4-diphenylphthalazine-*N*-oxide [5]. In addition, some benzoyl chloride, obviously formed by a free radical reaction with the solvent, was also obtained. The formation of 1,2-dibenzoylbenzene in the photolysis of **4b** does *not* take place *via* diphenylphthalazine, since the latter is stable towards UV irradiation even in the presence of oxygen.



1

a: R = H, X = 2,4,6-$Me_3C_6H_2SO_3$
b: R = H, X = Cl
c: R = Ph, X = 2,4,6-$Me_3C_6H_2SO_3$



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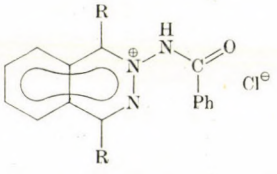

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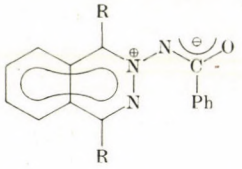
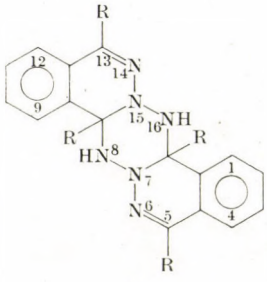


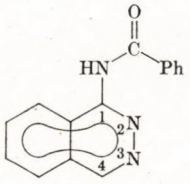
4

2–4, a: R = H. **b**: R = Ph



5

a R = H. **b**: R = Ph



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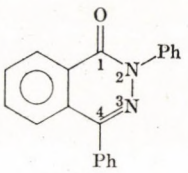

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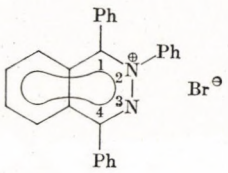

8

Experimental

2-Aminophthalazinium mesitylenesulfonate (1a)

An ethereal solution (250 ml) of *O*-mesitylenesulfonylhydroxylamine [1] (88 mmoles) was added at room temperature to a mixture of phthalazine (11 g; 85 mmoles), chloroform (30 ml) and ether (20 ml). The oily precipitate (20.1 g; 69%) turned rapidly crystalline on scratching, m.p. 95°C (from $CHCl_3$).

$C_{17}H_{19}N_3O_3S$. 1.5 H_2O (372.45). Calcd. N 11.28; S 8.61. Found N 11.38; S 8.50%.

The dry residue of the mother liquor of crude **1a** was taken up in acetone (10 ml) and allowed to stand at room temperature to yield 1.35 g of a colourless crystalline product, m.p. 183—184°C (from $CHCl_3$–light petroleum), which is probably identical with the mesitylenesulfonate of 2-(iminomethylene)-benzonitrile.

$C_{17}H_{18}N_2O_3S$ (330.34). Calcd. C 61.81; H 5.49; N 8.48. Found C 62.17; H 5.85; N 8.12%.

IR (KBr): $\nu C{\equiv}N$ 2160 cm^{-1}.

2-Aminophthalazinium chloride (1b)

(a) A mixture of **1a** (2.0 g; 5.8 mmoles), ethanol (15 ml) and 37% aqu. HCl (1.5 ml) was refluxed for 2 min to yield 0.6 g (57%) of **1b**, m.p. 208°C (d.; from EtOH) on cooling.

$C_8H_8ClN_3$ (181.62). Calcd. C 52.91; H 4.44; Cl 19.52; N 23.13. Found C 52.52; H 4.39; Cl 19.97; N 23.30%.

(b) A mixture of crude 8,8a,16,16a-tetrahidro-[1,2,4,5]-tetrazino[6,1-*a*; 3,4-*a*']diphthalazine (**5a**, see below) (3.1g; 10.7 mmoles), ethanol (20 ml) and 37% aqu. HCl (4 ml) was treated as described under *(a)* to yield 3.5 g (91%) of **1b**, m.p. 208—209°C (d.; from EtOH).

2-(Benzoylamino)-phthalazinium chloride (3a)

(a) A mixture of **1b** (2.5 g; 13.9 mmoles) and benzoyl chloride (5 ml; 43.5 mmoles) was heated for 20 min at 145—150°C (bath temperature). Evolution of HCl started at 90°C, and the mixture turned dark. The mixture was allowed to cool, and ether (30 ml) was added. The solvent was decanted from the gummy product which was triturated with another portion of ether (15 ml). The solvent was decanted and the residue refluxed for 5 min with EtOH (15 ml) whereby it gradually became crystalline on scratching. The mixture was allowed to cool, and crystallization of the product was completed by the addition of ether (50 ml) in portions. 3.40 g (86%) of **3a**, m.p. 213—214°C (d.; from EtOH) was obtained.

$C_{15}H_{12}ClN_3O$ (285.74). Calcd. Cl 12.41; N 14.70. Found Cl 12.96; N 15.07%.

IR (KBr): $\nu C{=}O$ 1680 cm^{-1}.

(b) A mixture of crude **5a** (see below) (0.5 g; 1.7 mmole) and PhCOCl (2 ml; 17 mmoles) was treated and worked up as described under *(a)* to yield 0.5 g (51%) of **3a**, m.p. 216°C (d.).

(c) A mixture of *N*-(2-phthalazinio)-benzamidate (**4a**, see below) (0.1 g; 0.4 mmole), ethanol (1 ml) and 37% aqu. HCl (0.2 ml) was boiled up. Crystallization of the product started on cooling and was completed by the addition of ether (1 vol). The yield of **3a**, m.p. 215°C (d.), was 0.1 g (87.6%).

8,8a,16,16a-Tetrahydro-[1,2,4,5]tetrazino[6,1-a; 3,4-a']diphthalazine (5a)

(a) 10% aqu. NaOH (10 ml; 2.8 mmoles) was added by drops under continuous stirring to a mixture of **1a** (8.0 g; 23.2 mmoles) and water (100 ml). A brown amorphous product precipitated gradually from the initially almost clear solution. The mixture was kept for 1/2 hr on a steam bath, and the product (2.7 g; 80%), m.p. 204°C (d.) was filtered off, after the mixture had been allowed to cool.

The product resisted all attempts at recrystallization.

(b) The chloride **1b** was similarly transformed into **5a**.

N-(2-Phthalazinio)-benzamidate (4a)

10% aqu. NaOH (5 ml; 14 mmoles) was added by drops to an aqueous solution (120 ml) of the chloride **3a** (3.0 g; 10.6 mmoles) to yield 1.85 (71%) of a crystalline product, m.p. 213—214°C (d.; from dioxane–light petroleum).

$C_{15}H_{11}N_3O$ (249.26). Calcd. C 72.27; H 4.45; N 16.86. Found C 71.95; H 4.45; N 17.19%.

IR (KBr): *no* νNH band.

NMR ($CDCl_3$, TMS): δ 9.55 ppm (m, 1 H, 1-H); $\sim$ 8.3 ppm (m, 3 H, 4-H + Ph, *o*-protons); $\sim$ 8.1 ppm (m, 4 H, 5-H–8 H); $\sim$ 7.5 ppm (3 H, Ph, *m*- and *p*-protons).

Vacuum sublimation

The benzamidate (**4a**) was sublimed at 1 torr at 180—250°C (bath temperature), and the sublimed product was examined by TLC (adsorbent: Kieselgel G; solvent: benzene-methanol, 5 : 1; detection: iodine vapour and aqu. K_2HgI_4 spray). As shown by comparison with authentic samples, the product consisted of a mixture of unchanged **4a**, phthalazine, 1-(benzoylamino)-phthalazine (**6**) and a compound of yet unknown structure.

An authentic sample of **6** was obtained as described in the literature [2].

1,4-Diphenylphthalazine

The Grignard reagent, obtained from bromobenzene (17 ml; 0.16 mole) and metallic Mg (4.0 g; 0.17 mole) in THF (60 ml), was added by drops, within 3 min, to a warm solution of 2,4-diphenyl-1(2*H*)-phthalazinone (**7**) [6]. A vigorous reaction took place. The resulting brown solution was refluxed for 9 hrs, allowed to stand overnight, and decomposed with saturated aqueous NH_4Cl solution (100 ml). The aqueous layer was extracted with 4 portions of THF (15 ml, each), and the combined THF solutions were worked up in the conventional manner to yield an oily product (**8**).

The latter was dissolved in a mixture of EtOH (50 ml) and 99% $N_2H_4 \cdot H_2O$ (15 ml), and the solution was gradually heated to its b.p. After the vigorous evolution of gas had ceased, the mixture was refluxed for 10 hrs and allowed to stand overnight to yield 10.6 g of diphenylphthalazine, m.p. and lit. m.p. [4, 5] 194°C, as the first crop. A less pure second crop (8.0 g, m.p. 189°C) was obtained by treating the dry residue of the mother liquor with benzene (40 ml) and light petroleum (20 ml). Total yield: 43.6%.

2-Amino-1,4-diphenylphthalazinium mesitylenesulfonate (1c)

An ethereal solution (60 ml) of *O*-mesitylenesulfonylhydroxylamine [1] ($\sim$38 mmoles) was added at room temperature to a solution of 1,4-diphenylphthalazine (8.4 g; 29.8 mmoles) in chloroform (100 ml). Heat was evolved. The mixture was kept overnight at room temperature, and about 2/3 of the solvent was evaporated. 2 Volumes of ether were added to precipitate 14.2 g (95.5%) of **1c**, m.p. 167°C, which was pure enough for use in the following experiments. A sample was purified for analysis by reprecipitating it from its $CHCl_3$ solution with light petroleum.

$C_{29}H_{27}N_3O_3S \cdot 2\ H_2O$ (533.71). Calcd. C 65.28; H 5.86; N 7.88. Found C 65.41; H 5.33; N 7.80%.

2-Benzoylamino-1,4-diphenylphthalazinium chloride (3b)

(a) An aqueous (90 ml) suspension of crude **1c** (8.0 g; 16 mmoles) was treated with the solution of NaOH (0.8 g; 20 mmoles) in water (10 ml) to yield a red precipitate of 4.5 g (94%) of the dimer **5b**, m.p. 135—138°C, which resisted all attempts at recrystallization.

(b) Benzoyl chloride (8 ml; 69 mmoles) was cautiously mixed with crude **5b** (5.7 g; 9.6 mmoles). Heat was evolved and a crystalline product was formed. The mixture was heated for 1 hr at 150°C (bath temperature). After being allowed to cool, the mixture was triturated with ether (20 ml), and the product was filtered off and thoroughly washed with ether to obtain 6.5 g (79.6%) of **3b**, m.p. 261°C (from EtOH).

$C_{27}H_{20}ClN_3O$ (437.93). Calcd. C 74.05; H 4.60; Cl 8.09; N 9.60. Found C 74.36; H 4.68; Cl 8.28; N 9.31%.

IR (KBr): $\nu C{=}O$ 1680 cm^{-1}.

N-(1,4-Diphenyl-2-phthalazinio)-benzamidate (4b)

A mixture of **3b** (0.5 g; 1.2 mmole), EtOH (5 ml), water (15 ml) and 10% aqueous NaOH (2 ml) was stirred for 15 min to yield 0.4 g (88%) of **4b**, m.p. 168—169°C (from 85% aqueous EtOH).

$C_{27}H_{19}N_3O \cdot H_2O$ (419.49). Calcd. C 77.31; H 5.05; N 10.02. Found C 77.28; H 5.38; N 9.64%.

IR (KBr): *no* $\nu C{=}O$ band.

Photolysis

A solution of **4b** (0.50 g; 1.3 mmole) in CH_2Cl_2 (400 ml) was irradiated through Pyrex for 48 hrs with a high pressure mercury immersion lamp (HPK 125, Philips) while a continuous stream of O_2 was introduced. The solvent was evaporated until crystallization started. Ether (4 ml) was added, and the product which, according to its IR spectrum, proved to be identical with 1,2-dibenzoylbenzene (0.15 g; 39.4%) was filtered off.

The filtrate of the product was strongly acidic (pH$\sim$1), and it contained benzoyl chloride (odour).

No 1,2-dibenzoylbenzene could be detected in the reaction mixture by TLC, when 1,4-diphenylphthalazine was irradiated for 30 hrs under the above conditions.

Thermolysis

(a) **4b** was kept for 1 hr at about 200°C (bath temperature). The residue was dissolved in EtOH and subjected to TLC under the conditions as described above for the vacuum sublimation products of **4a**. In addition to unchanged **4b**, only 1,4-diphenylphthalazine could be detected as the thermolysis product.

(b) In order to examine the volatile by-products, **4b** was kept successively between 180—200, 200—220 and 220—260°C (bath temperature), for 1 hr, each, and the volatile products were separately collected. The first fraction contained the water of crystallization of the starting **4b** in practically pure form. The second fraction was taken up in EtOH and subjected to TLC (conditions as above); it proved to be a mixture containing small amounts of ethyl *N*-phenylcarbamate. The third fraction was subjected to GLC analysis and was found to contain aniline and benzonitrile. The non-volatile residue was, according to TLC, a mixture of unchanged **4b**, 1,4-diphenylphthalazine and more degraded decomposition products of unknown structure.

*

IR spectra were taken by Miss M. Csirke, microanalyses were performed by Mrs. Zauer-Csüllög, and the GLC analysis was performed by Dr. S. Békássy.

REFERENCES

[1] Tamura, Y. *et al.:* Tetrahedron Letters **1972** (No. 40) 4133; Tetrahedron **29,** 2359 (1973); J. Org. Chem. **38,** 1239 (1973)
[2] Rodda, H. J.: J. Chem. Soc., **1956,** 3509
[3] Staunton, R. S., Topham, A.: J. Chem. Soc., **1953,** 1889
[4] Mustafa, A., Harhash, A. H., Saleh, A. A. Sh.: J. Am. Chem. Soc., **82,** 2735 (1960)
[5] Tomer, K. B. *et al.:* J. Am. Chem. Soc., **95,** 7402 (1973)
[6] Roser, W.: Ber., **18,** 805 (1885)

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ÜBER DIE SYNTHESE VON NEUEN ISOCHINOLINON-DERIVATEN MIT BIOLOGISCHER AKTIVITÄT

(KURZE MITTEILUNG)

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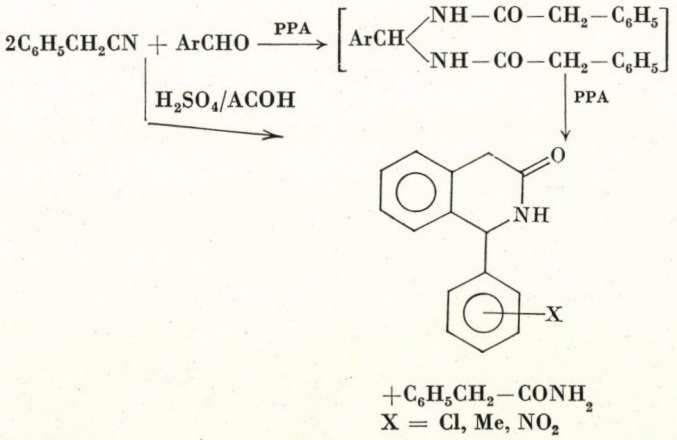
Bei der Untersuchung der zu 1-Aryl-1,4-dihydro-3(2*H*)-isochinolinonen führenden Kondensationsreaktion von aromatischen Aldehyden und Aralkylnitrilen wurde festgestellt, daß das Verfahren zur Synthese von 4-mono- oder dialkylsubstituierten Derivaten sowie im aromatischen Ring methoxy-substituierten Derivaten geeignet ist.

Beim Studium von Kondensationsreaktionen in nichtwäßrigen Medien, katalysiert durch Lewis- und Protonsäuren, wurde früher festgestellt [1], daß Phenylessigsäurenitril bzw. Phenylacetamid in polyphosphorsaurem Medium mit aromatischen Aldehyden in Reaktion tritt, wobei mit guter Ausbeute 1-Aryl-1,4-dihydro-3(2*H*)-isochinolinon gebildet wird. Auch wurde festgestellt [2], daß einige der durch uns synthetisierten Verbindungen eine bemerkenswerte biologische Aktivität besitzen, namentlich eine antikonvulsive Wirkung. Diese Beobachtung ist umsomehr interessant, als — aufgrund der biologischen Prüfungen — die genannten Isochinolinon-Derivate als eine neue Gruppe von Verbindungen mit antikonvulsiver Wirkung betrachtet werden können.

Im weiteren wurde festgestellt [3], daß diese Verbindungen auch aus den entsprechenden Aryliden-bis(säureamiden) hergestellt werden können. Aufgrund theoretischer Überlegungen nahmen wir an, daß in der Reaktion zwi-



schen Nitril bzw. Säureamid und Aldehyd als Zwischenstufe ebenfalls das bis-Amid gebildet wird, und daß das Endprodukt 1-Arylisochinolinon aus dessen Umwandlung entsteht.

Die Reaktion wurde ursprünglich nur mit Benzylcyanid durchgeführt. Bei der kinetischen Untersuchung der Reaktion [4] wurde auch die Reaktionsfähigkeit von Benzylcyaniden und Phenylacetamiden untersucht, die in der α-Stellung einen oder zwei Alkylsubstituenten enthalten. Für diese Untersuchungen wurden mehrere, in Stellung 4 substituierte Isochinolinon-Derivate

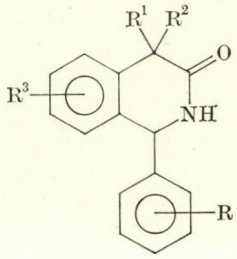


Tabelle I

Herstellung von 1-Aryl-1,4-dihydro-3(2H)

R	R^1	R^2	R^3	Verhältnis Nitril : Aldehyd	Reaktionszeit St.	Reaktionstemp. °C	Ausbeute, %	Schmp. Lsgm. der Umkrist.
4'-NO_2	Me	Me	H	1 : 1	1	120	72	191 EtOAc
4'-NO_2	Me	Me	7-Me	1 : 1	3	120	66	207 EtOH
3'-CF_3	Et	H	H	1 : 1	2	120	22	199 EtOH
4'-NO_2	iPr	H	H	2 : 1	5	120	33	203 C_6H_6
3'-Me	iPr	H	H	1 : 1	1	120	13	150 Benzin
4'-Cl	Me	Me	H	1 : 1	4	130	60	193 EtOH
3'-F	Me	Me	H	1 : 1	2	130	58	173 EtOH
H	$C_6H_5CH_2$	H	H	1 : 1	6	120	20	194 EtOAc
2',6'-diCl 3'-NO_2	H	H	H	2 : 1	3	120	92	278-80 Dioxan
2',6'-diCl	H	H	H	2 : 1	3	120	64	310 Dioxan

aus dem entsprechenden Nitril und Benzaldehyd hergestellt. Unter Berücksichtigung der Neigung des Benzyliden-bis(phenylacetamids) zur Cyklisation wurden diese Isochinolinon-Derivate auch aus den betreffenden bis-Amiden hergestellt [5]. Der Vergleich der direkten Reaktion aus Nitril und Aldehyd und jener aus bis-Amid sowie ihrer Ausbeuten scheint jedoch unsere frühere Annahme, wonach das bis-Amid ein Zwischenprodukt der aus Nitril und Aldehyd ausgehenden und zu Isochinolinon führenden Reaktion ist, nicht zu bestätigen. Es gelang uns nämlich, 4-Butyl-1-phenyl-1,4-dihydro-3(2*H*)-isochinolinon — wenn auch mit schlechter Ausbeute — aus dem entsprechenden Nitril und Aldehyd zu gewinnen, wogegen Benzyliden-bis(α-phenylcapronsäureamid) in Polyphosphorsäure ausschließlich zu Säureamid (und Aldehyd) zersetzt wird und keine Cyklisation erfolgt.

Bei den in der vorliegenden Arbeit beschriebenen Untersuchungen steckten wir uns das Ziel, die Ringschlußreaktion auf solche 1-Aryl-1,4-dihydro-3(2*H*)-isochinolinone auszudehnen, die in Stellung 4 mono- oder dialkylsubstituiert sind. Außerdem beabsichtigten wir, Methoxyderivate der Grundverbindung herzustellen. Außer dem Interesse in chemischer Hinsicht dachten

-isochinolinonen aus Nitril und Aldehyd

		Analyse					Bemerkung
$C_{17}H_{16}N_2O_3$	(296,33)	Ber.	C 68,91	H 5,44	N 9,45		Aus bis-Amid
		Gef.	C 68,94	H 5,68	N 9,56		77% [3]
$C_{18}H_{18}N_2O_3$	(310,35)	Ber.	C 69,65	H 5,85	N 9,03		
		Gef.	C 69,31	H 5,99	N 9,18		
$C_{18}H_{16}F_3NO$	(319,33)	Ber.	C 67,71	H 5,05	N 4,39		
		Gef.	C 67,88	H 4,98	N 4,13		
$C_{18}H_{18}N_2O_3$	(310,35)	Ber.	C 69,65	H 5,85	N 9,03		Aus bis-Amid
		Gef.	C 69,41	H 6,12	N 8,96		46% [3]
$C_{19}H_{19}NO$	(277,37)	Ber.	C 82,29	H 6,90	N 5,05		
		Gef.	C 82,39	H 7,15	N 5,03		
$C_{17}H_{16}ClNO$	(285,78)	Ber.	C 71,44	H 5,64	N 4,90	Cl 12,42	
		Gef.	C 71,35	H 5,69	N 5,09	Cl 12,40	
$C_{17}H_{16}FNO$	(269,32)	Ber.	C 75,79	H 5,99	N 5,20	F 7,05	
		Gef.	C 75,88	H 6,19	N 5,27	F 7,04	
$C_{22}H_{19}NO$	(313,40)	Ber.	C 84,31	H 6,11	N 4,46		
		Gef.	C 84,64	H 6,19	N 4,37		
$C_{15}H_{10}Cl_2N_2O_3$	(337,17)	Ber.			N 8,31		
		Gef.			N 8,50		
$C_{15}H_{11}Cl_2NO$	(292,17)	Ber.	C 61,66	H 3,80		Cl 24,27	
		Gef.	C 61,35	H 4,05		Cl 24,30	

wir dabei auch an die Möglichkeit der Synthese neuer, potentiell biologisch aktiver Verbindungen.

Die Daten der aus α-alkylierten Arylacetonitrilen und aromatischen Aldehyden erhaltenen Produkte sind in Tab. I zusammengefaßt.

Aus der Tabelle ist ersichtlich, daß die entsprechenden Isochinolinon-Derivate aus den in α-Stellung methylierten oder dimethylierten Nitrilen mit einer Ausbeute von 60—70% erhalten wurden. Ein Vergleich mit den Ausbeuten der analogen, jedoch in Stellung 4 unsubstituierten Verbindungen [1] zeigt keinen wesentlichen Unterschied. Eine wesentliche Verringerung der Ausbeute tritt jedoch ein, wenn die Nitrilkomponente in α-Stellung eine Äthyl- oder Isopropylgruppe enthält. Interessanterweise ist die Ausbeute auch bei der benzylsubstituierten Verbindung ähnlich schlecht.

Vor allem aus pharmakologischen Überlegungen heraus (zwecks Steigerung der Lipidlöslichkeit) wünschten wir Derivate mit Chlor in den Stellungen 2' und 6' herzustellen. Dabei war auch interessant, ob die beiden Substituenten in *ortho*-Stellung die Reaktion nicht hindern, da früher bereits festgestellt wurde [3], daß das 2'-Nitroderivat auf diesem Weg nicht hergestellt werden kann. Wie aus Tab. I ersichtlich ist, trat weder beim 2,6-Dichlor-, noch beim 2,6-Dichlor-3-nitrobenzaldehyd eine beobachtbare sterische Wirkung auf. Die

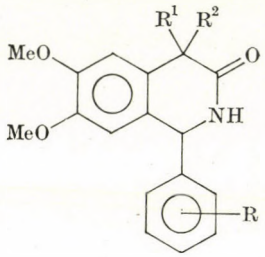


Tabelle II

Herstellung von 1-Aryl-1,4-dihydro-6,7-dimethoxy-3(2H)-isochinolinonen

R	R¹	R²	Verhältnis Nitril : Aldehyd	Reaktionszeit Temp. St.	°C	Ausbeute, %	Schmp. Lsgm. der Umkrist.
H	H	H	2 : 1	1	120	75	205 EtOH
3',4'-diOMe	H	H	2 : 1	1	120	75	180—82 C_6H_6
4'-NO_2	H	H	2 : 1	2	120	49	198—200 EtOH
H	Pr	H	1 : 1	2	120	29	189 EtOH

Klärung der Frage, ob 2-Nitrobenzaldehyd aus sterischen Gründen nicht mit Benzylcyanid in PPA reagiert, oder ob es vielleicht unter den Reaktionsbedingungen zersetzt wird, erfordert weitere Versuche.

Die bedeutende Wirkung von Methoxygruppen in Stellung 6 und 7 am Isochinolin-Gerüst auf die biologische Aktivität der Verbindung (z. B. Papaverin) brachte uns auf den Gedanken, ähnliche Derivate der Isochinolinone herzustellen. Die Ergebnisse sind in Tab. II zusammengefaßt.

Aus der Tabelle ist ersichtlich, daß die Gegenwart der Methoxygruppen das aus früheren Versuchen [5] sich ergebende Bild im wesentlichen nicht verändert: das in Stellung 4 eine längere Alkylgruppe (Propyl) enthaltende Produkt konnte nur mit schlechter Ausbeute hergestellt werden. Um die in der Tabelle angeführten Ausbeuten zu erreichen, mußte unser allgemeines Syntheseverfahren etwas modifiziert werden. PPA wurde auf 90 °C erhitzt, das Nitril zugegeben und das Gemisch weitere 5 Minuten lang bei 90 °C gehalten. Der Aldehyd wurde dann nicht auf einmal, sondern in drei Portionen, im Laufe von 30 Minuten zugegeben. Anschließend wurde während der in der Tabelle angeführten Reaktionszeit bei 120 °C gerührt und das Reaktionsgemisch aufgearbeitet. Bei der Reproduktion des bereits früher beschriebenen 6,7-Dimethoxyderivats wurde beobachtet, daß die Temperatur während des Rührens bei 120 °C spontan bis 150 °C anstieg. Durch Verhinderung dieses Temperaturanstiegs mittels Temperaturregelung konnten die Ausbeute sowie der Schmelzpunkt des Produkts erhöht werden.

1-Aryl-1,4-dihydro-3(2H)-isochinolinone

50 g Polyphosphorsäure 1 : 1 [1] wurde unter Rühren auf 90 °C erhitzt, 50 mmol Nitril zugegeben und das Gemisch 5 Minuten lang bei 90 °C gehalten. Danach wurde der Aldehyd im Verhältnis gemäß Tab. I bzw. II zugegeben, die Temperatur bis 120 °C erhöht, und es wurde während der in den Tabellen angeführten Reaktionszeit gerührt. Die viskose

aus aromatischen Aldehyden und 3,4-Dimethoxyphenylcarbonitrilen

	Analyse					Bemerkung
						Lit. Schmp. 198 °C Ausbeute 50% [1]
$C_{19}H_{21}NO_5$	(343,39)	Ber.	C 66,46	H 6,16	N 4,08	
		Gef.	C 66,39	H 6,32	N 4,01	
$C_{17}H_{16}N_2O_5$	(328,33)	Ber.	C 62,20	H 4,91	N 8,53	
		Gef.	C 62,19	H 5,53	N 8,52	
$C_{20}H_{22}NO_3$	(324,40)	Ber.	C 73,82	H 7,13	N 4,30	
		Gef.	C 73,69	H 7,25	N 4,28	

heiße Lösung wurde in Wasser gegossen, mit konz. NH_4OH alkalisch gemacht und wenn nötig das gummiartige Produkt zerrieben, bis es zu Pulver zerfiel. Danach wurde filtriert, mit Wasser neutral gewaschen, getrocknet und aus dem in den Tabellen angeführten Lösungsmittel umkristallisiert.

*

Herrn István NAGY sei an dieser Stelle für seine wertvolle technische Mitarbeit gedankt.

LITERATUR

[1] CSŰRÖS, Z., DEÁK, GY., HOFFMANN, I., TÖRÖK-KALMÁR, A.: Acta Chim. Acad. Sci. Hung., **60,** 177 (1969)
[2] Ungarisches Patent No. 5372; C. A. **78,** 159458 (1972)
[3] DEÁK, GY., GÁLL-ISTÓK, K., HAZAI, L., STERK, L.: Synthesis, **1975,** 393
[4] DEÁK, GY., GÁLL-ISTÓK, K., KÁLMÁN, ZS., HASKO-BREUER, J.: Acta Chim. (Budapest), **76,** 299 (1973)
[5] DEÁK, GY., GÁLL-ISTÓK, K., HAZAI, L.: Acta Chim. (Budapest), **84,** 477 (1975)

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REDUCTION OF DICARBOXYLIC ACID ESTERS WITH DIISOBUTYLALUMINIUM HYDRIDE

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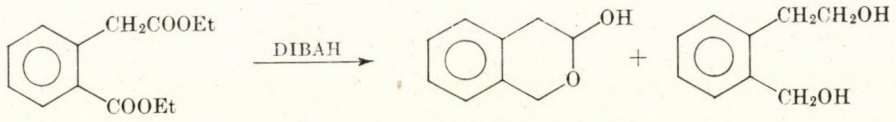
Reduction of diethyl homophthalate, diethyl phthalate, diethyl *cis*-1,2-cyclohexanedicarboxylate and diethyl glutarate with 1—4 equivalents of diisobutylaluminium hydride is reported. The crude reduction products were analyzed by gas chromatography. Reduction of diethyl homophthalate and diethyl phthalate with 3 equivalents of diisobutylaluminium hydride led to selective lactol formation.

Recently we have reported [1] a selective reduction of diethyl homophthalate to 3-hydroxyisochromane with 3 equivalents of diisobutylaluminium hydride (DIBAH). We have now extended this study to the reduction of dicarboxylic acid esters with 1–4 equivalents of DIBAH.

The dicarboxylic acid esters were treated in toluene, at low temperature, with 1–4 equivalents of DIBAH. After hydrolysis and concentration, the crude reduction products were analyzed by gas chromatography.

Reduction of diethyl homophthalate (**I**) with 1 or 2 equivalents of DIBAH led to 3-hydroxyisochromane (**II**) in a low yield. Homophthalic ester-aldehyde or dialdehyde were absent. Reaction with 3 equivalents of DIBAH afforded 100% of 3-hydroxyisochromane (**II**), as shown by GLC.



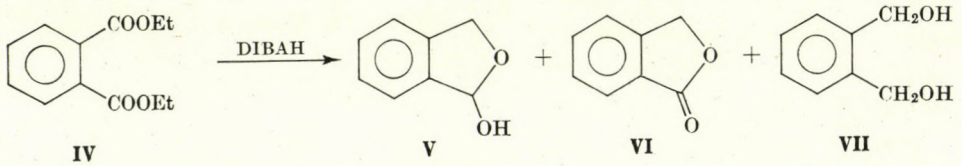
I **II** **III**

Table I

Product	DIBAH			
	1 eq. %	2 eq. %	3 eq. %	4 eq. %
Diethyl homophthalate (**I**)	87.5	53.4	—	—
3-Hydroxyisochromane (**II**)	10.7	42.5	100	33.0
Homophthalic alcohol (**III**)	—	—	—	67.0
Other (unidentified)	3.6	4.1	—	—

3-Hydroxyisochromane was, however, slowly reduced to homophthalic alcohol (**III**) under our conditions when **I** was treated with 4 equivalents of DIBAH (see Table I).

Similar treatment of diethyl phthalate with 1–4 equivalents of DIBAH led to analogous results. The only difference was that the reduction of diethyl phthalate also afforded phthalide (**VI**) as a by-product (Table II).



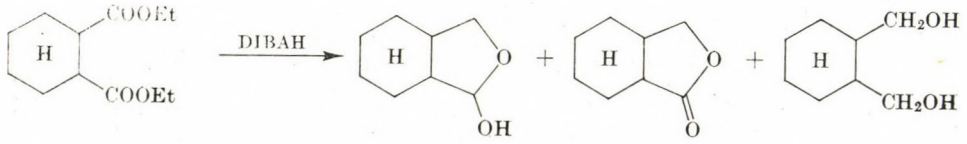
IV **V** **VI** **VII**

Table II

Product	DIBAH			
	1 eq. %	2 eq. %	3 eq. %	4 eq. %
Diethyl phthalate (**IV**)	92.0	68.0	—	—
Phthalide (**VI**)	—	2.5	17.0	11.5
Lactol (**V**)	8.0	29.5	82.0	20.0
Phthalalcohol (**VII**)	—	—	—	63.5
Other (unidentified)	—	—	1.0	5.0

Reduction of diethyl phthalate with three equivalents of DIBAH was less selective for lactol formation than the reduction of diethyl homophthalate. 1-Hydroxy-1,3-dihydroisobenzofuran (**V**) was identified by GLC comparison with an authentic sample prepared by the reduction of phthalide with one equivalent of DIBAH.

A similar series of reduction of diethyl *cis*-1,2-cyclohexanedicarboxylate (**VIII**) with 1–4 equivalents of DIBAH did not lead to selective lactol formation. The GLC data are listed in Table III.



VIII **IX** **X** **XI**

1-Hydroxy-perhydroisobenzofuran (**IX**) and *cis*-1,2-hydroxymethylcyclohexanecarboxylic acid lactone (**X**) were separated by chromatography on silica gel using chloroform as eluant. The spectrum of the lactol **IX** had strong infrared absorption bands at 3450 cm^{-1} (OH), 1130, 1050 cm^{-1} (C—O—C),

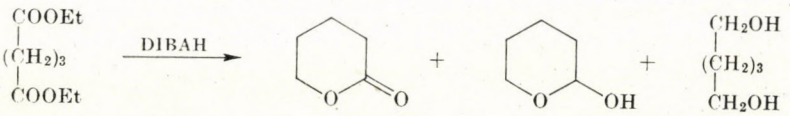
Table III

Product	DIBAH			
	1 eq. %	2 eq. %	3 eq. %	4 eq. %
Diethyl *cis*-1,2-cyclohexanedicarboxylate (**VIII**)	70.7	32.3	—	—
1-Hydroxy-perhydroisobenzofuran (**IX**)	18.0	33.5	38.0	12.9
Cis-1,2-hydroxymethylcyclohexanecarboxylic acid lactone (**X**)	8.8	19.1	20.0	6.9
Cis-1,2-bis(-hydroxymethyl)-cyclohexane (**XI**)	—	—	35.2	66.5
Other (unidentified)	1.6	3.5	6.8	3.0
	0.9	11.5	—	—
	—	—	—	10.7

and the lactone **X** had 1785 cm^{-1} (C=O). JONES oxidation [2] of 1-hydroxy-perhydroisobenzofuran (**IX**) gave the lactone **X** as shown by GLC.

Examination of the reduction of diethyl glutarate was carried out similarly. The yields obtained were low (10–20% of crude material) and the reduction did not show selectivity for lactol formation.

Reduction with 1 equivalent of DIBAH afforded 2-hydroxytetrahydropyran (**XIV**), valerolactone (**XIII**) and a large amount of unidentified product. Diethyl glutarate is the unique example of diesters examined which gave the totally reduced product, *i.e.* 1,5-pentanediol (**XV**), in a few per cent yield, on treatment with no more than 2 equivalents of DIBAH. Application of 4 equivalents of DIBAH led mainly to 1,5-pentanediol.



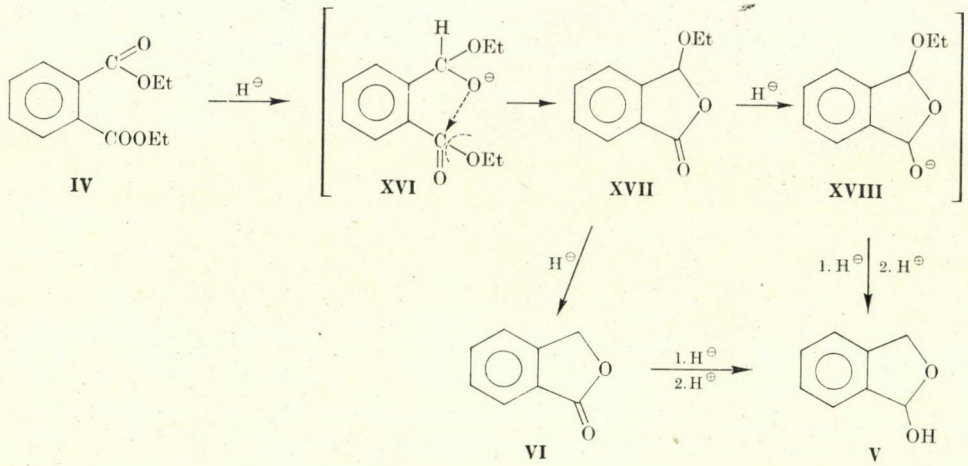
XII **XIII** **XIV** **XV**

2-Hydroxytetrahydropyran (**XIV**) was identified by comparison with an authentic sample prepared from 3,4-dihydro-2*H*-pyran by acid hydrolysis [3].

The GLC data are not listed, because they are not sufficiently informative in consequence of the low yields.

The results reported show that selective lactol formation has occurred only in the case of aromatic dicarboxylic acid esters (phthalate and homophthalate).

The selective formation of lactols may be reasonably explained by the mechanism shown below.



Since phthalic ester-aldehyde and dialdehyde were absent from the reaction products, it can be suggested that ring closure had taken place yielding the intermediate **XVII**. Lactol **V** could have arisen from intermediate **XVIII** or from phthalide (**VI**). As diethyl phthalate could also be detected besides **V** and **VI**, the intermediates **XVII** and **XVIII** should be more sensitive against the $H^{\ominus}$ attack than the starting material. The main reaction pathway seems to be **XVII** → **XVIII** → **V**, because the reduction of diethyl phthalate with 1 or 2 equivalents of DIBAH gave phthalide only in traces.

Experimental

Reduction of dicarboxylic acid esters with DIBAH

To a stirred solution of 0.05 mole of dicarboxylic acid diethyl ester in 100 ml of dry toluene there was added slowly 0.05—0.2 mole (1—4 equivalents) of diisobutylaluminium hydride in dry toluene (1 : 1) at −60°C, during 20—60 min. The reaction mixture was stirred for an additional hour at −60°C and then allowed to warm up to −10°C. At this temperature 200 ml of saturated sodium potassium tartrate solution was added; the organic layer was then separated and concentrated. The crude reduction products were analyzed on a Chrom III type gas chromatograph (80 cm × 5 mm Apieson M column at 205°C).

REFERENCES

[1] Kraiss, G., Povárny, M., Scheiber, P., Nádor, K.: Tetrahedron Letters **1973,** 2359
[2] Fieser, L. F., Fieser, M.: Reagents for Organic Synthesis, Vol. 1 p. 142 John Wiley and Sons, New York 1967
[3] Schniepp, L. E., Geller, H. H.: J. Am. Chem. Soc., **68,** 1646 (1946)

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DEVELOPMENT OF THE PETROLEUM REFINING TECHNOLOGIES

IN GRAPH THEORETICAL REPRESENTATION, II* MANUFACTURE OF OTTO ENGINE FUEL

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The quantitative indexes of the graphs representing the individual variants of Otto engine fuel manufacturing processes (thermal and catalytic cracking, reforming, synthetic processes), *i.e.* the graph elements, the path lengths, the number of cycles, plotted as a function of the time of introduction, show similarly to distillation an increasing trend, approaching a maximum. The change in octane number of the fuels produced has an identical trend.

Development of the manufacture of Otto engine fuel

It became clear early in automobile age, beginning at the turn of the century, that the exponentially growing number of cars would create fuel demands, that cannot be met either quantitatively or qualitatively by the production of gasoline obtained by the distillation of crude petroleum.**

Experiments started already in the second decade of our century on the production of motor fuel by the *chemical conversion* of the heavier fractions of petroleum. As a result of the experiments, new, advanced technologies have been introduced in the refineries, approaching the desired quality requirements.

In the following Otto engine fuel technologies — characteristic of the development — will be presented up to the 1950's (Figs 1—11). The curves of development shown in Figs 12, 13 and 14, are based on counting the graph elements. The figures were arranged in chronological order according to the year of realization of the individual technologies and the number of graph elements was plotted as a function of the years.

1. Cracking

It has been recognized early in the petroleum refining industry, based on directly fired distillation, that upon heating the residue after topping the light fractions, a light fraction can be obtained again. This operation became

* Part I of the series (Distillation) see: Acta Chimica (Budapest) Tomus 72, pp. 77—91 (1972), contains the definitions of symbols used here

** In 1911, the demand for gasoline in the USA exceeded that for kerosene. ([10] p. 99.)

general practice, particularly to increase the yield of kerosene. The essence of the phenomenon, the cracking of the molecules, was recognized already in 1855 by SILLIMAN, and proved experimentally by BERTHELOT in 1867 [10]. Refineries of the last century were cracking depending on the market situation (demand for kerosene). The apparatus is essentially the old: direct-fired still pot and condenser ([10] p. 390). The processes aimed at producing of gasoline were based on the principle of cracking.

1.1 Thermal cracking

The first gasoline producing process used industrially has been developed by BURTON *et al.*, and was protected by several patents. It was not the crude oil, but gas oil, or the fraction between light and heavy fuel oil that was cracked under pressure. Thermal cracking was carried out in a directly fired still. The first plant of this kind was built in 1912 by Standard Oil Co. of Indiana ([12] p. 136). The graph of the process is shown in Fig. 1. The graph is uniflow, open.

The main drawback of BURTON's process, besides being discontinuous, is overheating at the walls of the still, which could not be eliminated by the innovations introduced. Therefore, experiments were conducted to replace the pot by pipe cracking, following the example of pipe stills. Patents were filed for several processes of this kind, and some of these were actually realized (Holes-Hanley, Cross, Dubbs). Out of these, DUBBS' process will be shown here, which, after several modifications, is still in use today. An advantageous characteristic is of the "clean recirculation": the heavier part of the cracked-product is recycled for thermal cracking. The first plant of this kind was built in the USA in 1920—21 ([3] p. 219). Figure 2 shows the graph of the initial realization of a plant of this system. The base stock is fed into the dephlegmator, where it is mixed with the condensate from the crack vapours. The mixture

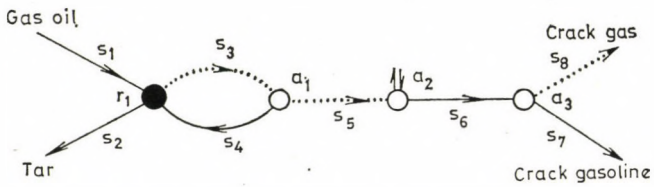

Fig. 1. Burton's thermal cracking process. USA. 1912
(According to Williamson—Doun: American Petroleum Industry. II. Fig. 4-4)
Theoretical graph. *Reactor:* r_1 cracking still. *Allactors:* a_1 dephlegmator, a_2 cooler, a_3 separator. *Conduits:* s_1 gas oil, s_2 tar, s_3 crack vapour, s_4 reflux, s_5 gasoline vapour, s_6 gasoline, s_7 crack gasoline, s_8 crack gas
Type of graph: uniflow, open
Number of graph elements: 12

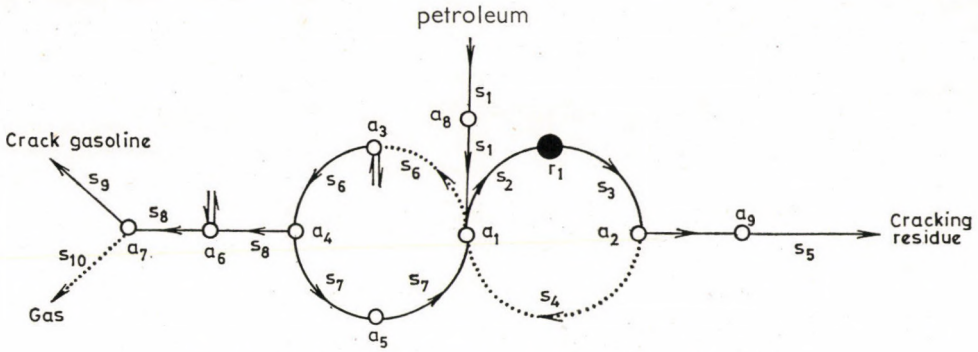

Fig. 2. Cracking plant, system Dubbs, USA. 1920—1921
(According to Bell: American Petroleum Refining, Fig. XIII. 9)
Theoretical graph. *Reactor:* r_1 pipe-still. *Allactors:* a_1 dephlegmator, a_2 expansion chamber, a_3 condenser, a_4 reflux collector, a_5 reflux pump, a_6 cooler, a_7 separator, a_8, a_9 pumps. *Conduits:* s_1 crude petroleum, s_2 substance for cracking, s_3 cracked substance, s_4 crack product, s_5 crack residue, s_6 dephlegmator head product, s_7 reflux, s_8 crack product, s_9 crack gasoline, s_{10} crack gas
Type of graph: uniflow cyclic (cumulated)
Number of graph elements: 24

is cracked in a pipe still under a pressure of 15—20 atm. The cracking residue, separating from the cracked substance in the expansion chamber, is lead away, while the vapours are directed to the dephlegmator. The head product of the dephlegmator is condensed. One part of the condensate is the reflux, and its main part is the crack product, from which the non-condensing gas is separated in a separator. The graph is cyclic, cumulated.*

The Dubbs process has been further developed. A process of this type is the system of *Universal Oil Products*, which differs from the above in that the substance to be cracked, together with a recirculated part of the cracked substance, are separated in the fractionating column into light and heavy distillates, and these are cracked in separate pipe stills at temperatures depending on the nature of the substance. The process was bought and applied in 1930 by several companies. Its graph is shown in Fig. 3. The graph is cyclic and consists of the cumulated connection of two cycles.

To achieve maximum gasoline yield, wherever possible, a second fractionating tower and a third furnace are inserted in Dubbs-type ([1] p. 265).

* Recent investigations show that there are certain frequently occurring types among the so-called 'cocurrent cyclic' graphs. These are:

1. cumulated cyclic graphs, in which the cyclic processes are connected with each other at a common angle point (see Figs 2 and 6);
2. conjugated graphs, in which the angle points of a wrapping circle are connected by internal cycles;
3. isolated cyclic systems, where the constituent cyclic processes are connected by directed edges between the angle points (see Figs 4 and 9).

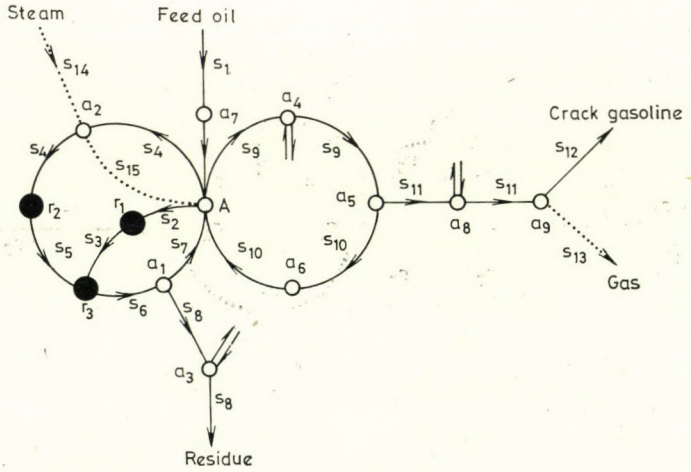

Fig. 3. Variant of system Dubbs by Universal Oil Comp. 1930
(According to H. Ruf: Kleine Technologie des Erdöls. Fig. 110)
Theoretical graph. *Reactors:* r_1 heavy oil furnace, r_2 light oil furnace, r_3 reaction chamber. *Allactors:* A fractionation column, a_1 flash chamber, a_2 stripping column, a_3, a_4 coolers, a_5 reflux receiver, a_6, a_7 pumps, a_8 cooler, a_9 separator. *Conduits:* s_1 feed oil, s_2 heavy oil, s_3 cracked heavy oil, s_4 light oil, s_5 cracked light oil, s_6 cracked substance, s_7 crack vapour, s_8 crack residue, s_9 head product of fractionation column, s_{10} reflux, s_{11} crack product, s_{12} crack gasoline, s_{13} crack gas, s_{14} steam, s_{15} recirculated fraction
Type of graph: cyclic, cumulated
Number of graph elements: 33

The graph of such a plant is shown in Fig. 4. Cracking is conducted to coke. The graph is cyclic, with two isolated cycles.

In the processes described, the cracking of oil is carried out in a so-called mixed phase (liquid and vapour phase). At the end of the 1920's vapour phase cracking processes were introduced. The feed is kerosene or gas oil, and thermal cracking is performed at high temperatures and low pressures. The Gyro, de Florenz and Pratt processes belong into this group. Gasoline manufactured by these processes has good antiknock characteristics, but owing to its high degree of unsaturation, it has a tendency to polymerization. Vapour phase cracking became an important intermediate operation of petrolchemistry (pyrolysis), but it was short-lived in the production of gasoline, and was replaced in the 1930's by catalytic processes ([3] p. 222).

1.2. Catalytic cracking processes

The petroleum refining industry of the USA increased its gasoline output more than 4 times and the output of cracked gasoline more than 9 times from 1919 to 1929 ([12] p. 395). In 1936 the output of cracked gasoline already exceeded the production of straight-run gasoline ([10] p. 191). The reason for

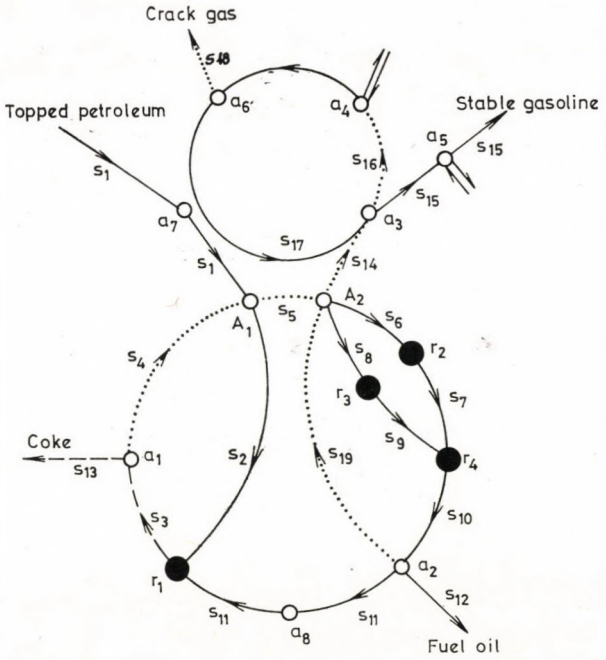

Fig. 4. Cracking plant system Dubbs with coke. USA. About 1940
(According to Winnacker—Küchler: Chemische Technologie. Vol. I. Fig. III-36)
Theoretical graph. *Reactors:* r_1 coke furnace, r_2 light oil cracking furnace, r_3 heavy oil cracking furnace, r_4 reactor chamber. *Allactors:* A_1, A_2 fractionation column, a_1 coke separator, a_2 stripper, a_3 stabilizer column, a_4 condenzer, a_5 cooler, a_6 separator, a_7, a_8 pumps. *Conduits:* s_1 toped petroleum, s_2 heavy oil reflux, s_3 coking product, s_4 crack vapour, s_5 head product of A_1, s_6 light oil, s_7 cracked light oil, s_8 heavy oil, s_9 cracked heavy oil, s_{10} cracked mixture, s_{11} heavy oil reflux, s_{12} fuel oil, s_{13} coke, s_{14} head product of A_2, s_{15} stable gasoline, s_{16} gasoline vapour, s_{17} reflux, s_{18} crack gas, s_{19} crack vapour
Type of graph: uniflow, cyclic
Number of graph elements: 37

the increase in cracked gasoline production is, in addition to the higher gasoline yield, the higher octane number. Catalytic processes have steadily gained ground. In the USA, the 1960 production of thermal cracking plants was 2.2 million bbl/day, while that of the catalytic plants 4.6 million bbl/day ([4] p. 195).

Though the effect of catalysts in thermal cracking has been known for decades, the development of a suitable catalyst and technology required the research work of several years.

The first process that proved to be satisfactory on industrial scale was developed by HOUDRY, and the first plant of this kind was started up in 1937 in the Paulsboro refinery of the *Sun Oil Co.* The process was operated with a fixed-bed, granular catalyst. Naphta, kerosene or gas oil were used as starting materials. The graph of the process is shown in Fig. 5. After heating in a pipe still, tar is separated from the vapours evolved, which are then

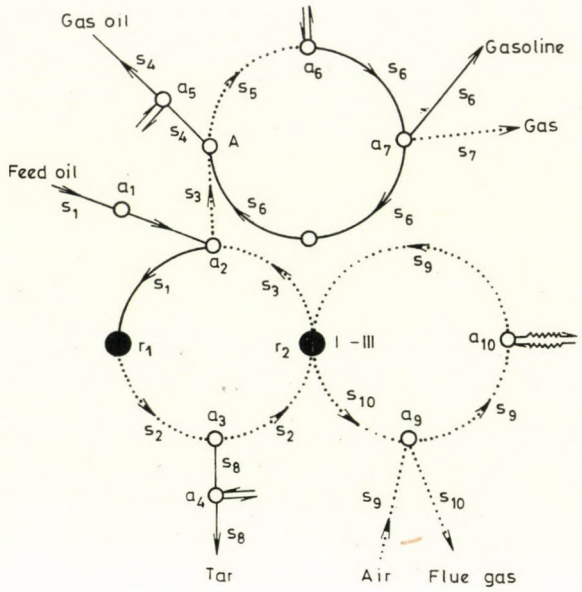

Fig. 5. Catalytic cracking Houdry's fixed bed process. Sun Oil Co. Paulsboro. 1937
(According to Nelson: Petroleum Refinery Engineering. Fig. 245)
Theoretical graph. *Reactors:* r_1 furnace, r_2 converters (I, II, III). *Allactors:* a_1 pump, a_2 heat exchanger, a_3 tar separator, a_4 tar cooler, a_5 gas oil cooler, a_6 gasolin cooler, a_7 separator, a_8 reflux pump, a_9 turbocompressor, a_{10} air heater, A fractionation column. *Conduits:* s_1 feed oil, s_2 feed oil vapour, s_3 cracked vapour, s_4 gas oil, s_5 crack gasoline vapour, s_6 crack gasoline, s_7 crack gas, s_8 tar, s_9 air, s_{10} flue gas
Type of graph: uniflow, cyclic (isolated and cumulated)
Number of graph elements: 42

introduced into one of the three reaction chambers filled with grained catalyst, for the cracking. After a certain period the reaction stops, owing to coke-formation, and the next chamber is switched on. The catalyst in the chamber switched off is regenerated: coke is burned off with hot air, and the chamber is blown out with steam. The cracked substance passes into the fractionating tower, the bottom product of which is cracked gas oil, and the head product cracked gasoline. The graph is cyclic, it consists of three cumulated and isolated cycles.

The equipment of the HOUDRY plant is complicated, the path of the gas is directed by programmed automatic control valves. The fixed-bed processes are increasingly replaced by moving-bed processes, where thermal cracking and regeneration of the catalyst are carried out in separate zones. The catalyst circulates in the system, the process is continuous. There are two kinds of moving-bed processes. In one of them, granulated catalyst is used, the moving of which was solved first mechanically, and later pneumatically. This principle was realized by the *Socony Vacuum Co.* in the so-called "*Thermophor Catalytic*

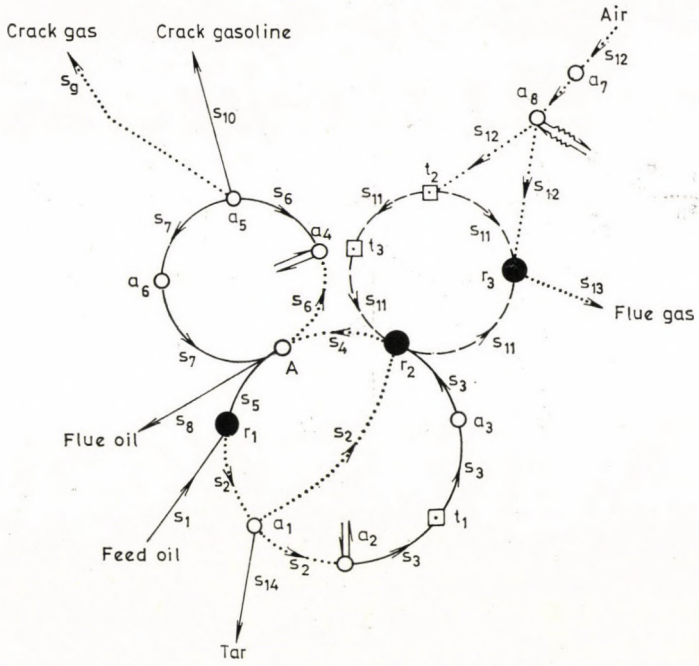

Fig. 6. Termophor catalytic cracking mowing bed process (T.C.C.) Socono Vacuum Comp USA. 1943

(According to Winnacker—Küchler: Chemische Technologie. Vol. I. Fig. III-42)
Theoretical graph. *Reactors:* r_1 pipe still, r_2 reactor, r_3 regenerator. *Allactors:* A fractionation tower, a_1 tar separator, a_2 condenser, a_3 pump, a_4 condenser, a_5 separator, a_6 reflux pump, a_7 compressor, a_8 air heater. *Conduits:* s_1 feed oil, s_2 feed oil vapour, s_3 cracked substance liquid, s_4 cracked substance gas, s_5 circulating oil, s_6 head product of tower A, a_7 reflux, s_8 fuel oil, s_9 crack gas, s_{10} crack gasoline, s_{11} catalyst, s_{12} air, s_{13} flue gas, s_{14} tar. *Storage:* t_1 condensate collector, t_2 transfer tank, t_3 catalyst tank
Type of graph: uniflow, cyclic (cumulated)
Number of graph elements: 41

Cracking" (T.C.C. Airlift) process in 1943. The graph of the process is shown in Fig. 6. The feed gas is oil or heavy oil, which is heated in a pipe still to 400—450°C. The non-evaporating part is separated. The vapour is introduced into the reactor, in which cracking takes place. In the lower part of the reactor, oil is blown off with steam from the catalyst, and passes into the fractionating tower for the separation of the products. The head product of the column is cracked distillate and gas. The catalyst, free of oil, drops from the reactor into the regeneration zone, where coke is burned off with air. The regenerated catalyst is raised pneumatically into the container above the reactor, from where it passes into the reactor. The graph is cyclic, and is composed of three cumulated cycles.

The second group of moving bed processes uses a vortex bed with fluidized catalyst. A process of this kind was realized in 1941 by *Kellog Corp.* in

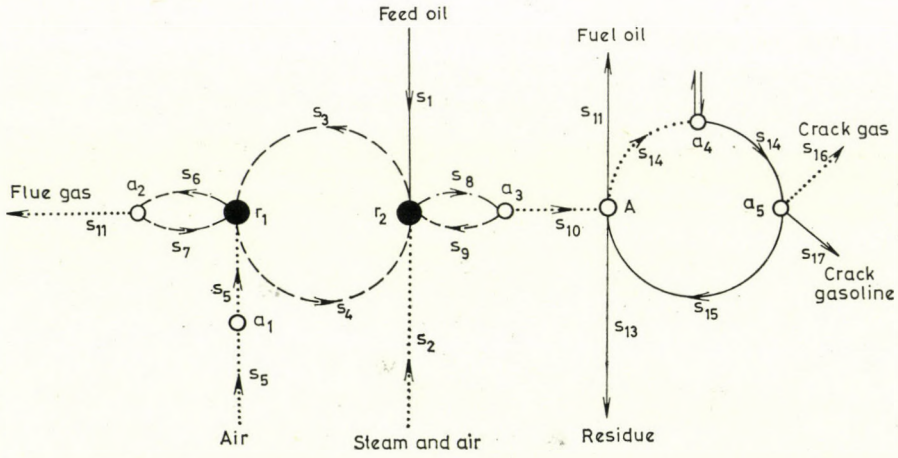

Fig. 7. Catalytic cracking fluidized bed process. Kellog Co. — Standard Oil. 1941
(According to H. Ruf: Kleine Technologie des Erdöls. Fig. 124)
Theoretical graph. *Reactors:* r_1 catalyst regenerator, r_2 reactor. *Allactors:* a_1 compressor, a_2, a_3 cyclones, a_4 condenser, a_5 separator, A fractionation column. *Conduits:* s_1 feed oil, s_2 steam and air, s_3 catalyst with deposited coke, s_4 regenerated catalyst, s_5 air, s_6 catalyst flue gas, s_7 catalyst powder, s_8 crack vapour with catalyst, s_9 catalyst powder, s_{10} crack vapour, s_{11} flue gas, s_{12} fuel oil, s_{13} residue, s_{14} head product of A, s_{15} reflux, s_{16} crack gas, s_{17} crack gasoline
Type of graph: uniflow, cyclic (cumulated and isolated)
Number of graph elements: 27

collaboration with the *Standard Oil Development Co.* The graph of the process is shown in Fig. 7. Cracking and regeneration of the catalyst takes place in separate zones, on the fluidized substance. Catalyst powder is separated by a cyclone from the cracked substance leaving the reactor, which passes then to the fractionating tower, where it is fractionated into its components. The head products of the column are cracked gasoline and gas. The graph is cyclic, and consists of three cumulated and an isolated cycles.

Later, the fluidization apparatus has been simplified by combining the reactor with the regenerator *(Kellog-Orthoflow)*.

2. Reforming

In thermal and catalytic cracking, olefins are also formed increasing the octane number. Though this increase is considerable, it is insufficient for modern engines, which need an octane renumberg of 100 or higher. Gasoline of this quality can be produced by the structural conversion of hydrocarbons. One group of these processes, in which aromatic hydrocarbons are formed, is called *reforming*. Aromatization can be achieved by thermal or catalytic reforming.

2.1. Thermal reforming is similar to thermal cracking processes. Its feed stock is generally naphtha, which is 'reformed' by heating at an adequate

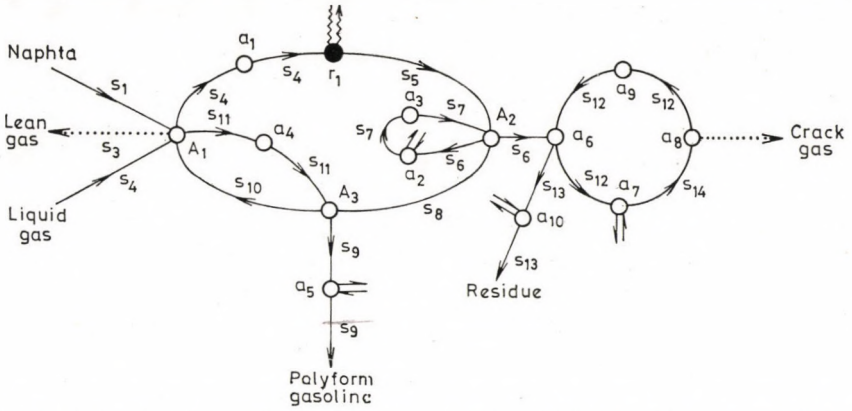

Fig. 8. Thermal reforming, polyforming. Pan American Refining Corp Texas City. 1935
(According to H. Ruf: Kleine Technologie des Erdöls, Fig. 130)
Theoretical graph. *Reactor:* r_1 reforming furnace. *Allactors:* a_1 pump, a_2 cooler, a_3, a_4 pumps, a_5 cooler, a_6 residue stripper, a_7 cooler, a_8 separator, a_9 pump, a_{10} cooler, A_1 absorber, A_2 fractionation tower, A_3 stabilizing column. *Conduits:* s_1 naphta, s_2 liquid gas, s_3 lean gas, s_4 basic substance, s_5 reformed substance, s_6 bottom product of A_2, s_7 cooling oil, s_8 head product of A_2, s_9 stable polyform gasoline, s_{10} head product of A_3, s_{11} reflux, s_{12}, s_{13} residues, s_{14} crack gas
Type of graph: uniflow, cyclic
Number of graph elements: 37

temperature and pressure in a furnace of special design. To avoid cracking, the reaction product is rapidly cooled dawn and fed into the fractionating tower. The head product of the tower is the 'reformate' containing besides aromatics substantial quantities of olefins, both of which increase the octane number. The process was used in several variants. One of these is polyforming, where reforming is coupled with polymerization, by feeding liquefied gas to the base stock. A plant of this kind was built in 1935 by the *Pan American Refining Co.* in its Texas City refinery ([7] p. 188). The graph of the process is shown in Fig. 8. The graph is cyclic, a cumulated cooling cycle and a residue stripping cycle are coupled to the large reforming cycle.

2.2 Catalytic reforming

In its 'Hydroforming' plant, built in 1940 in Leuna, the *I. G. Farben Industrie* began to manufacture toluene from hydrocarbons. The process is in essence catalytic reforming in the presence of hydrogen. During World War II, several plants of this kind were built in the USA for the production of TNT. From these were developed the *platforming* process, using Pt-catalisator deposited on Al_2O_3–SO_2 gel. In all these processes a hydrogen atmosphere is maintained. The first plant of this kind was started up in 1949 by the *Old Dutch Refining Co.*, Michigan ([7] p. 229). The graph of platforming is shown in Fig. 9; it is cyclic, two isolated cycles being coupled to the main production cycle.

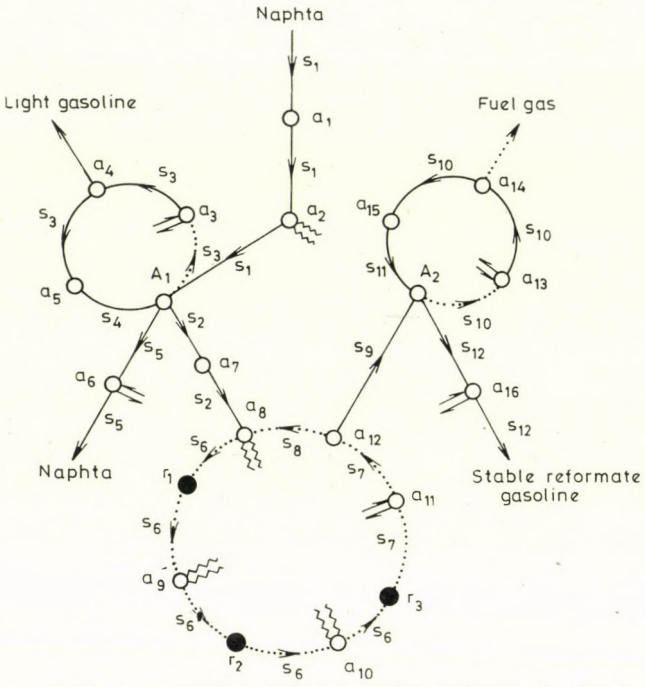

Fig. 9. Catalytic hydroforming. Platforming. Old Dutch Refining Co. Michigan. 1949
(According to H. Ruf: Kleine Technologie des Erdöls. Fig. 133)
Theoretical graph. *Reactors:* r_1 catalyst chamber I., r_2 catalyst chamber II., r_3 catalyst chamber III. *Allactors:* a_1 feeding pump, a_2 heat exchanger, a_3 condenser, a_4 receiver, a_5 pump, a_6 cooler, a_7 pump, a_8 preheating furnace, a_9 preheating furnace, a_{10} preheating furnace, a_{11} cooler, a_{12} separator, a_{13} condenser, a_{14} separator, a_{15} pump, a_{16} cooler, A_1 prefractionation column, A_2 fractionation column. *Conduits:* s_1 feed, s_2 mid product of A_1, s_3 head product of A_1, s_4 reflux, s_5 bottom product of A_1, s_6 path of platforming, s_7 platformed product, s_8 circulating H_2 gas, s_9 platformed product, s_{10} head product of A_2, s_{11} reflux of A_2, s_{12} stable reformed gasoline
Type of graph: uniflow, cyclic (isolated)
Number of graph elements: 47

3. Polymerization, alkylation

In the cracking and reforming processes, a substantial amount of saturated and unsaturated C_1–C_4 hydrocarbons is formed. The gas was used initially as fuel. Research aimed at better utilization, has led to the manufacture of high-quality gasolines by the polymerization and alkylation of the gases.

3.1. Polymerization

The first successful attempt at the utilization of the gases was the polymerization of low molecular weight olefins. Polymerization can be performed *thermally* or by the use of *catalysts*.

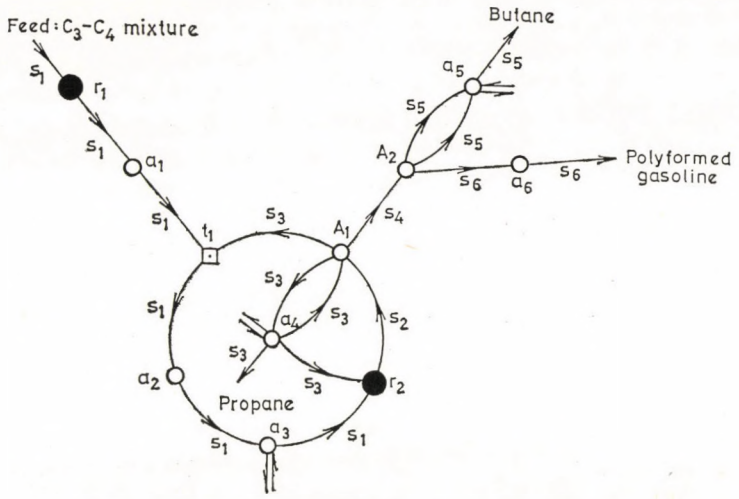

Fig. 10. Catalytic polymerization. Universal Oil Products. 1939
(According to Ullmann Enzyklopedie. 3rd Ed. Vol. 6. Fig. 57)
Theoretical graph. *Reactors:* r_1 alkaline washer, r_2 catalyst tower. *Allactors:* a_1 aqueous washer, a_2 pump, a_3 cooler, A_1 depropanizer column, a_4 propane cooler, A_2 debutanizer column, a_5 butane cooler, a_6 pump. *Storage:* t_1 feeding tank. *Conduits:* s_1 raw material mixture, s_2 polimerizate, s_3 propane, s_4 propane-free product, s_5 butane, s_6 polymer gasoline
Type of graph: uniflow, cyclic (cumulated and isolated)
Number of graph elements: 28

Thermal polymerization processes did not find widespread industrial application. Already in the 1930's, they were replaced by catalytic methods. Hydrogen fluoride or sulfuric acid can be used as catalyst. However, orthophosphoric acid is the most preferred catalyst, which is used with an inorganic support (kieselguhr, asbestos, etc.). The graph of this type of plant is shown in Fig. 10; it is cyclic, consisting of several (cumulated and isolated) cycles. Upon the polymerizate gives upon hydrogenation, a fuel with an octane rating of over 100. This product played an important role in World War II as an aviation fuel ([12] p. 630).

3.2. Alkylation means

In the petroleum refining industry alkylation means the process of linking olefins with isoparaffins. The alkylation process was discovered (1932—35) in the USA by IPATIEFF and SINES (U.O.P.); it can be performed thermally or catalytically with sulfuric acid. Several other companies have attained the same results. The first plant of this type was built in 1938 by *Humble Oil Co.* in Baytown, Texas. Several alkylating plants have been built in the USA, some of which used HF as catalyst; however, in most cases sulfuric acid was applied ([12] p. 602).

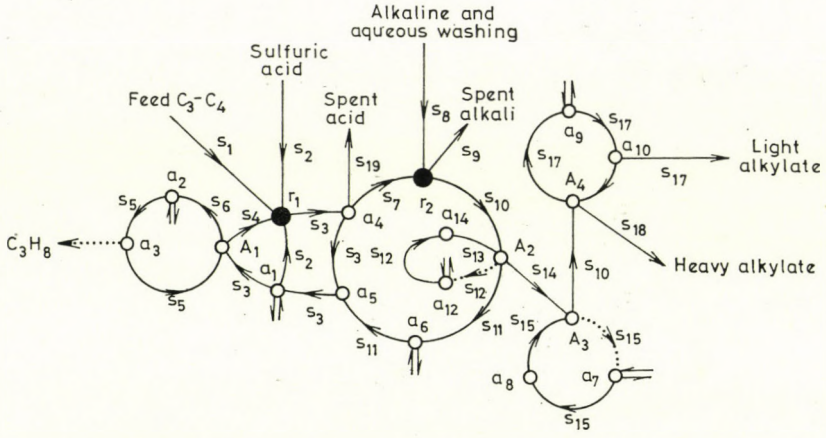

Fig. 11. Catalytic alkylation, sulfuric acid process. MW. Kellog Co. 1938
(According to Ullmann Enzyklopedie. 3rd Ed. Vol. 6. Fig. 58)
Theoretical graph. *Reactors:* r_1 emulsion circulator, r_2 alkaline washer. *Allactors:* a_1 self-cooler, A_1 depropanizer column, a_2 propane cooler, a_3 propane separator, a_4 acid separator, a_5 circulating pump, a_6 i-C_4 cooler, A_2 i-C_4 column, A_3 debutanizer column, a_7 butane cooler, a_8 butane tank, A_4 end-product column, a_9 cooler, a_{10} tank, a_{11} i-C_4 tank, a_{12} i-C_4 cooler. *Conduits:* s_1 feed, s_2 sulfuric acid, s_3 emulsion, s_4 propane-free emulsion, s_5 propane, s_6 propane reflux, s_7 acidic emulsion, s_8 alkali, water, s_9 spent alkali, s_{10} neutral substance, s_{11}, s_{12} i-C_4, s_{13} i-C_4 reflux, s_{14} i-C_4 free substance, s_{15} butane, s_{16} alkylate, s_{17} light alkylate, s_{18} heavy alkylate, s_{19} spent acid
Type of graph: uniflow, cyclic (multiply cumulated, isolated)
Number of graph elements: 59

On otherwise identical principles, the plants were built in different variations with respect to partial design features. Figure 11 shows the graph of the *Kellog Co.* process. The graph is cyclic, consisting of several cycles with cumulated connections.

In November 1939, six sulfuric acid plants produced 3500 bbl/day of aviation fuel ([12] p. 632).

4. Conclusions

4.1. With the exception of the graph of BURTON's discontinuous process (1912), the graphs of the manufacture of Otto engine fuel are cyclic, consisting of a varied combination of several process steps, to be traced back on plant management considerations. Figure 12 was plotted from data summarized in Table I, gives the changes of the *maximal path lengths*, and of *the cyclic processes* of graphs as a function of the time of introduction of the processes. Similarly as has been established in the course of the investigation of distillation [20], the diagram shows that *the complexity of the technologies approaches a maximum in the course of its development.*

4.2. It can be seen from Fig. 12 that in the majority of the processes investigated, the two complexity indexes of the technologies scatter widely

Table I

Data of the graphs of Otto engine fuel manufacture
(see Fig. 12)

Fig. No.	Year of introduction	System	No. of cycles	Path lengths	No. of graph elements
1	1912	Burton (Williamson)	1	5	16
2	1920/21	Dubbs (Bell)	2	10	29
3	1930	Dubbs (Universal)	4	12	38
8	1935	Pan American	4	16	43
5	1937	Houdry (Sun Oil)	3	15	42
11	1938	Kellog Co.	7	16	48
10	1939	Universal Oil	4	14	32
4	1940	Dubbs	5	14	42
7	1941	Kellog Co.	4	17	35
6	1943	Socony	4	12	46
9	1949	Old Dutch	3	23	48

around the trend line of development at about 1940, *i.e.* the time of World War II. The same fact is shown by Fig. 13, plotted from the data of Table II. This phenomenon can ascribed to the fact that *Otto engines were designed for steadily increasing compression* ([13] p. 26), *the operation of which needs suitable high octane gasoline.* (Table IV and Fig. 14 show the increasing demand with respect to octane number.) Naturally, the refineries wanted to meet market demands as soon as possible. Competition attained its goal at about the same time (World War II) as can be seen from Table III.

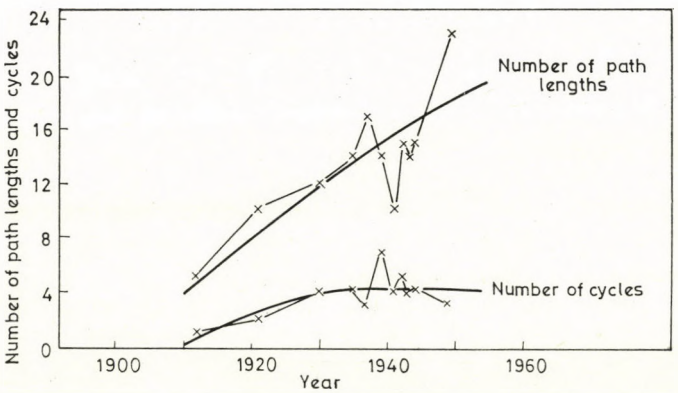

Fig. 12. Number of maximum path length and cycles in the graphs of Otto engine fuel manufacture (see Table I)

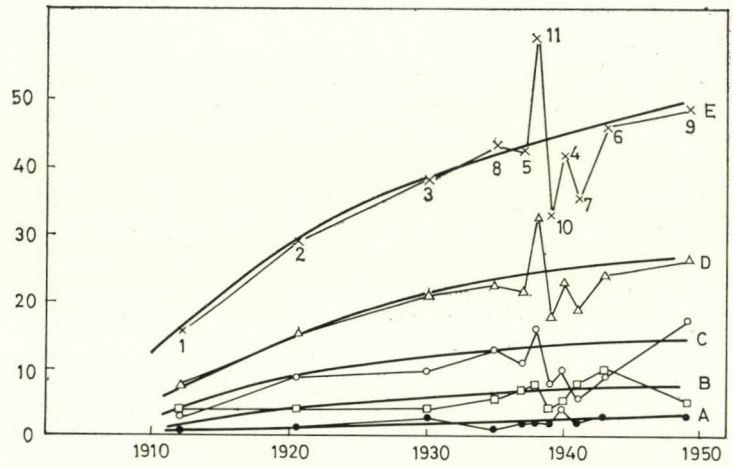

Fig. 13. Trend of the increase in the number of operational units and conduits of Otto engine fuel manufacture as a function of the years (see Table II)

4.3. In Fig. 13, the graph elements are separated into curves of development of reactors, allactors, storage tanks and pipings. The trend line of all graph elements shows an ascending tendency, as mentioned already under 4.1; the trend line of the reactors (curve A) ascends to the smallest extent, while that of the allactors (curve C) to a much greater extent. *This shows that in the process group investigated an increasing number of physical operations have been applied in the course of development, while chemical processes maintained an almost constant number.*

4.4. In Fig. 13 the scatter of the data from Figs 7, 10 and 11 around the trend lines (C, D, E) is remarkable. This can be attributed to the peculiarities of the discussed technologies.

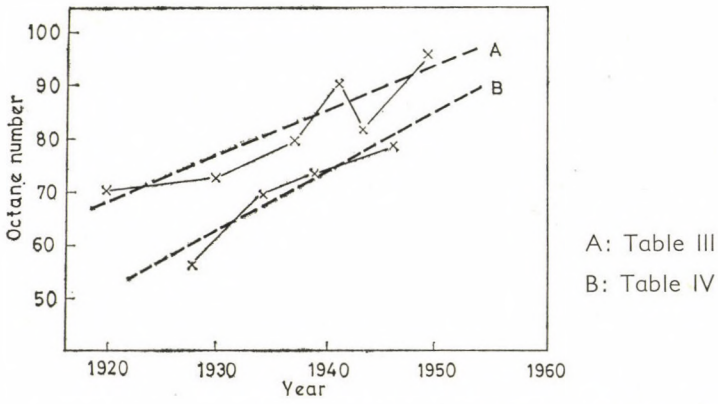

Fig. 14. Change in octane number as a function of the years (see Tables III and IV)

Table II

Number of graph elements
(see Fig. 13)

Fig. No.	Year of introduction	System	Edges	Allactor	Reactor	Storage*	Total
1	1912	Burton (Williamson)	8	3	1	4	16
2	1920/21	Dubbs (Bell)	15	9	1	4	29
3	1930	Dubbs (Universal)	21	10	3	4	38
8	1935	Pan American	23	13	1	6	43
5	1937	Houdry (Sun Oil)	22	11	2	7	42
11	1938	Kellog Co.	33	16	2	8	59
10	1939	Universal Oil	18	8	2	4	32
4	1940	Dubbs	23	10	4	5	42
7	1941	Kellog Co.	19	6	2	8	35
6	1943	Socony	24	9	3	10	46
9	1949	Old Dutch	26	17	3	5	51

* Including the storage units of incoming and outgoing substances, not shown in the figures

Figure 7 is the graph of the fluidized-bed catalytic cracking process of *Kellog* Co. ([4] p. 191). The reactor and the unit for catalyst regeneration fulfil several tasks. In the reactor, the feed is evaporated by the heat content of the hot pulverized catalyst introduced into the reactor and, at the same time, the reaction takes place in the fluidized bed. The catalyst powder and

Table III

*Technical and economical indexes of the chemical conversion technologies of petroleum**

Year of introduction	System	Gasoline yield (%)	Octane number
1912	Burton (Williamson)	20—35	—
1920	Dubbs (Bell)	40—35	65—75
1930	Dubbs (Universal)	50—65	70—74
1937	Houdry (Sun Oil)	30—50	77—81
1941	Kellog Co.	40—60	—83
1943	Socony	40—60	79—83
1949	Old Dutch	90	85—95

* From Tables III-38 and III-39 of WINNACKER—KÜCHLER: Chemische Technologie, Vol. I

coke are separated from the cracked vapours in a cyclone built into the reactor. The powder sinks to the bottom of the reactor, from where it is transported by an air current to regeneration. Air blown into the regenerator burns off coke from the catalyst, the temperature of which increases to 600°C. The regenerated catalyst powder is separated with a cyclone built into the regenerator from the flue gas. This means that the cyclones had to be drawn separate

Table IV

Change in the octane number recommended by the U. S. Bureau of Mines (see Fig. 14)

Year	Octane number (engine)
1928 (regular)	56
1934 (regular)	69
1939 (regular)	73
1946 (regular)	75.9
1946 (premium)	80.9

in the graphs. The regenerated catalyst sinks under its own weight into a communicating tube, from where it is carried by the feed oil stream into the reactor. It can be seen that no separate heating equipment is needed to provide for the required cracking temperature, and the catalyst is self-circulating in the system, without the need of any transportation equipment. Consequence: the diminution of graph elements. Fig. 10 represents, as has been seen, the catalytic polymerization process of *Universal Oil Co.* From the C_3–C_4 olefin mixture, the polymerizate is formed in a single run over the catalyst at a pressure of up to 100 atm. The unreacted gases are separated in two columns. The bottom product of the second column is polyform gasoline of high octane number. Thus, the number of the essential pieces of equipment is reduced to three.

Figure 11 represents catalytic alkylation. The process is not simple: it combines olefins with i–C_4 by heterogeneous catalysis, in which the catalyst is more than 90% sulfuric acid. The reaction takes place in an emulsion and is followed by separation, neutralization and washing. The unreacted hydrocarbons are separated in rectification columns, and finally, the end-product is also separated into two parts: light and heavy alkylates. This brief description explains also the high number of graph elements. These examples as well as the regular trend-curve sections, prove the effect of the constituting operations produced on the process. This effect appears in the mathematical model

of the evolution diagramm in that way, that the trend-curves of the operation unities and conduits are best expressed by the exponential function (Fig. 13)

$$y(x) = a + b^{-\frac{c}{x}}$$

where y the number of graph elements, a, b, c constants, x the number of the years.

The curve approaches to the limit $a + b$, if

$$x \to \infty$$

The constants of the function may be counted with the method of M. KORACH [22].

4.5. The introduction of technological graphs offers the possibility to represent numerically the development of chemical plant system types by mapping the generally increasing trend of the number of elements.

REFERENCES

[1] WINNACKER—KÜCHLER: Kémiai Technológia I. Műszaki Könyvkiadó, Budapest 1962
[2] NELSON: Petroleum Refinery Engineering. McGraw-Hill, New York 1960
[3] BELL, H. S.: American Petroleum Refining. D. Van Nostrand Co., New York 1959
[4] RUF, H.: Kleine Technologie des Erdöls. Birkhauser Vlg. Basel 1963
[5] KISSLING, R.: Chemische Technologie des Erdöls. Vieweg u. Sohn, Braunschweig 1915
[6] KRÁLIK—VAJTA—VÁMOS: Ásványolaj feldolgozó ipar. Népszava, Budapest 1951
[7] ULLMANN, F.: Enzyklopedie, 3rd ed. Vol. 6. Urban u. Schwarzenberg, München 1955
[8] KIRK—OTTMER: Encyclopedia of Chemical Technology, Vol. 10. Interescience Publ. Co., New York 1953
[9] SCHÖNWALDER: Erdöl in der Geschichte. Vlg. Huthig u. Dreyre, Mainz 1958
[10] CLARK, J. A.: The Chronological History of the Petroleum and Natural Gas Industries. Clark Book Co. Houston 1963
[11] WILLIAMSON, H. F., DAUN, A. R.: The American Petroleum Industry. The Age of Illumination. 1959. Northwestern University Press **(1859—1899)**
[12] WILLIAMSON, H. F., DAUN, A. R.: The American Petroleum Industry. The Age of Energy. 1899—1959. Northwestern University Press 1959
[13] PHILLIPOVICH, A.: Die Betriebsstoffe für Verbrennungskraftmaschinen. Springer Vlg. Wien 1949
[14] *World Petroleum Congress:* Petroleum Processing. NIM Dokumentációs és Fordítóiroda. Budapest 1967
[15] ENGLER—HÖFER: Das Erdöl. Vol. III. Die Technologie des Erdöls u. seiner Produkte. Vlg. Hirzel, Leipzig 1911
[16] THORPE, S.: Dictionary of Applied Chemistry, Vol. 9. Longsmans, Green and Co., London 1949
[17] FREUND, M.: Kőolajipar. Nehézipari Könyvkiadó, Budapest 1951
[18] SHERWOOD, H., TAYLOR, F.: A History of Industrial Chemistry. Heinemann, London 1959
[19] Das Erdöl und seine Verarbeitung. Vlg. Hüthig u. Dreyer, Mainz 1963
[20] KORACH, M., HASKÓ, L.: Acta Chim. (Budapest), **72,** pp. 77—91 (1972)
[21] FEHÉR, L.: Timföldgyártó technológiák folyamattani vizsgálata. Thesis, June, 1971
[22] KORACH, M.: Technical Chemistry as a Science. Conference of Applied Physical Chemistry. Veszprém, August, 2—6, 1971, p. 8

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INDEX

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РЕЗЮМЕ

Лигандное замещение и строение комплекса, XIII

ПМР спектры диамагнитных комплексов оснований Шиффа с Ni(II)

Й. ЧАСАР Т. САБО и Г. ДОМОИ

Были сняты и исследованы ПМР спектры хелатных комплексов типа Ni [HSAI—N—н—алкил]$_2$. На основе зависимости спектров от растворителя, концентрации и температуры были сделаны заключения относительно природы равновесных систем, устанавливающихся в инертных растворителях, полагая, что в зависимости от температуры и в растворах н-алкильных соединений могут образовываться парамагнитные тетраэдрические типы молекул.

Изучение гидратации макромолекул, I

Коэффициент самодиффузии воды в водных растворах поливинилового спирта

Д. ИНЗЕЛТ и П. ГРОФ

Коэффициент самодиффузии воды в водных растворах поливинилового спирта в интервале концентраций 0—10 вес.% был измерен при 25 и 35°С, используя метод капилляра с открытым концом. Вода была мечена O^{18} и содержание изотопов было определено с помощью масс-спектрометрии.

Коэффициент самодиффузии воды линейно уменьшается с добавлением пвс. Энергия активации самодиффузии воды равна (4,5 $\pm$ 1,4) ккал/моль. Было найдено, что степень гидратации равна 3,7—4 молекулам воды на одну гидроксильную группу в зависимости от формы макромолекулы. Плотность растворов линейно увеличивается с концентрацией макромолекул. Удельный специфический объем пвс равен 0,7344 и 0,7628 см^3/г при 25 35°С, соответсвенно.

Вязкости растворов значительно уменьшаются с концентрацией, однако, энергия активации ламинарного течения является постоянной и равна (7,4 $\pm$ 0,4) ккал/моль в изученном интервале концентраций.

Образование комплекса между никелем и 1-гидроксиэтан-1,1-дифосфокислотой

Р. РАУТШКЕ, Г. ЛЮКС и У. ШЛОССЕР

В водных растворах ионы никеля образуют комплексы с 1-гидроксиэтан-1,1-дифосфокислотой, которые, в свою очередь, протонируются в различной степени в зависимости от pH. С помощью спектрофотометрического метода были определены константы равновесия и константы протонирования для комплексов $NiH_2У$, $NiHУ^-$ и $NiУ^{-2}$.

Рагщепление гетерокольца изофлаваноидов с помощью нукле офильных реактивов, III

Кинетика разложения α-формил-2-гидроксидезоксибензоина до 2-гидроксидезоксибензоина

В. САБО и М. ЖУГА

Исследуя кинетику разложения α-формил-2-гидроксидезоксибензоин-енола (II) до 2-гидроксидезоксибензоина, было установлено, что гидроксильные ионы препятствуют разложению. Полагается, что сущность ингибирования заключается в том, что диссоциационное равновесие II ⇄ III смещается под действием гидроксильных ионов в направлении образования III, и образующийся таким образом дианион является неинактивным.

Были определены далее энергия и энтропия активации реакции разложения, а также константа вышеуказанного диссоциационного равновесия.

Исследование изомеризации ненасыщенных спиртов на металлических катализаторах с помощью импульсной техники

М. БАРТОК и И. ТЁРЁК

С помощью импульсной техники были исследованы превращения трех изомерных ненасыщенных спиртов (аллилкарбинол, кротиловый спирт и метивинилкарбинол) в присутствии водорода, в интервале температур 100—400°С на платиновых, палладиевых, родиевых, а также медных, никелевых и цинковых катализаторах типа Ренея, с термолитным носителем. Основные направления реакции (изомеризация до оксосоединения и гидрирование до насыщенного спирта) были исследованы в зависимости от различных экспериментальных параметров. На основе экспериментальных данных были сделаны заключения относительно механизма изомеризации.

Исследование шиффовых оснований салицилового альдегида с аминофенолами

Я. БАЛОГ и И. ЧАСАР

Были исследованы шиффовы основания салицилового альдегида с 2-, 3- и 4-аминофенолами. Изменения, наблюдаемые в н-бутанольном растворе, объясняются частичным распадом шиффовых оснований и образованием хинонамина.

Получение 2,4- и 2,2-замещенных 4Н-1,3-бензтиазинов

Й. САБО и И. ВАРГА

Производные 2-фенил-4*Н*-1,3-бензтиазин-4-она (I), взаимодействуя с реагентом Гриньяра — в зависимости от органической группы последнего — дают 4-гидрокси-2,4-замещенные 4*Н*-1,3-бензтиазины (III) и 2,2-замещенные производные 2,3-дигидро-4*Н*-1,3-бензтиазин-4-она (II). Продукты гидролиза соединения (III) подтверждают его строение.

Синтез N-метилолигопептидов с потенциальной антимикробной активностью

Ю. ШТВЕРТЕЦКИ и Ш. БАЮС

Циклические и ациклические N-метилолигопептиды, упрощенные аналоги грамицидина с потенциальной антимикробной активностью, были приготовлены из простых аминокислот. Для определения зависимости активности от структуры было изучено влия-

ние числа и конфигурации аминокислот и N-метиламинокислот, а также циклизации. Следующие молекулы: цикло(L-леуцил-L-пролил-L-леуцил-L-валил(или N-метил-L-валлил)-L-пролил-N-метил-O-леуцилглицил), L-треонил-L-леуцил-L-пролил-L-леуцил-L-валил(или N-метил-L-валил)-L-пролил-N-метил-O-леуцил-глицин и N -ацетил-цикло(L-треонил-L-леуцил-L-пролил-L-леуцил-L-валил(или N-метил-N-валил)-L-пропил-N-метил-*O*-метил-O-леуцил-глицил) необходимы в минимальной ингибирующей концентрации в области 6—50 г/мл против Mycobacterium tuberculosis $H_{37}R_V$ и в области 20—50 г/мл против Candida albicans, in vitro.

Электронодефицитные гетероароматические аммоинио-амидаты, VI

Синтез и некоторые реакции 10-еминоакридиновых солей и N-(10-акридинио)-амидатов

Б. АГАИ и К. ЛЕМПЕРТ

Акридин и 9-фенилакридин были Л-аминированы с помощбю О-мезитиленсульфонилгидроксиламина. Рбразующиеся N-(10-акридинио)-амидыт (1) были превращены в псевдооснования (2), а N-(10-акридинио)-амидаты (6) в соединение 7 подобного строения, а также их гидрохлориды. Были исследованы также некоторые реакции 2-псевдооснований.

Электронодефицитные гетероароматические аммонио-амидаты, VII

Синтез N-(2-фталазинио)- и N-(1,4-дифенил-2-фталазинио)-бензамидатов и их некоторые реакции

К. ЛЕМПЕРТ и К. ЗАУЭР

Описывается синтез, термолиз и фотолиз упомянутых в заглавии соединений.

Восстановление эфиров дикарбоксильных кислот с гидридом диизобутилалюминия

Г. КРАЙС, М. ПОВАРНИ и К. НАДОР

Было описано восстановление диэтилгомофталата, диэтил цис-1,2-циклогександикарбоксилата и диэтилглутарата за счет 1—4 эквивалентов гидрида диизобутилалюминия. Сырые продукты восстановления были анализированы с помощью газовой хроматографии. Восстановление диэтил гомофталата 3 эквивалентами гидрида диизобутилалюминия приводит к селективному образованию лактола.

Развитие промышленности рафинирования нефти, изображенное в свете теории графирования, II

Производство горючего для мотора Отто

М. КОРАХ и Л. ХАШКО

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THIN-LAYER pH-CHROMATOGRAPHY OF MONO- AND DIBASIC ORGANIC ACIDS ON BUFFERED SILICA GEL LAYERS

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(Research Institute for Pharmaceutical Chemistry, Budapest)

Received March 16, 1975

The equation of pH-R_f curve was derived in the case of mono- and dibasic acids and it was stated that on the basis of the pH-R_f curves mono- and dibasic acids can be distinguished from each other. Dissociation constants can be calculated from the data of pH-R_f curves with a good approximation. Experimental proofs for the theoretical correlations were provided by the TLC on buffered silica gel of *o*-phthalic, 3,5-dinitrobenzoic, *p*-nitrobenzoic and *p*-methoxybenzoic acids.

Organic electrolytes form a great and important group of compounds investigated chromatographically. Experimental data show that the R_f value of dissociating compounds is a function of the pH of the chromatographic system. On the basis of these data a special method, the so-called pH-chromatography has been developed. The essence of this method is the following: the investigated substance is developed in the same solvent system, but each strip of the stationary phase is adjusted to a given pH by previous buffering. The R_f values are plotted against pH graphically. Characteristic curves are obtained, on the basis of which it can be determined, whether the investigated unknown compund has an acidic, basic or amphoteric character or it is neutral. Another advantage of this method is that the separation of certain dissociating compounds, often very similar in character, can be improved by the suitable selection of the pH.

Theoretical relations and practical application of pH-chromatography were elaborated in the area of paper chromatography. The method gained special importance in the paper chromatography of different antibiotics. [1, 2, 3, 4, 5, 6] Many compounds of other types have been investigated and theoretical conclusions have been drawn from the experimental results. [7, 8 9 10, 11, 12]

The basic equations of partition chromatography were used for the derivation of pH—R_f-correlation. As it is well known the R_f value is a function of the partition coefficient:

$$R_f = \frac{\frac{q_S}{q_M}}{\frac{q_S}{q_M} + \alpha} \qquad (1)$$

where q_M represents the cross section of the mobile phase, q_S is the cross section of the stationary phase and α is the partition coefficient ($\alpha = c_S/c_M$, where c_M is the solute concentration in the mobile phase and c_S is the solute concentration in the stationary phase. (Denoting the ratio q_M/q_S by 'k') Eq. (1) can be written as follows:

$$R_f = \frac{k}{k + \alpha}. \tag{2}$$

In the case of dissociating substances the coefficient is a function of pH. The $\alpha = f(\text{pH})$ function was studied by GOLUMBIC [7], WAKSMUNDSKI and SOCZEWINSKI [9] and the following relationship was obtained:

$$\alpha = \alpha_0 \left(1 + \frac{K_d}{[H^+]}\right) \tag{3}$$

where α_0 is the partition coefficient of the undissociated acid and K_d is the dissociation constant of the acid.

Substituting Eq. (3) into Eq. (2) we obtain:

$$R_f = \frac{k}{k + \alpha_0 \left(1 + \frac{K_d}{[H^+]}\right)} = \frac{k}{k + \alpha_0 (1 + K_d \cdot 10^{pH})}. \tag{4}$$

Eq. (4) is the equation for pH—R_f-curves of monobasic acids. Such curves are shown in Figs 1, 2.

In a previous work [13] Eq. (4) was used to determine the dissociation constant of acids. It emerges from this equation, that by increasing $[H^+]$ the R_f value approaches a limit value, because if $[H^+] \gg K_d$, the ratio $K_d/[H^+]$ can be neglected beside 1, so

$$R_f = \frac{k}{k + \alpha_0} = R_{f,0} \tag{5}$$

$R_{f,0}$ is the R_f value of the undissociated acid. $R_{f,0}$ can be determined from the pH—R_f-curve, since the curve reaches a constant R_f-value after a given decrease in the pH of the stationary phase; the change of the R_f value in this part of the curve is less than the experimental error. This constant R_f value is equal to $R_{f,0}$ in Eq. (5).

By suitable transformation of Eq. (5) we obtain:

$$\frac{1}{R_{f,0}} = 1 + \frac{\alpha_0}{k}. \tag{6}$$

Dividing the numerator and denominator of the fraction in Eq. (4) by 'k' and using Eq. (6) we get the following expression:

$$R_f = \frac{R_{f,0}}{1 + (1 - R_{f,0}) \cdot \dfrac{K_d}{[H^+]}} = \frac{R_{f,0}}{1 + (1 - R_{f,0}) \cdot K_d \cdot 10^{pH}} . \tag{7}$$

Eq. (7) is suitable for the quantitative determination of the dissociation constant. This can be done in several ways. One of these, which was applied in a previous work [13] is based on the determination of the inflexion point of the pH—R_f-curve. When Eq. (7) is twice differentiated as the function of pH and the second differential quotient is made equal to zero, it can be stated, that the curve has its inflexion point at the following pH value:

$$pH_{infl} = \lg \frac{1}{(1 - R_{f,0}) \cdot K_d} . \tag{8}$$

It means, that

$$pK_d = pH_{infl} + \lg(1 - R_{f,0}) .$$

By means of pH_{infl} (determined from the curve graphically) and $R_{f,0}$ the value of pK_d can be determined. Eqs (7) and (8) reveal that at the inflexion point the value of $R_{f,\,infl}$ is equal to $R_{f,0}/2$, so that the graphical differentiation of the curve is not necessary. The pH-value of the inflexion point is the pH-value corresponding to $R_f = R_{f,0}/2$.

Another possibility of determining K_d is to determine the point of the curve, where $K_d = [H^+]$. On the basis of Eq. (7) the value of R_f, at this point, can be written as:

$$R_f' = \frac{R_{f,0}}{2 - R_{f,0}} . \tag{10}$$

The pH-value corresponding to R_f' is equal to the pK_d value of the acid.

The described considerations were extended to dibasic acids.

At the partition chromatography of a dibasic acid the following equilibria exist:

$$\begin{aligned} [H_2A]_M &\overset{\alpha_0}{\rightleftharpoons} [H_2A]_S \overset{K_1}{\rightleftharpoons} [H^+]_S + [HA^-]_S \\ [HA^-]_M &\overset{\beta_0}{\rightleftharpoons} [HA^-]_S \overset{K_2}{\rightleftharpoons} [H^+]_S + [A^{2-}]_S \cdot \end{aligned} \tag{11}$$

The concentration of A^{2-} in the mobile phase can be neglected. α_0 denotes the partition coefficient of the undissociated acid, β_0 denotes the partition coefficient of HA^- between the stationary and mobile phases. K_1 and K_2 are the dissociation constants of the acid.

The value of the partition coefficient is as follows:

$$\alpha = \frac{[H_2A]_S + [HA^-]_S + [A^{2-}]_S}{[H_2A]_M + [HA^-]_M} . \tag{12}$$

The value $[HA^-]_S$ must statisfy the following equations:

$$K_1 = \frac{[H^+]_S \cdot [HA^-]_S}{[H_2A]_S} \qquad K_2 = \frac{[H^+]_S \cdot [A^{2-}]_S}{[HA^-]_S} . \tag{13}$$

The partition coefficients are:

$$\alpha_0 = \frac{[H_2A]_S}{[H_2A]_M} \qquad \beta_0 = \frac{[HA^-]_S}{[HA^-]_M} . \tag{14}$$

Using equations (12), (13), (14) we obtain: ($[H^+]$ denotes the hydrogen ion concentration of the stationary phase)

$$\alpha = \frac{[H^+] + K_1 + \dfrac{K_1 \cdot K_2}{[H^+]}}{\dfrac{[H^+]}{\alpha_0} + \dfrac{K_1}{\beta_0}} . \tag{15}$$

The R_f-value on the basis of Eq. (2):

$$R_f = \frac{k}{k + \dfrac{[H^+] + K_1 + \dfrac{K_1 K_2}{[H^+]}}{\dfrac{[H^+]}{\alpha_0} + \dfrac{K_1}{\beta_0}}} = \frac{1}{1 + \dfrac{[H^+] + K_1 + \dfrac{K_1 K_2}{[H^+]}}{\dfrac{k}{\alpha_0}[H^+] + \dfrac{k}{\beta_0} \cdot K_1}} . \tag{16}$$

In the pH—R_f-curve of dibasic acids we found two horizontal parts (see curves of phthalic acid in Figs 1 and 2). It can be seen from Eq. (16), that at the pH values, where $[H^+] \gg K_2$, but $\ll K_1$, we may do some neglections:

$$R_f = \frac{1}{1 + \dfrac{\dfrac{[H^+]}{K_1} + 1 + \dfrac{K_2}{[H^+]}}{\dfrac{k}{\alpha_0}\dfrac{[H^+]}{K_1} + \dfrac{k}{\beta_0}}} \approx \frac{1}{1 + \dfrac{1}{\dfrac{k}{\beta_0}}} = \frac{1}{1 + \dfrac{\beta_0}{k}} = R_{f,2} . \tag{17}$$

Eq. (17) means, that the R_f value in this area is practically independent of the pH, the curve is within these pH-limits horizontal, the R_f value measured here is denoted as $R_{f,2}$. At pH values, where $[H^+] \gg K_1$, K_2 we may do neglections in Eq. (16) again:

$$R_f = \frac{1}{1 + \dfrac{\dfrac{[H^+]}{K_1} + 1 + \dfrac{K_2}{[H^+]}}{\dfrac{k}{\alpha_0}\dfrac{[H^+]}{K_1} + \dfrac{k}{\beta_0}}} \approx \frac{1}{1 + \dfrac{\dfrac{[H^+]}{K_1}}{\dfrac{k}{\alpha_0}\dfrac{[H^+]}{K_1}}} = \frac{1}{1 + \dfrac{\alpha_0}{k}} = R_{f,1} . \tag{18}$$

In this area, too, the R_f value is practically independent of the pH. The curve is horizontal. The R_f measured here is denoted as $R_{f,1}$.

Eq. (16) makes possible to determine dissociation constants. Using the right side of Eq. (17) and (18) R_f can be expressed as

$$R_f = \frac{1}{1 + \dfrac{[H^+] + K_1 + \dfrac{K_1 K_2}{[H^+]}}{\dfrac{R_{f,1}}{1 - R_{f,1}}[H^+] + \dfrac{R_{f,2}}{1 - R_{f,2}} \cdot K_1}}. \tag{19}$$

At the point, where $[H^+] = K_1$ (pH $= pK_1$) the corresponding R_f value (R_f^*) can be calculated according to the following equation:

$$R_f^* = \frac{1}{1 + \dfrac{2K_1 + K_2}{K_1 \dfrac{R_{f,1}}{1 - R_{f,1}} + \dfrac{R_{f,2}}{1 - R_{f,2}} \cdot K_1}}. \tag{20}$$

Considering that $K_1 \gg K_2$, we may allow the following approximation:

$$R_f^* \approx \frac{1}{1 + \dfrac{2}{\dfrac{R_{f,1}}{1 - R_{f,1}} + \dfrac{R_{f,2}}{1 - R_{f,2}}}}. \tag{21}$$

Having read $R_{f,1}$ and $R_{f,2}$ from the pH—R_f curve we are able to calculate R_f^* and then read the corresponding pH value from the curve; this pH is equal to pK_1.

Similarly, when $[H^+] = K_2$ (pH $= pK_2$), the corresponding R_f value (R_f^{**}) can be expressed as

$$R_f^{**} = \frac{1}{1 + \dfrac{K_2 + 2K_1}{\dfrac{R_{f,1}}{1 - R_{f,1}} \cdot K_2 + \dfrac{R_{f,2}}{1 - R_{f,2}} \cdot K_1}} \approx \frac{1}{1 + \dfrac{2(1 - R_{f,2})}{R_{f,2}}}. \tag{22}$$

The pH value corresponding to R_f^{**} is equal to pK_2.

Experimental

Experimental evidence for the correlations described above was given by silica gel thin-layer chromatography. The advantage of this method is its wide range of applicability, some experimental difficulties, however, may arise. As it is well known, silica gel itself behaves like a buffer against acids an bases. While in paper chromatography the buffering of the stationary phase can be carried out by simple soaking of the paper in a buffer solution, in TLC on

buffered silica gel it is not enough to replace water by a buffer solution when preparing the plates, especially, when we want to perform quantitative determinations. When silica gel is suspended in a buffer solution, it behaves in such a way, that the pH value of the stationary phase prepared from the gel will not be equal to that of the original buffer solution. Therefore the pH of the suspension must be adjusted each time to the desired value by titration. The preparation of the plates was done as follows.

Buffer solutions were prepared in pH range between 1.5 and 8.0. In the range of 2.5—8.0 suitable mixture of 0.1 *M* citric acid and 0.2 *M* Na_2HPO_4 were used, at pH values below 2.5 the solutions of 0.1 *M* sodium citrate and 0.1 *M* HCl were mixed in the necessary proportions. The pH values of the buffers were measured on a Radelkis type pH meter, using glasss electrode; the accuracy was ± 0.02 pH unit. Then 30 g Kieslegel HF_{254} was suspended in 200 ml of buffer solution and allowed to stand for an hour at room temperature After an hour the pH of the suspension was measured and the required buffer component (HCl, citric acid, Na_2HPO_4 or 0.1 *N* NaOH solutions) was mixed in small portions into the suspension, until the pH of the suspension was adjusted to the original pH value of the buffer. Then the suspension was allowed to stand for a day. Measuring the pH value on the next day we found that it did not change, so the silica gel and the buffer were in equilibrium. The buffer solution was then removed from the silica gel by decantation until only 70 ml remained on the 30 g Kieselgel. This suspension was used for the preparation of the plates by means of a CAMAG apparatus. The thickness of the layer was 300 μ. The plates were air-dried at room temperature for a day.

Chromatographic investigations were carried out with the following aromatic acids: phthalic acid (PA), *p*-methoxybenzoic acid (PMBA), 3,5-dinitrobenzoic acid (3.5-DNBA) and *p*-nitrobenzoic acid (PNBA). 50—100 μg of the acids were applied using methanolic solutions. Development was carried out in diethyl ether and diisopropyl ether, respectively, saturated with the respective buffer solution in advance. The plates were developed in grinded chromatographic tanks. The distance of the solvent front from the origin was 15 cm and was marked before beginning the development. The detection of the spots was carried out by means of an UV lamp at 254 nm. R_f values were calculated and plotted against pH.

Discussion

pH—R_f curves can be utilized for quantitative evaluation only if the chromatographic solvents used had been perfectly chosen. That means that the $R_{f,0}$ value (in the case of dibasic acids $R_{f,1}$) must not be very near to 1.0, because in this case the accuracy of measurement is poor. The other condition is that the R_f value approaches to zero at pH values higher than 7, because this proves that the completely dissociated form of the acid did not enter into the mobile, organic phase. This is a support for the correctness of the assumption described in the theoretical part. These conditions were fulfilled in the case of diisopropyl ether by each of the four acids, but in the case of diethyl ether were met only by phthalic acid and *p*-methoxybenzoic acid. The $R_{f,0}$ of nitro acids was very near to 1.0 in diethyl ether.

Experimental data are summarized in Tables I and II. Each R_f value is the average of 3 parallel chromatographic runs. The deviation between two parallel R_f values was below 0.03.

Plotting R_f against pH is shown in Figs 1 and 2. It can be seen that the curve of the *o*-phthalic acid shows two steps, whereas the curve of monobasic acids only one. Characteristic data were calculated from the curves according to the methods described in the theoretical part. Dissociation constants obtained this way were compared to the values given in the literature (see Tables III and IV). K_d values were found in Beilstein: Handbuch der organischen Chemie **9,** 389, 414 and 793; **10,** 155.

Table I

R_f values of o-phthalic and p-methoxybenzoic acid in saturated diethyl ether at different pH values

pH	*o*-phthalic acid	*p*-methoxy-benzoic acid
1.61	0.91	0.91
2.05	0.90	0.90
2.55	0.88	0.90
3.05	0.83	0.91
3.43	0.72	0.90
4.07	0.53	0.91
4.49	0.51	0.87
5.02	0.17	0.76
6.05	0.02	0.35
7.02	0	0.08
8.15	0	0

Table II

R_f values of acids in buffer-saturated diisopropyl ether at different pH values

pH	Phthalic acid	PMBA	PNBA	3,5-DNBA
1.61	0.39	0.70	0.85	0.80
2.05	0.37	0.70	0.85	0.78
2.55	0.34	0.71	0.84	0.74
3.05	0.29	0.70	0.83	0.64
3.43	0.23	0.68	0.72	0.45
4.07	0.16	0.64	0.60	0.27
4.49	0.15	0.59	0.44	0.15
5.40	0.02	0.29	0.10	0.02
6.05	0.02	0.10	0.02	0
7.02	0	0	0	0
8.15	0	0	0	0

Table III

Characteristic data and calculated pK_d values of monobasic acids compared with the pK_d values given in the literatures

Acid	pH_{infl}	$R_{f,0}$	R'_f	pK_d calcd. with pH_{infl}	pK_d calcd. with R'_f	pK_d lit.
PMBA (in diethyl ether)	5.6	0.91	0.83	4.65	4.60	4.50
PMBA (in diiprop ether)	5.1	0.70	0.54	4.58	4.50	4.50
3,5-DNBA (in diiprop ether)	3.5	0.80	0.67	2.80	2.90	2.77
PNBA (in diiprop ether)	4.3	0.85	0.74	3.48	3.50	3.42

Table IV

Characteristic data and calculated pK_d values of phthalic acid, compared with pK_d values given in the literature

Solvent	$R_{f,1}$	$R_{f,2}$	R_f*	R_f**	pK_1	pK_2	pK_1 lit	pK_2 lit
Diethyl ether	0.91	0.51	0.84	0.35	2.9	4.65	2.89	4.41
Diiprop ether	0.39	0.16	0.30	0.11	2.9	4.60		

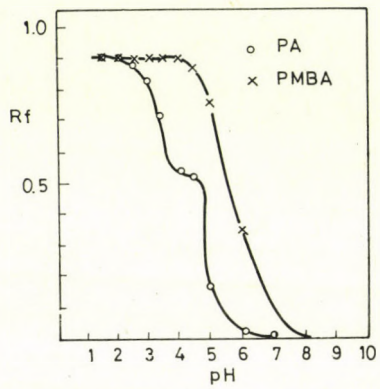

Fig. 1. pH-R_f curves of *o*-phthalic and *p*-methoxybenzoic acid in buffer-saturated diethyl ether

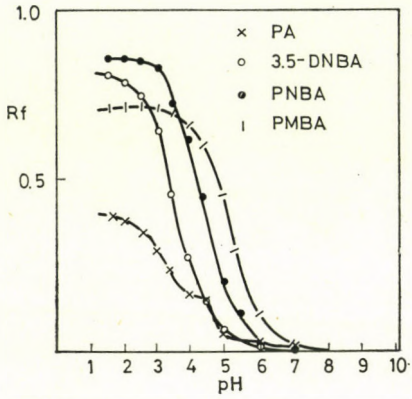

Fig. 2. pH-R_f curves of *o*-phthalic, *p*-methoxybenzoic, 3,5-dinitrobenzoic acid and *p*-nitrobenzoic acids in buffer-saturated diisopropyl ether

An advantage of the described method is that it allows the elucidation of the acidic character of an unknown compound, which may be present in the sample only in small amount and cannot be isolated in pure solid state. Whether the compound is a monobasic or dibasic acid can be stated in this way and the dissociation constants can be determined with good approximation, as it was shown in Tables III and IV. These data may facilitate the identification of the unknown compound. In the case of a known acid it can be calculated what R_f value can be expected at a given pH of the stationary phase, so a suitable pH for the chromatography can be chosen.

REFERENCES

[1] BETINA, V.: Nature **182,** 796 (1958).
[2] BETINA, V., NEMEC, P.: Nature **187,** 1111 (1960).
[3] BETINA, V.: Chem. zvesti **13,** 51 (1959)
[4] BETINA, V.: Chem. zvesti **15,** 750 (1961)
[5] BETINA, V.: Chem. zvesti **15,** 661 (1961)

[6] DUKOVICHNAYA, D. E.: Antibiotiki **8**, 939 (1963)
[7] GOLUMBIC, C., ORCHIN, M., WELLER, S. J.: J. Am. Chem. Soc. **71**, 2624 (1949)
[8] BÜCHI, G., SOLIVA, M.: Pharm. Acta Helv. **30**, 154 (1959)
[9] WAKSMUNDSKI, A., SOCZEWINSKI, E.: J. Chromatogr. **3**, 252 (1960)
[10] VACEK, Z., STOTA, Z., STANEK, J.: J. Chromatogr. **19**, 572 (1965)
[11] LAYOLE, J. *et al.*: J. Chromatogr. **76**, 441 (1973)
[12] KUCHER, M. *et. al.*: J. Chromatogr. **92**, 381 (1974)
[13] IGLÓY, M.: Magy. Kém. Lapja **18**, 622 (1963)

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EFFECT OF SILICON SUBSTITUTION ON THE THERMAL STABILITY OF POLYMERS

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Thermal degradation of poly-styrene-dimethyl-silane has been studied by pyrolysis gas chromatography. The composition and distribution of the volatile pyrolysis products show that the decomposition of this polymer is governed by the same rules as that of polystyrene and polydimethyl-silane. This observation is a further confirmation of our previous experiences on poly-alkylene-siloxanes and polyvinyl-silanes. The presence of the silicon atom does not influence importantly the decomposition mechanism of the hydrocarbon chain.

In a recent work we have introduced a new concept to explain phenomena of thermostability [1], which we called 'energetic retardation effect'. There are two relevant groups of observations made by many authors: (i) the intrinsic thermostability (which seems to be mostly of kinetic and not thermodynamic in nature) is very often not in a close and simple correlation with bond structure, and (ii) the kinetics of degradation can be described by a simple kinetic equation only in the simplest cases, *e.g.* if degradation occurs by simple depolymerization. The second observation can also be expressed by stating that degradation is often not a simple, thermally activated reaction [2], thus the activation energy has no meaning in the classical sense, and that the kinetic equation cannot be obtained simply in terms of remaining weight fraction or conversion [3]. As an explanation we have proposed, in contrast to the theory of chemical (or thermal) activation, that during the heat treatment a simple physical interaction between the transmitted energy and the macromolecule may be anticipated, consequently, on account of 'trapping' or 'cageing' of energy or dissipation by a non-destructive mode, sufficient localization on one or another bond occurs at a much higher temperature than it would if equipartition in the Boltzmannian sense were valid. Thus at a critical temperature — where 'cages' are opened or another way is found by the system to lift energetic retardation — degradation suddenly occurs at a high rate, being affected not only by the excess thermal energy 'pumped' into the system at this critical temperature. As the activation energy is usually determined by measuring the temperature dependence of the reaction rate, this apparently strong effect of heating just above this critical temperature results in an apparently high activation energy of the order of 100 kcal mol^{-1} or higher.

In several papers we tried to clarify the influence of the silicon atom or a siloxane unit on the thermal stability and the mechanism of polymer degradation. We have shown that poly-alkylenesiloxanes are degraded just like polyalkylenes and siloxanes separately [4]; polyvinyltrimethylsilane and polyvinylphenyldimethylsilane are degraded according to the scheme of polypropylene [5] and copolymers of the last two substances with styrene behave again like the separate homopolymeric systems [6]. The series of these experiments is now completed with results on polystyrenedimethylsilylane, PSDS, to be reported in this paper. Conclusions will be drawn on all the polymers mentioned regarding the influence of silicon. Owing to its relatively large mass, silicon is extremely interesting from the point of view of the energetic retardation effect, therefore, we found it necessary to obtain information on its role in the degradation of PSDS.

Experimental

PSDS was synthesized according to NEFEDOW *et al.* [7] from a mixture of dimethyldichlorsilanes and styrene in tetrahydrofuran by the reaction with metallic lithium. The components were added in equimolar amounts, which, according to analytical results, were retained also in the polymer. The data of elemental analysis and the values calculated for the equimolar amounts of the components are:

Calcd.	C 74.04;	H 8.64;	Si 17.28.
Found	C 70.97;	H 8.35;	Si 17.09%.

The PSDS samples were pyrolyzed by the technique used in this laboratory [8]. For the separation of pyrolysis products an OV-101 coated glass capillary column was used. The number of benzylene and silylene parts in the product has been counted on the basis of the gas chromatographic retention data and the relative responses given in a modified flame ionization detector sensitized for silicon [9].

Results and discussion

The results of pyrolysis at 400°C are shown in Fig. 1, where weight fractions of the products, normalized to styrene, are plotted against the retention time. The gas chromatographic separation was carried out on a column OV—1 as the stationary phase, using a temperature program of 10°/min from 40 to 260°C. The retention time of some standards are marked on the retention time scale. The silylene and benzylene content of the other products are given as well. The mole ration of styrene and the sum of the other products proved to be 1 : 1 at 350°C and 1 : 1.7 at 400°C.

The following conclusions are of importance.

1. Neither oligomers of styrene, nor those of dimethylsilylene are to be observed, which demonstrates that true alternating copolymerization has occurred. Dimeric and trimeric styrene and cyclic dimethylsilylene penta- and hexamers were checked and found to be absent.

2. The predominant product of pyrolysis seems to be styrene, which means that primary chain cleavage — at least up to 350°C — occurs at the Si–C-bond, and styrene-ended macroradicals always split off styrene as does polystyrene. As this produces silicon-ended macroradicals too which cannot

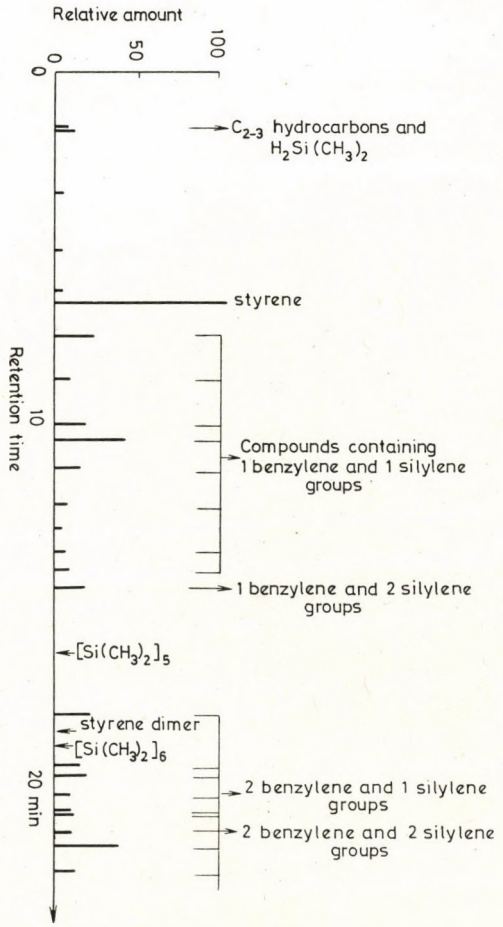

Fig. 1

split off any starting monomer, large amounts of silylene and benzylene containing molecules are formed on account of some hydrogen migration, transfer or back-biting mechanism.

3. As well known, hydrogen migration is favoured in slicicon-containing molecules and also during pyrolysis, as in the case being effected by electron-impact too [10]. The same holds true here for the formation of $H_2Si(CH_3)_2$, which is the product of two such steps.

4. The mole ratio of styrene and all the other products is about 1 : 1 at 350°C, which again supports the conclusion of paragraph 2. This ratio is shifted to 1 : 1 7 at 400°C in favour of non-styrene compounds, showing that at higher pyrolysis temperatures, the rates of formation and decomposition of silicon-ended macroradicals become higher.

5. The fact that $H_2Si(CH_3)_2$, which requires double hydrogen transfer, and the compounds which contain one or two benzylene units are formed together demonstrates the relatively high stability of silicon-ended free radicals, a know fact in silylene chemistry.

Conclusion

The main finding of the present study is that the presence of the silicon atom in the substituted hydrocarbon chain does not appreciably influence the general properties of this chain, since the decomposition of this macromolecule (which may be considered as a polystyrene–polysilylene copolymer) are governed essentially by the same factors as that of pure polystyrene and polysilylene. The inductive effect of the silicon or any other interaction of this atom with the α-phenyl group seems to have no importance from the point of view of thermal degradation. No interaction with silicon influencing the decomposition has been observed in our previous works either [4—6], thus the generalization seems justified that the enhanced thermal stability of silicon-containing organic polymers or copolymers may be attributed to the higher mass of the silicon atom, and probably not any quantum-chemical interaction due to empty *d*-orbitals. This finding confirms the existence of the energetic retardation effect. In addition, no polymers of this type follow simple degradation kinetics, which again can be explained by this picture.

REFERENCES

[1] Székely, T., Blazsó, M., Till, F., Várhegyi, G.: J. Thermal. Anal. (to be published)
[2] Székely, T., Blazsó, M., Till, F.: IVème Conference Européenne des Plastiques et des Caoutchoucs, Paris, 1974
[3] Székely, T., Till, F., Várhegyi, G.: Proc. IV. ICTA Conference, Budapest 1974.
[4] Blazsó, M., Garzó, G., Székely, T., Andrianov, K. A., Volkova, L. M.: J. Organometal. Chem., **54**, 105 (1973)
[5] Blazsó, M., Székely, T.: Eur. Polym. J., **10**, 115 (1974)
[6] Blazsó, M., Székely, T.: Eur. Polym. J., **10**, 733 (1974)
[7] Nefedov, O. M., Manalov, M. N., Petrov, D. A.: Konf. Vysokomolekul. Soedin., 1962, pp. 67—74 (1964)
[8] Blazsó, M., Garzó, G., Székely, T.: Chromatographia, **5**, 485 (1972)
[9] Garzó, G., Fritz, D.: Gas Chromatography. p. 150, Ed. Littlewood Institute of Petroroleum, 1966
[10] Tamás, J., Újszászi, K., Bujtás, G.: Acta Chim. Acad. Sci. Hung., **62**, 335 (1969)

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AMINOPHTHALAZINONE DERIVATIVES, I

REACTION OF AMINO ALCOHOLS WITH 4-CHLORO-1(2*H*)-PHTHALAZINONE

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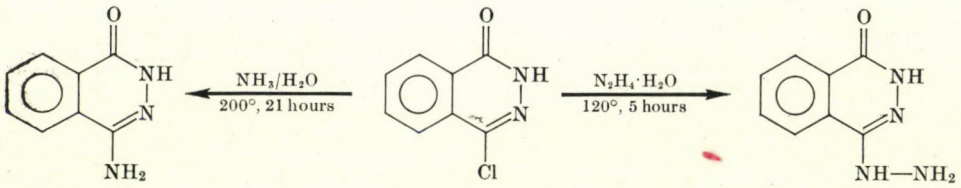
4-Chloro-1 (2*H*)-phthalazinone (**1**) reacts with relative ease with amino alcohols to give 4-(hydroxyalkylamino)-1(2*H*)-phthalazinone derivatives (**5**). The reactivity of **1**, which is known to be stable to amines [3, 4], is enhanced by the formation of transitory amino alcohol addition. The reactivity-increasing role of alcohol addition is proved by the fact that **1** gives the corresponding aminophthalazinone derivative (**5k**) with diethylaminoethylamine in ethylene glycol solution at 150°C in 20 hrs in a yield of 55%, whereas under identical conditions but in the absence of ethylene glycol no substitution occurs.

Several experiments aiming at the preparation of 4-amino-1(2*H*)-phthalazinone derivatives have been carried out in the past [1, 2, 3, 4], yet no generally applicable synthesis is known; thus this group of compounds has remained practically inaccessible. The purpose of the series starting with the present paper is to assist in improving this situation. In addition to being a preparative contribution, this work serves also a practical purpose, as some members known so far of this new group of compounds exhibit considerable biological activity.

4-Chloro-1(2*H*)-phthalazinone (**1**), a compound readily obtainable from phthalic acid hydrazide, seems to be an ideal starting material for the synthesis of 4-N-substituted aminophthalazinone derivatives (**5**). One example is the observation of STEPHENSON [1] made as early as 1944, according to which **1** could be converted with aqueous ammonia at about 200°C to 4-amino-1(2*H*)-phthalazinone (**2**). A similar successful reaction was reported in 1967 by KÖHLER [2], who obtained the analogous 4-hydrazino derivative (**3**) with 100% hydrazine hydrate in an excellent yield. However, attempts to generalize the reaction remained unsuccessful. HAWORTH and ROBINSON [3] found 4-chloro-1(2*H*)-phthalazinone (**1**) completely resistant to diethylaminoethylamine, and recently FLITSCH and PETERS [4] had the same experience in the attempted reaction with aniline. Our own experiments confirmed the statements published in the literature; heating of **1** with diethylaminoethylamine for 20 hours at 150°C did not convert the compound to 4-(2-diethylaminoethylamino)-1(2*H*)-phthalazinone (**5k**).



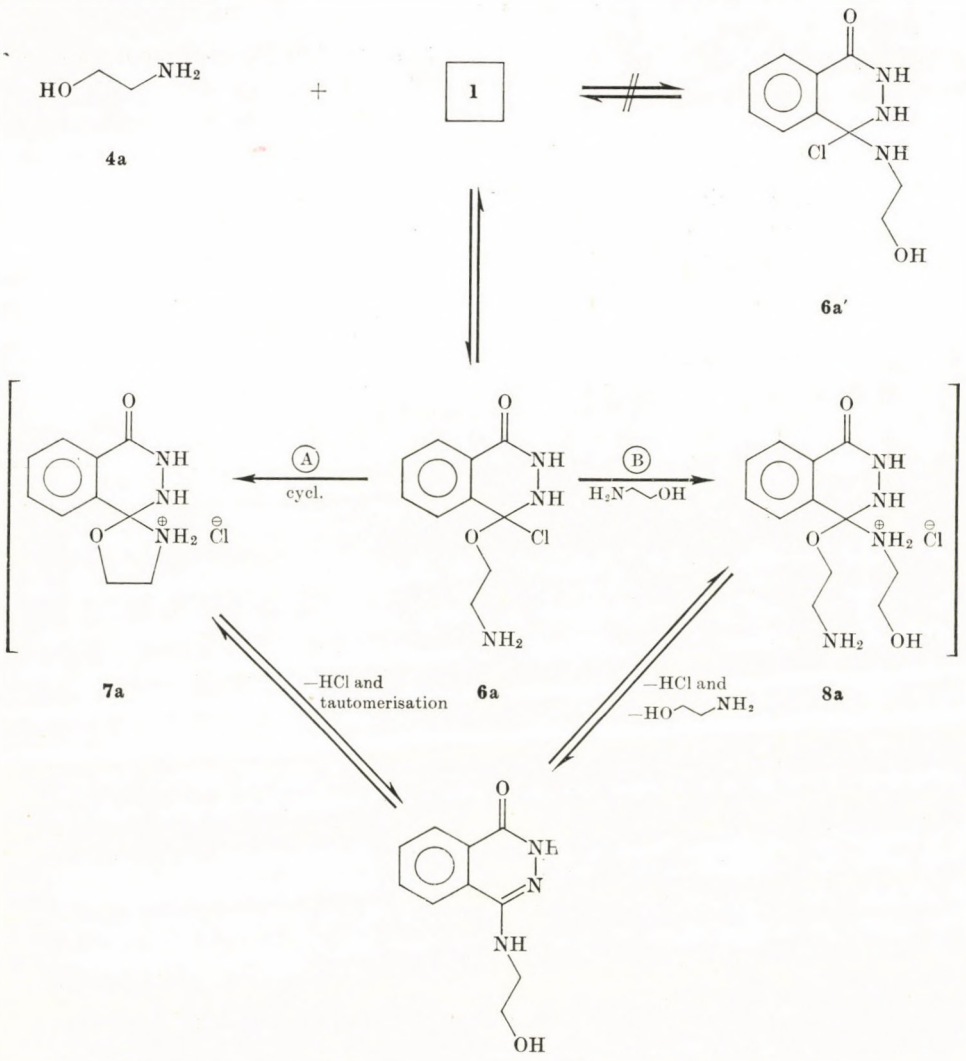
2 (48%) **1** **3** (90%)

According to one of our earlier observations [5], **1** and ethanolamine give very easily 4-(2-hydroxyethylamino)-1(2*H*)-phthalazinone (**5a**), the so-called β-type open desmotrope of spiroxazone. Therefore, this conversion has been studied more extensively. It has been found that the substitution process proceeds with relative ease giving various yields, depending on the structure of the amino alcohol; in general, the reaction is satisfactory from the preparative point of view (see Table I).

The poor reactivity of the chlorophthalazinone (**1**) is due to its structure, because halogens linked to a C-atom adjacent to a double bond, similarly to vinyl halides, are hardly accessible to substitution reactions. The high stability of **1** to alkali solutions (practically no change when boiled with 5% sodium hydroxide for 10 hours) can be attributed to this structure. HILL and EHRLICH [6] reported in 1971 that the rate constant of the nucleophilic substitution process between **1** and sodium methoxide is by orders of magnitude lower, than the substitution rate constant of 1,4-dichlorophthalazinone, known as a reactive compound [3].

According to data in the literature [7] and our own experiences [5, 8], the C = N groups of various heterocycles (among others, spiroxazone derivatives) can reversibly add nucleophilic reagents (*e.g.* water or alcohols). We explain the considerable increase in exchangeability of the chlorine atom in chlorophthalazinone (**1**) in the presence of amino alcohols, on the basis of the facts mentioned above, by transitory alcohol addition (*e.g.* **1** → **6**); the vinyl halide character of **1** ceases by the addition, so that the chlorine atom becomes more mobile.

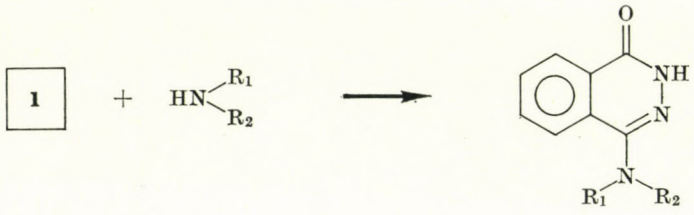
The activating effect of alcohol addition is supported by the fact that **1** reacts with diethylaminoethylamine in the presence of ethylene glycol to give 4-(2-diethylaminoethylamino)-1(2*H*)-phthalazinone (**5k**) in 55% yield, whereas in the absence of ethylene glycol no substitution takes place under identical experimental conditions. At the same time this experiment makes probable that the amino alcohol (*e.g.* ethanolamine) molecule adds to the C = N double bond of **1** primarily by means of its hydroxyl group (→ **6a**), while amine addition (→ **6a'**) seems to be considerably less, or might totally be absent.



According to our assumption, the substitution reaction may proceed with 2- and 3-amino alcohols by two routes (*A* and *B*). According to mechanism *A*, the transitory adduct **6a** formed, *e.g.*, with ethanolamine, gives an α-type spirane (**7a**) in an intramolecular reaction [5], and this is tautomerized in alkaline medium (by the action of the excess amino alcohol) to the non-cyclic β-tautomer (**5a**). Reaction route *B* presumes an intermolecular interaction (**6a** → **8a**), and the process is terminated by the decomposition of the amino alcohol adduct (**8a** → **5a**). This latter mechanism (*B*) may prevail,

Table I

*Reaction of 4-chloro-1-(2H)-phthalazinone (**1**) with amino alcohols (**4**) and with diethylaminoethylamine (**4k**)*



4 **5**

	Amine (4), product (5)		Reaction			Note
	R_1	R_2	temperature, C°	time, hr	Yield, %	
a	H	$-(CH_2)_2-OH$	170	6	88	
b	H	$-(CH_2)_3-OH$	190	6	69	
c	H	$-(CH_2)_4-OH$	180*	5	95	
d	H	$-(CH_2)_5-OH$	180*	5	86	
e	H	$-(CH_2)_6-OH$	180*	5	92	
f	H	$-CH_2-CH(CH_3)-OH$	160	10	83	
g	H	$-CH(C_2H_5)-CH_2-OH$	180	14	24	
				32	70	
				50	—	polymer
h	H	$-C(CH_3)_2-CH_2-OH$	170	50	4.2**	
i	CH_3	$-(CH_2)_2-OH$	160	6	46.1**	about 34%
				8	46.4**	phthalic acid
				12	46.5**	hydrazide by-product
j	Ph	$-(CH_2)_2-OH$	160*	12	—	
k	H	$-(CH_2)_2-N(C_2H_5)_2$	150	20	—	
				20	55	in ethylene glycol solution

* Under reduced pressure or in inert gas atmosphere
** On the basis of chlorine determination

and plays indubitably a role in the reaction with ethylaminoethylamine in ethylene glycol solution (where the formation of an ethylene glycol adduct of type **6** is possible), further in the cases of 4-amino-1-butanol (**4c**), 5-amino-1-pentanol (**4d**) and 6-amino-1-hexanol (**4e**).

2-Amino-1-butanol (**4g**) and particularly 2-amino-2-methyl-1-propanol (**4h**), shielded sterically at the N-terminal, are less reactive (*cf.* Table I). Since 1-amino-2-propanol (**4f**), containing a secondary hydroxyl group, also readily reacts with chlorophthalazinone, successful substitutions can be expected mainly with amino alcohols which are not shielded at the N-terminal; the

process is less influenced by the primary or secondary character of the amino alcohol. A substitution with lower conversion (46%), but proceeding rapidly (within 6 hours at 160°C) can also be achieved with 2-methyl-aminoethanol, which is of the secondary amine type (**4i**). In the case of **4i**, the lower yield is not due to steric reasons, but to an undesired side reaction (formation of phthalic acid hydrazide); such side reactions were not observed in the case of amino alcohols containing primary amino group. 2-Anilinoethanol (**4j**) practically fails to react with chlorophthalazinone under the given experimental conditions (160°C, 12 hours).

The most important infrared spectral data of the hydroxyalkylaminophthalazinone derivatives (**5**) prepared are listed in Table II. The chemical properties and tautomeric transformations of the new compounds will be discussed in a following part of this series.

Table II

*The most important bands in the IR spectra of aminophthalazinone derivatives (**5**) recorded in KBr pellets*

	νNH νOH	ν CO_{amide}	ν Ar	δ NH	ν C—O	1,2-disubst. Ar ring
5b	3450—2800	1639	1591 1475	1559 1533	1077	780
5c	3400—2750	1647	1588 1480	1540 1558	1078	782
5d	3400—2750	1647	1589 1481	1540 1558	1046	782
5e	3400—2800	1648	1590 1480	1559 1541	1080	780
5f	3450—2700	1644	1585 1480	1550 (sh) 1539	 1128	781
5g	3400—2800	1647	1597 1482	1553 1542 (sh)	1050	773
5h	3400—2800	1650	1596 1481	1564 1543	1062	787
5i	3300—2700	1641	1609 1582 1496	—	1080	790
5k	ν NH: 3334 ν NH_{amide}: 3200—2400	1662	1597 1500 1487	1557	—	762

Experimental

M. p. 's were determined with a Boetius micro melting point apparatus. Infrared spectra were recorded in KBr pills with a spectrometer Model UR-10 (Zeiss, Jena).

4-Chlorophthalazinone (1)

This compound was prepared from phthalic acid hydrazide, according to the method of RADULESCU and GEORGESCU [9] in phosphorus oxychloride solution with phosphorus pentachloride, in 93% yield; after recrystallization from glacial acetic acid (300 ml solvent per 20 g of raw product) colourless needles, m. p. 276—278°C (lit. m. p. 274°C, sublimation).

$C_8H_5ClN_2O$ (180.6). Calcd. Cl 19.6 Found Cl 19.5, 19.6%.

IR spectrum: ν NH 3250—2750; ν CO_{amide} 1670; ν Ar 1610, 1592, 1490; 1,2 aromatic disubstitution 775 cm^{-1}.

Stability to alkali solution. 4-Chlorophthalazinone (0.18 g; m. p. 276—278°C) was dissolved in 5% NaOH solution (10 ml) and boiled for 10 hrs. Neutralization after cooling gave back 0.17 g of unchanged substance, which melted completely up to 270°C; as shown by the IR spectrum, it did not contain a detectable quantity of phthalic acid hydrazide. The aqueous mother liquor gave slightly positive chloride reaction.

Calcd. Cl 19.6 Found 19.5%.

4-(2-Hydroxyethylamino)-1(2*H*)-phthalazinone (5a; β-type isomer of spiroxazone [5])

A mixture of 180 g (1 mole) of 4-chlorophthalazinone and 305 g (5 moles) of ethanolamine was gently refluxed 6 hrs in a flask equipped with an air cooling tube. The suspension dissolved in about 1 hr. The excess of ethanolamine was distilled off at reduced pressure (10—20 torr); about 150 g of ethanolamine can be recovered in this way. The distillation residue was diluted with 3 liter of water. The colourless, crystalline substance which separated was filtered off and washed with water to obtain 166—180 g (81—88%) of the product. From a large quantity of water, it crystallized in colourless needles, containing no trace of chlorophthalazinone; m. p. 254—256°C. The IR spectrum was identical with that of an authentic sample prepared as described in the literature [5].

4-(3-Hydroxypropylamino)-1(2*H*)-phthalazinone (5b; β-type isomer of homospiroxazone [5])

According to the process described above (190°C; 6 hrs), 4-chloropthalazinone (18.0 g; 0.1 mole) and 3-aminopropanol (37.5 g; 0.5 mole) gave 15.1 g (69%) of **5b**. From water, it crystallized as colourless, thin needles, m. p. 193—194°C.

$C_{11}H_{13}N_3O_2$ (219.2). — Calcd. C 60.3; H 6.0; N 19.2. Found C 60.4; H 5.9; N 19.3%.

IR spectrum: see Table II.

4-(4-Hydroxybutylamino)-1(2*H*)-phthalazinone (5c)

In a flask equipped with a reflux condenser, a mixture of the chlorophthalazinone (3.6 g; 0.02 mole) and 4-amino-1-butanol (6 g; 0.066 mole) was heated for 5 hrs. at 180°C and 100—150 torr pressure. The homogeneous melt was diluted with 100 ml of water. After neutralization and short standing the colourless crystals were filtered off (4.42 g; 94.8%; no halogen present) and recrystallized; from water: colourless, elongated plates; from ethanol: prisms; m. p. 214—216°C.

$C_{12}H_{15}N_3O_2$ (233.3). Calcd. C 61.8; H 6.5; N 18.0. Found C 61.6; H 6.4; N 18.2%.

IR spectrum: see Table II.

4-(5-Hydroxypentylamino)-1(2*H*)-phthalazinone (5d)

A mixture of the chlorophthalazinone (3.6 g; 0.02 mole) and 5-amino-1-pentanol (6 g; 0.058 mole) was heated 5 hrs as described above, at 180°C and 150—200 torr pressure. Dilution with water gave 4.90 g (86.4%) of a colourless powder, containing only traces of halogen, which crystallized from ethanol in small needles, m. p. 179—180°C.

$C_{13}H_{17}N_3O_2$ (247.3). Calcd. C 63.1; H 6.9; N 17.0. Found C 62.8; H 6.8; N 17.1%.

IR spectrum: see Table II.

4-(6-Hydroxyhexylamino)-1(2*H*)-phthalazinone (5e)

In a small ground flask fitted with an air condenser, a mixture of 6-amino-1-hexanol (3 g; 0.026 mole) and chlorophthalazinone (1.8 g; 0.01 mole) was heated on an oil bath for 5 hrs. at 180°C and 60—80 torr pressure. The melt was mixed with water (100 ml), neutralized with hydrochloric acid, and the solid which separated was filtered off to yield 2.41 g (92%) of

the raw product, which was free of halogens. It was sparingly soluble in water. Colourless powder, m. p. 180—182°C (from ethanol).

$C_{14}H_{19}N_3O_2$ (261.3). Calcd. C 64.3; H 7.3; N 16.1. Found C 64.1; H 7.2; N 16.3%.

IR spectrum: see Table II.

4-(2-Hydroxy-2-methylethylamino)-1(2*H*)-phthalazinone (5f)

A mixture of chlorophthalazinone (9.0 g; 0.05 mole) and 1-amino-2-propanol (18.7 g; 0.25 mole) was gently boiled for 10 hrs and the excess of amino alcohol removed by distillation on a water pump. The solid residue was suspended in water, filtered off and washed with water to obtain 9.13 g (82.8%) of the product. Recrystallization from much water gave colourless, small needles, m. p. 231—233 °C (recrystallization observed between 200 and 210 °C).

$C_{11}H_{13}N_3O_2$ (219.2). Calcd. C 60.3; H 6.0; N 19.2. Found C 60.5; H 6.1; N 19.3%.

IR spectrum: see Table II.

4-(1-Ethyl-2-hydroxyethylamino)-1(2*H*)-phthalazinone (5g)

Chlorophthalazinone (9.0 g; 0.05 mole) was suspended in 2-amino-1-butanol (22.25 g; 0.25 mole), and gently boiled in a flask equipped with an air condenser tube, for the time given in Table I. After cooling, the reaction mixture was diluted with much water, the crystals which separated were filtered off and washed with water until free of chloride. The chloropthalazinone content of the samples was assayed by determining the chlorine content.

Composition of the mixture

Reaction time, hrs.	Cl%	1, %	5g, %
14	15.0	76	24
32	5.8	30	70
50		polymer	

Purification. 1.40 g of the mixture (chlorophthalazinone content 30%) was acetylated in 30 ml of abs. pyridine with 3 ml of acetic anhydride at room temperature. On the next day, water was added to the clear solution, and pyridine was removed by vacuum distillation. The air dry product (1.70 g) was suspended in chloroform (30 ml), the undissolved chlorophthalazinone was removed by filtration, the filtrate was evaporated to dryness and the distillation residue hydrolyzed by boliling for 5 hrs with a mixture of water (30 ml) and conc. HCl (9 ml). The acid solution was evaporated in vacuum, and the residual salt was recrystallized from a large amount of water. Colourless plates; yield 0.80 g; m. p. 246°C.

$C_{12}H_{15}N_3O_2$ (233.3). Calcd. C 61.8; H 6.5; N 18.0. Found C 61.6; H 6.4; N 18.1%.

IR spectrum: see Table II.

4-(1,1-Dimethyl-2-hydroxyethylamino)-1(2*H*)-phthalazinone (5h)

A mixture of 2-amino-2-methyl-1-propanol (22.25 g; 0.25 mole) and chlorophthalazinone (9.0 g; 0.05 mole) was gently boiled for 50 hrs, then diluted with 500 ml of water. The solid product which separated (5.45 g) was filtered off, and washed with water until free of chloride. On the basis of its halogen content (Cl 17.6%) the material was a mixture of chlorophthalazinone (91%) and **5h** (9%). This corresponds to 4.2% yield in the mixture. The mixture was purified in the same way as 4-(1-ethyl-2-hydroxyethylamino)-1(2*H*)-phthalazinone. Recrystallization from a large amount of water yielded microscopic prisms (0.38 g; 3.26%), m. p. 270—271°C.

$C_{12}H_{15}N_3O_2$ (233.3). Calcd. C 61.8; H 6.5; N 18.0. Found C 61.9; H 6.6; N 18.8%.

IR spectrum: see Table II.

4-[N-Methyl-(2-hydroxyethyl)-amino]-1(2*H*)-phthalazinone (5i)

A mixture of chlorophthalazinone (9.0 g; 0.05 mole) and 2-methylaminoethanol (15 g; 0.2 mole) was gently boiled for the time given in Table I. After cooling, the syrup was diluted with water (200 ml), and evaporated in vacuum, while raising the temperature of the bath

gradually to 100°C. The solidifying mass was suspended in a small amount of water, filtered off and washed with water. (From the alkaline mother liquor 2.78 g (34.3%) of phthalic acid hydrazide, identified on the basis of its IR spectrum, separated on acidification with hydrochloric acid.) Yield: 5.05—5.10 g (46.1—46.5%), depending on the duration of heating. Recrystallization from water or from ethanol gave colourless needles, m. p. 138—139 °C.

$C_{11}H_{13}N_3O_2$ (219.2). Calcd. C 60.3; H 6.0; N 19.2. Found C 60.2; H 6.1; N 19.4%.

IR spectrum: see Table II.

Reaction of chlorophthalazinone with 2-anilinoethanol

A mixture of anilinoethanol (4 ml; about 0.03 mole) and chloropthalazinone (1.8 g; 0.01 mole) was heated on a bath at 160°C and about 60 torr pressure for 12 hrs. The mixture which solidified on cooling, was suspended in 50% aqueous ethanol, filtered, and the solid washed with 50% ethanol. As shown by the IR spectrum, the resulting colourless, crystalline substance (1.75 g) was unchanged chlorophthalazinone.

4-(2-Diethylaminoethylamino)-1(2*H*)-phthalazinone (5k)

(*a*) A mixture of anhydrous diethylaminoethylamine (5 ml) and chlorophthalazinone (0.90 g; 0.005) mole was boiled for 20 hrs. The amine was removed by vacuum distillation, the solid residue suspended in water and filtrred. 0.85 g of unchanged chloropthalazinone was obtained, which was identified on the basis of the IR spectrum.

(*b*) A mixture of chlorophthalazinone (4.5 g; 0.025 mole), diethylaminoethylamine (6.4 g; 0.05 mole) and ethylene glycol (20 ml) was heated for 20 hrs on a bath at 150°C. The volatile components were removed on a water pump, distilling from a bath of 190—200 °C. The distillation residue, which solidified to a hard resin on cooling, was covered with 250 ml of water; this caused disintegration into a colourless powder. The substance obtained on filtration (1.43 g) was unchanged chlorophthalazinone. The volume of the aqueous filtrate was reduced by evaporation to about 50 ml, and made alkaline with solid sodium hydroxide. The emulsion produced crystallized on rather long standing to yield 3.63 g (55.4%) of the product. Recrystallization from hot water and clarification with activated carbon gave colourless prisms, m. p. 168—170 °C.

$C_{14}H_{20}N_4O$ (260.3). Calcd. C 64.6; H 7.7; N 21.5. Found C 64.7; H 7.5; N 21.3%.

IR spectrum: see Table II.

*

The author's thanks are due to Dr F. RUFF for his help in the evaluation of the infrared spectra. The elementary analyses were made in the microanalytical laboratory (leader: Dr. H. MEDZIHRADSZKY). The BRISTOL Laboratories (USA, Syracuse, N. Y.) supported our work by supplying the starting materials. Their help is gratefully acknowledged.

REFERENCES

[1] STEPHENSON, E. F. M.: J. Chem. Soc. **1944,** 678
[2] KÖHLER, W., BUBNER, M., ULBRICHT, G.: Chem. Ber. **100,** 1073 (1967)
[3] HAWORTH, R. D., ROBINSON, S.: J. Chem. Soc. **1948,** 777
[4] FLITSCH, W., PETERS, H.: Chem. Ber. **102,** 1304 (1969)
[5] KÖRMENDY, K., SOHÁR, P., PFISZTNER-FREUD, Á., RUFF, F.: Acta Chim. Acad. Sci. Hung. **60,** 151 (1969)
[6] HILL, J. H. M., EHRLICH, J. H.: J. Org. Chem. **36,** 3248 (1971)
[7] ALBERT, A.: Angew. Chem. **79,** 913 (1967)
[8] KÖRMENDY, K.: Amine, amide and hydrazine additions of cyclic imino ethers. Thesis. In Hungarian. Budapest 1965
[9] RADULESCU, D., GEORGESCU, V.: Bull. soc. chim. **37,** 881 (1925)

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BASICHE DERIVATE VON GLUTAMYLPEPTIDEN, III

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Es wurden die basischen Glutamylpeptide: α- und γ-Tri-L-glutaminsäure-tetra-(2-dimethylamino-äthyl)-amid (**XIV**; $n = 3$ und **XVI**; $n = 3$), α-Tetra-L-glutaminsäure-penta-(2-dimethylaminoäthyl)-amid (**XIV**; $n = 4$), α-Penta-L-glutaminsäure-hexa-(2-dimethylamino-äthyl)-amid (**XIV**; $n = 5$), α-Tri-[L-glutaminsäure-γ-(2-dimethylamino-äthyl)-amid] (**XX**; $n = 3$) und L-Pyroglutamyl-L-glutaminsäure-di-(2-dimethylamino-äthyl)-amid (**XVIII**) hergestellt, und zwar durch Umsetzung der entsprechenden zwei, drei, vier bzw. fünf und sechs aktive Estergruppen enthaltenden Carbobenzoxy-L-oligoglutaminsäure-Derivate (**III, VI, VIII, X**) mit berechneten Mengen von 2-Dimethylamino-äthylamin und darauffolgender hydrogenolytischer Abspaltung der Schutzgruppen.

Die Verbindungen **III, VI, VIII, X** wurden aus den entsprechenden Derivaten der L-Glutaminsäure aufgebaut, deren Carboxylgruppen, die in die Peptidbindung nicht einbezogen werden sollten, in Form von *p*-Nitrophenylestergruppen geschützt waren. Die peptidische Verknüpfung der Komponenten erfolgte durch Aktivierung der freien Carboxylgruppe der acylierenden Komponente durch Bildung eines gemischten Anhydrids. Eine in einem Fall beobachtete Nebenreaktion wird diskutiert.*

In unseren früheren Mitteilungen [1, 2] hatten wir über die Synthese der isomeren 2-Dimethylamino-äthylamide und des bis-Dimethylamino-äthylamid der L-Glutaminsäure, weiterhin der in verschiedenen Stellungen mit 2-Dimethyl-amino-äthylamin amidierten Derivate der α- und γ-L-Glutamyl-L-glutaminsäure berichtet. Als Fortsetzung dieser Arbeit berichten wir jetzt über die Synthese der mit 2-Dimethylaminoäthylamin 3, 4, 5, 6 fach amidierten Derivate einiger Oligopeptide der L-Glutaminsäure und über ein basisches Derivat der Pyroglutamyl-L-glutaminsäure.

Die mit 2-Dimethylamino-äthylamin zwei- und dreifach amidierten Glutamyl-glutaminsäuren (**XIV, XVI, XX**; $n = 2$) wurden schon [2] aus den entsprechenden, geschützten, zwei bis drei aktive Estergruppen enthaltenden Glutamyl-glutaminsäure-Derivaten hergestellt.

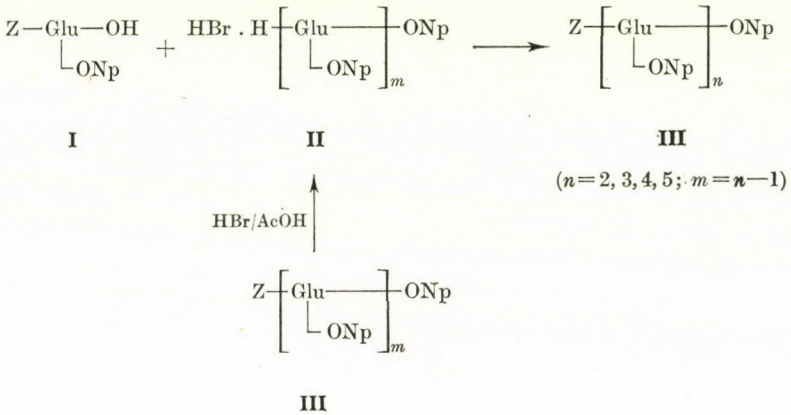
Die aktive Estergruppen enthaltenden, geschützten L-Glutamyl-L-glutaminsäure-Derivate (**III, VI, X**; $n = 2$) wurden aus solchen L-Glutaminsäure-Derivaten aufgebaut, deren Carboxylgruppen, die in die Peptidbindung nicht einbezogen werden sollten, mit *p*-Nitrophenol verestert waren [2]. Wir haben gefunden, daß die Umsetzung der aufgezählten Komponenten zu den entsprechenden Dipeptidderivaten durch Anwendung der Methode der gemischten Anhydride mit recht guter Ausbeute verläuft. Die hergestellten, aktive Ester-

* Die in dieser Arbeit gebrauchten, abgekürzten Bezeichnungen der Aminosäuren, Aminosäuresreste, Schutzgruppen und Reagenzien richten sich nach dem Vorschlag der IUPAC-IUB Commission in Biochemical Nomenclature (siehe z. B. J. Biol. Chem. **241**, 527, 2491 (1966).

gruppen enthaltenden, geschützten L-Glutamyl-L-glutaminsäure- Derivate wurden dann unter ganz milden Reaktionsbedingungen mit 2-Dimethylaminoäthylamin zu den entsprechenden basischen Amidderivaten umgesetzt (**XIII**, **XV**, **XIX**; $n = 2$) [2].

Im Laufe unserer neueren Untersuchungen gelang es uns, dieses oben beschriebene Prinzip für die Synthese der basischen Derivate von Glutamyloligopeptiden zu verwenden.

Die aktive Estergruppen in höchster Zahl enthaltenden, geschützten α-Glutamyl-oligopeptide (**III**) wurden mit der "stepwise" Methode aufgebaut. An die entsprechenden C-terminalen Peptidkomponenten, deren Carboxylgruppen in Form von *p*-Nitrophenylestern geschützt waren, wurde Carbobenzoxy-L-glutaminsäure-γ-*p*-nitrophenylester (**I**) [1] angeknüpft:

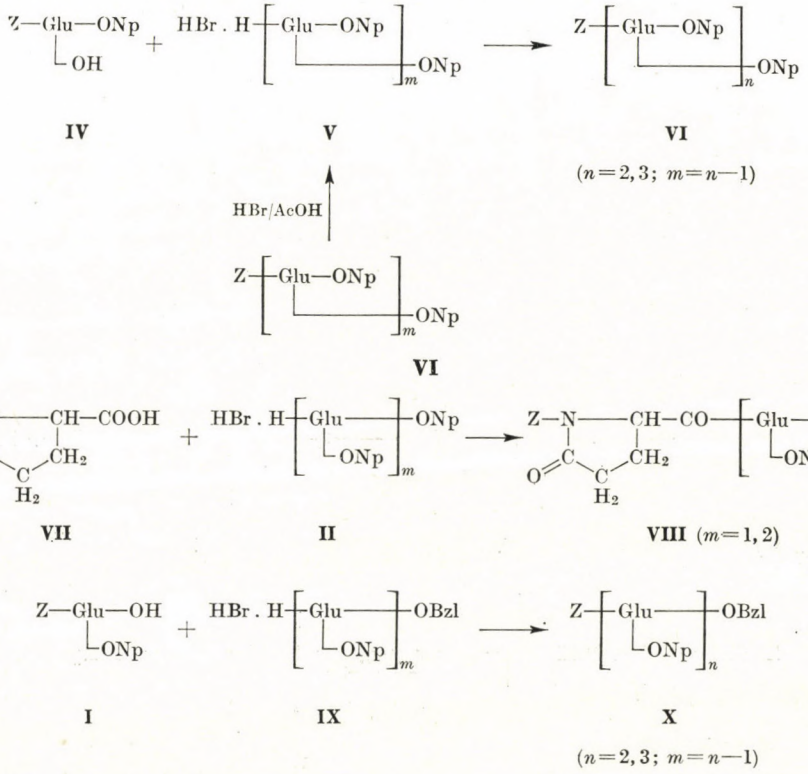


Aus diesem geschützten Derivat kann die folgende C-terminale Komponente der Serie durch Acidolyse mit HBr/AcOH gewonnen werden. Die Serie wurde bis zur Gliederzahl $n = 5$ fortgesetzt.

Wir haben gefunden, daß gute Ausbeuten bei der Peptidknüpfung sich durch Anwendung der Methode der gemischte Anhydride erreichen ließen, besonders dann, wenn zur Bereitung des gemischten Anhydrids des Carbobenzoxy-L-glutaminsäure-γ-*p*-nitrophenylesters Chlorameisensäure-isobutylester eingesetzt wurde.

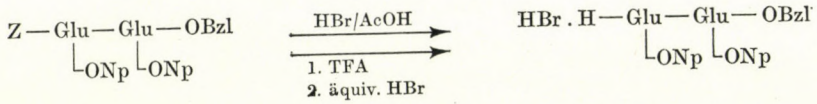
Die C-terminalen Peptidkomponenten bzw. deren Hydrobromide (**II**) waren aus den bereits hergestellten Carbobenzoxy-geschützten Derivaten (**III**) durch Einwirkung von Bromwasserstoff-Eisessig gewinnbar. Beim Verdünnen des Reaktionsgemisches mit Äther fiel das Hydrobromid in kristalliner Form aus und ließ sich dann in Acetonitril, nach Zusatz von Triäthylamin, mit Carbobenzoxy-L-glutaminsäure-γ-*p*-nitrophenylester (**I**) durch Anwendung der Anhydrid-Methode glatt zu dem entsprechenden Endprodukt umsetzen, das sich beim Verrühren des Reaktionsgemisches mit verdünnter Salzsäure gleich in kristalliner Form ausschied.

Bei der Analyse der erhaltenen Oligopeptidderivate wurde auf die quantitative Bestimmung der *p*-Nitrophenylestergruppen stets großes Gewicht gelegt. Diese Bestimmung ließ sich mit großer Genauigkeit auf spektroskopischem Wege durchführen, nämlich durch Ermittlung der Extinktion bei 400 nm in 0,1*N* Natronlauge. Nach dem Erfolg dieser Versuche waren wir bestrebt, auch einige andere Glutamylpeptide herzustellen, z.B.: γ-Glutamylpeptide, Pyroglutamylpeptide und solche α-Glutamylpeptide, deren C-terminale α-Carboxylgruppen in Form von Benzylestern vorlagen.



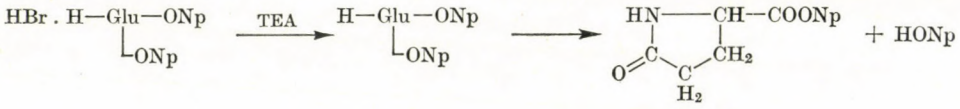
Zum Anknüpfen der N-terminalen Komponente wurden Carbobenzoxy-L-glutaminsäure-α-*p*-nitrophenylester (**IV**) [2], Carbobenzoxy-L-glutaminsäure-γ-*p*-nitrophenylester (**I**) [1] und Carbobenzoxy-L-pyroglutaminsäure (**VII**) [3] angewandt.

In den ersten zwei Fällen wurden die früher hergestellten Hydrobromide (**V, II**), im dritten Fall wurde das α-L-Glutamyl-(γ-*p*-nitrophenylester)-L-glutaminsäure-α-benzyl-γ-*p*-nitrophenylester-hydrobromid (**IX**; $m = 2$) jetzt als C-terminale Komponente gewählt. Nach unseren Erfahrungen kann dieses Hydrobromid (**IX**; $m = 2$) aus Carbobenzoxy-α-L-glutamyl-(γ-*p*-nitrophenylester)-L-glutaminsäure-α-benzyl-γ-*p*-nitrophenylester (**X**; $n = 2$) durch Acidolyse gewonnen werden:

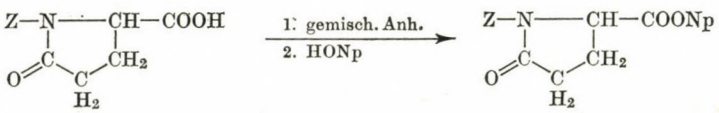


X ($n = 2$) **IX** ($m = 2$)

Wir haben gefunden, daß nur eine sehr beschränkte Einwirkungsdauer — einige Minuten — des Bromwasserstoff-Eisessigs zur Herstellung des Hydrobromids notwendig ist [2]. Es war aber vorteilhafter, nach der Methode von KHOSLA *et al.* [4] für die selektive Acidolyse Trifluoressigsäure zu benützen. Bei dieser Methode verläuft die Spaltung der Carbobenzoxy-Gruppe ohne Acidolyse der Benzylestergruppe. Nur in einem einzigen Fall konnte die Entstehung eines unerwünschten Nebenproduktes dieser Reaktionen beobachtet werden: bei der Herstellung des Pyroglutaminsäurederivates (**VIII**; $m = 1$) wurde aus der Mutterlauge als Nebenprodukt Carbobenzoxy-L-pyroglutaminsäure-*p*-nitrophenylester (**XII**) [5] isoliert. Dies wird verständlich, wenn man annimmt, daß aus der anzuknüpfenden C-terminalen Komponente (**Va**) durch intramolekulare Acylierung wenig Pyroglutaminsäure-*p*-nitrophenylester und *p*-Nitrophenol entsteht (**Va** → **XI** + HONp). Letzteres würde dann mit dem aus der Carbobenzoxy-L-pyroglutaminsäure hergestellten gemischten Anhydrid sofort weiter reagieren.

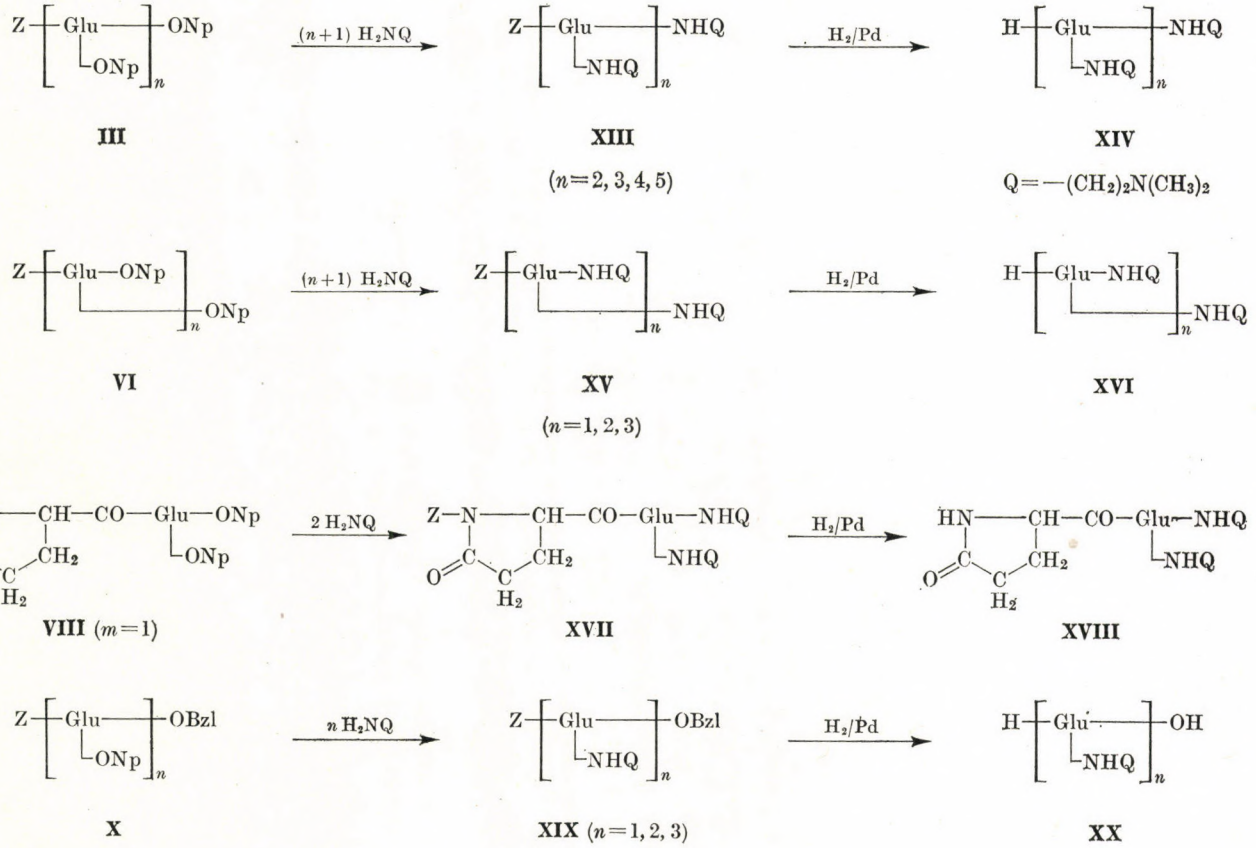


V (n=1) **Va** **XI**



VII **XII**

Es gelang uns, die Amidierung der Glutamyloligopeptidderivate (**III, VI, VIII, X**) durch Einwirkung der berechneten Menge von 2-Dimethylamino-äthylamin (Q-NH_2 in den Formeln) in Essigester bei Raumtemperatur. Die in Essigester weniger löslichen Komponenten wurden durch Zusatz von etwas Dimethylformamid in Lösung gebracht. Die auf diese Weise hergestellten, mehrere 2-Dimethylamino-äthylamid-Gruppen enthaltenden Oligopeptidderivate fielen unmittelbar (oder nach Zusatz von Äther) aus dem Reaktionsgemisch als Kristallprodukte an. Zum Schluß wurde die N-terminale Schutzgruppe (und die C-terminale Benzylestergruppe) der gewonnenen basischen Oligopeptidderivate durch Hydrogenolyse entfernt:


Z-[Glu(ONp)-ONp]n-ONp
(n+1) H2NQ
Z-[Glu(NHQ)-NHQ]n-NHQ
H2/Pd
H-[Glu(NHQ)-NHQ]n-NHQ
III
XIII
(n=2, 3, 4, 5)
XIV
Q=—(CH2)2N(CH3)2
Z-[Glu-ONp]n-ONp
(n+1) H2NQ
Z-[Glu-NHQ]n-NHQ
H2/Pd
H-[Glu-NHQ]n-NHQ
VI
XV
(n=1, 2, 3)
XVI
Z-N-CH-CO-Glu-ONp
2 H2NQ
Z-N-CH-CO-Glu-NHQ
H2/Pd
HN-CH-CO-Glu-NHQ
VIII (m=1)
XVII
XVIII
Z-[Glu(ONp)]n-OBzl
n H2NQ
Z-[Glu(NHQ)]n-OBzl
H2/Pd
H-[Glu(NHQ)]n-OH
X
XIX (n=1, 2, 3)
XX

Die Reinheit und Identität der Produkte und Endprodukte wurde durch Elementaranalysen, Infrarotspektren, titrimetrisch bestimmten Äquivalentzahlen, elektrophoretischen und chromatographischen Untersuchungen und schließlich durch Abbau mit Leucinaminopeptidase vielseitig geprüft.

Über weitere enzymatische Untersuchungen der hergestellten basischen Derivate von Glutaminsäure-oligopeptiden wird in anderen Mitteilungen [6] berichtet.

Beschreibung der Versuche

Die Äquivalentzahl der beschriebenen basischen Amidderivate wurde durch Titrierung ihrer Lösung in 99,9%iger Essigsäure mit einer 0,1*N* essigsauren Perchlorsäurelösung unter Anwendung von Kristallviolett als Indikator [1, 2] bestimmt.

Bestimmung der p-Nitrophenylester-Gruppen [2]

Es wurde die Extinktion einer Lösung von 1,0 mg der zu untersuchenden Substanz in 25 ml 0,1*N* Natronlauge bei 400 nm gemessen. Das als Vergleichssubstanz herangezogene *p*-Nitrophenol hat bei dieser Wellenlänge eine molare Extinktion von 18400.

Bestimmung der R_F-Werte

durch Dünnschichtchromatographie an Silikagel-G (Stahl, Merck).
Lösungsmittel:
1 = *n*-Butanol–Essigsäure–Wasser 4 : 1 : 5
2 = *sek*-Butanol-85%-ige Ameisensäure–Wasser 75 : 15 : 10
3 = Propanol–Wasser 7 : 3
4 = *n*-Butanol–Essigsäure–Wasser 4 : 1 : 1
5 = *n*-Butanol–Essigsäure–Pyridin–Wasser 30 : 6 : 20 : 24
6 = *n*-Butanol–Essigsäure–Pyridin–Wasser 30 : 60 : 20 : 24
7 = Essigester–Pyridin–Eisessig–Wasser 60 : 20 : 60 : 11
8 = Acetonitril–Essigsäure–Chloroform 6 : 1 : 3
9 = Chloroform–Essigsäure 95 : 5
10 = *n*-Butanol–Dimethylformamid–Essigsäure–Pyridin–Wasser 15 : 15 : 60 : 20 : 24

Die elektrophoretische Charakterisierung der Syntheseprodukte erfolgte bei 1500 V, pH 1,8 und einer Laufzeit von 1,5 Stunden [6]. Als Trägermaterial diente Whatman-1-Papier.

Der *enzymatische Abbau* der Syntheseprodukte wurde mit Leucinaminopeptidase unter Standardbedingungen durchgeführt und elektrophoretisch untersucht [6].

Allgemeines Verfahren zur Herstellung aktive Estergruppen enthaltender Glutamylpeptide

Eine stark gerührte und gekühlte (—20 °C) Lösung von 2,01 g (5,0 mmol) Carbobenzoxy--L-glutaminsäure -*γ*-*p*-nitrophenylester (**I**) [1] und 0,70 ml (5,0 mmol) Triäthylamin in 35 ml Acetonitril wird tropfenweise mit 0,70 ml (5,0 mmol) Chlorameisensäure-isobutylester, nach 20 Minuten mit 5,0 mmol des entsprechenden Aminosäure- oder Peptidester-hydrobromids in mehreren Portionen und abermals tropfenweise mit einer Lösung von 0,70 ml (5,0 mmol) Triäthylamin in 5 ml kaltem Acetonitril versetzt. Man rührt noch zwei—drei weitere Stunden bei —20 °C und vermengt das Gemisch mit 300 ml 0,05*N* Salzsäure. Das kristallin ausgeschiedene Produkt wird am nächsten Tag abfiltriert, mit Wasser gewaschen, getrocknet und schließlich umkristallisiert.

Allgemeines Verfahren zur Herstellung von mit aktiven Estergruppen völlig veresterten Glutamylpeptidester-hydrobromiden

Eine Suspension von 1 g Carbobenzoxy-glutamylpeptidester in 3 ml Eissessig wurde bei Raumtemperatur mit 3 ml 30%iger Bromwasserstoff-Essigsäure versetzt und die klare Lösung nach 30—60 Minuten in 100 ml Äther gegossen. Nach einigen Tagen wurde der Niederschlag abfiltriert, mit Äther gewaschen, im Vakuumexsiccator über Ätzkali und konz. Schwefelsäure getrocknet.

α-L-Glutamyl-(γ-p-nitrophenylester)-L-glutaminsäure-di-p-nitrophenylester-hydrobromid (II; $m = 2$)

wurde nach dem allgemeinen Verfahren aus Carbobenzoxy-α-L-glutamyl-(γ-*p*-nitrophenylester)-L-glutaminsäure-di-*p*-nitrophenylester (**III**; $m = 2$) [2] hergestellt. Ausbeute 0,9 g (96,9% d. Th.). Schmp. 106—109 °C; $[\alpha]_D^{20} = -6{,}1°$ ($c = 2{,}1$; Dimethylformamid). $R_F =$ = 0,4(3), 0,5(1).

$C_{28}H_{26}N_5O_{13}Br$ (720,5). Ber. C 46,6; H 3,6; N 9,7; Br 11,1; ONp 57,1. Gef. C 45,9; H 4,0; N 9,6; Br 10,4; ONp 56,5%.

Carbobenzoxy-α-tri-L-glutaminsäure-tetra-p-nitrophenylester (III; $n = 3$)

Es wurden nach dem allgemeinen Verfahren aus Carbobenzoxy-L-glutaminsäure-γ-*p*-nitrophenylester (**I**) und α-L-Glutamyl-(γ-*p*-nitrophenylester)-L-glutaminsäure-di-*p*-nitrophenylester-hydrobromid (**II**; $n = 2$) 3,6 g (70% d. Th.) des aus Acetonitril umkristallisierten Tripeptidderivates gewonnen. Schmp. 185—186 °C, $[\alpha]_D^{20} = -25{,}2°$ ($c = 2$, Dimethylformamid); $R_F = 0{,}05(9)$.

$C_{47}H_{41}O_{20}N_7$ (1023,8). Ber. C 55,1; H 4,0; N 9,5; Z 13,1; ONp 54,0. Gef. C 54,7; H 4,2; N 8,9; Z 13,1; ONp 53,8%.

Charakteristische Banden des IR-Spektrums (KBr-Tablette): $\nu_{C=O}$ (COONp): 1765 cm^{-1}, $\nu_{C=O}$ (Z): 1700 cm^{-1}, $\nu_{C=O}$ (Amid-I): 1645 cm^{-1}.

α-Tri-L-glutaminsäure-tetra-p-nitrophenylester-hydrobromid (II; $m = 3$)

wurde nach dem allgemeinen Verfahren aus Carbobenzoxy-α-tri-L-glutaminsäure-tetra-*p*-nitrophenylester (**III**; $m = 3$) hergestellt. Ausbeute 0,72 g (71% d. Th.). Schmp. 166—168 °C; $[\alpha]_D^{20} = -14{,}2°$ ($c = 0{,}7$; Dimethylformamid); $R_F = 0{,}47(4)$.

$C_{39}H_{36}N_7O_{18}Br$ (970,7). Ber. C 48,2; H 3,7; N 10,1; ONp 56,9. Gef. C 48,0; H 4,0; N 9,8; ONp 55,3%.

Carbobenzoxy-α-tetra-L-glutaminsäure-penta-p-nitrophenylester (III; $m = 4$)

Es wurde nach dem allgemeinen Verfahren aus Carbobenzoxy-L-glutaminsäure-γ-*p*-nitrophenylester (**I**) und α-tri-L-Glutaminsäure-tetra-*p*-nitrophenylester-hydrobromid (**II**; $n = 3$) 3,8 g (60% d. Th.) des aus Acetonitril umkristallisierten Tetrapeptidderivates gewinnen. Schmp. 169—171 °C; $[\alpha]_D^{20} = -19{,}6°$ ($c = 1{,}0$; Dimethylformamid); $R_F = 0{,}9(4)$.

$C_{58}H_{51}O_{25}N_9$ (1274,0). Ber. C 54,6; H 4,1; N 9,9; ONp 54,2. Gef. C 54,8; H 4,5; N 9,3; ONp 52,5%.

Charakteristische Banden des IR-Spektrums (KBr-Tablette): $\nu_{C=O}$ (COONp): 1768 cm^{-1}, $\nu_{C=O}$(Z): 1700 cm^{-1}, $\nu_{C=O}$ (Amid—I): 1650 cm^{-1}.

α-Tetra-L-glutaminsäure-penta-p-nitrophenylester-hydrobromid (II; $m = 4$)

wurde nach dem allgemeinen Verfahren aus 1 mmol Carbobenzoxy-α-tetra-L-glutaminsäure--penta-*p*-nitrophenylester (**III**; $m = 4$) hergestellt, und aus Tetrahydrofuran–Äther umkristallisiert. Ausbeute 0,85 g (70% d. Th.). Schmp.; 157—159 °C. $[\alpha]_D^{20} = -11{,}2°$ ($c = 2$; Dimethylformamid); $R_F = 0{,}38(3)$, 0,2(4).

$C_{50}H_{46}O_{23}N_9Br$ (1219,9). Ber. C 49,2; H 3,8; N 10,4; Br 6,5; ONp 56,5. Gef. C 49,9; H 4,2; N 10,2; Br 6,1; ONp 54,4%.

Carboxybenzoxy-α-penta-L-glutaminsäure-hexa-p-nitrophenylester (III; $n = 5$)

wurde nach dem allgemeinen Verfahren aus Carbobenzoxy-L-glutaminsäure-γ-*p*-nitrophenylester (**I**) bzw. aus dessen gemischtem Anhydrid und α-Tetra-L-glutaminsäure-penta-*p*-nitrophenylester- hydrobromid (**II**; $m = 4$) hergestellt. Die aus Acetonitril–Äther dreimal umkristallisierte Substanz wog 0,51 g (44% d. Th.). Schmp. 166—167 °C.

$C_{69}H_{61}O_{30}N_{11}$ (1524,3). Ber. C 54,6; H 3,9; ONp 54,6. Gef. C 54,2; H 4,3; ONp 53,2%.

Charakteristische Banden des IR-Spektrums (KBr-Tablette): $\nu_{C=O}$(COONp): 1765 cm^{-1}, $\nu_{C=O}$(Z): 1700 cm^{-1}; $\nu_{C=O}$(Amid—I): 1645 cm^{-1}.

γ-L-Glutamyl-(α-p-nitrophenylester)-L-glutaminsäure-di-p-nitrophenylester-hydrobromid (V; $m = 2$)

wurde nach dem allgemeinen Verfahren aus Carbobenzoxy-γ-L-glutamyl-(α-*p*-nitrophenylester)--L-glutaminsäure-*p*-nitrophenylester (**VI**; $m = 2$) hergestellt. Ausbeute 0,69 g (73,8% d. Th.). Schmp. 152—155 °C.

$C_{28}H_{26}O_{13}N_5Br$ (720,4). Ber. ONp 57,7. Gef. ONp 56,9%.

Carbobenzoxy-γ-tri-L-glutaminsäure-tetra-p-nitrophenylester (VI; $n = 3$)

Es wurden nach dem allgemeinen Verfahren (Lösungsmittel: Acetonitril–Dimethylformamid 3 : 1) aus Carbobenzoxy-L-glutaminsäure-α-*p*-nitrophenylester (**IV**) und γ-L-Glutamyl-(α-*p*-nitrophenylester)-L-glutaminsäure-di-*p*-nitrophenylester-hydrobromid (**V**; $m = 2$) 4,1 g (79,8% d. Th.) des aus Äthanol und einmal aus Acetonitril umkristallisierten Tripeptidderivates gewonnen. Schmp. 185—187 °C; $[\alpha]_D^{20} = -31{,}0°$ ($c = 2$; Dimethylformamid).

$C_{47}H_{41}O_{20}N_7$ (1023,9). Ber. C 54,9, H 4,0, N 9,5, ONp 54,0. Gef. C 55,1, H 4,2, N 8,9, ONp 53,7%.

Charakteristische Banden des IR-Spektrums (KBr-Tablette): $\nu_{C=O}$(COONp): 1765 cm^{-1}; $\nu_{C=O}$(Z): 1700 cm^{-1}; $\nu_{C=O}$(Amid—I): 1645 cm^{-1}.

Carbobenzoxy-L-pyroglutamyl-L-glutaminsäure-di-p-nitrophenylester (VIII; $m = 1$)

wurde nach dem allgemeinen Verfahren aus Carbobenzoxy-L-pyroglutaminsäure (**VII**) (Lösungsmittel: Acetonitril–Dimethylformamid 10 : 1) und L-Glutaminsäure-di-*p*-nitrophenylesterhydrobromid (**II**; $m = 1$) [2] hergestellt. Die aus Äthanol umristallisierte Substanz wog 1,15 g (36,4% d. Th.). Schmp: 179—180 °C. $[\alpha]_D^{20} = -40{,}5°$ ($c = 2$; Dimethylformamid).

$C_{30}H_{26}O_{12}N_4$ (644,5). Ber. C 56,9; H 4,1; N 8,8; ONp 42,7. Gef. C 57,2; H 4,4; N 8,5; ONp 41,9%.

Charakteristische Banden des IR-Spektrums (KBr-Tablette): $\nu_{C=O}$(COONp): 1765 cm^{-1}; $\nu_{C=O}$ (Amid—I): 1660 cm^{-1}; ν_{OCNCO}: 1765 und 1700 cm^{-1}.

Aus der Mutterlauge der Kristallisation war Carbobenzoxy-L-pyroglutaminsäure-*p*-nitrophenylester (**XII**) nach zweitägigem Stehen ausgeschieden. 0,50 g (26% d. Th.). Schmp: 138—140°. $[\alpha]_D^{20} = -51{,}0$ °C ($c = 1{,}09$; Tetrahydrofuran). Literaturangabe [5]: Schmp. 140—141°; $[\alpha]_D^{20} = -50{,}6$ °C ($c = 1{,}01$; Tetrahydrofuran).

$C_{19}H_{16}O_7N_2$ (384,3). Ber. C 59,5; H 4,2, N 7,3, ONp 31,8. Gef. C 59,5, H 4,6, N 7,1 ONp 31,2%.

Charakteristische Banden des IR-Spektrums (KBr-Tablette): $\nu_{C=O}$ (COONp): 1765 cm^{-1}; ν_{OCNCO}: 1780 und 1702 cm^{-1}; $\nu_{C=O}$(Z): 1690 cm^{-1}.

α-L-Glutamyl-(γ-p-nitrophenylester)-L-glutaminsäure-α-benzyl-γ-p-nitrophenylester-hydrobromid (IX; $m = 2$)

Verfahren A. Man versetzte eine Lösung von 1 g (1,2 mmol) Carbobenzoxy-α-L-glutamyl-(γ-*p*-nitrophenylester)-L-glutaminsäure-α-benzyl-γ-*p*-nitrophenylester (**X**; $n = 2$) in 5 ml Eisessig mit 5 ml 30%igem Bromwasserstoff-Eisessig und goß nach 4 Minuten die klare Lösung zu 200 ml Äther. Nach zweitägigem Stehen wurde der ausgeschiedene flockige Niederschlag abfiltriert, mit Äther gewaschen und im Vakuumexsiccator über Ätzkali und konz. Schwefelsäure getrocknet. Ausbeute 0,65 g (69,5% d. Th.). Schmp. 150—151 °C; $[\alpha]_D^{20} = -21{,}9$ °C ($c = 1{,}5$; Dimethylformamid); $R_F = 0{,}77(6)$.

$C_{29}H_{29}N_4O_{11}Br$ (689,3). Ber. C 50,5, H 4,2, ONp 40,0. Gef. C 51,0. H 4,5, ONp 39,4%.

Charakteristische Banden des IR-Spektrums (KBr-Tablette): $\nu_{C=O}$(COOBzl): 1740 cm^{-1}; $\nu_{C=O}$(COONp): 1760 cm^{-1}; $\nu_{C=O}$(Amid—I): 1650 cm^{-1}; ν_{N-C}(Amid—II): 1530 cm^{-1}.

Verfahren B. Eine Lösung von 1 g (1,2 mmol) Carbobenzoxy-α-L-glutamyl-(γ-*p*-nitrophenylester)-L-glutaminsäure-α-benzyl-γ-*p*-nitrophenylester (**X**; $n = 2$) in 12 ml Trifluoressigsäure ließ man drei Stunden bei 38 °C stehen und trieb danach das Lösungsmittel bei Unterdruck ab. Der Rückstand wurde mit 1 ml 30%igem Bromwasserstoff-Eisessig verrührt und die klare Lösung in 200 ml Äther gegossen. Nach einigen Tagen wurde der Niederschlag abfiltriert, mit Äther gewaschen, im Vakuumexsiccator über Ätzkali und konz. Schwefelsäure getrocknet und aus Eisessig–Äther umkristallisiert. Ausbeute 0,60 g (65,2% d. Th.), Schmp. 154—155 °C; $R_F = 0{,}93(7)$.

Ber. C 50,5, H 4,2, ONp 40,0. Gef. C 50,8, H 4,5, ONp 39,3%.

Carbobenzoxy-α-di-L-glutamyl-(γ-p-nitrophenylester)-L-glutaminsäure-α-benzyl-γ-p-nitrophenylester (X; $n = 3$)

wurde nach dem allgemeinen Verfahren aus Carbobenzoxy-L-glutaminsäure-γ-*p*-nitrophenylester (**I**) und α-L-Glutamyl(γ-*p*-nitrophenylester)-L-glutaminsäure-α-henzyl-γ-*p*-nitrophenylester-hydrobromid (**IX**; $m = 2$) hergestellt und aus Äthanol umkristallisiert. Ausbeute 2,6 g (53,0% d. Th.).

Schmp. 166—168 °C, $[\alpha]_D^{20} = -39{,}6°$ ($c = 1{,}0$; Dimethylformamid), $R_F = 0{,}49(7)$.

$C_{49}H_{44}N_6O_{18}$ (992,0). Ber. C 58,2, H 4,4, ONp 41,6. Gef. C 58,0, H 4,7, ONp 40,7%.

Charakteristische Banden des IR-Spektrums (KBr-Tablette): $\nu_{C=O}$(COOBzl): 1730 cm^{-1}; $\nu_{C=O}$(COONp): 1765 cm^{-1}; $\nu_{C=O}$(Z): 1695 cm^{-1}; $\nu_{C=O}$(Amid—I) 1655 cm^{-1}; ν_{N-C} (Amid—II): 1530 cm^{-1}; ν_{NH}: 3300 cm^{-1}.

Carbobenzoxy-L-pyroglutamyl-α-L-glutamyl-(γ-p-nitrophenylester)-L-glutaminsäure-di-p-nitrophenylester (VIII; $m = 2$)

wurde nach dem allgemeinen Verfahren (Lösungsmittel: Acetonitril–Dimethylformamid 10 : 1) aus Carbobenzoxy-L-pyroglutaminsäure (**VII**) und α-L-Glutamyl(γ-*p*-nitrophenylester)-L-glutaminsäure-di-*p*-nitrophenylester-hydrobromid (**II**; $m = 2$) hergestellt. Die aus Äthanol zweimal umkristallisierte Substanz wog 1 g (37,4% d. Th.). Schmp. 100—102 °C.

$C_{41}H_{36}O_{17}N_6$ (884,6). Ber. C 55,6; H 4,1; N 9,5; ONp 46,8. Gef. C 54,8; H 4,2; N 9,4; ONp 45,9%.

Charakteristische Banden des IR-Spektrums (KBr-Tablette): $\nu_{C=O}$(COONp): 1765 cm^{-1}; $\nu_{C=O}$(Amid-I): 1660 cm^{-1}; ν_{OCNCO}: 1765 und 1700 cm^{-1}.

Allgemeines Verfahren zur Amidierung von aktive Estergruppen enthaltenden Carbobenzoxy-glutamylpeptiden mit 2-Dimethylamino-äthylamin

Man löst 1,0 mmol des aktive Estergruppen enthaltenden Carbobenzoxy-glutamylpeptids in 10—20 ml Essigester, dem man — falls die Substanz in Essigester schwer löslich ist — einige ml Dimethylformamid zufügt. Die mit Eis gekühlte und gerührte Lösung wird tropfenweise mit 0,12 ml (1,0 mmol) 2-Dimethylaminoäthylamin pro aktive Estergruppe versetzt, weitere 2 Stunden gerührt und nachher bei Raumtemperatur 24 Stunden stehen gelassen. Man kühlt das Gemisch mit Eis wiederum ab, filtriert nachher das ausgeschiedene Kristallgut und wäscht mit Äther das beigemengte *p*-Nitrophenol heraus.

Carbobenzoxy-α-tri-L-glutaminsäure-tetra-(2-dimethylamino-äthyl-amid (XIII; $n = 3$)

Es wurden nach dem allgemeinen Verfahren aus Carbobenzoxy-α-tri-L-glutaminsäure-tetra-*p*-nitrophenylester (**III**; $n = 3$) 0,75 g (91,5% d. Th.) des aus Dimethylformamid-Essigester umkristallisierten, amidierten Produktes gewonnen. Schmp. 200—201 °C; $[\alpha]_D^{20} = -24{,}1°$ ($c = 1{,}1$; N-Salzsäure); $[\alpha]_D^{20} = -18{,}1$ °C ($c = 1{,}0$; Trifluoräthanol); $[\alpha]_D^{20} = -13{,}1°$ ($c = 0{,}9$; Trifluoressigsäure), $R_F = 0{,}17(5)$; 0,26(6).

$C_{39}H_{69}N_{11}O_8$ (820,1). Ber. C 57,1; H 8,4; N 18,7; Äquivalentzahl 205,0. Gef. C 56,8 H 8,5; N 19,0%; Äquivalentzahl 204,9.

Carbobenzoxy-α-tetra-L-glutaminsäure-penta-(2-dimethylamino-äthyl)-amid (XIV; $n = 4$)

Es wurden nach dem allgemeinen Verfahren aus Carbobenzoxy-α-tetra-L-glutaminsäure-penta-*p*-nitrophenylester (**III**; $n = 4$) 0,86 g (84,4% d. Th.) des aus Dimethylformamid–Essigester umkristallisierten Umsetzungsproduktes vom Schmp. 208—209°C gewonnen.

$[\alpha]_D^{20} = -27{,}5°$ ($c = 2$; N Salzsäure); $[\alpha]_D^{20} = -13{,}6°$ ($c = 0{,}9$, Trifluoräthanol); $R_F = 0{,}13(5)$.

$C_{48}H_{86}N_4O_{10}$ (1019,3). Ber. C 56,2; H 8,4; N 19,2; Äquivalentzahl 203,8. Gef. C 55,9; H 8,3; N 18,8%; Äquivalentzahl 205,5.

Carbobenzoxy-α-penta-L-glutaminsäure-hexa-(2-dimethylamino-äthyl)-amid (XIII; $n = 5$)

Es wurde nach dem allgemeinen Verfahren (Lösungsmittel: Dimethylformamid) aus Carbobenzoxy-α-penta-L-glutaminsäure-hexa-*p*-nitrophenylester (**III**; $n = 5$) 1 g (82% d. Th.) des aus Dimethylformamid–Essigester umkristallisierten, amidierten Produktes gewonnen. Schmp. 218—220 °C. $R_F = 0{,}15(6)$.

$C_{57}H_{103}N_{17}O_{12}$ (1218,6). Ber. C 56,2; H 8,5; N 19,5%. Äquivalentzahl 203,1. Gef. C 56,0 H 8,2; N 19,1%; Äquivalentzahl 203,8.

Carbobenzoxy-γ-tri-L-glutaminsäure-tetra-(2-dimethylamino-äthyl)-amid (XV; $n = 3$)

Es wurden nach dem allgemeinen Verfahren aus Carbobenzoxy-γ-tri-L-glutaminsäure-tetra-*p*-nitrophenylester (**VI**; $n = 3$) 0,70 g (85,4% d. Th.) des aus Dimethylformamid–Essigester umkristallisierten, amidierten Produktes gewonnen. Schmp. 208—209 °C. $R_F =$ = 0,18(5); 0,25(6).

$C_{39}H_{69}N_{11}O_8$ (820,1). Ber. C 57,1, H 8,4, N 18,7, Äquivalentzahl 205,0. Gef. C 56,9, H 8,6, N 18,8; Äquivalentzahl 204,6.

Carbobenzoxy-α-di-L-glutamyl-[γ-(2-dimethylamino-äthyl)-amid]-L-glutaminsäure-γ--(2-dimethylamino-äthyl)-amid-α-benzylester XIX; $n = 3$)

Es wurden nach dem allgemeinen Verfahren aus α-Di-L-glutamyl(γ-*p*-nitrophenylester)--L-glutaminsäure-α-benzyl-γ-*p*-nitrophenylester (**X**; $n = 3$) 0,65 g (72,5% d. Th.) des aus Essigester–Methanol–Äther umkristallisierten amidierten Derivates gewonnen. Schmp. 174—175 °C. $[\alpha]_D^{20} = -14{,}7°$ ($c = 1{,}02$; Dimethylformamid); $R_F = 0{,}39(7)$.

$C_{42}H_{65}N_9O_9$ (839,7). Ber. C 60,0; H 7,7; N 15,0; Äquivalentzahl 279,9. Gef. C 59,1; H 8,0; N 15,4%; Äquivalentzahl 279,2.

Charakteristische Banden des IR-Spektrums (KBr-Tablette): $\nu_{C=O}$(COOBzl): 1735 cm^{-1}; $\nu_{C=O}$(Z): 1700 cm^{-1}; $\nu_{C=O}$(Amid—I): 1645 cm^{-1}; ν_{N-C}(Amid—II): 1528 cm^{-1}; ν_{NH}: 3300 cm^{-1}.

Carbobenzoxy-L-pyroglutamyl-L-glutaminsäure-di-(2-dimethylamino-äthyl)-amid (XVII)

Eine eiskalte und gerührte Lösung von 1,27 g (2 mmol) Carbobenzoxy-L-pyroglutamyl--L-glutaminsäure-di-*p*-nitrophenylester (**VIII**; $m = 1$) in 10 ml Essigester und 5 ml Dimethylformamid wurde mit 0,48 ml (4 mmol) 2-Dimethylamino-äthylamin tropfenweise versetzt, dann das Gemisch bei —20°C noch 4 Stunden weiter gerührt, schließlich über Nacht bei 0 °C stehen gelassen. Die Lösung wurde bei 0,2 Torr Druck eingedampft, dann der Rückstand mit Äther ausgefällt, aus Äthanol–Äther umkristallisiert. Ausbeute 0,72 g (68,6% d. Th.). Schmp. 154—156 °C; $[\alpha]_D^{20} = -47{,}8°$ ($c = 2{,}0$; Methanol).

$C_{26}H_{40}O_6N_6$ (532,6). Ber. C 58,6; H 7,5; N 15,8; Äquivalentzahl 266,3. Gef. C 58,4; H 7,4; N 14,9%; Äquivalentzahl 265,4.

Charakteristische Banden des IR-Spektrums (KBr-Tablette): ν_{OCNCO}: 1790 und 1705 cm^{-1}; $\nu_{C=O}$ (Amid I): 1645 cm^{-1}; ν_{N-CH_3,CH_3}: 2765, 2790, 2820 cm^{-1}.

Allgemeines Verfahren zur Abspaltung der N-Schutzgruppe

Durch eine geschüttelte Lösung von 0,6 mmol des Carbobenzoxy-glutamylpeptids in 15 ml Methanol läßt man in Gegenwart von 0,2 g 10%iger Pd-Aktivkohle so lange einen Wasserstoffstrom streichen, bis das heraustretende Gas kohlendioxydfrei geworden ist. Das Filtrat wird bei Unterdruck eingedampft und der Rückstand aus Äthanol–Äther umkristallisiert.

α-Tri-L-glutaminsäure-tetra-(2-dimethylamino-äthyl)-amid (XIV; $n = 3$)

Aus dem geschützten Derivat **XIII** ($n = 3$) wurden 0,35 g (84,9% d. Th.) der Verbindung **XIV** ($n = 4$) gewonnen. Schmp. nicht charakteristisch. $R_F = 0{,}10(6)$. Nach den elektrophoretischen Reinheitsuntersuchungen ist **XIV** ($n = 3$) eine einheitliche Substanz.

$C_{31}H_{63}N_{11}O_6$ (685,9). Ber. C 54,3; H 9,2; N 22,4. Gef. C 54,1; H 9,0; N 22,2%.

α-Tetra-L-glutaminsäure-penta-(2-dimethylamino-äthyl)-amid (XIV; $n = 4$)

Aus dem geschützten Derivat **XIII** ($n = 4$) wurden 0,41 g (77,2% d. Th.) der Verbindung **XIV** ($n = 4$) gewonnen. Schmp. 160 °C; $R_F = 0{,}08(6)$.

$C_{40}H_{80}N_{14}O_8$ (885,2). Ber. C 54,2; H 9,1; N 22,1. Gef. C 53,9; H 9,3; N 21,8%.

Nach den elektrophoretischen Reinheitsuntersuchungen ist **XIV** ($n = 4$) eine einheitliche Substanz.

Der enzymatische Abbau mit Leucinaminopeptidase wurde unter Standardbedingungen [6] durchgeführt. Im enzymatischen Hydrolysat wurden nur L-Glutaminsäure-γ-(2-dimethylamino-äthyl)-amid und 2-Dimethylamino-äthylamin gefunden.

α-Penta-L-glutaminsäure-hexa-(-2-dimethylamino-äthyl)-amid (XIV; $n = 5$)

Aus dem geschützten Derivat in Dimethylformamid–Äthanol–Methanol wurden 0,59 g (90,0% d. Th.) der Verbindung **XIV** ($n = 5$) gewonnen. Schmp. ~ 165° (Zers.). $R_F = 0{,}35(10)$.

$C_{49}H_{97}N_{17}O_{10}$ (1084,4). Ber. C 54,2; H 8,9; N 21,9. Gef. C 53,9; H 8,7; N 21,7%.

Nach dem elektrophoretischen Reinheitsuntersuchungen ist **XIV** ($n = 5$) eine einheitliche Substanz.

Der enzymatische Abbau mit Leucinaminopeptidase wurde unter Standardbedingungen durchgeführt. Im enzymatischen Hydrolysat wurden nur L-Glutaminsäure-γ-(2-dimethylamino-äthyl)-amid und 2-Dimethylamino-äthylamin gefunden.

γ-Tri-L-glutaminsäure-tetra-(2-dimethylamino-äthyl)-amid (XVI; $n = 3$)

Aus dem geschützten Derivat (**XV**; $n = 3$) wurden 0,40 g (97,2% d. Th.) der Verbindung **XVI** ($n = 3$) gewonnen. $R_F = 0{,}11(6)$.

Nach den elektrophoretischen Reinheitsuntersuchungen ist **XVI** ($n = 3$) eine einheitliche Substanz.

$C_{31}H_{63}N_{11}O_6$ (685,9). Ber. C 54,3; H 9,2; N 22,4. Gef. C 54,4; H 9,3; N 22,1%.

α-Tri-[L-glutaminsäure-γ-(2-dimethylamino-äthyl)-amid] XX; ($n = 3$)

Aus dem geschützten Derivat (**XIX**; $n = 3$) konnten nach dem allgemeinen Verfahren die Carbobenzoxy- und Benzylester-Schutzgruppen in einer Stunde entfernt werden. Man erhielt 0,3 g (81,5% d. Th.) der Verbindung **XX** ($n = 3$). $R_F = 0{,}15(1)$.

Nach den elektrophoretischen Reinheitsuntersuchungen ist **XX** ($n = 3$) eine einheitliche Substanz.

$C_{27}H_{52}N_9O_7$ (614,8). Ber. C 52,5; H 8,5; N 20,4. Gef. C 52,0; H 8,1; N 19,9%.

Der enzymatische Abbau mit Leucinaminopeptidase wurde unter Standardbedingungen durchgeführt. Im enzymatischen Hydrolysat wurde nur L-Glutaminsäure-γ-(2-dimethylamino-äthyl)-amid gefunden.

L-Pyroglutamyl-L-glutaminsäure-di-(2-dimethylamino-äthyl)-amid (XVIII)

Aus dem geschützten Derivat (**XVII**) wurden 0,23 g (96,2% d. Th.) der stark hydroskopischen Verbindung **XVIII** gewonnen. Schmp. 150—152 °C.

Nach den elektrophoretischen Reinheitsuntersuchungen ist **XVIII** eine einheitliche, ninhydrinnegative, chlorpositive Substanz.

$C_{18}H_{34}N_6O_4$ (398,5). Ber. C 54,2; H 8,6; N 21,1. Gef. C 53,9; H 8,9; N 20,9%.

*

Wir danken auch an dieser Stelle für die Durchführung der zahlreichen Mikroanalysen Frau H. MEDZIHRADSZKY-SCHWEIGER, Frau S. KUTASSI, weiterhin für die IR-spektroskopischen Aufnahmen und ihre Auswertung Herrn F. RUFF. Für die gewissenhafte experimentelle Mitarbeit sei Frl. A. SCHWARTZ, Frl. M. DUKAI, Frau E. PÉTERI und Herrn J. KÖKÖSI ebenfalls gedankt.

LITERATUR

[1] KÓTAI, A., SZÓKÁN, GY., BRUCKNER, V.: Acta Chim. Acad. Sci. Hung. **64**, 285 (1970)
[2] SZÓKÁN, GY., KÓTAI, A., DOBÓ, GY.: Acta Chim. Acad. Sci. Hung. **65**, 375 (1970)
[3] GIBIAN, H., KLIEGER, E.: Ann. **640**, 145 (1961)
[4] KHOSLA, M. C., ANAND, N.: Ind. J. Chem. **1**, 49 (1963)
[5] KLIEGER, E., GIBIAN, H.: Ann. **649**, 183 (1961)
[6] SZÓKÁN, GY., KÓTAI, A.: Ann. Univ. Sci. Budapest, Rol. Eötvös nom., Sect. Chim. **XIII**, 39 (1972)

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SYNTHESIS OF 2*H*-1,3-BENZOTHIAZINE DERIVATIVES, I

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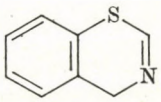
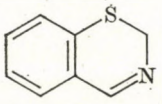
Condensation of aliphatic and aromatic acid amides with formaldehyde and 3,4-dimethoxythiophenol in pyridine gave 2*H*-1,3-benzothiazine derivatives. This is a new process for the synthesis of 2*H*-1,3-benzothiazine and its 4-substituted derivatives.

Chemical investigations on 1,3-benzothiazines have been in progress for about 20 years. Of the two theoretically possible isomers (**I** and **II**), only the preparation of 4*H*-1,3-benzothiazine (**I**), and its substituted and 2,3-dihydro derivatives have been achieved.



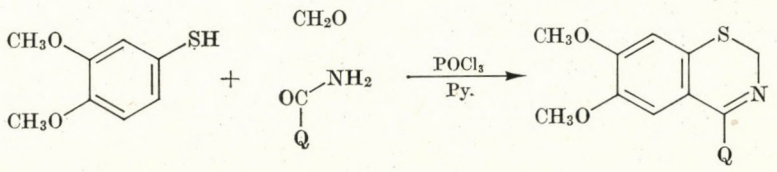
I



II

Up to the beginning of our work, we did not find reference in the literature to the synthesis of 2*H*-1,3-benzothiazine and its 4-substituted derivatives. An investigation of this problem seemed therefore interesting.

The desired 2*H*-1,3-benzothiazine derivatives (**Va, b, c**) have been prepared in pyridine as solvent, by the condensation of aromatic or aliphatic acid amides (**III**) and 3,4-dimethoxythiophenol (**IV**) with formaldehyde, in the presence of phosphorus oxychloride as the dehydrating agent.



IV **III** **V**

a Q = H

b Q = Me

c Q = Ph

Cyclization experiments with other aldehydes remained unsuccessful.

The structures of the 2*H*-1,3-benzothiazine derivatives obtained were verified by elementary analysis, hydrolysis experiments, and on the basis of their IR and NMR spectra. (Spectroscopic data are given in Tables I and II.)

Table I

IR data proving the structure of the compounds **Va-c, VIII** *and* **IX** *(KBr pellets), cm*$^{-1}$

Compound	ν ($\overset{+}{=}$NH) band	ν C=O band	ν C=N band	Methoxy bands	Aromatic bands
Va-hydro chloride	3100—2000* diffuse 1950—1850 broad	—	1630**	2840, 1260 1200, 1175	1590, 1535, 1500, 1490, 1440, 840, 810
Vb	—	—	1550	2840, 1270—1260, 1170, 1040	1615, 1590, 1500, 1470, 875, 800
Vc	—	—	1545	2840, 2820, 1270— 1260, 1065, 1030	1595, 1500, 870, 830 800, 735, 720
VIII	—	1655—1645	—	2840, 1270, 1210, 1170, 1060—1050	1595, 1580, 1560, 1500 895, 875, 865, 810, 790, 730, 720, 710, 690
IX	—	—	—	2835, 1250, 1235, 1170, 1145, 1020	1590, 1580, 1505, 880, 845, 800, 770

* The diffuse absorption has maximum at about 2550 cm^{-1}
** C=N^{+} band of the immonium group

Table II

NMR data of compounds **Va—c, VIII** *and* **IX,** *in deuterochloroform solution, ppm (δ_{TMS}=0ppm)*

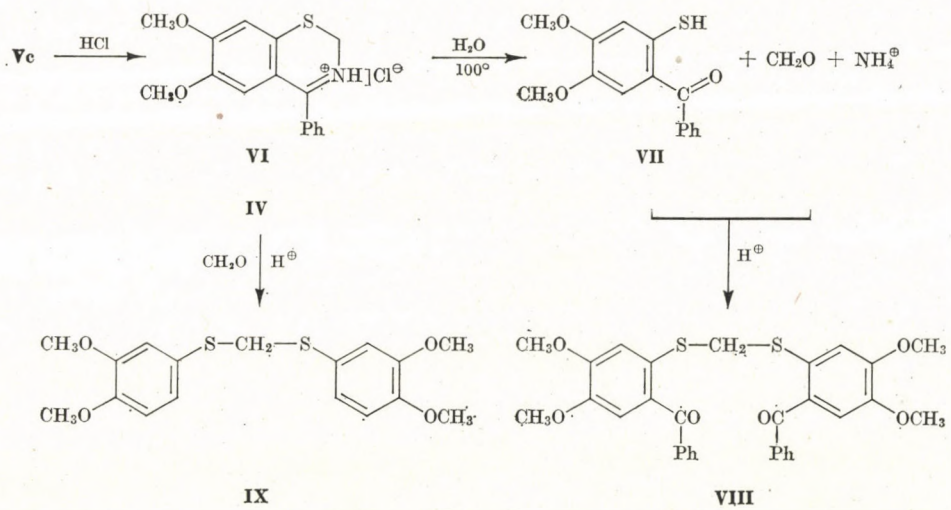
Compound	δ CH_3	δ OCH_3	δ CH_2	δ (=CH) (C—4)	ArH			ν ArH *m* [Hz]
					(C—5) (V,IX) (C—3) (VIII)	(C—8) (V) (C—6) (VIII) (C—2) (IX)	C—6	
Va-hydro chloride*	— 	3.85 *s*, 3H 4.00 *s*, 3H	5.05 *s*, 2H	9.00 *s*, 1H	7.69 *s*, 1H	7.25 *s*, 1H	—	—
Vb	2.37 *s*, 3H	3.88 *s*, 6H	4.50 *s*, 2H	—	7.00 *s*, 1H	6.73 *s*, 1H	—	—
Vc	— 	3.70 *s*, 3H 3.95 *s*, 3H	4.70 *s*, 2H	—	6.90 *s*, 1H	6.78 *s*, 1H	—	410—470 5H
VIII	— 	3.75 *s*, 6H 3.80 *s*, 6H	4.05 *s*, 2H	—	6.90 *s*, 2H	6.70 *s*, 2H	—	420—470 10H
IX	— 	3.88 *s*, 12 H	4.22 *s*, 2 H	—	6.83** *d*, 2H	7.02** *d*, 2H	7.05** 2x*d*, 2H	—

* Solvent: DMSO—d_6; the signal SN^{+}H merged into the δ OH signal of the water content of the solvent, was observed at about 4.05 ppm.

** ABX spectrum, where the symbols A, B and X correspond to the ring protons at C—6, C—5 and C—2, respectively, and $I_{AB} = 8$ Hz, $I_{AX} = 2$ Hz, $I_{BX} = 2 \sim 0$ Hz.

As expected, 2*H*-1,3-benzothiazine derivatives (**Va, b, c**) are stronger bases than 4*H*-1,3-benzothiazines. Their hydrochlorides are readily soluble in water, and are not hydrolyzed to the corresponding base. With picric acid, they form well crystallized picrates.

In order to prove the structure, the 4-phenyl-2*H*-1,3-benzothiazine derivative (**Vc**) was hydrolyzed by heating for 6 days in a sealed tube in vacuum with 15% aqueous hydrochlorid acid solution at 100°C; the end of the reaction was indicated by the disappearance of the orange-yellow colour of the benzothiazinium chloride (**VI**). Of the hydrolysis products of the 2*H*-1,3-benzothiazine ring, the 2-mercaptobenzophenone derivative (**VII**) and formaldehyde condensed in acid medium to give the thioacetal derivative **VIII**, which was isolated. The $\nu C = O$ band appearing at 1665—1655 cm^{-1} in the IR spectrum of **VIII** proved the presence of the benzoyl group, while the signal of an intensity corresponding to two protons and appearing at 4.25 ppm in the NMR spectrum, afforded evidence for the thioacetal ($-S-CH_2-S-$) structure. For comparison, we used the NMR spectrum of the thioacetal derivative **IX**, prepared by the condensation of the thiophenol derivative **IV** and formaldehyde; this also had the $-S-CH_2-S-$ signal at 4.25 ppm.



After the termination of our investigations, a paper published by GRUBER, *et al.* [1] reported the synthesis of 2,4-disubstitued 2*H*-1,3-benzothiazine derivatives by the thermolysis of 2-(arylthio)-2-(trifluoromethyl)-4-(isopropyl)-oxazolin-5-one derivatives.

Presumably, our cyclization reactions lead through intermediate products to the 2*H*-1,3-benzothiazines. Studies on the course of the reaction are in progress and will be reported in our next communication.

Experimental

M.p.s. are uncorrected.
IR spectra were recorded with a Perkin-Elmer 457 instrument. NMR spectra were obtained at room temperature with a JEOL 60-HL (60MHz) spectrometer, using TMS internal standard.

1. 6,7-Dimethoxy-2*H*-1,3-benzothiazine (Va)

0.45 g (0.01 mole) of formamide, 0.03 g of potassium carbonate and 0.9 ml of 35% aqueous formaldehyde were dissolved with heating in 5 ml of pyridine. After cooling, 1.7 g (0.01 mole) of 3,4-dimethoxythiophenol and, under constant stirring and cooling, 2 ml of phosphorus oxychloride were added to the solution, which was then allowed to stand. The mixture was heated for 30 min on a boiling water bath, and it was then decomposed by pouring it on ice. The mixture was made alkaline with sodium carbonate, it was extracted with ether, and the solvent and pyridine were evaporated in vacuum. The residue was dissolved in benzene, extracted with 10 ml of 10% HCl, the solution was made alkaline with sodium carbonate and extracted with ether. The ether extract was dried over anhydrous sodium sulfate. The solvent was evaporated and the residual colourless oil, which proved to be chromatographically homogeneous, was dissolved in 1 ml of ethanol and precipitated as the picrate (0.05 g); yellow crystals, m. p. 189—191°C (d.) (from ethanol).

$C_{16}H_{14}N_4O_9S$ (438.37). Calcd. C 43,84; H 3.22; N 12.75; S 7.31. Found C 43.44;H 3.15; N 12.26; S 7.59%.

The hydrochloride forms orange-yellow crystals, m. p. 194—195°C (d.) (from ethanol–ether).

$C_{10}H_{12}ClNO_2S$ (245.73). Calcd. C 48.87; H 4.92; Cl 14.43. Found C 48.46; H 5.04; Cl 14.05%.

2. 4-Methyl-6,7-dimethoxy-2*H*-1,3-benzothiazine (Vb)

0.59 g (0.01 mole) of acetamide, 0.03 g of potassium carbonate and 0.9 ml of 35% formaldehyde were dissolved with heating in 5 ml of pyridine. After cooling, 1.7 g (0.01 mole) of 3,4-dimethoxythiophenol was added, and the mixture was condensed with 2 ml of phosphorus oxychloride and processed as described for Experiment 1. The aqueous solution obtained in the hydrochloric acid extraction was heated for 30 min on a boiling water bath. The viscous, oily reaction product was converted to the picrate (0.11 g), yellow crystals, m. p. 195—196°C (d.) (from ethanol).

$C_{17}H_{16}N_4O_9S$ (452.4). Calcd. C 45.13; H 3.57; N 12.38. Found C 45.21; H 3.72; N 12.20%.

The base liberated from the picrate appeared as pale yellow crystals, m. p. 110—111°C (from ethanol).

$C_{11}H_{13}NO_2S$ (223.28). Calcd. C 59.17; H 5.87; N 6.27. Found C 58.99; H 5,90; N 6.29%.

The hydrochloride formed yellow crystalls, m. p. 190—191°C (d.) (from ethanol).

$C_{11}H_{14}ClNO_2S$ (259.75). Calcd. C 50.51; H 5.43; N 5.39; Cl 13.61. Found C 50.64; H 5.68; N 5. 39; Cl 13.55%.

3. 4-Phenyl-6,7-dimethoxy-2*H*-1,3-benzothiazine (Vc)

1.21 g (0.01 mole) of benzamide, 0.03 g of potassium carbonate and 0.9 ml of 35% formaldehyde were dissolved in 5 ml of warm pyridine. After cooling, 1.7 g (0.01 mole) of 3,4-dimethoxythiophenol and 2 ml of phosphorus oxychloride were added, as described for Experiment 1, and the mixture was processed similarly. The hydrochloric acid extract was heated 1 hr on a boiling water bath. The product was isolated as the picrate (0.1 g), yellow crystals, m. p. 222—223°C (d.) (from ethanol).

$C_{22}H_{18}O_9N_4S$ (514.24) Calcd. C 51.39; H 3.53; N 10.89; S 6.24. Found C 51.60; H 3.70; N 10.65; S 6.10%.

The base liberated from the picrate gave pale yellow prisms, m. p. 142—143°C (from ethanol).

$C_{16}H_{15}NO_2S$ (285.35). Calcd. C 67.34; H 5.30; N 4.91. Found C 67.50; H 5.47; N 4.75%.

The hydrochloride appeared as orange-yellow crystals, m. p. 182—183°C (d.) (from ethanol, ether).

$C_{16}H_{16}ClNO_2S$ (321.82). Calcd. C 59.71; H 5.01; Cl 11.02. Found C 59.85; H 5.20; Cl 11.12%.

4. Hydrolysis of 4-diphenyl-6,7-dimethoxy-2*H*-1,3-benzothiazine (Vc)

0.285 g (0.001 mole) of 4-phenyl-6,7-dimethoxy-2*H*-1,3-benzothiazine was dissolved in 15 ml of 15% hydrochloric acid, and the solution was heated on a boiling water bath, in a tube sealed under vacuum, for 6 days, until the disappearance of the orange-yellow colour of 4-phenyl-6,7-dimethoxy-2*H*-1,3-benzothiazinium chloride. After cooling, the mixture was extracted with benzene, the benzene extract was washed with water and dried over anhydrous sodium sulfate; the solvent was then evaporated. The residue was crystallized from methanol to obtain bis(2-benzoyl-4,5-dimethoxyphenylmercapto)methane (**VIII**) (0.2 g), pale yellow prisms, m. p. 161—161.5 °C (from methanol).

$C_{31}H_{28}O_6S_2$ (560.60) Calcd. C 66.41; H 5.03. Found C 66.10; H 4.98%.

5. Bis(3,4-dimethoxyphenylmercapto)methane (IX)

0.17 g (0.001 mole) of 3,4-dimethoxythiophenol was dissolved in 10 ml of ethanol; 0.5 ml of 37% formaldehyde and 5 ml of 10% HCl were added, and the reaction mixture was heated to the boiling point. After cooling, it was diluted with water and the reaction product extracted with benzene. The solvent was evaporated and the residue crystallized from ethanol (0.10 g); colourless needles, m. p. 123—124°C (from ethanol).

$C_{17}H_{20}O_4S_2$ (352.46) Calcd. C 57.93; H 5.72; S 18.19. Found C 57.59; H 5.87; S 18.43%.

*

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REFERENCE

[1] Gruber, P., Müller, L., Steglich, W.: Chem. Ber. **106**, 2863 (1973)

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SYNTHESIS OF O-α-D-GLUCOPYRANOSYL-(1 → 4)-O-β-D-GLUCOPYRANOSYL-(1 → 6)-D-GLUCOSE

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The KOENIGS—KNORR reaction of benzyl 2,3,4-tri-O-benzyl-β-D-glucopyranoside (**2**) with α-acetobromomaltose (**4**) gave the trisaccharide derivative (**5**) in 68% yield. After removal of the protecting groups, reduction with $NaBH_4$ and acetylation gave the alditol derivative (**8**). In the NMR spectrum of **8** the slightest chemical shift induced by $Pr(fod)_3$ was observed for C_1—H, thus the determination of the steric position of this hydrogen atom was possible. Deacetylation of **5** followed by benzalation, benzylation and hydrogenolysis with $LiAlH_4$—$AlCl_3$ gave the fully benzylated trisaccharide (**12**) containing only a single primary free hydroxyl group. The structures of the products were proved by the IR and NMR spectra.

For an NMR spectroscopic examination of the rare earth complexes of higher-membered oligosaccharides, we needed a trisaccharide derivative containing different types of bonds, as well as interglycosidic linkages of different anomeric configurations. For this purpose O-α-D-glucopyranosyl-(1 → 4)-O-β-D-glucopyranosyl-(1 → 6)-D-glucose was synthesized. Two methods are known in the literature for the preparation of the peracetyl derivative of this trisaccharide: the KOENIGS—KNORR [1] and the orthoester syntheses [2].

These known methods were unsuitable for us to obtain intermediates with a potential possibility of further transformation into higher-membered oligosaccharides. The synthesis starting with benzyl 2,3,4-tri-O-benzyl-β-D-glucopyranoside (**2**) — made by the stereoselective hydrogenolysis [3, 4] of benzyl 2,3-di-O-benzyl-4,6-O-benzylidene-β-D-glucopyranoside (**1**) [5] with $LiAlH_4$-$AlCl_3$ in 92% yield — satisfies the above-mentioned requirement. The structure of **2** was confirmed by the NMR spectrum of the methyl ether derivative (**3**), too, prepared by the procedure of KUHN *et al.* [6]. The protons of the OCH_3 group appear as sharp singlets with a chemical shift of $\delta = 3.39$ ppm; this is in good accordance with the published values [3, 7, 8].

The reaction of **2** with α-acetobromomaltose (**4**) [9] in 1 : 1 benzene-nitromethane in the presence of $Hg(CN)_2$ catalyst afforded the benzyl glycoside of the partially acetylated and benzylated trisaccharide (**5**) in a yield of 67.8%. The 60 MHz NMR spectrum of **5** is of higher order, direct assignation being impossible; from among the three anomeric protons only the signal assignable to the α-linkage of the maltose moiety is separated from the others.

The signals of the two β-glycosidic linkages are shielded mainly by the AB quartets of the benzyl protons. At the same time in agreement with the analytical data and chromatographic examination, the NMR spectrum unequivocally proved the purity of the crystalline **5**. Catalytic debenzylation of **5** with palladium-on-carbon in ethyl acetate followed by saponification with ZEMPLÉN's method [10] resulted in the amorphous trisaccharide (**6**). The acetylation of **6** yielded the corresponding hendecaacetate (**7**), a compound reported in the literature [1]. The reduction of **6** with $NaBH_4$ followed by acetylation gave crystalline 1,2,3,4,5-penta-O-acetyl-6-O-(hepta-O-acetyl-β-maltosyl)-D-glucitol (**8**). The NMR spectrum of **8** recorded in $CDCl_3$ in the presence of $Pr(fod)_3^*$ [11] showed that from among the two interglycosidic linkages the shift induced was slightest for the proton of the β-glycosidic bond. It appeared at $\delta = 3.41$ ppm, differentiated from the signals of the protons of the skeleton and the α-glycosidic linkage, the coupling constant being $J_{1',2} = 8.5$ Hz, characteristic of a *trans diaxial* steric relation.

In the same way, the anomeric configuration of the glycosidic linkage formed in the synthesis of **5** was also exactly identified.

The crystalline compound **9**, obtained by the saponification of **5**, was converted into the corresponding benzylidene derivative (**10**). Benzylation of the crystalline **10** with benzyl bromide and NaH in DMF resulted in crystalline benzyl 2,3,4-tri-O-benzyl-6-O-(2,3,6,2',3'-penta-O-benzyl-4',6'-O-benzylidene-β-maltosyl)-β-D-glucopyranoside (**11**). The structure of **11** was confirmed by its IR and NMR spectra. Hydrogenolysis of **11** with $LiAlH_4$-$AlCl_3$ reagent, similarly to all the 3-O-benzyl-4,6-O-benzylidene-D-glucopyranoside derivatives examined by us [3,4], gave with stereoselective ring cleavage a fully-benzylated trisaccharide (**12**) containing free hydroxyl only at the primary carbon atom of the non-reducing end-group. This compound (**12**), with only one free hydroxyl group and with protecting groups which are readily removable under mild conditions, is very suitable for further transformation into higher-membered oligosaccharides.

The structure of **12** was proved by methylation to **13** and the NMR spectrum of the latter. The protons of the $-OCH_3$ group appear at $\delta = 3.42$ ppm as a singlet, this value being characteristic of the chemical shift of the 6-O-methyl group.

Experimental

M. p. 's were determined on a Kofler hot-stage apparatus and were uncorrected. Optical rotations were measured with a Polamat (Zeiss) automatic photoelectric polarimeter. NMR spectra were recorded on a Varian A60A (60 MHz) and a Jeol MH-100 (100 MHz) instrument using TMS as internal standard. The thin-layer chromatographic examinatons were carried out on silica gel (Kieselgel G; E. Merck, Darmstadt). 50% sulfuric acid was used for detection.

* $Pr(fod)_3$ stands for tris(2,2-dimethyl-6,6,7,7,8,8,8-heptafluoro-3,5-octanedionato) praseodymium(III).

Benzyl 2,3,4-tri-O-benzyl-β-D-glucopyranoside (2)

To a solution of **1** [6] (3 g) in 1 : 1 ether–dichloromethane (60 ml) 1 g of $LiAlH_4$ was added in 3—4 portions over a period of 10—12 min at room temperature with stirring, and the mixture was slowly heated to reflux. To the hot reaction mixture $AlCl_3$ (3 g) in ether (30 ml) was added in portions over a period of 30 min, and refluxing was continued for 2 hrs until **1** could no longer be detected. After cooling, the excess of $LiAlH_4$ was decomposed with ethyl acetate (8—10 ml) and $Al(OH)_3$ was precipitated by the addition of water (cca. 15 ml). After dilution with ether (50 ml) the organic layer was separated, washed with water (3 × 20 ml), dried over Na_2SO_4 and evaporated. Recrystallization of the crystalline residue gave pure **2** (2.76 g; 92%), m. p. 106 °C (lit. [12] m. p. 105—106°C); $[\alpha]_D$ −11.5° (c = 2.1, chloroform) (lit. [12] $[\alpha]_D$ −9.2° (c = 1.0, chloroform)). R_f 0.42 (benzene–methanol, 97 : 3).

$C_{34}H_{36}O_6$ (540.6). Calcd. C 75.53; H 6.71. Found C 75.44; H 6.63%.

Benzyl 2,3,4-O-benzyl-6-O-methyl-β-D-glucopyranoside (3)

A mixture of **2** (1.0 g), methyl iodide (1.25 ml) and Ag_2O (1.25 g) in 15 ml of dimethylformamide was shaken for 24 hrs. After dilution with chloroform (50 ml) the mixture was filtered, the filtrate was successively washed with 1% KCN solution (3 × 20 ml) and water (3 × 20 ml), dried ($CaCl_2$) and evaporated. Crystallization from cyclohexane (7 ml) afforded **3** (0.92 g; 90%), m. p. 122—124 °C; $[\alpha]_D$ −21.6° (c = 1.05, chloroform). R_f 0.69 (benzene–methanol, 98 : 2).

NMR: δ = 7.31 ppm (m, 20 H, aromatic); 5.18—4.40 (m, 9 H, 4 benzyl, 1 anomeric); 3.85—3.40 (m 6 H, skeleton); 3.39 (s, 3 H, OCH_3).

$C_{35}H_{38}O_6$ (554.6). Calcd. C 75.76; H 6.90. Found C 74.89; H 6.69%.

Benzyl 2,3,4-tri-O-benzyl-6-O-(hepta-O-acetyl-β-maltosyl)-β-D-glucopyranoside (5)

Compound **2** (2.16 g; $4 \cdot 10^{-4}$ moles) was dissolved in a mixture of benzene (60 ml) and nitromethane (60 ml) and the solution was concentrated at atmospheric pressure to 40 ml. After cooling to 40 °C, $Hg(CN)_2$ (1.01 g; $4 \cdot 10^{-4}$ moles) and **4** (2.79 g; $4 \cdot 10^{-4}$ moles) were added, and the mixture was stirred at 40 °C with the exclusion of moisture. After 2 hrs TLC indicated the absence of the starting material (**2**). The inorganic salts were removed from the cooled solution by filtration, the filtrate was evaporated and the residue dissolved in chloroform (100 ml). The mixture was filtered and the filtrate successively washed with 5% KI solution (3 × 20 ml), water (2 × 30 ml), dried (Na_2SO_4) and evaporated. The residue was crystallized from ethanol (40 ml) and then recrystallized three times to yield pure **5** (2.85 g; 67.8%), m. p. 146—147 °C; $[\alpha]_D$ +33.6° (c = 2, chloroform).

NMR (in $CDCl_3$): δ = 7.55—7.16 (m, 20 H, aromatic); 5.26 (d, 1 H, $C_{1''}$—H, J = 2 Hz); 5.50—3.30 (m, 28 H, skeleton and benzyl protons); 2.20—1.83 (m, 21 H, 7 Ac).

$C_{60}H_{70}O_{23}$ (1159.2). Calcd. C 62.26; H 6.09. Found C 62.20; H 6.24%.

O-α-D-glucopyranosyl-(1 → 4)-O-β-D-glucopyranosyl-(1 → 6)-β-D-glucopyranose (6)

Compound **5** (2.0 g) was hydrogenated in 120 ml of ethyl acetate in the presence of 10% palladium-on-carbon (0.2 g) for 24 hrs until no more hydrogen was absorbed and the starting material (**4**) disappeared. The catalyst was removed by filtration and the filtrate evaporated to dryness. In order to get rid of the last traces of water, dry benzene was repeatedly distilled from the residue. The syrupy product (1.32 g; 96%) obtained was dissolved in abs. methanol (50 ml) and saponified with 0.1M $NaOCH_3$ solution (0.5 ml). The methanolic solution was deionized with Dowex 50—8X ion exchange resin and evaporated. The yield of the amorphous product was 0.81 g (93%). $[\alpha]_D$ +62° (c = 1.2, water). R_f 0.26 (n-butanol-pyridine-water, 6 : 4 : 3).

$C_{18}H_{32}O_{16}$ (504.4). Calcd. C 42.89; H 6.40. Found C 43.50; H 6.21%.

O-[2,3,4,6-Tetra-O-acetyl-α-D-glucopyranosyl-]-(1 → 4)-O-[2,3,6-tri-O-acetyl-β-D-glucopyranosyl-]-1 (→ 6)-0-1,2,3,4-tetra-O-acetyl-β-D-glucopyranose (7)

Compound **6** (210 mg) was acetylated with acetic anhydride (3 ml) and sodium acetate (200 mg) for 1 hr at 95 °C. After cooling, the reaction mixture was poured into ice-water. The dusty material which precipited was crystallized from ethanol (38 ml) to obtain 314 mg (78.3%) of **7**, m. p. 239—240 °C; $[\alpha]_D$ +60.1° (c = 0.43, chloroform). (Lit. [1] m. p. 242 °C, lit. [1] $[\alpha]_D$ +42.5° (chloroform). R_f 0.31 (benzene – methanol, 95 : 5).

6-O-(Hepta-O-acetyl-β-maltosyl)-1,2,3,4,5-penta-O-acetyl-D-glucitol (8)

100 mg of **6** was reduced with $NaBH_4$ (50 mg) in water (2 ml) for 16 hrs. After neutralization with acetic acid the solution was evaporated to dryness. The traces of water were removed by repeated addition and distillation of methanol (5 × 20 ml). The residue was dried over P_2O_5 and acetylated at room temperature with acetic anhydride (5 ml) in pyridien (5 ml). The mixture was then poured into ice-water and extracted with chloroform (50 ml). The organic layer was washed with 0.5*M* sulfuric acid (3 × 20 ml) and water (5 × 40 ml) until neutral. After drying over Na_2SO_4 and evaporation of the solvent, the syrupy residue was crystallized from ethanol (5 ml) to yield **8** (160 mg; 80%), m. p. 148—149 °C; $[\alpha]_D$ +47° (*c* = 0.25, chloroform).

$C_{42}H_{58}O_{28}$ (1010.9). Calcd. C 49.89; H 5.78. Found C 50.25; H 6.12%.

NMR (with 2 : 1 proportion of **8** and $Pr(fod)_3$ in $CDCl_3$): δ = 3.41 (d, 1 H, J = 8.5)Hz); 1.82, 1.53, 1.50, 1.41, 1.30, 1.28, 1.20, 1.18, 1.15, 1.10, 1.02, 0.83 (singlets, 12 Ac).

Benzyl 2,3,4-tri-O-benzyl-6-O-(β-maltosyl)-β-D-glucopyranoside (9)

Compound **5** (2.5 g) was saponified in abs. methanol (25 ml) with 0.1*N* $NaOCH_3$ solution (0.5 ml). After standing for 24 hrs the beginning of spontaneous crystallization was observed. Recrystallization from methanol (15 ml) afforded **9** (1.04 g; 75.2%), m. p. 113—114 °C; $[\alpha]_D$ +50.5° (*c* = 0.5, pyridine). R_f 0.41 (benzene—methanol, 8 : 2).

$C_{48}H_{56}O_{16}$ (864.9). Calcd. C 63.86; H 6.52. Found C 64.20; H 6.41%.

Benzyl 2,3,4-tri-O-benzyl-6-O-(4′,6′-O-benzylidene-β-maltosyl)-β-D-glucopyranoside (10)

Compound **9** (1.57 g) was shaken with benzaldehyde (10 ml) and $ZnCl_2$ (3.0 g) for 6 hrs. The mixture was poured into ice-water, the aqueous phase was separated and the residue was rubbed with 20 ml of petroleum ether. The crude product was crystallized from ethanol (12 ml) to gave compound **10** (1.52 g; 87.8%), m. p. 111—113 °C; $[\alpha]_D$ +30.5° (*c* = 1.0, pyridine). R_f 0.59 (benzene–methanol, 8 : 2).

$C_{53}H_{60}O_{16}$ (953.0). Calcd. C 66.69; H 6.43. Found C 67.15; H 6.42%.

Benzyl 2,3,4-tri-O-benzyl-6-O-(2,3,6,2′,3′-penta-O-benzyl-4′,6′-O-benzylidene-β-maltosyl)-β-D-glucopyranoside (11)

Compound **10** (1.43 g) was dissolved in DMF (7 ml) and stirred with 0.5 g NaH for 1 hr. The solution was then cooled in an ice-bath and treated with benzyl bromide (2 ml). Stirring was continued for further 12 hrs at room temperature. The mixture was poured into 50% aqueous ethanol; the syrupy material which separated soon solidified. Crystallization from ethanol (30 ml) gave **11** (1.04 g; 50.4%), m. p. 95—96 °C; $[\alpha]_D$ +45° (*c* = 0.65, chloroform).

$C_{88}H_{90}O_{16}$ (1403.6). Calcd. C 75.29; H 6.46. Found C 74.67; H 6.38%.

NMR (in $CDCl_3$): δ = 7.26 (m, 50 H, aromatic), 5.52 (*s*, 1 H, benzylidene), 5.08—3.30 (m, 39 H, skeleton and benzyl protons).

Benzyl 2,3,4-tri-O-benzyl-6-O-(2,3,6,2′,3′,4′-hexa-O-benzyl-β-maltosyl)-D-glucopyranoside (12)

1.0 g of **11** was dissolved in a 1 : 1 mixture of ether and dichloromethane (40 ml) and treated with $LiAlH_4$ (0.3 g) and a solution of $AlCl_3$ (0.9 g) in ether (15 ml). After 2 hrs TLC indicated the absence of starting material. Compound **12** was isolated in the same way as described for **2**. The syrupy product was crystallized from ethanol (12 ml). The yield was 0.62 g (62%), m. p. 81—82°C; $[\alpha]_D$ +41° (*c* = 0.75, chloroform).

IR (KBr): 3500—3200 cm^{-1} (broad, polymeric OH).

$C_{88}H_{92}O_{16}$ (1405.6). Calcd. C 75.27; H 6.50. Found C 75.70; H 6.52%.

0.2 g of **12** was methylated according to Kuhn's procedure, as described for **3**. The syrupy product was purified by preparative thin-layer chromatography with 95 : 5 benzene–methanol as the eluant to give **13**. The IR spectrum of **13** does not contain hydroxy band.

NMR (in $CDCl_3$): δ = 3.42 ppm (s, 3 H, OCH_3).

*

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REFERENCES

[1] NICHOLS, Jr., S. H., EVANS, W. L., MCDOWELL, H. D.: J. Am. Chem. Soc. **62,** 1754 (1940)
[2] KOCHETKOV, N. K., KHORLIN, A. J., BOCHKOV, A. F.: Tetrehedron **23,** 693 (1967)
[3] NÁNÁSI, P., LIPTÁK, A.: Magy. Kém. Folyóirat **80,** 217 (1974)
[4] LIPTÁK, A., JODÁL, I., NÁNÁSI, P.: Carbohyd. Res. **44,** 1 (1977)
[5] KLEMER, A.: Ber. **92,** 218 (1959)
[6] KUHN, R., TRISCHMAN, A., LÖW, I.: Angew. Chem. **67,** 32 (1955)
[7] RATHBONE, E. B., STEPHEN, A. M.: Tetrahedron Letters **1970,** 1339
[8] GROS, E. G., MASTRONARDI, I. O., FRASKA, A. R.: Carbohyd. Res. **16,** 232 (1971)
[9] FISCHER, E. G., ARMSTRONG, E. F.: Ber. **35,** 3153 (1902)
[10] ZEMPLÉN, G.: Ber. **59,** 1254 (1926)
[11] SIEVERS, R. E., RONDEAU, R. E.: J. Am. Chem. Soc. **93,** 1522 (1971)
[12] ZISSIS, E., FLETSCHER, H. G.: Carbohyd. Res. **12,** 361 (1970)

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SYNTHESIS OF THE NEW AMINO ACID γ-CARBOXY-GLUTAMIC ACID AND ITS DERIVATIVES

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The synthesis of the new amino acid γ-carboxyglutamic acid (Gla) and some of its derivatives is described. The key compounds, Boc- and Z-DL-Gla($OtBu$)$_2$-OBzl, were prepared by condensation of di-*t*-butyl malonate and the corresponding protected dehydroalanine.

The new amino acid γ-carboxyglutamic acid (Gla*) has recently been discovered in the N-terminal, Ca^{2+} binding region of prothrombin, a vitamin K-dependent clotting factor [1, 2]. This amino acid gives prothrombin the Ca^{2+} binding ability being necessary for its activation, *i.e.* its proteolytic transformation into the enzyme thrombin. Abnormal prothrombin, induced by vitamin K antagonists, that does not bind Ca^{2+}, contains Glu residues instead of Gla. Apparently, the modified glutamic acid, Gla, can be an essential ingredient in the prothrombin molecule as well as in the other vitamin K-dependent clotting factors (VII, IX, X).

In this paper we describe the synthesis of DL—Gla and some of its derivatives.

As the most obvious route to Gla, the reaction of malonic ester with a suitable protected O-tosyl-serine, β-chloroalanine and dehydroalanine derivative, respectively, was studied.** The protecting groups for malonic acid and for the amino acid component were selected in view of the requirements of peptide synthesis, namely, selectively removable protecting groups were used for blocking the α-amino function of Gla as well as its α- and γ-carboxyl groups. Thus, di-*t*-butyl malonate was allowed to react with the appropriate Boc- or Z-amino acid benzyl ester. As each version of these condensations seemed to proceed *via* the dehydroalanine derivative, this reaction is described in detail.

Boc-Ser-OBzl (**1**) prepared from Boc-Ser [5] was converted into Boc-Dha-OBzl (**2**) *via* Boc-Ser(Tos)-OBzl. In benzene solution, di-*t*-butyl malonate

* Amino acids and amino acid derivatives are written in their abbreviated forms as recommended [3]. The following additional symbols have been used: Gla = γ-carboxyglutamic acid, Dha = dehydroalanine, DCHA = dicyclohexylamine, TFA = trifluoroacetic acid.

** Meanwhile a paper was published by H. R. MORRIS *et al.* [4] giving a scant account of a similar synthesis of DL-Gla, *i.e.* preparation of Z-DL-Gla(OBzl)$_2$-OBzl from Z-DL-Ala(Cl)-OBzl and its conversion to DL-Gla. HBr. In January 1975, Dr. MORRIS kindly provided us with the manuscript of this paper and a sample of synthetic Gla.

[6] was allowed to react with **2** at a molecular ratio of 3 : 2 in the presence of sodium di-*t*-butyl malonate. The ensuing Boc-DL-Gla(O*t*Bu)$_2$-OBzl (**3**) was isolated in crystalline state. With 85% formic acid the Boc group of **3** could be selectively removed [7]. H-DL-Gla(O*t*Bu)$_2$-OBzl (**4**) thus obtained was isolated as crystalline oxalate (**4a**). Both hydrogenolysis and alkaline hydrolysis of **3** afforded Boc-DL-Gla(O*t*Bu)$_2$-OH (**5**) which could be crystallized as the DCHA salt (**5a**).

$$\text{BOC-Ser-OH} \xrightarrow[\text{DCHA}]{\text{Bzl-Br}} \text{BOC-Ser-OBzl} \xrightarrow[\text{NEt}_3]{\text{Tos-Cl}} \underset{\text{(without isolation)}}{\text{BOC-Ser(Tos)-OBzl}}$$

$$\xrightarrow{\text{NEt}_3} \text{BOC-Dha-OBzl} \xrightarrow[\text{and its Na-salt}]{\text{di-}t\text{-butyl malonate}} \text{BOC-DL-Gla}(O\text{t}\text{Bu})_2\text{-OBzl}$$

$$\text{BOC-DL-Gla}(O\text{t}\text{Bu})_2\text{-OBzl} \begin{cases} \xrightarrow[20\,^\circ\text{C}]{\text{HCOOH}} \text{H-DL-Gla}(O\text{t}\text{Bu})_2\text{-OBzl} \\ \xrightarrow{\text{H}_2/\text{Pd}} \text{BOC-DL-Gla}(O\text{t}\text{Bu})_2\text{-OH} \\ \xrightarrow[\text{MeOH}]{\text{KOH}} \text{BOC-DL-Gla}(O\text{t}\text{Bu})_2\text{-OH} \end{cases}$$

In a similar way, Z-Dha-OBzl (**6**) prepared from Z-Ser(Tos)-OBzl [8] was converted into Z-DL-Gla(O*t*Bu)$_2$-OBzl (**7**). Z-DL-Gla(O*t*Bu)$_2$-OH (**8**) was obtained from **7** by alkaline hydrolysis, and was crystallized as the DCHA salt (**8a**). Hydrogenolysis of **8** gave the crystalline H-DL-Gla(O*t*Bu)$_2$-OH (**9**).

$$\text{Z-Ser-OH} \xrightarrow[\text{DCHA}]{\text{Bzl-Br}} \text{Z-Ser-OBzl} \xrightarrow[\text{NEt}_3\text{/Py}]{\text{Tos-Cl}} \text{Z-Ser(Tos)-OBzl}$$

$$\xrightarrow[\text{EtOAc}]{\text{Et}_2\text{NH}} \text{Z-Dha-OBzl} \xrightarrow[\text{and its Na-salt}]{\text{di-}t\text{-butyl malonate}} \text{Z-DL-Gla}(O\text{t}\text{Bu})_2\text{-OBzl}$$

$$\text{Z-DL-Gla}(O\text{t}\text{Bu})_2\text{-OBzl} \xrightarrow{\text{KOH/MeOH}} \text{Z-DL-Gla}(O\text{t}\text{Bu})_2\text{-OH}$$

$$\text{Z-DL-Gla}(O\text{t}\text{Bu})_2\text{-OH} \xrightarrow{\text{H}_2/\text{Pd}} \text{H-DL-Gla}(O\text{t}\text{Bu})_2\text{-OH}$$

Removal of the blocking groups of either **5** or **9** with TFA yielded DL-Gla in the form of a trifluoroacetate. After lyophilization, an amorphous non-hygroscopic material was obtained with a low TFA content (0.15—0.25 equivalent) which could be crystallized from aqueous ethanol. Crystalline DL-Gla (**10**) had a sharp decomposition point, 156.5—157°C, and seemed to be homogeneous in TLC and electrophoresis.

Experimental

All m. p. 's are uncorrected. Thin-layer chromatograms were run on Silica gel G in the following solvent systems (composition by volume): (1) ethyl acetate–pyridine–acetic acid–water (120 : 20 : 6 : 11); (2) ethyl acetate–pyridine–acetic acid–water (240 : 20 : 6 : 11), (3)

n-butanol–acetic acid–water (3 : 1 : 1); (4) ethyl acetate; (5) ethyl acetate–*n*-hexane (1 : 3); (6) ethyl acetate–*n*-hexane (1 : 5). All evaporations were carried out in a rotary evaporator under diminished pressure, after drying the organic solutions over Na_2SO_4.

Boc-Ser-OBzl (1)

Boc-Ser [5] (20.5 g; 100 mmoles) and DCHA (21 ml; 102 mmoles) were dissolved in benzene (250 ml) and after the addition of benzyl bromide (10 ml; 97 mmoles), the clear solution was refluxed for 6 hrs. The DCHA·HBr which separated was filtered off and the filtrate washed successively with 1*N* HCl, 1*M* $NaHCO_3$ and water, dried and evaporated. The oily residue (25 g; 85%) showed a single spot in TLC: R_f^2 0.86—0.94.

Its structure was supported by the IR and NMR spectra.

Boc-Dha-OBzl (2)

To a solution of **1** (24.2 g; 82 moles) in ethyl acetate (200 ml) tosyl chloride (15.6 g; 82 mmoles) was added at 5—8°C, followed by triethylamine (23 ml; 164 mmoles). After standing at room temperature overnight, the mixture was refluxed for 10 min, then cooled and the salts which precipitated were filtered off. The filtrate was washed successively with 1*M* $NaHCO_3$ and water, then dried and evaporated. The residue was applied onto a column (Kieselgel 40, 0.063—0.200 mm, Reanal, Budapest; 400 g) and eluted with a mixture of ethyl acetate–*n*-hexane (3 : 1), to obtain 18.2 g (80%) of **2**, R_f^4 0.68—0.72.

Its structure was supported by the IR and NMR spectra.

Boc-DL-Gla(O*t*Bu)$_2$-OBzl (3)

Di-*t*-butyl malonate [6] (13 g; 60 mmoles) was dissolved in benzene (100 ml) and, after chilling to —5°C, sodium hydride (0.4 g 50% dispersion in oil; 8.7 mmoles) was added with caution. When the evolution of hydrogen ceased, the solution was refluxed for 10 min and was mixed, after cooling, with a solution of **2** (11.1 g; 40 mmoles) in benzene (400 ml). The resulting solution was concentrated to half volume and allowed to stand at room temperature overnight. The mixture was neutralized with acetic acid (0.6 ml), diluted with benzene (300 ml), and washed successively with 1*M* citric acid, 1*M* $NaHCO_3$ and water, then dried and evaporated to dryness. The residue was dissolved in light petroleum (300 ml) and seeded with pure **3** (obtained in a previous experiment by column chromatography on Kieselgel 40 with ethyl acetate–*n*-hexane (1 : 5)). After cooling overnight, the crystals were filtered off, washed with light petroleum and dried to obtain 13.5 g (68%) of **3**; m. p. 112—114 °C, R_f^6 0.38—0.42.

$C_{26}H_{39}O_8N$ (493.48). Calcd. C 63.26; H 7.96; N 2.83. Found C 63.09; H 7.97; N 2.82%.

DL-Gla(O*t*Bu)$_2$-OBzl. (COOH)$_2$ (4a)

A suspension of **3** (0.5 g; 1 mmole) in 85% formic acid (17 ml) was stirred for 1 hr. The clear solution was diluted with water (50 ml), the unchanged starting material (about 0.02 g; 4%) was filtered off and the filtrate concentrated. The residue was re-evaporated with water, dried by destillation with benzene and dissolved in ether (10 ml). On the addition of a slight excess of ethereal oxalic acid, **4a** separated. After filtration, washing with ether and drying. 0.31 g (64%) of the desired compound was obtained, m. p. 104—106 °C, R_f^4 0.85—0.90.

$C_{23}H_{33}O_{10}N$ (483.50). Calcd. C 57.13; H 6.88; N 2.90. Found C 57.25; H 6.92; N 2.88%.

Boc-DL-Gla(O*t*Bu)$_2$-OH. DCHA (5a)

(*a*) Alkaline hydrolysis. Compound **3** (1.35 g; 2.8 mmoles) was dissolved in 0.5*N* methanolic potassium hydroxide (5.6 ml) and the solution was stirred for 4 hrs. After adding acetic acid (0.3 ml), the solvent was evaporated, the residue dissolved in ethyl acetate and washed with 1*N* HCl and water, then dried and the solvent was evaporated. The oily residue was dissolved in ether (5 ml) and combined with a slight excess of ethereal DCHA. The solution was treated with *n*-hexane until turbidity appeared and was then stored in a refrigerator. 1.38 g (84%) of **5a** deposited as crystals, m. p. 166—168 °C, R_f^2 0.85—0.92.

$C_{31}H_{56}O_8N_2$ (584.77). Calcd. C 63.67; H 6.88; N 2.90. Found C 63.80; H 6.95; N 2.95%.

(*b*)Hydrogenolysis. A solution of **3** (2.45 g; 5 mmoles) in tetrahydrofuran (20 ml) was hydrogenated in the presence of palladized charcoal. When hydrogen absorption was completed, the catalyst was removed by filtration, and the filtrate was evaporated to yield 2 g (99%) of **5** which could be converted into the DCHA salt as described above.

Z-Dha-OBzl (6)

A solution of Z-Ser(Tos)-OBzl [8] (24.2 g; 50 mmoles) in ethyl acetate (200 ml) was treated below 10°C with diethylamine (5.3 ml; 51.5 mmoles). Stirring was continued without cooling for 3 hrs. The salts which precipitated were filtered off, and the filtrate was washed successively with 1*N* HCl, 1*M* $NaHCO_3$ and water, then dried and evaporated. 12.76 g (82%) of **6** was obtained as a thick oil, which solidified under *n*-hexane in a refrigerator, m. p. 57—60 °C R_f^5 0.62—0.68.

Z-DL-Gla(O*t*Bu)$_2$-OBzl (7)

Di-*t*-butyl malonate [5] (3.25 g; 15 mmoles) was dissolved in benzene (20 ml) and treated with sodium hydride (0.092 g; 1.95 mmoles) as described in the preparation of **3**. The solution thus obtained was combined with **6** (3.11 g; 10 mmoles) in benzene (10 ml). After standing overnight, the mixture was neutralized with acetic acid, evaporated, and the residue was applied onto a column made with 100 g of Kieselgel 40 (0.063—0.200 mm, Reanal, Budapest) in a mixture of ethyl acetate–*n*-hexane (1 : 5). Elution with the same mixture afforded 4.33 g (82%) of **7** as a pale yellow oil, R_f^5 0.45—0.50

Z-DL-Gla(O*t*Bu)$_2$-OH. DCHA (8a)

Compound **7** (1.48 g; 2.8 mmoles) was dissolved in 0.5*M* methanolic potassium hydroxide (5.6 ml) and stirred for 4 hrs. After neutralization with acetic acid the solvent was evaporated and the residue dissolved in ethyl acetate (20 ml), washed successively with 1*N* HCl and water then dried and evaporated to give **8**. This was dissolved in ether (15 ml) and the solution was combined with a slight excess of ethereal DCHA, then saturated with *n*-hexane (about 100 ml). On cooling **8a** crystallized (1.12 g; 64.7%), m. p. 135—137 °C, R_f^1 0.42—0.47.

$C_{34}H_{45}O_8N_2$ (618.79). Calcd. C 65.99; H 8.79; N 4.53. Found C 65.84; H 8.86; N 4.57%

DL-Gla(O*t*Bu)$_2$-OH (9)

Compound **8a** (1.1 g; 1.77 mmoles) was distributed between ethyl acetate (10 ml) and 1*N* H_2SO_4 (10 ml). The organic layer was washed with 1*N* H_2SO_4 and water, then dried and evaporated. The remaining oily **8** was dissolved in dioxane (10 ml) and hydrogenated in the presence of palladized charcoal. When the consumption of hydrogen stopped, the mixture was diluted with water (3 ml) and the catalyst was filtered off. The filtrate was evaporated to give white powder which was triturated with ether, filtered and washed with ether. 0.33 g (58%) of **9** was thus obtained, m. p. 143—145 °C, R_f^1 0.15—0.25.

$C_{14}H_{25}O_6N \cdot H_2O$ (321.46). Calcd. C 52.30; H 8.46; N 4.36. Found C 52.67; H 8.49; N 4.20%.

DL-Gla (10)

Boc-DL-Gla(O*t*Bu)$_2$-OH(**5**, 0.806; 2 mmoles) or DL-Gla(O*t*Bu)$_2$-OH (**9**, 0.642 g; 2 mmoles) was dissolved in TFA (4 ml) and kept at room temperature overnight. The TFA salt of **10** (0.60 g; 98%) which precipitated on treatment with ether was dissolved in water (20 ml) and lyophilized. This procedure was repeated three times and the material thus obtained (0.40 g) was dissolved in water (2 ml) and ethanol (2 ml) was added. The crystals were filtered off, washed with a small portion of ethanol, ether and, after drying, separately with water (3 × 0.3 ml); 0.19 g (50%) of **10** was obtained. A second crop of Gla (0.08 g; 20%) of the same purity was isolated, from the combined organic filtrates by dilution with ether; m. p. 156.5—157 °C (d.), R_f^3 0.28—0.34. Paper electophoresis of **10** in a pyridine acetate buffer of pH 6.5 showed a single ninhydrine-positive spot at a mobility relative to Asp, R_f 1.35—1.40. On a JLC—5AH amino acid analyser a retention time of 21 min was obtained for Gla (35 and 52 min for Asp and Glu, respectively), using LC—R-1 resin (column: 50 cm), at 40 °C, in 0.2*N* sodium citrate buffer (pH 3.25) at a flow rate of 100 ml/hour.*

$C_6H_9O_6N$ (191.14). Calcd. C 37.70; H 4.75; O 50.22; N 7.32. Found C 37.67; H 5.00; O 50.20; N 7.23%.

* These experiments were kindly performed by A. PATTHY.

REFERENCES

[1] STENFLO, J., FERNLUND, P., EGAN, W., ROEPSTORFF, P.: Proc. Nat. Acad. Sci. USA **71,** 2730 (1974)
[2] MAGNUSSON, S., SOTTRUP-JENSEN, L., PETERSEN, T. E., MORRIS, H. R., DELL, A.: FEBS Letters **44,** 189 (1974)
[3] Tentative Rules of the IUPAC—IUB Commission on Biochemical Nomenclature: Biochem. J. **126,** 773 (1972)
[4] MORRIS, H. R., THOMPSON, R., DELL, A.: Biochem. Biophys. Res. Commun. **62,** 856 (1975)
[5] OTSUKA, H., INOUYE, K., SHINOKAZI, F., KANAYAMA, M.: Bull. Chem. Soc. Jap. **39,** 1171 (1966)
[6] FONKEN, G., JOHNSON, W.: J. Am. Chem. Soc. **74,** 831 (1952)
[7] KINOSHITA, H., KOTAKE, H.: Chemistry Letters **1974,** 631
[8] PHOTAKI, I.: J. Am. Chem. Soc. **85,** 1123 (1963)

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HEXITOL DERIVATIVES CONTAINING A 1,4-OXATHIANE RING V*
PUMMERER REARRANGEMENT OF SULFOXIDES

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The Pummerer rearrangement of type **II** thioanhydrohexitol sulfoxides to the corresponding glucothioseptanose derivatives (**IV**) is described. Further oxidation of the dimesyl derivative **IVa** gave a mixture of two sulfoxide isomers (**V**). Deacetylation of the tri-*O*-acetate **IVb** afforded 2,5-anhydro-6-deoxy-6-thio-D-glucothioseptanose **VII**.

In earlier papers of this series [1—4] we described the synthesis of differently substituted 1,6-thioanhydrohexitols. Now we report on the possibility of converting these compounds (**I**) *via* their sulfoxides (**II**) by the Pummerer rearrangement [5] into hexose derivatives (**IV**).

As a model compound 2,5-anhydro-3,4-di-*O*-methylsulfonyl-1,6-thioanhydro-D-glucitol *S*-oxide (**IIa**) was used, which could be obtained from **Ia** by oxidation with sodium periodate [4], hydrogen peroxide [4] or *m*-chloroperbenzoic acid. When a solution of **IIa** in acetic anhydride was heated at 50°C for 3 hrs, the starting material was completely converted, and the Pummerer rearrangement product **IVa** could be isolated in a yield of 73%. As the sulfoxide group in **IIa** is flanked by two methylene groups, theoretically four isomers can be formed in this reaction, containing the acetyl group at C-1 (D-glucose) or at C-6 (L-gulose), and either axially (α) or equatorially (β) oriented. According to the NMR spectrum of **IVa** only one isomer was fromed, as the signal of the newly introduced acetoxyl group appeared as a singlet at δ 2.20 ppm. The signal of H-3 gives a doublet of doublets at δ 5.33 ppm and H-4 a doublet at δ 5.72 ppm, similarly to compound **Ia** [1]. The signal of H-2 which appears in the spectrum of **Ia** as a multiplet (due to the prevailing $J_{1,2}$; $J_{1',2}$ and $J_{2,3}$ couplings) gives in the case of the acetoxy derivative **IVa** a distinct doublet of doublets at δ 4.73 ppm, indicating substitution of one proton at C-1 by the acetoxyl group. The α-orientation of this group was established from the following data. From among all signals of the parent compound **Ia**, only that of the axially oriented H-6′ proton was shifted significantly (δ 3.15 → 3.45 ppm) in the acetoxy derivative **IVa**, besides the signal of the H-1 proton, being geminal to the acetoxyl group. This strong downfield shift can only be explained by a sterically close '*syn axial*' arrangement of the acetoxyl group at C-1 to

* Part IV: Acta Chim. (Budapest) **86**, 285 (1975)

the *axial* H-6′ proton. On the other hand, the two doublets of H-6 (2.49 ppm) and H-6′ (3.47 ppm) appear with different shapes, as that of the equatorially oriented H-6 proton gives broad signals, due to long-range coupling [4] with the similarly equatorially oriented H-1 proton ($J_{1,6} > 0$). According to these considerations, the product of the Pummerer rearrangement is 1-*O*-acetyl-2,5-anhydro-6-deoxy-3,4-di-*O*-methylsulfonyl-6-thio-α-D-glucothioseptanose (**IVa**).

Despite the fact that the sulfur atom of the original thio ether link is already part of a monothioacetal group in compound **IVa**, it can be oxidized to the sulfoxide **Va**. Nevertheless, in this case the two theoretically possible isomers, containing an equatorially and axially oriented S—O bond are formed in a ratio of about 1:1, as indicated by the NMR spectrum in which the acetoxyl group gives two singlets at δ 2.12 and 2.20 ppm. The two isomers differ in the shift of the mesyl groups as well but, due to overlapping, only three of them can be indicated at δ 3.37, 3.43 and 3.47 ppm. All efforts to separate these two isomers failed.

The sulfoxide mixture **Va** was submitted to the Pummerer reaction to convert it into the dialdehydothioacetal **VI**. No rearrangement took, however, place at 50 °C or at 80°C. At 110°C the starting material was consumed after 8 hrs, but the product, which could only be isolated as a chromatographycally pure solid foam, decomposed on standing at room temperature.

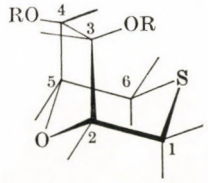
As **IVa** could not be deacetylated with sodium methoxide without further decomposition of the molecule, the synthesis of the corresponding 1,3,4-tri-*O*-acetyl derivative **IVb** was attempted. As intermediate the sulfoxide **IIb** was needed, which was prepared from the 3,4-dihydroxy derivative **Ic** [2] by oxidation and subsequent acetylation (**Ic** → **IIc** → **IIb**), or by a reversed order of these reactions (**Ic** → **Ib** → **IIb**). It is worthwile mentioning that treatment of **Ic** with sodium periodate resulted in exclusive oxidation of the sulfur atom and no splitting between the two vicinal hydroxyl groups did occur. McCORMICK and McELHINNEY [6] observed a similar selectivity when oxidizing 3,4-dihydroxytetrahydrothiophene with periodate.

The diacetylsulfoxide **IIb** proved to be more resistant to the Pummerer reaction than the dimesyl analogue **IIa**, as no reaction took place at 50 °C. At 80 °C the rearrangement was completed in 5 hrs and the hexose derivative **IVb** could be isolated as a colorless syrup in 90% yield. The *gluco* configuration of this compound was proved by its NMR spectra, confirming location of the newly introduced acetoxyl group at C-1. The spectrum is similar to that of **IVa**, the doublet of H-1 appearing at δ 5.40 ppm, whereas H-2 gives a doublet of doublets at δ 4.70 ppm, completely separated from the multiplet of H-5 at δ 4.35 ppm. The H-6 and H-6′ protons give two doublets of doublets at δ 2.51 and 3.42 ppm, respectively; the former appear as broad signals, due to the prevailing long-range coupling with H-1 ($J_{1,6} > 0$). The three singlets of the acetoxyl groups can be detected at δ 2.18, 2.16 and 2.13 ppm, respectively.

When oxidation of the thioacetal **IVb** to the corresponding sulfoxide **Vb** was carried out similarly to the conversion of the dimesyl analogue (**IVa** to **Va**), only a syrupy product was obtained which decomposed rapidly on standing at room temperature.

Deacetylation of the triacetate **IVb** by sodium methoxide afforded 2,5-anhydro-6-deoxy-6-thio-D-glucothioseptanose (**VII**) as a water-soluble, amorphous material.

The sulfones **IIIa** and **IIIb** remained unchanged under the conditions of the Pummerer rearrangement even at 110 °C.



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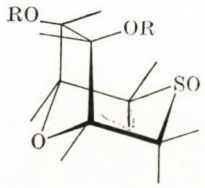
Ic R = H



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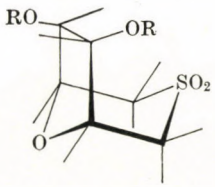

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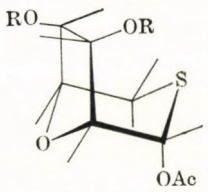

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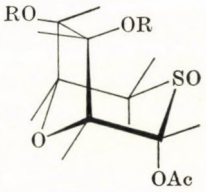

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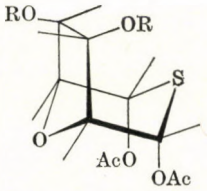
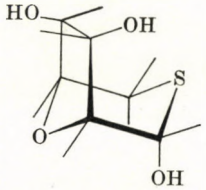
Vb R = Ac



VI R = Ms



VII

Experimental

M. p. 's are uncorrected. TLC was effected on microscope slides coated with Silica Gel G. Spraying with a mixture of 0.1*M* potassium permanganate and 1*M* sulfuric acid (1 : 1) and heating to 105 °C was used for detection. The NMR spectra were recorded at 60 MHz with a Varian A-60D spectometer, using $CDCl_3$ solutions with TMS as internal standard, at room temperature. All evaporations were carried out in a rotary evaporator under reduced pressure, after drying the organic solutions over sodium sulfate.

2,5-Anhydro-3,4-di-*O*-methylsulfonyl-1,6-thioanhydro-D-glucitol *S*-oxide (IIa)

A solution of compound **Ia** [1,2] (3.2 g) in dry chloroform (32 ml) was treated with *m*-chloroperbenzoic acid (83.5% purity, 2.26 g). The temperature of the reaction mixture rose to 50 °C. After 1 hr it was poured, with stirring, into a slurry of potassium carbonate (7 g) in acetone (100 ml). The solid material was filtered off and washed with dry acetone. The combined filtrates were evaporated and the residue was recrystallized from 5% aqueous sodium hydrogen carbonate solution to yield 2.13 g (63.7%) of **IIa**; m.p. 190—192°C, alone as well as in admixture with an authentic sample [1, 2].

3,4-Di-*O*-acetyl-2,5-anhydro-1,6-thioanhydro-D-glucitol *S*-oxide (IIb)

A solution of the dihydroxy-*S*-oxide **IIc** (0.18 g) in pyridine (0.5 ml) was treated with acetic anhydride (0.4 ml). The reaction mixture was kept at room temperature for 2 days and was then evaporated. The residue was mixed with ether, filtered off and recrystallized from ethyl acetate–light petroleum to yield pure **IIb** (0.13 g; 50%), m.p. 128—130 °C, alone and in admixture with an authentic sample [4].

2,5-Anhydro-1,6-thioanhydro-D-glucitol *S*-oxide (IIc)

A solution of compound **Ic** [2] (0.32 g) in methanol (10 ml) was treated with a solution of sodium periodate (0.46 g) in water (4 ml). The slurry which formed immediately was stirred for 1 hr at room temperature. The precipitated salts were filtered off and washed with methanol. The residue of the evaporated filtrate was dissolved in water (2 ml) and treated with methanol (2 ml). After keeping the mixture overnight at −5 °C, the precipitated material was filtered off. The filtrate was evaporated, the residue re-evaporated with ethanol, and filtrated with acetone to yield pure **IIc** (0.25 g; 70%); m.p. 170—171°C; R_f 0.60 (ethyl acetate–ethanol (2 : 1); $[\alpha]_D^{20}$ −23° ($c = 1$, water).

$C_6H_{10}O_4S$ (178.21). Calcd. C 40.44; H 5.66; S 17.99. Found C 40.35; H 5.61; S 17.68%

3,4-Di-*O*-acetyl-2,5-anhydro-1,6-thioanhydro-D-glucitol *S*,*S*-dioxide (IIIb)

A solution of the dihydroxysulfone **IIIc** (0.39 g) in pyridine (2 ml) was treated with acetic anhydride (1 ml). After keeping the reaction mixture at room temperature overnight, it was poured into water. The precipitate was filtered off and recrystallized from water to yield **IIIc** (0.28 g; 50%), m.p. 166—168 °C, alone and in admixture with an authentic sample [4].

2,5-Anhydro-1,6-D-glucitol *S*,*S*-dioxide (IIIc)

A solution of compound **Ic** [2] (1.52 g) in acetic acid (10 ml) was treated with 33% aqueous hydrogen peroxide (3 ml). After 3 days at room temperature the reaction mixture was evaporated and twice re-evaporated with water. The solid residue was mixed with ethanol and filtered off to yield **IIIc** (1.25 g; 64.4%), m.p. 133—135 °C; $[\alpha]_D^{20}$ −23° ($c = 1$, water).

$C_6H_{10}O_5S$ (194.21). Calcd. C 37.11; H 5.19; S 16.51. Found C 36.95; H 5.25; S 16.52%.

1-*O*-Acetyl-2,5-anhydro-6-deoxy-3,4-di-*O*-methylsulfonyl-6-thio-α-D-glucothioseptanose (IVa)

A solution of the sulfoxide **IIa** (6.7 g) in acetic anhydride (70 ml) was heated at 50°C for 4 hrs. The residue obtained after evaporation was recrystallized from acetic acid (5 ml) to yield compound **IVa** (5.65 g; 73.5%); m.p. 154—155°C (d.); R_f 0.75 (water std butanol), 0.5 (carbon tetrachloride–ethyl acetate 1 : 1); $[\alpha]_D^{20}$ + 154° ($c = 1$, chloroform), + 170.5° ($c = 1$, DMF). The compound could be recrystallized from methanol, but the m.p. decreased to 137—140 °C.

NMR data: δ5.72 (*d*, H-4), 5.55 (*d*, H-1), 5.33 (2 × *d*, H-3), (4.73 2 × *d*, H-2), 4.70 (*m*, H-5), 3.47 (2 × *d*, H-6'), 2.49 (2 × *d*, broad, H-6), 3.24 and 3.20 (2 × *s*, mesyl CH_3), 2.20 ppm (*s*, acetyl CH_3). Coupling constants: $J_{1,2} = 2$, $J_{2,3} = 7$, $J_{3,4} = 3$, $J_{4,5} \approx 0$, $J_{5,6} \approx \approx 2.5$, $J_{5,6'} = 2.5$, $J_{1,6} > 0$ Hz.

$C_{10}H_{16}O_9S_3$ (376.43). Calcd. C 31.91; H 4.29; S 25.56. Found C 32.12; H 4.45; S 25.40%.

1,3,4-Tri-*O*-acetyl-1,5-anhydro-6-deoxy-6-thio-α-D-glucothioseptanose (IVb)

A solution of compound **IIb** (2.62 g) in acetic anhydride (26 ml) was heated at 80 °C for 5 hrs. After evaporation and re-evaporation with ethanol the residue was dissolved in chloroform and washed with water, aqueous sodium hydrogen carbonate and water. Evaporation of the dried solution afforded **IVb** as a colorless syrup (2.7 g; 90%); $[\alpha]_D^{20}$ + 95° ($c = 1$, chloroform).

NMR data: δ5.66 (*d*, H-4), 5.40 (*d*,H-1), 5.38 (2 × *d*, H-3), 4.70 (2 × *d*, H-2), 4.35 (*m*, H-5), 3.42 (2 × *d* H-6'), 2.51 (2 × *d*, broad, H-6), 2.18, 2.16 and 2.13 ppm (3 × *s*, acetyl CH_3). The coupling constants are, within the limit of error, identical with those of compound **IVa**.

$C_{12}H_{16}O_7S$ (304.31). Calcd. C 47.35; H 5.30; S 10.53. Found C 47.16; H 5.15; S 10.32%.

1-*O*-Acetyl-2,5-anhydro-6-deoxy-3,4-di-*O*-methylsulfonyl-6-thio-α-D-glucothioseptanose *S*-oxide (Va)

Compound **IVa** (3.8 g) was dissolved with gentle heating in acetic acid (100 ml). 33% aqueous hydrogen peroxide (1.1 ml) was added to the cooled solution and the reaction mixture was allowed to stand at room temperature overnight. Then it was evaporated below 30 °C and the residue washed with water to yield compound **Va** (3.63 g; 92.6%); m.p. 148—150 °C (d.); $[\alpha]_D^{20}$ + 165° (c = 1, DMF); R_f 0.40 (carbon tetrachloride–ethyl acetate 1 : 1; the spot can be detected with potassium iodide).

$C_{10}H_{16}O_{10}S_3$ (392.43). Calcd. C 30.60; H 4.11; S 24.51. Found C 30.78; H 4.09; S 24.78%.

2,5-Anhydro-6-deoxy-6-thio-D-glucothioseptanose (VII)

A solution of compound **IVb** (1.4 g) in dry methanol (15 ml) was treated with 4.3*N* sodium methoxide (1.2 ml). After 1 hr at room temperature the solution was neutralized with 1*N* HCl and evaporated. The residue was purified by column chromatography on silicic acid (ethyl acetate) using ethyl acetate–ethanol (5 : 1) for elution. The fractions of R_f 0.55 were evaporated to yield **VII** as a solid foam (0.55 g; 67%); $[\alpha]_D^{20}$ + 66° (c = 1, water; no mutarotation was observed). Compound **VII** reduced Fehling's solution immediately at room temperature.

$C_6H_{10}O_4S$ (178.21). Calcd. C 40.44; H 5.66; S 17.99. Found C 40.19; H 5.89; S 17.72%.

REFERENCES

[1] KUSZMANN, J., SOHÁR, P.: Cabohyd. Res. **27,** 157 (1973)
[2] KUSZMANN, J., SOHÁR, P.: Acta Chim. Budapest **83,** 373 (1974)
[3] KUSZMANN, J., SOHÁR, P., HORVÁTH, GY., MÉHESFALVI-VAJNA, ZS.: Tetrahedron **30,** 3905 (1974)
[4] SOHÁR, P., KUSZMANN, J.: Acta Chim. (Budapest) **86,** 285 (1975)
[5] KUSZMANN, J., SOHÁR, P., HORVÁTH, GY.: Tetrahedron **27,** 5055 (1971)
[6] MCCORMICK, J. E., MCELHINNEY, R. S.: Chem. Commun. **1969,** 171

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THE OXIDATIVE REARRANGEMENT OF CHALCONES BY THALLIUM(III)NITRATE, V*

THE SYNTHESIS OF 3'-HYDROXYRETUSIN-8-METHYL ETHER AND NEW SYNTHESIS OF RETUSIN AND ITS 8-METHYL ETHER, THREE NATURAL ISOFLAVONES FROM TROPICAL WOODS

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The synthesis of 7,8-dihydroxy-4'-methoxyisoflavone (retusin, **1**), 4',8-dimethoxy-7-hydroxyisoflavone (8-*O*-methylretusin, **2**) and 3',7-dihydroxy-4',8-dimethoxyisoflavone (3'-hydroxy-8-*O*-methylretusin, **3**) was accomplished by oxidative rearrangement of the corresponding chalcones by $Tl(NO_3)_3$ as the key step.

From the heartwood of *Dalbergia retusa*, a tree indigenous to Panama, two new isoflavones, 7,8-dihydroxy-4'-methoxyisoflavone (**1**), named retusin and its 8-methyl ether (**2**), the first natural isoflavones possessing this particular oxygenation pattern, have been isolated by JURD *et al.* [2] in 1972. The structures of these isoflavones have been determined by spectroscopic and chemical means, as well as by identifying the phenyl benzyl ketone obtained from the degradation of retusin (**1**) with 2,3,4-trihydroxyphenyl 4'-methoxybenzyl [5] ketone prepared by synthesis. This ketone was recyclized to **1** and also converted to 8-*O*-methylretusin (**2**) by selective benzylation (at C_7-O) of its diacetate followed by deacetylation methylation and debenzylation [2].

In 1974 **1** and **2** have been re-isolated by HAYASHI and THOMSON from the heartwood of the tropical tree *Dipteryx odorata* [3] along with a new component, 3',7-dihydroxy-4',8-dimethoxyisoflavone (3'-hydroxy-8-*O*-methylretusin, **3**). The structure **3** has been deduced from spectroscopic evidence; its synthesis has not been reported.

In this paper we describe the utilization of the oxidative rearrangement of chalcones by thallium(III) nitrate (TTN) [4] for the first synthesis of **3** and for convenient new syntheses of **1** and **2**.

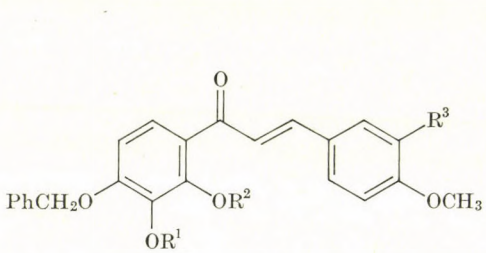
For the synthesis of retusin (**1**), first 2-hydroxy-3,4-dibenzyloxyacetophenone [5] was condensed with anisaldehyde to give the chalcone **4**. The use of gallacetophenone was precluded by its oxidizability. In order to increase solubility in methanol and avoid side reactions, **4** was converted to its acetate (**5**). This was treated in methanol with TTN to give the acetal **16** by oxidative rearrangement [6]; this was not isolated, but deacetylated and cyclized by acid to 7,8-di-*O*-benzylretusin (**10**). Catalytic debenzylation of **10** afforded 7,8-dihydroxy-4'-methoxyisoflavone (**1**), which was identical in every respect

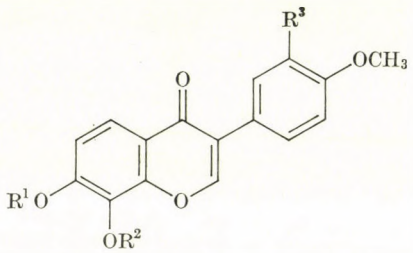
* For Part IV, see ref. [1].

with natural retusin (m.p., mixed m.p., IR and NMR spectra, further the m.p. of the diacetate (**11**)).

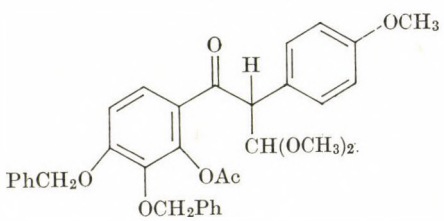
A similar sequence starting with 4-benzyloxy-2-hydroxy-3-methoxyacetophenone [5] and comprising the chalcone **6**, its acetate **7** and 7-*O*-benzyl-8-*O*-methylretusin (**12**), afforded 4', 8-dimethoxy-7-hydroxyisoflavone (**2**) identified by its UV spectrum and the m.p. of its acetate (**13**) with natural 8-*O*-methylretusin. Synthetic **2** showed a slightly higher m.p. (228—229°C) than the natural product (223—224 °C).

In order to accomplish the synthesis of **3**, the above acetophenone was condensed with 3-benzyloxy-4-methoxybenzaldehyde [7] to give the chalcone **8**. Oxidation of its acetate (**9**) gave rise to the isoflavone **14**, which was debenzylated to 3',7-dihydroxy-4',8-dimethoxyisoflavone (**3**). The synthetic sample was identified with natural 3'-hydroxy-8-*O*-methylretusin by m.p., mixed m.p., IR spectrum and by the m.p. of the diacetate (**15**).





	R^1	R^2	R^3		R^1	R^2	R^3
4	$PhCH_2$	H	H	**1**	H	H	H
5	$PhCH_2$	CH_3CO	H	**2**	H	CH_3	H
6	CH_3	H	H	**3**	H	CH_3	OH
7	CH_3	CH_3CO	H	**10**	$PhCH_2$	$PhCH_2$	H
8	CH_3	H	$PhCH_2O$	**11**	CH_3CO	CH_3CO	H
9	CH_3	CH_3CO	$PhCH_2O$	**12**	$PhCH_2$	CH_3	H
				13	CH_3CO	CH_3	H
				14	$PhCH_2$	CH_3	$PhCH_2O$
				15	CH_3CO	CH_3	CH_3CO_2



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Experimental

3′,4′-Dibenzyloxy-2′-hydroxy-4-methoxychalcone (4)

To a solution of 3,4-dibenzyloxy-2-hydroxyacetophenone (4.7 g) [5] and anisaldehyde (5 ml) in hot ethanol (100 ml) 50% aqueous potassium hydroxide (100 ml) was added and the mixture heated for 15 min on a steam bath. To the cooled solution ice was added and it was neutralized with 10% HCl. The precipitate was separated and recrystallized from methanol–acetone 1 : 1 (400 ml) to give 4.4 g (76%) of the almost pure chalcone; orange needles, m.p. 140—141 °C (from acetic acid).

$C_{30}H_{26}O_5$ (466.5). Calcd. C 77.23; H 5.67. Found C 77.27; H 5.71%.

2′-Acetoxy-3′,4′-dibenzyloxy-4-methoxychalcone (5)

Acetylation of **4** (3.0 g) with acetic anhydride in pyridine gave, after recrystallization from ethanol, compound **5** (2.4 g, 72%) as yellow needles, m.p. 131—132 °C.

$C_{32}H_{28}O_6$ (508.5). Calcd. C 75.57; H 5.55. Found C 75.29; H 5.57%.

7,8-Dibenzyloxy-4′-methoxyisoflavone (10)

To a solution of **5** (2.3 g) in 50 ml of dry methanol and 50 ml of chloroform, $Tl(NO_3)_3 \cdot 3H_2O$ (2.5 g) was added in portions over a period of 30 min at about 40 °C. After 4 hrs the reaction mixture was filtered, neutralized with 1*N* NaOMe, filtered again and evaporated to a small volume. After the addition of water, the organic material was extracted with chloroform, the solvent evaporated, the residue dissolved in methanol and boiled, after the addition of a few of 1*N* NaOMe, for 15 min. After acidification with 10% aqueous HCl, boiling was continued for 1 hr. The product separated on cooling and was recrystallized from methanol to obtain small, colorless needles (0.58 g, 31%), m.p. 116—117 °C.

$C_{30}H_{24}O_5$ (464.5). Calcid. C 77.57; H 5.21. Found C 77.26; H 5.35%.

7,8-Dihydroxy-4′-methoxyisoflavone; retusin (1)

Catalytic hydrogenation of **10** (0.58 g) in the presence of palladium-on-charcoal in acetone gave, after repeated crystallizations from methanol, compound **1** (73 mg; 21%) as colorless prisms, m.p. 247—249 °C (lit. [2] m.p. 249 °C).

7,8-Diacetoxy-4′-methoxyisoflavone; retusin diacetate (11)

Acetylation of **1** (50 mg) gave the diacetate (48 mg; 83%) as colorless needles, m.p. 165—166 °C (from methanol (lit. [2] m.p. 166 °C).

4′-Benzyloxy-3′,4-dimethoxy-2′hydroxychalcone (6)

Reaction of 4-benzyloxy-2-hydroxy-3-methoxyacetophenone (4.7 g) [5] with anisaldehyde (4.0 ml), as described for chalcone **4**, gave after two recrystallizations from acetic acid compound **6** (3.7 g; 57%) as orange plates, m.p. 143—145°C.

$C_{24}H_{22}O_5$ (390.4). Calcd. C 73.83; H 5.68. Found C 74.01; H 5.93%.

2′-Acetoxy-4′-benzyloxy-3′,4-dimethoxychalcone (7)

Acetylation of **6** (1.0 g) gave yellow crystals (0.7 g; 61%), m.p. 88—89 °C (from methanol).

$C_{26}H_{24}O_6$ (432.5). Calcd. C 72.21; H 5.59%. Found C 72.09; H 5.61%.

7-Benzyloxy-4′,8-dimethoxyisoflavone (12)

Transformation of **7** (2.6 g), as described for **4**, in MeOH–$CHCl_3$ (4 : 1, 50 ml) gave almost pure **12** (1.0 g; 43%); colorless plates (from methanol), m.p. 135—136°C.

$C_{24}H_{20}O_5$ (388.4). Calcd. C 74.21; H 5.19. Found C 66.75; 4,72%.

7-Acetoxy-4′,8-dimethoxyisoflavone; 8-*O*-methylretusin acetate (13)

Catalytic debenzylation of **12** (0.58 g) in acetone and acetylation of the product afforded after two recrystallizations from ethanol compound **13** (0.10 g; 20%) as colorless needles, m.p. 123—124 °C (lit. [2] m.p. 124—125 °C).

4′,8-Dimethoxy-7-hydroxyisoflavone; 8-*O*-methylretusin (2)

Deacetylation of **13** (50 mg) with NaOMe gave **2** (34 mg) as colorless prisms of m.p. 228—229 °C (lit. [2] m.p. 223—224 °C).

3,4′-Dibenzyloxy-3′,4-dimethoxy-2′-hydroxychalcone (8)

Reaction of 4-benzyloxy-2-hydroxy-3-methoxyacetophenone (5 g) [5] with 3-benzyloxy--4methoxybenzaldehyde (6 g) [7], as described for chalcone **4**, gave after three recrystallizations from acetic acid orange plates (2.9 g; 34%), m.p. 138—139 °C.

$C_{31}H_{28}O_6$ (496.5). Calcd. C 74.98; H 5.68. Found C 74.87; H 5.73%.

2′-Acetoxy-3,4′-dibenzyloxy-3′,4-dimethoxychalcone (9)

Acetylation of **8** (1.8 g) gave colorless plates (1.7 g; 92%), m.p. 152—153 °C (from acetic acid).

$C_{33}H_{30}O_7$ (538.6). Calcd. C 73.59; H 5.61. Found C 73.79; H 5.60%.

3′,7-Dibenzyloxy-4′,8-dimethoxyisoflavone (14)

Transformation of **9** (1.5 g) in methanol–chloroform (1 : 1, 100 ml) gave pure **14** (0.69 g; 50%), m.p. 151—152.5 °C, unchanged on recrystallization from methanol.

$C_{31}H_{26}O_6$ (494.5). Calcd. C 75.29; H 5.43. Found C 75.29; H 5.30%.

3′,7-Diacetoxy-4′,8-dimethoxyisoflavone; 3′-hydroxy-8-*O*-methylretusin diacetate (15)

Catalytic debenzylation of **14** (0.50 g) in acetone and acetylation of the product yielded, after recrystallization from methanol, compound **15** as colorless needles (0.13 g), m.p. 168—170°C (lit. [3] m.p. 163—165 °C).

3′7-Dihydroxy-4′,8-dimethoxyisoflavone; 3′-hydroxy-8-*O*-methylretusin (3)

Deacetylation of **15** (50 mg) with NaOMe gave colorless prisms (26 mg), m.p. 207—209 °C (from methanol) (lit. [3] m.p. 208—210 °C).

*

We are grateful to Dr. L. JURD (Berkeley, U.S.A.) and to Prof. R. H. THOMSON (Aberdeen, Scotland) for samples of the natural products.

REFERENCES

[1] ANTUS, S., FARKAS, L., KARDOS-BALOGH, ZS., NÓGRÁDI, M.: Chem. Ber. **108,** 3883. (1975)
[2] JURD, L., STEVENS, K., MANNERS, G.: Tetrahedron Letters, **1972,** 2149; Phytochemistry **11,** 2535 (1972)
[3] HAYASHI, TERUO, THOMSON, R. H.: Phytochemistry, **13,** 1943 (1974)
[4] ANTUS, S., FARKAS, L., GOTTSEGEN, A., NÓGRÁDI, M.: J. C. S. Chem. Commun., **1972,** 825; J. Chem. Soc. Perkin I **1974,** 305
[5] KHANNA, R. H., SESHARDI, T. R.: Indian. J. Chem., **1963,** 1, 385
[6] MCKILLOP, A., SWANN, B., TAYLOR, E. C.: Tetrahedron Letters, **1970,** 5281; J. Am. Chem. Soc. **95,** 3641 (1973)
[7] BOGNÁR, R., STEFANOVSKIY, J.: Tetrahedron, **8,** 143 (1962)

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KINETIC STUDY OF THE ISOMERIZATION OF 5-VINYL-BICYCLO(2.2.1.)HEPTENE-2 CATALYZED BY $Co(N_2)(PPh_3)_3$

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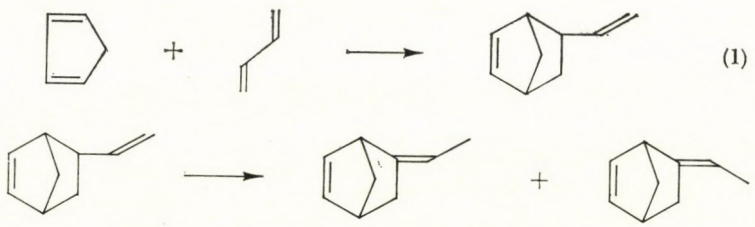
5-Vinylbicyclo(2.2.1.)heptene-2 can be isomerized to 5-ethylidenebicyclo(2.2.1.) heptene-2 by $Co(N_2)(PPh_3)_3$ in toluene solution at 50—70°. The following rate law was found to apply:

$$-\frac{d\,[vbh]}{dt} = \frac{k_4K_1K_2K_3K_5\,[Co]\,[vbh]^2}{K_5\,[S]\,[PPh_3] + K_2K_5\,[S]}$$

where [Co], [*vbh*], [PPh_3] and [S] are the concentrations of the catalyst, 5-vinylbicyclo (2.2.1) heptene-2, triphenyl phosphine and the solvent, respectively. The 1,3 hydrogen shift is assumed to proceed through a π-allyl mechanism.

Introduction

Since the discovery that 5-ethylidenebicyclo (2. 2. 1.) heptene-2* [1] can be used for the ethylene-propylene mixed polymerization giving terpolymers, which contain double bonds suitable for vulcanization, and exhibit better properties than the ethylene–propylene co-polymer, more attention was paid to its preparation. The isomerization of *vbh* to *ebh* (2) is presently the only way for large scale production which may be considered since *vbh* can be prepared with the Diels-Alder reaction from butadiene and cyclopentadiene (1) [2]



(1)

(2)

vbh exo ebh endo

both which are formed in large amounts in gasoline pyrolysis.

* *ebh* = abbreviation for 5-ethylidenebicyclo(2.2.1.)heptene-2
vbh = abbreviation for 5-vinylbicyclo(2.2.1.)heptene-2

FVOZDEVA *et al.* [3] have found, that the isomerization of *vbh* can be carried out at 20° with high reaction rate and practically 100% yield using metallic potassium in liquid ammonia. Using $NaAl_2O_3$ as a catalyst at 40° high yields could be achieved, too [4]. $Fe(CO)_5$ was used successfully for the same isomerization in hydrocarbon solvents at 80—200° under argon [5], and Ziegler-type catalysts composed from cobalt(II) acetylacetonate and trialkylaluminium were also very effective [6].

Encouraged by our earlier results of isomerization of hexenes catalyzed by $Co(N_2)(PPh_3)_3$ [7] we applied this catalyst also for the isomerization of *vbh* to *ebh*.

Results and discussion

The kinetic measurements were carried out in toluene at 50—70° and the reaction was followed by GLC. Besides the *exo*- and *endo*-isomers of *ebh* (which were not determined separately) less than 1% ethyl-bicycloheptadiene was found as the only by-product.

The results of a typical experiment are shown in Fig. 1 plotting the reciprocal concentration of *vbh* againts reaction time. The straight line obtained indicates a second order dependence on *vbh*. The reaction rates obtained at varying catalyst concentrations can be seen in Fig. 2. The straight line suggests a first order dependence with respect to catalyst concentration. High concentrations of added free triphenyl phosphine reduce the reaction rate; the effect of added PPh_3 is shown in Fig. 3.

If no triphenyl phosphine is added the following empirical rate equation (3) results:

$$-\frac{d[vbh]}{dt} = \underbrace{k_{obs}[Co(N_2)(PPh_3)_3]}_{k_2'}[vbh]^2 . \qquad (3)$$

Performing experiments at different temperatures and determining the corresponding k_{obs} values the following activation parameters were calculated:

$$\Delta E_a = 25.0 \text{ kcal.mole}^{-1}$$

$$\Delta H^{\ddagger} = 24.3 \text{ kcal.mole}^{-1}$$

$$\Delta S^{\ddagger} = 4.0 \text{ cal.mole}^{-1}.\text{K}^{-1}$$

Experiments showed that at temperatures between 50—70° and in aromatic solvents, like benzene or toluene, $Co(N_2)(PPh_3)_3$ looses dinitrogen in a fast and irreversible reaction (4).

$$Co(N_2)(PPh_3)_3 + (S) \xrightarrow{\text{fast}} Co(S)(PPh_3)_3 + N_2 . \qquad (4)$$

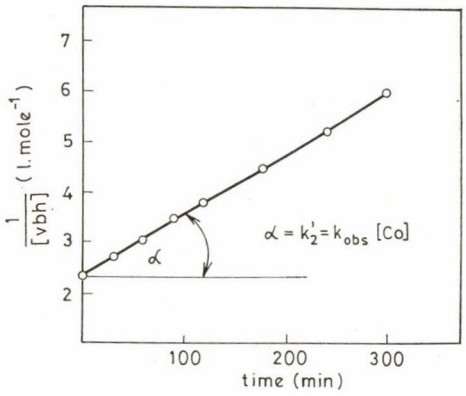


Fig. 1. A typical *vbh* isomerization experiment catalyzed by Co(N)$(PPh_3)_3$. Solvent: 10 ml toluene; catalyst concentration: 3.9×10^{-2} mole · l^{-1}; olefin concentration: 0.419 mole l^{-1}; temp. 60°

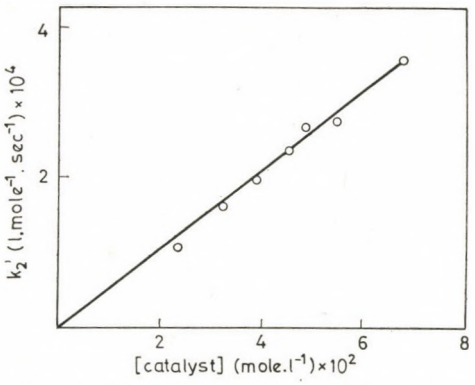


Fig. 2. The influence of catalyst concentration on the isomerization rate of *vbh*. Solvent: toluene; *vbh* concentration: 0.419 mole · l^{-1}; temp. 60°

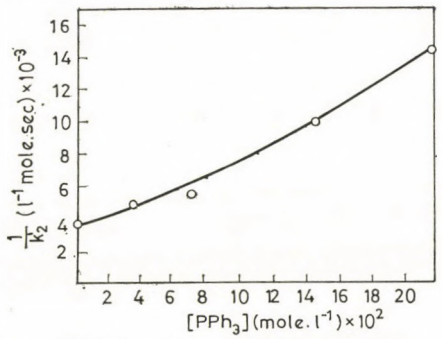


Fig. 3. The influence of free added phosphine on the reciprocal reaction rate. Solvent: toluene; catalyst concentration: 4.9×10^{-2} mole · l^{-1}; *vbh* concentration: 0.42 mole · l^{-1}; temp. 6

Reaction (4) could not be reversed even at 50 atm dinitrogen pressure. The reaction was followed by the evolution of N_2 and by the vanishing intensity of the infrared N,N stretching frequency. No signals in the ^{1}H-NMR spectrum attributable to Co–H bonds were found.

Based on the kinetic data the following mechanism is suggested:

$$Co(S)(PPh_3)_3 \overset{K_1}{\rightleftharpoons} Co(S)(PPh_3)_2 + PPh_3 \qquad (5)$$

$$Co(S)(PPh_3)_2 + vbh \overset{K_2}{\rightleftharpoons} Co(vbh)(PPh_3)_2 + (S) \qquad (6)$$

$$Co(vbh)(PPh_3)_2 + vbh \overset{K_3}{\rightleftharpoons} Co(vbh)_2(PPh_3)_2 \qquad (7)$$

$$Co(vbh)_2(PPh_3)_2 \xrightarrow{k_4} Co(vbh)(ebh)(PPh_3)_2 \qquad (8)$$

$$Co(vbh)(ebh)(PPh_3)_2 + vbh \overset{K_5}{\rightleftharpoons} Co(vbh)_2(PPh_3)_2 + ebh \qquad (9)$$

If reaction (8) is regarded as the rate determining step the reaction rate may be expressed by Eq. (10)

$$-\frac{d[vbh]}{dt} = k_4 [Co(vbh)_2(PPh_3)_2] \ . \tag{10}$$

The total amount of cobalt [Co] is present in the reaction mixture in the following forms:

$$[Co] = [Co(S)(PPh_3)_3] + [Co(S)(PPh_3)_2] + [Co(vbh)(PPh_3)_2] + [Co(vbh)_2(PPh_3)_2] + [Co(vbh)(ebh)(PPh_3)_2] \tag{11}$$

and the concentrations of the different species depend on the equilibria (5), (6), (7) and (9) as shown in Eqs (12)—(15).

$$K_1 = \frac{[Co(S)(PPh_3)_2][PPh_3]}{[Co(S)(PPh_3)_3]} \tag{12}$$

$$K_2 = \frac{[Co(vbh)(PPh_3)_2][S]}{[Co(S)(PPh_3)_2][vbh]} \tag{13}$$

$$K_3 = \frac{[Co(vbh)_2(PPh_3)_2]}{[Co(vbh)(PPh_3)_2][vbh]} \tag{14}$$

$$K_5 = \frac{[Co(vbh)_2(PPh_3)_2][ebh]}{[Co(vhb)(ebh)(PPh_3)_2][vbh]} \ . \tag{15}$$

Substituting Eqs (12)—(15) into Eq. (11) the dependence of $Co(vbh)_2(PPh_3)_2$ on the total catalyst concentration may be obtained (16).

$$[Co] = [Co(vbh)_2(PPh_3)_2]\left\{\frac{[PPh_3][S]}{K_1K_2K_3[vbh]^2} + \frac{[S]}{K_2K_3[vbh]^2} + \frac{1}{K_3[vbh]} + 1 + \frac{[ebh]}{K_5[vbh]}\right. \tag{16}$$

(10) and (16) lead to Eq. (17) for the rate expression.

$$-\frac{d[vbh]}{dt} = \frac{k_4K_1K_2K_3K_5[Co][vbh]^2}{K_5[PPh_3][S] + K_1K_5[S]K_1K_2K_5[vbh]} + \frac{k_4K_1K_2K_3K_5[Co][vbh]^2}{K_1K_2K_3K_5][vbh]^2 + K_1K_2K_3[vbh][ebh]} \ . \tag{17}$$

If K_2 and K_3 are assumed to be small, K_1 may be determined from the phosphine inhibition experiments. If no phosphine is added, Eq. (12) may be written in the form (18) since $[Co(S)(PPh_3)_3] = [Co] - [PPh_3]$.

$$K_1 = \frac{[PPh_3]^2}{[Co] - [PPh_3]} \tag{18}$$

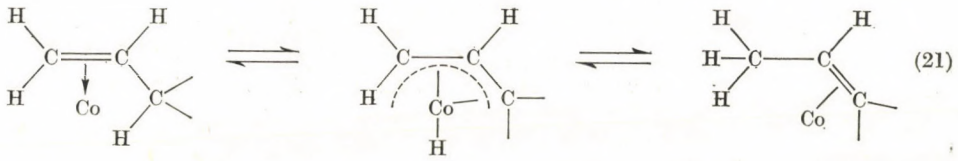
Using free added phosphine Eq. (18) modifies to Eq. (19)

$$K_1 = \frac{[PPh_3'] \{[PPh_3'] + [PPh_3]_{add}\}}{[Co] - [PPh_3']} \tag{19}$$

where $[PPh_3']$ is the phosphine concentration originating from the catalyst complex if free added phosphine is present. Using Eqs (18) and (19) K_1 can be calculated and its value is included in Table I.

The assumption, that constants K_2 and K_3 are small simplifies (17) to Eq. (20) which is in accordance with the experimental results obtained:

$$-\frac{d[vbh]}{dt} = \frac{k_4 K_1 K_2 K_3 K_5 [Co] [vbh]^2}{K_5 [S] [PPh_3] + K_1 K_5 [S]} \tag{20}$$



(21)

Concerning the fine mechanism of *vbh* isomerization several plausible pathways may be suggested. One of these is represented in Eq. (21) according to which the C–H bond of the cobalt–olefin complex at the allylic position undergoes oxidative addition to Co(O) giving a hydrido π-allyl cobalt(II) complex. 1,3 Hydrogen shifts in π-allyl complexes [8] are well documented and we suggest this as the most probable mechanism of *vbh* isomerization.

Table I

The rate constants k_{obs} at different temperatures and the equilibrium constant K_1 and degree of dissociation at 60°

Temp. (°C)	$k_{obs} \times 10^3$ (mole^{-2}l^{2}sec^{-1})	$K_1 \times 10^2$ (mole l^{-1})	degree of dissociation (%)
50	1.62		
60	5.22	6.95	68*
70	15.65		

* at 4.9×10^{-2} mole · l^{-1} catalyst concentration

Experimental

Preparation of 5-vinylbicyclo(2.2.1.)heptene-2 (vbh)

vbh was prepared according to the literature [2]. A mixture of 330 g (6.1 mole) butadiene and 200 g (3.33 mole) freshly prepared cyclopentadiene were condenzed at −10° into an autoclave. 0.5 g hydrochinone was added and the reaction mixture was kept at 140—145° for 2—4 hrs. After cooling the product was distilled over a filled column (50 cm) and the fraction at 70—75°/85 mmHg (30—35 g, 85—90%) was collected. This was further purified through preparativ GLC (6 m tricresyl phosphate column, 130°) giving *vbh* in 99.5% purity, which consisted of 21% *endo*-and 79% *exo*-isomer.

The preparation of $Co(N_2)(PPh_2)_2$

This was prepared by known method [9] using cobalt(II) acetylacetonate and diethyl aluminium ethoxide.

The isomerization of vbh

Into a thermostated reaction vessel, equipped with a serum cap and a bulb containing a weighed amount of the catalyst, the prepurified solvent and *vbh* were injected with a hypodermic syringe, stirred magnetically and the catalyst added by a bulb. At regular time intervals samples were taken, treated with Na_2CO_3 and analysed by GLC (6 m tricresyl phosphate column, 130°).

REFERENCES

[1] GERMAN, R., HANK, R., VAUGHAN, G.: Kautschuk, Gummi, Kunststoffe, **19,** 67 (1966)
[2] PLATE, A. F., BELIKOVA, N. A.: Zh. Obshch. Khim., **30,** 3945 (1960)
[3] FVOZDEVA, N. A., BELIKOVA, N. A., PLATE, A. P.: Dokl. Acad. Nauk, SSSR, **189,** 1009 (1969)
[4] Neth. Patent, 6 613 870
[5] French Patent, 1 556 198
[6] French Patent, 1 556 199
[7] KOVÁCS, J., SPEIER, G., MARKÓ, L.: Inorg. Chim. Acta, **4,** 412 (1970)
[8] BÖNNEMANN, H.: Angew. Chem., **82,** 699 (1970)
[9] SPEIER, G., MARKÓ, L.: Inorg. Chim. Acta, **3,** 127 (1969)

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NEIGHBOURING GROUP PARTICIPATION IN THE AMINOLYSIS OF ESTERS IN A NON-HYDROXYLIC SOLVENT

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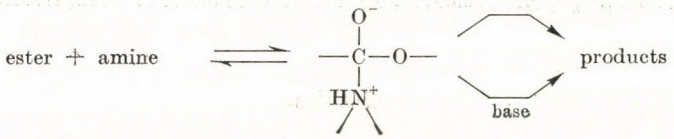
The piperidinolysis in chlorobenzene of 5-nitro-, 5-chloro-, 2-methyl-, and unsubstituted 8-acetoxyquinoline and *p*-nitrophenyl acetate was studied. The high reactivity of the quinoline esters, the strictly second order kinetics, and the effect of substituents on the reaction rate were interpreted as results of intramolecular general base participation by the tertiary nitrogen.

Since the active sites of several proteolytic enzymes lie in hydrophobic locations [1], enzyme model investigations in non-hydroxylic solvents [2—4] are in some respect more relevant than similar studies in water [5]. As a model reaction, the aminolysis of *p*-nitrophenyl acetate (*p*-NPA) in chlorobenzene was studied, which takes place according to a two-step mechanism, involving the rate determining collapse of a zwitterionic tetrahedral intermediate [3]:

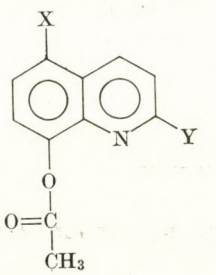


The slight acceleration effect of pyridine on the rate of this reaction was shown to be a general base catalysis [4].

The reactions of esters with aliphatic amines in this solvent followed a two-term rate equation [3, 4]:

$$-\frac{d\,[\text{Ester}]}{dt} = (k_2\,[\text{Amine}] + k_3\,[\text{Amine}]^2)\,[\text{Ester}]\ . \qquad (2)$$

In this paper we wish to report kinetic data on the piperidinolysis in chlorobenzene of substituted 8-acetoxyquinolines (**I—IV**), systems in which a tertiary nitrogen atom is in suitable position to catalyze the reaction. For comparison, the reaction of *p*-NPA was studied.



	X	Y
I	H	H
II	H	CH_3
III	Cl	H
IV	NO_2	H

Experimental

Materials. Chlorobenzene and piperidine were distilled prior to use. Quinoline esters and *p*-NPA were prepared from the hydroxy compounds according to literature methods. Melting points [6—9] and analytical data for the esters are given in Table I.

Kinetics. All the kinetics were performed spectrophotometrically with a UNICAM spectrophotometer SP 800 connected to a RADELKIS Recorder OH-814/1, in 3-ml Teflon-stoppered, 10-mm fused silica cells, contained in the thermostated cell holder. In all runs, at least 15-fold excess of amine over the ester (initial concentration 10^{-4}M) was used. The reactions were followed to ten half-lives, and the rate constants were calculated in the usual manner. Analysis of the infinity spectra showed that the production of phenolic compounds was quantitative.

Table I

Melting points and analytical data

Ester	M. p., °C	Lit. m. p., °C	Ref. or analysis
I	54.5—55.5	56—57	6
II	63.5—65.5	63—64	7
III	83—84	82—84	8
IV	112—113		a
p-NPA	78— 79	79	9

[a] Calcd. for $C_{11}H_8N_2O_4$: C, 56.89; H, 3.44; N, 12.07. Found: C, 56.52; H, 3.75; N, 12.31%

Results

In the presence of a great excess of amine over ester, all spectrophotometrically determined rate constants (k_{obs}) were found to be pseudo-first order.

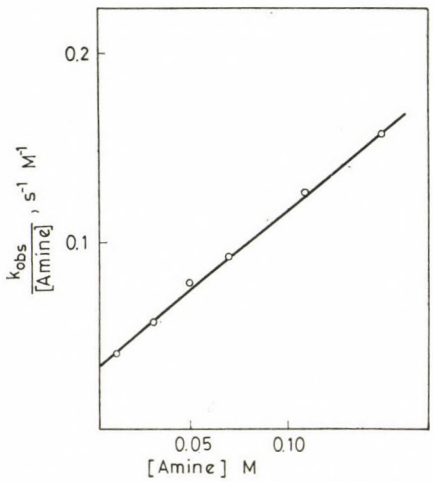


Fig. 1. k_{obs}/[Amine] *vs.* [Amine] plot for the piperidinolysis of *p*-NPA in chlorobenzene at 25 °C

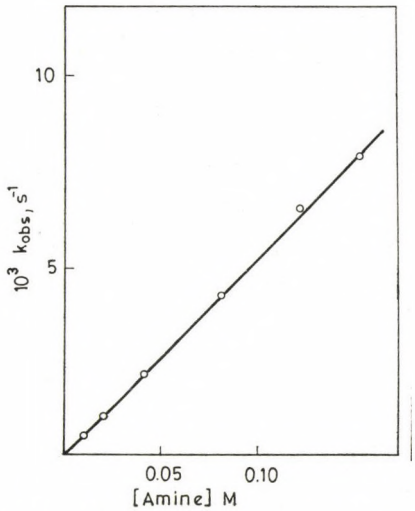


Fig. 2. k_{obs} *vs.* [Amine] plot for the piperidinolysis of **I** in chlorobenzene at 25 °C

Table II

Second and third order rate constants for the piperidinolysis of the esters in chlorobenzene at 25°C; pK_a values for the leaving groups of the esters in 75% ethanol–water[a] *at 25 °C*

Ester	k_2, $M^{-1}s^{-1}$	k_3, $M^{-2}s^{-1}$	pK_a	
			proton	proton gained
I	$5.35 \cdot 10^{-2}$	—	11.30	4.33
II	$2.50 \cdot 10^{-3}$	—	11.63[b]	4.45[b]
III	$2.60 \cdot 10^{-1}$	—	10.45	3.68
IV	$2.24 \cdot 10$	—	7.10	2.80
p-NPA	$3.50 \cdot 10^{-2}$	$8.20 \cdot 10^{-1}$	(7.89)[c]	—

[a] SCHULMAN, S. G., GERSHON, H.: J. Phys. Chem. **72,** 3692 (1968);
[b] KOVI, P. J., MILLER, C. L., SCHULMAN, S. G.: Anal. Chim. Acta **62,** 59 (1972);
[c] in 50 % ethanol–water, COHEN, L. A., JONES, W. M.: J. Am. Chem. Soc. **84,** 3397 (1963)

The reaction of *p*-NPA follows Eq. (2); the k_{obs}/[Amine] *vs.* [Amine] plot is linear, and has a non-zero intercept (Fig. 1). Piperidinolysis of the quinoline esters, however, follows strictly second order kinetics, the k_{obs} *vs.* [Amine] plot being linear with zero intercept (Fig. 2). Rate constants along with literature pK_a data are listed in Table II.

Rate constants for the reactions of *p*-NPA and **I** determined at different temperatures, and enthalpies and entropies of activation obtained from the rate values are given in Table III.

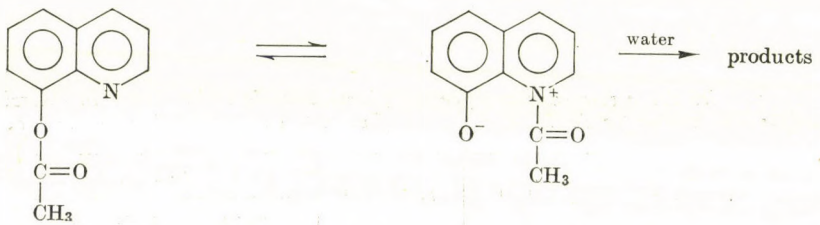
Table III

Rate constants for the piperidinolysis of p-NPA and **I** *in chlorobenzene at different temperatures; activation parameters at 25 °C*

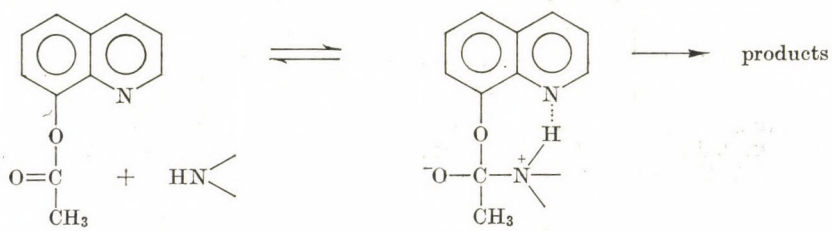
		t, °C					$\Delta H^{\ddagger}_{25}$ kcal/mole	$-\Delta S^{\ddagger}_{25}$ e. u.
		20.1	25.0	33.8	39.3	44.9		
p-NPA	$10^2 k_2$, $M^{-1}s^{-1}$	2.75	3.50	4.14	7.12	8.70	7.8	39
	k_3, $M^{-2}s^{-1}$	0.80	0.82	0.91	1.08	1.11	2.2	52
I	$10^2 k_2$, $M^{-1}s^{-1}$	4.46	5.35	7.59	10.0	12.2	7.0	41

Discussion

The high reactivity of the esters of 8-hydroxyquinoline to water was explained by an intramolecular nucleophilic catalysis mechanism [8, 10] involving the reversible formation of a highly reactive acylammonium intermediate:



On the other hand, for the aminolysis reactions in 90% dioxane–water [11] and in water [6], an intramolecular general base catalysis by the tertiary nitrogen was suggested:



The data in Table II show that in the reactions of quinoline esters term k_3 of Eq. (2) is undetectable, and only the least reactive compound **II** has a k_2 value lower than that of the 'active ester' *p*-NPA.

The introduction of an electron-withdrawing substituent in the 5-position of the quinoline ring of **I**—**IV** results in increased reactivity. The reactivity sequence for these compounds ($NO_2 > Cl > H$) is the same as for the pyrrolidinolysis of *p*-substituted phenyl acetates in this solvent [3]: the weaker basic the leaving phenoxy group, the higher the reactivity of the ester.

Similarities in the kinetic behaviour of the esters **I**—**IV** suggest that they react with the same mechanism. The strictly second order kinetics not observed so far for reactions of esters with aliphatic amines in chlorobenzene, as well as the high reactivity of quinoline esters can only be explained by the catalytic participation of the neighbouring tertiary nitrogen.

The efficiency of this intramolecular catalysis should clearly depend on the basicity of the nitrogen atom. Therefore, it is striking that the ester with the most basic nitrogen has the lowest reactivity. This finding can be explained by the different solvent effect on the influence of the substituents on the pK_a value of the phenolic hydroxyl group and the tertiary nitrogen atom. Changing the solvent from protic to dipolar aprotic results in an increased sensitivity to substitution of the phenolic pK_a [12], but it does not alter that of a tertiary nitrogen base [13]. Thus, the reactivity sequence for compounds **I**—**IV** is determined primarily by the more sensitive phenolic basicities.

General base catalysis may be subjected to steric hindrance [14], yet nucleophilic catalysis is much more sensitive to steric factors: *e.g.*, introduction of a methyl substituent in the 2-position of pyridine causes complete loss of nucleophilicity [15]. Since the tertiary nitrogen of **II** remained catalytically effective despite the presence of a C-2 methyl group, it can act only as a general base, *i.e.* according to Eq. (4).

The activation parameters shown in Table III are also in accordance with the mechanism proposed: their values for the second order rate constant of *p*-NPA and **I** are characteristic of bimolecular reactions, while those for the third order rate constant of *p*-NPA are consistent with a termolecular mechanism [16].

REFERENCES

[1] KRIEGER, M., KAY, L. M., STROUD, R. M.: J. Mol. Biol. **83,** 209 (1974)
[2] SNELL, R. L., KWOK, W., KIM, Y.: J. Am. Chem. Soc. **89,** 6728 (1967)
[3] MENGER, F. M., SMITH, J. H.: J. Am. Chem. Soc. **94,** 3824 (1972)
[4] SU, C., WATSON, J. W.: J. Am. Chem. Soc. **96,** 1854 (1974)
[5] JENCKS, W. P.: "Catalysis in Chemistry and Enzymology", New York, McGraw Hill, 1969
[6] FELTON, S. M., BRUICE, T. C.: J. Am. Chem. Soc. **91,** 6721 (1969)
[7] BÜCHI, K., AEBI, A., DEFLORIN, A., HURNI, H.: Helv. Chim. Acta **39,** 1676 (1956)
[8] BILLO, E. J., GRAHAM, R. P., CALWAY, P. G.: Talanta **17,** 180 (1970)
[9] ZAHN, H., SCHADE, F.: Ber. **96,** 1747 (1963)
[10] BARCA, R. H., FREISER, H.: J. Am. Chem. Soc. **88,** 3744 (1966)
[11] JAKUBKE, H. D., VOIGT, A.: Ber. **99,** 2419 (1966)
[12] KALFUS, K., SOCHA, J., VECERA, M.: Coll. Czechoslov. Chem. Commun. **39,** 275 (1974)
[13] DYUMAEV, K. M., KOROLEV, B. A., LOHOV, R. E.: Zh. Obsch. Khim. **41,** 2520 (1972)
[14] AKAHORI, Y.: Chem. Pharm. Bull. **13,** 352 (1965)
[15] BUTLER, A. R., GOLD, V.: J. Chem. Soc. **1961,** 4362
[16] SCHALEGER, L. L., LONG, F. A.: Advan. Phys. Org. Chem. **1,** 1 (1963)

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ELECTRON DEFICIENT HETEROAROMATIC AMMONIO-AMIDATES, VIII*

THE SYNTHESIS OF *N*-(PYRIDINIO)-BENZENESULFONAMIDATES BY RING TRANSFORMATION OF (1-PHENYLSULFONYL-2-PYRAZOLIN-5-YL)-METHYL KETONES

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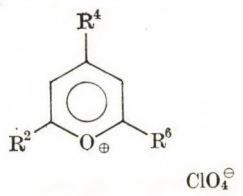
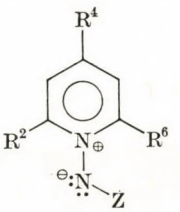
The reaction of pyrylium perchlorates (**1d-g**) and benzenesulfonohydrazide furnishes pyrazolinylmethyl ketones (**4d-4f**) or mixtures of the phenylsulfonylhydrazones of the pyrazolinylmethyl ketones (**4b**, **4c**), and pyridiniosulfonamidates (**2b**, **2c**). When treated with acids, the ketones **4** are converted, depending on the nature of the substituents R, into a variety of products, such as pyrylium salts, pyridiniosulfonamidates and pyrazoles. Alkaline treatment of **4c**, too, gives the amidate **2c**.

The Schneider synthesis [1, 2] of *N*-(1-pyridinio)-amides **2** (*e.g.*, Z = = Ph), based upon the reaction of pyrylium salts (**1**) with hydrazines, has been shown [3] to involve the intermediacy of monohydrazones (**3**) of enediones. An alternative mode of cyclization of the latter may lead to the formation of (2-pyrazolin-5-yl)methyl ketones (**4**) which, once formed, may not be transformed into the pyridinioamides **2** any more [2].



1



2

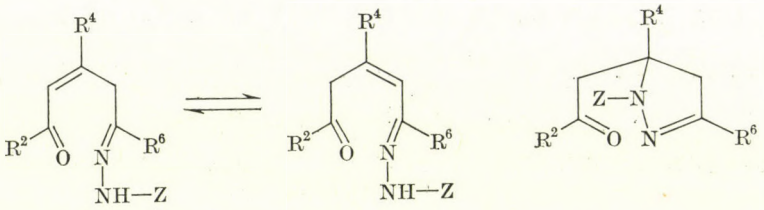
1

	R^2	R^4	R^6
a	Ph	Ph	Ph
b	Ph	H	Ph
c	Me	Ph	Ph
d	Me	*m*—$O_2NC_6H_4$	*m*—$O_2NC_6H_4$
e	Me	*p*—$O_2NC_6H_4$	*p*—$O_2NC_6H_4$
f	Ph	Ph	*p*—$O_2NC_6H_4$
g	Ph	Ph	*p*—BrC_6H_4

2 (a—e: Z = $PhSO_2$)

	R^2	R^4	R^6
a	Me	Ph	Ph
b	Me	*m*—$O_2NC_6H_4$	*m*—$O_2NC_6H_4$
c	Me	*p*—$O_2NC_6H_4$	*p*—$O_2NC_6H_4$
d	Ph	Ph	*p*—$O_2NC_6H_4$
e	Ph	Ph	*p*—BrC_6H_4

* Part VII: K. LEMPERT and K. ZAUER, Acta Chim. (Budapest) **88**, 81 (1976),



3 4

4 (a—f: Z = $PhSO_2$)

	R^2	R^4	R^6
a	Me	Ph	Ph
b	Me	*m*—$O_2NC_6H_4$	*m*—$O_2NC_6H_4$
c	Me	*p*—$O_2NC_6H_4$	*p*—$O_2NC_6H_4$
d	Ph	Ph	*p*—$O_2NC_6H_4$
e	Ph	Ph	*p*—BrC_6H_4
f	*p*—BrC_6H_4	Ph	Ph

When pyrylium salts **1a-c** were allowed to react with benzenesulfonohydrazide, the corresponding (1-phenyl-sulfonyl-2-pyrazolin-5-yl)methyl ketones **4** (Z = $PhSO_2$) (or their phenylsulfonylhydrazones) were obtained as the only products [4]. One of these ketones (**4a**), when refluxed with a mixture of acetic and perchloric acids, was smoothly transformed into **2a**, constituting thereby the first example of the ring transformation of a pyrazolinylmethyl ketone into a pyridiniosulfonamidate [4].

In the present paper we wish to describe further examples of such ring transformations which may be induced both by acids and bases.

The starting (1-phenylsulfonyl-2-pyrazolin-5-yl)methyl ketones **4b-f** were obtained by allowing to react the pyrylium perchlorates **1d-g** with excess benzenesulfonohydrazides. In several cases, depending on the nature of the substituents R^2, R^4 and R^6, the phenylsulfonylhydrazones were obtained rather than the free ketones **4**, and the corresponding pyridinioamidates **2** or their perchlorates were obtained as by-products (see Experimental). The phenylsulfonylhydrazones were converted into the ketones **4** by refluxing their HCOOH solutions. Treatment of **4c**-phenylsulfonylhydrazone with ethanolic NaOH furnished, involving 1 : 2 elimination of the side-chain and of a proton attached to C-4, and subsequent dephenylsulfonation, 3,5-bis(*p*-nitrophenyl)pyrazole [5]. This is analogous to the behaviour of **4a**-oxime under similar conditions [6].

In all cases in which R^2 and R^6 of the starting pyrylium salts (**1**) are not identical, the formation of either or both of two isomeric ketones **4** could be expected. The structures of the ketones actually formed from **1d** and **1e** follow from the position of their $\nu C = O$ bands in the IR spectrum which clearly

proves that both α-carbon atoms are of the saturated aliphatic type. The structure of the ketone obtained from **1f**, on the other hand, must be **4d**, since one of the products resulting on treatment with $HClO_4$/AcOH (see below) is 3(5)-*p*-nitrophenyl-5(3)-phenylpyrazole, which proves that one of the *un*substituted phenyl groups is part of the side chain. A mixture of the expected two ketones **4e** and **4f** was obtained from **1g**. Owing to its poor solubility in 1--propanol, **4f** could be isolated in pure form. The structure of the latter follows from the nature of its photolysis products: 3,5-diphenylpyrazolium benzenesulfonate, (3,5-diphenyl-4-pyrazolyl)phenyl sulfone and *p*-bromoacetophenone (*c.f.* Ref. [7]).

Attempts to prepare the ethylene hemithioketal of **4c** by allowing to react the ketone and 2-mercaptoethanol in refluxing toluene in the presence of *p*-toluenesulfonic acid, or in HCOOH in the presence of BF_3 failed: the pyridinioamidate **2c** was obtained instead of the expected product. In order to clarify the reason of the different behaviour of **4a** [6] and **4c** under the conditions of ketalization, the action of acids on **4c** was studied.

When treated with $HClO_4$ in AcOH at 110°C or refluxed with *p*-toluenesulfonic acid in toluene, **4c** was transformed into **2c**. The same transformation was brought about by ethanolic NaOH at room temperature. The latter transformation was unexpected, since type **4** ketones are, in general, transformed by bases (in addition to a variety of other products) into pyridines, rather than into pyridinioamides and pyridinioamidates, respectively. (*C.f.* the reaction of **4e** + **4f** and KOH described below, and Ref's [6] and [8].)

4b was similarly converted into **2b**, when refluxed with *p*-toluenesulfonic acid and 2,2-dimethoxypropane in dioxane–MeOH. The behaviour of **4d** is more complex: when heated with $HClO_4$ in AcOH, it furnished **1f**, 3,5-diphenylpyrazole and **2d**. The mixture of the two isomeric ketones **4e** and **4f**, when similarly treated gave **1g** as the main product, and traces of the amidate **2e**. On treatment with ethanolic KOH, **4e** + **4f** was converted into 2-(*p*-bromophenyl)-4,6-diphenylpyridine.

Experimental

Synthesis of pyrylium salts

(*a*) 70% $HClO_4$ aq. (1 ml) was added by drops under cooling and continuous stirring into a solution of *m*-nitroacetophenone (2.0 g; 12 mmoles) in Ac_2O (5 ml). The resulting orange-yellow solution was kept for 48 hrs at room temperature. EtOAc was added to precipitate 0.72 g (13.7%) of **1d**, orange-yellow crystals, m.p. 228—230 °C, which were chemically pure without recrystallization.

$C_{18}H_{13}ClN_2O_9$ (436.76). Calcd. Cl 8.12; N 6.41. Found Cl 8.29; N 6.40%.

IR (KBr): 1635 (pyrylium), 1535 + 1355 (νNO_2), 1095 cm^{-1} ($\nu ClO_4^{\ominus}$).

(*b*) A mixture of 1,3-diphenyl-2-propen-1-one (1.04 g; 5 mmoles), *p*-nitroacetophenone (0.84 g; 5 mmoles), trityl perchlorate (1.70 g; 5 mmoles) and AcOH (5 ml) was refluxed for 30 min. The dark green solution was allowed to stand for 2 days at room temperature, and

the green crystals of **1f** (1.56 g; 69%) were filtered off; m.p. 259—262 °C (from DMF–EtOH), lit. [9] m.p. 260—261°C.

(*c*) When *p*-nitroacetophenone was replaced by *p*-bromoacetophenone, **1g**, m.p. 271—272° (from AcOH–$MeNO_2$), lit. [10] m.p. 272 °C, was similarly obtained in 77% yield.

Reactions of pyrylium perchlorates (1d—g) with benzenesulfonohaydrazide

(*a*) A mixture of **1d** (0.3 g; 0.69 mmole), benzenesulfonohydrazide (0.45 g; 2.6 mmoles), CH_2Cl_2 (3 ml) and EtOH (2 ml) was stirred at room temperature until, within a few min, a clear red solution resulted. The dry residue was recrystallized from EtOAc–EtOH to yield 0.15 g (37%) of **2b**-perchlorate, m.p. 255—257 °C.

IR (KBr): *no* νC=O band; νNO_2: 1535 + 1360, $\nu ClO_4^{\ominus}$: 1100 cm^{-1}.

Treatment of the perchlorate with ethanolic NaOH furnished **2b**, m.p. 261—262°. Molecular composition (established by high-resolution mass spectrometry): $C_{24}H_{18}N_4O_6S$.

IR (KBr): 1630 (pyridinium), 1530 + 1350 (νNO_2), 1280 + 1140 cm^{-1} ($\nu^{\ominus}NSO_2$).

MS (70 eV, 280 °C), principal peaks: 490 ($M^{+\cdot}$, 0.4%), 349 (M — $PhSO_2$, 15%), 335 (M — $PhSO_2N$; 62%), 319 (3%), 305 (5%), 303 (349 — NO_2, 12%), 289 (335 — NO_2, 100%), 243 (289 — NO_2; 40%), 242 (20%), 157 (30%), 141 ($PhSO_2^{+\cdot}$, 30%), 120.5 (9%), 114 (11%), 94 (20%), 93 (30%), 77 (140%), 51 (40%), 39 (10%). Metastables: 349 $\xrightarrow{-46}$ 303, 335 $\xrightarrow{-30}$ 305, 335 $\xrightarrow{-46}$ 289, 289 $\xrightarrow{-46}$ 243.

The filtrate of crude **2b**-perchlorate was diluted with 5 volumes of HCOOH and refluxed for 1 hr to yield 0.07 g (20%) of **4b**, m.p. 185—186°C (from AcOH).

$C_{24}H_{20}N_4O_7S$ (508.50). Calcd. N 11.02. Found N 11.16%.

IR (KBr): νC=O 1715, νNO_2 1535 + 1360, νSO_2 1360 + 1175 cm^{-1}.

(*b*) Benzenesulfonohydrazide (1.5 g; 8.7 mmoles) was added to a suspension of **1e** [11] (1.0 g; 2.4 mmoles) in a mixture of CH_2Cl_2 (15 ml) and MeOH (12 ml). The mixture was shaken for a few minutes at room temperature until a clear red solution resulted. The dry residue of the latter was recrystallized from DMF–EtOH to yield 0.86 g of **4c**-phenylsulfonylhydrazone. Addition of EtOH to the filtrate furnished a mixture (0.3 g) of the above product and **2c** which was worked up by TLC (adsorbent: Kieselgel Merck; solvent: benzene–AcOH, 20 : 3) to yield 0.07 g of **4c**-phenylsulfonylhydrazone (R_f = 0.58) and 0.18 g of **2c** (R_f = 0).

4c-phenylsulfonylhydrazone, purified by extraction of its contaminants with boiling EtOH and boiling AcOH, total yield 58.5%, m.p. 214—215 °C.

$C_{30}H_{26}N_6O_8S_2$ (662.70). Calcd. C 54.38; H 3.96; N 12.69. Found C 54.30; H 3.86; N 12.58%

IR (KBr): νNH 3235, νNO_2 1535/1520 d + 1360, νSO_2 1350 + 1175 cm^{-1}.

2c, yield 11.3%, m.p. 239—241°C (from DMF–EtOH).

$C_{24}H_{18}N_4O_6S$ (490.49). Calcd. C 58.77; H 3.70; N 11.43. Found C 58.75; H 3.70; N 11.35%.

IR (KBr): νNO_2 1525 + 1350, $\nu^{\ominus}NSO_2$ 1285 + 1135 cm^{-1}.

4c-phenylsulfonylhydrazone (0.1 g; 0.15 mmole) was refluxed with HCOOH (0.5 ml) for 90 min. to yield 0.07 g (92%) of **4c**, m.p. 239—240 °C (from EtOH–pyridine).

$C_{24}H_{20}N_4O_7S$ (508.50). Calcd. C 56.69; H 3.97; N 11.02. Found C 56.77; H 4.27; N 11.00%.

IR (KBr): νC=O 1710, νNO_2 1530/1520 d + 1350, νSO_2 1350 + 1170 cm^{-1}.

4c-phenylsulfonylhydrazone (0.2 g; 0.31 mmole) was stirred at room temperature for 24 hrs with 0.2*N* ethanolic NaOH (88 ml). The originally red solution gradually turned yellow. The dry residue was triturated with water; the insoluble material was separated by centrifuging, dried and recrystallized from EtOH to yield 0.065 g (65.5%) of 3,5-bis(*p*-nitrophenyl)-pyrazole, m.p. 266—268°, lit. [5] m.p. 266 °C.

(*c*) A suspension of **1f** (0.5 g; 1.1 mmole) and benzenesulfonohydrazide (0.6 g; 3.5 mmoles) in EtOH (5 ml) was stirred at 50°C for 1 hr. A clear solution was transiently formed from which the light green crystals of crude **4d**, 0.52 g (91%), soon started to separate. Recrystallization from $MeNO_2$–EtOH furnished cream coloured crystals, m.p. 215—216 °C.

$C_{29}H_{23}N_3O_5S$ (525.57). Calcd. C 66.28; H 4.41; N 7.99; O 15.22. Found C 66.60; H 4.72; N 8.14; O 14.97%.

IR (KBr): νC=O 1690, νNO_2 1520 + 1360, νSO_2 1350 + 1175 cm^{-1}.

(*d*) $\mathbf{1}_g$ and benzenesulfonohydrazide furnished under similar conditions a mixture of **4e** and **4f** (total yield 46%). When repeatedly extracted with boiling EtOH or 1-propanol, pure **4f** (11%), m.p. 194—196 °C (from AcOH), was obtained as the insoluble residue.

$C_{29}H_{23}BrN_2O_3S$ (559.47). Calcd. C 62.29; H 4.14; N 5.01; **4e** + **4f**, found C 62.17; H 4.40; N 4.88%.

4f, IR (KBr): νC=O 1690, νSO_2 1355 + 1170 cm^{-1}.

Photolysis of 4f*

A nitrogen-purged $CHCl_3$ solution (625 ml) of **4f** (1.25 g; 2.24 mmoles) was irradiated with a high-pressure mercury immersion lamp through pyrex until, according to TLC, the starting **4f** completely disappeared (3 hrs). The dry residue was taken up in CH_2Cl_2. Overnight 0.065 g (8%) of crystalline (3,5-diphenyl-4-pyrazolyl) phenyl sulfone [7], m.p. 302 °C, deposited. The dry residue of the filtrate was taken up in benzene to yield 0.028 g (8%) of 3,5-diphenylpyrazolium benzenesulfonate, m.p. 228—234 °C, as the insoluble residue. An authentic sample, obtained by allowing to react 3,5-diphenylpyrazole and benzenesulfonic acid in EtOH, had m.p. 229—234 °C.

IR (KBr): νNH 3200—2400, $\nu SO_3^{\ominus}$ 1180, 1050, 605 cm^{-1}.

The mother liquor of the sulfonate was chromatographed on a column of Al_2O_3. (Solvents: benzene–EtOAc, 4 : 1, and EtOAc.) One of the fractions contained *p*-bromoacetophenone (3%), identified as its 2,4-dinitrophenylhydrazone, m.p. and mixed m. p. with an authentic sample 230°C, lit. [12] m.p. 235—237 °C.

Reactions of the ketones 4

(*a*) A mixture of **4c** (0.35 g; 0.69 mmole), 70% aq. $HClO_4$ (1 ml) and AcOH (1 ml) was heated for 15 min at 110 °C and poured into water. The precipitate was filtered off, washed with water, dried and stirred for 30 min with benzene at room temperature. The insoluble part was recrystallized from EtOAc to yield 0.16 g (47.5%) of **2c**, identical according to m.p. and IR spectra with a sample obtained as described above.

(*b*) **4c** was refluxed with toluene for 20 hrs in the presence of a catalytic amount of *p*-toluenesulfonic acid. According to TLC, the starting **4c** was completely converted at this point into **2c**.

(*c*) **4c** (0.02 g) was stirred with 0.2*N* ethanolic NaOH (9 ml) at ambient temperature. (At elevated temperatures profound decomposition takes place.) The mixture turned dark. 0.011 g (75%) of **2c**, identified by its IR spectrum, was obtained.

(*d*) A mixture of **4b** (0.20 g; 0.4 mmole), *p*-toluenesulfonic acid (0.01 g), 2,2-dimethoxypropane (2.5 ml), anhydrous MeOH and dioxane (5 ml, each) was refluxed for 4 hrs to yield 0.07 g (35%) of **2b**, identified by its IR spectrum, as the insoluble residue.

(*e*) A mixture of **4d** (0.5 g; 0.95 mmole), 70% aq. $HClO_4$ (1.8 ml) and AcOH (10 ml) was heated for 15 min at 110 °C and poured into water. The precipitate was filtered off, washed with water, dried and stirred for 30 min with benzene (100 ml). The insoluble residue was extracted with boiling DMF and washed with hot EtOAc to yield 0.05 g (10.5%) of **2d**, m.p. 255—257°C.

$C_{29}H_{21}N_3O_4S$ (507.48). Calcd. C 68.63; H 4.17; N 8.28. Found C 68.50; H 4.31; N 7.92%.

IR (KBr): νNO_2 1515 + 1350, $\nu^{\ominus}NSO_2$ 1280 + 1130 cm^{-1}.

When EtOH was added to the DMF solution, 0.14 g (33.0%) of **1f**, identified by m.p. and IR spectra with an authentic sample (see above), was obtained.

Alternatively, **2d** (0.075 g; 15%) was isolated from its mixture with **1f** by decomposing the latter with boiling 0.5*N* ethanolic KOH (8 ml).

The dry residue of the original benzene solution was worked up by TLC (adsorbent: Kieselgel G, Merck; solvent: benzene–$CHCl_3$–EtOAc, 8 : 1 : 1) to yield 0.03 g (12.5%) 3(5)-*p*-nitrophenyl-5(3)-phenylpyrazole, m.p. 274—276 °C, lit. [13] 272—275°C, and 0.05 g (10.5%) **2d**, m.p. 255—257 °C.

(*f*) A mixture (1.0 g; 1.8 mmole) of **4e** + **4f** was heated with 70% aq. $HClO_4$ (4.2 ml) in AcOH (13 ml) for 15 min at 110 °C, and poured into water. The crystalline precipitate was filtered off, washed with water, dried and triturated with benzene. The insoluble residue was recrystallized from $MeNO_2$–AcOH to yield 0.3 g (34%) of **1g**, identified by m.p. and IR spectra with an authentic sample (see above). The dry residue of the benzene solution (0.01 g), m.p. 248—251 °C, proved, according to its IR spectrum, to be identical with **2e**.

IR (KBr): $\nu^{\ominus}NSO_2$ 1285 + 1135 cm^{-1}.

(*g*) A mixture of **4e** + **4f** (2.5 g; 4.5 mmoles) was refluxed for 30 min. with 0.3*N* ethanolic KOH (600 ml). About 9/10 of the solvent was distilled off, and the solution was poured

* The authors are indebted to Mr. T. Loránd for having performed this preliminary experiment.

into water. The solid product was recrystallized from EtOH–EtOAc to yield 0.66 g (33%) of 2-(*p*-bromophenyl)-4,6-diphenylpyridine, m.p. 151—153°, lit. [10] m.p. 154 °C.

*

The authors are indebted to Dr. F. RUFF and Dr. MEDZIHRADSZKY-SCHWEIGER and staffs for the IR spectra and microanalyses, respectively, and to Dr. J. TAMÁS for the mass spectrum.

REFERENCES

[1] SCHNEIDER, W., SEEBACH, F.: Ber. dtsch. chem. Ges. **54,** 2285 (1921)
[2] DIMROTH, K., *et al.:* Ann. **604,** 221 (1957)
[3] BALABAN, A. T.: Tetrahedron **24,** 5059 (1968)
[4] LEMPERT-SRÉTER, M., LEMPERT, K.: Acta Chim. Acad. Sci. Hung. **65,** 443 (1970)
[5] LIPP, M., DELLACKER, F., MUNNES, S.: Ann. **618,** 110 (1958)
[6] LEMPERT-SRÉTER, M., LEMPERT, K.: Tetrahedron **31** 1677 (1975).
[7] LEMPERT-SRÉTER, M., LEMPERT, K., TAMÁS, J.: Acta Chim. (Budapest) **80,** 455 (1974)
[8] SNIECKUS, V., KAN, G.: Chem. Communications 1208 (1970)
[9] DIMROTH, K.: Liebigs Ann. Chem. **661,** 1 (1963)
[10] SIMALTY-SIEMIATYCKI, M.: Bull. soc. chim. France, **1965,** 1945
[11] DOROFEENKO, G. N., DEMODENKO, E. I., KRIVUN, S. V.: Izv. Vyssh. Ucheb. Zaved. Khim. Khim. Tekhnol. **10,** 3047 (1967); Chem. Abstr. **68,** 29529 (1968)
[12] SMITH, L. I., HOLLY, E. D.: J. Am. Chem. Soc. **78,** 1475 (1956)
[13] CUSMANO, S.: Gazz. Chim. Ital. **82,** 191 (1952)

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THE SOLVENT POLYMERIZATION AND COPOLYMERIZATION OF MONOALKYL ITACONATES*

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Regularities of the solvent polymerization of monobutyl and monooctyl itaconates and their copolymerization with acrylonitrile were studied; the initiation was effected by azobis (isobutyronitrile) or gamma-irradiation. The main characteristic kinetic parameters of the homopolymerization were determined. Results of the homopolymerization were determined. Results of the copolymerizations have proved unambiguously that the higher the polarity of the solvent, the greater its interaction with the monomers. The medium-dependent dissociation of the free carboxyl groups considerably influences the course of the polymerization and copolymerization.

Monoalkyl itaconates as olefin dicarboxylic acid derivatives may supply valuable new theoretical information about the relationship between structure and polymerization reactivity. Further, while several publications deal with the homopolymerization of itaconic acid [1] and itaconic diesters [2, 3], no data are available for monoalkyl itaconates except for those reporting on some of their applications in preparative organic chemistry [4].

The present paper covers the kinetic regularities of the γ-irradiation-induced and azobis-isobutyronitrile (AIBN)-initiated polymerization of β-monobutyl and β-monooctyl itaconate and their copolymerizations with acrylonitrile (AN) in various solvents.

Experimental

The monomers were synthesized on the analogy of β-monomethyl itaconate [4]. Before use, β-monobutyl itaconate (MBI) and β-monooctyl itaconate (MOI) were recrystallized from a 1 : 3 mixture of benzene and petroleum ether (m.p. 41°C) and from pure petroleum ether (m.p. 58 °C), respectively. Kinetic measurements of polymerization were performed by dilatometry, usually in tetrahydrofuran (THF) solution of 50% w/w. The polymers from both monomers were precipitated by light petroleum. Molecular weight determination of the polymers was made in THF solutions at 25 °C. The radiation-induced polymerizations were also carried out in THF solutions by γ-irradiation from a ^{60}Co source.

Copolymerizations with AN were conducted in various solvents, namely in THF, acetic acid and benzene. The copolymer products were soluble in chloroform as contrasted with the homopolymers. The composition of copolymers and relative reactivity ratios of the monomers were determined by the Kjeldahl method and by the Fineman-Ross method, respectively.

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Results and discussion

Kinetic curves of the polymerization of MBI and MOI are shown in Figs 1 and 2, respectively, with the same initiator concentration at different temperatures.

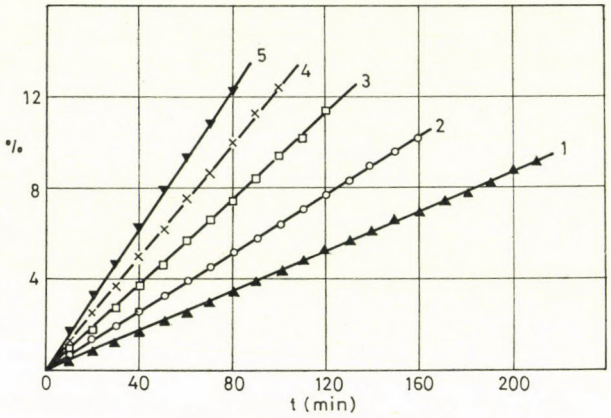


Fig. 1. Kinetic curves of the polymerization of MBI at different temperatures, with the same initiator concentration. (Numbering of the curves corresponds to that in Table I)

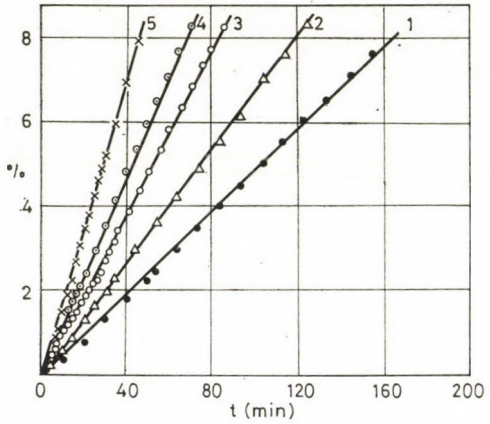


Fig. 2. Kinetic curves of the polymerization of MOI at different temperatures, with the same initiator concentration. (Numbering of the curves corresponds to that in Table II)

The rate of polymerization as a function of temperature gives 14.42 and 14.31 kcal/mole for the overall activation energy of MBI and MOI, respectively. These values are relatively low in comparison with the usual activation energies (*e.g.* that of the polymerization of methyl methacrylate is 19.5 kcal/mole [6]). Since the activation energy of initiation by AIBN (E_{in}) is 30.8 kcal/mole,

it follows from the above data that the difference between the activation energy of propagation (E_p) and termination ($1/2\ E_t$) is

$$E_p - 1/2\ E_t = -0.98 \text{ kcal/mole for MBI and}$$

$$E_p - 1/2\ E_t = -1.09 \text{ kcal/mole for MOI.}$$

The unusual negative or very small values of ($E_p - 1/2E_t$) may lead to the conclusion that the activation energy of termination is very high due possibly to steric hindrance by the bulky substituent, as well as to the electrostatic repelling power arising from the partial dissociation of the carboxyl group beside the growing radical. In addition, the high E_t value and a probable disproportionation mechanism of the termination step are supported by the relatively low values of the characteristic viscosity, shown in Tables I and II, where the other directly obtained experimental data are also included. Fig. 3 presents the overall polymerization rates at 60 °C, plotted against the square root of the initiator concentration; the relation appears to be linear in both cases. The characteristic viscosities of the polymer products decrease in proportion with the increase of temperature and the initiator concentration. The latter proportionally suggests that chain transfer to the monomer is not

Table I

Characteristic data of the polymerization of β-monobutyl itaconate initiated by azobis (isobutyronitrile)

No.	Temp. °C	AIBN concentration, mole/l	Monomer concentratton, mole/l	Rate of polymerization, $V \cdot 10^5$ mole/l sec	$[\eta]$, g/100 ml
1	45	0.124	2.54	1.85	0.10
2	50	0.124	2.53	2.79	0.09
3	55	0.123	2.52	3.95	0.07
4	60	0.123	2.51	5.18	0.06
5	65	0.123	2.49	6.44	0.05
6	60	0.017	3.11	3.87	0.08
7	60	0.029	3.11	5.51	—
8	60	0.057	3.11	7.96	0.07
9	60	0.114	3.11	10.8	0.06
10	60	0.201	3.11	14.3	0.06
11	60	0.180	1.45	1.03	0.05
12	60	0.123	1.98	1.89	0.06
13	60	0.046	2.51	5.18	0.07
14	60	0.043	3.11	9.929	0.06

Table II

Characteristic data of the polymerization of β-monooctyl itaconate initiated by azobis (isobutyronitrile)

No.	Temp. °C	AIBN concentration, mole/l.	Monomer concentration, mole/l	Rate of polymerization, $V \cdot 10^5$ mole/l sec	$[\eta]$ g/100 ml
1	40	0.106	2.34	1.87	0.31
2	45	0.108	2.33	2.58	0.28
3	50	0.127	2.32	3.67	0.25
4	55	0.107	2.30	4.47	0.23
5	60	0.111	2.29	6.65	0.19
6	60	0.014	2.29	2.64	0.29
7	60	0.032	2.29	3.12	0.28
8	60	0.084	2.29	4.81	0.21
9	60	0.185	2.29	6.91	0.16
10	60	0.266	2.29	7.97	0.15
11	60	0.418	0.72	0.56	—
12	60	0.236	1.11	1.10	0.18
13	60	0.187	1.49	2.05	0.10
14	60	0.131	1.91	4.10	0.25

characteristic of the kinetics of polymerization of either monomer. Fig. 4 shows the polymerization rate as a function of the monomer concentration at 60 °C. It is clearly seen that the rates of homopolymerization of MBI and MOI are proportional to the square of the monomer concentration. Such a quadratic function is not rare [6], the exponent of the monomer concentration

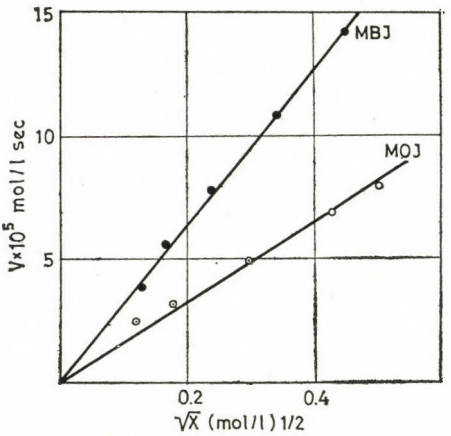


Fig. 3. The rate of polymerization as a function of the initiator concentration at 60 °C

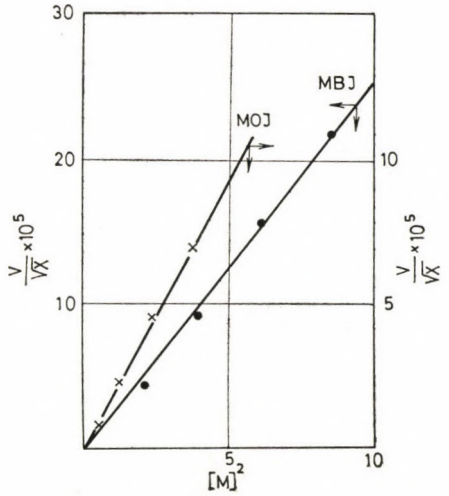


Fig. 4. The rate of polymerization as a function of the square of monomer concentration at 60 °C

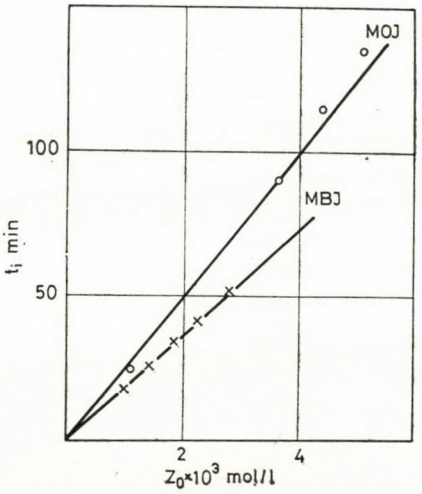


Fig. 5. Duration of the inhibition period as a function of the concentration of Banfield-radicals

is higher than the unity for great many monomers in their kinetic equations and even an exponent of 2 is not exceptional. For the further characterization of the kinetics of polymerization, the rate of the initiation step was also determined by means of the Banfield-radical which has proved suitable for such purposes [7]. Fig. 5 represents the inhibition period (t_i) plotted against the concentration of inhibitor (z_o) demonstrating that this relation is linear. The

Table III

Kinetic data of the polymerization of β-monobutyl itaconate inhibited by Banfield -radicals

No.	AIBN concentration, mole/l	Inhibitor concentration, mole/l	Inhibition period, t_i, sec	Rate of polymerization, $V \cdot 10^5$, mole/l sec	Rate of initiation, $V_i \cdot 10^7$ mole/l sec
1	0.056	—	—	7.34	9.01
2	0.058	0.009	1 000	7.23	8.57
3	0.057	0.0014	1 560	7.12	8.97
4	0.056	0.0019	2 100	6.91	9.05
5	0.057	0.0024	2 700	6.90	8.89
6	0.055	0.0028	3 090	6.91	9.06

Table IV

Kinetic data of the polymerization of β-monooctyl itaconate inhibited by Banfield-radicals

No.	AIBN concentration, mole/l	Inhibitor concentration, mole/l	Inhibition period, t_i, sec	Rate of polymerization, $V \cdot 10^5$, mole/l sec	Rate of initiation, $V_i \cdot 10^7$ mole/l sec
1	0.014	—	—	5.03	6.67
2	0.107	0.0019	1 440	4.95	13.19
3	0.104	0.0026	2 700	4.33	9.63
4	0.108	0.0036	5 400	4.11	6.66
5	0.109	0.0044	6 900	3.90	6.37
6	0.106	0.0051	7 980	3.20	6.39

other experimental conditions are collected in Tables III and IV. From the rate of initiation and from the overall rate of the process,

$k_p/k_t^{1/2}$ can be calculated when the concentration of the monomer is known:

$k_p/k_t^{1/2} = 8.1 \cdot 10^{-3}$ mole$^{-3/2}$lit$^{3/2}$sec$^{-1/2}$ (for MBI at 60 °C)

$k_p/k^{t1/2} = 11.7 \cdot 10^{-3}$ mole$^{-3/2}$lit$^{3/2}$sec$^{-1/2}$ (for MOI at 60 °C).

The ratios of the propagation constant (k_p) to the termination constant (k_t) are quite high for both monomers indicating a relatively high reactivity of the growing radical. According to the experimental results, the chain length of the ester group in the monoalkyl itaconates does not influence appreciably the magnitude of $k_p/k_t^{1/2}$. As the rate of initiation is known, the radical utilization

factor can be calculated. The decomposition constant (k_d) is calculated for AIBN at 60°C, according to Tobolsky and applied for the utilization factor:

$$f_{\text{AIBN}} = 0.90 \text{ (for MBI at 60°C)}$$
$$f_{\text{AIBN}} = 0.40 \text{ (for MOI at 60°C).}$$

Fig. 6 shows the kinetic curves of the γ-radiation-induced polymerization of MBI and MOI at the same dose rate at different temperatures. It can be seen that the rate of polymerization does not depend on the temperature. In view of the Arrhenius law, it means that

$$E_p - 1/2\, E_t = 0$$

since $E_{in} = 0$, in both cases. It also suggests a relatively high activation energy of termination which is in good agreement with the experimental data of the AIBN-induced polymerizations. Fig. 7 shows the linear relation between the

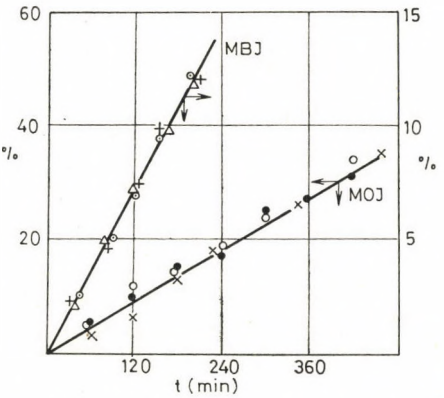


Fig. 6. Kinetic curves of the radiation-induced polymerization of MBI and MOI at different temperatures, with the same dose rate. (MBI: + 60 °C; ⊙ 50 °C; Δ 40 °C; MOI: × 65 °C; ○ 55 °C; ● 45 °C.)

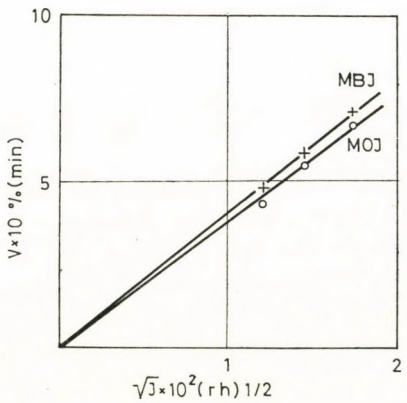


Fig. 7. Rate of the radiation-induced polymerization of MBI and MOI as a function of the dose rate at 60 and 65 °C, respectively

rate of the radiation-induced polymerization and the square root of the dose rate. The experimental conditions and the characteristic data of the polymer products are presented in Tables V and VI. The molecular weights of both

Table V

Characteristic data of the polymerization of β-monobutyl itaconate initiated by gamma-irradiation

No.	Temperature, °C	Dose rate, r/hr · 10^4	Monomer concentration, mole/l	Rate of polymerization, %/hr	$[\eta]$ g/100 ml
1	40	2.04	3.16	3.57	0.33
2	50	2.04	3.14	3.57	0.32
3	60	2.04	3.11	3.57	0.31
4	60	1.48	3.11	2.97	0.31
5	60	3.03	3.11	4.32	0.29

Table VI

Characteristic data of the gamma-radiation-induced polymerization of β-monooctyl itaconate

No.	Temperature, °C	Dose rate r/hr · 10^4	Monomer concentration, mole/l	Rate of polymerization, %/hr	$[\eta]$ g/100 ml
1	45	2.04	2.33	4.5	0.20
2	55	2.04	2.30	4.5	0.14
3	65	2.04	2.28	4.5	0.14
4	65	1.48	2.28	2.7	0.13
5	65	3.03	2.28	4.8	0.20

polymers formed in the high-energy radiation-induced polymerization are essentially independent of the dose rate and temperature.

Composition curves for the copolymerization of MBI with AN are shown in Fig. 8 using acetic acid, tetrahydrofuran and benzene as solvent. It is readily seen that the azeotropic composition of the copolymerization curves is shifted by the solvent in the sequence: acetic acid, tetrahydrofuran, benzene. The same is valid for the MOI/AN system (Fig. 9).

The relative reactivity ratios and Q-e values are collected in Table VII. It is found that the 'e' values of MBI and MOI are getting more negative with the above-mentioned shift of the azeotropic composition indicating that the dissociation of the free carboxyl groups is getting higher depending on the solvent. It is also revealed by Table VII that a change in the solvent from benzene to acetic acid markedly alters the copolymerization constants. Under the copolymerization conditions employed, the free carboxyl groups of the MBI

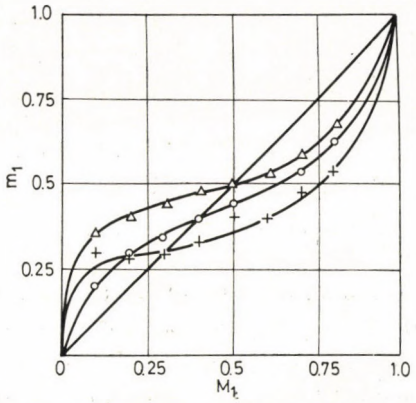


Fig. 8. Composition curves for the copolymerization of MBI in various solvents. (Δ Acetic acid, o tetrahydrofuran, + benzene)

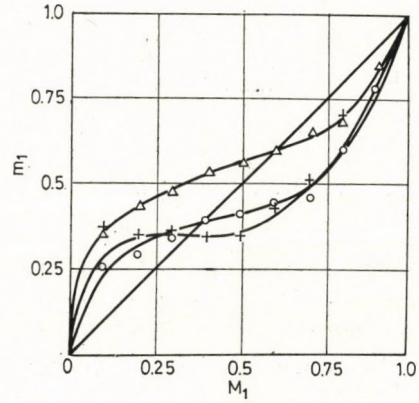
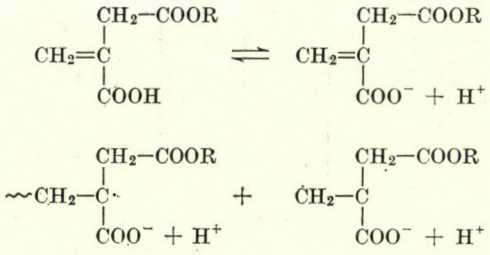


Fig. 9. Composition curves for the copolymerization of MOI in various solvents. (Δ Acetic acid, o tetrahydrofuran, + benzene)

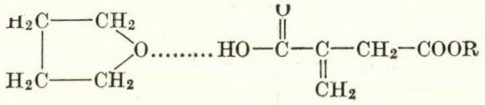
Table VII

Solvent	Monobutyl itaconate				Monooctyl itaconate			
	r_{AN}	r_{MBI}	Q_{MBI}	e_{MBI}	r_{AN}	r_{MOI}	Q_{MOI}	e_{MOI}
Benzene	0.15	0.72	0.92	−0.29	0.20	0.88	0.90	−0.12
Tetrahydrofuran	0.20	0.42	0.45	−0.37	0.30	0.45	0.37	−0.21
Acetic acid	0.25	0.20	0.30	−0.53	0.40	0.11	0.18	−0.58

and MOI molecules may presumably be present in a more or less dissociated state, depending on the solvent, according to the following pattern:



Accordingly, a part of the molecules involved in the polymerization becomes free radical with negative charge, acting as a definite electron donor. This is supported by the *Q-e* values as well. In addition, the negative shift of the '*e*' values may also be explained by an interaction of the solvent molecules with the monoalkyl itaconate molecules, controlled by the polarity of the solvent, resulting probably in a hydrogen-bonded complex, after breaking down the original hydrogen bonds in itaconate dimers:



This effect causes a partial ionization of the carboxyl groups enhancing the electron density on the C = C double bond. This explains why the '*e*' values of MBI and MOI are getting more negative, while the *Q* values are reduced in the same sequence. It may probably be due to the fact that the complex formed from monoalkyl itaconate and the solvent has reduced mobility in the reaction with the radical, owing to steric hindrances.

REFERENCES

[1] TATE, B. E.: Edv. Polym. Sci. **5,** 214 (1967)
[2] NAGAI, S., YOSHIDA, K.: Kobunshi Kagaku **17,** 478 (1960)
[3] NAGAI, S., YOSHIDA, K.: Kobunshi Kagaku **17,** 79 (1960)
[4] BAKER, B. R., SCHAUB, R. E., WILLIAMS, J. H.: J. Org. Chem. **17,** 117 (1952)
[5] FINEMANN, M., ROSS, S.: J. Polyme. Sci. **2,** 101 (1947)
[6] BAGDASARYAN, KH. S.: "Theory of the Radical Polymerization" (in Hungarian) Akadémiai Kiadó Budapest, 1961
[7] FÖLDESNÉ-BEREZSNICH, T., TÜDŐS, F.: Magy. Kém. Folyóirat, **70,** 201 (1964)

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RECENSIONES

G. A. GOROKHOVSKII: *Dispersion Polymers and Metals in Dynamic Contact*

Kiev, Naukova Dumka, 1972. pp. 152 × (in Russian)

Plastics are widely used in the modern technical design of frictioning mechanical constructions. This fact emphasizes particularly the significance of the physicochemical and mechanical phenomena occurring at the surface of metals in contact with plastics.

The study of such phenomena is difficult because the moving connections function under complicated external forces. Besides, frictioning metal–plastics surfaces constitute a heterogeneous system. The monograph of G. A. GOROKHOVSKII discusses the mechanism of surface dispersion of dynamically contacting plastics and metal surfaces in detail. Modern methods which have been elaborated by the author are described. These make it possible to control such processes and hence permit advantageous alterations in the structure and mechanical properties of the contacting layers.

The problems discussed in the monograph can be divided into two close connected sections. In the first part the author gives a survey on the relationships of the surface dispersion processes taking place on the dynamic contact of polymer and metal surfaces as well on the parallel structural changes with particular emphasis on the mechanochemical process at the boundary layers. Among these processes a novel feature of the mechanically degraded active polymer is described — namely, it activates the dispersion of the solid metal surface. These phenomenon play an important role in the processing technologies of metals.

In the second part the author describes in detail the effect of the external low-molecular medium on the dispersion of contacting polymer–metal surfaces. A particularly detailed description is given of the effect of gaseous, organic and electrolytic media on the structural changes on the contacting surfaces and on the mechanochemical processes at the interlayers.

I. Physicomechanical properties of polymers and metals.

II. Dispersion of and structural changes in polymers due to frictional load.

III. Dispersion of and structural changes in metals in dynamic contact with polymers.

IV. Effect of the medium on the dispersion of contacting polymers and metals.

V. Mechanism of surface dispersion in moving, hinged plastics metal joints.

The book was written for scientists and engineers, particularly for materials specialists and those interested in physicochemical mechanics.

GY. HARDY

Trends in Macromolecular Science. Midland Macromolecular Monographs. Vol. 1.

Edited by Hans Georg Elias. Gordon and Breach Science Publishers, London, New York, Paris 1973. pp. 131.

This volume contains the lectures which were given at the Scientific Symposium held on the occasion of dedication of the Midland Macromolecular Institute.

The first part of the book carries the dedication addresses and a description of the Midland Macromolecular Institute. One can perfectly agree with the program of the newly established institute. (Synthesis of macromolecules of industrial and biological significance, their reactions, physical properties, supermolecular structure and processing).

Two short lectures by Nobel Prizewinner Professor P. J. FLORY (The Challenge to Macromolecular Science, Molecular Configurations in Bulk Polymers) are followed by Professor Ch. G. OVERBERGER's summary of his investigation on the synthesis of polymers contain-

ing biologically active groups and their behaviour as polymer reagents, entitled "Organic Chemistry of Macromolecules". In the lecture of Professor M. CALVIN the chemical composition and formation of the secondary and tertiary structures of polypeptides and polynucleotides as well as their biological functions in the living cell, self-organizing behaviour, physicochemical problems of cell formation and the chemistry of life in molecular and supermolecular aspects of cellular systems are briefly outlined.

"Polymers in Medicine" is the title of the lecture of D. J. LYMAN. He gives a description of the behaviour of plastics in contact with the cardiovascular system in the living organism and explains the possibilities of achieving a better compatibility. These experiments are very promising from the viewpoints of the replacement of damaged organs and diseased tissues.

The paper by E. H. ANDREWS "Sructure-Property Relationships in a Polymer" gives an idea about the control of the structure of solid polymers at a higher than the molecular level and about the way of achieving the desired physical properties.

The last lecture in the book is that by T. ALFREY, "Mechanical Fabrication of Thermoplastic Polymers". It deals with those factors which are at our disposal for influencing the properties of a polymeric end-product (uni-and biaxial orientation, composites: fiber reinforcement, multi-layer films).

Most of the speakers are pioneers of the areas of macromolecular science they have surveyed. Particularly valuable parts of their lectures are those which review the historical background of the area and expound the present trend of evolution. The initation of this series of monographs is a welcome event and the specialists expect its continuation with great interest.

GY. HARDY

Advances in Polymer Science. Vol. 12.

Springer Verlag, Berlin—Heidelberg—New York, 1973. pp. 190, 63 Figures.

Four reviews are published in volume 12 of the series Advances in Polymer Scienc.

The review by K. OSAKI "Viscoelastic Properties of Dilute Polymer Solutions" gives a good survey on the theories and experimental methods concerned with this field. Particularly valuable are the chapters about the viscoelastic properties of infinitely dilute solutions of flexible polymers and about the viscoelastic behavior determined in a wide frequency range, because these can be considered as the first surveys of these topics. The author points out properly that in the last decade sufficient experimental data have been accumulated about the conditions influencing the behaviour of polymer solutions namely, about the effects of frequency, different polymers and solvents, temperature and molecular weight. The comparison of these data with the theories consolidated hitherto makes it necessary to investigate the hydrodynamic properties of dissolved polymer molecules and to describe on molecular basis the behaviour of dissolved polymer molecules at high frequencies.

W. L. CARRICK in his review, entitled "The Mechanism of Olefin Polymerizations by Ziegler-Natta Catalysts" undertakes a difficult task. On these catalyst systems many reports and large volumes of comprehensive books have already been published. The cocatalyst interactions, the nature of active sites, the polymerization mechanism, the activation of olefins and the stereoregularity are the problems which are promised by the author to be elucidated. Answers are furnished for all these problems but without supporting the statements by suitable experimental evidence. Hence, not too much is told to readers who are experienced in macromolecular chemistry.

The survey of C. TOSI and CIAMPELLI, "Applications of Infrared Spectroscopy to Ethylene–Propylene Copolymers" is an excellent and systematic summary of information on the title subject which is scattered here and there in the literature. The most outstanding chapters are those about the structural analysis of C_2—C_3 random copolymers, the distribution of C_2 and C_3 units, the crystallinity and the infrared analysis of C_2—C_3 diene terpolymers.

The "ESR Study of Photodegradation of Polymers" by K. TSUJI is important from both the theoretical and the practical points of view. After a short introduction on the fundamental steps in the photodegradation of polymers, a systematic description follows about the radicals which are produced under UV irradiation on different polymers and are detectable by ESR spectroscopy. The knowledge of the structure of these different radical products furnishes important information about the mechanism of photodegradation processes for several polymers. This information is essential for the photostabilization of polymers or to produce polymer systems which are decomposing under the influence of light.

The four reviews included in Volume 12 of Advances in Polymer Science are indeed concerned with important and timely problems of polymer physics and chemistry. The work of specialists interested in the subjects covered by this volume can be greatly promoted by these surveys.

GY. HARDY

^{13}C — *Kernresonanzspektroskopie.* J. T. CLERC, E. PRETSCH and S. STERNHELL: *Methoden der Analyse in der Chemie*, Vol. 16.

Akademische Verlaggesellschaft, Frankfurt am Main, 1973, pp. 142.

A very useful book. Part of the Analytical Methods in Chemistry Series of the German Academic Press, this small-size, hard cover volume gives the organic chemist readable introduction to the basic principles, and a practical guide to the use of the Fourier tansform carbon-13 NMR method.

Since the advent (in the early 70's) of commercially available, computer-controlled Fourier transform (FT) NMR instruments, ^{13}C NMR (or CMR) spectrometry has become a powerful research tool. Its successful application in organic and bioorganic studies is widely documented in a fast growing body of publications. Although similar in many respects to the more familiar proton NMR, Fourier transform carbon-13 resonance offers a number of distinctive new features that may extensively be exploited to enhance the amount and quality of chemical information. Most of these features are related to the novel experimental technique termed Fourier transform NMR method. When initiating his knowledge in carbon-13 NMR spectroscopy, the chemist has therefore to learn some basic FT instrumentation and experimental techniques in addition to the fundamental correlations between ^{13}C NMR spectral parameters — chemical shifts, coupling constants, relaxation times — and chemical structure. The existing texts by LEVY and NELSON (Carbon-13 Nuclear Magnetic Resonance for Organic Chemists) and by STOTHERS (Carbon-13 NMR Spectroscopy) provide excellent introduction and reference sources on these matters. This new book, nevertheless, seems to fulfil an important task: it is aimed mainly at initiating the first steps of the novice in this new field. Clarity rather than completeness, outline style instead of detailed explanations are the virtues that had helped the authors in achieving their goal.

The book may be divided into two major sections. Three introductory chapters give a first insight into the basic principles of a pulsed Fourier transform NMR experiment, explain the importance and nature of relaxation processes and provide some general information on carbon-13 chemical shifts and ^{13}C — ^{1}H coupling constants. The remaining four chapters are devoted to practical aspects of CMR. This section of the book includes (in that order) a brief description of various types of heteronuclear ^{13}C — $\{^{1}H\}$ double resonance experiments, a presentation of NMR solvents, solvent effects on carbon-13 chemical shifts and reference substances, extensive tables of chemical shifts for the major classes of organic compounds, including additivity parameters and easy-to-use simple formulas to predict shift values for individual carbons. By far the greatest in volume (83 pages), this chapter is introduced with a brief discussion of the basic assignment techniques and the data tables for each class of compounds are complete with references to leading articles. The final chapter deals with some fundamental aspects of Fourier transformation, selection of experimental parameters, practical hints for data acquisition and major instrumental requirements.

L. RADICS

P. SYKES: *Reaktionsaufklärung. Methoden und Kriterien der organischen Reaktionsmechanistik*

Verlag Chemie Physik Verlag, Weinheim, BRD *Taschentext.* Band 8. 1973

Die erste Ausgabe des Buches erfolgte in englischer Sprache im Verlag Longman Group Ltd. (London) im Jahre 1972 und kann als Ergänzung des weitverbreiteten, in vielen Auflagen erschienenen Buches des Verfassers (Reaktionsmechanismen der organischen Chemie — eine Einführung. 5. Aufl. Verlag Chemie, 1972) betrachtet werden. Es werden hier die

Methoden und Wege behandelt, deren Anwendung bzw. Befolgung die Aufklärung des Mechanismus der untersuchten Reaktion ermöglicht. Der erste Abschnitt erörtert die Bedeutung der kinetischen Daten und gibt ein kurzgefaßtes (insgesamt etwa 40 Seiten), gut nutzbares Bild über das zu Verfügung stehende, Chemiker jedoch für den nicht immer übersichtliche Kenntnismaterial. Der zweite Abschnitt behandelt die Anwendungsmöglichkeiten markierter Verbindungen, der dritte die verschiedenen Verfahren zum Untersuchen der reaktiven Intermediäre. Die Zusammenhänge zwischen Mechanismus und Stereochemie werden in einem relat'v größeren Umfang behandelt, zunächst allgemein und danach an Beispielen von Substitutions-, Additions-, Eliminations- und Umlagerungsreaktionen. Im fünften Abschnitt werden Zusammenhänge zwischen Struktur und Reaktions bereitschafterörtert; hier wird die Hammett-Gleichung sowie die lineare Beziehung der freien Energie diskutiert. Im letzten Abschnitt wird — anhand von konkreten Beispielen — die mühsame, aufregende, letzten Endes jedoch stets eine hohe intellektuelle Genugtuung bereitende Arbeit der Aufklärung des Reaktionsmechanismus vorgeführt. Das Buch ist im dem für den Verfasser charakteritistischen klaren Stil geschrieben und läßt sich mit Genuß lesen. Es ist höchst lobenswert, daß der Verlag Chemie dieses Buch nun auch den nur deutsch lesenden Chemikern zugänglich gemacht hat.

Band 15. Herausgegeben von H. Friebolin. *NMR-Spektroskopie. Eine Einführung mit Übungen.* 1974.

Im ersten Augenblick erscheint es als ein fast unmögliches Unterfangen in einem Umfang von nur 210 Seiten ein umfassenden Bild der Kernresonanzspektroskopie zu geben, dieser gegenwärtig in der chemischen Forschung bereits unerläßlichen physikalischen Methode der Strukturaufklärung, die während ihrer 25jährigen Laufbahn einen fabelhaften Aufstieg erlebt hat und deren Ergebnisse in Hunderten von Büchern behandelt wurden. Nach dem Lesen des Buches überzeugt man sich dennoch, daß seine Veröffentlichung in der Taschentext-Folge ein gute Idee war. Der Leser gelangt zu einem wertvollen Kenntnismaterial und lernt nicht nur die Grundprinzipien und wichtigsten Anwendungsmöglichkeiten der NMR-Spektroskopie kennen, sondern auch einige völlig neue, spezielle Ergebnisse, so z.B. die Protonenresonanzspektroskopie an Hochpolymeren, die ^{13}C-Resonanzspektroskopie und kann sogar über die zur Zeit nur begrenzt angewendeten "chemical-shift"-Reagenzien lesen. Die Übungsbeispiele im zweiten Teil erleichtern das Üben dieser wichtigen Methode, während die Literaturverzeichnisse am Ende der einzelnen Abschnitte zur allgemeineren Orientierung Hilfe leisten. Das Buch sollte seinen Platz auf dem Bücherregal eines jedem organischen Chemikers finden, der Interesse für das Neue hat.

GY. DEÁK

I. ROUTH: *Experiments in Organic and Biochemistry*

W. B. Saunders Co., Philadelphia — London — Toronto 1974 VIII + 172 pp.

The linking together of the two large disciplines, chemistry and biochemistry, in the course of university teaching, is not without its problems both from the scientific and the didactical point of views. As far as practical work is concerned, a special problem is posed by attempts at an intensive utilization of the generally very little time granted for this in the curricula; this means the selection of experiments that can be carried out with simple equipment yet are really instructive and of a high level.

Those who are acquainted with "Essentials of General, Organic and Biochemistry" by ROUTH, EYMAN, and BURTON (2nd ed. 1973) will peruse this newer, short book with much interest since it approaches the same domain from the practical side.

The dominance of an organic chemical view is obvious at the first glance; this is reflected by the arrangement of the chapters of about equal length, *viz.:* 1. Introduction to laboratory techniques. 2. Introduction to organic compounds. 3. Hydrocarbons. 4. Alcohols, ethers, aldehydes and ketones. 5. Acids, salts, esters, amides and amines. 6. Heterocyclic compounds. 7. Carbohydrates. 8. Lipids. 9. Proteins. 10. Nucleic acids. 11. Enzymes. 12. Digestion and metabolism. 13. Body fluids. 14. Drugs.

However, also the experiments in organic chemistry contain work of biochemical relevance, *e.g.* 7. — 9. Fermentation of carbohydrates.

Generally the experiments are started with some preparative task and this is followed in every case by a manysided study of the properties of the substances involved. This is a very valuable feature of the book and one which raises it above the level held by most of a similar kind. Yet we think that the usefulness of this book is due primarily to the question–answer sections which follow the experimental parts. These form a link between the theoretical

problems of chemistry and biochemistry and thus ensure that the carrying out of the experiments will be more than simple mechanical work according to directions.

Among the experiments choice by preference and amplification on the basis of individual experiences are possible. The whole work is easy to survey so that it can be recommended for use by those who do not study chemistry or biochemistry as their principal subject, *e.g.* for medical or agricultural students.

Numerous formulas and figures make this book very expressive and easy to handle.

P. NÁNÁSI

I. HARGITTAI: *The Electron Diffraction Interatomic Distance*. First part of Vol. 21. of the series "A kémia legújabb eredményei" (in Hungarian)

Akadémiai Kiadó, Budapest, 1974. pp. 173.

The accurate geometry of small and medium size molecules can be studied with the aid of electron diffraction in the gas phase, combined with the methods of spectroscopy. The molecular geometry can be described in terms of the interatomic distances obtained from the "radial distribution" and refined in a proper least squares adjustment of the weighted function of the "molecular intensity". Theoretically, a rigid molecule consisting of n atoms can be constructed from $n(n\text{-}1)/2$ interatomic distances (*i.e.* in the gas phase there is no way to fix the molecules in a vector space as it can be done in the crystalline state), if the number of atoms is no more than 20—30 and if these distances are free of distorsion. In practice, however, the "equilibrium" interatomic distances differ from the "average" interatomic distances measured by electron diffraction, owing to the rotational and vibrational movements of the molecules. Among the vibrational effects the well-known "shrinkage" effect might be mentioned, which has the greatest influence upon the observed interatomic distances. On the other hand, *e.g.* the internal rotation of the molecules is not only a source of problems, but it is of great importance in structural chemistry revealing the conformational equilibria in the gas phase. The problems are due to the fact that the number of the most probable conformers, especially if the number of atoms is great, increase the disturbing coincidences between the identical or nearly identical interatomic distances formed between different kinds of atoms. This "burden" of the electron diffraction might generally be eliminated by the complex application of the results of microwave and IR spectroscopy.

These questions of the gas electron diffraction method are discussed in the well-written booklet of HARGITTAI. In the first chapter he presents a good comparison of the methods of diffraction and spectroscopy from the point of view of the accurate determination of the interatomic distances and molecular geometry. In the second chapter the author deals with the theory (using clear mathematics) and technique of the gas electron diffraction method, using his own rich contribution to both the technique and structure analysis as examples. The third chapter presents a description of the so-called "average structures". The fourth and fifth chapters are devoted to the discussion of the problems of vibrational effects and large-amplitude intramolecular motions. The sixth chapter gives several examples for the successful combination of data obtained by electron diffraction and spectroscopy in the analysis of molecular structures. The booklet is concluded by an ample list of references.

It is a pleasure to recommend this work to anyone (especially to crystallographers, quantum chemists, spectroscopists etc.) who are interested in the analysis of molecular structures by electron diffraction in the gas phase. It is highly recommendable to translate this booklet into English or any other foreign language.

A. KÁLMÁN

J. SCHORMÜLLER: *Lehrbuch der Lebensmittelchemie*. Zweite, völlig neubearbeitete Auflage

Springer-Verlag, Berlin—Heidelberg—New York 1974, 831 Seiten

Die Lebensprozesse des menschlichen Organismus sind mit ständigem Stoff- und Energieverbrauch verbunden. Der Mensch benötigt also stets Lebensmittel, und zwar, in engem Zusammenhang mit dem Anstieg der Bevölkerung der Erde, immer *mehr* und immer *bessere*

landwirtschaftliche Produkte und Lebensmittelerzeugnisse, welche die mit den zeitgemäßen Erkenntnissen der Ernährungswissenschaft konformen Bedürfnisse *auch qualitativ* völlig befriedigen. In der gegenwärtigen Entwicklungsphase der Lebensmittelchemie, die sich zwangsläufig mit der Herkunft, der quantitativen und qualitativen Zusammensetzung, der Herstellung, Konservierung und Kontrolle der Lebensmittel befaßt, handelt es sich folglich nicht allein um die zur Beurteilung der Reinheit, der Unverfälschtheit usw. unerläßlichen Parameter sowie um die zu Veränderungen derselben führenden Auswirkungen der Produktions- und Industrieverfahren, sondern es müssen auch jene Veränderungen erschlossen werden, die verschiedene physiologische und nichtphysiologische Faktoren in den Rohstoffen und Fertigprodukten hervorrufen sowie die Möglichkeiten ihrer Verhinderung, damit die Lebensmitteltechnologie diese Erkenntnisse nutzbar machen kann. Die Lebensmittelchemie muß bestrebt sein, die Zusammenhänge zwischen der Struktur der in den Lebensmitteln vorkommenden Verbindungen und ihren organoleptischen Eigenschaften, sowie Zusammenhänge zwischen Struktur und physiologischer Wirkung zu klären. Aus dem Gesagten folgt, daß die moderne Lebensmittelchemie angewandte Biochemie ist, die mit der Erkenntnis rechnet, daß Lebensmittel dynamische Systeme, sich ständig verändernde Stoffe, Produkte von Lebensprozessen sind, die der Aufrechterhaltung von Lebensprozessen dienen; zugleich muß es aber die zeitgemäße Lebensmittelchemie auch ermöglichen, das gesamte — oft enzyklopädische — Kenntnismaterial auffindbar zu machen, das den Fachmann für den Kampf gegen die auch gegenwärtig vorkommenden Mißbräuche mit Lebensmitteln rüstet. Alldies ist eine große und äußerst komplexe Aufgabe, deren zufriedenstellende Lösung noch durch verschiedene didaktische Überlegungen erschwert wird, nämlich durch die Lehrgangvorschriften des betreffenden Landes bzw. der betreffenden Hochschule, für die das Lehrbuch der Lebensmittelchemie bestimmt ist.

Professor SCHORMÜLLER, dieser seit dem Erscheinen seines Buches leider verschiedene, hervorragende Fachmann und Wissenschaftler, emeritierter Professor des Lehrstuhls für Lebensmittelchemie und Lebensmitteltechnologie der Technischen Hochschule Berlin-Charlottenburg, veröffentlichte sein Lehrbuch erstmals 1961, fundiert auf gründliche Erwägungen aller Erfahrungen eines langen, erfolgreichen Lebens, später arbeitete er das Werk völlig um, unter Berücksichtigung der stürmischen Entwicklung der Theorie und Praxis, und diese zweite Auflage gelangte 1974 in die Hände der interessierten Leser. Im Werk sind, über lebensmittelchemische Kenntnisse im engeren Sinne, auch die Technologien kurz zusammengefaßt, welche die Zusammensetzung und Qualität der Lebensmittel unmittelbar beeinflussen; gesetzliche Bestimmungen zur Regelung der Qualität und des Vertriebs von Lebensmitteln sind ebenfalls kurz berührt. Biochemische Beziehungen werden nur im notwendigsten Ausmaß und in solchen Fällen erörtert, wo ihre Kenntnis zum Verständnis des Vorgangs unerläßlich ist (z.B. Ranzigwerden, Antioxidanzien). Die skizzenhafte Behandlung des juristischen und biochemischen Kenntnismaterials wird dadurch ermöglicht — wie das vom Verfasser selbst, im Vorwort der zweiten Auflage auch betont wird — daß diese Fragen ausführlich in Arbeiten anderer Kollegen behandelt werden.

Das übrigbleibende, immer noch gewaltige Kenntnismaterial gliedert sich in zwei Hauptteile: im ersten Teil behandelt der Verfasser — nach einem kurzen historischen Überblick — die chemischen Komponenten der Lebensmittel (Proteine, Lipide, Kohlenhydrate, anorganische Bestandteile, Vitamine, Enzyme), die Grundlagen der Ernährungswissenschaft, die allgemeinen Erzeugungsmethoden der Lebensmittel, die physikalischen und chemischen Verfahren der Lebensmittelkonsevierung und die Lebensmittelfarbstoffe; dieser Teil umfaßt 312 Seiten, d. h. also, die kleinere Hälfte des Buches. Der zweite Teil enthält die ausführlichere Erörterung der tierischen Lebensmittel, der Speisefette und -öle, der Lebensmittel pflanzlichen Ursprungs, innerhalb der letzteren der Genußmittel, d.h. alkoholische Getränke, Gewürze, Kaffee, Tee, Kakao und Schokolade, Tabak — und endlich wird Trinkwasser und Industriewasser, Luft und Gebrauchsgegenstände (z.B. Küchengeschirr, Verpackungsmaterial, zugelassene Farbstoffe zum Färben derselben usw.) behandelt. Die chemischen und technologischen Kenntnisse werden durch gut gewählte Wirtschaftsdaten ergänzt und durch Tabellen der wichtigsten Zusammensetzungsparameter veranschaulicht. Das Verständnis der Technologien wird durch schematische Darstellungen der Prozesse und der Maschinen und durch Bilder erleichtert. Gegenäber der ersten Auflage erfolgte nicht allein eine bemerkenswerte Modernisierung des gesamten Materials, sondern es wurden zahlreiche neue Kapitel zugefügt, wie z.B. die Ausführungen über kalorienarme und kalorienreiche Lebensmittel, die Proteinversorgung der Welt, einige in neuerer Zeit erkannte Bestandteile der Lebensmittel, die Fleischproduktion und der Fleischkonsum, das Gewicht des Tabaks usw. Das Literaturverzeichnis (179 Hinweise) sollte dem weiteren Studium, der Erweiterung der Kenntnisse dienen, es enthält jedoch — wie bereits in der Rezension der ersten Auflage bemerkt wurde — nur die wichtigsten Publikationen der westlichen Welt und kann deshalb die erstrangig wichtige, der

internationalen wissenschaftlichen Zusammenarbeit dienende, edle Aufgabe der allgemeinen Information nicht erfüllen. Die technische Ausführung, der Druck und die äußere Erscheinung des Buches lobt die Arbeit des Verlags.

L. TELEGDY–KOVÁTS

Handbuch der Starke in Einzeldarstellungen IX—1. (Eine Monographiereihe, herausgegeben von H. Ullmann) R. A. SCHUTZ: *Die Rheologie auf dem Stärkegebiet*

(121 Seiten, 54 Abbildungen, 3 Tabellen, Literaturverzeichnis)

Die allgemeine Entwicklung der makromolekularen Chemie sowie die stetig zunehmende Anwendung von Stärke und stärkehaltigen Rohstoffen in der Lebensmittel-, Textil-, Papier-, Futter- und pharmazeutischen Industrie wirft ständig neue theoretische und praktische Probleme auf, deren Lösung auf die Fachleute des Gebiets wartet. Deshalb begrüßen wir das Erscheinen der neuen Monographie;über die rheologischen Fragen auf dem Stärkegebiet, die in der durch Professor Ullmann angeregten Serie erschien.

Die ersten zwei Abschnitte der Monographie behandeln einige Grundfragen der allgemeinen Rheologie und geben eine Übersicht über die wichtigsten rheometrischen Methoden. Der dritte Abschnitt befaßt sich mit der Rheologie verdünnter Stärkelösungen, wobei besonderes Gewicht auf die Schlußfolgerungen gelegt wird, die aus den rheologischen Meßergebnissen hinsichtlich der physikalisch-chemischen Eigenschaften der Stärke gezogen werden können. Die abschließenden drei Abschnitte behandeln des Schlüsselvorgang der Stärkeanwendung, nämlich die Verkleisterung, wobei einerseits dieser Vorgang und seine Rheologie, anderseits die rheologischen Eigenschaften der verkleisterten Stärke erörtert werden.

Es hat viele Vorteile, daß die Monographie die Grundbegriffe der Rheologie und die Grundlagen der Rheometrie beinhaltet. Auf dem Stärkegebiet arbeitende finden dadurch kurz und logisch aufgebaut die wichtigsten theoretischen Anweisungen sowie die Gesichtspunkte für die Wahl des Meßverfahrens und des Meßinstruments. Besonders hervorzuheben ist dabei das Bestreben des Verfassers, die Grenzen der empirischen Meßverfahren und die Vorteile und Notwendigkeit der Anwendung der absoluten Rheometrie klar vorzuführen. Aus dieser vorteilhaften Lösung folgt jedoch auch das Problem, daß der Verfasser — infolge des beschränkten Umfangs der Monographie — in vielen Fällen gezwungen war, die mathematische Behandlung stark zu vereinfachen und unter den Meßverfahren stark zu selektieren.

Recht gut gelungen ist die Beschreibung der mit dem Verkleisterungsvorgang in Zusammenhang stehenden rheologischen Erscheinungen. Ein großes Verdienst dieses Abschnittes ist, daß der Verfasser, auch aufgrund eigener Erfahrungen, die theoretischen Kenntnisse und Prüfmethoden gut;mit den Bedürfnissen der Praxis vereinigen konnte. Allein der Lebensmittelwissenschaftler hat vielleicht das Gefühl, daß die Rheologie einiger stärkehaltiger komplexer Systeme, die in der Lebensmittelindustrie vorkommen, mehr Raum verdient hätte. Ich denke dabei vor allem an Stärke–Zucker–Protein–Lipid-Komplexsysteme, die besonders in der Süßwaren-, Getreide- und Futterindustrie von Bedeutung sind.

Ein reichhaltiges, zeitgemäß zusammengefaßtes Material findet der Leser über die rheologischen Eigenschaften der verkleisterten Stärke. In diesem Abschnitt ist auch die Behandlung der rheologischen Eigenschaften verschiedener Stärkederivate wertvoll.

Der Abschnitt über die viskoelastischen Eigenschaften verkleisterte Stärke enthaltender Systeme macht mit neuen, äußerst wertvollen und interessanten Ergebnissen und Problemen bekannt.

Das reichhaltige Literaturverzeichnis ist — trotz seines beschränkten Umfangs — jenen Lesern gut behilflich, die sich in Einzelfragen zu vertiefen wünschen.

Es ist zu erwarten, daß die Fachleute in der Stärkeforschung und -verarbeitung die neue, in ihrer Auffassung zeitgemäße Monographie von Schutz mit viel Interesse und Nutzen lesen werden.

R. LÁSZTITY

Recent Development in the Chemistry of Natural Carbon Compounds. Volume VI

Editors: R. BOGNÁR, V. BRUCKNER and Cs. SZÁNTAY, Akadémiai Kiadó, Budapest, 1975. 198 pages

Volume VI of this series contains valuable reviews of three different domains of organic compounds.

One of these domains is covered by the first review by E. WINTERFELD, titled "Approaches to Camptothecin" (p. 11—34, 123 formulas and 29 references to literature). In this review the experiments for the synthesis of camptothecin are surveyed by the author.

The compound camptothecin has been isolated in the middle of the sixties by W. WALL *et. al.* from the bark of *Camptotheca acuminata.* Its structure was established and the pharmacological investigations detected its activity against leukaemia.

Owing to this remarkable physiological effect several research teams dealt with the total synthesis of the compound. The problem was rather complex because in addition to building up the heterocyclic ring system also an extremely reactive α-hydroxylactone group must be formed.

In the first part of the review the author presents a survey of investigations carried out concerning the synthesis of the chromphore of camptothecin then describes the total syntheses of camptothecin performed in different ways by six research teams. Of these various syntheses that carried out by the author and his research team is of particular interest because the key issue in this synthesis consists in the "in vitro" realization of the indole–quinoline conversion similar to the actual biogenesis of the compound.

The final part of the review reported experimental results which though they did not lead to the total synthesis of camptothecin still resulted in interesting intermediates.

In the review discussing this very actual problem literature available up to the beginning of 1973 is taken into account. However, on considering the intensive research activity on this field, as mentioned also by the author, novel results of researches can be expected soon.

The second review by A. KLÁSEK and O. WEINBERGOVA (p. 35—134, 7 tables, 226 numbered and several no-numbered formulas, 420 references to literature) carries the title "The Pyrrolysidine Alkaloids". This review is an up-to-date summary of monographs published earlier concerning the pyrrolysidine alkaloids and of other publications which appeared until 1973/1974. The dynamic and impressive nature of the review is due to the included ontstanding results of the authors themselves in the field of the chemistry of pyrrolysidine alkaloids and of the investigation of their biological effects. In order to facilitate the systematization of the ramified mass of data the review is divided into five chapters and a number of subchapters. The accumulated knowledge is discussed by the authors in the individual chapters along a consequent structural scheme and in a perceptible way. The brief introduction comprising three pages is very informative. Chapter II contains the description of the structure determination, stereochemistry and absolute configuration, further the synthesis of the so-called necines (mono-, di- and trialcohols possessing a pyrrolysidine or 1,2-didehydropyrrolysidine skeleton).

In Chapter III the most important knowledge concerning the structure, stereochemistry, absolute configuration and synthesis of the extremely sensitive so-called necic acids having a complicated structure (mono-, di- and trihydroxy- saturated or unsaturated mono-, di- and tricarboxylic acids, their stereoisomers and/or mono- or dilactones which are C_{10} adipic acid derivatives, C_5 acids, derivatives of α-isopropylbutyric acid, C_6, C_8 or C_{10} derivatives of glutaric acid) is summarized.

In Chapter IV, in turn, the structure and absolute configuration, further the synthesis and biosynthesis of the pyrrolysidine alkaloids are discussed. Besides the ester-type alkaloids formed from necines and necic acids also free necines occur in certain plants. The authors deal at first with these free necines then with the esters according to the following consecutive order bases on the structures: monoester, non-cyclic diester, and macrocyclic diester alkaloids. These latter are systematized according to the number of members (12, 13, 11) of the macrocycle. Chapter IV is terminated by the description of the physical and spectroscopical properties of the pyrrolysidine alkaloids. Throughout the review, the authors point to the still unsolved problems of structural, mainly stereostructural nature and to unrealized syntheses, summarizing in this way the necessity or possibilities of further researches.

The biological propertes are discussed in Chapter V by describing and investigating the mutagen, carcinogen and anti-tumor effects and the mechanisms of these effects.

The third domain of organic compounds is represented by the review "Advances in the Synthetic Chemistry of Glucosaminides" by A. Ya. KHORLIN and S. E. ZURABYAN (p. 136—190, 3 tables, 145 formulas and 229 references to literature).

The structure elucidation and the synthesis of the aminosugar-containing oligosaccharides of prominent biological importance is one of the domains of carbohydrate chemistry exhibiting the most dynamic development. Though some earlier monographs dealing with the synthesis of the glycosides of 2-amino-2-deoxy sugars are already available, the publication of an up-to-date review was timely and very useful — just because the rapid advances in research.

The review of the authors comprises the literature of the synthesis of glycosaminides available up to the first half of 1973, following a logical, well constructed critical order of discussion. After a short survey of the production of alkyl and aryl glycosaminides the application of the Koenigs–Knorr reaction is treated in detail. An interesting remark of the authors is (supported also by the data reported by them in the review) that extended, systematic investigations concerning the role of the aglycone components are lacking though the Koenigs–Knorr reaction, as an almost classical method, is most frequently used also at present.

The best elaborated part of the review is the discussion of the chemistry of 2-substituted glyco-(2',1' : 4,5)-2-oxazolines and its use in the synthesis of glycosaminides. This is not a mere chance because significant results were attained in this field just by the laboratory of the authors. The next chapters deal with the problems of the synthesis methods of 1,2-*cis*-2-amino-2-deoxyglycosides just under development, with the achievements attained in the enzymatic synthesis of the aminosugar-containing oligosaccharides and with the preparation of S- and N-glycosaminides.

The presented 229 references may help significantly the studies of researchers active in this field.

On reading carefully the critical remarks concerning the deficiencies of the individual methods and the limits of their applicability, and comparing the number of the already systematically produced oligosaccharides presented in the accurately constructed tables of the review with the number of native carbohydrates whose structure has been elucidated but whose actual synthesis has not been carried out up to the present, the magnitude of the problems in the chemistry of carbohydrates which are still to be solved is quite apparent. Therefore, in our opinion a significant peculiarity of this review is its inspiring nature.

S. MAKLEIT

Atlas of Thermoanalytical Curves

Volume 4. Edited by G. LIPTAY, Akadémiai Kiadó, Budapest 1975 (With 75 diagrams)

In the last decades the use of thermal analysis has become a widespread and important tool for almost all types of research in technical and natural sciences and for industrial routine tests. The various methods of thermoanalytical procedures play a significant role in fields extending from the investigation of biological materials to the study of reactions taking place in solid phase and in melts.

The discovery of the novel method of derivative thermogravimetry by Hungarian scientist (F. PAULIK, J. PAULIK and L. ERDEY) and the development of the novel complex instrument (the derivatograph) represented an important step in the advance of thermoanalytical methods.

A significant advantage offered by this instrument is that thermogravimetric (TG), derivative thermogravimetric (DTG), differential thermoanalytical (DTA) and even thermodilatometric (TD) measurements can be carried out at the same time under identical experimental conditions.

In order to permit the comparison and evalution of results obtained in various laboratories with various instruments, it was necessary to standardize the parameters of investigation.

The international team that has undertaken the preparation of the derivatographic atlas of various substances by investigations carried out under standardized conditions has performed indeed a praisable work.

The recently published Volume 4 comprises a collection of thermograms of 75 inorganic salts, metal complexes, organic acids, organic analytical reagents, minerals and natural biological materials, obtained by derivatography under accurately specified experimental conditions, with remarks and references to the literature. Volumes 1—4 published thus far contain a total of 275 thermoanalytical diagrams of various substances.

The collection is extremely useful for all control and research laboratories possessing a thermobalance and carrying out thermal investigations.

The amount of data (weight of substance, rate of heating, reference substance, material of crucible, puritiy of sample, ets.) supplied with each diagram makes possible the comparison of the diagrams with the results of measurements carried out with a thermobalance of any type.

The book is a laudable example of successful international cooperation and sincere praise is due to the scientists working in the laboratories of various countries who performed the investigations and produced the measured data. Also the merits of the editor and his associates for their organizing and editorial activities, as well as those of Akadémiai Kiadó must be acknowledged here; they have made possible the successive publication of the extremely useful material comprising a great amount of important information.

J. INCZÉDY

G. J. MOODY, J. D. R. THOMAS: *Practical Electrophoresis*

Merrow Publishing Co. Ltd., England 1975, 104 pages, 22 figures, 9 tables.

The book consists of 12 chapters. After explaining basic principles, it discusses all the main variants of electrophoretic methods used in practice. It deals with paper and cellulose acetate membrane electrophoresis, and with different variants of gel electrophoresis, such as starch, acrylamide and agar gel electrophoresis, further with the special fields of gel electrophoresis, thus with immune electrophoresis, isoelectric focussing and isotachophoresis. The last chapter of the book discusses problems of non-aqueous and mixed-medium electrophoresis.

The book, illustrated by clear, critical, nicely constructed figures, gives very useful information for all those who wish to introduce or adapt some form of electrophoresis under their own conditions. In particular, it will be of valuable help for clinical laboratories.

The Appendix of the book summarizes the electrophoretic products of 20 predominantly British companies. The book is complemented by 104 references, including many modern data. The subject index of 6 pages is rather informative.

T. DÉVÉNYI

Topics in Current Chemistry (Fortschritte der chemischen Forschung) Vol. 56. *Theoretical Inorganic Chemistry*

Springer Verlag, Berlin, Heidelberg, New York 1975. pp 159.

The 56. volume of Topics in Current Chemistry includes 4 articles three of them discuss topics which are of interest from the coordination chemistry point of view and the fourth one contributes to our knowledge in the field of plasma chemistry.

The first review (66 pages with 210 references) is entitled "Continuum Effects Indicated by Hard and Soft Anti-bases (Lewis Acids) and Bases" and written by Ch. K. JÖRGENSEN. The review starts with a historical introduction into the subject mentioning some problems connected to chemical affinity, complex formation constants, the PEARSON concept on hard and soft acids and bases, and preparative chemistry. In the second chapter the author deals with spontaneous deviations from the highest symmetry available in the case of copper (II), palladium(II), mercury(II), lead(II) complexes. Then in a chapter each he mentions some problems connected to electric dipolar polarizability, and the efficiences of quantum chemistry for the more involved understanding of bonding in complexes. In the final chapter softness parameters, hydration and ionization energies are discussed. Emphasis has been laid among others on AHRLAND's softness parameters, KLOPMAN's approach, and on the ionization energies of valence eletrons, partly filled shells, and inner shells.

The second article (24 pages with 74 references) written by H. BRUNNER and entitled "Stereochemistry of the Reactions of Optically Active Organometallic Transition Metal Compounds" describes the stereochemical results obtained with the new optically active organometallic compounds, subdivided according to the stereochemical outcome into retention, inversion, racemization and epimerization reactions. Among the retention reactions the ligand transformations and sulphur dioxide insertion are discussed. Role change of ligands. Walden

inversion and carbon monoxide insertion are described as inversion reactions. Most of the new organometallic compounds are optically stable in solution, and the solutions retain their optical rotations unchanged for long periods of time. Some complexes, however, are configurationally labile in solution, their rotational value decrease without participation of other reagents. Examples of this kind are treated in subchapters entitled "Dissociation Reactions" and "Intramolecular Epimerization Reactions". The racemization and epimerization reactions that occur when optically active organometallic complexes interact with other reagents are described in a separate subchapter.

The third article (47 pages with 122 references) is entitled "Dynamics of Intramolecular Metal-Centered Rearrangement Reactions of Tris-Chelate Complexes" and written by L. H. PIGNOLET. Since several reviews have appeared in the last 10 years which deal with inter- and intramolecular rearrangement reactions of metal complexes the author limited his review to intramolecular metal-centered rearrangement reactions of six-coordinate tris-chelate complexes. After a brief introduction the author describes the dynamic nuclear magnetic resonance technique which permits detailed mechanistic conclusions *via* the observation of site interchanges. Then he outlines in some detail the various intramolecular rearrangement mechanisms and modes which tris-chelate complexes can undergo: mechanism *via* idealized transtition states and permutational rearrangement reactions. The next chapter gives the results of the experimental studies on a) tris(dithiocarbamates), b) tris(tropolonates), c) tris(β-diketonates), d) mixed ligand complexes, and e) miscellaneous tris(didentates).

The author explains the results by considering the effect of ground state geometry as determined from X-ray data on the kinetic parameters and mechanism of rearrangement, and finally discusses the influence of electronic configuration on the dynamics.

"A Theoretical Approach to Heterogeneous Reactions in Non-Isothermal Low Pressure Plasma" is the title of the fourth article (21 pages with 67 references) and is written by S. VEPŘEK. The purpose of the author of this review article is to develop and verify a reasonably simplified theoretical approach to heterogeneous reaction in a non-isothermal low pressure plasma. He considered a simple statistical model of the plasma which has brought about a better understanding of the dependence of the chemical composition of the plasma on energy. The author discussed the chemical transport in low pressure plasma and described how the theoretical approach helped in planning experiments. The main subjects of the review are the theoretical aspects of plasma chemical vapour deposition (CVD) processes, and further the use of the sputtering technique, CVD of the solid in the plasma, as well as the direct oxidation and nitridation of solid surfaces by the plasma. It is also shown in the article that plasma of intense low pressure discharges offers new techniques of crystal growth.

The first, second and third articles can be highly recommended primarily to chemists active or interested in the field of coordination, inorganic and organometallic chemistry, the fourth one to those working in high temperature chemistry or in solid state physics and technology.

E. KŐRÖS

INDEX

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РЕЗЮМЕ

Тонкослойная pH-хроматография моно- и диосновных органических кислот на буферном слое силикагеля

М. БИДЛО-ИГЛОИ

Уравнение кривой pH—R_f было определено в случае моно- и диосновных кислот и было найдено, что на основе кривых pH—R_f моно- и диосновные кислоты могут быть отличены друг от друга. Константы диссоциации могут быть рассчитаны на основе кривых pH—R_f с хорошим приближением. Теоретические зависимости демонстрировались экспериментальными данными ТСХ на буферном силикагеле для следующих органических кислот: о-фталевая, 3,5-динитробензойная, п-нитробензойная и п-метоксибензойная кислоты.

Эффект кремниевого замещения на термическую стабильность полимеров

Т. СЕКЕЙ и М. БЛАЖО

Термическая деградация полистирол-диметилсилана была исследована с помощью пиролитической газовой хроматографии. Состав и распределение летучих продуктов пиролиза указывают на то, что разложение данного полимера протекает согласно тем же закономерностям, наблюдаемым в разложении полистирола и полидиметилсилана. Это заключение является дальнейшим подтверждением более ранних наблюдений авторов в случае полиалкиленсилоксанов и поливинилсиланов. Присутствие атома кремния принципиально не оказывает влияния на механизм разложения углеводородной цепочки.

Производные аминофталазинона, I

Реакция аминоспиртов с 4-хлор-1(2H)-фталазиноном

К. КЁРМЕНДИ

4-Хлор-1(2H)-фталазинон (**1**) сравнительно легко реагирует с аминоспиртами, давая при этом производные 4-(гидроксиалкиламино)-1(2H)-фталазинона (**5**). Реакционность соединения **1**, до сих пор известного своей стабильностью по отношению к аминам [3, 4], повышается за счет промежуточного присоединения аминоспиртов. Роль спиртового присоединения в увеличении реакционной способности подтверждается тем, что соединение **1** с диэтиламиноэтиламином в этиленгликольном растворе при 150°C, за 20 часов дает с 55%-ым выходом соответствующее производное аминофталазинона (**5k**), в то время как без этиленгликоля в тех же самых экспериментальных условиях замещение не происходит.

Основные пептидные производные глутаминовой кислоты, III

ДЬ. СОКАН и А. КОТАИ

Производные карбобензокси-L-олигоглутаминовой кислоты, содержащие две, три, четыре или пять и шесть активных эфирных групп (III, VI, VIII, X) подвергались взаимодействию с расчетным количеством 2-диметиламино-этиламина, а затем производилось

гидрогенолитическое отщепление защитных групп. Так были получены следующие основные пептиды глутаминовой кислоты: тетра-(2-диметиламиноэтил)-амид α- и γ-три-L-глутаминовой кислоты (XIV, $n = 3$ и XVI, $n = 3$), пента-(2-диметиламиноэтил)-амид α-тетра-L-глутаминовой кислоты XIV, $n = 4$), гекса-(2-диметиламиноэтил)-амид α-пента-L-глутаминовой кислоты (XIV, $n = 5$), α-три-[L-глутаминокислый-γ-(2-диметиламиноэтил)-амид] (XX, $n = 3$) и ди-(2-диметиламиноэтил)-амид L-пироглутамил-L-глутаминовой кислоты.

Соединения III,VI, VIII и X были получены из таких производных L-глутаминовой кислоты, в случае которых свободные карбоксильные группы были защищены п-нитрофенилэфирными группами. Образование пептидной связи происходило за счет смешанного ангидрида, образованного с участием карбоксильной свободной группы ацилирующего компонента. Интерпретируется побочная реакция, наблюдаемая в одном из случаев.

Получение производных 2*H*—1,3-бензтиазина, I

Й. САБО, Л. ФОДОР, И. ВАРГА и П. ШОХАР

Конденсация алифатических и ароматических амидов кислот с формальдегидом в пиридоновом растворе приводит к образованию производных 2*H*-1,3-бензтиазина. Это новый способ получения 2*H*-1,3-бензтиазина и его 4-замещенных производных.

Синтез O-α-D-глюкопиранозил-(1→4)-O-β-D-глюкопиранозил-(1→6)-D-глюкозы

П. НАНАШИ, А. ЛИПТАК и Л. ЯНОШИ

Реакция Кёнигс—Кнорра для бензил 2,3,4-три-O-бензил-β-D-глюкопиранозида (2) с α-ацетобромомальтозой (4) дает трисахаридное производное (5) с 68%-ым выходом. После удаления защитных групп с последующим восстановлением $NaBH_4$ и ацетилированием были получены производные альдитоля (8). В спектре ЯМР соединения *8* небольшой химический сдвиг за счет $Pr(fod)_3$ был обнаружен при C_1—H, и, т.о., стало возможным определение стерического расположения C_1—H. Деацетилирование *5* с последующим бензалированием, бензилированием и гидрогенолизом с помощью реактива $LiAlH_4 - AlCl_3$ дает полностью бензилированный трисахарид (12), содержащий только одну первичную свободную гидроксильную группу. Структура продуктов была доказана на основе их ИК и ЯМР спектров.

Синтез новой аминокислоты — γ-карбоксиглутаминовой кислоты и ее производных

Ш. БАЮС и А. ЮХАС

Описывается синтез новой аминокислоты — γ-карбоксиглутаминовой кислоты (Gla) и ее некоторых производных. Ключевые соединения Boc- и Z—DL—$Gla(OtBu)_2$-OBzl были приготовлены за счет конденсации ди-*трет*-бутил-малоната с соответствующим блокированным дегидроаланином.

Гекситоловые производные, содержащие 1,4-оксатиановое кольцо, V

Перегруппировка Пуммерера для сульфоксидов

Й. КУСМАН и П. ШОХАР

Описывается перегруппировка Пуммерера тиоангидрогекситольных сульфоксидов типа II до соответствующих производных глюкотиосептанозы (IV). При дальнейшем окислении димезильных производных IVa образуется смесь двух сульфоксидных изомеров (V). Деацетилирование три-O-ацетата IV/0 приводит к образованию 2,5-ангидр-6-деокси-6-тио-D-глюкотиосептанозы (VII).

Окислительная перегруппировка халконов с помощью нитрата таллия(III),V

Синтез 8-метилового эфира 3′-гидросиретузина и новый синтез ретузина и его 8-метилового эфира — трех природных изофлавонов тропической древесины

Л. ФАРКАШ и А. ВОЛЬФНЕР

Синтез 7,8-дигидрокси-4′-метоксиизофлавона (ретузина, **1**), 4′,8-диметокси-7-гидроксиизофлавона (8-*O*-метилретузина, **2**) и 3′,7-дигидрокси-4′,8-диметоксиизофлавона (3′-гидрокси-8-*O*-метилретузина, **3**) был осуществлен на основе окислительной перегруппировки соответствующих халконов с помощью $Tl(NO_3)_2$, как ключевой ступени.

Кинетические исследование изомеризации 5-винилбицикло (2.2.1.) гептена-2, катализированной $Co(N_2)$ $(PPh_3)_3$

Й. КОВАЧ, В. ПРИЦКОВ, Г. ШПЕЙЕР и Л. МАРКО

5-Винилбицикло(2.2.1)гептен-2 изомеризуется под влиянием $Co(N_2)(PPh_3)_3$ в растворе толуола при 50—70°C в 5-этилиденбицикло(2.2.1)гептен-2. Скорость реакции была выражена следующим уравнением:

$$-\frac{d\,[vbh]}{dt} = \frac{k_4K_1K_2K_3K_5\,[Co]\,[vbh]^2}{K_5\,[S]\,[PPh_3] + K_2K_5\,[S]}$$

где [Co], [vbh], $[PPh_3]$ и [S] обозначают концентрации катализатора, 5-винилбицикло-(2.2.1)гептена-2, трифенилфосфина и растворителя, соответственно. Полагается, что 1,3 смещение водорода протекает по π-аллильному механизму.

Участие соседних групп в аминолизе эфиров в негидроксильных группах

Т. КЁМИВЕШ, А. Ф. МАРТОН и Ф. ДУТКА

Был изучен пиперидинолиз 5-нитро-, 5-хлор-, 5-метил- и незамещенных 8-ацетоксихинолина и п-нитрофенилацетата в хлорбензоле. Высокая реактивность хинолиновых эфиров, строгий второй порядок кинетики, а также влияние заместителей на скорость реакции были интерпретированы на основе участия 1-аза-азота в качестве интрамолекулярного основания.

Электронодефицитные гетероароматические аммонио-амидаты, VIII

Синтез N-(пиридино)-бензолсульфонамидатов с помощью трансформирования кольца [(1-фенилсульфонил-2-пиразолин-5-ил)-метил]-кетонов

М. ЛЕМПЕРТ-ШРЕТЕР и К. ЛЕМПЕРТ

Пирилиму-перхлораты (**1d—g**), взаимодействуя с бензолсульфонгидразидом, превращаются в (пиразилинилметил)-кетоны (4d—f), а также дают смесь фенилсульфонилгидразона кетона 4b и 4c с соответствующим пиридиниосульфонамидатом (**2b**, **2c**). Под влиянием кислоты кетоны *4*, в зависимости от природы заместителя R, дают различные продукты: пирилийные соли, пиридиносульфонамидаты и пиразолы. Соединение **4c** под влиянием щелочи превращается в амидат **2c**.

Исследование полимеризации и сополимеризации β-моноалкилитаконатов в растворе

К. НИТРАИ, НГУЕН НГОК ЛАН и ДЬ. ХАРДИ

Были изучены закономерности полимеризации в растворе в случае монобутилитаконата и монооктилитаконата, инициированной азо-бис-(изобутиронитрилом) и γ-облучением, а также их сополимеризация с акрилонитрилом как с сомономером. Были определены основные характерные кинетические параметры. Результаты по сополимеризации однозначно указывают на то, что с увеличением полярности растворителей их взаимодействие с мономерами увеличивается. Диссоциация свободных карбоксильных групп, зависящая от среды, значительно влияет на ход как полимеризации, так и сополимеризации.

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COMPUTER SIMULATION OF ZONE REFINING

E. BRANDT-PETRIK,* L. CSER** and J. NAGY*

(Technical University of Budapest)

Received May 17, 1974

Zone melting has been used for the purification of organic liquids. Using test data, a simple simulation for zone melting has been carried out.
The method helps predict the probable efficiency of further experiments.

Zone melting, whose first important application was in the purification of materials used in semiconductor technology, is now widely utilized for the purification of metals, organic and inorganic compounds.

After the process of zone melting had been clarified experimentally [1], theoretical principles were discussed and conclusions were drawn [2, 3, 4]. The field of zone melting has grown rapidly, hundreds of chemicals have been raised to new levels of purity by zone refining.

We have performed zone melting to remove micro-impurities from organic solvents. The results of the experiments with benzene and the apparatus used have been described [5].

The concentration distribution upon *normal freezing* is exponential and can be described by the equation

$$c = kx_0 (1\text{-}g)^{k-1} \tag{1}$$

in which c is the impurity concentration in g fractions of the sample length and x_0 is that in the original liquid.

The effective distribution coefficient k can be read directly from the nomogram plotted using the above equation if the values of $\frac{c}{x_0}$ and g are known.

The basic differential equation to be considered as the mathematical model of *zone refining*, was derived independently by REISS [6], and LORD [7], in the form of

$$\frac{l}{k} dc_n(z) = [c_{n-1}(z+1) - c_n(z)]\, dz \tag{2}$$

* Department of Inorganic Chemistry
** Computer Center of Mechanical Engineering Faculty

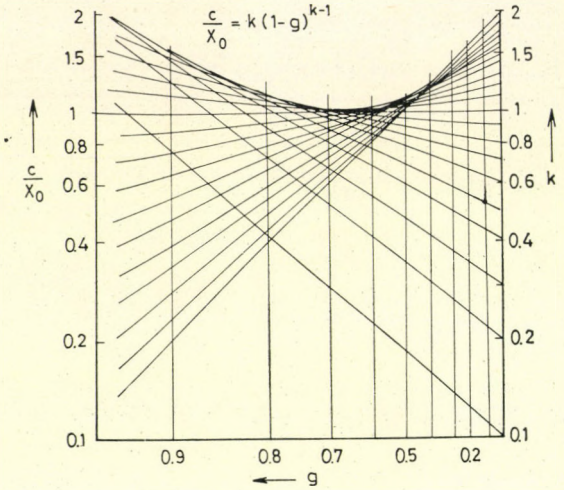

Fig. 1. Nomogram for values of the distribution coefficient k

where

l = zone length;
z = distance covered by the molten zone;
$c_n(z)$ = concentration after the n-th zone step, as a function of z;
$c_{n-1}(z)$ = concentration after the $(n\text{-}1)$-th step and
k = effective partition coefficient.

The equation describes the situation up to a length of $z = L_0 - l$, *i.e.* until the zone reaches the end of the rod. From this on, normal freezing begins.

The solution of the differential equation of zone refining is very complicated [1], thus it can only be evaluated numerically by high-speed computers.

In order to describe zone refining theoretically, we have attempted to find a simple model to simulate the process (melting, freezing). The advantage of this approach is that the initial concentration along the solidified rod does not have to be constant.

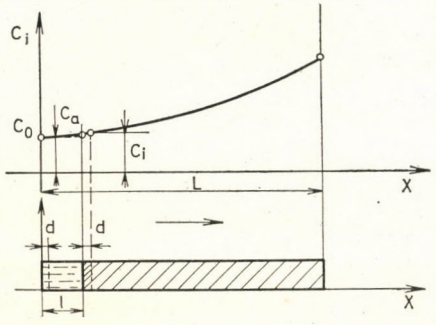

Fig. 2. Model of the simulation

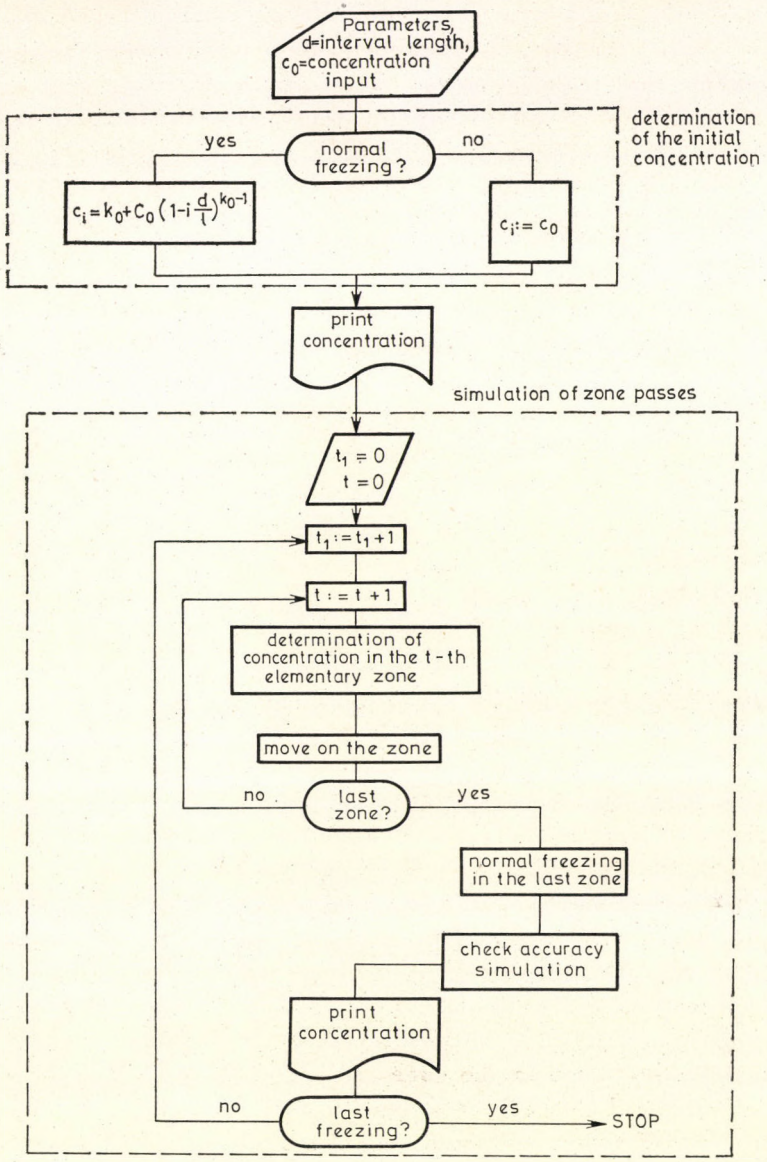

Fig. 3. Block diagram

In Fig. 2 c_i denotes the initial concentration distribution in the solidified rod.

The principle of the simulation is that the average concentration (c_a) is calculated in the molten zone of length l. After the zone has moved on by distance d, the solute will be separated in an amount of kc_ad and in concentra-

tion kc_a at the front of the rod. The amount of material in the zone changes by the same quantity but an amount $c_i d$ of melts to it from the zone end.

Provided that region d moves on in a finite number of steps and that solidification at the zone end is independent of melting at the front, the average

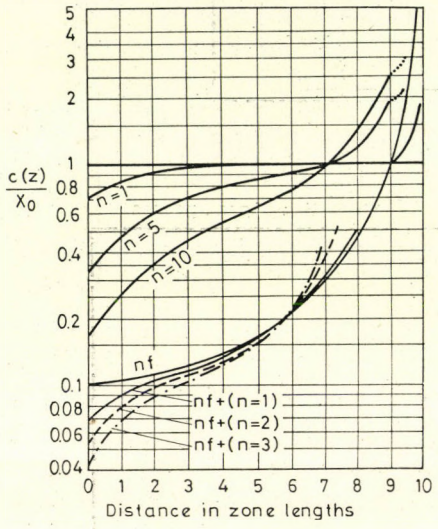

Fig. 4. Computed curves of distribution

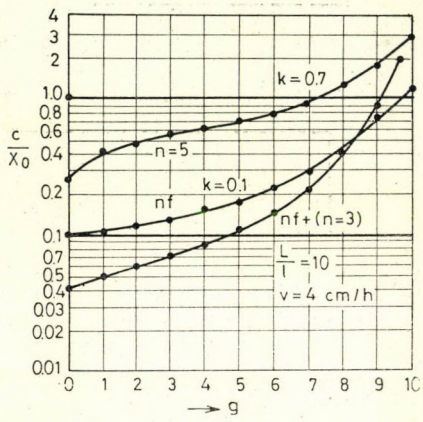

Fig. 5. Computed distribution curves

concentration in the travelling molten zone can be calculated by substracting the solidified, and by adding the molten portions.

The zone then moves on in a step of d until it reaches the end of the rod. The molten material of a zone length at the end of the rod is solidified *via* normal freezing with the corresponding concentration distribution.

The algorithm of the simulation is shown in the block diagram of Fig. 3. The program was written in ALGOL language (Odra code).

The parameters obtained in the zone refining of benzene have been used in the computations; the results are plotted in Figs 4 and 5.

On comparing the experimental and computed distribution curves, the following can be established:

1. The concentration distribution upon normal freezing (if k is known from the experiments) agrees well with that determined experimentally;

2. The calculated distribution curves for zone refining are of the same type as the experimental ones, but are more smoother and more characteristic; This indicates that the parameters affecting the process in the real zone are subject to certain fluctuations (both the zone length and the partition coefficient), which causes slight fluctuations in the distribution, too;

3. If the simulation is performed with the k value determined experimentally, the concentration at the beginning of the rod and the type of the concentration distribution are in agreement with the experimental results;

4. In principle, after 2—3 passes, computation with the true parameters can simulate additional passes in order to decide the degree of purification that can be achieved and whether it is economical carry on zoning.

5. It was possible to simulate combined zoning, consisting of one normal freezing and three zone melting passes. The conditions of the experiments did not permit 10 subsequent passes, but in this way it was possible to compare the effect of tenfold zoning with that of the combined process.

To evaluate the error of simulation, the impurity levels before and after refining were computed and compared. In principle, the values should be identical but with different distributions.

Since in the simulation procedure the zone moved on in finite steps of d, the summation disclosed a smaller amount of impurity at the end than at the beginning of computed zoning.

The high-speed computer permits very small d steps, thus the relative theoretical error of the method is around a few hundredth of one per cent and only rarely increases to the order of 0.1%.

Simulations may supplement and assist in experiments, but can never replace them. Their significance lies in revealing the nature of the process and in permitting to predict the probable outcome of further experiments.

REFERENCES

[1] W. G. PFANN: Zone Melting. Wiley, New York, London, Sydney 1966
[2] E. F. G. HERINGTON: Zone Melting of Organic Compounds. Wiley, Oxford 1963 Moszkva „Mir" 1965
[3] H. SCHILDKNECHT: Zonenschmelzen. Verlag Chemie, Weinheim 1964
[4] WILCOX, W. R., FRIEDENBERG, R., BLACK, N.: Chem. Rev., **64**, 187 (1964)
[5] BRANDT-PETRIK, E., NAGY, J.: Periodica Polytechnica, Chem. Eng., **16** (1972)
[6] REISS, H.: Trans. AIME, **200**, 1053 1954
[7] LORD, N. W.: Trans. AIME, **197**, 1531 1953

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REACTION OF *n*-HEXANE AND WATER VAPOUR ON SUPPORTED NICKEL CATALYSTS AT 1 ATM*

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Received November 21, 1974, in revised form April 16, 1975

It was found experimentally that the composition of the product mixture formed in the decomposition of *n*-hexane by water vapour corresponds to the equilibrium composition in the temperature and conversion ranges employed on catalysts of two different grain sizes (the undecomposed hexane being regarded as a diluent gas).

Apart from methane, no compounds with carbon atom chains shorter than that of the *n*-hexane were found among the reaction products (disregarding the cracking at higher temperatures, above 570 °C).

Unsaturated and aromatic hydrocarbons did not influence the operation of the catalyst.

Introduction

The industrial utilization of the catalytic conversion of low-boiling petrol cuts with water vapour is of ever greater economic importance all over the world. At the relatively low temperature of 500°C the reaction can be used to prepare a gas mixture rich in methane and hydrogen, which can be further employed for various purposes.

The industrial procedures are generally carried out in the temperature range 400—535°C, and in the pressure interval 1—25 atm. Since the overall reaction is slightly exothermic under such conditions, the reagents are preheated to the appropriate temperature and led through a catalyst bed in a thermally insulated reactor. The heat evolved is sufficient to maintain the reaction, and the process does not require further heat input.

The composition of the product mixture leaving the reactor is controlled by the equilibrium corresponding to the conditions. Since every system which contains the same elements in the same proportions leads to the same thermodynamic equilibrium, no matter how complicated the starting compounds, the equilibrium composition of the end-products can be established in advance if the pressure, temperature and C : H : O proportions of the starting compounds are known. (If the system also contains an inert gas, then this must naturally be taken into consideration.)

* The work described was supported by the High Pressure Institute.

If a paraffin hydrocarbon and water vapour are heated above 400°C, only carbon monoxide, carbon dioxide, methane, hydrogen, water and possibly solid carbon can be present in measurable amounts in the equilibrium mixture. At higher temperatures the equilibrium is shifted in the direction of hydrogen formation, and at lower temperatures in the direction of methane formation. The formation of carbon in the reaction is not desirable. Equilibrium carbon formation in the given temperature interval can be avoided by appropriate selection of the hydrocarbon : water vapour ratio of the initial mixture. If the transformation of the hydrocarbon in the reaction is not complete (with the exception of the case when the starting hydrocarbon is methane), the 'equilibrium composition' of the reaction mixture cannot be established in the previous manner, since the system at equilibrium may not contain hydrocarbons with molecular weights higher than that of methane. However, if it is assumed that the original hydrocarbon is present in the system merely as an inert diluting gas, then a pseudoequilibrium composition of the end-products can be established in advance in this case too. Naturally, the 'equilibrium' composition is then a function not only of the pressure, the temperature and the starting composition, but also of the degree of conversion.

There is no clear-cut standpoint as regards the mechanism of the reaction. It was earlier assumed that adsorption of the hydrocarbon is followed by splitting of the carbon chain on the surface of the catalyst, and the residual carbon chain fragments then react with water vapour [1].

That the decomposition of hydrocarbons by water vapour takes place via hydrocarbons of lower molecular weight appears to be supported by the plant and pilot-plant observation that, in the course of the deactivation of the catalyst bed, hydrocarbons of various chain lengths, but mainly olefinic, are present before the appearance of the undecomposed hydrocarbon in the product.

From recent results [2—6] it was concluded that the decomposition of hydrocarbons by water vapour at higher pressures (15—30 atm) first leads to the formation of hydrogen and carbon monoxide; these then interact to yield methane. In parallel with the reactions mentioned, a number of authors [1, 3, 7—9] have also observed establishment of equilibrium in the water gas reaction. The exact kinetics of the reaction have not been clarified, however.

The aim of the research reported in the present paper was to establish the catalytic properties of a 15% nickel on alumina catalyst with the aid of *n*-hexane – water vapour model reaction at 1 atm.

Experimental

Apparatus

The investigations were carried out in the apparatus to be seen in Fig. 1. The catalyst was placed in a quartz reactor, and the temperature was measured with the thermocouple in the concentrically attached quartz capillary. The water vapour was fed from a flask under the reactor, by the aid of boiling with a given electric power. Nitrogen saturated with hexane was introduced to the water vapour.

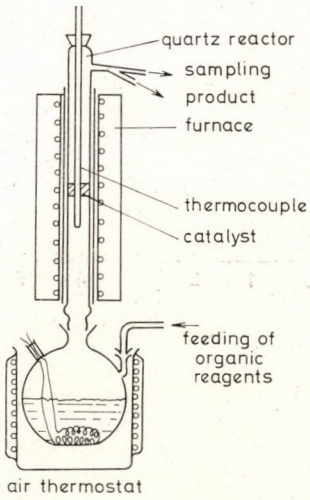

Fig. 1. Experimental apparatus

The gas mixture leaving the reactor was passed through a dry-ice trap, where the water vapour and unreacted hexane condensed, and the rate of the product gas was then measured with a wet drum meter. The gas rates given in the Experimental section refer to room temperature and to the state saturated with water vapour. Samples were taken from the reaction mixture at intervals, and their compositions were determined gas-chromatographically.

n-Hexane of 99.5% purity was used in the experiments; the main impurity was cyclohexane. The distilled water had been boiled immediately before use. The nitrogen used as carrier gas was taken from a cylinder and was freed from oxygen by passage through a copper-containing catalyst.

The catalyst employed had a grain diameter of 3.6 mm, and contained 15 wt.% nickel on alumina. It was prepared by Leunawerke (GDR) on the basis of a procedure elaborated in the High Pressure Institute. It was used either in the original grain size, or after crushing to 0.6—0.8 mm. The specific surface of the catalyst, as determined by the BET method, was 150 m^2/g; the nickel surface, measured by hydrogen chemisorption, was 3.6 m^2/g; and the total pore volume was 0.282 cm^3/g. The pore distribution was as follows:

Pore radius (A)	Pore volume (cm^3)
0—10	0.0684
10—20	0.048
20—40	0.094
above 40	0.072

The pore distribution was determined by oxygen adsorption at liquid nitrogen temperature. The Kelvin equation was used without correction.

Variation of catalyst activity as a function of time in the n-hexane decomposition reaction

From the aspect of evaluation and comparison of the experimental results, it is essential that the activity of the catalyst should possibly not change during each experiment, and that the activities of the catalysts used in different experiments should as possible be the same.

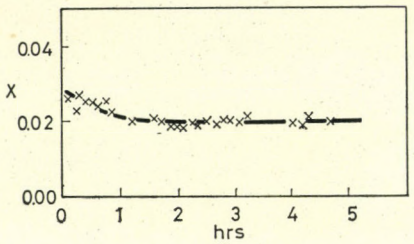

Fig. 2. Variation of the activity of the catalyst in the *n*-hexane – water vapour reaction

Measurements were always made with fresh catalyst, to ensure as far as possible identical initial states.

After addition of the appropriate amount of catalyst, a stream of hydrogen was passed through the reactor while it was heated up to the appropriate temperature. Only after this was the reaction mixture let into the catalyst bed.

The rate and composition of the product gas were measured, and from these the volume flows of the individual components were calculated, together with the degree of conversion relating to *n*-hexane.

It was found in the experiments that the activity of the catalyst initially decreased, and then reached some constant value after being used for about one hour.

Figure 2 shows the degrees of conversion measured at 420 °C as a function of the duration of the experiment on 1.25 g of the catalyst with a grain diameter of 3.6 mm. The gas mixture was admitted at a rate of 930 cm^3/min. It contained water vapour and *n*-hexane in a mole ratio of 12 : 1.

Temperature distribution in the catalyst bed

The temperature of the catalyst bed used in the *n*-hexane – water vapour reaction was not the same at every point. Temperature-drops of 10–50 °C were observed along the catalyst bed, depending on the conversion and on the input rate. For this reason the temperature distribution in the catalyst bed was determined in a number of cases. The temperature of an

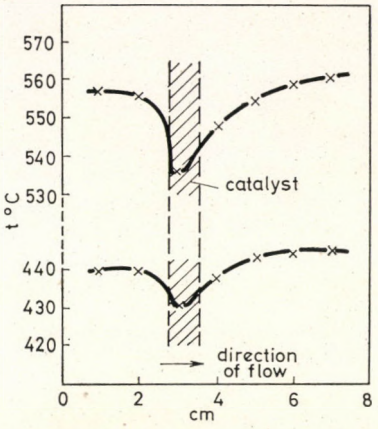

Fig. 3. Temperature distribution along the reactor in the *n*-hexane – water vapour reaction. Feed rate: 940 cm^3/min; catalyst: 1.25 g; H_2O: *n*-hexane = 17:1

experiment was subsequently taken as the lowest temperature measured in the differential catalyst layer.

Figure 3 shows two characteristic temperature distributions as a function of the length of the reactor. The amount of catalyst employed in the experiment was 1.25 g, the input rate was 940 cm^3/min, and the water vapour: hexane mole ratio in the feed mixture was 17 : 1.

Equilibrium calculations

The equilibrium concentrations of the products and the water vapour were calculated as a function of the degree of conversion and of the temperature, on the assumption that the unconverted hydrocarbon is present as an inert diluent gas.

Figure 4 gives the equilibrium product distribution in vol.% (referred to the dry gas mixture) in the decomposition of *n*-hexane by water vapour, as a function of the degree of conversion at various temperatures; the composition of the feed mixture was 18 : 3 : 1 = H_2O : N_2 : *n*-hexane. The same values are depicted in Fig. 5 as a function of the temperature, at various degrees of conversion.

The equilibrium concentration of *carbon dioxide* initially increases rapidly with the conversion, but later barely changes. Below a conversion of 10% the equlibrium concentration of carbon dioxide is practically independent of the temperature in the range 400—550 °C, and at higher conversions, too, the temperature dependence is slight. Up to about 500 °C the amount of carbon dioxide in the equilibrium mixture increases to a small extent, but after this decreases.

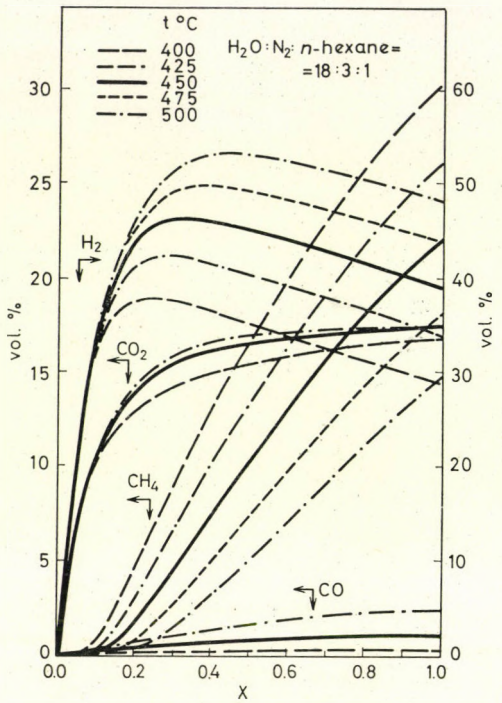

Fig. 4. Variation of equilibrium composition with the conversion. Mole ratio of feed mixture $H_2O : N_2$: *n*-hexane = 18 : 3 : 1

The equilibrium concentration of *methane* depends strongly on both the conversion and the temperature. At constant temperature the concentration of methane initially increases only very slightly with the increase of the conversion, but the concentration increase is later very rapid. With elevation of the temperature, the initial section with low slope extends to an ever larger range of conversion. This means that at constant conversion the equilibrium concentration of methane falls with the rise of temperature. It can readily be seen from the diagrams that at conversions below 10% under the given feed conditions at temperatures above 450 °C the equilibrium methane concentration is extremely low so that the equilibrium product mixture practically does not contain methane.

The equilibrium concentration of *carbon monoxide* rises with the increase of both the conversion and the temperature. Even at a conversion of 20% and a temperature of 550 °C, however, the concentration does not reach 1 vol.%

Up to a conversion of about 20% the equilibrium concentration of *hydrogen* runs fairly parallel to that of carbon dioxide, increasing steeply with increase of the conversion. As a result of a further increase in the conversion, the value passes through a maximum and falls fairly uniformly, corresponding

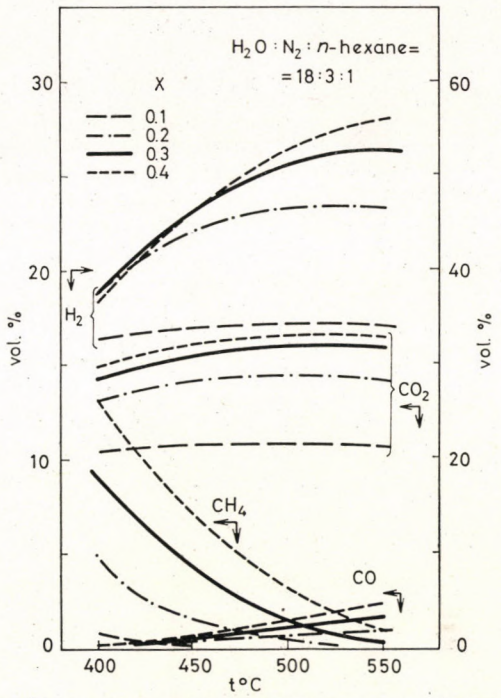

Fig. 5. Variation of equilibrium composition with temperature. Mole ratio of feed mixture $H_2O : N_2$ *n*-hexane = 18 : 3 : 1

to the formation of methane. Up to a conversion of about 10% the equilibrium concentration of hydrogen is practically independent of temperature, but at higher conversions it rises with the increase of temperature.

Variation of the feed composition naturally also affects the equilibrium composition of the product. A decrease in the water vapour concentration of the feed mixture results in increases in the concentrations of the products methane and carbon monoxide, and decreases in the concentrations of hydrogen and carbon dioxide. Of these components, methane and hydrogen are the most sensitive to the feed composition (above a certain water vapour concentration). Figure 6 shows the equilibrium concentrations of carbon dioxide and methane as a function of the degree of conversion for a feed mixture of composition $H_2O : N_2$: n-hexane = 15 : 3 : 1.

Results and conclusions

Temperature dependence of the decomposition of n-hexane by water vapour

The temperature dependence of the decomposition of *n*-hexane by water vapour was studied on catalysts with two different grain diameters (3.6 and 0.6—0.8 mm).

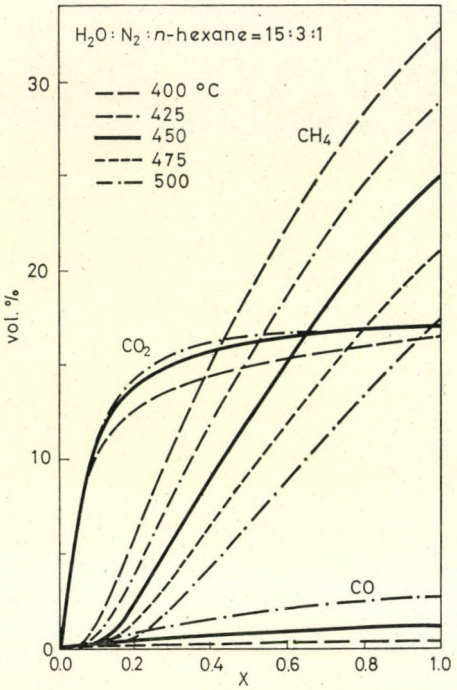

Fig. 6. Equilibrium concentrations of the carbon-containing components in the dry gas mixture. Mole ratio of feed mixture $H_2O : N_2 : n$-hexane = 15 : 3 : 1

In these experiments the reaction was begun at a comparatively low temperature, where it already proceeds at a measurable rate: 400—420 °C. The volume flows of the product components formed during the reaction were determined after establishment of the steady state at various temperatures.

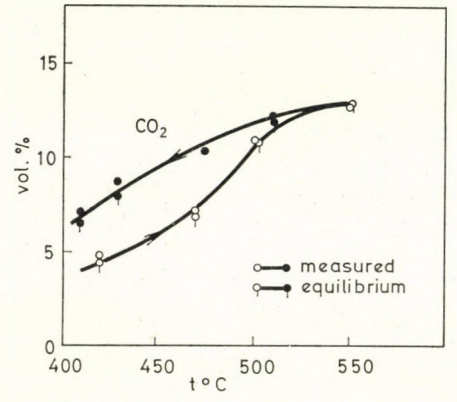

Fig. 7. Variation of carbon dioxide concentration of the product mixture as a function of temperature on catalyst grains 3.6 mm in diameter. Empty and full symbols are measured on equilibrium points taken in the direction of increasing and decreasing temperature respectively. Feed rate: 930 cm^3/min; catalyst: 1.26 g; H_2O: *n*-hexane = 17.5 : 1

The temperature dependence of the reaction was measured with feed mixtures containing various mole ratios of *n*-hexane and water vapour (1 : 4—1 : 18), and at temperatures increasing and decreasing in the range 400—550 °C.

In the range of low conversions at temperatures between 400 and 550 °C, the products of the reaction for both catalyst grain sizes were carbon dioxide

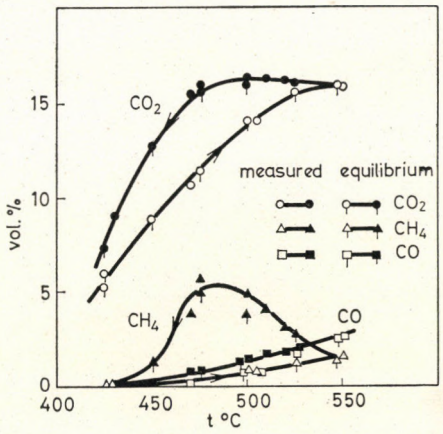

Fig. 8. Temperature dependence of the concentrations of the carbon-containing products on catalyst grains 0.7 mm in diameter. Empty and full symbols are measured on equilibrium points taken in the direction of increasing and decreasing temperature, respectively. Feed rate: 920 cm^3/min; catalyst: 1.26 g; H_2O: *n*-hexane = 17 : 1

and hydrogen, with some carbon monoxide and methane. With increasing conversion, the concentrations of the products methane and carbon monoxide also increase.

When the reaction mixture was fed into an empty reactor at 400—580 °C, no transformation at all was observed. The mixture left the reactor unchanged.

Figure 7 shows the carbon dioxide concentration (expressed in vol.%) of the product mixture formed on 1.26 g of catalyst with a grain diameter of 3.6 mm, as a function of temperature. The equilibrium values corresponding to the given reaction conditions are also indicated in the diagram. The concentration of methane is not plotted, for in the entire measurement series the conversion remained below 15%, and thus the equilibrium and experimentally measured concentrations of methane did not attain 0.1 vol.%. The concentration of carbon monoxide is not shown for similar reasons.

Figure 8 gives the values (in vol.%) of the carbon-containing components of the product formed on 1.26 g of the catalyst fraction with a grain diameter of 0.6—0.8 mm, as a function of temperature. The values corresponding to the equilibrium composition are similarly given in this diagram.

The activities of the catalysts with the different grain sizes both exhibit

hysteresis as a function of temperature; this means that in a certain temperature interval the degree of conversion of the reaction and the composition of the product depend on the direction from which the temperature is approached. In the direction of increasing temperature a lower degree of conversion was

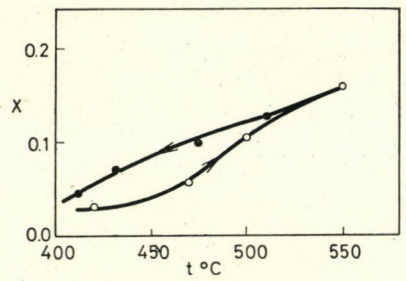

Fig. 9. Variation of the degree of conversion with the temperature on 1.26 g catalyst with a grain diameter of 3.6 mm. Experimental conditions as in Fig. 7

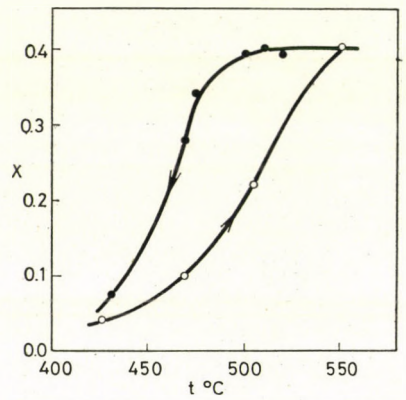

Fig. 10. Variation of the degree of conversion with the temperature on 1.26 g catalyst with a grain diameter of 0.7mm. Experimental conditions as in Fig. 8

observed than if the same temperature was approached from above (Figs 9 and 10).

It can be established that for both grain sizes the composition of the reaction product in the temperature and conversion ranges employed on these catalysts had a value corresponding to the equilibrium composition. This means, therefore, that the rate-determining step is the reaction between hydrocarbon and water vapour, and that the equilibrium between the primary products formed sets in very rapidly, even at the lowest conversions. Conclusions as to the sequence of consecutive steps in the reaction can thus not be drawn from these experiments.

The shape of the methane concentration curve in Fig. 8 is of interest. If the measurement is performed in the direction of increasing temperatures, the concentration of methane in the product mixture scarcely changes. This is a consequence of the fact that while the degree of conversion increases with the increase of temperature, at the same time the equilibrium concentration of methane decreases to roughly the same extent; this results in a curve the shape of which barely changes in the Figure. If the measurement is carried out in the direction of decreasing temperatures, the concentration of methane increases for a time in accordance with the higher conversion values and the lower temperature, and then, below a certain conversion, falls rapidly. Overall, therefore, as a result of the two opposing effects we obtain a curve with a maximum.

On comparison of the measurements made on the two sizes of catalyst grains (Figs 9 and 10), it can readily be seen that at lower temperatures the two catalysts act roughly identically (kinetic interval); then, above a certain temperature (430—440 °C), the gas production of the catalyst with the smaller grains increases compared to the value observed for the larger grains.

This phenomenon can be explained in that at temperatures around 430 °C a pore-diffusion appears on the coarser-grained catalyst, and with the elevation of the temperature this becomes increasingly more significant.

Studies on the change of the carbon atom number

In the conversion interval 0.02—0.40 in the concentration range employed on the two types of catalyst, apart from methane no other hydrocarbon, either saturated or unsaturated, was ever observed below 570 °C.

At temperatures higher than 570 °C, various hydrocarbons, mainly olefinic, with chain lengths less than that of hexane appeared in the product gas. In such cases a considerable deposit of soot was also observed in the catalyst bed and on the walls of the reactor.

The explanation of the phenomenon is that at higher temperatures hexane may also undergo thermal decomposition, resulting in the occurrence of such compounds.

Effect of impurities

A study was made of the effects of aromatic and olefinic hydrocarbon impurities on the activity of the catalyst. Benzene was used as an aromatic compound, and *cis*-2-pentene as an unsaturated hydrocarbon.

These compounds were mixed with hexane in the saturator, in an initial concentration of about 5%. The composition varied during the experiment, in consequence of the differing volatilities.

The compounds were not observed to exhibit any modifying effect on the catalyst.

Other types of hydrocarbons did not appear in the reaction mixture in the case of benzene. The temperature employed in the experiments is already high for the hydrogenation of benzene and the equilibrium is shifted in the direction of benzene formation, and thus benzene is rather formed from the cyclohexane impurity present in the *n*-hexane.

In the case of pentene as impurity, some pentane can also be detected in the mixture, but no other hydrocarbon can be observed here either.

REFERENCES

[1] COCKERHAM, R. G., PERCIVAL, G., YARWOOD, T. A.: J. Inst. Gas Eng., **5**, 109 (1965)
[2] BHATTA, K. S. M., DIXON, G. M.: Trans. Faraday, Soc., **63**, 2217 (1967)
[3] BHATTA, K. S. M., DIXON, G. M.: Ind. Eng. Chem., **8**, 324 (1969)
[4] PHILLIPS, T. R., MULHALL, J., TURNER, G. E.: J. Catal., **15**, 233 (1969)
[5] PHILILPS, T. R., YARWOOD, T. A., MULHALL, J., TURNER, G. E.: J. Catal., **17**, 28 (1970)
[6] ROGERS, M. C. F., CROOKS, W. M.: J. Appl. Chem., **16**, 253 (1966)
[7] DENT, F. J.: Proc. Joint Conf. Gasif. Processes **1962**, B. 1. (1963)
[8] LIHON, D. A.: Chem. Process. Eng., **46**, 487 (1965)
[9] DAVIES, H. S., HUMPHERIES, K. J., HEBDEN, D., PERCY, D. A.: Inst. Gas Eng. J., **7**, 707 (1967)

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REACTION OF OCTANES AND PROPANE WITH WATER VAPOUR ON SUPPORTED NICKEL CATALYSTS AT 1 ATM*

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The controlling step in the decomposition of propane, *n*-octane and iso-octane by water vapour on an alumina supported nickel catalyst is the reaction of the hydrocarbon and water vapour. Equilibrium is established between the reaction products and the unreacted water vapour at various hydrocarbon conversions.

In the reaction of hydrocarbon and water vapour on a magnesium silicate supported catalyst the composition of the product gas apparently corresponds to the equilibrium composition only under conditions where the formation of methane is practically insignificant. In all other cases in the decompositions of both the octanes and propane by water vapour, the catalyst produces much more carbon dioxide and hydrogen than the equilibrium values, and much less methane.

Up to a certain temperature limit, and at various conversions, compounds containing more than one carbon atom were not found among the reaction products. The various normal and isoparaffins reaching the surface of the catalyst are thus able to leave it only in a totally disintegrated state, in the form of compounds containing only a single carbon atom.

At 450 °C the products are formed from the hydrocarbons in question at the same rate, and therefore the rates measured on the model compounds can be used to draw conclusions on the rates of reaction of hydrocarbon mixtures with water vapour too.

Introduction

In an earlier publication [1], a study of the reaction of *n*-hexane with water vapour at 1 atm on aluminium oxide supported nickel catalysts, was reported. It was found that in the decomposition of *n*-hexane by water vapour the step controlling the reaction is that between *n*-hexane and water vapour, while under the conditions employed equilibrium was established between the reaction products at all conversion values.

The aim of the present work was to extend the investigations relating to *n*-hexane to other paraffins, *n*-octane, iso-octane and propane were selected as model compounds.

* The work described was supported by High Pressure Institute.

Experimental

Apparatus

Investigations were made in the apparatus described earlier [1], with the difference that when propane was fed, its flow rate was measured with a differential manometer; when feeding octane, however, the liquid hydrocarbon was injected by means of a peristaltic pump, vapourized and then mixed with the water vapour.

Since the cross sections of the elastic silicone rubber tubes necessary for the peristaltic pump changed continuously after use, as a consequence of the swelling effect of the hydrocarbons, and the tubes finally deteriorated completely, an indirect method was employed: the pump was used to feed water into a vessel, fitted with two outlets, which was completely filled with the appropriate liquid hydrocarbon. The water was admitted through one of the outlets so as to form a layer under the hydrocarbon; since the two liquids are practically immiscible, a volume of hydrocarbon equivalent to the volume of water was expelled through the other outlet.

The reaction products were analyzed by a gas chromatograph.

The *n*-octane and iso-octane used were of p. a. purity. The distilled water fed had previously been boiled out. At the beginning of the experiments the propane used contained 7% ethane and 3% butane + isobutane. These impurities were taken into account in the measurements by determining the average carbon atom number of the gas mixture and using this value in the calculations. During use of the propane, the composition of the gas mixture did not remain unchanged: the concentration of the more volatile ethane decreased, whereas the gas mixture became enriched in butanes, which are less volatile than propane. The average carbon atom number in the experiments varied in the range 2.96—3.08.

Catalysts

One of the catalysts examined was the same as that used in the experiments with *n*-hexane; grains about 3.6 mm in diameter, containing 13 wt.% nickel supported on alumina. The physical parameters of the catalyst were given earlier [1].

Experiments were also carried out with a magnesium silicate supported nickel catalyst. This was prepared by $Ni(NO_3)_2$-$Mg(NO_3)_2$ impregnation of an enstatite based support, followed by heat treatment and reduction. The product contained 6—7% nickel. The fraction with a grain diameter of 2.0—2.5 mm was used in this work.

Experimental method

Fresh catalyst was taken for every experiment. It was placed in the reactor and heated up to the appropriate temperature in a stream of hydrogen, and the reaction mixture was then admitted to the catalyst bed.

After establishment of the steady state, the rate and composition of the product gas were measured. These were used to determine the partial volume flows (relating to 25 °C and 1 atm) of the components produced by the catalyst in unit time, and the degree of conversion of the hydrocarbon was calculated.

In each experimental series (a fixed amount of catalyst and a fixed feed rate), the composition of the product mixture was measured at several temperatures, first in the direction of increasing temperatures, and then in the direction of decreasing temperatures.

Material balance calculations

The material balance was primarily established to check the correctness of the experimental results.

If the residual unreacted liquid hydrocarbon and the water are removed from the product gas, then the following material balance can be written for

the carbon-containing components:

$$v_t = \left(4 + \frac{1}{n}\right) v_{CO_2} + \left(3 + \frac{1}{n}\right) v_{CO} + \frac{1}{n} v_{CH_4} \tag{1}$$

v_t is the rate of flow of the product gas, and v_{CO_2}, v_{CO} and v_{CH_4} the partial rates of the corresponding components, expressed in cm^3/min; n in the equation is the number of carbon atoms present in one molecule of the liquid hydrocarbon.

The amount of hydrogen formed in unit time during the reaction can be calculated from the following relation:

$$v_{H_2} = \frac{\left(2 + \frac{1}{n}\right) v_t + v_{CO_2} - 3v_{CH_4}}{3 + \frac{1}{n}} \tag{2}$$

If the residual hydrocarbon is not removed from the product gas (as in case of propane), then the total volume of the product gas is related as follows to the partial volumes:

$$v_t - 4\, v_{CO_2} - v_{CO} = v^\circ \tag{3}$$

where v° is the feed rate of propane.

The amount of hydrogen formed in the reaction can be calculated from the following relation:

$$v_{H_2} = \frac{(2n + 1)(v_t - v^\circ) + (n - 1)(v_{CO_2} - 3v_{CH_4})}{3n} \tag{4}$$

The material balance was given by consideration of the following reactions:

$$C_nH_{2n+2} + 2n\, H_2O = n\, CO_2 + (3n + 1)\, H_2 \tag{5}$$

$$C_nH_{2n+2} + n\, H_2O = n\, CO + (2n + 1)\, H_2 \tag{6}$$

$$CO_2 + 4\, H_2 \rightleftharpoons CH_4 + 2\, H_2O \tag{7}$$

$$CO + 3\, H_2 \rightleftharpoons CH_4 + H_2O \tag{8}$$

The experimental results could in general be well described by equations (1)—(8). For example, the standard deviation of the propane feed rate, calculated *via* equation (3), was 1.3 cm^3/min, while at the same time the estimated

uncertainty of the measurement of the propane feed rate was $\pm$ 1 cm³/min. Only in a few exceptional experiments, carried out under extreme conditions, could it be shown that a material imbalance was caused by some other reaction (carbon deposition or cracking).

In the knowledge of the hydrocarbon feed rate and the amounts of carbon dioxide, methane and carbon monoxide formed in unit time, the degree of conversion (x) was calculated from the following relation:

$$x = \frac{(v_{CO_2} + v_{CH_4} + v_{CO})}{nv^0} \cdot 100\%$$

Experimental results

Investigations on alumina-supported nickel catalyst

Reaction of octanes and water vapour

In the study of the decompositions of *n*-octane and iso-octane by water vapour, the results were similar to those obtained earlier for the reaction of *n*-hexane with water vapour.

The results of measurements made at increasing and at decreasing temperatures do not agree: a catalyst proved more active at a given temperature if it was approached from higher temperatures than in case of approaching from the direction of lower temperatures (Fig. 1).

In these experiments, too, the reaction rate was controlled by the rate of decomposition of the hydrocarbon, while the reaction products (the undecomposed hydrocarbon being treated as a diluent gas) were present in concentrations corresponding to the equilibrium composition (Fig. 2).

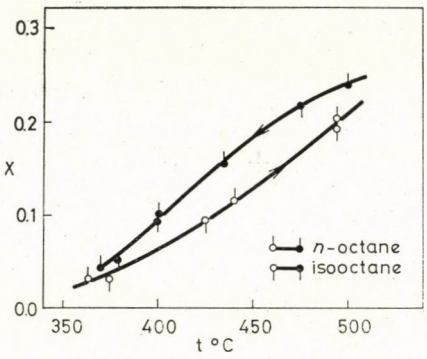

Fig. 1. Variation of the degree of conversion with the temperature in the decompositions of *n*-octane and iso-octane by water vapour on 5.0 g catalyst. Feed rate: 1020 cm³/min; H_2O: octane = 17 : 1. The empty and filled symbols are points measured in the direction of increasing or decreasing temperature, respectively

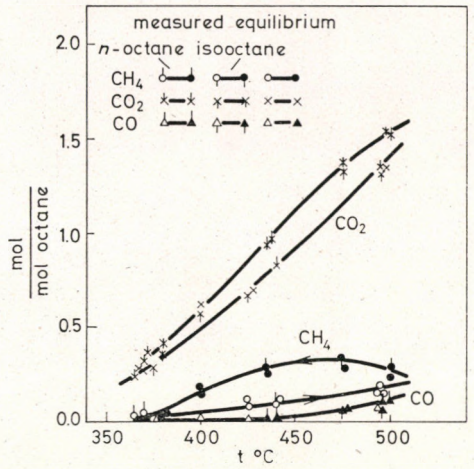

Fig. 2. Amounts of carbon-containing components formed from 1 mol octane fed, as a function of temperature. Feed rate: 1020 cm^3/min; H_2O : octane = 17 : 1; catalyst: 5.0 g

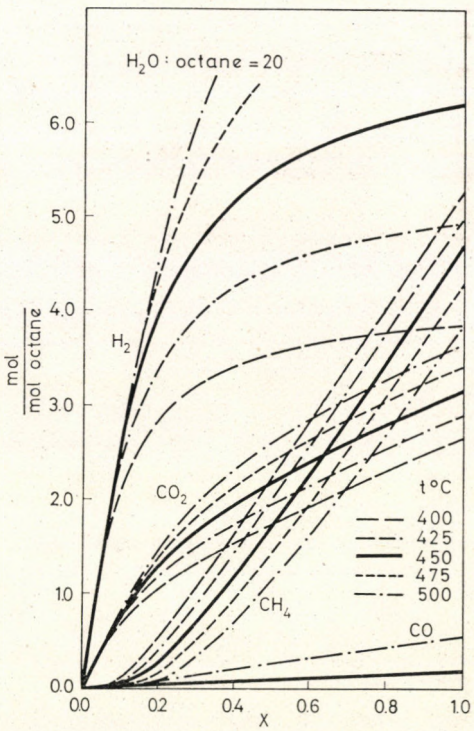

Fig. 3. Equilibrium amounts of products formed from 1 mol octane fed in the octane – water vapour reaction, as a function of the conversion. H_2O : octane = 20 : 1

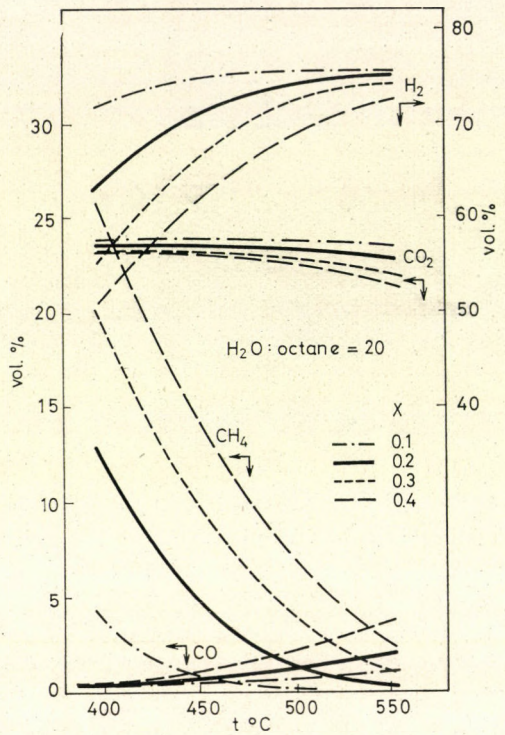

Fig. 4. Variation of the equilibrium composition of the dry gas mixture with the temperature H_2O : octane = 20 : 1

Figure 3 shows the equilibrium amounts (expressed in mol) of the products formed from 1.0 mol octane, at a molar feed ratio $H_2O : C_8H_{18} = 20 : 1$, as a function of the conversion, and Fig. 4 the composition of the equilibrium product (expressed in vol.%) as a function of the temperature at various degrees of conversion. These diagrams too are similar to the equilibrium product distribution in the *n*-hexane – water vapour reaction. At low conversions in the temperature interval of 400—500 °C the main products of the reaction are again carbon dioxide and hydrogen; methane and carbon monoxide are formed in negligible amounts. With the increase of the conversion, the methane concentration of the equilibrium product also increases, at the expense of the carbon dioxide and hydrogen concentrations. At 400—480 °C the amount of carbon monoxide increases to only a very slight extent with the increase of the conversion or the temperature, but at higher temperatures the temperature dependence becomes increasingly steeper.

Increase of the water vapour concentration in the feed mixture suppresses the formation of both methane and carbon monoxide, similarly as in the decomposition of *n*-hexane by water vapour.

When experiments were carried out at low conversions, apart from the unreacted substances, the product contained practically only carbon dioxide and hydrogen corresponding to the equilibrium. The investigations were therefore extended to a conversion range where the formation of methane, too, was appreciable.

Figure 2 shows the rates of formation of the carbon-containing products in the *n*-octane – water vapour and iso-octane – water vapour reactions under

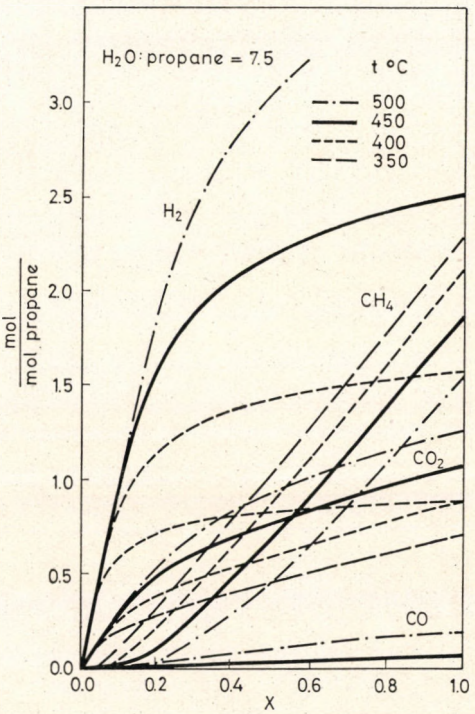

Fig. 5. Equilibrium amounts of products formed from 1 mol propane fed in the propane–water vapour reaction, as a function of the conversion. H_2O : propane = 7.5 : 1

similar experimental conditions, referred to an octane feed of 1.0 mol, as a function of the temperature. The diagram also indicates the equilibrium values corresponding to the given experimental conditions at some temperatures.

From Figs 1 and 2 it can be established that, within the limits of experimental error, the reactions of *n*-octane and iso-octane with water vapour on the catalyst under the same experimental conditions proceed with the same conversions; the product compositions are also identical, and correspond to the equilibrium composition.

Cracking of octanes

At temperatures below 500 °C, apart from methane, no other hydrocarbons were formed in the decompositions of the two octanes with water vapour. At temperatures above 500 °C, on the other hand, cracking was observed in all cases, even at the highest feed ratio used ($H_2O : C_8H_{18} \sim 30$). It must be noted that the concentration of the cracking products (ethane, ethylene,

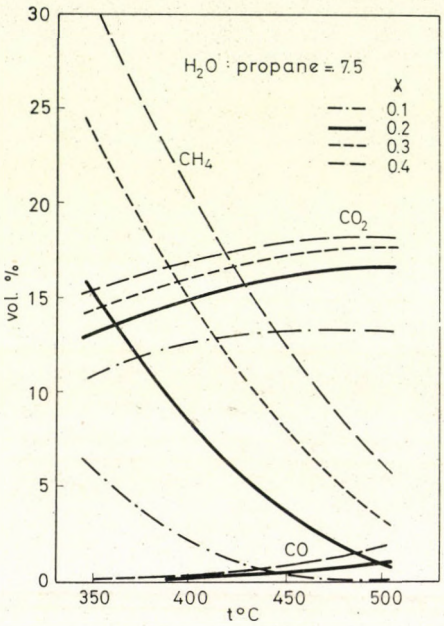

Fig. 6. Variation of the equilibrium composition of the dry gas mixture with the temperature. H_2O : propane = 7.5 : 1

propylene, pentane, pentene) was at most a few tenths of a per cent, but the deposition of carbon was at times very considerable. For example, with a feed ratio of $H_2O : C_8H_{18} = 8 : 1$ at 550 °C for 1—2 hrs at relatively low conversions (6—7%), the deposition of carbon was so extensive that the catalyst grains underwent disintegration.

The possibility of formation of lower molecular weight hydrocarbons was examined at low flow rates, at a conversion of 80—90%, on a longer catalyst bed. It was found that in experiments below 500 °C, apart from methane, no hydrocarbons with chain lengths shorter than that of the feed hydrocarbon were formed in the decompositions of the two octanes with water vapour.

Reaction of propane and water vapour

Figures 5 and 6 show the equilibrium amounts (expressed in mol) of the products formed from 1 mol propane fed in the propane – water vapour reaction, at a feed ratio H_2O : propane = 7.5 : 1.

The equilibrium product distribution is very similar to that observed in the decomposition of hexane or octane by water vapour. At low conversions the main products of the reaction here too are carbon dioxide and hydrogen.

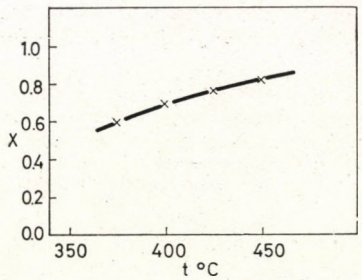

Fig. 7. Variation of the degree of conversion with the temperature in the decomposition of propane by water vapour on 8.1 g catalyst. Feed rate: 990 cm^3/min; H_2O : propane = 8.8 : 1

Hysteresis was also observed in the experiments with propane. In measurements carried out in the direction of decreasing temperatures, the catalyst decomposed the propane with higher conversion than when measurements were made in the direction of increasing temperatures. In these experiments too equilibrium was established between the reaction products, even at a conversion of 50—60%. This shows that at a given feed composition and pressure the composition of the product depends only on the temperature and the conversion of the hydrocarbon. Here again mainly carbon dioxide and hydrogen were formed at low conversions in the temperature range employed, together with some methane and carbon monoxide.

The decomposition of propane by water vapour was studied at high conversions (60—80%) on an 8 g catalyst bed at 375—450 °C, and the results are illustrated in Figs 7 and 8. Figure 8 also shows the equilibrium amounts of the carbon-containing components formed under the given conditions from 1 mol propane fed. It can be seen that at conversions higher than 60% the catalyst produces somewhat more carbon dioxide and less methane than the equilibrium amounts. Under the given conditions the equilibrium and experimentally measured quantities of carbon monoxide are very low compared to those of the other product components, their absolute values being of the same order as the measurement errors. The difference between the experimentally measured and equilibrium values is not too large, never attaining 10%.

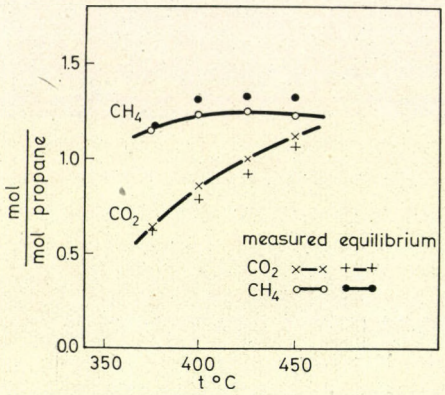

Fig. 8. Temperature dependence of the amounts of carbon dioxide and methane formed in the propane – water vapour reaction from 1 mol propane fed. Feed rate: 990 cm^3/min; H_2O : propane = 8.8 : 1; catalyst: 8.1 g

The equilibrium composition was the product composition observed at a temperature higher by 20 °C than the lowest temperature measured in the catalyst bed.

Cracking was not observed in the temperature range 350—600 °C in the decomposition of propane by water vapour. However, considerable deposition of carbon occurs here too if the water vapour : propane ratio is low.

Decomposition properties of various hydrocarbons

The decomposition properties of the individual hydrocarbons were studied at various feed compositions.

Figures 9 and 10 show the degrees of conversion observed in the direction of decreasing temperatures in the decompositions of the octanes and propane by water vapour, as a function of the feed composition; to facilitate comparison, the composition is given as the mole ratio water vapour : carbon atom. The curves depicted are made up of values interpolated to 400, 450 and 500 °C from the appropriate experimental curves. The experiments were carried out on 1.25 g catalyst, with a total feed rate of 1000 $\pm$ 20 cm^3/min (calculated for a gas state assumed to be at 25 °C and 1 atm).

As a function of the water vapour concentration of the feed, the amount of octane or propane decomposed passes through a maximum. For the hydrocarbons studied, the maximum transformation occurs in the interval H_2O : C = = 2—3.

Figures 11 and 12 show the amounts of carbon dioxide formed from 1 mol octane or propane fed, as a function of the mole ratio H_2O : C of the feed mix-

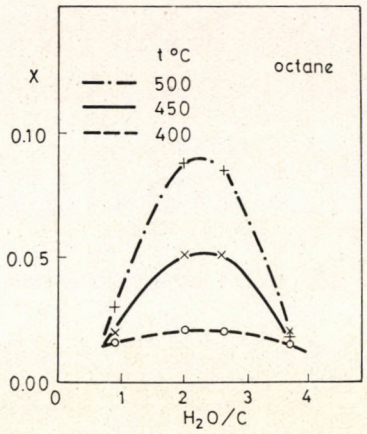

Fig. 9. Variation of the degree of conversion with the feed composition in the decompositions of the octanes with water vapour. Feed rate: 1000 ± 20 cm³/min; catalyst: 1.25 g

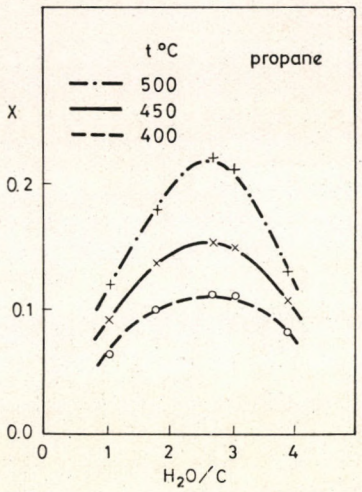

Fig. 10. Variation of the degree of conversion with the feed composition in the decomposition of propane by water vapour. Feed rate: 1000 ± 20 cm³/min; catalyst: 1.25 g

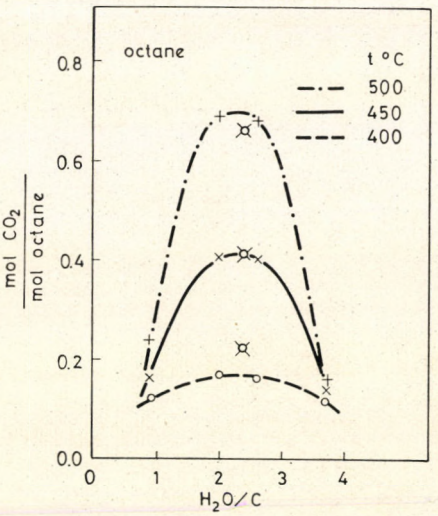

Fig. 11. Variation of the amount of carbon dioxide formed from 1 mol octane fed, with the feed composition, in the octane – water vapour reaction. The symbol ⌑ refers to *n*-hexane. Feed rate: 1000 ± 20 cm³/min; catalyst: 1.25 g

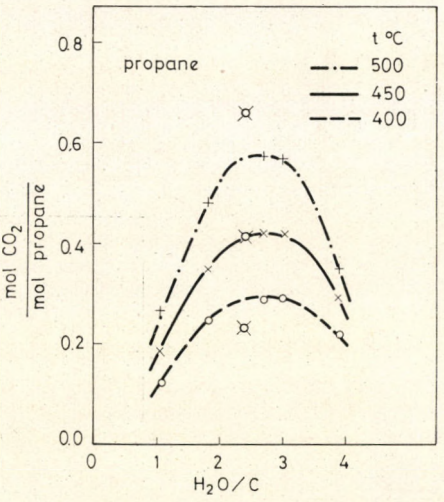

Fig. 12. Variation of the amount of carbon dioxide formed from 1 mol propane fed, with the feed composition, in the propane – water vapour reaction. The symbol ⌑ refers to *n*-hexane. Feed rate: 1000 ± 20 cm³/min; catalyst: 1.25 g

ture. Also depicted are the amounts of carbon dioxide formed in the *n*-hexane – water vapour reaction under similar experimental conditions, at one feed composition.

It is interesting to observe that at a medium temperature, 450°C, in the concentration range $H_2O : C = 2—3$, a fixed amount of carbon dioxide is formed from a given amount of hydrocarbon, regardless of how many carbon atoms the hydrocarbon contains.

Investigations on magnesium silicate-supported nickel catalysts

The reactions of the octanes and propane were also studied on a magnesium silicate-supported nickel catalyst.

Reactions of octanes and water vapour

No differences were observed in the experiments with *n*-octane and iso-octane. Under given experimental conditions the catalyst decomposed the two octanes with the same conversion, and the reaction products too were the same.

At low conversions this catalyst too produced mainly hydrogen and carbon dioxide, with some methane and carbon monoxide. Here again the composition of the product is rather close to the equilibrium composition (regarding the undecomposed hydrocarbon as a diluent gas).

If a higher conversion was achieved by decreasing the flow rate, when the methane concentration at equilibrium is also appreciable, the composition of the product mixture was not the equilibrium one: the catalyst produced somewhat more carbon dioxide and hydrogen and less methane than the

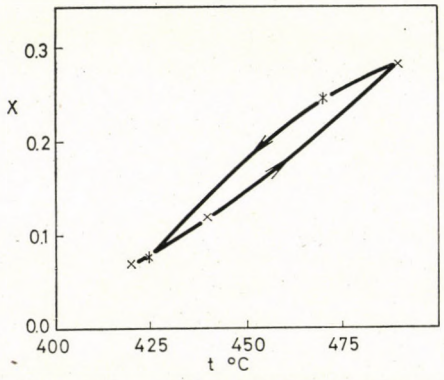

Fig. 13. Variation of the degree of conversion with the temperature in the decomposition of *n*-octane by water vapour on a magnesium silicate-supported catalyst. Feed rate: 1020 cm^3/min; $H_2O : C = 3.1 : 1$; catalyst: 2.5 g

equilibrium quantities. The amount of carbon monoxide formed in the reaction is very low, and is very sensitive to the accuracy of the analysis, the difference from the equilibrium value having the same order as the experimental errors.

Figures 13 and 14 give the conversions of *n*-octane measured on 2.5 g catalyst with a grain diameter of 2.0—2.5 mm and the amounts of carbon

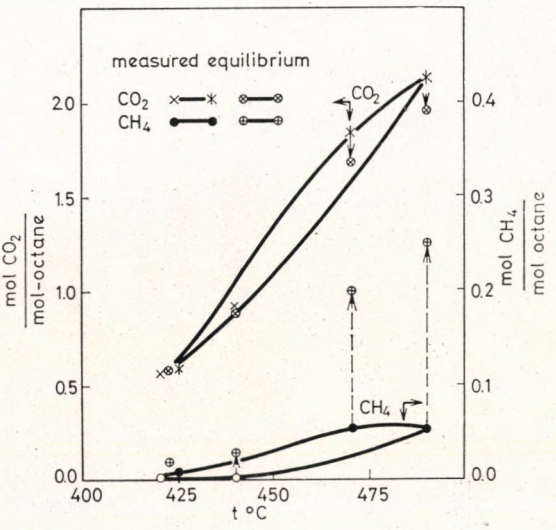

Fig. 14. Temperature dependence of the amounts of carbon dioxide and methane formed from 1 mol *n*-octane fed on a magnesium silicate-supported catalyst. Feed rate: 1020 cm³/min; $H_2O : C = 3.1 : 1$; catalyst = 2.5 g

dioxide and methane (expressed in mol) formed from 1 mol of *n*-octane fed, as a function of the temperature.

Figure 14 also shows the equilibrium product distribution corresponding to Fig. 13.

When the measurements were made at still higher conversions, the difference from equilibrium was even more marked (Figs 15 and 16).

Reaction of propane and water vapour

The results of experiments with propane were very similar to those observed in the decompositions of the octanes with water vapour.

At low conversions, when mainly carbon dioxide and hydrogen are formed in the reaction, the controlling step of the reaction is only the decomposition of the hydrocarbon; the concentrations of the products are close to the equlilibrium product distribution.

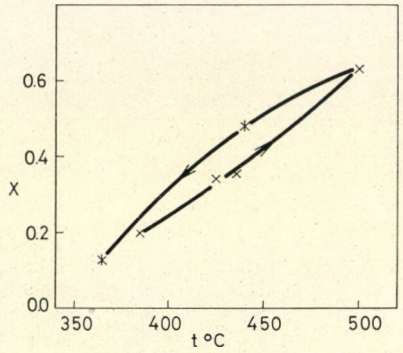

Fig. 15. Variation of the degree of conversion with the temperature in the decomposition of *n*-octane by water vapour on a magnesium silicate-supported catalyst. Feed rate: 1030 cm^3/min; $H_2O : C = 3.1 : 1$; catalyst: 5.0 g

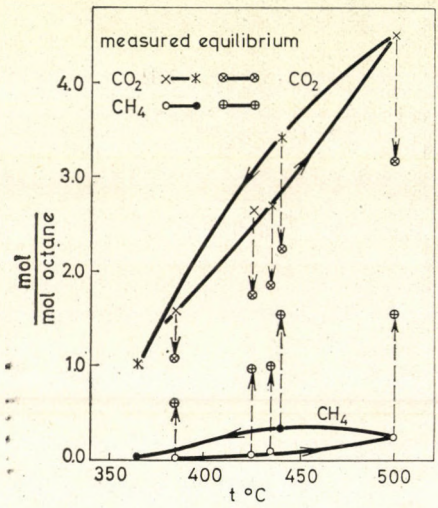

Fig. 16. Temperature dependence of the amounts of carbon dioxide and methane formed from 1 mol *n*-octane fed on a magnesium silicate-supported catalyst. Feed rate: 1030 cm^3/min; $H_2O : C = 3.1 : 1$; catalyst: 5.0 g

With increasing conversion, however, the composition of the product in the decomposition of propane on the magnesium silicate supported catalyst does not correspond to the equilibrium composition either. Compared to the equilibrium amounts, the catalyst produces more carbon dioxide and hydrogen and less methane.

Figures 17 and 18 show the amounts of carbon dioxide and methane formed from 1 mol propane on 5.0 g catalyst at two different feed compositions, and the amounts corresponding to equilibrium. The corresponding conversions are given in Fig. 19, as a function of the temperature.

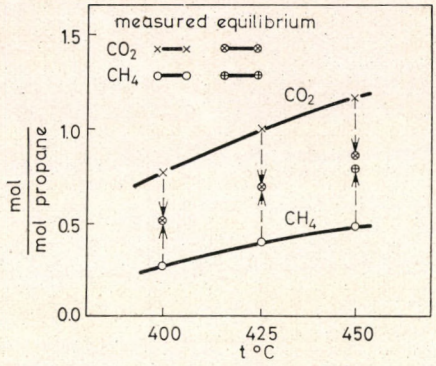

Fig. 17. Temperature dependence of the amounts of carbon dioxide and methane formed from 1 mol propane fed on a magnesium silicate-supported catalyst. Feed rate: 950 cm³/min; $H_2O : C = 2.7 : 1$; catalyst: 5.0 g

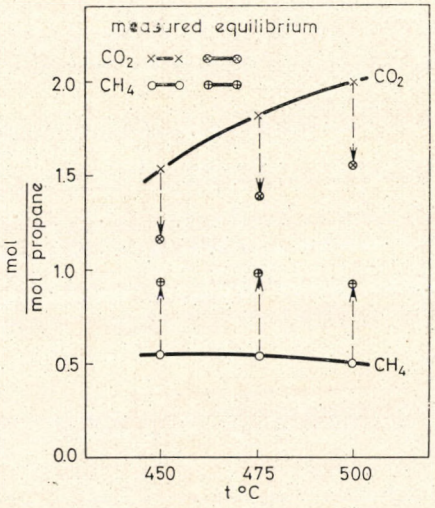

Fig. 18. Temperature dependence of the amounts of carbon dioxide and methane formed from 1 mol propane fed on a magnesium silicate-supported catalyst. Feed rate: 920 cm³/min; $H_2O : C = 3.9 : 1$; catalyst: 5.0 g

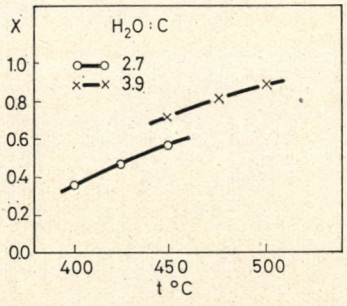

Fig. 19. Temperature dependence of conversion values corresponding to Figs 17 and 18

Discussion

From the experimental results obtained on the magnesium silicate-supported catalyst it may be concluded that for all of the hydrocarbons examined the reaction of the hydrocarbon with water vapour is composed of two steps. In the first step of the reaction, the hydrocarbon and water vapour interact in a strongly endothermic process to give hydrogen and carbon dioxide with a little carbon monoxide. Then, in the second step the primary reaction products interact, with the formation of methane and water vapour.

The assumed reaction steps are thus:

$$C_nH_{2n+2} + 2n\ H_2O = n\ CO_2 + (3n + 1)\ H_2 \tag{5}$$

$$CO_2 + 4\ H_2 = CH_4 + 2\ H_2O \tag{7}$$

The small amounts of carbon monoxide always present in the reaction mixture at the temperatures employed may be formed from the hydrocarbon in parallel to the carbon dioxide:

$$C_nH_{2n+2} + n\ H_2O = n\ CO + (2n + 1)\ H_2 \tag{6}$$

or in the water gas reaction:

$$CO_2 + H_2 = CO + H_2O \tag{9}$$

It is very difficult to establish which of the oxides of carbon is formed first, for the catalyst promotes not only the hydrocarbon – water vapour, but also the water gas reaction. In the temperature interval under consideration, however, the equilibrium of the water gas reaction is shifted in the direction of carbon dioxide and hydrogen, and even a very small amount of carbon monoxide is sufficient for equilibrium to be established. Not even this gives exact information as to the excess of the appropriate oxide of carbon compared to the equilibrium amount, as the uncertainty of the analysis is comparable to the amount of carbon monoxide.

Overall, it may be stated that in the decompositions of these hydrocarbons by water vapour carbon dioxide, hydrogen and a small quantity of carbon monoxide first leave the surface of the catalyst, their relative concentrations roughly corresponding to the values calculated from the water gas equilibrium.

In the second step of the reaction, methane is formed according to equation (7) as a result of the interaction of carbon dioxide and hydrogen formed in the first step. Naturally, the carbon monoxide too may react with hydrogen to yield methane:

$$CO + 3\ H_2 = CH_4 + H_2O \tag{8}$$

but because of the low equilibrium concentration of carbon monoxide this amount is insignificant in practice.

The experiments on the two types of catalysts therefore exhibit a substantial difference in the rate of formation of methane. On the aluminium oxide supported catalyst the rates of the water gas reaction and the methane formation reaction following decomposition of the hydrocarbon are high, and equilibrium of the product components and the unreacted water vapour is established even at the highest hydrocarbon conversions. On the magnesium silicate supported catalyst the equilibrium of the water gas reaction is well approximated to, even at high hydrocarbon conversions, but the approach of the methane formation reaction to equilibrium is slow, and at high hydrocarbon conversions the deviation from the equilibrium of reaction (7) is significant. From the results of measurements on the magnesium silicate supported catalyst, where the amount of carbon dioxide in the product mixture increases compared to the equilibrium value with the increase of the conversion, whereas that of methane decreases, it naturally does not follow that with the increase of the conversion the departure from equilibrium is all the grater.

For the experiments illustrated in Figs 17 and 18, the apparent equilibrium constant calculated from the composition of the departing gas:

$$Ky = \frac{y_{CH_4} \cdot y_{H_2O}^2}{y_{CO_2} \cdot y_{H_2}^4}$$

is compared in Table I with the thermodynamic equilibrium constants at various degrees of conversion.

It is readily seen that the quotient K_{measd}/K_p increases with the temperature, and thus the composition approaches that at equilibrium. Even at a hydrocarbon conversion of 88%, however, the apparent equilibrium constant is only about one tenth of what would be expected at the given temperature.

No difference was found in the experiments with *n*-octane and iso-octane. Accordingly, it may be assumed that other isomeric paraffins also behave sim-

Table I

t °C	x	K_{measd}	K_p	H_2O/C_{feed}	$\frac{K_{measd}}{K_p}$
400	0.35	42.4	1340		0.032
425	0.47	18.7	417	2.7	0.045
450	0.56	9.5	140		0.068
450	0.71	11.5	140		0.082
475	0.82	4.2	50.3	3.9	0.085
500	0.88	2.1	19.2		0.111

ilarly. This is apparently not supported by the findings of PHILLIPS *et al.* [2], who mixed unspecified 'branched-chain hydrocarbons' to an equimolar mixture of hexane and heptane, and then decomposed this reaction mixture with water vapour. At partial conversions it was found that hydrocarbons with molecular weights lower than those of the feed hydrocarbons appeared in the reaction mixture. The hydrocarbon fragments were reported to comprise only a small fraction of the products. The other conditions of the experiment do not emerge from the article, however, and it is possible, therefore, that the cracking of one or other of the components began under the given conditions, and this resulted in the appearance of the hydrocarbon fragments.

In the laboratory the catalysts can be studied more conveniently with pure hydrocarbons than with hydrocarbon mixtures. Industrial reactors for the decomposition of hydrocarbons, however, are generally fed with mixtures. On the basis of the investigations reported it can be stated that from studies with a model substance (*e.g.* propane) conclusions may be drawn with certainty on the rate of transformation of a hydrocarbon mixture, for at the temperature most favourable for the reaction (450 °C) the products were formed at the same rate from all four hydrocarbons examined, in the case of a fixed H_2O/C ratio.

REFERENCES

[1] TRAPLY, G., PARLAGH, GY., RÁCZ, GY., STEINGASZNER, P., SZÉKELY, GY.: Acta Chim. (Budapest) In press
[2] PHILLIPS, T. R., MULHALL, J., TURNER, G. E.: J. Catal., **15**, 233 (1969)

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TIN (IV) DERIVATIVES OF SCHIFF BASES DERIVED FROM PENTANE-2,4-DIONE AND AMINOALCOHOLS

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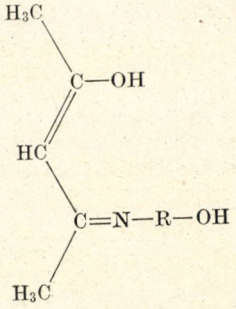
Reactions of tin(IV) chloride with Schiff bases of the general formula $CH_3C(OH)=CHC(CH_3)=NROH$ (where R = $(CH_2)_2$, $CH_2CH(CH_3)$, $(CH_2)_3$ and $CH(C_2H_5)CH_2$ have been investigated at different stoichiometric ratios. The resulting products $SnCl_4(SBH_2)$ and $SnCl_4(SBH_2)_2$ (where SBH_2 represents the Schiff base molecule) have been isolated in almost quantitative yields. Tentative structures are proposed on the basis of elemental analyses, IR spectra and conductivity measurements.

Introduction

The reactions of tin(IV) chloride with nitrogen containing ligands have been studied [1—3]. In earlier communications [4—5] from this laboratory, the reactions of tin(IV) chloride with the Schiff bases derived from benzaldehyde or *o*-hydroxyacetophenone and aminoalcohols have been reported and several new derivatives isolated for the first time. However, the reactions of tin(IV) chloride with the Schiff bases derived from pentane-2,4-dione and aminoalcohols have not been investigated so far. It was, therefore, considered of interest to undertake studies of the resulting tin(IV)-Schiff base derivatives of general formulae $SnCl_4(SBH_2)$ and $SnCl_4(SBH_2)_2$ (where SBH_2 is a Schiff base (**I**) obtained by the condensation of pentane-2,4-dione with aminoalcohols such as 2-aminoethanol-1, 1-aminopropanol-2, 3-aminopropanol-1 and 2-aminobutanol-1) having the central metal atom in a 6- and 8-coordinate environment respectively.



(where R = $(CH_2)_2$, $CH_2CH(CH_3)$, $(CH_2)_3$ and $CH(C_2H_5)CH_2$)

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Experimental

All reactions were carried out in a glass apparatus with interchangeable quickfit joint, under strictly anhydrous conditions. Benzene (BDH) was first refluxed over sodium wire for several hours and then distilled azeotropically with ethanol. Tin(IV) chloride (Reidel) was kept over copper turnings and redistilled before use. Dimethylformamide (BDH) was purified as described earlier [4]. The middle fraction boiling at 55 ± 1 °C/35 mm was collected and stored in blackened and stoppered pyrex flasks. The specific conductivity of the solvent was found to be $0.5—1.5 \times 10^{-7}$ ohm^{-1} at 25 ± 1°C.

Preparation of Schiff bases

Schiff bases of pentane-2,4-dione were prepared by mixing the reactants, *i. e.* pentane--2,4-dione and an aminoalcohol in a 1 : 1 mole ratio in the presence of benzene and refluxing for several hours, followed by the removal of water–benzene azeotrope. These were distilled before use and their analyses and physical characteristics are listed in Table I.

Table I

Physical properties and analyses of the Schiff bases

No.	Schiff base	State and m.p. (°C)	B. p. (°C/mm)	Analysis (%)		
				C Found (Calcd.)	H Found (Calcd.)	N Found (Calcd.)
1.	Pentane-2,4-dione-2--hydroxyethylimine ($C_7H_{13}NO_2$)	Yellow solid 71—72	114—115/0.2	58.83 (58.72)	9.25 (9.15)	9.58 (9.77)
2.	Pentane-2,4-dione-2-hydroxy-1-propylimine ($C_8H_{15}NO_2$)	Viscous yellow liquid	112/0.3	61.35 (61.12)	9.86 (9.62)	8.83 (8.90)
3.	Pentane-2,4-dione-3-hydroxy-1-propylimine ($C_8H_{15}NO_2$)*	Pale yellow crystalline solid 81—82	110—111/0.3	61.01 (61.12)	9.78 (9.62)	8.78 (8.90)
4.	Pentane-2,4-dione-1-hydroxy-2-butylimine ($C_9H_{17}NO_2$)	Deep yellow liquid	111/0.4	62.97 (63.16)	9.81 (9.94)	8.01 (8.18)

* Used for distinguishing between compounds of the same molecular formula

Preparation of tin(IV) complexes

The reactions of tin(IV) chloride with the Schiff bases have been carried out at mole ratios of 1 : 1 and 1 : 2. Tin(IV) chloride was dissolved in benzene and the calculated amount of the Schiff base was then slowly added with shaking. An exothermic reaction took place and the solid compound separated immediately. After decanting the solvent, the resulting solids were repeatedly washed with dry benzene and the products dried under reduced pressure. These have been found to be insoluble in most of the common organic solvents but soluble in DMF. The details of their analyses, their physical properties and molar conductance are reported in Table II.

Table II

Synthesis and characteristics of tin(IV) Schiff base complexes

No.	Tin tetrachloride (g)	Schiff base (g)	Mole ratio	Compound, yield (g) nature	Analysis (%)			Molar conductance (ohm^{-1} cm^2 mol^{-1})
					Sn Found (Calcd.)	Cl Found (Calcd.)	N Found (Calcd.)	
1.	1.25	$C_7H_{13}NO_2$ 0.68	1 : 1	$SnCl_4(C_7H_{13}NO_2)$ (1.93), white solid	28.78 (29.43)	35.37 (35.20)	3.44 (3.47)	8.31
2.	0.76	$C_7H_{13}NO_2$ 0.97	1 : 2	$SnCl_4(C_7H_{13}NO_2)_2$ (1.73), brown semisolid	21.41 (21.72)	25.64 (25.98)	4.88 (5.12)	7.11
3.	1.58	$C_8H_{15}NO_2$ 0.95	1 : 1	$SnCl_4(C_8H_{15}NO_2)$ (2.53), white solid	28.00 (28.44)	34.38 (34.02)	3.20 (3.35)	6.72
4.	1.57	$C_8H_{15}NO_2$ 1.90	1 : 2	$SnCl_4(C_8H_{15}NO_2)_2$ (3.4), yellow semisolid	20.98 (20.66)	24.97 (24.72)	4.64 (4.87)	6.85
5.	1.18	$C_8H_{15}NO_2$* 0.71	1 : 1	$SnCl_4(C_8H_{15}NO_2)$* (1.75), yellow semisolid	27.99 (28.44)	33.42 (34.02)	3.45 (3.25)	8.41
6.	0.74	$C_8H_{15}NO_2$* 0.89	1 : 2	$SnCl_4(C_8H_{15}NO_2)_2$* (1.59), yellow semisolid	20.40 (20.66)	24.49 (24.72)	4.82 (4.87)	8.60
7.	1.35	$C_9H_{17}NO_2$ 0.88	1 : 1	$SnCl_4(C_9H_{17}NO_2)$ (2.23), white solid	27.12 (27.51)	32.48 (32.92)	3.33 (3.24)	8.31
8.	1.05	$C_9H_{17}NO_2$ 1.38	1 : 2	$SnCl_4(C_9H_{17}NO_2)_2$ (2.27), pale yellow solid	19.50 (19.70)	23.11 (23.57)	4.60 (4.64)	8.81

Analytical methods and physical measurements

Tin was determined gravimetrically as tin oxide, chlorine as silver chloride and nitrogen by Kjeldahl's method.

Conductance measurements were made using a Tesla RLC bridge, using a cell with a constant of 0.74 cm^{-1}.

The infrared spectra of the ligands and the complexes were recorded is nujol mull on a Perkin Elmer 337 Grating IR Spectrophotometer in the 4000—400 cm^{-1} range.

Results and discussion

The low molar conductance values falling in the range of 6.72—8.81 $ohm^{-1}\ cm^2\ mol^{-1}$ (Table II), determined in DMF at 10^{-3} *M* concentration and 25 $\pm$ 1 °C indicate the nonelectrolyte nature of the complexes. Their limited solubilities in common organic solvents, however, did not permit the determination of their molecular weights.

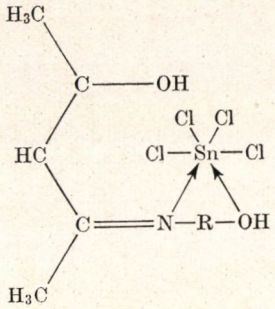
All the ligands have been shown to form 1 : 1 and 1 : 2 complexes, $SnCl_4$ (SBH_2) and $SnCl_4(SBH_2)_2$, when the benzene solutions of the reactants are mixed together. The reactions at mole ratios of 1 : 3 and higher have been found to give $SnCl_4(SBH_2)_2$ type of derivatives only.

The IR spectra of the Schiff bases show a carbonyl absorption within the range of 1680—1660 cm^{-1} characteristic of the keto form. Another medium intensity band is observed at $\sim$1601 cm^{-1} and this may be due to the conjugated, hydrogen bonded carbonyl, the C = C and the C = N vibrations. In the metal–Schiff base complexes these peaks are observed in nearly the same region.

As the Schiff bases possess the functional group NOH and if only the nitrogen is coordinated to the metal atom, the 1 : 1 complex will be pentacoordinate. However, in the case of tin(IV), hexacoordinate complexes have been reported [6, 7] to be more stable and KOGAN *et al.* [8] have shown the formation of a 1 : 2 complex only in the reaction between tin(IV) chloride and the Schiff bases of pentane-2,4-dione with aromatic amines.

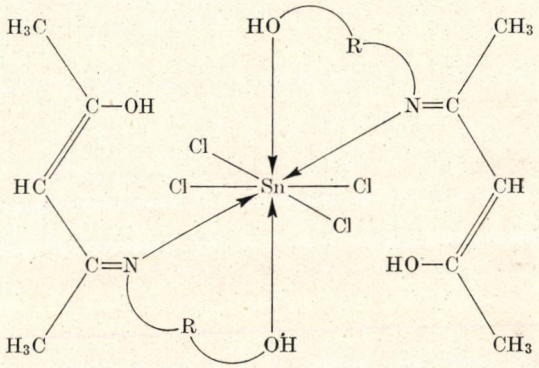
A similar hexacoordinate environment for tin(IV) can be postulated in the derivatives synthesized during the course of the present investigations. This is only possible if the oxygen of the alcohol group may also coordinate to the metal atom forming a Sn←0 bond. This is reflected in the 400—460 cm^{-1} region of the IR spectra of tin(IV) complexes with oxygen donor ligands [9—12]. However, owing to the lack of facilities for recording the spectra in this range, this could not be observed in these complexes.

Thus in the $SnCl_4(SBH_2)$ type complexes, a coordination number of six with an octahedral geometry seems to be possible (**II**).



II

In the $SnCl_4(SBH_2)_2$ type derivatives, the central metal atom may probably be octacoordinated [4, 5, 13—16] and can be represented by the following structure (**III**).



III

*

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REFERENCES

[1] FARANGLIA, G., MAGGIO, F., BOSCO, R., CEFALU, R., BARBIERI, R.: Inorg. Nucl. Chem. Lett., **5**, 177 (1969)
[2] KOGAN, V. A., SOKOLOV, V. P., OSIPOV, O. A.: Zh. Obsch. Khim., **40**, 883 (1970)
[3] BIRADAR, N. S., KULKARNI, V. H.: J. Inorg. Nucl. Chem., **33**, 3781 (1971)
[4] SINGH, O. P., PRASAD, N. R., TANDON, J. P.: Z. Naturforsch., **30b**, 46 (1975)
[5] SINGH, O. P., PRASAD, R. N., TANDON, J. P.: Acta Chim. (Budapest) (In press)
[6] SINGH, O. P., TANDON, J. P.: (private communication)

[7] KOGAN, V. A., OSIPOV, O. A., MINKIN, V. I., SOKOLOV, V. P.: Zh. Neorg. Khim., **10**, 83 (1965)
[8] KOGAN, V. A., SOKOLOV, V. P., OSIPOV, O. A.: Zh. Obsch. Khim., **40**, 833 (1970)
[9] PAUL, R. C., CHADHA, S. L.: J. Inorg. Nucl. Chem., **32**, 3204 (1970)
[10] PAUL, R. C., SINGH, P., CHADHA, S. L., MAKHANI, H. S.: J. Inorg. Nucl. Chem., **32**, 2141 (1970)
[11] TANAKA, T., KAMITANI, T.: Inorg. Chim. Acta, **2**, 175 (1968)
[12] HUNTER, S. H., LANGFORD, V. M., RODLEY, G. A., WILKINS, C. J.: J. Chem. Soc. (A) 305 (1968)
[13] RAMAIAH, K., MARTIN, D. F.: Chem. Comm., 130 (1965)
[14] MEUTTERTIES, E. L., WRIGHT, C. M.: J. Amer. Chem. Soc., **86**, 5132 (1964)
[15] KROENKA, W. J., KENNEY, M. E.: Inorg. Chem., **3**, 251 (1964)
[16] GARNER, G. D., SUTTON, D., WALLWORK, S. C.: J. Chem. Soc. (A), 1949 (1967)

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KINETIC EQUATIONS OF MULTISTEP ELECTRODE PROCESSES, II

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An equation for the polarization curve of the ionization of a metal and the neutralization of the metal ion proceeding by a multistep mechanism is given for the case when a complex-forming agent is present in the solution and the consecutive steps involving electrochemical and chemical reactions as well as diffusion of the product, occur at rates of the same order of magnitude. The kinetic parameters corresponding to a given rate-determining step have been derived.

In a former communication [1] we have given a relationship for the polarization curve of m consecutive electrode processes. We have assumed that there is an excess of inert electrolyte in the solution and the intermediates of the reaction practically do not diffuse away from the electrode surface and do not react with each other or with the components of the solution. These conditions ensure that only consecutive processes occur and the intermediates are consumed only in first order reactions. Under these conditions steady-state polarization curve can be described equation (1).

$$j = z_m \frac{1 - \prod_{i=1}^{m} \frac{k_{ki}}{k_{a_i}} c_{m,\infty}}{\sum_{i=1}^{m} \left[n_i \prod_{j=0}^{i-1} k_{kj} \left(\prod_{l=1}^{i} k_{a_l} \right)^{-1} \right]_i} \tag{1}$$

where $k_{k_0} = 1$, k_{k_i} and k_{a_i} are the rate constants of the corresponding electrode processes which are exponential functions of the electrode potential.

Equation (1) is valid also for consecutive processes in which one or several steps are not electrochemical but chemical reactions. This expression leads to correct results also when the first or the last of the consecutive processes is the diffusion of the starting substance or of the final product. However, for these non-electrochemical steps is $n_i = z_m$.

In an electrolyte containing a complex forming substance it is unlikely that the ionization of the metal or the neutralization of the metal ion in the complex should occur in one step if the coordination number of the complex in solution and also the charge number of the central metal atom are higher than one [2, 3]. According to the Franck–Condon effect, it is to be expected that the activated complexes of the cathode and the anode processes (partici-

pating in the gain or loss of the electron) will have the same structure [4]. On the basis of this assumption and considering that possible adsorption of the ligands on the metal surface before the ionization of the metal, the ionization of the metal and the neutralization of the metal complexes can be described by the following consecutive processes [5],

$$M + \nu_1 K^{n-} \underset{\vec{k}_1}{\overset{\vec{k}_1}{\rightleftharpoons}} (M K_{\nu_1}^{\nu_1 n-})_0 \qquad \text{(I)}$$

$$(M K_{\nu_1}^{\nu_1 n-})_0 \underset{k_{k_2}}{\overset{k_{a_2}}{\rightleftharpoons}} (M K_{\nu_1}^{(z_1-\nu_1 n)+})_0 + z_1 e \qquad \text{(II)}$$

$$(M K_{\nu_1}^{(z_1-\nu_1 n)+})_0 + (\nu_2 - \nu_1) K^{n-} \underset{\vec{k}_3}{\overset{\vec{k}_3}{\rightleftharpoons}} (M K_{\nu_2}^{(z_1-\nu_2 n)+})_0 \qquad \text{(III)}$$

$$(M K_{\nu_2}^{(z_1-\nu_2 n)+})_0 \underset{k_{k_4}}{\overset{k_{a_4}}{\rightleftharpoons}} (M K_{\nu_2}^{(z-\nu_2 n)+})_0 + (z - z_1) e \qquad \text{(IV)}$$

$$(M K_{\nu_2}^{(z-\nu_2 n)+})_0 + (\nu - \nu_2) K^{n-} \underset{\vec{k}_5}{\overset{\vec{k}_5}{\rightleftharpoons}} (M K_{\nu}^{(z-\nu n)+})_0 \qquad \text{(V)}$$

$$(M K_{\nu}^{(z-\nu n)+})_0 \underset{zX}{\overset{zX}{\rightleftharpoons}} M K_{\nu}^{(z-\nu n)+} \qquad \text{(VI)}$$

where M is the metal or the metal ion, K^{n-} is the ligand ion ($n = 0, 1, 2$) and ν_1, ν_2 and ν are the numbers of ligands bound, z_1 and z are the charge numbers of the metal ion; the rate constants* are written above the arrows that indicate the direction of the reactions, the subscript 'o' refers to the components at the surface of the electrode. The overall process (I)—(VI) involves consecutive chemical (I), (III) and (V), electrochemical (II) and (IV), and diffusion process (VI). Obviously, all the consecutive processes occur on the surface of the electrode and if K^{n-} is present in high concentration, this concentration does not change during the process. Therefore, steps (I), (III) and (V) can be regarded as first order reactions and the ligand concentration c_k can be included into the rate constant. If expression (1) is applied to process (I)—(VI), the equation of the polarization curve can be given as

$$j = \frac{zX\,(\vec{k}_1 k_{a_2} \vec{k}_3 k_{a_4} \vec{k}_5 c_k^{\nu} - \overleftarrow{k}_1 k_{k_2} \overleftarrow{k}_3 k_{k_4} \overleftarrow{k}_5 c_{MK})}{X\vec{k}_3 k_{a_4} \vec{k}_5 c_k^{(\nu-\nu_1)}(z k_{a_2} + z_1 \overleftarrow{k}_1) + X\overleftarrow{k}_1 k_{k_2} \vec{k}_5 c_k^{(\nu-\nu_2)}(z k_{a_4} + (z - z_1)\overleftarrow{k}_3) + \overleftarrow{k}_1 k_{k_2} \overleftarrow{k}_3 k_{k_4}\,(zX + \overleftarrow{k}_5)} \qquad (3)$$

where c_{MK} is the bulk concentration of the complex ion produced.

* The rate constant of diffusion is zX. In the case of a rotating disc electrode

$$X = 0.62\, F D^{2/3} \nu^{-1/6} (2\pi f)^{1/2} \qquad (2)$$

where D is the diffusion coefficient of the product, ν is the kinematic viscosity of the solution and f is the number of revolutions of the electrode [6].

Equation (3) is valid if all the rate constants are of the same order of magnitude and the reactants are adsorbed only on an insignificant fraction of the electrode surface. If the rate constant of any step is significantly lower than those of the other steps, this 'slow step' will determine the kinetics of the process and for the reactions preceding the slow step an equilibrium will be established. The kinetic parameters for process (I)—(VI) (kinetic order with respect to the ligand and the apparent transfer coefficient) are shown in Table I for various rate-determining steps. It is clear that conclusions concerning the rate-determining step of the process may be drawn from the slope of the polarization curve and from the reaction order with respect to the ligand even in only the anodic or cathodic polarization curve is studied. It cannot be decided on the basis of the parameters in Table I whether step (V) or (VI) is rate-determining. However, even in this case a decision is possible according

Table I

Slow reaction step	Kinetic order with respect to K^{n-}		Apparent transfer coefficient	
	anodic	cathodic	anodic	cathodic
I	ν_1	$-(\nu-\nu_1)$	0	z
II	ν_1	$-(\nu-\nu_1)$	$\alpha_2 z_1$	$(z-z_1\alpha_2)$
III	ν_2	$-(\nu-\nu_2)$	z_1	$(z-z_1)$
IV	ν_2	$-(\nu-\nu_2)$	$z_1+(z-z_1)\alpha_4$	$(1-\alpha_4)\ (z-z_1)$
V	ν	0	z	0
VI	ν	0	z	0

to how the polarization curve is affected by the stirring of the solution. If the rate increases with increasing speed of stirring or upon faster rotation of a disc electrode, then the polarization is of the diffusion type, whereas the lack of such an effect points to reaction polarization. Thus in the former case step (VI) and the latter case step (V) is rate-determining.

If in a solution of the ligand, the ionization of the metal and the neutralization of the metal ion occur *via* one charge transfer reaction, then the process can often be described [7] by reactions (I), (II), (III) and (VI). On applying relationship (1) or (3) to this four-step process, the following equation is obtained for the polarization curve.

$$j = \frac{\vec{k}_1 k_{a_2} \vec{k}_3 c_k^{\nu} - \overleftarrow{k}_1 k_{k_2} \overleftarrow{k}_3 c_{MK}}{\vec{k}_3 c_K^{(\nu-\nu_1)}(k_{a_2}+\overleftarrow{k}_1)+\overleftarrow{k}_1 k_{k_2}+\dfrac{\overleftarrow{k}_1 k_{k_2}\overleftarrow{k}_3}{zX}} \qquad (4)$$

if $z = z_1$, $\nu_2 = \nu$ and $\alpha_2 = \alpha$. In Table II are listed the kinetic parameters referring to reaction series of (I), (II), (III) and (VI) for the case when one of the steps is 'slow'. On the basis of the kinetic parameters it can be decided also in this case which of the reaction steps determines the rate of the process. Possible deviations from the parameters shown in Tables I and II may be caused not only by the circumstance that several processes have comparable rate constants but also the fact that the surface concentration of the activated complex of the charge transfer reaction is affected by the electrode potential [7].

Table II

Slow reaction step	Kinetic order with respect to K^{-n}		Apparent transfer coefficient	
	anodic	cathodic	anodic	cathodic
I	ν_1	$-(\nu-\nu_1)$	0	z
II	ν_1	$-(\nu-\nu_1)$	αz	$(1-\alpha)z$
III	ν	0	z	0
VI	ν	0	z	0

Expressions (3) and (4) demonstrate that in the case of a process occurring *via* steps (I) — (VI), the effect of diffusion can always be eliminated by the well-known rotating disc electrode [8, 9, 10] since j^{-1} will always be given by correlation.

$$j^{-1} = A + B f^{-1/2} \tag{5}$$

where the reciprocal of A defines the equation of the polarization curve determined by process [(I)—(VI)] unaffected by diffusion.

As we have shown previously [10], the anodic dissolution of copper in anhydrous acetic acid containing chloride ions proceeds *via* the sequence (I)—(II)—(III)—(VI).

REFERENCES

[1] KISS, L., FARKAS, J.: Magy. Kém. Foly., **80,** 542 (1974); Acta Chim. (Budapest) **84,** 161 (1975)
[2] KORYTA, J. (ed. Delahay, P.): Advances in Electrochemistry and Electrochemical Engineering, Vol. 6, p. 289. Interscience Publ. 1967
[3] KRAVTSOV, V. I.: Elektrodnye processy v rastvorakh kompleksov metallov. Izd. LGU. 1969
[4] LIBBY, W. F.: J. Phys. Chem., **56,** 683 (1952)
[5] KOLOTYRKIN, Ja. M.: Usp. Khim., **31,** 322 (1962)
[6] KISS, L., VARSÁNYI, L. M.: Magy. Kém. Foly., **80,** 29 (1974); Acta Chim. (Budapest) **81,** 61 (1974)
[7] KRAVTSOV, V. I.: Electrokhim., **9,** 1702 (1975)

[8] FRUMKIN, A., TEODORADZE, G.: Z. Elektrochem., **62**, 251 (1958)
JAHN, D., VIELSTICH, J.: Electrochem. Soc., **109**, 849 (1962)
[9] KISS, L., VARSÁNYI, L. M.: Magy. Kém. Foly., **80**, 225 (1974); Acta Chim. (Budapest) **83**, 165 (1974)
[10] KISS, L., VARSÁNYI, L. M.: Magy. Kém. Foly., **81**, 43 (1975); Acta Chim. (Budapest) **85**, 399 (1975)

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INFRARED SPECTROPHOTOMETRIC INVESTIGATION OF ALKOXYSILANE-CHLOROSILANE CONDENSATION REACTIONS, I

IR METHOD FOR ANALYSIS OF REACTION MIXTURES

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IR spectrophotometry was used for the determination of all components in the condensation reaction of dimethyldichlorosilane with dimethyldiethoxysilane, dimethyldi-*n*-propoxysilane or dimethyldi-*sec*-butoxysilane. The spectra of the components expected in the course of the reactions were recorded separately and in their respective mixtures. Analytical bands suitable for their determination were selected and characterized from the point of view of quantitative applicability too.

Introduction

Organosilicon compounds with different groups, *e.g.* alkoxysilanes and chlorosilanes condense in the presence of catalyst according to the following equation:

$$\equiv Si-OR + Cl-Si\equiv \xrightarrow{\text{catalyst}} \equiv Si-O-Si\equiv + RCl \qquad (1)$$

This reaction is called sometimes as heterofunctional condensation and leads to the formation of siloxane polymers while a by-product of small molecular weight eliminates. The method is a reasonably simple way for the preparation of polysiloxanes even in the case of a special — *e.g.* asymmetrical — structure too [1].

In connection with this process the main aspects of investigations were the search of the most advantageous catalyst on one side and the clearing up the way of action of the catalyst on the other side [2, 3]. The path of the process, the different reaction steps, however, are still obscure probably because of the lack of an appropiate analytical method.

Some analytical methods have been applied to investigate this type of reactions, they did not give, however, sufficient information in details on the process, moreover they required at the same time some lenghty preparations. ANDRIANOV *et al.* followed the reaction of organosilicon acetates with chlorosilanes by conventional chemical methods, namely by the titration each of the functional groups of the starting materials and those of the expected products in each samples [4]. CSÁKVÁRI and others studied the condensation of alkoxy-

chlorosilane where the evolved product was gaseous alkylchloride. The process was followed by measurement of this only product by repeated weighting after freezing it out in a deeply cooled receiver [3, 5]. In other cases only the composition of the end-product was analyzed by means of gas chromatography, NMR or IR spectroscopy and from these results conclusion was drawn on the path of the reaction or on the side reactions [2, 6].

Our aim was to develop an IR spectrophotometric method for the simultaneous determination of as many components of the reaction mixture as possible all over the process. Infrared spectrophotometry offers a lot of advantages. It is reasonably rapid, easy to perform and is suitable for both qualitative and quantitative analytical purposes. From the point of view of kinetic measurements it has an additional advantage; an IR measurement does not interfere with the reaction examined unlike *e.g.* to gas chromatography.

Here we report on an infrared analytical method worked out for three systems, namely for dimethyldichlorosilane(D)—dimethyldiethoxysilane (D_{OEt}), dimethylchlorosilane—dimethyldi-*n*-propoxysilane(D_{OPr}), and dimethyldichlorosilane—dimethyldi-*sec*-butoxysilane(D_{OBut}) systems.

In these systems we had to consider the presence of the following components: One of the starting materials in every case was D, the other partner was D_{OEt}, D_{OPr} and D_{OBut}, respectively. The additional components expected were dimethylethoxychlorosilane($D_{OEt,Cl}$), dimethyl-*n*-propoxychlorosilane ($D_{OPr,Cl}$) and dimethyl-*sec*-butoxychlorosilane($D_{OBut,Cl}$) respectively, furthermore ethyl chloride, *n*-propyl chloride or *sec*-butyl chloride as well as the siloxane polymer produced independently of the starting mixture.

Experimental

Instrumentation

All infrared spectra were taken by a Perkin—Elmer Model Typ 225 infrared spectrophotometer. The spectra of the materials in cyclohexane solution were recorded in the region of 1400—400 cm^{-1}.

The error of the wave number data was smaller than ± 1 cm^{-1} for sharp bands.

The samples examined were placed in CsI-liquid cell of 0.05—0.1 mm path width. The reference cell was a CsI-micrometer cell which contained only the solvent.

As the samples were corrosive and hydrolyzed readily the cell has to have been stoppered tight. The cell constructed was covered by a thick silicone rubber gasket put between the two metallic plates at the spacer around the side of the windows. The vulcanized silicone rubber made a perfect proof and it did not disturb the measurements because it was soluble neither in cyclohexane nor in the organosilicone compounds. It could be pulled off easily from the plates at the disassembling of the cell.

Materials

Dimethyldichlorosilane was obtained from commercial sources and it was further purified by distillation using a fractionating column. Dimethyldiethoxysilane, dimethyldi-*n*-propoxysilane and dimethyldi-*sec*-butoxysilane were prepared according to NAGY *et al.* by treatment of dimethyldichlorosilane with the suitable alcohol in the presence of pyridine

or aniline [7]. Dimethylalkoxychlorosilanes were obtained by the partial alcoholysis of dimethyldichlorosilane with the respective alcohol. *n*-Propyl chloride and *sec*-butyl chloride were synthetized by the method of Copenhaver from the suitable alcohol and conc. sulphuric acid and zinc chloride [8]. Reagent grade cyclohexane was used as a solvent both in IR-measurements and in the condensation reaction.

Spectra and analytical bands of the components

In order to follow the pathway of all the components during the reaction independent analytical bands had to be found for each of the materials. However, due to the similarity of the chemical composition and spectra of

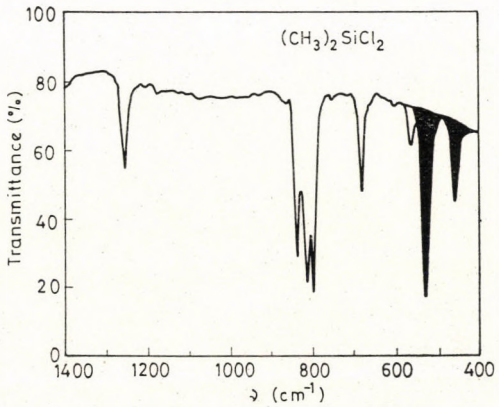

Fig. 1. Spectrum of $(CH_3)_2SiCl_2$ in cyclohexane solution (c_D: 0.2 *M*)

the reactants it was not an easy task. The spectra of the components expected in the reactions of the three systems studied are to be seen on Figs 1, 2, 3 and 4. The analytical bands of the materials are designed with black on the figures. One of the components of the ethoxy-system, ethyl chloride leaves the reaction mixture being gaseous at room temperature; for this we did not care for its IR determination. On the other hand in the course of the condensation reaction a mixture of linear and cyclic siloxanes of different polymerization degree is formed thus, these siloxanes also could not be modelled in advance.

Compounds examined belong to the most fundamental materials of the organosilicon chemistry, therefore they have been examined already from a lot of aspects. The IR spectra of all these materials are known except dimethylalkoxychlorosilanes. Numerous communications deal with the assignment of their IR spectra.

Absorptions characteristic of D are the asymmetrical and symmetrical Si—Cl stretching frequencies at 535 cm^{-1} and at 465 cm^{-1}. The Si—Cl bands were the basis of the analytical method for the determination of D as impurity in trimethylchlorosilane [9].

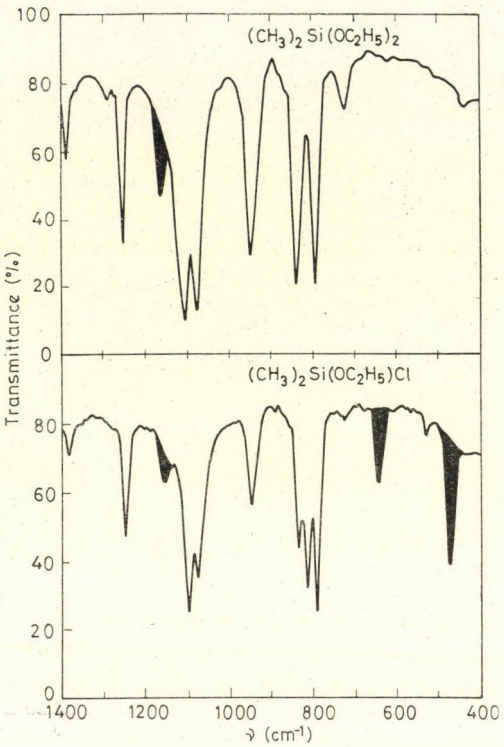

Fig. 2. Spectra of $(CH_3)_2Si(OC_2H_5)_2$ and $(CH_3)_2Si(OC_2H_5)Cl$ in cyclohexane solution (c_{DOEt}:0.2M; $c_{DOEt,Cl}$: 0.2M)

The CH-rocking frequency of the Si–OR group is suitable for analysis which appears in the region of 1150—1170 cm^{-1} in the spectra of every D_{OR} examined [10, 11, 12].

The $D_{OR,Cl}$-s have three analytical bands suitable for analysis in these systems. The Si—Cl stretching frequency appears at 485 cm^{-1} in the case of $D_{OR,Cl}$-s and the CH-rocking frequency at quite the same wave number like in the spectra of the respective D_{OR}-s. $D_{OR,Cl}$ compounds have one band more at 660—650 cm^{-1} which seems to be suitable for analytical purpose. This band can probably be assigned to the SiC_2 stretching frequency on the basis of assignment of other compounds with similar $-Si(CH_3)_2$ skeleton.

The analytical bands of the alkyl chlorides to be measured are the C—Cl stretching frequencies in the region of 730—560 cm^{-1} [13, 14]. In the case of *n*-propyl chloride the C—Cl stretching vibration usable lies at 730 cm^{-1} and in the case of *sec*-butyl chloride at 610 cm^{-1}.

In spite of its utility IR method is not very sensitive, however, to distinguish in molecular weight of the siloxane polymer. There was no unique analytical band for the quantitative determination of siloxanes in these sys-

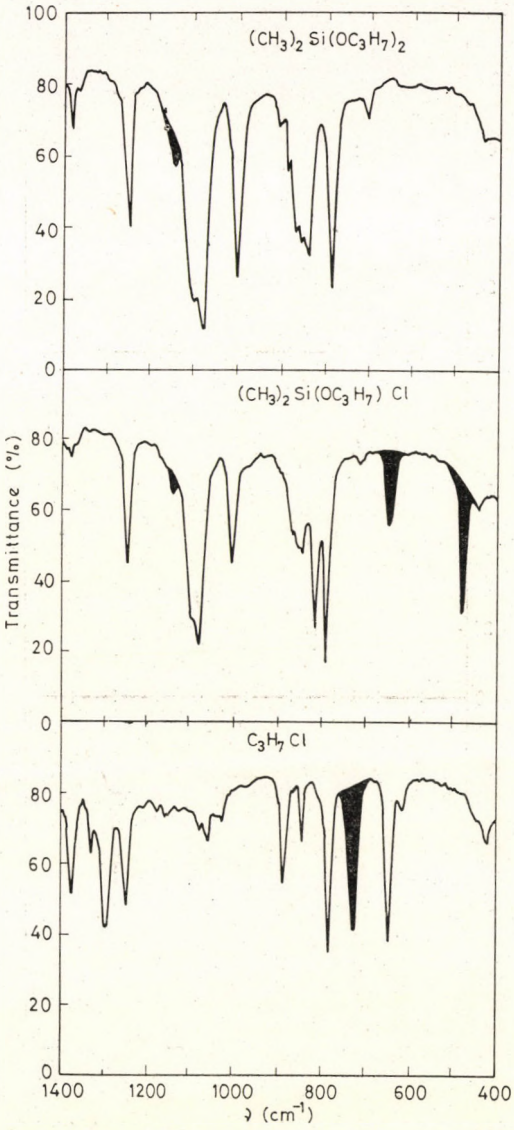

Fig. 3. Spectra of $(CH_3)_2Si(OC_3H_7)_2$ and $(CH_3)_2Si(OC_3H_7)Cl$ and C_3H_7Cl in cyclohexane solution (c_{DOPr}: 0.2*M*; $c_{DOPr,Cl}$: 0.2*M*; c_{Pr-Cl}: 2*M*)

tems. Qualitatively they could be followed in the region of 1000—1100 cm^{-1}, in the range of the asymmetrical Si—O—Si stretching frequencies, as it will be shown in the second part.

The spectra taken on the synthetic mixtures of different composition show the absence of any intermolecular interactions either with the solvent or other components. The analytical bands chosen follow Berr's law, thus, they

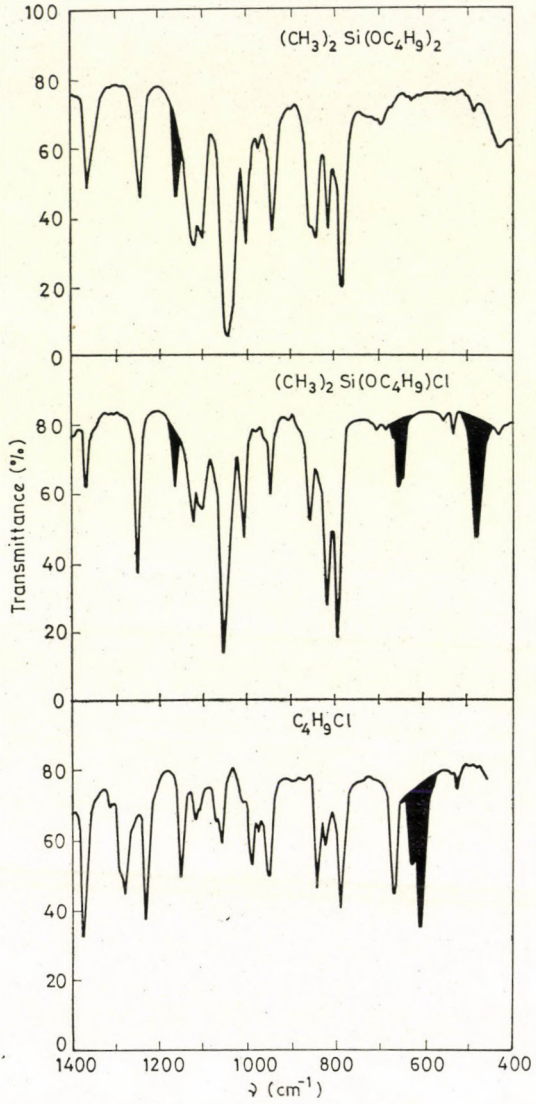

Fig. 4. Spectra of $(CH_3)_2Si(OC_4H_9)_2$, $(CH_3)_2Si(OC_4H_9)Cl$ and C_4H_9Cl in cyclohexane solution (c_{DOBut}: 0.2*M*; $c_{DOBut,Cl}$: 0.2*M*; c_{But-Cl}: 2*M*)

are usable for quantitative measurements. Lower detection limit was determined in the respective mixtures at each analytical bands. The analytical bands and the detection limit belonging to them are summarized in Table I. Figs 5, 6, and 7 show the spectra of the synthetic mixtures of D—D_{OEt}, D—D_{OPr} and D—D_{OBut} systems. The analytical bands are designed with black and with the letters of Table I.

Table I

Analytical bands of the compounds

Compounds	Band (cm^{-1})	Intensity	Lower detection limit (c[M])*
$(CH_3)_2SiCl_2$	535 (E)	vs	$9 \cdot 10^{-4}$
	465 (F)	m	$3 \cdot 10^{-3}$
$(CH_3)_2Si(OC_2H_5)_2$	1165 (A)	m	$5 \cdot 10^{-3}$
$(CH_3)_2Si(OC_2H_5)Cl$	1165 (B)	m	$1 \cdot 10^{-2}$
	660 (C)	m	$5 \cdot 10^{-3}$
	485 (D)	s	$2 \cdot 10^{-3}$
$(CH_3)_2Si(OC_3H_7)_2$	1150 (A)	m	$2 \cdot 10^{-2}$
$(CH_3)_2Si(OC_3H_7)Cl$	1150 (B)	m	$2 \cdot 10^{-2}$
	665 (C)	m	$5 \cdot 10^{-3}$
	485 (D)	s	$2 \cdot 10^{-3}$
C_3H_7Cl	730 (G)	m	$2 \cdot 10^{-2}$
$(CH_3)_2Si(OC_4H_9)_2$	1170 (A)	m	$3 \cdot 10^{-3}$
$(CH_3)_2Si(OC_4H_9)Cl$	1170 (B)	m	$8 \cdot 10^{-3}$
	660, 650 (C)	m	$6 \cdot 10^{-3}$
	485 (D)	s	$3 \cdot 10^{-3}$
C_4H_9Cl	610 (G)	m	$1 \cdot 10^{-2}$

* Calculated for 0.1 mm path width

The analytical bands of *n*-propyl chloride and *sec*-butyl chloride (band G) appear separately in the synthetic mixtures. The analytical band of D at 535 cm^{-1} (band E) also appears separately in the spectra of the three systems, thus D can be easily and exactly determined at this band. The band at 465 cm^{-1} of D (band F) and that of $D_{OR,Cl}$ at 485 cm^{-1} (band D) overlapp partially, thus the determination of these two compounds encounters difficulties at the mentioned bands. Fortunately there is another analytical band for $D_{OR,Cl}$ at 660 cm^{-1} (band C) like for D at 535 cm^{-1} (band E). D_{OR}-s have only one analytical band at 1150—1170 cm^{-1} unfortunately at quite the same wave number like the respective $D_{OR,Cl}$. For this reason D_{OR}-s can be determined quantitatively by using the concentration of the respective $D_{OR,Cl}$ calculated at another isolated peak *e.g.* at 660 cm^{-1}. (The absorbance at band B calculated from the known concentration of $D_{OR,Cl}$ was substracted from the total absorbance determined at band A, B.)

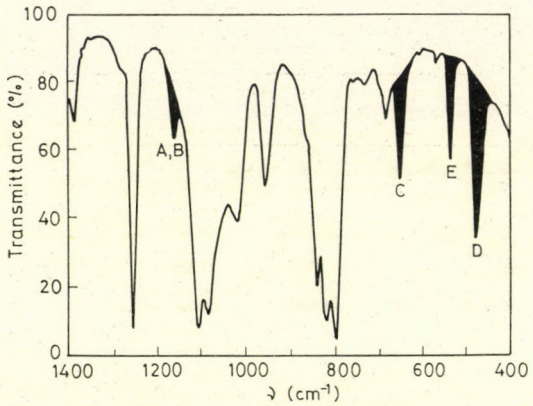

Fig. 5. Spectrum of a synthetic mixture of the components of D—D_{OEt} system in cyclohexane solution (c_D: 0.1*M*; c_{DOEt}: 0.2*M*; $c_{DOEt,Cl}$: 0.2*M*)

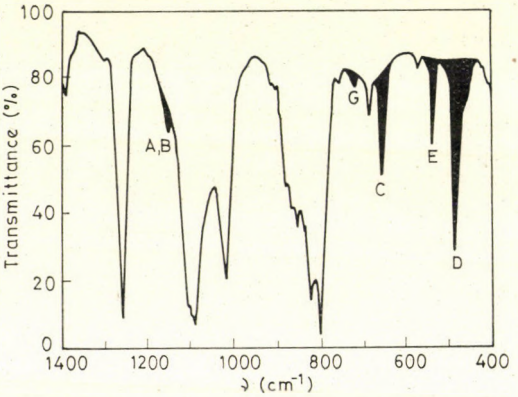

Fig. 6. Spectrum of a synthetic mixture of the components of D—D_{OPr} system in cyclohexane solution (c_D: 0.1*M*; c_{DOPr}: 0.2*M*; $c_{DOPr,Cl}$: 0.2*M*; c_{Pr-Cl}: 0.66*M*)

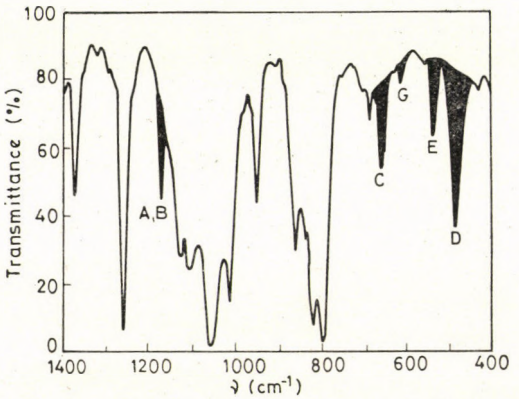

Fig. 7. Spectrum of a synthetic mixture of the components of D—D_{But} system in cyclohexane solution (c_D: 0.15*M*; c_{DOBut}: 0.2*M*; $c_{DOBut,Cl}$: 0.2*M*; c_{But-Cl}: 0.66*M*)

The informations obtained illustrate the utility of IR spectrophotometry for the analysis of these reaction mixtures, and this method seems to be applicable to study the condensation processes.

REFERENCES

[1] USP 2 542 641 (1947) Doyle, C. D.
USP 2 485 928 (1947) Servais, P. C.
French Pat. 1 037 111 (1947) Phylip, C. S.
[2] Székely, T., Rösner, P., Gömöry, P.: Acta Chim. Acad. Sci. Hung., **61,** 233 (1969)
[3] Csákvári, B., Fábry, L., Gömöry, P., Keömley, G.: Radiochem. Radioanal. Lett., **15/6,** 393 (1973)
[4] Andrianov, K. A., Sokolov, N. N., Khrustaleva, E. N.: Zhurn. Obschtch., Chim., **26,** 1102 (1956)
[5] Andrianov, K. A., Ganina, T. N., Sokolov, N. N.: Zhurn. Obschtch. Chim., **26,** 1961 (1956)
[6] Andrianov, K. A., Vasileva, T. V., Dyachenko, R. A., Dyachenko, B. I., Yastrebov, V. V., Raifelb, J. E.: Zhurn. Obschtch. Chim., **41/5,** 1090 (1971)
[7] Nagy, J., Ferenczi-Gresz, S., Barta, I., Borbély-Kuszmann, A.: Acta Chim. (Budapest), **69,** 397 (1971)
[8] Whaley, A. M., Copenhaver, J. E.: J. Am. Chem. Soc., **60,** 2497 (1938)
[9] Brown, P., Smith, A. L.: Anal. Chem., **30,** 1016 (1958)
[10] Richard, R. E., Thomson, H. W.: J. Chem. Soc., **1949,** 124
[11] Marchand, A., Valade, J.: J. Organometal. Chem., **12,** 305 (1968)
[12] Smith, A. L.: Spectrochim. Acta, **16,** 87 (1959)
[13] Mizushima, S.: Structure of Molecules and Internal Rotation, Academic Press, New York (1954)
[14] Shipmann, J. J., Folt, V. L., Krimm, S.: Spectrochim. Acta, **18,** 1603 (1962)

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INFRARED SPECTROPHOTOMETRIC INVESTIGATION OF ALKOXYSILANE–CHLOROSILANE CONDENSATION REACTIONS, II

THE COURSE OF THE CONDENSATION REACTION OF DIMETHYLDICHLOROSILANE WITH DIMETHYLDI-*sec*-BUTOXYSILANE

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Fe-Cl_3-catalyzed condensation of dimethyldichlorosilane with dimethyldi-*sec*-butoxysilane was studied. Infrared spectrophotometry was applied to follow the process. It was found that the reaction consists of two steps. The first is a very rapid radical exchange between the difunctional alkoxysilane and chlorosilane producing dimethylalkoxychlorosilane. This compound is the starting monomer of the consecutive condensational step. It has been established that the condensation is irreversible and practically absent of side-reactions.

Introduction

In the first part of this series we have described an infrared spectrophotometric analytical method for three alkoxysilane–chlorosilane systems. The method is suitable for the determination of the compounds expected in the condensation reaction. In our present work this method was applied to follow the $FeCl_3$-catalyzed condensation of dimethyldichlorosilane (D) with dimethyldi-*sec*-butoxysilane (D_{OBut}).

Considerations on the possible reaction path

From the point of view of preparation of longer chain linear or cyclic siloxanes monomers at least difunctional have of practical importance. For this reason we studied the condensation of difunctional compounds.

The spectrophotometric method enabled us to study the different processes occurring in the reaction mixture. For this reason it seemed to be advisable to think over the probable reaction steps and side-reactions as well as the products expected in their course.

From the monomers with alkoxy and chlorine functional groups polysiloxanes arise, the respective alkyl chloride eliminates according to the simplest reaction path described in some publications [1, 2, 3].

$$n\,\mathrm{RO{-}Si(CH_3)_2{-}OR} + n\,\mathrm{Cl{-}Si(CH_3)_2{-}Cl} \xrightarrow{\text{catalyst}} \xrightarrow{\text{catalyst}} (2n-1)\,\mathrm{RCl} + \mathrm{RO{-}[Si(CH_3)_2{-}O]_{(2n-1)}{-}Si(CH_3)_2{-}Cl} \qquad (1)$$

Beside this an other condensation process can also be supposed from these starting materials. $FeCl_3$ has been widely used as a catalyst in the field of organosilicon chemistry. Thus, it can be supposed that this catalyst offers advantageous conditions to the reaction of monomers containing identical functional groups, namely to the self-condensation of dialkoxysilanes. They react with the elimination of ether:

$$n\,\mathrm{RO{-}Si(CH_3)_2{-}OR} \xrightarrow{\text{catalyst}} (n-1)\,\mathrm{R_2O} + \mathrm{RO{-}[Si(CH_3)_2{-}O]_{n-1}{-}Si(CH_3)_2{-}OR} \qquad (2)$$

Under the applied experimental conditions this reaction may proceed further. Ethers and chlorosilanes, which are present in the reaction mixture, may react with each other producing siloxanes and alkyl chloride [4]:

$$n\,\mathrm{R_2O} + n\,\mathrm{Cl{-}[Si(CH_3)_2{-}O]_n{-}Si(CH_3)_2{-}} \longrightarrow n\,\mathrm{RCl} + n\,\mathrm{RO{-}[Si(CH_3)_2{-}O]_n{-}[Si(CH_3)_2{-}} \qquad (3)$$

Thus two different paths with the same end-products can be supposed for the formation of siloxanes.

In addition an other type of reaction was observed in the course of some investigations performed from other aspects in similar organosilicon systems. It was established that organosilicon compounds containing both the chlorine and alkoxy groups in the same molecule disproportionate already at room temperature [5, 6]. VAN WAZER and MOEDRITZER pointed out that a radical exchange occurs in the mixture of di- or trifunctional organosilicon halides and dimethylamino- or methoxy- or ethoxysilanes without a catalyst, and this reaction reaches an equilibrium after 8—17 hrs and at high temperature (120 °C) [7, 8]. In our system also a catalyst is present and this fact may modify

the results mentioned above. In spite of that following radical exchange reaction had to be presumed;

$$n\,RO-\underset{\underset{CH_3}{|}}{\overset{\overset{CH_3}{|}}{Si}}-OR + n\,Cl-\underset{\underset{CH_3}{|}}{\overset{\overset{CH_3}{|}}{Si}}-Cl \rightleftharpoons 2n\,RO-\underset{\underset{CH_3}{|}}{\overset{\overset{CH_3}{|}}{Si}}-Cl \qquad (4)$$

An additional reaction should be taken into consideration, namely the hydrolysis of chlorosilanes. This undesirable sidereaction usually occurs in a few per cent even in spite of the most careful manipulation.

From the scope of the difunctional systems the $FeCl_3$-catalyzed condensation of D with D_{OBut} was chosen as a model process. The reason for this choise was that in this system the low-molecular product of the condensation, *sec*-butyl chloride of relatively high boiling point (67.3 °C) does not leave the system at the temperature (60 °C), where the reaction proceeds with a moderate rate.

Experimental

The condensation reaction was carried out under constant stirring in a 100 cm^3 jacketed reaction vessel thermostated to 60°C. The reaction mixture contained the cyclohexane solution of the starting materials, D and D_{OBut} in 2 *M* concentration each and 1 weight per cent anhydrous $FeCl_3$. In six hrs the reaction had completed. Time by time samples were withdrawn from the reaction mixture, without opening the vessel, by a hypodermic syringe through a silicon rubber stopper. To stop the reaction, samples in a small vessel were quenched by putting them into melting ice.

The process was followed by infrared spectrophotometry. The concentration of the components were calculated from the IR-spectra on the basis of Beer's law. Calibration curves were taken for each components at their respective analytical bands (see Part I). The peak height was determined by the base-line technique, only in one case we had to characterize the band intensity by integral absorbance which was calculated mathematically. The adsorbance data were corrected to 0.1 mm cell width in every case. These values were plotted against the concentration of the compounds. Figs 1, 2, 3 and 4 show the calibration curves.

The linear dependence of the absorbance on the concentration data was characterized by the correlation coefficient (r) calculated by the method of least squares. By this method

Table I

Correlation coefficients of calibration curves, standard and mean deviations of measured data

Compound	Analytical band, cm^{-1}	r	s (%)	$s_{\bar{k}}$ (%)
$(CH_3)_2SiCl_2$	535 (E)	0.9957	7.9	2.99
	465 (F)	0.9965	7.1	2.54
$(CH_3)_2Si(OC_4H_9)_2$	1170 (A)	0.9987	8.3	3.16
$(CH_3)_2Si(OC_4H_9)Cl$	1170 (B)	0.9973	9.6	3.63
	660 (C)	0.9986	3.6	1.30
	485 (D)	0.9974	5.6	1.89
C_4H_9Cl	610 (G)	0.9983	2.6	1.01

we calculated also the equation of the straight line of best fit of the measured data points. The linearity of our calibration curves indicates the validity of Beer's-law, for each compound $r > 0.99$ was obtained. (Table I)

The standard deviations (s) and the mean deviations (s_k) of the data were calculated to estimate the precision of the analytical method outlined and the reliability of a typical analytical application.

The data are given in Table I.

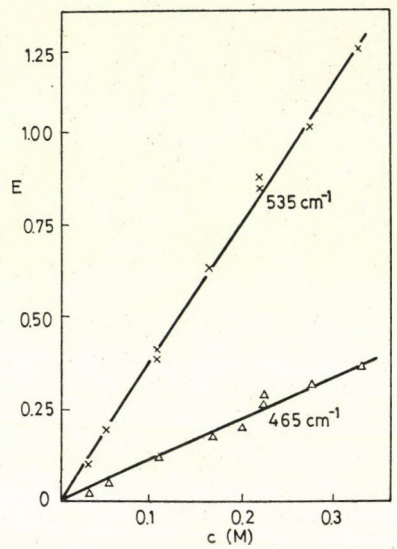

Fig. 1. Calibration curves of dimethyl dichlorosilane

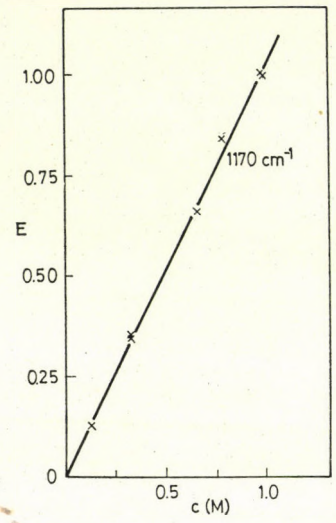

Fig. 2. Calibration curves of dimethyldi-*sec*-butoxysilane

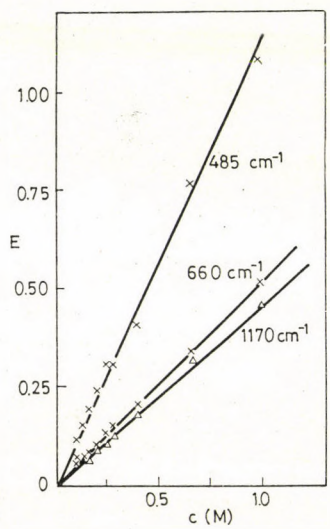

Fig. 3. Calibration curves of dimethyl-*sec*-butoxychlorosilane

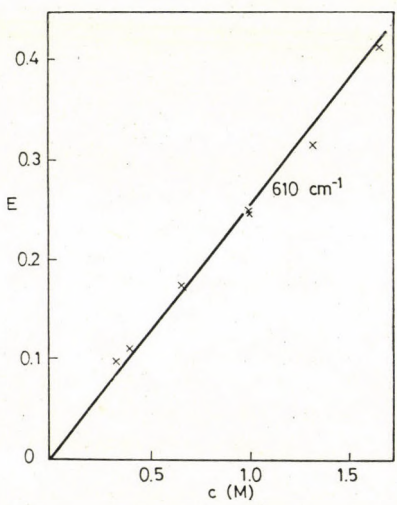

Fig. 4. Calibration curves of butyl chloride

Results and discussion

The reaction between D and D_{OBut} was carried out under the conditions described in the experimental part. In the thermostated reaction mixture the reaction was started by the addition of the catalyst. We checked the spectra of the reaction mixture time by time and tried to interpret the changes of the spectra by taking into consideration the supposed side-reactions too.

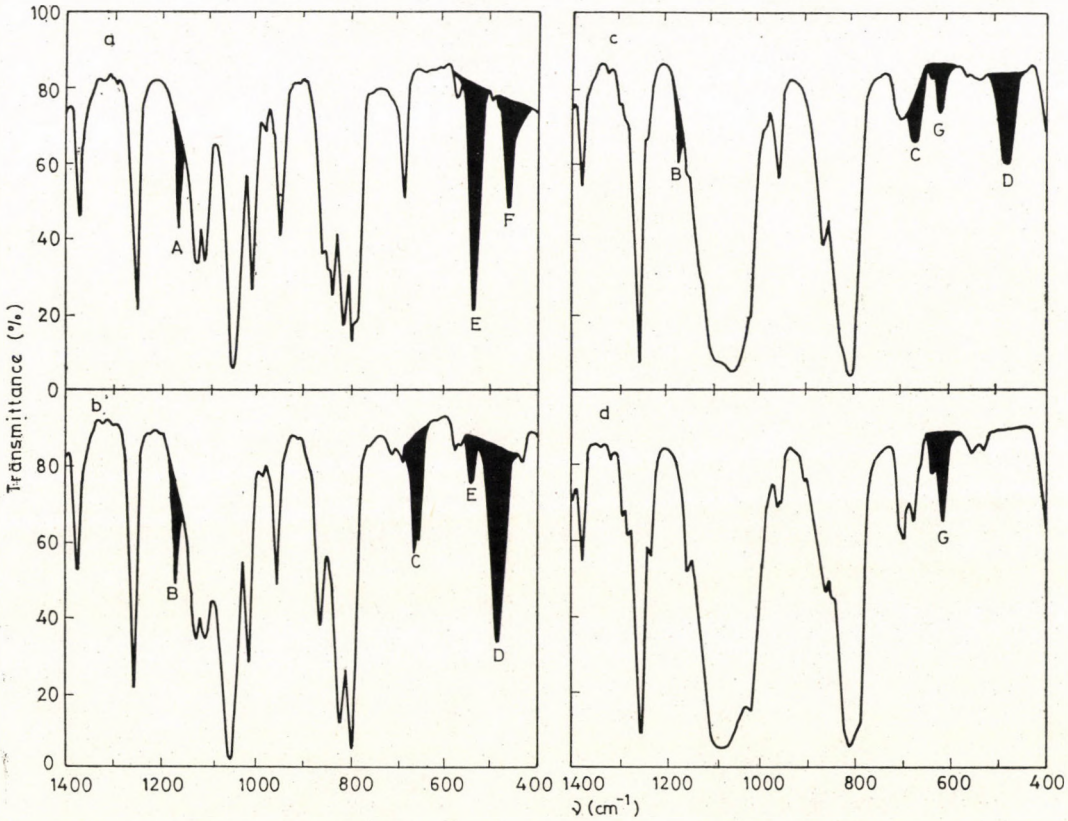

Fig. 5. Spectra on the samples withdrawn from the reaction mixture of D and D_{OBut} *a.* 0th minute, *b.* 2th minute, *c.* 90th minute, *d.* at the end of the reaction

On part *a* of Fig. 5 spectrum of the sample can be seen which was taken from the mixture before adding the catalyst, on *b* that in the 2, on *c* that in the 90th minute and finally on *d* at the end of the reaction. The characteristic analytical bands are designed with black and with the letters of Table I.

The following changes on the spectra were observable:

At the beginning of the reaction only D and D_{OBut} were in the mixture (spectrum *a*). Comparing spectrum *a* with *b*, however, it could be seen that

the characteristic peak of D at 535 cm^{-1} (band E) disappeared almost completely in the second minute, although no butyl chloride has been formed yet. Furthermore the band at 1170 cm^{-1} (band A, B) characteristic of the CH-vibrations of *sec*-butoxy group seemed to be unchanged. Simultaneously a strong band appeared at 485 cm^{-1} (band D) and a doublett band at 660—650 cm^{-1} (band C). These two new bands and the CH-rocking frequency at 1170 cm^{-1} continuously decreased, then entirely disappeared during the reaction (spectra *c* and *d*), while the characteristic band of butyl chloride at 610 cm^{-1} (band G) appeared and increased. The strong and wide peak in the region of 1100—1000 cm^{-1} showed the formation of Si—O—Si bonds.

It could be concluded that simultaneously with the disappearing of the analytical band of D a new compound was formed immediately after the beginning of the reaction. This compound was recognized as dimethyl-*sec*-butoxy-chlorosilane ($D_{OBut,Cl}$). One of its analytical bands lies at 1170 cm^{-1} (band B), the other two one at 660 cm^{-1} (band C) and at 485 cm^{-1} (band D).

This result is consistent with the findings of the authors mentioned above [7, 8]. Although they investigated systems containing compounds of higher reactivity (*e.g.* ethoxy-, methoxy- or dimethylamino compounds) than the *sec*-butoxy substituted one, we have found that the radical exchange reaction proceeded also in the mixture of D and D_{OBut} without any catalyst, and it also led to an equilibrium. The reaction is described by equation (4) where R = C_4H_9. We determined the equilibrium constant at 60 °C approaching the equilibrium from both sides; its value was found to be about 10^{-4} for the process starting from the compound in the right-hand side of equation (4). Obviously the equilibrium lies well in the direction of the conversion to $D_{OBut,Cl}$.

Under the conditions of the condensation that is at 60 °C in the presence of the catalyst the radical exchange reaction proceeded much more rapidly. The system attained similar state with the catalyst in about two minutes as without a catalyst in about fifty hours. In the presence of the catalyst the radical exchange even more progressed since the quantity of $D_{OBut,Cl}$ formed was immediately consumed by condensation. Due to its high rate the first step, the radical exchange, could not be followed by the IR-method. However the consecutive condensation of its product, $D_{OBut,Cl}$ was a much slower step, thus it could be followed easily.

We performed three experiments which aimed to verify whether the formed $D_{OBut,Cl}$ was the starting monomer of the condensation producing siloxane-polymers. In the first experiment the mixture of D and D_{OBut} was thermostated at 60 °C for 60 hrs before adding the catalyst. Within this time the equilibrium was set up. The equilibrium mixture contained practically only $D_{OBut,Cl}$. The condensation was initiated by the addition of the catalyst.

In the second experiment the catalyst and the reactants were added together to the reaction mixture.

In the third case the starting material was a synthetized $D_{OBut,Cl}$, consequently the mixture did not contain D and D_{OBut} at all.

The course of the three reactions is illustrated in Fig. 6. The consumption of butoxy groups was calculated from the peak height at 1170 cm^{-1}. The curves going upwards show the rise of butyl chloride calculated from the peak height at 610 cm^{-1}. The three curves correspond satisfactorily which indicate the identity of the reactions. The monomer is $D_{OBut,Cl}$ in all the three cases.

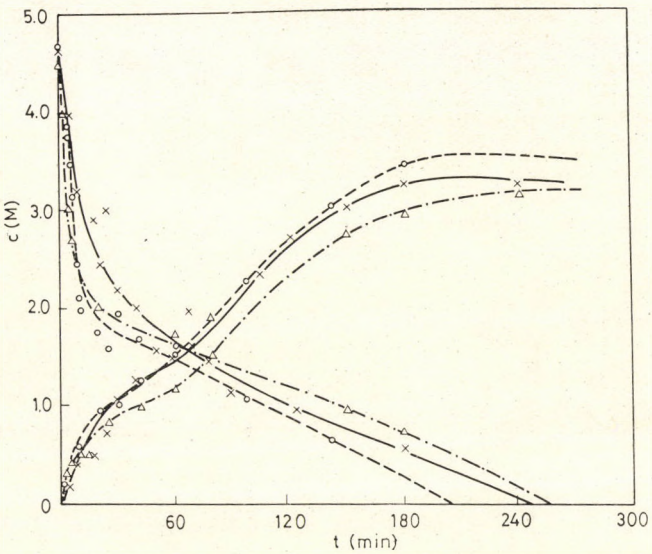

Fig. 6. Paths of reactions of D with D_{OBut} and that of $D_{OBut,Cl}$. — — — — — reaction in the equilibrium mixture of D and D_{OBut}, ———— reaction of D with D_{OBut} without the previous setting of the equlibrium, — · — · — reaction of $D_{OBut,Cl}$

$D_{OBut,Cl}$ monomer can follow the same routes as the monomers containing two identical functional groups. It is also supposed that it takes part in reactions analogous to reaction (1) or (2)—(3), *i.e.*:

$$n\ RO-\overset{|}{\underset{|}{Si}}-Cl \xrightarrow{\text{catalyst}} RO-[Si-O]_{\overline{n-1}}Si-Cl + (n-1)\ RCl \qquad (5)$$

$$n\ RO-\overset{|}{\underset{|}{Si}}-Cl \xrightarrow{\text{catalyst}} n/2\ Cl-Si-O-Si-Cl + n/2\ R_2O \qquad (6)$$

$$R_2O + Cl-[Si-O]_n-Si- \xrightarrow{\text{catalyst}} RO-[Si-O]_n-Si + RCl \qquad (7)$$

If the two steps of the homofunctional condensational route [reactions (6) — (7)] occur, di-*sec*-butylether(But_2O) and chlorine terminated oligomers also should be found in the reaction mixture. Figure 7 shows the spectrum of the cyclohexane solution of But_2O. The band at 1330 cm^{-1} is the only one which does not overlap any bands of the other components, thus it would be suitable for analysis in this system. But under the concentration conditions

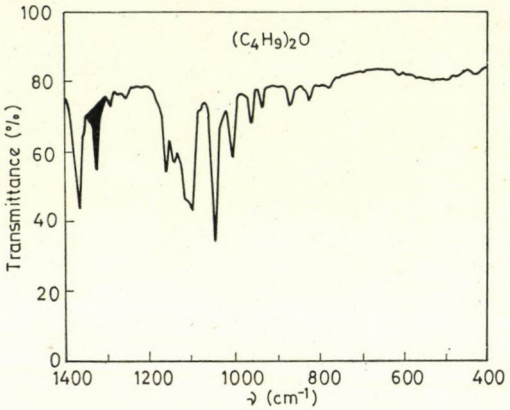

Fig. 7. Spectrum of *sec*-butyl ether in cyclohexane solution

of the reaction this band was not sharp and strong enough to state unambiguously from the IR spectra alone whether But_2O was in the reaction mixture even in a small quantity at all.

To solve this question we performed low temperature IR measurements. At the temperature of liquid nitrogen (—190 °C) the peak height considerably grows and the overlapping bands split in some cases, thus, the stronger bands of But_2O might be noticed in the case of small concentration. The low temperature measurements showed that no But_2O was present in the mixture. This result was supported by gas chromatographic measurements too. For the GC measurements the quenched samples of the reaction mixture could be used only after extracting the catalyst and the corrosive components with water. In the mixture But_2O could be detected by gas chromatography, its quantity, however, was only of 0.01 per cent referred to cyclohexane.

This result verify the absence of the homofunctional condensation step.

On the other hand it could be noticed from the subsequent spectra of the reaction mixture that all of the three analytical bands of $D_{OR,Cl}$ decreased in the course of the reaction, however, with not the same rate. The SiC_2 frequency at 660 cm^{-1} decreased more slowly than the characteristic band of SiOR at 1170 cm^{-1}. Beside its decrease the Si–Cl band at 485 cm^{-1} widened towards

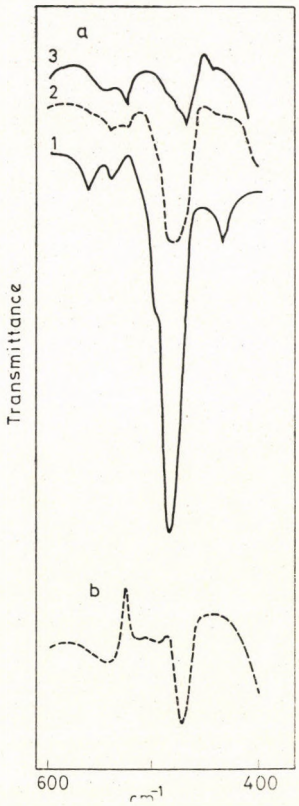

Fig. 8. The shift of the Si—Cl stretching frequency in the course of the condensation of dimethyl-*sec*-butoxychlorosilane. *a.* curve 1: 0th minute, curve 2: 60th minute, curve 3: 240th minute. *b.* differential spectrum belonging to curve 2

the smaller wavenumbers, and then shifted to 470 cm^{-1}. (Figure 8 *a*). At the end of the reaction all of these bands disappeared.

In agreement with previous finding [9], the band at 470 cm^{-1} was found to be the Si–Cl stretching frequency of the linear oligomer formed in the condensation. The shift of the Si–Cl band in the course of polymerization provided us with the possibility to determine the concentration of the monomer and the oligomers separately.

The intensity of the overlapping peaks at 485—470 cm^{-1} was proportional to the total quantity of the Si–Cl groups. These two Si–Cl bands never separated in the course of the reaction, therefore the total concentration of the Si–Cl groups was proportional to the area of these absorptional bands, that is to the integral absorbance. This was calculated from the data.

The amount of the terminal Si–Cl groups of the linear oligomer chains was determined by differential spectra. We recorded the spectra of the reaction

mixture against the cyclohexane solution of $D_{OBut,Cl}$ (monomer) and butyl chloride. In the reference solution the concentration of $D_{OBut,Cl}$ was chosen equal to that of the sample. Thus, the peak height at 470 cm^{-1} was proportional to the concentration of the oligomer Si–Cl group because of the complete compensation of the peak at 485 cm^{-1}. In Fig. 8*b* the differential spectrum can be seen corresponding to curve 2 of Fig. 8*a*.

The concentration of the Si–Cl groups present in the monomer equals to the difference between the two former ones.

The analytical band at 1170 cm^{-1} (band B) was suitable for the quantitative determination of $D_{OR,Cl}$ without any difficulties all over the course of the reaction. The third band at 660 cm^{-1} (band C) could be also used up to a 60 per cent conversion. The wavenumber and intensity of the SiC_2 stretching vibrations also depends on the degree of polymerization [9]. For the last third period of the reaction the continuous shift of this band extended to a very wide region, and meanwhile the band was overlapping other ones.

In the last period of the reaction the equilibration of the formed siloxanes could be observed. This process was noticed in the region of 1000—1100 cm^{-1} where the appeared Si–O–Si vibrations were still changing when the functional groups had been used up already. The changes of the Si–O–Si vibrations could not be followed accurately, however, in this system because of overlapping of the bands.

Finally the reversibility of the condensation step was studied. We modelled the backward reaction in two systems.

Mixtures of a cyclic siloxane (octamethylcyclotetrasiloxane) and butyl chloride as well as that of a linear siloxane and butyl chloride were thermostated under the conditions of the condensation in the presence of the catalyst for five hours. Process indicating reversibility did not occur, bands characteristic of Si–Cl or Si–OR groups did not appear. The only effect which could be detected was the equilibration of the originally homogeneous siloxane by the action of the catalyst.

On the basis of this result we supposed that the condensation of $D_{OBut,Cl}$ formed by radical exchange follows only the heterofunctional route [reaction (5)]. This fact may be taken as proved if the concentration of the components corresponds to the material balance characteristic the of heterofunctional route. This can be written by two equations:

$$c_{\text{total Si–Cl}} = c_{\text{total Si–OR}} \tag{8}$$

$$c_{\text{total Si–Cl}} + c_{\text{RCl}} = c_{\text{total Si–OR}} + c_{\text{RCl}} = \text{constant} \tag{9}$$

In Fig. 9 the changes of concentrations of the materials are plotted against time. The quantity of Si–OR groups was measured at 1170 cm^{-1}, the total concentration of Si–Cl bonds was calculated by integral absorbance.

Amount of Si–Cl bonds being in oligomers was determined from differential spectra, and the concentration of monomer Si–Cl was given by the difference of the two formers. Concentration of formed butyl chloride was measured at 610 cm^{-1}.

It can be seen that the curve illustrating the change of the concentration of butoxy groups corresponds well to the curve illustrating the total concentra-

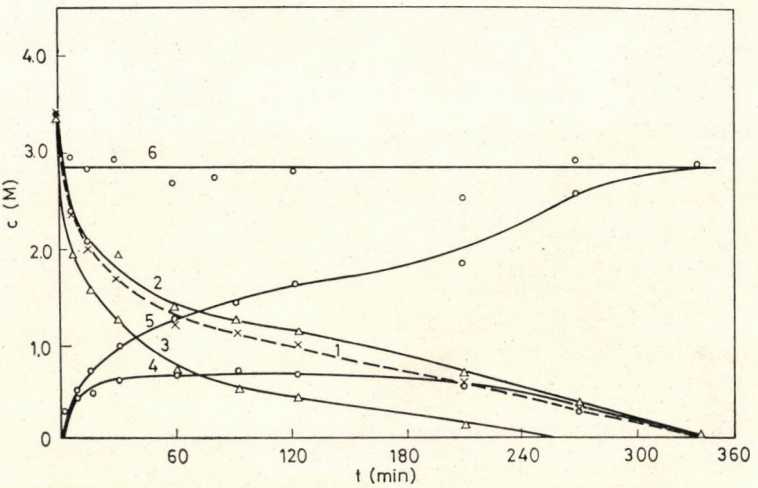

Fig. 9. Change of concentration of functional groups during the reaction of $D_{OBut,Cl}$, curve 1: concentration of Si—OR, curve 2: concentration of total Si—Cl, curve 3: concentration of monomer Si—Cl, curve 4: concentration of oligomer Si—Cl, curve 5: concentration of butyl chloride, curve 6: balance of materials of the reaction

tion of Si–Cl groups. This shows that equation (8) holds all over the course of the reaction, with other words the quantity of Si–Cl groups equals that of the Si–OR groups.

Curve 6 illustrates the current sum of the concentration of the total chlorosilanes and that of the formed butyl chloride. Table II contains the same data. It can be seen that the sum of the concentration of the starting materials and end-products is really constant during the reaction except the first few minutes. (In the first minutes a small percentage of the chlorosilanes hydrolyzed as it could be expected.)

The results obtained can be extended to the reactions of dimethyldichlorosilane with other difunctional alkoxysilanes, namely with dimethyldiethoxysilane and dimethyldi-*n*-propoxysilane. Some qualitative experiments were performed in these systems too. It was pointed out that the starting dichlorosilane and dialkoxysilane were transformed to the respective alkoxychlorosilane both under the conditions of the condensation and without the catalyst.

Table II

Material balance for the heterofunctional route

Time, min	$c_{\text{total SiCl}}$ M	c_{ROCl} M	Sum
0	3.27	—	3.27
1	3.00	0.31	3.31
7	2.39	0.51	2.90
15	2.07	0.74	2.81
30	1.39	0.98	2.91
60	1.40	1.36	2.76
92	1.27	1.44	2.71
124	1.13	1.62	2.75
180	0.86	1.86	2.72
210	0.68	(1.78)	(2.46)
270	0.33	2.49	2.82
333	—	2.78	2.78
393	—	2.74	2.74

This process is also an equilibrium reaction shifted considerably to the direction of alkoxychlorosilanes. Also in the case of these systems the formed alkoxychlorosilanes take part in the condensation reaction.

REFERENCES

[1] Székely, T., Rösner, P., Gömöry, P.: Acta Chim. Acad. Sci. Hung., **61,** 233 (1969)
[2] Andrianov, K. A., Mantrova, V. M.: Zhurn. Obschtch. Chim., **27,** 1243 (1957)
[3] Csákvári, B., Fábry, L., Gömöry, P., Keömley, G.: Radiochem. Radioanal. Lett., **15/6,** 393 (1973)
[4] Eaborn, C.: Organosilicon Compounds, p. 186. Butterwords Sci. Publ. London 1968
[5] Wolnow, J. N.: Zhurn. Obschtch. Chim., **17,** 1428 (1947)
[6] Kessler, G., Kriegsmann, H.: Z. anorg. allgem. Chem., **342,** 63 (1966)
[7] Van Wazer, J., Moedritzer, K.: J. Inorg. Nucl. Chem., **26/5,** 734 (1964)
[8] Moedritzer, K., van Wazer, J.: Inorg. Chem., **6,** 93 (1967)
[9] Smith, A. L.: Spectrochim. Acta, **19,** 849 (1962)

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SYNTHESIS OF SOME N-SALICYLSULFONYL-AMINO ACID DERIVATIVES, II

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Syntheses of N-(3-Carboxy-4-hydroxyphenylsulfonyl)-Gly and the corresponding derivatives of Ser, Tyr and Orn (**II—V**), as well as their O-acetyl, carbomethoxy and some hydrazide derivatives (**VI—XVII**) are described. **III, IV, VII** and **VIII** were found to be active against a number of microorganisms.

Introduction

Previously salicylates and some salicylsulfonamide derivatives were found to have hypoglycaemic and other pharmacological activities [1—8]. Recently we have reported the synthesis of some N-salicylsulfonyl-amino acids which were expected to possess some biological activities [9]. However, the effect of variations of the functional groups in both the salicylic and amino acid moieties on the biological and pharmacological activities has not yet been studied.

The present investigation involved the synthesis of some O-acetyl, Carbomethoxy and Carboxyhydrazide derivatives (**II—XVII**) and studies of their microbiological activities.

Results and discussion

N-(3-Carboxy-4-hydroxyphenylsulfonyl)-amino acids (**II—V**) were readily prepared by the reaction of 5-chlorosulfonyl salicylic acid (**I**). [10] with the appropriate amino acid in ether–sodium hydroxide medium. All N-salicylsulfonyl-amino acid derivatives were chromatographically homogeneous (detection with benzidine), and gave a violet colour with $FeCl_3$. IR (**II**) ν_{max}^{KBr} : 1180, 1175, 1360 (SO_2): 3390, 3420 (SO_2NH); 1690 (Ar—COOH); 1310, 1360, (R—COOH); 1120, 3420 (Ar—OH) and OH/COOH hydrogen bond, and 1080, 1030, 910, 840, 800, 720, 610 cm^{-1} (1,2,4-trisubstituted benzene) confirming the structure of (**II**). The IR spectra, chromatographic, electrophoretic and elemental analyses of **II—V** were consistent with the structures given (*cf.*

Table I

N-(3-Carboxy-4-hydroxyphenylsulfonyl)-amino

Compound (Type)	R	R_1	R_2 and amino acid residue	Yield, %	M. p., °C
II—(A)	H	OH	H; Gly-	84	309—310°
III—(A)	H	OH	$-CH_2OH$; DL-Ser-	72	340° charred
IV—(A)	H	OH	P—CH_2—C_6H_4—OH; L-Tyr-	66	292—294°
V—(B)	H	OH	DL-Orn-	80	282—284°
VI—(A)	$COCH_3$	OH	H; Gly-	81	350°
VII—(A)	$COCH_3$	OH	$-CH_2OCOCH_3$; DL-Ser-	60	60—64° hygroscopic
VIII—(A)	$COCH_3$	OH	P · CH_2—C_6H_4—$OCOCH_3$ L-Tyr-	73	350°
IX—(B)	$COCH_3$	OH	DL-Orn-	70	295—298°
X—(A)	H	OCH_3	H; Gly-	92	290—294°
XI—(A)	H	OCH_3	$-CH_2OH$; DL-Ser-	60	280—282°
XII—(A)	H	OCH_3	P—CH_2—C_6H_4—OH; L-Tyr-	66	277—280°
XIII—(B)	H	OCH_3	DL-Orn-	61	350°
XIV—(A)	$COCH_3$	OCH_3	H; Gly-	73	269—271°
XV—(A)	H	N_2H_3	H; Gly-	78	196—200°
XVI—(A)	H	N_2H_3	$-CH_2OH$; Ser-	75	200—202°
XVII—(B)	H	N_2H_3	Orn-	67	207—210°

$[\alpha]_D^{20}$ For **IV:** −9.8 ($c = 0.5$, methanol); **VIII:** −12 ($c = 1$, DMF); **XII:** −16.5 $c = 1$,

Table I). Complete acid hydrolysis of **II** [9] gave a ninhydrin-positive spot of glycine.

N-(3-Carboxy-4-acetoxyphenylsulfonyl)-Gly (**VI**) was prepared by the acetylation of **II**. In the case of Ser and Tyr, acetylation of **III** and **IV** required the use of excess acetic anyhdride, when the hydroxyl groups of both the salicyl and amino acid residues were acetylated. Spot tests for compounds **VI**—**IX** showed the absence of hydroxyl, and the structures of the compounds were confirmed by elemental analysis and IR spectroscopy.

N-(3-Carbomethoxy-4-hydroxyphenylsulfonyl)-Gly-OMe (**X**) was prepared by dissolving **II** in a cooled solution of dry methanol, and adding pure thionyl chloride. Esterification of **III** and **IV** containing Ser and Tyr was effected using the same conditions as in the synthesis of **X**. The methyl esters

acid derivatives

R_f	E_{cm}	Formula (Mol. wt.)	Analysis %, Calcd./Found		
			C	H	N
0.57	5	$C_9H_9NO_7S$	39.2	3.25	5.09
		(275.23)	39.5	3.55	5.12
0.47	7	$C_{10}H_{11}NO_8S$	39.34	3.60	4.57
		(305.26)	39.85	3.61	4.59
0.49	5.3	$C_{16}H_{15}NO_8S$	50.31	3.92	3.66
		(371.35)	50.64	4.21	3.92
0.5	5	$C_{19}H_{20}N_2O_{10}S_2$	42.85	3.75	5.26
		(500.49)	42.95	3.86	5.27
0.85	11	$C_{11}H_{11}NO_8S$	41.63	3.46	4.40
		(319.27)	41.65	3.63	4.45
0.71	10.5	$C_{14}H_{15}NO_{10}S \cdot H_2O$	41.27	4.17	3.44
		(407.33)	41.35	4.19	3.54
0.83	6.8	$C_{20}H_{19}NO_{10}S$	51.53	4.79	3.06
		(465.42)	51.63	4.95	3.11
0.83	7	$C_{23}H_{24}N_2O_{14}S_2$	44.80	3.89	4.54
		(616.56)	45.01	3.99	4.68
0.53	6	$C_{11}H_{13}NO_7S$	43.56	4.29	4.62
		(303.29)	43.86	4.59	4.65
0.54	6.3	$C_{12}H_{15}NO_8S$	43.15	4.49	4.19
		(333.31)	43.25	4.50	4.21
0.63	5.5	$C_{18}H_{19}NO_8S$	52.8	4.64	3.42
		(409.41)	53.11	4.65	3.45
0.58	7.4	$C_{22}H_{26}N_2O_{12}S_2$	45.97	4.52	4.87
		(754.57)	46.15	4.75	5.11
0.64	6	$C_{12}H_{15}NO_8S$	43.23	4.50	4.20
		(333.31)	43.33	4.60	4.45
0.65	—	$C_{19}H_{13}N_5O_5S$	35.64	4.29	23.10
		(303.29)	35.75	4.32	23.75
0.7	—	$C_{10}H_{15}N_5O_6S$	36.03	4.53	21.02
		(333.32)	36.26	4.68	21.13
0.72	—	$C_{19}H_{26}N_8O_9S_2$	39.72	4.52	19.51
		(574.58)	39.83	4.56	19.63

dioxane)

(**X**—**XII**) were shown to be homogeneous and no side reactions were observed. IR (**X**) ν_{max}^{KBr}: 1440—1330 ($COOCH_3$); 1130, 1305, 1360 (SO_2); 3440 (SO_2NH); 1220—40, 3440 (Ar—OH); 1080. 1030, 910, 840, 800 and 720 cm^{-1} confirming the structure of **X**. All the methyl esters gave positive hydroxamate reactions.

The synthesis of N-(3-Carbomethoxy-4-acetoxy-phenylsulfonyl)-Gly-OMe (**XIV**) was achieved by acetylation of the methyl ester **X**. The attempted esterification of the acetoxy derivative **VI** failed; the reaction led to partial deacetylation and a mixture containing three different unseparable components was obtained. The methyl ester **X** was readily acetylated to give **XIV** in 73% yield; the product contained neither free hydroxyl nor carboxyl groups.

Previously several sulfohydrazides have been investigated and found to be effective as antituberculosis drugs [11—13]. Therefore, some N-salicyl-

sulfonyl amino acid hydrazides were prepared and investigated in our laboratory. Hydrazinolysis of the methyl ester **X** gave the hydrazide **XV** containing two hydrazide groups in both the salicylic and amino acid moieties. The synthesis of the hydrazide derivatives of serine was easily achieved and the hydroxyl groups of the seryl or salicyl residues were not affected. Similarly, the serine peptide hydrazides were previously synthesized using the same procedure [14].

Compounds **II**—**XVII** are now prepared and characterized for the first time.

N-(3-carboxy-4-hydroxyphenylsulfonyl)-DL-Ser (**III**) and L-Tyr (**IV**) and the corresponding O-acetyl derivatives (**VII** and **VIII**) were found to be active against *Bacillus subtilis*, *Esch. coli*, *Staphilococcus aureus*, but inactive against *Proteus vulgaris* and *Azotobacter crococcum*. The remaining carbomethoxy and hydrazide derivatives were found to be inactive against all the tested microorganisms. Other pharmacological studies are still in progress.

Experimental

Rf_1 [15]: *n*-butanol–pyridine–acetic acid–water (15 : 10 : 3 : 12). E: pyridine–acetate buffer pH 5.6 600 V, 2 hr. [15].

N-(3-Carboxy-4-hydroxyphenylsulfonyl)-Gly (II)

Glycine (1.7 g; 0.023 mole) was dissolved in water (20 ml) and 2*N* sodium hydroxide (25 ml) was added to the solution. The reaction mixture was cooled to 0 °C, and a solution of 5-chlorosulfonylsalicylic acid (**I**) [10] (5.4 g; 10.023 mole) in 25 ml ether was added dropwise during 30 min. The temperature of the reaction mixture was maintained at 0 °C until the addition had been completed and the reaction mixture was shaken for additional 4 hrs at 20 °C. The solution was cooled at 0 °C and acidified with 6*N* HCl to Congo Red indicator. Some crystalline material was filtered off and the solution concentrated in vacuum. The residual material was crystallized from methanol and the soluble N-(3-carboxy-4-hydroxyphenylsulfonyl)-Gly precipitated from methanol–ether.

N-(3-Carboxy-4-hydroxyphenylsulfonyl)-DL-Ser (II) and -L-Tyr (IV)

These compounds were prepared as described for **II**.

N^2,N^5-Di-(3-carboxy-4-hydroxyphenylsulfonyl)-DL-Orn (V)

DL-Ornithine HCl (3.369 g; 0.02 mole) was dissolved in water (30 ml), 2*N* sodium hydroxide (40 ml) was added and the mixture cooled to 0 °C. A solution of 5-chlorosulfonylsalicylic acid (**I**) (9.8 g; 0.042 mole) in ether (50 ml) was added in portions, while maintaining the temperature of the reaction mixture at 0 °C and the pH at 9—10. The reaction mixture was shaken for additional 4 hrs and processed as described for **II**.

N-(3-Carboxy-4-acetoxyphenylsulfonyl)-Gly (VI)

Compound **II** (1.9 g; 0.007 mole) was dissolved in acetic anhydride (15 ml) and 5 drops of conc. H_2SO_4 were added. The reaction mixture was heated to 50—60 °C. The mixture was allowed to cool, water (50 ml) was added, and after stiring the solvent was evaporated in vacuum. The crude product which separated was filtered off and recrystallized from methanol–ether.

N-(3-Carboxy-4-acetoxyphenylsulfonyl)-DL-Ser (Ac) (VII); -L-Tyr (Ac) (VIII) and di-DL-Orn (IX)

These compounds were prepared starting from **III**—**V** (0.007 mole) acetic anhydride (25 ml) and conc. H_2SO_4 (8 drops), using the procedure described for **VI**. The products (**VII**—**VIII**) gave negative tests for hydroxyl.

N-(3-Carbomethoxy-4-hydroxyphenylsulfonyl)-Gly-OMe (X) -DL-Ser-OMe (XI), -L-Tyr-OMe and N^2,N^5-di-DL-Orn-OMe (XIII)

II—**V** (0.001 mole) was dissolved in absolute methanol (60 ml), cooled to —10 °C and pure thionyl chloride (0.022 mole) was added by drops. The temperature of the the reaction mixture was kept at —5 °C during the process of addition and stirring was continued for additional 3 hrs, at room temperature. The mixture was allowed to stand for 24 hrs at 20 °C and the solvent evaporated in vacuum. Methanol was added and re-evaporated several times, then the crude product was recrystallized from methanol–ether. The products (**X**—**XIII**) were chromatographically homogeneous (detection with benzidine) and had positive hydroxamate reactions.

N-(3-Carbomethoxy-4-acetoxyphenylsulfonyl)-Gly-OMe (XIV)

Compound **X** (2.1 g.; 0.007 mole), was added to a mixture of acetic anhydride (12 ml) conc. H_2SO_4; (5 drops); the rest of the procedure was described for (**VI**).
The material was crystallized from methanol to give white needles.

N-(3-Carboxyhydrazide-4-hydroxyphenylsulfonyl)-Gly-N_2H_3 (XV)

Compound **X** (0.006 mole) was added gradually to hydrazine hydrate (8 ml) and the reaction mixture was refluxed for 2 hrs. The solution was concentrated in vacuum and the residual material poured into crushed ice. The crude product was filtered off and recrystallized from water–acetic acid. The product (**XV**) was chromatographically homogeneous (detection with benzidine and silver nitrate).

N-(3-Carboxyhydrazide-4-hydroxyphenylsulfonyl)-DL-Ser-N_2H_3 (XVI)

Compound **XI** (0.8 g; 0.025 mole) was dissolved in dry methanol (30 ml) and hydrazine hydrate (2.5 ml) was added. After standing for 24 hrs at room temperature and 5 hrs at 0°C, the solvent was evaporated in vacuum, another portion of methanol was added and then re-evaporated. The residual material was crystallized from methanol–acetone (1 : 1).

N^2,N^5-(3-Carboxyhydrazide-4-hydroxyphenylsulfonyl)$_2$-Orn-N_2H_3 (XVIII)

Compound **XIII** (1.1 g; 0.002 mole) was added gradually to warm hydrazine hydrate (10 ml); and the rest of the procedure was as described for **XV**.

REFERENCES

[1] MARSHALL, M., SIGAL, T.: J. Org. Chem., **23,** 927 (1958)
[2] ENGLE, D. J.: Prot. Expt. Biol. Med., **75,** 673 (1950)
[3] ENGLE, D. J.: J. Am. Pharm. Assoc., **42,** 247 (1953)
[4] FISHGOLD, J. T., FIELD, J., HALLV, E.: Am. J. Physiol., **164,** 427 (1951)
[5] EL-GENDY, M. A., ABOU-OUF, A. A.: Egypt. J. Pharm. Sci., **14,** 197 (1973)
[6] FANG, V., FOGE, O., ROBINSON, S. M., JENKINS, H. I.: J. Pharm. Sci., **57,** 2111 (1968)
[7] MCLAMORE, W. M. *et al.:* Am. Y. Acad. Sci., **74,** 443 (1958)
[8] ABOU-OUF, A. A., YOUSEF, A. F., EL-GENDY, M. A.: Acta. Chim. (Budapest) **69,** 210 (1971)

[9] EL-NAGGAR, A. M., ISLAM, A. M., HANNOUT, I. B., GAAFAR, M. M.: Ind. J. Chem., **13** (3), 248 (1975)
[10] STEWART, E. H.: J. Chem. Soc., **122**, 2555 (1922)
[11] CHRITTA, C.: Chem. Abstr., **52**, 15462c (1958)
[12] RIST, M. *et al.:* Compt. Rend. Soc. Biol., **130**, 972 (1939)
[13] RAIFORD, L. C., STEWART, E. H.: J. Am. Chem. Soc., **57**, 2172 (1935)
[14] PODDUBNAYA, N. A., EL-NAGGAR, A. M.: Zhur. Obsch. Khim., **36**, 219 (1966)
[15] EL-NAGGAR, A. M.: Ind. J. Chem., **9**, 1326 (1971)

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OXAZEPINES AND THIAZEPINES, II*

SYNTHESIS OF 2,3-DIHYDRO-2,4-DIPHENYL-1,5-BENZOTHIAZEPINES BY THE REACTION OF 2-AMINOTHIOPHENOL WITH CHALCONES SUBSTITUTED IN RING B

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The reactions with 2-aminothiophenol of sixteen chalcones (**I**—**XVI**), variously substituted in ring B, have been studied in hot, anhydrous toluene. In the majority of the cases, *i. e.* with **I**—**X**, the β-phenyl-β-(2-aminophenylmercapto)propiophenones (**XVII**—**XXVI**) are formed: with **XI** and **XII** mixtures of the corresponding propiophenone (**XXVII** and **XXVIII**) and 2,3-dihydro-2,4-diphenyl-1,5-benzothiazepine derivatives (**XXXIX** and **XL**) are obtained: the presence of strongly electron-withdrawing substituents (**XIII**—**XVI**) leads to 1,5-benzothiazepines (**XLI**—**XLIV**). Boiling of the β-phenyl-β-(2-aminophenylmercapto)-propiophenones (**XVII**—**XXVIII**) in the presence of acetic acid catalyst in methanol, converts these compounds into 2,3-dihydro-2,4-diphenyl-1,5-benzothiazepines (**XXIX**—**XL**).

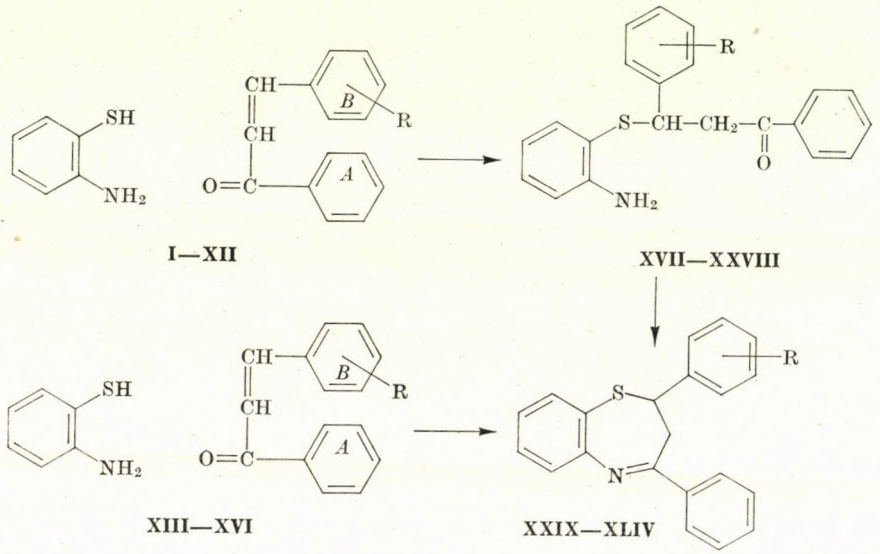
The synthesis of dihydro-1,5-benzothiazepines by the reaction of 2-aminothiophenol with α, β-unsaturated ketones is described in the literature [2—5]. Ried and Marx [2] studied the reaction of 2-aminothiophenol with thienyl analogues of chalcones. They found that in the presence of piperidine catalyst a nucleophilic addition occurred between the β-carbon atom of the unsaturated ketone and the mercapto group to give β-(2-aminophenylmercapto)-ketones which could be converted by means of hydrochloric acid catalyst into the corresponding dihydro-1,5-benzothiazepines. When the hydrochloride of 2-aminothiophenol was made to react with α, β-unsaturated ketones, the thiazepines were obtained in a single step. Muskalo [3] prepared N-substituted dihydro-1,5-benzothiazepines which contained an unsaturated bond in position Δ^3, by the reaction of N-substituted 2-aminothiophenols with α, β-unsaturated ketones. Hideg-Hankovszky and Hideg [4] synthesized 2,3-dihydro-1,5-benzothiazepine derivatives by boiling β-methyl-vinyl-pyridyl ketones, heterocyclic acrylophenones, pyridyl-acrylonaphtones and 2-acrylidenetetraline-1-ones with 2-aminothiophenol in xylene solution.

Stephens and Field [5] described the reaction of unsubstituted chalcone (**I**) with 2-aminothiophenol. The two compounds were allowed to react in methanolic solution in the presence of piperidine catalyst, to obtain β-phenyl-β-(2-aminophenylmercapto)-propiophenone (**XVII**) (m.p. 134—135°C, ν C = O 1670 cm^{-1}). Boiling of **XVII** in methanolic solution containing a catalytic

* Part I, see Ref. [1]

amount of acetic acid, converted **XVII** into 2,3-dihydro-2,4-diphenyl-1,5-benzothiazepine (**XXIX**) (m.p. 114—115 °C, ν C = N 1613 cm^{-1}).

In the course of earlier work concerning the chemical transformations [6, 7] and the spectral characteristics [8, 9] of chalcones and chalcone epoxides, we studied the effect of the substituents of the aromatic ring upon the electronic structure of these molecules and, through this, upon the direction of their chemical reactions. Partly in connection with these works, partly as a continuation of other investigations on the synthesis, structure elucidation and chemical conversions of benzothiazepines, we have now studied the reactions of 1-amino-2-mercapto compounds with chalcones. In this paper the reactions of 2-aminothiophenol with chalcones, variously substituted in their ring B, will be reported.



I, XVII, XXIX: R = H
II, XVIII, XXX: R = 4-CH_3
III, XIX, XXXI: R = 3-OCH_3
IV, XX, XXXII: R = 4-OCH_3
V, XXI, XXXIII: R = 3,4-$(OCH_3)_2$
VI, XXII, XXXIV: R = 3,4,5-$(OCH_3)_3$
VII, XXIII, XXXV: R = 3,4-OCH_2O
VIII, XXIV, XXXVI: R = 3-Cl
IX, XXV, XXXVII: R = 4-Cl
X, XXVI, XXXVIII: R = 2,6-$(Cl)_2$
XI, XXVII, XXXIX: R = 2-OCH_3
XII, XXVIII, XL: R = 2-Cl
XIII, XLI: R = 3-NO_2
XIV, XLII: R = 4-NO_2
XV, XLIII: R = 2,4-$(Cl)_2$
XVI, XLIV: R = 3,4-$Cl))_2$

The primary aim of these experiments was a study of the effect of substituents in ring B of the chalcone on the pathway of the reaction. The reactions had to be carried out without catalysis since, as shown by the results reported by RIED and MARX [2], the presence of catalyst can markedly alter the course of these reactions, and this effect had to be precluded. This is why we chose reaction conditions similar to those described by HIDEG-HANKOVSZKY and HIDEG [4].

Table I

Physical constants and analysis data of β-phenyl-β-(2-aminophenylmercapto)-propiophenones

	M. p., °C	Yield, %	Overall formula	Molecular weight	Analysis, %					
					Calculated			Found		
					C	H	N	C	H	N
XVII	142—143	72.0	$C_{21}H_{19}ONS$	333.36	75.67	5.70	4.20	75.60	5.79	4.29
XVIII	149—150	63.4	$C_{22}H_{21}ONS$	347.39	76.08	6.05	4.03	75.96	6.02	4.14
XIX	106—107	63.8	$C_{22}H_{21}O_2NS$	363.39	72.72	5.78	3.85	72.63	5.88	3.94
XX	124—125	68.8	$C_{22}H_{21}O_2NS$	363.39	72.72	5.78	3.85	72.28	5.74	3.99
XXI	143—144	71.7	$C_{23}H_{23}O_3NS$	393.41	70.22	5.85	3.56	70.61	5.91	3.64
XXII	125—126	64.2	$C_{24}H_{25}O_4NS$	423.44	68.08	5.91	3.30	68.04	5.93	3.41
XXIII	128—129	70.2	$C_{22}H_{19}O_3NS$	377.37	70.02	5.03	3.71	70.49	5.11	3.58
XXIV	107—108	70.8	$C_{21}H_{18}ONSCl$	367.80	68.47	4.93	3.83	68.97	5.07	4.01
XXV	138—139	63.8	$C_{21}H_{18}ONSCl$	367.80	68.47	4.93	3.83	68.80	5.04	3.81
XXVI	178—179	62.5	$C_{21}H_{17}ONSCl_2$	402.26	62.68	4.22	3.48	62.54	4.32	3.59
XXVII	92— 93	16.6	$C_{22}H_{21}O_2NS$	363.39	72.72	5.78	3.85	72.58	5.92	3.94
XXVIII	101—102	21.7	$C_{21}H_{18}ONSCl$	367.80	68.47	4.93	3.83	68.87	4.98	3.89

Sixteen chalcones variously substituted in ring B were boiled each for 3 hours in anhydrous toluene with a small excess of 2-aminothiophenol and, depending on the substituent, the following compounds were obtained. From unsubstituted chalcone (**I**), from chalcones with electron donor substituents (**II**—**VII**) or from those with slightly electron-withdrawing substituents (**VIII**—**X**) only β-phenyl-β-(2-aminophenylmercapto)-propiophenones (**XVII**—**XXVI**) were obtained. From compounds with a methoxyl group (**XI**) or chlorine (**XII**) in position C-2, a mixture of the propiophenone (**XXVII**, **XXVIII**, and 2,3-dihydro-2,4-diphenyl-1,5-benzothiazepine (**XXXIX**, **XL**) was formed due in part,probably, to steric effects. However, in the case of strongly electron-withdrawing substituents (**XIII**—**XVI**) only the 1,5-benzothiazepines (**XLI**—**XLIV**) were isolated. These different pathways of the reaction with 2-aminothiophenol, shown by chalcones with substituents of different electronic character can be interpreted as being due to the significant change in electron density on the β-carbon caused by the substituent [8, 9] which thus enhances, or weakens, nucleophilic addition on the mercapto group and also affects the rate of the condensation step. Thus, in the presence of strong electron acceptor substituents (**XIII**—**XVI**) condensation is also accomplished during boiling in toluene.

The β-phenyl-β-(2-aminophenylmercapto)-propiophenones (**XVII**—**XXVIII**) were converted into 2,3-dihydro-2,4-diphenyl-1,5-benzothiazepines (**XXIX**—**XL**) by boiling them in anhydrous methanol in the presence of acetic acid catalyst.

Table II

IR and UV spectral data of β-phenyl-β-(2-aminophenylmercapto)-propiophenones

	Infrared		Ultraviolet λ_{max} [nm] (log ε)
	ν C=O [cm^{-1}]	ν NH$_2$ [cm^{-1}]	
XVII	1682	3349, 3442	310 (3.75), 242 (4.31)
XVIII	1680	3530, 3445	310 (3.70), 242 (4.38)
XIX	1682	3354, 3444	308 (3.69), 284 (3.73), 242 (4.29)
XX	1680	3360, 3460	310 (3.66), 238 (4.45)
XXI	1676	3344, 3443	308 (3.66), 282 (3.81), 242 (4.42)
XXII	1677	3339, 3420	312 (3.67), 242 (4.39), 204 (4.77)
XXIII	1677	3346, 3443	294 (3.88), 242 (4.38), 204 (4.77)
XXIV	1677	3360, 3460	308 (3.82), 244 (4.30)
XXV	1680	3360, 3461	312 (3.98), 228 (4.51)
XXVI	1682	3359, 3462	320 (3.62), 243 (4.38)
XXVII	1680	3341, 3440	308 (3.68), 282 (3.81), 242 (4.37)
XXVIII	1679	3357, 3442	310 (3.79), 242 (4.38)

Table III

Physical constants and analysis data of 2,3-dihydro-2,4-diphenyl-1,5-benzothiazepines

	M. p., °C	Yield, %	Overall formula	Molecular weight	Analysis, %					
					Calculated			Found		
					C	H	N	C	H	N
XXIX	115—116	74.4	$C_{21}H_{17}NS$	315.35	79.96	5.39	4.44	79.86	5.45	4.38
XXX	114—116	84.6	$C_{22}H_{19}NS$	329.37	80.24	5.77	4.25	79.78	5.93	4.19
XXXI	104—105	75.4	$C_{22}H_{19}ONS$	345.37	76.52	5.50	4.05	76.32	5.66	3.99
XXXII	127—128	63.8	$C_{22}H_{19}ONS$	345.37	76.52	5.50	4.05	76.51	5.67	4.02
XXXIII	118—119	65.9	$C_{23}H_{21}O_2NS$	375.40	73.60	5.60	3.73	73.86	5.74	3.82
XXXIV	145—146	70.2	$C_{24}H_{23}O_3NS$	405.42	71.11	5.67	3.45	71.06	5.75	3.51
XXXV	133—134	65.9	$C_{22}H_{17}O_2NS$	359.36	73.54	4.73	3.89	73.11	4.84	3.82
XXXVI	104—105	74.4	$C_{21}H_{16}NSCl$	349.79	72.01	4.57	4.01	71.71	4.64	3.98
XXXVII	128—129	74.7	$C_{21}H_{16}NSCl$	349.79	72.01	4.57	4.01	72.62	4.63	3.93
XXXVIII	119—120	68.0	$C_{21}H_{15}NSCl_2$	384.24	65.62	3.90	3.64	65.59	3.98	3.77
XXXIX	168—169	35.3	$C_{22}H_{19}ONS$	345.37	76.52	5.50	4.05	76.40	5.63	4.04
XL	148—149	20.4	$C_{21}H_{16}NSCl$	349.79	72.01	4.57	4.01	71.10	4.62	4.08
XLI	168—169	52.7	$C_{21}H_{16}O_2N_2S$	360.34	69.97	4.44	7.77	69.74	4.56	7.62
XLII	180—181	77.7	$C_{21}H_{16}O_2N_2S$	360.34	69.97	4.44	7.77	70.34	4.51	7.69
XLIII	181—182	70.3	$C_{21}H_{15}NSCl_2$	384.24	65.62	3.90	3.64	65.32	3.93	3.63
XLIV	172—173	73.0	$C_{21}H_{15}NSCl_2$	384.24	65.62	3.90	3.64	65.84	4.01	3.59

In Table II infrared and ultraviolet spectral data of the β-phenyl-β-(2-aminophenylmercapto)-propiophenones (**XVII**—**XXVIII**), and in Table IV those of the 2,3-dihydro-2,4-diphenyl-1,5-benzothiazepines (**XXIX**—**XLIV**) are shown. The C = O and NH_2 bands appearing in the infrared spectra of **XVII**—**XXVIII**, and the —C = N— bands of **XXIX**—**XLIV** unequivocally prove that these compounds have the structures ascribed them. In the infrared spectra of **XXIX**—**XLIV** no NH band is found: this also proves that the double bond is not in the Δ^3-position.

The assigned structures of compounds **XVII**, **XXI**, **XXV**, **XXXI** and **XXXVI** have also been confirmed by ^{1}H—NMR spectroscopy: the data are shown in Table V.

Table IV

IR and UV spectral data of 2,3-dihydro-2,4-diphenyl-1,5-benzothiazepines

	Infrared ν C = N [cm^{-1}]	Ultraviolet λ_{max} [nm] (log ε)
XXIX	1608	336 (3.63), 260 (4.27)
XXX	1610	336 (3.72), 261 (4.32)
XXXI	1608	338 (3.62), 262 (4.27)
XXXII	1609	335 (3.75), 261 (4.34), 231 (4.33)
XXXIII	1608	335 (3.67), 291* (4.01), 261 (4.32), 237 (4.29)
XXXIV	1606	330 (3.65), 261 (4.32)
XXXV	1604	330 (3.75), 296* (4.09), 261 (4.36)
XXXVI	1609	335 (3.64), 261 (4.29)
XXXVII	1609	340 (3.64), 262 (4.30)
XXXVIII	1610	335 (3.57), 262 (4.22)
XXXIX**	1608	335 (3.70), 264 (4.35)
XL	1610	335 (3.66), 262 (4.24)
XLI	1611	342 (3.66), 262 (4.39)
XLII**	1611	323 (3.96), 265 (4.46)
XLIII**	1610	340 (3.56), 265 (4.18), 236 (4.18)
XLIV**	1610	340 (3.62), 264 (4.25), 236 (4.25)

* shoulder

** UV data recorded in dioxane

Experimental

M. p.'s are uncorrected.

The UV spectra were recorded in ethanolic solutions, with the exception of **XXXIX**, **XLII**—**XLIV**, with a UNICAM SP 800 instrument: the IR spectra were obtained (in KBr pellets) with a UNICAM SP 200G instrument. The NMR spectra were recorded with a JEOL MH 100 instrument in deuterochloroform (internal standard TMS $\delta = 0$ ppm), at room temperature.

Table V

^{1}H-NMR spectra (δ ppm)

	Aromatic	—CH—	—CH_2—	—NH_2	2 OCH_3
XVII	6.40—7.92 m	4.73 t	3.62 q	4.20 s	—
XXI	6.32—7.79 m	4.61 t	3.60 q	3.95 s	3.68 s and 3.75 s
XXV	6.39—7.88 m	4.68 t	3.56 q	4.18 s	—

The NH_2 signal is extinguished by D_2O

	Aromatic	—CH—	—CH_2—	OCH_3
XXXI	6.78—8.04 m	4.90 q	2.84—3.40 m	3.68 s
XXXVI	6.85—8.02 m	4.86 q	2.78—3.37 m	—

These spectra are not affected by D_2O

The chalcones were prepared by the condensation of acetophenone and substituted benzaldehydes in aqueous ethanolic solution in the presence of sodium hydroxide catalyst, as described in the literature [10—14].

β-Phenyl-β-(2-aminophenylmercapto)-propiophenones

The chalcone (**I—X**) (10 mmoles) and 2-aminothiophenol (12 mmoles) were dissolved in dry toluene, and refluxed for 3 hrs in an apparatus provided with a water separator: the solvent was then removed under reduced pressure. The residue was recrystallized from methanol: in this way the compounds **XVII—XXVI** were obtained (Tables I and II).

The chalcones **XI** and **XII** gave a mixture of the corresponding propiophenone (**XXVII** and **XXVIII**) (Tables I and II) and 1,5-benzothiazepine (**XXXIX** and **XL**) (Tables III and IV): this mixture was separated by fractional crystallization from methanol. From the chalcones **XIII—XVI** the 1,5-benzothiazepines (**XLI—XLIV**) were prepared (Tables III and IV).

2,3-Dihydro-2,4-diphenyl-1,5-benzothiazepines

β-Phenyl-β-(2-aminophenylmercapto)-propiophenone (**XVII—XXVIII**) (0.5 g) was refluxed for 1 hr in a mixture of anhydrous methanol (20 ml) and glacial acetic acid (1 ml). The product which separated after cooling was recrystallized from methanol: in this way compounds **XXIX—XL** were obtained (Tables III and IV).

*

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REFERENCES

[1] LÉVAI, A., BOGNÁR, R.: in "Topics in Flavonoid Chemistry and Biochemistry" (ed. L. Farkas, M. Gábor, F. Kállay) Akadémiai Kiadó Budapest, and Elsevier Publ. Co., Amsterdam 1975
[2] RIED, W., MARX, W.: Chem. Ber., **90,** 2683 (1957)
[3] MUSKALO, L. K.: Zh. Obschh. Khim., **28,** 507 (1958)
[4] HIDEG-HANKOVSZKY, O., HIDEG, K.: Acta Chim. Acad. Sci. Hung., **68,** 403 (1971)
[5] STEPHENS, W. D., FIELD, L.: J. Org. Chem., **24,** 1576 (1959)
[6] LITKEI, GY., BOGNÁR, R.: Kémiai Közl., **34,** 249)1970)
[7] LITKEI, GY., BOGNÁR, R., DINYA, Z.: Acta Chim. (Budapest), **71,** 403 (1972)
[8] DINYA, Z., BOGNÁR, R.: Kémiai Közl., **37,** 1 (1972)
[9] DINYA, Z., LITKEI, GY., BOGNÁR, R., MÁTYÁS, GY.: Magy. Kém. Foly., **78,** 504 (1972); Acta Chim. (Budapest) **77,** 323 (1973)
[10] FREDERICK, J., DIPPY, J., LEWIS, R. L.: Rec. trav. chim., **56,** 1000 (1937); C. A. **32,** 521 (1938)
[11] BRADSHER, C. K., BROWN, F. C., BLUE, W. B.: J. Amer. Chem. Soc., **71,** 3570 (1949)
[12] ISHIWATA, S., SUZUKI, K.: J. Pharm. Soc. Japan, **70,** 195 (1950)
[13] DAVEY, W., GWILT, J. R.: J. Chem. Soc., **1957,** 1008
[14] DAVEY, W., TIVEY, D. J.: J. Chem. Soc., **1958,** 1230

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SYNTHESIS OF OLIGO-β-L-ASPARTIC ACID DERIVATIVES

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The synthesis of oligo-β-L-aspartic acid derivatives **(Ia, b)** containing up to six aspartic acid residues is described. Benzyloxycarbonyl and *t*-butyl ester groups were used to protect the amino and carboxyl groups, respectively. The peptide bonds were formed by the dicyclohexylcarbodiimide method. Column chromatography on silica gel was used to purify the protected peptides with 4—6 aspartic acid residues **(IVc—e)**. Free oligopeptides **(VIIa—e)** were prepared by treatment with trifluoroacetic acid followed by catalytic hydrogenation. The protected derivatives **(IVa—e)** were characterized by TLC. The purity of the free oligo-β-L-aspartic acids was checked by means of TLC and high voltage paper electrophoresis.

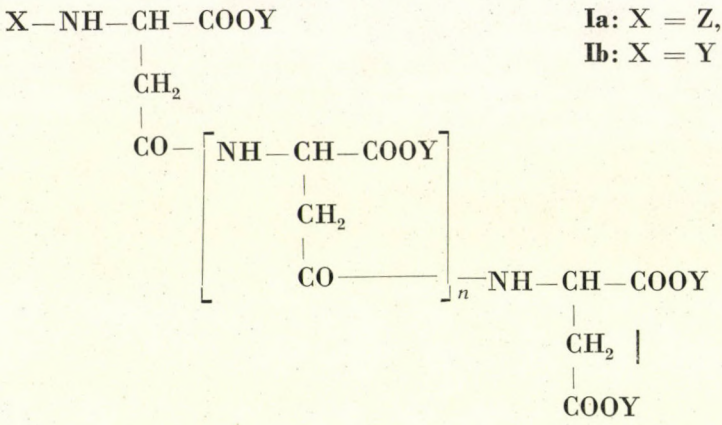
The demand for monotone oligopeptides of well-defined structure containing γ-glutamic acid or β-aspartic acid residues has been increased recently in the fields of biochemical and physicochemical investigations. Pteroyl-oligo-γ-L-glutamic acids are the major forms of folic acid (vitamin Bc) [1] and the biological and pharmacological activity of pteroyl-L-aspartic acid is also well known [2]. The syntheses by different methods of oligo-γ-L-glutamic acids with up to seven glutamic acid residues have been described in a previous paper [3]. From a comparison of the optical rotatory dispersion spectra of these model compounds with that of natural poly-γ-D-glutamic acid, conclusions have also been drawn concerning the secondary structure of this macromolecule [4].

In order to obtain more detailed information about the chiroptical properties of monotone oligopeptides built up from γ- or β-linked amino acid residues, we have synthesized a series of oligo-β-L-aspartic acid derivatives **(Ia,b)**. The preparation of pteroyl-oligo-β-L-aspartic acids is also in progress.

The synthesis of β-L-aspartyl-L-aspartic acid *via* tribenzyl N-benzyloxycarbonyl-β-L-aspartyl-L-aspartate has been described by YOUNG *et al.* [5]. No oligo-β-L-aspartic acids with more than two aspartic acid residues, however, have been reported as yet.

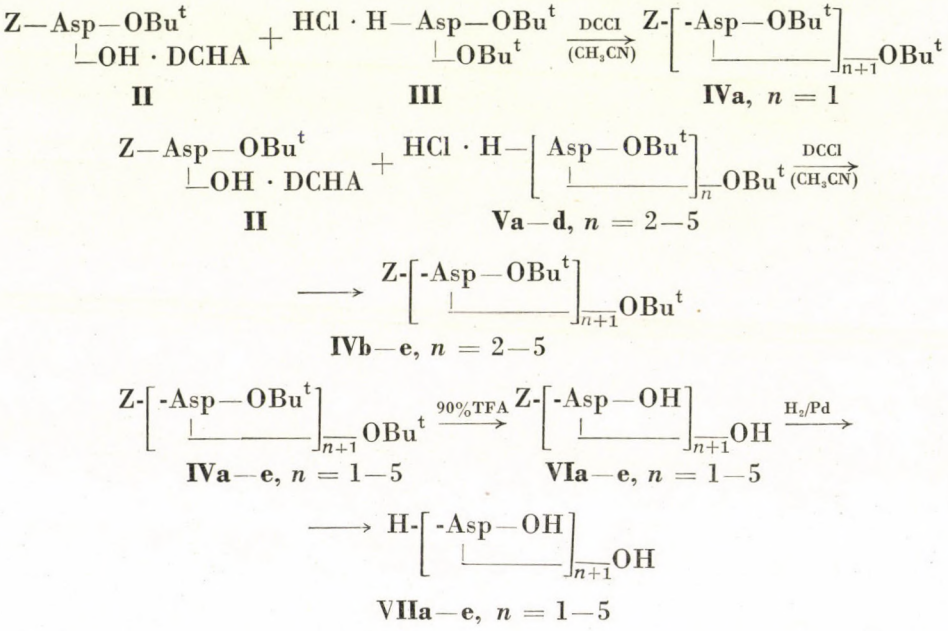
On the basis of experiences in the syntheses of oligo-γ-L-glutamic acids [3], we have chosen the benzyloxycarbonyl and *t*-butyl groups for the protection of the amino and carboxyl terminals, respectively.

Derivatives of aspartic acid used as starting materials in the syntheses were α-*t*-butyl N-benzyloxycarbonyl-L-aspartate dicyclohexylammonium salt



Ia: X = Z, Y = Bu^t; $n = 0-4$
Ib: X = Y = H; $n = 0-4$

(**II**) [6] and di-*t*-butyl L-aspartate hydrochloride (**III**) [7,8]. The synthesis of the oligo-β-L-aspartic acids was accomplished according to the general scheme summarized below [9].



Selective fission of the benzyloxycarbonyl group of the protected oligopeptide derivatives **IVa—e** was effected by catalytic hydrogenation (palladium(10%)-on-charcoal) in the presence of hydrochloric acid, and the appropriate oligopeptide ester hydrochloride salts (**Va—d**) were obtained in good yields (85—100%). After failing in an attempt at preparing the protected dipeptide derivative (**IVa**) by means of α-*t*-butyl N-carbobenzoxy-L-aspartate pentachloro-

phenyl ester [10] as acylating agent, we chose the dicyclohexylcarbodiimide method [11] for building the peptide bond. While the protected derivatives **IVa** and **IVb** were obtained in high chromatographic purity after crystallization, the protected oligopeptides with 4—6 aspartic acid residues (**IVc—e**) had to be purified by column chromatography on silica gel. The free oligopeptides **VIIa—e** were prepared by removing the *t*-butyl and benzyloxycarbonyl groups of the protected derivatives **IVa—e** by treatment with 90% trifluoroacetic acid for 3—5 hrs [3], followed by catalytic hydrogenation.

Table I

Synthesis of oligo-β-L-aspartic acids (**VIIa—e**)

Compound	Starting materials **IVa—e** (mmole)	Intermediates **VIa—e** R_f *(b)*	Yield, %
VIIa	2.18	0.35	92.5
VIIb	1.11	0.30	74.5
VIIc	1.34	0.25	93.5
VIId	0.56	0.20	90
VIIe	0.49	0.15	87

Characterization and purity control of oligo-β-L-aspartic acid derivatives

(*a*) *t-Butyl N-benzyloxycarbonyl-oligo-β-L-aspartates* (**IVa—e**)

The protected oligo-β-L-aspartic acid derivatives are crystalline substances with well defined melting points. Their purity was checked by TLC (Fig. 1) on silica gel (DC-Alufolien, Kieselgel 60 F_{254}, Merck), using a solvent mixture of ethyl acetate–cyclohexane (1 : 1) capable of separating the protected derivatives containing different numbers of aspartic acid residues. Each protected peptide showed one single chlorine-positive spot of significantly different R_f value indicating the homogeneity of these substances. The analytical data were also in good agreement with the calculated values.

(*b*) *t-Butyl oligo-β-L-aspartate hydrochlorides* (**Va—d**) (Table II)

The hydrochloride salts are gel-like substances having no definite melting points. As they could not be obtained as crystalline substances, their purity was controlled in an indirect way. Starting from the homogeneous protected derivatives **IVa—e**, the removal of the benzyloxycarbonyl group was followed by TLC on silica gel (DC-Alufolien, Kieselgel 60 F_{254}, Merck), using the above solvent mixture. In this mixture the hydrochloride salt derivatives showed only one ninhydrine-positive spot of a lower R_f value than the chlorine-positive spot of the appropriate protected derivative, indicating the completeness of the

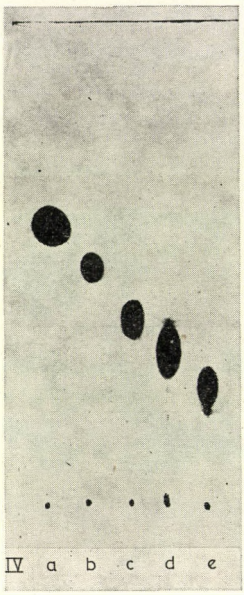


Fig. 1. Thin-layer chromatogram of *t*-butyl N-benzyloxycarbonyl-oligo-β-L-aspartates (**IVa—e**) on silica gel (DC-Alufolien, Kieselgel 60 F_{254}, Merck) in ethyl acetate–cyclohexane (1 : 1), detected by the chlorine–tolidine test. R_f values: **IVa** 0.57, **IVb** 0.49, **IVc** 0.39, **IVd** 0.32 and **IVe** 0.25.

catalytic hydrogenation in each case. The gel-like hydrochloride salts were thoroughly dried in a vacuum desiccator over conc. H_2SO_4 and KOH, and characterized by chlorine analysis and TLC using different solvent mixtures.

Table II

Chromatographic and analytical data of t-butyl oligo-β-L-aspartate hydrochlorides (**Va—d**)

Compound	Formula	Mol. wt.	Cl %		Chromatography (R_f)*	
			Calcd.	Found	Solvent *f*	Solvent *g*
Va	$C_{20}H_{36}N_2O_7 \cdot HCl$	452.7	7.85	8.10	0.52	0.58
Vb	$C_{28}H_{49}N_3O_{10} \cdot HCl$	624.0	5.70	6.20	0.43	0.48
Vc	$C_{36}H_{62}N_4O_{13} \cdot HCl$	795.3	4.45	4.80	0.36	0.43
Vd	$C_{44}H_{75}N_5O_{16} \cdot HCl$	966.6	3.65	4.40	0.23	0.31

* Kieselgel G nach Stahl, Merck

(*c*) *Oligo-β-L-aspartic acids* (**VIIa—e**) (Table III)

The oligo-β-L-aspartic acids are amorphous solids with some water content bound so strongly that it could not be removed even at 100°C in a vacuum desiccator over conc. H_2SO_4 (or P_2O_5) and KOH. The data of elemental analysis,

Table III

Physical constants and analytical data of oligo-β-L-aspartic acids (**VIIa—e**)

Compound	$[\alpha]_D^{20}$ (0.5*N* HCl)	TLC (R_f) solvent *b*	TLC (R_f) solvent *c*	High voltage electrophor. (R_f)[1] pH 1.8[2]	High voltage electrophor. pH 6.5[3]	Formula	Mol. wt.	C, % Calcd.	C, % Found	H, % Calcd.	H, % Found	N, % Calcd.	N, % Found
VIIa	+18.5 (c 2.0)	0.30	—	0.50	1.17	$C_8H_{12}N_2O_7$ $C_8H_{12}N_2O_7 \cdot 1/2H_2O$	248.2 257.2	38.7 37.35	38.0	4.85 5.10	5.7	11.3 10.9	9.4
VIIb	+6.0 (c 2.0)	0.25	0.50	0.40	1.30	$C_{12}H_{17}N_3O_{10}$ $C_{12}H_{17}N_3O_{10} \cdot 1/2H_2O$	363.3 372.3	39.65 38.7	38.9	4.7 4.85	5.05	11.55 11.3	9.7
VIIc	+16.1 (c 1.0)	0.10	0.45	0.30	1.30	$C_{16}H_{22}N_4O_{13}$ $C_{16}H_{22}N_4O_{13} \cdot 1/2H_2O$	478.3 487.3	40.15 39.4	39.85	4.65 4.75	5.05	11.7 11.5	10.65
VIId	+6.1 (c 1.0)	—	0.40	0.20	1.30	$C_{20}H_{27}N_5O_{16}$ $C_{20}H_{27}N_5O_{16} \cdot 1/2H_2O$	593.4 602.4	40.5 39.85	39.3	4.6 4.7	4.9	11.8 11.6	10.4
VIIe	+8.7 (c 2.0)	—	0.35	0.15	1.30	$C_{24}H_{32}N_6O_{19}$ $C_{24}H_{32}N_6O_{19} \cdot 1/2H_2O$	708.5 717.5	40.7 40.2	39.8	4.55 4.65	4.95	11.85 11.7	11.0

[1] Relative to aspartic acid
[2] Acetic acid–formic acid–water (80 : 20 : 900)
[3] Pyridine–acetic acid–water (100 : 3 : 894)

ranging over relatively small intervals (C 38.7—40.7%; H 4.85—4.55%; N 11.3—11.85%, calculated for the water-free substances) are not characteristic of the purity of the free acids **VIIa—e** with water content. In consequence of this difficulty, the oligo-β-L-aspartic acids were characterized by TLC using different solvent mixtures and especially high voltage electrophoresis on Whatman 3MM paper at 1500 V, pH 1.8 and 6.5. According to these investigations, the free acids may be said to be satisfactorily pure, meaning that degradation products due to peptide bond cleavage in the course of the 90% trifluoroacetic acid treatment, or other contaminations containing *t*-butyl groups, can only be detected to a very small extent. Analytical data and R_f values are summarized in Table III together with the values of optical rotation. The investigation of the chiroptical properties of the synthesized oligo-β-L-aspartic acid derivatives will be reported elsewhere.

Experimental

M. p.'s are uncorrected and were taken on a Tottoli apparatus. The optical rotations were measured with an OPTON-REPM 12 spectropolarimeter (Xenon high pressure lamp). Before microanalyses, the samples were dried in a vacuum desiccator over P_2O_5 for 8—10 hrs at a temperature selected according to the melting point of the substance in question. Thin-layer chromatograms were made on silica gel (Kieselgel-G nach Stahl, Merck) or DC-Alufolien (Kieselgel 60 F_{254}, Merck) using the following solvent mixtures:

a) *n*-butyl alcohol–pyridine–acetic acid–water (30 : 20 : 6 : 24)
b) *n*-butyl alcohol–pyridine–acetic acid–water (3 : 5 : 3 : 3)
c) *n*-butyl alcohol–pyridine–acetic acid–water (4 : 7 : 4 : 9)
d) *n*-butyl alcohol–acetic acid–water (4 : 1 : 1)
e) ethyl acetate–cyclohexane (1 : 1)
f) ethyl acetate–cyclohexane (3 : 2)
g) acetic acid–water (1 : 9)

Starting materials

α-*t*-Butyl N-benzyloxycarbonyl-L-aspartate dicyclohexylammonium salt (II)

From 57.5 g of α-*t*-butyl β-methyl N-benzyloxycarbonyl-L-aspartate, prepared by the method of GREGORY *et al.* [6], 45 g (52%) of α-*t*-butyl N-benzyloxycarbonyl-L-aspartate dicyclohexylammonium salt was obtained, m. p. 118—119 °C; $[\alpha]_D^{25}$ —2,4° (c 1.0, ethanol). The physical constants reported in the literature [6] are: m. p. 119—120 °C; $[\alpha]_D^{25}$ —2.5° (c 1.0, ethanol).

Di-*t*-butyl L-aspartate hydrochloride (III)

Starting from 13.3 g (0.1 mole) of L-aspartic acid — according to the method of ROESKE [8] — 11.0 g (39%) of the hydrochloride III was obtained, m. p. 149—150 °C. (The m. p. reported by TASCHNER *et al.* [7] is 151—152 °C.)

Tri-α-*t*-butyl N-benzyloxycarbonyl-β-di-L-aspartate (IVa)

15.5 g (30.7 mmoles) of α-*t*-butyl N-benzyloxycarbonyl-L-aspartate dicyclohexylammonium salt was dissolved in acetonitrile (120 ml) and a suspension of 9.4 g (33.4 mmoles) of di-*t*-butyl L-aspartate hydrochloride in 80 ml acetonitrile was added to the solution. After 2 hrs stirring the dicyclohexylammonium hydrochloride was filtered off and, at 0 °C, 6.32 g

(30.7 mmoles) of dicyclohexylcarbodiimide was added to the filtrate. After 2 hrs stirring at room temperature the reaction mixture was allowed to stand overnight. Dicyclohexylurea was filtered off and the solution evaporated under reduced pressure. The remaining oil was dissolved in ether (120 ml), washed with ice-cold 0.5*N* H_2SO_4 (2 × 40 ml), 10% $NaHCO_3$ solution (3×40 ml) and 10% NaCl solution (40 ml), then dried (Na_2SO_4) and evaporated to dryness. The remaining oily substance was recrystallized from a mixture of ether (35 ml) and petroleum ether (60 ml) to give 11.4 g (67.5%) of the protected dipeptide (**IVa**); m. p. 70—72 °C, $[\alpha]_D^{25}$ —23.0° (*c* 1.0, dimethylformamide).

$C_{28}H_{42}N_2O_9$ (550.65). Calcd. C 61.05; H 7.7; N 5.1. Found C 60.7; H 7.65; N 5.15%.

General methods

(A) Preparation of *t*-butyl oligo-β-L-aspartate hydrochlorides (Va—d) (Table II).

The *t*-butyl N-benzyloxycarbonyl-oligo-β-L-aspartates (**IVa—e**) were dissolved in methanol (5—10 ml per mmole) and hydrogenated at room temperature and atmospheric pressure over prehydrogenated palladium (10%)-on-charcoal catalyst (50—100 mg per mmole) in the presence of 1.2 equivalent of hydrogen chloride, until the evolution of carbon dioxide ceased (2—5 hrs). After removal of the catalyst, the solution was evaporated to dryness and the remaining solid gel-like substance dried in a vacuum desiccator over conc. H_2SO_4 and KOH. The yields ranged from 85 to 100%.

(B) Syntheses of *t*-butyl N-benzyloxycarbonyl oligo-β-L-aspartates (IVb—e)

10 mmoles of *t*-butyl N-benzyloxycarbonyl-L-aspartate dicyclohexylammonium salt (**II**) was dissolved in acetonitrile (30 ml per 10 mmoles) and a solution of 10 mmoles of the appropriate *t*-butyl oligo-β-L-aspartate hydrochloride (**Va—d**) dissolved in acetonitrile (20—30 ml per 10 mmoles), was added to the first solution. After stirring at room temperature for 2 hrs the dicyclohexylammonium hydrochloride was filtered off and 10 mmoles of dicyclohexylcarbodiimide were added to the filtrate at 0 °C. After another 2 hrs stirring at room temperature, the mixture was allowed to stand overnight. The dicyclohexylurea was filtered off and the filtrate evaporated under reduced pressure. The remaining oil was dissolved in ether (100—150 ml) and the solution washed with ice-cold 0.5*N* H_2SO_4 (3×50 ml), 10% $NaHCO_3$ (3×50 ml) and water (50 ml), then dried (Na_2SO_4) and evaporated to dryness.

Protected tripeptide derivative (IVb, n = 2)

The crude product prepared from 38.5 mmoles of the starting materials **II** and **Va** as described above, was purified by crystallization from a mixture of ether and petroleum ether. Yield: 21.0 g (75.5%), m. p. 93—95 °C, $[\alpha]_D^{25}$ —22.1° (*c* 1, dimethylformamide).

$C_{36}H_{55}N_3O_{12}$ (721.85). Calcd. C 59.9; H 7.65; N 5.8. Found C 60.55; H 8.50; N 5.95%.

Protected tetrapeptide derivative (IVc, n = 3)

From 16 mmoles of the starting materials **II** and **Vb**, a crude product (13.6 g) was obtained, which was purified by column chromatography on silica gel (Kieselgel 60, Merck; 42×2.5 cm), using a mixture of ethyl acetate–cyclohexane (1 : 1) as eluant. The fractions containing the chromatographically pure product were collected to obtain, after crystallization from a mixture of ethyl acetate, ether and petroleum ether, 9.8 g (68.5%) of the crystalline tetrapeptide, m. p. 97—99 °C, $[\alpha]_D^{25}$ —19.3° (*c* 1.0, dimethylformamide).

$C_{44}H_{68}N_4O_{15}$ (893.05). Calcd. C 59.2; H 7.65; N 6.25. Found C 59.3; H 7.9; N 6.85%.

Protected pentapeptide derivative (IVd, n = 4)

From 10 mmoles of the starting materials **II** and **Vc**, 9.8 g of a crude product was obtained which was purified by column chromatography on silica gel (Kieselgel 60, Merck; 40×2.5 cm), using a mixture of ethyl acetate–cyclohexane (1 : 1) as eluant. The fractions containing the chromatographically pure product were collected and evaporated to dryness to give 8.0 g (75%) of an amorphous substance, m. p. 121—123 °C, $[\alpha]_D^{25}$ —18.7° (*c* 1.0, dimethylformamide).

$C_{52}H_{81}N_5O_{18}$ (1064.25). Calcd. C 58.7; H. 7.65; N 6.6. Found C 58.9; H 7.85; N 6.85%.

Protected hexapeptide derivative (IVe, n = 5)

From 4.75 mmoles of the starting materials **II** and **Vd**, after evaporation of the acetonitrile solution, a solid product was obtained, which could only be dissolved in chloroform. According to the general procedure described above, another solid (3.6 g) was obtained which was purified by column chromatography on silica gel (Kieselgel 60, Merck; 42 × 2.5 cm) using the above mixture as eluant. The fractions containing the chromatographically pure product were collected to yield 3.2 g (54%) of **IVe**, m. p. 157—162 °C; $[\alpha]_D^{25}$ —20.0 (*c* 1.0, dimethylformamide).

$C_{60}H_{94}O_{21}N_6$ (1235.44). Calcd. 58.5; H 7.7; N 6.8. Found C 57.65; H 7.8; N 7.15%.

(C) Preparation of the oligo-β-L-aspartic acids (VIIa—e) (*cf.* Table I)

The appropriate *t*-butyl N-benzyloxycarbonyl oligo-β-L-aspartate (0.4—2.5 mmoles) was dissolved in ice-cold 90% trifluoroacetic acid (15—25 ml per mmole) and kept at 0 °C for 1 hr, and at room temperature for further 2—4 hrs. The cleavage procedure was followed by means of TLC (Table III), and continued until a single chlorine-positive spot could only be detected on the layer. The solution was then evaporated under reduced pressure (bath temperature 35 °C) and the residue taken up in dry ether. The precipitated solid was filtered off, washed with ether and dried in a vacuum desiccator over conc. H_2SO_4 and KOH.

The N-benzyloxycarbonyl-oligo-β-L-aspartic acids were dissolved in methanol (30—50 ml per mmoles) and hydrogenated at room temperature and pressure over prehydrogenated palladium (10%)-on-charcoal catalyst (100—150 mg per mmoles) until the evolution of carbon dioxide ceased (1—3 hrs). After removal of the catalyst, the solution was evaporated under reduced pressure and the remaining solid dried in a vacuum desiccator over conc. H_2SO_4 and KOH. The overall yields ranged from 75 to 95%. Physical constants and analytical data of the oligo-β-L-aspartic acids **VIIa—e** are summarized in Table III.

*

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REFERENCES

[1] BLAKELEY, R. L.: in "The Biochemistry of Folic Acid and Related Pteridines", pp. 25—49. North Holland Publishing Co., Amsterdam 1969;
BINKLEY, S. B., BIRD, O. D., BLOOM, E. S., BROWN, R. A., CALKINS, D. G., CAMPBELL, C. J., EMMETT, E. D., PFIFFNER, J. J.: Science, **100,** 36 (1944)
[2] EHRHART, G., RUSCHIG, H.: in "Arzneimittel" Vol. 5, p. 362. Verlag Chemie, Weinheim/Bergstr., 1972
[3] KAJTÁR, M., HOLLÓSI, M.: Acta Chim. Acad. Sci. Hung., **65,** 403 (1970)
[4] KAJTÁR, M., BRUCKNER, V.: Tetrahedron Letters, **1966,** 4318;
KAJTÁR, M.: Kémiai Közl., **28,** 251 (1967)
[5] BRYANT, P. M., MOORE, R. H., PIMLOTT, P. J., YOUNG, G. T.: J. Chem. Soc., **1959,** 3868
[6] GREGORY, H., MORLEY, J. S., SMITH, J. M., SMITHERS, M. J.: J. Chem. Soc., (C) **1968,** 715
[7] TASCHNER, E., CHIMIAK, A., BATOR, B., SOKOLOWSKA, T.: Ann., **646,** 134 (1961)
[8] ROESKE, R. W.: Chem. and Ind., **1959,** 1121
[9] IUPAC—IUB Commission on Biochemical Nomenclature, Abbreviated Designation of Amino Acid Derivatives and Peptides, Tentative Rules, J. Biol. Chem., **241,** 2491 (1966)
[10] KOVÁCS, J., BALLINA, R., RODIN, R. L., BALASUBRAMANIAN, D., APPLEQUIST, J.: J. Am. Chem. Soc., **87,** 119 (1965)
[11] SHEEHAN, J. C., HESS, G. P.: J. Am. Chem., Soc., **77,** 1067 (1955)

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THE REACTIVITY OF THE CARBONYL GROUP IN FLAVONOID COMPOUNDS, II

BASICITY OF THE ANALOGUES OF FLAVONE AND FLAVANONE

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The basicity of the carbonyl group in 1-thiaflavones, 1-azaflavones and -flavanones, and the rates of formation of the 1,2-dinitrophenylhydrazones have been determined. In the compounds studied the basicity of the carbonyl group increases in the sequence O < S < NH, while the nitrogen in 1-azaflavanone lowers the basicity of the carbonyl group owing to its precedence during protonation. The rates of formation of the 2,4-dinitrophenylhydrazones decrease in the order O > S > NH; in the attempted proton-catalyzed reaction of 1-azaflavone, owing to the presence of the enolic tautomer form, the hydrazone is not formed at all.

Thiaflavonoids and azaflavonoids (2-phenyl-4-quinolone and 2-phenyl-2,3-dihydro-4-quinolone) are analogues of the natural flavonoid compounds widely distributed in the vegetable kingdom. The influence of the S and N atom in the hetero ring on the UV spectral characteristics [1] and on the reactivity of the carbonyl group in these compounds [2] has been studied.

Few data can be found in the literature on the physical and chemical properties of thia- and azaflavonoids. For the characterization of their reactivity we have utilized the dependence of the basicity of the C = O group and the reaction rate of 2,4-dinitrophenylhydrazone formation [3] on the hetero substitution, determined according to the method described in an earlier communication [4].

As it is known, aromatic ketones are coloured when dissolved in a strong mineral acid. This phenomenon, halochromy, is due to the ionic form resulting from protonation of the carbonyl group [5, 6, 11].

The proton acceptor character of the C = O group, *i.e.* its basicity, is a measure of its polarization depending on the structure and substitutions, thus it allows the determination of the relative electron density of the carbonyl group.

Experimental

Of the compounds studied, the thia analogues were prepared according to [7], the aza derivatives according to [8] or [9]. The UV spectra were recorded with a UNICAM SP 800 instrument at concentrations of $1 \cdot 10^{-4}$ or $5 \cdot 10^{-5}$ *M*. The spectral data of the compounds studied are shown in Table I. The 2,4-dinitrophenylhydrazones of the compounds were

prepared as described in a former communication [3]. The rate of hydrazone formation was also determined according to the method described previously.

The melting points, the spectral data of the 2,4-dinitrophenylhydrazones, and the reaction rates are shown in Table II.

Table I

UV spectral data of flavanone, flavone, and the 1-thia- and 1-aza analogues

Compound	λ_{max} (ethanol)		
	band I (ε)	band II (ε)	band III (ε)
Flavanone	320 (3650)	252 (9400)	214 (30800)
1-Thiaflavanone	348 (3400)	256 (7850)*	240 (30300)
1-Azaflavanone (2-phenyl-2,3-dihydro-4-quinolone)	373 (3450)	260 (8000)*	235 (26500)
Flavone	298 (21600)	252 (17400)	215 (17000)*
1-Thiaflavone	345 (7600)	265 (15200)	225 (11500)
1-Azaflavone (2-phenyl-4-quinolone)	333 (9400)	256 (38200)	210 (35500)

* shoulder

Table II

Melting points and spectral data of 2,4-dinitrophenylhydrazones; reaction rate constants determined at 25 °C

Compound	Mp., °C	λ_{max} (dioxane)	$k/s^{-1} \cdot 10^{-3}$
Flavanone-2,4-DNPH	250—252*	383 (27400)	255.00
1-Thiaflavanone-DNPH	235—237	385 (24600)	153.00
1-Azaflavanone-DNPH	242—244	408 (21400)	316.00
Flavone-2,4-DNPH	283—285	425 (26400)	0.18

* R. Mozingo, H. Adkins: J. A.m Chem. Soc., **60,** 669 (1938) mp. 254—255 °C
F. Kállay, G. Janzsó, I. Koczor, Tetrahedron, **23,** 417 (1967) 252—255 °C

Determination of basicity constants

The ethanolic (5% ethanol) aqueous sulfuric acid solution were freshly prepared by dilution of analytical grade 99.5% sulfuric acid. The H_0 values for the various sulfuric acid concentrations given in g/l were calculated using the original Hammett base, the unsubstituted chalcone related to the flavonoids [6]; these being known, the basicity of the flavonoids and of their analogues were obtained by means of the formula [6, 10]:

$$pK_{BH^+} = H_0 + log \frac{C_{BH^+}}{C_B} = H_0 + log \frac{\varepsilon - \varepsilon_B}{\varepsilon_{BH^+} - \varepsilon}$$

where H_0 is the acidity value of the ethanolic aqueous sulfuric acid solution, and the quotient $\frac{C_{BH^+}}{C_B}$ is the ratio between the concentrations of the protonated form and the free base at a given value of H_0.

These concentrations were determined by spectrophotometry since there is an essential difference between the absorptions of the ionic and non-ionic forms (Table III).

Table III

Absorption spectral data and calculated basicity constants of the neutral (B) and the protonated (BH^+) forms of flavonoids and flavonoid analogues

Compound	B form*		BH+ form**		pK_{BH^+}
	λ_{max}	(ε)	λ_{max}	(ε)	
Flavanone	255 (11000)	325 (3800)	295 (18200)	410 (3600)	-6.5 ± 0.02
1-Thiaflavanone	235 (29000)	265 (9000)***	255 (18000)	307 (9000)	
		355 (3400)	480 (4000)		-5.65 ± 0.05
1-Azaflavanone	235 (25000)	260 (8000)***	250 (14000)	285 (2000)	-6.75 ± 0.09 (a)
		375 (4000)			-0.65 ± 0.05 (b)
Flavone	253 (22000)	302 (23600)	250 (20000)	348 (30000)	-1.52 ± 0.05
1-Thiaflavone	265 (20000)	350 (8000)	265 (38000)	380 (9200)	-1.15 ± 0.05
1-Azaflavone	255 (3400)··	320 (12000)	265 (30000)	315 (18000)	$+1.82 \pm 0.06$

* 1.985% H_2SO_4 ** 96.5% H_2SO_4 ··pH =2

*** shoulder

(a) pK_{BH^+} calculated at 250 nm

(b) pK_{BH^+} calculated at 235 nm and 310 nm

Figs 1, 2, 3, and 4 show the changes in the spectra due to protonation, *i. e.* to the emergence of the ionic form. The curves obtained at various sulfuric acid concentrations intersect at an isosbestic point, proving the existance of an equilibrium system [6, 10].

In this system, the equilibrium is shifted toward complete protonation when the concentration of the sulfuric acid is increased, remaining then unaffected by further increase of the concentration. (In the case of flavanone we found that the curve recorded at 99.5% sulfuric acid concentration did not pass through the isosbestic point; also the character of the curve was entirely different from the spectra recorded in more dilute sulfuric acid solutions. This curve certainly has no connection with protonation.)

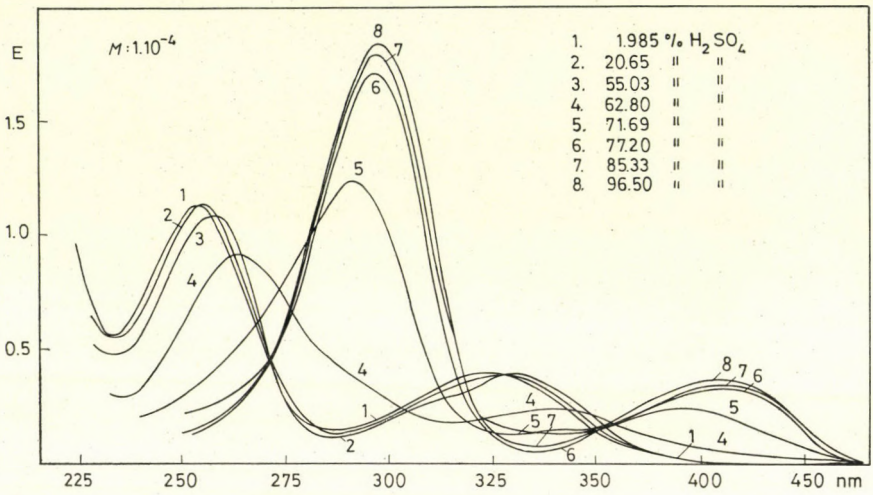


Fig. 1. Effect of the concentration of sulfuric acid on the spectrum of flavanone ($1 \cdot 10^{-4}$ *M*

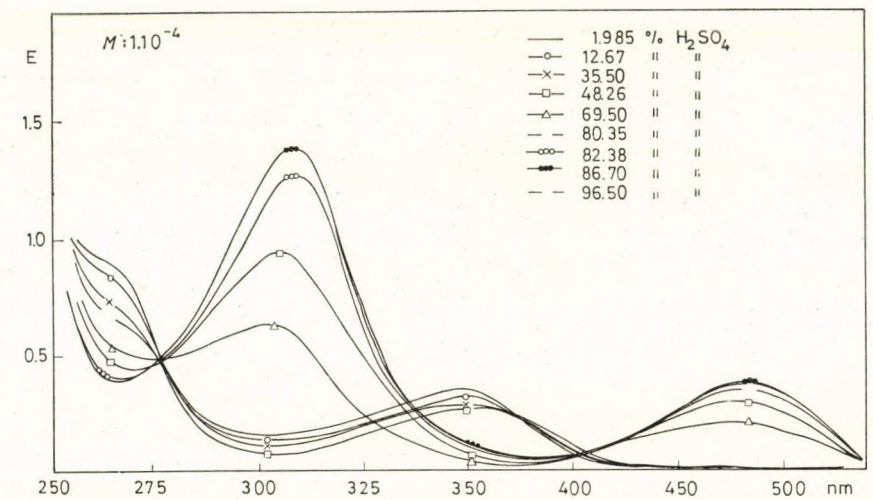


Fig. 2. Effect of the concentration of sulfuric acid on the spectrum of 1-thiaflavanone ($1 \cdot 10^{-4}$ *M*)

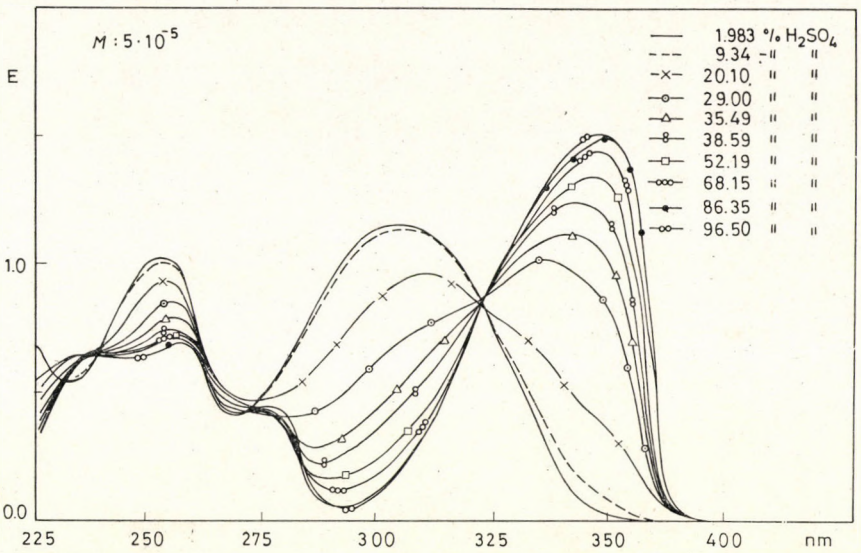


Fig. 3. Effect of the concentration of sulfuric acid on the spectrum of flavone ($5 \cdot 10^{-5}$ *M*)

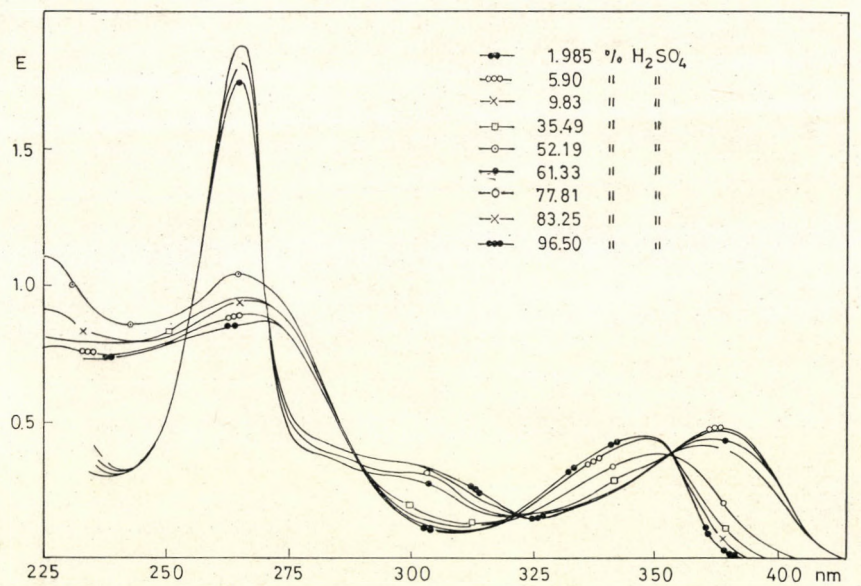


Fig. 4. Effect of the concentration of sulfuric acid on the spectrum of 1-thiaflavone ($5 \cdot 10^{-5}$ *M*)

When the extinction values read at a given wavelength on the curves that pass through the isosbestic point are plotted as a function of H_0, a so-called titration curve can be drawn. The H_0 pertinent to the bisection point (inflexion) of this curve gives the pK_{BH^+} value sought. The basicity constants thus calculated and the molar extinction values at the wavelengths used in these calculations are shown in Table III.

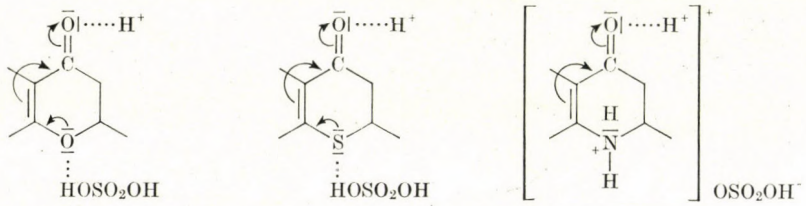
Discussion

According to the data in Table I replacement of the hetero oxygen in flavanone by sulfur or nitrogen causes a bathochromic shift of all the three bands as compared with flavanone, while the intensities change only slightly.

Most conspicuous are the bathochromic shift of band I and its broadening; this is due to increased participation of the non-bonding electrons of the hetero atom in conjugation. Substitution by S and NH causes a shift of +28 nm and +53 nm, respectively.

The changes in the spectra of the analogues of flavone are not so unequivocal. The 'two-band spectrum' can be found also here in every case, yet substitution produces not only a bathochromic shift, but also the intensity ratios are changed, thus spectra of different character are obtained. Substitution by S and NH causes a shift of only 48 nm and 36 nm, respectively, of band I, while the intensity of band II is more than doubled as compared with the intensity of band II of flavons.

A similar anomaly is observed as a result of substitution with NH, in the reactivity of the C = O group. Flavanone and thiaflavanone have relatively low basicity. 50% ionization is achieved with sulfuric acid concentrations as high as about 70%. This low basicity must be due — as suggested by the spectra taken in sulfuric acid, (Figs 1 and 2) — to solvatation of a non-bonding electron pair of the hetero atom in flavanone and 1-thiaflavanone, in addition to protonation of the C = O group. Accordingly, the spectra reveal the presence of two equilibrium systems, one of them corresponding to solvatation (lower H_2SO_4 concentrations), and the other to protonation of the C = O group higher concentrations:



a b c

According to Table III the proton affinity, *i.e.* the basicity, of the C = O group in the flavanone series changes in the sequence NH > S > O. The abnormally high basicity of the compound containing the NH group is conspicuous, and its explanation was found by a detailed study of the spectra. In contradistinction to the cases of flavanone and 1-thiaflavanone increasing concentrations of sulfuric acid did not cause a shift and higher intensity of band I (longer) wavelengths of 1-azaflavanone; on the contrary, the intensity

decreased, and in concentrated sulfuric acid the band completely dissappeared. (Fig. 5). This we ascribe to the circumstance that the protonated non-bonding electron pair of the nitrogen atom cannot participate in the conjugation (*c*). This supports our earlier view [3] according to which, and at variance with GAFFILD's [14] ORD and CD investigations, band I in all the flavanone analogues is an '*ortho* charge transfer' band. The pK_{BH+} values calculated from the intensity changes of band I and III thus reflect the protonation of the

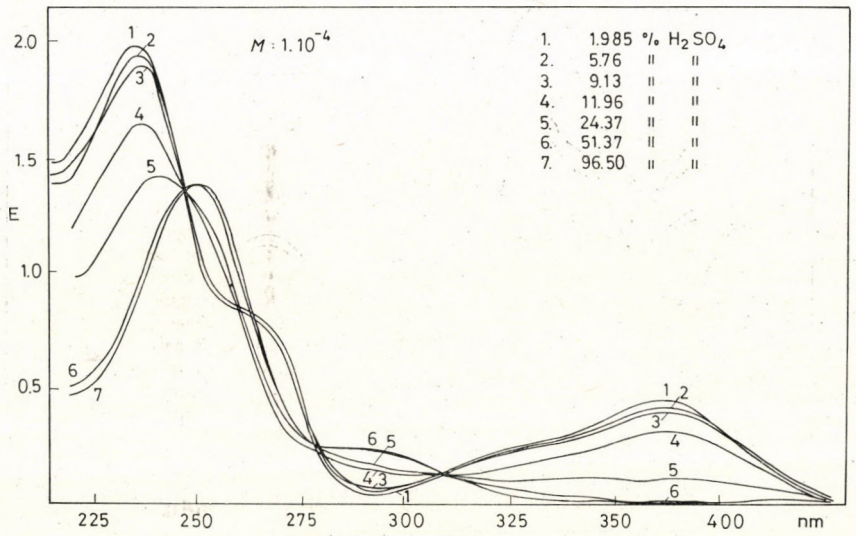


Fig. 5. Effect of the concentration of sulfuric acid on the spectrum of 1-azaflavanone ($1 \cdot 10^{-4}$ *M*)

NH group $pK_1 = -0.65$ instead of that of the C = O group, whereas $pK_2 = -6.75$ obtained from the intensity values of the 250 nm band gives the basicity of the C = O group.

The basicities of the compounds in the flavone series are much higher than those of the flavanone homologues, and this supports the idea of a quasi-aromatic character of the γ-pyrone and thiapyrone structures [13, 15]. This high basicity well represents the change in the energy state of the π-electron system during protonation. At the same time, no change in the spectrum of 1-azaflavone is detectable when the concentration of sulfuric acid is increased; in this way the basicity of this compound cannot be determined either.

Similarly negative results were obtained when the preparation of the 2,4-dinitrophenylhydrazone of 1-azaflavone was attempted. As shown in Table II, even 1-thiaflavone-DNPH could not be isolated, though an increase of its concentration in the course of kinetic measurements could be clearly

followed. Thus, in the case of derivatives which contain sulfur, the reaction rates in the flavone and flavonone series are as expected. The sulfur atom, owing to its electron donor character, increased the charge density on the carbon atom of the carbonyl group, therefore it decreased the rate of the proton-catalyzed nucleophilic reaction. In the case of 1-thiaflavone this rate-decreasing effect is so strong that, though the progress of the reaction can be detected

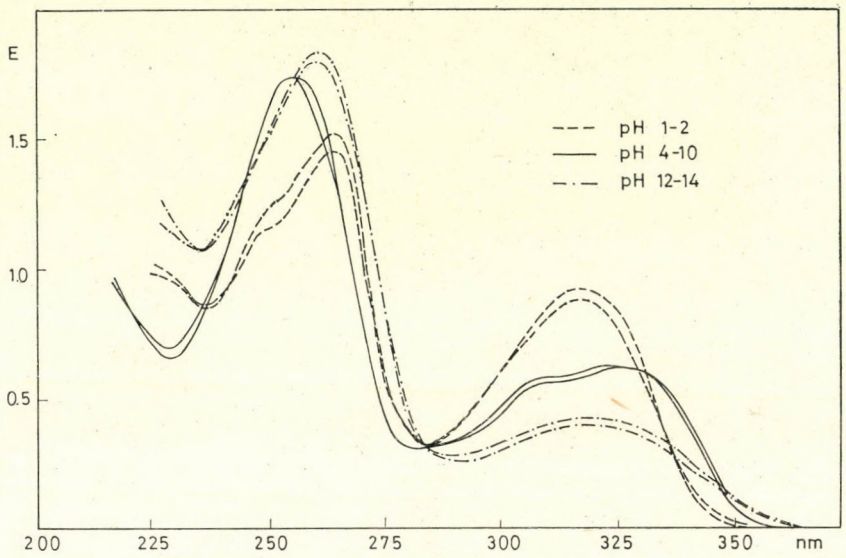


Fig. 6. Effect of pH on the spectrum of 1-azaflavone ($5 \cdot 10^{-5}$ *M*)

by spectroscopy, the reaction would require several weeks, therefore the calculation of its rate is not feasible.

In spite of its electron donor character, the NH group caused an increase of the rate of the reaction between 1-azaflavanone and 2,4-dinitrophenylhydrazine. This can be explained by the fact that in the proton-catalyzed reaction also the NH group is protonated, therefore the hetero atom plays no part, or has a positive role, during the hydrazone formation.

The same effect should be expected in the case of 1-azaflavone. Here, however, the formation of hydrazone was not detected either by preparative or by kinetic methods. Similarly negative results were obtained in every one of the usual colour tests for flavonoids, as well as in reactions used for the detection of the C = O group [11, 12, 13]. These negative experiments as well as irregularities in the basicity determinations and in the ultraviolet spectra taken in ethanol, prompted us to study, within narrow pH intervals, the pH-dependence of the spectrum of 1-azaflavone. As shown in Fig. 6, three pH

regions can be distinguished on the basis of these spectra, which obviously correspond to different structural forms. If the intensity measured at the λ_{max} points is plotted as a function of pH, the existence of these three states is quite conspicuous (Fig. 7).

All this and the negative results mentioned above support our view: the presence of the enolic tautomer form must be taken into consideration in these

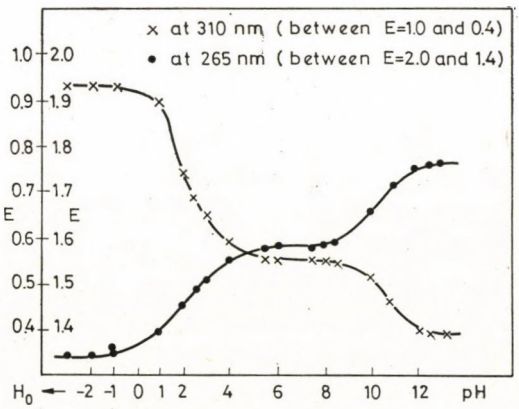
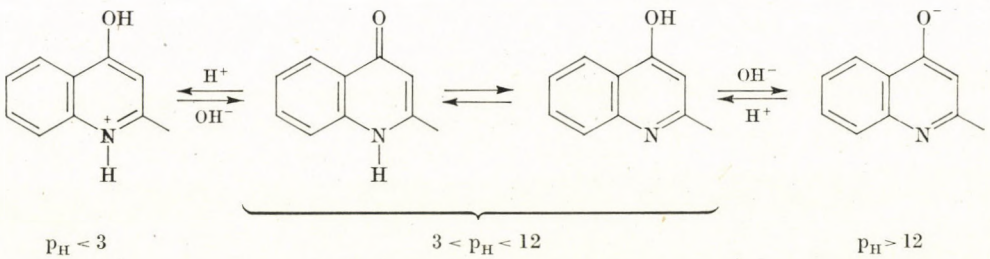


Fig. 7. Change of the intensity at λ_{max} 265 nm and 310 nm of the spectrum of 1-azaflavone as a function of the pH.

compounds, and the pH-dependent changes in the spectrum suggest the following structural transformation:



In Fig. 6 the curves drawn for pH 1 and pH 2 show the protonated BH^+ form, the curves for pH 3—12 are those of the enolic tautomer form, and the curves for pH 12 and pH 14 suggest dissociation of the enolic form. On the basis of the curves obtained in buffers, the basicity of the carbonyl group is +1.82, which is very high compared with the basicity of flavone. This high value explains the readiness for enolization.

REFERENCES

[1] DÁVID, É. R., RÁKOSI, M., BÁLINT, J., JANZSÓ, G. in "Absorption Spectra in the Ultraviolet and Visible Region" edited by L. Láng, Vol. I, 1961; Vol. IV, 1964; Vol. VII, 1966; Vol. XIX, 1974, Akadémiai Kiadó Budapest
[2] DÁVID, É. R., BOGNÁR, R.: Acta Chim. (Budapest) **84**, 335 (1975)
[3] DÁVID, R. É., LITKEI, GY., BOGNÁR, R.: Acta Univ. Phys. et Chim. Debr., **1971**, 215
[4] DÁVID, É. R., RÁKOSI, M., BÁLINT, J., BOGNÁR, R.: Acta Univ. Phys. et Chim. Debr., **1970**, 163
[5] TOLMACHEV, A. I., SHULESKHO, L. M., KISHILENKO, A. A.: Obschch. Him., **1968** 118,
[6] PAUL, M. A., LONG, F. A.: Chem. Rev., **57**, 1 (1957)
[7] ARNDT, F., FLAMMING, W., SCHOLZ, E., LESENSOHN, V.: Chem. Ber., **56**, 1268 (1923)
[8] MANNICH, C., DANNEHL, M.: Chem. Ber., **71**, 1899 (1938)
[9] FUSON, R. C., BURNESS, D. M.: J. Am. Chem. Soc., **68**, 1270 (1946)
[10] DAVIS, M. T., GEISSMAN, T. A.: J. Am. Chem. Soc., **76**, 3507 (1954)
[11] GEISSMAN, T. A.: The Chemistry of Flavonoid Compounds, Pergamon Press, Oxford 1962
[12] LÉGRÁDI, L.: Mikrochim. Acta **1967** (603)
[13] PATAI, S.: The Chemistry of the Carbonyl Group Interscience, John Wiley and Sons London 1966
[14] GAFFILD, W.: Tetrahedron **26**, 4013 (1970)
[15] ZAHRADNIK, R., PÁRKÁNYI, C., KOUTECKY, J.: Coll. Czechoslov. Chem. Commun. **27**, 1242 (1962)

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THE ACID-CATALYZED REARRANGEMENT OF THE N-NITRO DERIVATIVES OF 2-AMINOTHIAZOLE, II

MECHANISM OF THE REARRANGEMENT OF 2-THIAZOLYLNITRAMINES

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Concurrent rearrangements of 2-(N-methyl)-(^{15}N)-nitraminothiazole and 2-N-(D$_3$-methyl)-nitraminothiazole, as well as of 2-(N-methyl)-nitraminothiazole with natural isotope content and 2-(N-D$_3$-methyl)-(^{15}N)-nitraminothiazole have been studied. The results indicate a partially intermolecular, partially intramolecular mechanism of rearrangement of 2-thiazolylnitramines to give the corresponding 5-nitro derivatives.

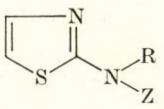
The detection of solvent and substrate isotope effects and general acid catalysis in the rearrangement of N-2-thiazolylnitramines [1] has shown that the rearrangement of these heteroaromatic nitramines, yielding the corresponding 5-nitro derivatives, involves a special mechanism different from that of the aromatic nitramine rearrangement. The present paper records the results of an investigation on the mechanism of the rearrangement of thiazolylnitramines.

The intra- or intermolecular character is one of the most interesting questions of aromatic rearrangements, thus also of the nitramine rearrangement. Recent investigations have shown [2] that for the aromatic nitramine rearrangement both inter- and intramolecular pathways can be claimed. Among the previous studies on the rearrangement of heteroaromatic nitramines in the pyridine series an intramolecular pathway was indicated in the presence of ^{15}N-labelled NO_2 ions [3]. Nitration of the added mesitylene [4], or taking the molecular distances into consideration [5] led the investigators to the conclusion that the nitramine rearrangement in the thiazole series was an intermolecular reaction.

However, recent investigations of aromatic rearrangements have shown that the above mentioned data are insufficient for decision of the intra- or intermolecular character. The ^{15}N labelling technique cannot be used as a criterion for distinguishing in this respect if the rate of an exchange reaction between the substrate and the labelled ion is far greater than that of the rearrangement [6]. On the other hand, nitration of the added scavenger is also attributable to electrophilic attack by the protonated substrate [7].

The question can be settled by concurrent rearrangements of two different derivatives of the same compound [2]. A requirement in using this method is that the rates of rearrangement of the two derivatives must be similar. For this reason, concurrent rearrangements of isotopic isomers of the same compound labelled in two different positions [8] can be expecially instructive. Therefore the $^{15}NO_2$- and/or CD_3-labelled analogues of 2-(N-methyl)-nitraminothiazole have been synthesized and rearranged concurrently. The compounds are listed in Table I.

Table I



	R	Z	Mol. wt.
1	CH_3	NO_2	159
2	H	$^{15}NO_2$	146
3	CH_3	$^{15}NO_2$	160
4	CD_3	$^{15}NO_2$	163
5	CD_3	NO_2	162

A purely intramolecular rearrangement of an equimolar mixture of **3** and **5** will not alter the distribution of the molecular weights, which can be well followed by MS, as the rearranged sample would also contain the components of mol. wt. 160 and 162 in 1 : 1 proportion. On the other hand if the NO_2 migration is only intermolecular, the components of mol. wt. 159, 160, 162 and 163 will be formed with equal probability. Thus the appearance of the components of mol. wt. 159 and 163 is characteristic of the intermolecular character of the process, and from their relative abundance the 'degree of intermolecularity' [2] can be concluded.

Similarly, in the course of the concurrent intramolecular rearrangement of an equimolar mixture of **1** and **4**, the distribution of the molecular weights would not change (159 : 193 = 1 : 1), whereas a pure intermolecular rearrangement process could produce the same distribution, as the above mentioned intermolecular reaction. Here the intermolecular character of the process and its degree can be detected by the appearance and relative abundance of the components of mol. wt. 160 and 162.

Experimental

2-(N-methyl)-nitraminothiazole (1)

This compound was prepared according to DICKEY *et al.* [5]; m. p. 269 °C (lit. m. p. 269 °C).

2-(^{15}N)-nitraminothiazole (2)

2-Aminothiazole (1.0 g; mmoles) was dissolved at +5—+10 °C in 1 ml of 96% sulfuric acid; to the solution there was added a solution of $K^{15}NO_3$ (1.03 g; 10 mmoles) and 96% sulfuric acid (1 ml). The solution was maintained at 0— —5 °C for 10 min and stirred with 1 ml of ethanol for 10 min. It was poured onto 5 g ice, the white crystals which separated were filtered off by suction, washed with water and dried to obtain 366 mg (2.5 mmoles) of the product m. p. 198 °C.

Dimethyl sulfate-D_6

2 ml of CD_3OD was added by drops into 4.64 (40 mmoles) of chlorosulfonic acid at —15 °C, then the mixture was fractionated. B. $p._{20}$: 124—126 °C. Yield: 1.92 g (14.5 mmoles).

2-(N-methyl)-(^{15}N)-nitraminothiazole (3)

2-(^{15}N)-nitraminothiazole (2) (182 mg; 1.25 mmole) was dissolved in a solution of 0.2 g (2 mmoles) Na_2CO_3 in 5 ml of water, then dimethyl sulfate (274 mg; 2.16 mmoles) was added by drops to the solution. It was then stirred for 2 hrs. After standing overnight it was filtered by suction, washed with water and dried over P_2O_5. Yield: 153 mg (0.96 mmole), white crystals, m. p. 268 °C.

2-(N-D_3-methyl)-(^{15}N)-nitraminothiazole (4)

2-(^{15}N)-Nitraminothiazole (182 mg; 1.25 mmole) was dissolved in a solution of 0.2 g (2 mmoles) Na_2CO_3 in 5 ml of water, then D_6-dimethyl sulfate (280 mg; 2.12 mmoles) was added dropwise into the solution. It was stirred for 2 hrs. After standing overnight it was filtered by suction, washed with water and dried over P_2O_5. Yield: 140 mg (0.86 mmole); m. p. 267 °C.

2-(N-D_3-methyl)-nitraminothiazole (5)

2-Nitraminothiazole (180 mg; 1.25 mmole) was dissolved in a solution of 0.2 g (2 mmoles) Na_2CO_3 in 5 ml of water, then D_6-dimethyl sulfate (280 mg; 2.12 mmoles) was added into the solution. After stirring 2 hrs, the mixture was kept overnight at room temperature. The white crystals which separated were filtered off, washed with water and dried over P_2O_5. Yield: 148 mg (0.92 mmole), m. p. 268 °C.

Concurrent rearrangements of (1) and (4), and of (3) and (5)

A mixture of the appropriate quantities (0.31 mmole) of the two nitramines was dissolved in 0.5 ml of 96% sulfuric acid at 0 °C, then the solution was thermostated to 25 ± 1 °C for 2 hrs. It was then pured onto 3 g of ice, and naturalized to pH 7 with a saturated solution of sodium carbonate. The yellow crystals were filtered off and recrystallized twice from glacial acetic acid.

Mass spectrometric measurements

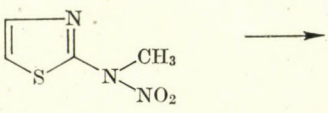
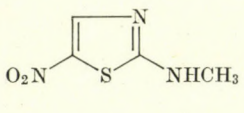
The mass spectra of the starting materials and those of the rearrangement products were obtained with an MH—1303 type, single-focussing mass spectrometer. In the experiments 50 eV ionizing electron energy and an ion accelerating potential of 2kV were used. The temperature of the ionization chamber was about 150 °C. A direct sample inlet technique was applied; the temperature of the sample holder was about 100—110 °C.

Results and discussion

The partial 50 eV mass spectra of the starting materials (**1**, **3**, **4**, **5**), the rearrangement product of **1** (compound **6**) and those of the compounds resulting from the concurrent rearrangements (**7**, **8**) are recorded in Table II.

Table II

Partial (50 eV) mass spectra of compounds 1, 3, 4 and 5 and the rearrangement products (6, 7, 8)

Compounds	Ionic abudances, %							Type of ions
								
	1	**3** ($^{15}NO_2$)	**5** (CD_3)	(CD_3, $4^{15}NO_2$)	**6** (from 1*)	**7** (from 1±4)	**8** (from 3+5)	
Mol. wt.	159	160	162	163	159	159—163	159—163	
165				2.5		1.3	1.1	
164			2.9	3.2		2.9	1.7	
163			3.8	48.1		29.9	14.2	
162		2.5	53.4	2.9		15.8	35.3	M^+
161	2.5	3.1	2.0		4.6	3.2	3.5	
160	3.1	45.3			5.5	14.5	30.5	
159	46.4	2.3			90.1	31.1	14.1	
m/e								
118			5.0	5.2		1.1	1.0	
117			7.1	7.5		1.5	1.4	
116			100.0	100.0		21.5	21.4	$(M-NO_2)^+$
115	4.9	5.7	4.5	3.5	2.8	3.3	3.4	
114	6.4	7.0			3.7	2.1	1.9	
113	100.0	100.0			51.3	22.5	23.5	

* See Ref. [5]

Taking the natural isotope abudance into account, it can be established from the spectra that the deuterium content in CD_3 group is about 98.8—99% and the ^{15}N label of the NO_2 group is about 96%. The intensity of the peaks given for the N-nitro compounds is expressed in percentage of the total ion current of the $(M-NO_2)^+$ type ions. For the peaks of the rearranged samples the abundances are given in percentage of the total abundance of the molecular ions with different *m/e* ratios. The $M^+/(M-NO_2)^+$ abundance ratio is about 0.5 for the starting N-nitro compound and is about 1.8 for the rearranged

products. This difference is due to the lower stability of the molecular ions of the former isomers and gives an opportunity to follow the progress of the rearrangement reaction. It can be established that both samples (**7** and **8**) contain products characteristic of intermolecular rearrangement, but their abundance is less than that of the compounds having molecular weights which correspond to the starting material. Thus the rearrangement shows a mixed, partially infra- and partially intermolecular character.

Table III shows the calculated ionic abundances arisen if the concurrent rearrangement of **3** and **5** would be only inter- or intramolecular, finally for the case when the proportion of the frequency of the intra- or intermolecular reaction is 1 : 1. As Table III shows, this last calculated ratio approaches well the measured values.

Table III

Study of the intra- or intermolecular character of the rearrangement on the basis of mass shifts in the mass spectrum of compound 8

m/e	Ionic abundance, %			
	Measured	Calculated		
		intramol.	intermol.	intra : inter = 1:1
165	1.1		1.1	1.1
164	1.7	2.3	2.6	2.5
163	14.2	3.1	22.7	13.0
162	35.3	45.3	23.9	35.0
161	3.5	4.5	3.5	3.8
160	30.5	42.6	22.8	33.0
159	14.1	2.16	22.3	13.0

The abundance ratio measured for the concurrent, rearrangement producing **7** from **1** + **4** can also be well approached by supposing the equal frequency of the intra- and intermolecular rearrangements. Thus the degree of intermolecularity for the rearrangement of 2-(N-methyl)-nitraminothiazole is about 50%.

The partial intramolecular mechanism of the reaction can be interpreted similarly to the case of N-methyl-N-nitroaniline derivatives [2]. Thus the intramolecular part of the rearrangement takes place within a solvate cage, by direct collapse of the protonated aminothiazolyl- and nitronium-fragments, while dissociation and later recombination of these fragments results in the intermolecular portion of the rearrangement.

*

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REFERENCES

[1] NEMES, A., TÓTH, G.: Acta Chim. (Budapest) (In press)
[2] WHITE, W. N., GOLDEN, T. T.: J. Org. Chem., **35**, 2759 (1970)
[3] GELLER, B. A., SAMSVAT, L. S.: Zh. Obsch. Khim., **34**, 613 (1964)
[4] KASMAN, S., TAURINS, A.: Can. J. Chem., **34**, 1261 (1956)
[5] DICKEY, J. B., TOWNE, E. B., WRIGHT, G. F.: J. Org. Chem., **20**, 499 (1955)
[6] MORGAN, T. D. B., WILLIAMS, D. L. H.:, J. Chem., Soc. Perkin II **1972**, 74
[7] BANTHORPE, D. V.: in the "Chemistry of the Amino Group" (E. D. G. Patai), p. 639. Interscience Publ., New York 1968
[8] TÓTH, G., TOLDY, L., TAMÁS, J., ZÓLYOMI, G.: Tetrahedron, **28**, 167 (1972)

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RECENSIONES

Extraction Chromatography

Edited by T. BRAUN, and G. GHERSINI. Journal of Chromatography Library; Volume 2 (pp. 566, 629 references). Akadémiai Kiadó, Budapest 1975

The actual research profile of a scientific or an operational domain cannot be always deduced ethymologically from its designation. Itself an historical survival of pioneer days, the word 'chromatography' was restricted once to the separation of coloured organic substances. On the other hand, the name 'extraction chromatography' looks like a synonym of the term 'partition chromatography' used since about 30 years; in fact, it is used for the designation of a much narrower field, *viz.* of inorganic ion analyses by reversed phase partition chromatography. Here also the cause is to be found in an evolutionary process; it was not the professional scientists of partition chromatography who have expanded their study to include inorganic ions but rather the 'extraction analysis' of inorganic analysts has taken advantage of the excellent possibilities offered by the chromatographic column; thus the method has become known in the literature under the name 'extraction chromatography' and is the chromatographic variant of inorganic analysis by extraction.

This we felt appropriate to explain by way of introduction because the work to be reviewed offers much more than the 'explained' designation suggests: but those who — based upon a word for word evaluation of the title — expect a comprehensive discussion of the correlations of liquid–liquid extrcation and chromatography will not be disappointed either.

Chapters 1—5, and 13—15, about 70% of the book, will be of interest for every expert in chromatography. Chapters 6, 11, and 12 deserve the attention of many inorganic analysts; the remaining 15% of the book deals with special topics: analytical problems concerning the actinides, the lanthanides, fission products and radio-toxicology.

Already in the first chapter a very laudable feature of this book leaps to the eye. Beyond the mere deduction of theoretical relationships, a very careful analysis of the significance of the parameters, and of the influence of the constants involved in the formulae is given, notably of the influence exerted upon the numerical value of the quantity characterized by the formula. It draws attention to factors that cause a significant change only when extreme experimental conditions prevail while within a precisely circumscribed set of experiments they can be left out of consideration. Such a discussion method, which transcends the qualitative presentation of the correlations, requires the knowledge of the numerical values of the physical constants involved in the equations. The various chapters of this work are unusually abundance in information of this kind. For data not included in the relevant Tables, references to the literature are given; finally, if no notice of the experimental determination of some factor has been published up to the time the book went to press, the authors draw special attention to such a deficiency. — Incidentally, in the first chapter a very clear and expert presentation is given of the changes in thermodynamic activities due to the special circumstances preyailing in a chromatographic column and of the dynamic factors of the chromatographic process.

The first half of the second chapter shows the classical mathematical approach to the chromatographic operation proceeding *via* assumed static, theoretical plates of equilibria. For the reader who now enters this field the first time it will be, perhaps, a bit inconvenient that the interpretation of the theoretical number of plates is left to the second chapter, yet the numerical value of the "HETP" and the static and dynamic factors which affect it are mentioned in the first chapter already. — The second half deals with the striking analogies of inorganic 'extraction analysis' and extraction chromatography, and with the practical possibilities of an exchange of information made possible by these analogies.

From a general view of chromatography, the third chapter is a very wealth of informations on useful techniques, devices and formulae. All the tricks can be learnt from this

chapter of what chromatographers call the art of column packing. The methods of how to standardize the support material, the approved methods of how to apply the stationary phase, the selection of optimum overall dimensions of the column and optimum parameters for its operation are described, and in a manner made very informative by figures and tables.

The fourth and the fifth chapters describe, first generally then in detail the stationary parts of the device, *i. e.* the support material and the extractants on it. In our opinion, this sequence would have been didactically preferable to the one in the book, *i. e.* stationary phase, then support material, for the discussion of the role of these two. Otherwise, these chapters give a faultless exposition of the theme.

In an imposing manner the sixth chapter evidences that nowadays for nearly every column in the Periodic Table, from the alkalies to the halogens, an extraction chromatographic technique has been elaborated for the separation of the elements in the group. Perhaps the authors should have given in this chapter a more detailed description of the preparation samples and of the detection of the various elements (ions), since with these details added, a wider public would have been Table to critically evaluate the complete chain of analytical steps, *i. e.* sample preparation, chromatography, detection and measurement, and to compare this technique with other, traditional or novel, analytical methods. As pointed out in the book, its eleventh chapter is, actually, related to the theme of the fourth, yet presents in itself a full picture of the equilibrium and dynamic aspects of the formation of metal chelates, of their partition in solvents, and of the chromatographic utilization of this partition. The chapters which discuss the enrichment of trace impurities by a factor of up to 10^6, or those which inform about redox reactions performed on a chromatographic column, all merit the attention of analysts in general, while the studies described in the last chapters on the use of closed-cell or permeable solid synthetic foams as supports, on the control of a pulsating flow of the eluent, and on generally valid theoretical and practical relationships between laminar (paper, thin-layer)- and column-chromatography embody valuable progress in chromatographic science as a whole.

In connection with the generally well balanced edition of this book some critical remarks might be appropriate. The reader misses the harmony of the various nomenclatures used in the individual chapters and a uniform list and explanation of the symbols since this would have prevented writing the same correlation, *e. g.* for the number of theoretical steps, differently in the various chapters; at the same time a given letter, *e. g.* the Greek beta denotes various concepts in various chapters. Also the volume of the work is unnecessarily enlarged by repeated definition, and symbolization of concepts. It would have been well to use a uniform notation of the valence of metal ions: calcium is $Ca^{2}+$. Ca(II). or even Ca: this last form, without the charge given, leads to the formula, to be seen on p. 98, bordering on the incorrect, *viz.* $Ca < NH_4$.

The typographical aspect of the book conforms to the puritanic forms now very much in vogue. This seems to be an unavoidable prerequisite of speedy production and tolarable price. Even so, perhaps by the more frequent utilization of italics, some typographical variety and better arrangement might have been attained. There are very few typographical errors, and only one of them that on p. 17, distorts the sense: in the term $[B]_{org}/[B]_{aq}$ the slash is missing, thus K seems to be the product and not the quotient of the two concentrations. The text is easy to read, line drawings, and tables are clearly printed and yield maximum information.

The book adds valuable knowledge, a host of numerical data and correlations to our chromatographic experience, thus helps the planning, control, and evaluation of tests, by numerical calculation. Neither are valuable hints lacking on how operations might be best carried out in practice; also the description of the substances used is nearly complete in the various chapters.

This thorough introduction to extraction chromatography offers new possibilities for a broad public of inorganic analytical chemists; scientists in some special fields are spared the pains of collecting the vast, and often hardly accessible literature. Finally, its clear, smooth style should also be mentioned in praise of this book.

A. USKERT

Topics in Current Chemistry, Vol. 53, Gas-Phase Electron Diffraction

Springer Verlag, Berlin—Heidelberg—New York 1975

This book is an excellent appraisal for the electron diffraction method as a modern and efficient tool in structural chemistry as it presents an abundance of interesting and well-organized structural information collected by this technique. In fact, the title of the volume is somewhat unfortunate and not informative enough since it is the results and not the technique that are described and discussed.

The volume consists of three independent chapters that are connected by the expertise of the authors in the fields reviewed and their successful attempts to look for empirical trends in the compound series discussed. The three chapters are the following.

Arne HAALAND: *Organometallic Compounds Studied by Gas-Phase Electron Diffraction*, pp. 1—23 (with 114 references, 2 Tables, 11 Figures)

As stated by the author, selected groups of compounds are dealt with in the Chapter and the emerging structural patterns are discussed in terms of simple molecular orbital theory, the valence shell electron pair repulsion model and nonbond interactions. The compounds of beryllium, magnesium, boron, and aluminium, cyclopentadienyl derivatives of other main-group elements, and also of the transition elements are considered. In addition to presenting the structutal information gained by electron diffraction (and originating primarily from the Oslo school), correlation is sought and shown between the electron diffraction results and information from other techniques including theoretical calculations, and also between structural and physical-chemical properties.

Lev VILKOV and L. S. KHAIKIN: *Stereochemistry of Compounds Containing Bonds between Si, P, S, Cl and N or O*, pp. 25—70 (with 234 references, 28 Tables, 12 Figures)*

The stereochemistry of a very large class of compounds is covered, *viz.* molecules with Si—N, P—N, S—N, Cl—N, Si—O, P—O, S—O, Cl—O bonds. The unique character of the structural properties of these compounds originates from what is interpreted to be $d\pi-p\pi$ interactions between the third row and second row elements.

Apparently all the data on gas-phase molecular geometry obtained by either electron diffraction or microwave spectroscopy, and published to date, are collected. A concise presentation of the main structural results on the basis of the original papers is given. The authors successfully aim at classifying and generalizing the available data in terms of the classical structural theory rather than presenting arguments in favour of one or the other of the current theories. The Chapter is concluded by a short discussion dealing with some interesting stereochemical patterns shown by the bond angles at three-coordinate nitrogen and two-coordinate oxygen. Some variations in the bond distances are also considered.

Akimichi YOKOZEKI and Simon H. BAUER: *The Geometric and Dynamic Structures of Fluorocarbons and Related Compounds*, pp. 71—119 (with 313 references, 26 Tables, 15 Figures)

Gas-phase structural data on fluorocarbons and related compounds are collected and discussed focusing attention to the effects of fluorine for hydrogen substitution in hydrocarbons and related substances.

After a short review of fluorine for hydrogen substitution effects in di- and triatomic species, a survey of C—F bonds, which have been investigated, is given. The effect of fluorine for hydrogen substitution on the rest of the molecule is also examined in detail. Special attention is paid to the important phenomena of intramolecular motions and related internal rotations about single bonds. Comments on selected inorganic fluorides conclude the Chapter.

One is surprised by the abundance of structural data on C—F bonds, and also, as a result of the authors' careful work, which apparently was an investigation on its own, by the abundance of interesting patterns and correlations that emerge as the changes in the number of fluorine atoms attached to the central carbon atom, the carbon hybridization state and environmental factors are examined.

The editors and the publisher have to be congratulated for compiling this volume of authoritative, critical and interesting reviews of very rapidly developing areas of structural chemistry and for publishing it with a speed that favourably compares with journal articles.

I. HARGITTAI

* A more consistent way of putting the authors' name would have been, *e. g.* Lev V. VILKOV and Leonid S. KHAIKIN.

INDEX

PHYSICAL AND INORGANIC CHEMISTRY

ORGANIC CHEMISTRY

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РЕЗЮМЕ

Симуляция процесса зонного плавления с помощью ЭВМ на основе его математической модели

Э. БРАНДТ-ПЕТРИК, Л. ЧЕР и Й. НАДЬ

Зонное плавление было использовано для очистки органических жидкостей. Используя пробные данные, была произведена простая симуляция зонного плавления. Метод позволяет предсказать вероятную эффективность дальнейших экспериментов.

Реакция октанов и пропана с водяным паром на никелевом катализаторе с носителем под давлением 1 атм

Г. ТРАПЛИ, ДЬ. ПАРЛАГ, ДЬ. РАЦ, П. ШТЕЙНГАСНЕР и ДЬ. СЕКЕЙ

Реакцией, определяющей скорость процесса разложения пропана, н-октана и изооктана с помощью водяного пара на никелевом катализаторе с носителем окиси алюминия, является реакция углеводорода с водяным паром. При различных конверсиях углеводородов между продуктами реакции и непрореагировавшим водяным паром устанавливается равновесие.

В экспериментах, проведенных на катализаторах с носителем силиката магния, состав газовых продуктов лишь в таких условиях соответствовал равновесному составу, при которых образованием метана практически можно пренебречь. Во всех других случаях, как для октанов, так и для пропана, при разложении их водяным паром на катализаторе, образуется гораздо больше — по сравнению с равновесными величинами — двуокиси углерода, водорода и гораздо меньше метана.

Среди продуктов реакции, до определенной температуры, при различных степенях конверсии не было найдено соединения, содержащего более одного атома углерода. Т. о., нормальные и изопарафиновые углеводороды с длинной или короткой цепочкой, попадая на поверхность катализатора, удаляются с нее лишь в совершенно расщепленном состоянии, в виде соединения, содержащего единственный атом углерода.

Образование продуктов из исследованных углеводородов при 450°C протекает с одинаковой скоростью, и поэтому полагается, что на основе скоростей, измеренных на модельных соединениях, можно судить о скоростях реакций водяного пара со смесями углеводородов.

Реакция н-гексана с водяным паром на никелевом катализаторе с носителем при давлении 1 атм

Г. ТРАПЛИ, ДЬ. ПАРЛАГ, ДЬ. РАЦ, П. ШТЕЙНГАСНЕР и ДЬ. СЕКЕЙ

На основе экспериментальных данных было установлено, что на изученном катализаторе — независимо от размера зерен — в исследованном интервале температур и конверсий, состав продуктов реакции, образующихся при разложении н-гексана с помощью водяного пара, соответствует равновесному составу, рассматривая неразложенный гексан в качестве разбавляющего газа.

Среди продуктов реакции, помимо метана, не были найдены соединения с числом углеродных атомов, меньшим чем в н-гексане, исключая крекинг, протекающий только при повышенных температурах, выше 570°C.

Ненасыщенные и ароматические углеводороды не оказывают влияния на работу катализаторов.

Соединения олова(IV) с шиффовыми основаниями, образованными из пентан-2,4-диона и аминоспиртов

О. П. СИНГ и ДЖ. П. ТАНДОН

Реакции хлорида олова(IV) с шиффовыми основаниями с общей формулой CH_3C-(OH) : $CHC(CH_3)$: NROH (где R = $-(CH_2)_2$-, $-CH_2-CH(CH_3)$-, $-(CH_2)_3$- и $-CH(C_2H_5)-CH_2$-) были исследованы, используя различные стехиометрические соотношения компонентов. Результатующие продукты $SnCl_4$. SBH_2 и $SnCl_4(SBH_2)_2$ (где SBH_2 представляет молекулы шиффового основания) были изолированы с почти количественными выходами. На основе результатов элементарного анализа, ИК спектров и кондуктометрических измерений предлагаются некоторые вероятные структуры.

О кинетических уравнениях многостадийных электродных процессов, II

Л. КИШ и Л. М. ВАРШАНИ

Было выведено и рассмотрено уравнение кривой поляризации для многостадийной ионизации металлов и восстановления металлических ионов, для такого случая, когда раствор содержит комплексообразующие компоненты. На кинетику процесса влияют все последовательные стадии, среди которых имеются электрохимические и химические реакции, а также диффузия конечного продукта ионизации. Были определены кинетические параметры, получающиеся в случае одной замедленной стадии.

ИК спектрофотометрическое исследование реакции конденсации алкоксисиланов с хлорсиланами, I

Применение метода ИК для анализа реакционной смеси

Э. МАТРАИ и Ш. ДОБОШ

На основе ИК спектрофотометрии был разработан аналитический метод определения всех компонентов в реакции конденсации, протекающей между диметилдихлорсиланом и диметилдиэтоксисиланом, диметил-ди-н-пропоксисиланом, а также диметил-ди-втор-бутоксисиланом. Были сняты спектры чистых компонентов, ожидаемых в ходе реакции, а также их соответствующих смесей. Были выбраны полосы поглощения, пригодные для аналитических целей, которые и были охарактеризованы для количественных измерений.

ИК спектрофотометрическое исследование реакции конденсации алкоксисиланов с хлорсиланами, II

Реакция конденсации диметилдихлорсилана с диметил-ди-втор-бутоксисиланом

Э. МАТРАИ, Ш. ДОБОШ и Т. СЕКЕИ

Была исследована конденсация диметилдихлорсилана с диметил-ди-втор-бутоксисиланом, катализированная $FeCl_3$. За процессом следили с помощью ИК спектрофотометрии. Результаты указывают на то, что реакция протекает в двух ступенях. На первой ступени происходит очень быстрый обмен радикалов между бифункциональным алкоксисиланом и хлорсиланом, который приводит к образованию диметилалкоксихлорсилана. Это соединение представляет собой исходный мономер для следующей ступени конденсации. Было установлено, что конденсация является необратимой реакцией. Практически не протекает других побочных реакций.

Синтез некоторых производных N-салицилсульфонил-аминокислот, II

А. М. ЭЛЬ-НАГГАР и М. М. ГААФАР

Был описан синтез N(3-карбокси-4-гидроксифенилсульфонил) Gly и соответствующих производных Ser, Tyr и Orn (II—V), а также их О-ацетил, карбометокси и некоторых гидразидных производных (VI—XVII). Было найдено, что соединения III, IV, VII и VIII являются активными против многих микроорганизмов.

Синтез производных олиго-β-L-аспарагиновой кислоты

М. КАЙТАР, М. ХОЛЛОШИ и Ж. РЕЙДЛ

Описывается синтез производных олиго-β-L-аспарагиновой кислоты (Ia, b) с числом остатков аспарагиновой кислоты до шести. Бензилоксикарбонильная и *трет*-бутилэфирная группы были использованы для защиты амино и карбоксильных групп, соответственно. Пептидные связи были образованы с помощью дициклогексилкарбодиимидного метода. Колонная хроматография на силикагеле была использована для очистки блокированных пептидов с остатками аспарагиновой кислоты от 4 до 6 (IVc—e). Свободные олигопептиды (VIIa—e) были приготовлены обработкой трифторуксусной кислотой с последующим каталитическим гидрированием. Блокированные производные (IVa—e) были охарактеризованы с помощью ТСХ. Чистота свободных олиго-β-L-аспарагиновых кислот контролировалась с помощью ТСХ и высоковольтного бумажного электрофореза.

Оксазепины и тиазепины, II

Получение 2,3-дигидро-2,4-дифенил-1,5-бензотиазепинов на основе реакции взаимодействия 2-аминотиофенола с «B» кольцом замещенных халконов

А. ЛЕВАИ и Р. БОГНАР

Была исследована реакция взаимодействия 16 халконов, замещенных различным образом в «B» кольце (I—XVI), с 2-аминотиофенолом, протекающая в абсолютном толуольном растворе. Было установлено, что в данных условиях реакции в большинстве случаев (I—X) образуется смесь β-фенил-β-(2-аминофенилмеркапто)-пропиофенонов (XVII—XXVI), в двух случаях (XI, XII) соответствующих пропиофенонов (XXVII, XXVIII), с производными 2,3-дигидро-2,4-дифенил-1,5-бензотиазепина (XXXIX, XL). При наличии сильных электроноакцепторных заместителей (XIII—XVI) образуются 1,5-бензотиазепины (XLI, XLIV). β-Фенил-β-(2-аминофенилмеркапто)-пропиофеноны (XVII—XXVIII) в абс. метанольном растворе и в присутствии уксусной кислоты, как катализатора, при кипячении превращаются в 2,3-дигидро-2,4-дифенил-1,5-бензотиазепины (XXIX—XL).

Исследование реакционной способности карбонильной группы флавоноидных соединений, II

Основность флавонных и флаванонных аналогов

Р. Е. ДАВИД, Г. ЯНЖО, Й. БАЛИНТ и Р. БОГНАР

Были определены основность карбонильной группы 1-тиа- и 1-азафлавонов и флаванонов, а также скорость образования (2,4-динитрофенил)-гидразона. В изученных соединениях основность карбонильной группы увеличивается в следующем порядке $O < S < NH$, в то время как азот 1-азафлаванона, вследствие первичной протонизации уменьшает основность карбонильной группы. Скорость образования (2,4-динитрофенил)-гидразона, в свою очередь, уменьшается в следующем порядке $O > S > NH$, а в случае 1-азафлавона, из-за присутствия энольной таутомерной формы, образование фенилгидразона в протоннокатализированной реакции вообще и не протекает.

Перегруппировка N-нитропроизводных 2-аминотиазоля, катализированная кислотами, II

Исследование характера перегруппировки 2-тиазолил нитраминов

Г. ТОТ, А. НЕМЕШ, Й. ТАМАШ и Й. ВОЛЬФОРД

Была исследована конкурирующая перегруппировка 2-(N-метил)-(N^{15})-нитраминотиазоля и 2-N-(D_3-метил)-нитраминотиазоля, а также 2-(N-метил)-нитраминотиазоля с природным содержанием изотопа и 2-(N-D_3-метил)-(N^{15})-нитраминотиазоля. Результаты указывают на частично интермолекулярный и частично интрамолекулярный механизм перегруппировки 2-тиазолил нитраминов, приводящий к образованию 5-нитропроизводных.

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GAS CHROMATOGRAPHIC ANALYSIS OF A MIXTURE OF N_2, CO, CO_2, Cl_2, HCl AND $COCl_2$ USING A GAS DENSITY BALANCE DETECTOR

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Received June 17, 1974

Separation of the title compounds by injecting two samples on two columns is reported. Separation and detector conditions required by the corrosive nature of the mixture are discussed.

Introduction

During the reductive chlorination of alumina containing ores, metal chlorides as $AlCl_3$, $SiCl_4$ and $FeCl_3$ are retained in a cold trap. The effluent gas after the cold trap is usually a mixture of nitrogen, carbon dioxide, hydrogen chloride, chlorine and phosgene.

According to our present knowledge the complete separation of this mixture on a single column at ambient or higher temperatures is impossible. For the separation of a similar gas mixture H. RUNGE used [1] a 9 m long column packed with 5% Aroclor 1232 on Haloport F. No separation was obtained for N_2 and CO, separation for (N_2 + CO) and CO_2 and for CO_2 and HCl resp. was rather poor even on this extremely long column.

The method proposed by P. K. BASU *et al.* [2] has utilized three columns and three detectors in series for the separation and quantitative determination of argon, nitrogen, carbon monoxide, carbon dioxide, chlorine and phosgene.

The first column contained 15% Kel F on a PTFE packing. Argon, nitrogen, carbon monoxide, and carbon dioxide were eluted as one combined peak while chlorine and phosgene were separated. The gases eluted from the first column passed on to the second column which was packed with silica gel and gave a combined peak of argon, nitrogen and carbon monoxide and separated peaks for carbon dioxide and chlorine. The argon, nitrogen and carbon monoxide were then separated by the third column.

The method recommended here for the separation of the title compounds requires two injections into two columns from each gaseous sample and the chromatograms are detected and recorded separately.

The analytical method reported utilizes a gas density balance detector in order to avoid filament corrosion by Cl_2 and especially by HCl. The GDB detec-

tor enables further the quantitative evaluation of the chromatogram without any calibration procedure. Details of the quantitation of the chromatogram are not included in this paper.

Experimental

Analyses were performed on a Carlo Erba Model C gas chromatograph, modified according to Fig. 1. Pressure regulator, gas sampler, and column switching valve were Carlo Erba products, while gas density balance detector was a Gow Mac Model 11—625 coupled to the TC power supply of the apparatus. The filament current in the detector was 185 mA.

Separation conditions and their discussion

Informations on the separation are given in Table I.

The mixture was injected first to column *A*. When the chromatogram has been recorded, the carrier gas was directed to column *B* and a second injection was performed.

Table I

	Column *A*	Column *B*
Column material	PTFE tubing	PTFE tubing
Length × ID	3m × 4 mm	4.3 m × 4 mm
Support material	Chromosorb WAW	
Stationary phase	240 cm length Aroclor 1232, 20% and 60 cm length nitrobenzene 20% in series	Porapak R
Column temperature	ambient	ambient
Carrier gas	H_2–N_2 mixture; volume ratio 1 : 1	H_2–N_2 mixture; volume ratio 1 : 1
Flow rate; measuring	70 ml/min	70 ml/min
reference	140 ml/min	140 ml/min
Separated:	(N_2 + CO + CO_2); HCl, Cl_2; $COCl_2$	N_2; CO; CO_2
Irreversibly retained	—	HCl; Cl_2; $COCl_2$

A highly inert support material, preferably PTFE is recommended in the literature for the gas chromatography of chlorine and hydrogen chloride [1, 2]. Successful use of a diatomaceous earth support was also reported [3]. According to our experiments the symmetry of the chlorine and hydrogen chloride peaks was approximately the same on a heavily loaded Chromosorb W (acid washed) support and on a lightly loaded Haloport F (PTFE) support. As powdered PTFE is soft and difficult to pack properly into the column, Chromosorb WAW was chosen.

The best separation for (N_2 + CO + CO_2)–hydrogen chloride-chlorine at ambient temperature was achieved with Aroclor 1232 and nitrobenzene as the stationary phases. However, on the former the separation of the (N_2 + + CO + CO_2)–hydrogen chloride, while on the latter that of hydrogen chloride–chlorine was rather poor. Mixing the two phases, separation could be optimized. On the basis of the additivity of adjusted retention data while mixing the phases, the relative length of column sections packed with nitrobenzene and Aroclor respectively — required for the optimum separation — were calculated.

The separation of nitrogen and carbon monoxide on Porapak R is not complete at room temperature even on a 430 cm long column. To achieve complete separation, 0 °C column temperature is needed.

The choice of the carrier gas is crucial point for the method if a GDB detector is used. The detector demands the use of a carrier gas having considerably different MW compared to the compounds to be detected. Therefore the use of conventional carrier gases, as nitrogen (MW: 28) and argon (MW: 40) should be excluded. (MW_{CO}: 28; MW_{CO_2}: 44 and MW_{HCl}: 36.5).

From the operating principles of the GDB [4] it comes further, that the optimum carrier gas flow rate for hydrogen and for helium is 300 ml/min and for Freon 1.2 (MW: 121) 5 ml/min. Both the extremely high and extremely low gas velocities are disadventageous for the separation. A hydrogen–nitrogen gas mixture proved to be a satisfactory carrier gas in both respects.

Because of the corrosive nature and the water solubility of chlorine and hydrogen chloride a thoroughly dry system is needed for the analysis. Besides the drier tubes indicated in Fig. 1, traces of water were to be removed from time to time by injecting $SiCl_4$ into column *A*. This was especially important, when small amounts of hydrogen chloride were to be detected. Besides there was also a column conditioning effect with hydrogen chloride. Several hydrogen chloride injections (some hundred microliters) were required each day before consistent quantitative values were obtained.

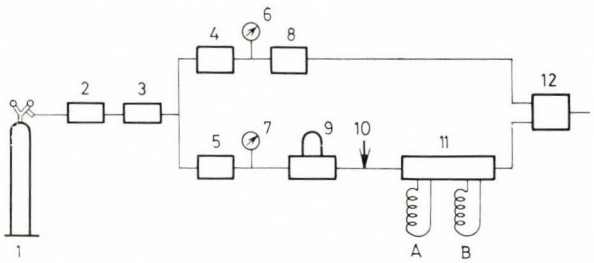

Fig. 1. Block diagram of the gas chromatograph used. 1: Carrier gas supply; 2: drier tube filled with 5 A molecular sieve; 3: drier tube filled with Sicapent; 4,5: pressure regulators; 6,7: manometers; 8: flow regulator; 9: gas sampling valve; 10: sample injection port; 11: column switching valve, *A*, *B* Columns; 12: GDB detector

Results

Fig. 2*a* shows typical chromatogram of a 0.9 ml sample containing nitrogen, carbon monoxide, carbon dioxide, hydrogen chloride, chlorine and phosgene on the Aroclor–nitrobenzene column. In Fig. 2*b* the chromatogram of nitrogen, carbon monoxide and carbon dioxide on the Porapak column at ambient temperature is demonstrated.

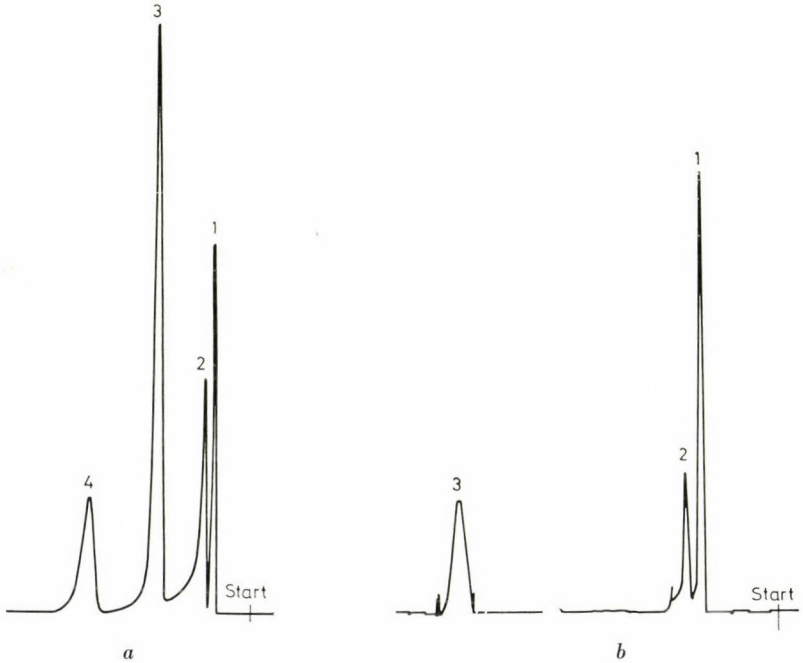

Fig. 2. a) Chromagotram on column *A:* 1. N_2 + CO + CO_2, 2. HCl, 3. Cl_2, 4. $COCl_2$. *b)* Chromatogram on column *B:* 1. N_2, 2. CO, 3. CO_2. Sample volume: 0.9 ml; temperature: ambient; carrier gas: 70 ml/min

Table II

Substance	Column	Elution time (min)
N_2 + CO + CO_2	*A*	0.9
HCl	*A*	1.2
Cl_2	*A*	2.3
$COCl_2$	*A*	4.1
N_2	*B*	1.2
CO	*B*	2.3
CO_2	*B*	8.3

After the injection of approximately 50 Cl_2-containing samples, no deterioration of the Porapak column was observed.

Oxigen and carbon monoxide if both were present would interfere with one another. However, oxygen is quite unlikely to be present in the product gases of a reductive chlorination.

Table II shows the elution times observed for the different components.

The relative amounts of the nitrogen, carbon monoxide and carbon dioxide were calculated from the chromatogram on column *B*. This information enabled the quantitative evaluation of the chromatogram on column *A*.

The same separation could have been performed with one injection only if two columns and two detectors had been connected in series. However, in this case GDB should have been avoided and two TC-s to be used.

The authors thank Mr. F. TILL for his valuable technical help.

REFERENCES

[1] RUNGE, H.: Z. Anal. Chem. **189,** 111 (1962)
[2] BASU, P. K., KING, C. J., LYNN, S.: J. Chrom. Sci., **10,** 479 (1972)
[3] RUTHVEN, D. M., KENNEY, C. N.: Analyst **91,** 603 (1966)
[4] Instruction Manual of the Gow Mac Gas Density Detector Gow-Mac Instruments Co.

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pH-METRIC STUDIES ON TERNARY SYSTEMS: OXOVANADIUM (IV)–8-HYDROXYQUINOLINE-5-SULFONIC ACID–DIHYDRIC PHENOLIC COMPOUNDS

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Mixed chelate formation in a system containing vanadyl ion, 8-hydroxyquinoline-5-sulfonic acid (HQSA) and tiron or chromotropic acid salt (CS) has been studied pH-metrically at an ionic strength of 0.1 *M* (KNO_3) and 30 ± 0.5 °C. Stability constants of the resulting 1 : 1 : 1 mixed ligand complexes have been determined and in terms of the secondary ligands found to decrease in the order: chromotropic acid > tiron.

Introduction

The literature records some studies on ternary chelates with 8-hydroxyquinoline-5-sulfonic acid as one of the ligands [1–7]. In an earlier communication [8], pH-metric studies on the interaction of oxovanadium(IV) with salicylic (SA), 5-sulfosalicylic (SSA) and 8-hydroxyquinoline-5-sulfonic (HQSA) acids in the presence of SA, SSA, phthalic and maleic acids were described. In the present paper these studies have been extended to the ternary systems VO^{2+}–HQSA–dihydric phenolic compounds.

Experimental

A stock solution of vanadyl sulfate was prepared. 8-Hydroxy-quinoline-5-sulfonic acid (Kodak) was recrystallized from water and weighed out directly for each investigation on account of its low solubility. Solutions of tiron (E. Merck) and chromotropic acid salt (E. Merck) were prepared by direct weighing; their purity was checked by potentiometric titrations against 0.1 *M* KOH. The titrations of solutions containing tiron and CS were carried out under an inert atmosphere of purified nitrogen owing to their sensitivity to atmospheric oxidation. The pH measurements were carried out at 30 ± 0.5 °C with a Cambridge pH-meter standardized with 0.05 *M* potassium hydrogen phthalate.

The following pH-metric titrations were performed:

1. 10 ml (0.025*M*) ligand.
2. 10 ml (0.025 *M*) each of the ligand and vanadyl sulfate [VO^{2+} : ligand, 1 : 1]
3. 10 ml (0.025 *M*) each of the primary and secondary ligands and vanadyl sulfate [VO^{2+} : primary ligand : secondary ligand, 1 : 1 : 1].

The ionic strengths of all solutions were kept constant (μ = 0.1 KNO_3) by adding 5 ml 1 *M* potassium nitrate to each solution. The final volume was increased to 50 ml before each titration.

Results and discussion

The potentiometric titration curves for 8-hydroxyquinoline-5-sulfonic acid (Curve 1, Figs 1 and 2), tiron (Curve 3, Fig. 1) and chromotropic acid salt (Curve 3, Fig. 2) exhibit well defined inflections at $m = 1$ (where m represents

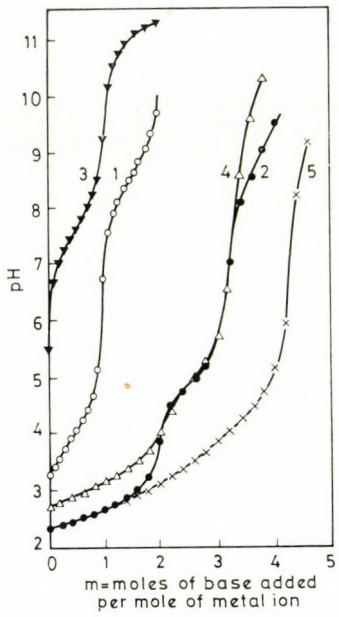

Fig. 1.

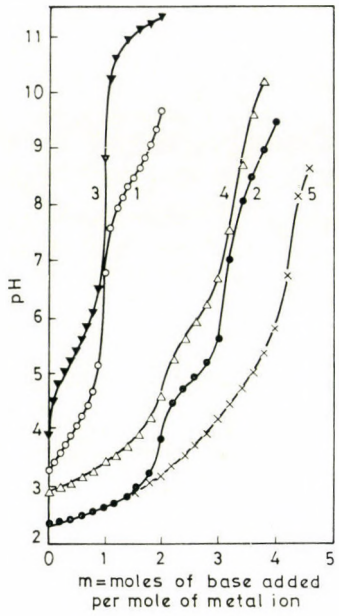

Fig. 2.

the amount of base (mole) added per mole of the metal ion), followed by another poor inflection at $m = 2$ in the case of HQSA and long steep buffer regions in the case of tiron and CS in the high pH region, indicating two separate neutralization steps. The values of the dissociation constants of these ligands have been taken from the literature (Table I).

Table I

Dissociation constants of the ligands, and equilibrium and hydrolysis constants of the 1 : 1 VO^{2+}–HQSA chelate

Ligand	pk_1	pk_2	$-\log K_1$	$-\log K_H$
8-Hydroxyquinoline-5-sulfonic acid	4.06 [8]	8.49 [8]	2.07 [8]	5.79 [8]
Tiron	7.56 [12]	12.48 [2]		
Chromotropic acid salt	5.34 [12]	15.60 [2]		

As reported earlier [8, 9], the potentiometric titration curves of vanadyl sulfate with KOH in the presence of an equimolar concentration of HQSA [8] (Curve 2, Figs 1 and 2), tiron [9] (Curve 4, Fig. 1) and chromotropic acid [9] (Curve 4, Fig. 2) may be explained on the basis of the formation of the normal 1 : 1 chelate and its further conversion into the corresponding monohydroxo derivative.

A comparison of curves 5, Figs 1 and 2, representing the potentiometric titration of vanadyl sulfate in the presence of equimolar concentrations of HQSA (H_2A) and one of the dihydric phenolic compounds with the composite curve representing the titrations of the free ligand and the binary system, indicates that the formation of a 1 : 1 : 1 mixed ligand chelate, MAL is the only possibility in the ternary systems studied. Further, from the analysis of the potentiometric titration curves and the stability constants it may be inferred that the mixed ligand chelate formation occurs through the formation of a 1 : 1 VO^{2+}–HQSA chelate.

The lowering of curves, which is a measure of mixed ligand chelate formation, occurs after $m = 1.0$ in the system, VO^{2+}–HQSA–tiron and $m = 1.2$ in the VO^{2+}–HQSA–CS system. This probably indicates that the formation of the mixed ligand chelate takes place in overlapping steps. This receives support from the analysis of the potentiometric data given below.

The formation of a 1 : 1 : 1 mixed ligand chelate in the above systems may be described as

$$VOA + H_2L \rightleftharpoons VOAL^{2-} + 2H^+ \tag{i}$$

and the overall reaction for the formation of the 1 : 1 : 1 ternary chelate as

$$VO^{2+} + H_2A + H_2L \rightleftharpoons VOAL^{2-} + 4H^+ \tag{ii}$$

If K′ and K″ are the equilibrium constants of reactions (i) and (ii), respectively, then

$$K' = \frac{[VOAL^{2-}][H^+]^2}{[VOA][H_2L]} \tag{1}$$

and

$$K'' = \frac{[VOAL^{2-}][H^+]^4}{[VO^{2+}][H_2A][H_2L]} \tag{2}$$

If T_M, T_A and T_L represent the total concentrations of the metal, the primary and secondary ligand species, respectively, and T_{OH} is the concentration of the base added to the reaction mixture during the titration, the following material balance equations are obtained.

$$T_M = [VO^{2+}]+[VO(OH)^+]+2[\{VO(OH)\}_2^{2+}]+[VOA]+ \\ +[VO(OH)A^-]+[VOAL^{2-}]$$

$$T_A = [H_2A]+[HA^-]+[VOA]+[VO(OH)A^-]+[VOAL^{2-}] \tag{4}$$

$$T_L = [H_2L]+[VOAL^{2-}] \tag{5}$$

$$T_{OH} + [H^+]=[VO(OH)^+]+2[\{VO(OH)\}_2^{2+}]+2[VOA]+ \\ +3[VO(OH)A^-]+4[VOAL^{2-}]+[HA^-] \tag{6}$$

In the pH range studied, the concentrations of OH^-, A^{2-}, HL^- and L^{2-} were negligible compared with those of the other species present in the reaction mixture. However, the concentrations of the hydrolyzed species of the free vanadyl ions were taken into account, since chelation in these cases also occurs at pH > 3.5. For this purpose, values of the hydrolysis constants reported by ROSSOTTI and ROSSOTTI [10] have been used.

In the above 1 : 1 : 1 systems, it may be shown that:

$$a[VO^{2+}]^3 + b[VO^{2+}]^2 + c[VO^{2+}] - d = 0 \tag{7}$$

where

$$a = \frac{2\times 10^{-6.88}}{[H^+]^2}\left(\frac{2K_1}{[H^+]^2} + \frac{K_H}{[H^+]^3}\right),$$

$$b = \frac{2\times 10^{-68.8}}{[H^+]^2}\left\{1+2\left(1+\frac{k_1}{[H^+]}\right)\right\} + \left(1+\frac{10^{-6.0}}{[H^+]}\right)\left(\frac{2K_1}{[H^+]^2} + \frac{K_H}{[H^+]^3}\right),$$

$$c = \left(1+\frac{k_1}{[H^+]}\right) + \left(1+\frac{10^{-6.0}}{[H^+]}\right)\left\{1+2\left(1+\frac{k_1}{[H^+]}\right)\right\},$$

and

$$d = (4T_M - T_{OH} - [H^+])\left(1+\frac{k_1}{[H^+]}\right).$$

Here k_1 is the first dissociation constant of HQSA, and K_1 and K_H are the equilibrium and hydrolysis constants, respectively, of the 1 : 1 VO^{2+}–HQSA chelate. The equilibrium concentration of the free vanadyl ions present in the reaction mixture may be determined by solving Eq. (7) by NEWTON—RAPHSON method [11]. The concentrations of other species involved in the equilibrium relations can then be calculated from the above equations together with the values of equilibrium constants K′ and K″.

Stability of the 1 : 1 : 1 mixed ligand chelates

In these systems, the stability constants of the ternary complexes can be defined as:

$$K_{MAL} = \frac{[VOAL^{2-}]}{[VOA][L^{2-}]} \tag{8}$$

or

$$K_{MAL} = \frac{K'}{k_1' k_2'} \tag{9}$$

where K′ is the equilibrium constant defined by Eq. (i), and k_1' and k_2' are the

dissociation constants of the dihydric phenolic compounds. Further, the overall stability constant of the 1 : 1 : 1 mixed ligand chelate,

$$K'_{MAL} = \frac{[VOAL^{2-}]}{[VO^{2+}][A^{2-}][L^{2-}]} \tag{10}$$

may be calculated from the expression

$$K'_{MAL} = \frac{K''}{k_1 k_2 k'_1 k'_2} \tag{11}$$

where K' represents the equilibrium constant of the overall reaction (ii). The values of the equilibrium and chelate formation constants of the ternary complexes are presented in Table II.

Table II

Equilibrium and chelate formation constants of mixed ligand chelates

System	—log K′	—log K″	log K_{MAL}	log K'_{MAL}
VO^{2+}–HQSA–tiron	4.48±0.07	6.55±0.07	15.56±0.07	26.04±0.07
VO^{2+}–HQSA–CS	5.06±0.04	7.13±0.04	15.88±0.04	26.36±0.04

In these systems, a poor inflection at $m \sim 4$ probably indicates the decomposition of the mixed ligand chelate into another species, which is supported by a gradual decrease in the values of the stability constants of the ternary chelates at $m > 2.0$.

In the pH range of 5—6, the titration curves rise above $m = 4$. This may be explained by the formation of the monohydroxo derivative ($VO(OH)A^-$) of the 1 : 1 VO^{2+}–HQSA chelate and of the hydrolyzed species of the free vanadyl ions along with the formation of the ternary chelates. The concentrations of these species were also taken into account during the calculation of the ternary systems.

A comparison of the data given in Table II indicates the following stability order of the ternary complexes with regard to the secondary ligand: chromotropic acid > tiron; this is in accordance with their relative basicities.

*

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REFERENCES

[1] INTORRE, B. J., MARTELL, A. E.: J. Amer. Chem. Soc., **83,** 3618 (1961)
[2] L'HEUREUX, G. A., MARTELL, A. E.: J. Inorg. Nucl. Chem., **28,** 481 (1966)
[3] CAREY, G. H., MARTELL, A. E.: J. Amer. Chem. Soc., **89,** 2859 (1967)
[4] CONDIKE, G. F., MARTELL, A. E.: J. Inorg. Nucl. Chem., **31,** 2455 (1969)
[5] BOHIGIAN, T. A., Jr., MARTELL, A. E.: *ibid*, **29,** 453 (1967)
[6] SCHARFF, J. P., PARIS, M. R.: Bull. Soc. Chim. France, **5,** 1782 (1967)
[7] SCHARFF, J. P., PARIS, M. R.: C. R. Acad. Sci., Ser. C **263,** 935 (1966)
[8] SINGH, S. P., TANDON, J. P.: Monatsh., Chem. **106,** 271 (1975)
[9] CHABEREK, S., Jr., GUSTAFSON, R. L., COURTNEY, R. C., MARTELL, A. E.: J. Amer. Chem. Soc., **81,** 515 (1959)
[10] ROSSOTTI, F. J. C., ROSSOTTI, H. S.: Acta. Chem. Scand., **9,** 1177 (1955)
[11] BARD, A. I.: Chemical Equilibrium, p. 172. Harper, London 1966
[12] LAL, K., AGARWAL, R. P.: J. Less-Common Metals, **12,** 269 (1967)

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INFRARED SPECTROPHOTOMETRIC STUDY OF CHARGE-TRANSFER COMPLEXES OF SOME SYMMETRICAL TRINITROBENZENE DERIVATIVES WITH AROMATIC COMPOUNDS

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The IRspectra of addition compounds of some symmetrical trinitrobenzene derivatives with aromatic compounds are analysed in order to investigate the type of interaction. The shifts in the NH_2 bands of aromatic amines and asymmetric NO_2 bands of the symmetrical trinitrobenzene derivatives are considered to differentiate between CT complexes and molecular complexes. Solvent effects is also studied to clarify the nature of the reaction between picryl chloride and aromatic amines.

Introduction

The formation of molecular complexes of the charge-transfer type was previously studied by several authors [1—4] taking a number of aromatic compounds including amines with different basicities as donors, and trinitrobenzene or picric acid as acceptors. The recent work on charge-transfer complexes of picric acid [1] with amines revealed that there is a possibility for the formation of proton transfer compounds with moderately basic amines. The type of interaction with aromatic amines can be disclosed by investigating the NH_2, NO_2 and γ_{C-H} bands in comparison to those of the individual molecules.

In the present investigation the possibility of proton transfer or salt formation is greatly reduced by using 2,4,6-trinitrobenzene derivatives containing CH_3, OCH_3 or Cl substituents in position 1 instead of the OH group of picric acid.

MULLIKEN [5] on investigating the benzidine–1,3,5-trinitrobenzene molecular compound, showed that the structure of such compound is that the $-NH_2$ group is positioned between two $-NO_2$ groups which favours bonding between the $-NH_2$ and $-NO_2$ groups.

NAKAMOTO [6] attributed the absorption bands within the 400—600 nm region in the visible spectra of *sym*-trinitrobenzene-aniline derivatives to intermolecular charge-transfer resulting from an inter-benzenoid overlap of the π-orbitals.

POWEL and HUGSE [7] on studying the hexamethylbenzene-picryl chloride molecular complexes found that both picryl chloride and hexamethyl-

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benzene molecules are planar except for the *ortho*-NO_2 groups of picryl chloride which are forced out of plane of the ring due to steric effect of the chlorine atom.

In the present investigation, the IR spectra of some addition products of *sym*-2,4,6-trinitrobenzene derivatives with aromatic compounds, essentially amines of different basicities, are investigated.

Experimental

1. Trinitrobenzene derivatives: 2,4,6-trinitrotoluene [8], 2,4,6-trinitroanisol [9] and 2,4,6-trinitrochlorobenzene [10] were prepared as described in the literature; they were purified by repeated crystallization from an appropriate solvent.

2. Amines: the solid amines were obtained from the commercial sources and purified by repeated crystallization from the appropriate solvent till constant m.p. The liquid amines were purified by vacuum distillation; the head and tail portions were rejected.

3. The addition compounds were prepared by mixing hot saturated equimolar ethanolic solutions of the donor compound (condensed ring hydrocarbon or aromatic amine) and the trinitrobenzene derivatives. From the hot saturated solutions the compounds separated as fine crystals having yellow, organe-yellow, organe or red colour. Some compounds were crystallized from solvents of different polarities *viz.* acetone, chloroform, benzene, dioxane and methanol.

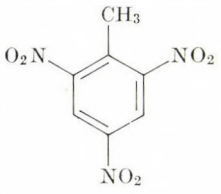
4. Ethanol used as solvent was purified according to the method of MANSKE [11]. Other solvents were purified by recommended procedures [12].

5. The IR spectra of the addition products were recorded for solid thin films between two NaCl plates or as KBr discs on a Unicam S.P. 200 infrared spectrophotometer.

Results and discussion

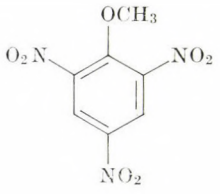
A detailed study of the different parts of the spectra in which changes occur, due to the addition compound formation, would be discussed.

The acceptor molecules used are *sym*-trinitrobenzene derivatives and the donor molecules are naphthalene, anthracene, or substituted aniline derivatives of varying basicity.



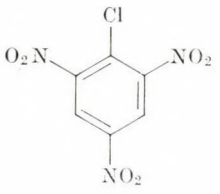
TNT

I



TNA

II



TNCB

III

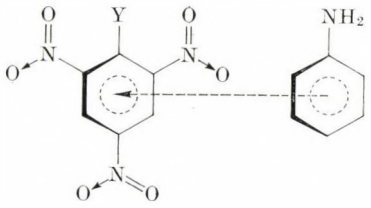
Compound (**I**) could act as a good acceptor compared to (**II**) since the *sym*-trinitrobenzene portion would suffer less electron donation from the $-CH_3$ group than the OCH_3 group.

Salt formation in the case of (**I**) and (**II**) is highly improbable while with (**III**) the possibility for covalent compound formation is liable when

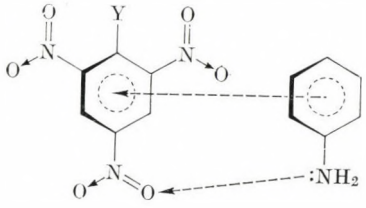
using strongly basic amines. This suggestion is based on the study carried out by RAYAN and HUMFRAY [13] who measured the rate of nucleophilic substitution of the picryl chloride using a number of amines.

The bonding in the addition compounds formed takes place through $\pi - \pi^*$ or $n - \pi^*$ interactions. The latter occurs with aromatic amines when the $-NH_2$ group is positioned facing one of the $-NO_2$ groups. The type of addition compound formed will depend on the charge density on the donor system.

It is supposed that the aromatic trinitro compounds (**I**), (**II**) and (**III**) could bound with the amines through two types of interaction namely, $\pi - \pi^*$ or $\pi - \pi^*$ in addition to the $n - \pi^*$. The possibility for intermolecular hydrogen bonding between the amino and nitro groups should not be excluded.



(a) $\pi - \pi^*$ bonding



(b) $\pi - \pi^*$ and $n - \pi^*$ bonding

TNT, compound (I)

The addition compounds obtained are typical examples of charge-transfer complexes in which TNT is a strong electron acceptor.

i) Bands due to ν_{CH_3} and ν_{NH_2} are observed within the 2900—3000 and 3200—3500 cm^{-1} regions. The ν_{CH_3} are not apparently changed while the ν_{NH_2} band acquire a slight red shift compared to the free amines indicating the formation of a weak intermolecular hydrogen bonding between the $-NO_2$ group and $-NH_2$ group of the amine or an intermolecular charge transfer of the $n - \pi^*$ type.

ii) Bands of the *asym* $-NO_2$ vibrations are more splitted in the molecular complex. They are also shifted to higher or lower frequencies. The bands due to the *sym* $-NO_2$ vibrations are splitted indicating a greater differentiation in the characteristic bond energies of these group. The $-NO_2$ groups involved in H-bonding with the $-NH_2$ group or those displaying increased charge acceptance from the donor molecule, especially of the $n - \pi^*$ type, would lead to bands at lower frequencies. The $-NO_2$ groups leading to bands at higher frequency would be less polarized in the molecular complex through decreased charge transfer to them from the benzene ring. This would take place under specific increased charge migration to the $-NO_2$ groups involved in the intermolecular hydrogen bonding with the $-NH_2$ groups.

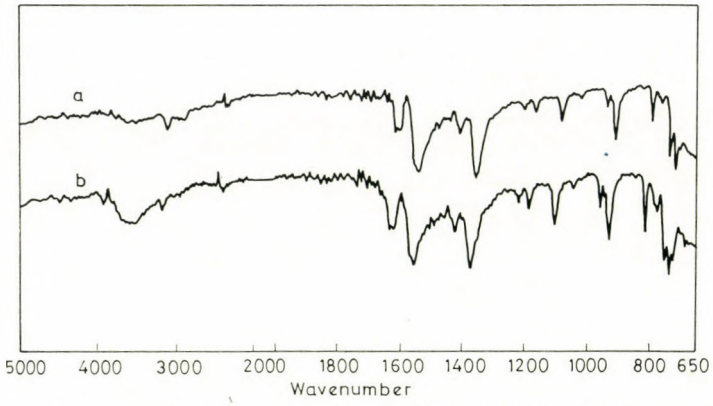


Fig. 1. Potentiometric titration curves of normal and mixed ligand chelate systems of VO (IV) having 8-hydroxyquinoline-5-sulphonic acid and tiron as ligands. Curve 1, HQSA; 2,1 : 1 VO (IV) — HQSA; 3, tiron; 4., 1 : 1 VO (IV)–tiron; 5, 1 : 1 : 1 VO (IV) — HQSA–tiron

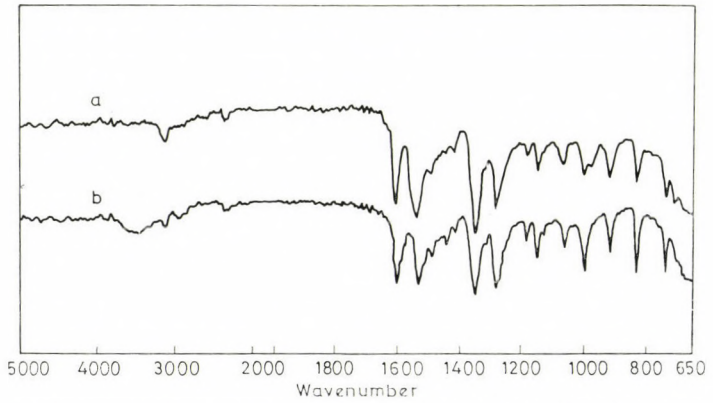


Fig. 2. Potentiometric titration curves of normal and mixed ligand chelate systems of VO (IV) having 8-hydroxyquinoline-5-sulphonic acid and chromatotropic acid (CS) as ligands. Curve 1, HQSA; 2, 1 : 1 VO (IV) — HQSA; 3, CS: 4, VO (IV)–CS; 5,1 : 1 : 1 VO (IV)–HQSA–CS

iii) The ν_{C-N} and γ_{C-H} are slightly influenced indicating a weak interaction between components of the addition compound.

The addition compounds formed have low m.p.'s which is characteristic of molecular complexes. Also the compounds display different colours as shown in Table I.

TNA, compound (II)

This type of addition compounds also represent an example of charge-transfer complexes. The spectra of the addition compounds show some shifts compared to the individual components.

i) Bands due to the ν_{OCH_3} and ν_{NH_2} are still observed but those for the ν_{NH_2} acquire slight red shifts as in case of the addition compounds with (**I**) and can be explained on the same basis.

ii) The bands due to the *asym.* $-NO_2$ vibrations are more splitted compared to the parent compound (**II**). However the *sym* $-NO_2$ bands are sharp as in (**II**). The ν_{C-H} and γ_{C-N} bands are nearly unaffected indicating weaker interaction than (**I**). The same trends of colour observed with components of group (**I**) are obtained in the case of group (**II**). Also the melting points of group (**II**) are lower than the parent compound, (*c.f.*, Table I).

The spectral shifts in (**II**) are smaller compared to (**I**) indicating a weaker acceptor character of the former. This, as stated above, is due to the higher donor character of the OCH_3 group compared to the $-CH_3$ group.

TNCB, compound (III)

From the spectral changes with the compounds obtained, the reaction of (**III**) with aromatic amines would lead to the formation of two types of compounds.

i) Compounds involving covalent bonding leading to derivatives of the diphenylamine type

RAYAN and HUMFRAY [13] stated that covalent addition compounds are formed by the reaction of (**III**) with aromatic amines of moderate or high basicities. The N-atom of the amine would act as an attacking nucleophile for the polarized C–Cl bond which results in the removal of the Cl atom giving

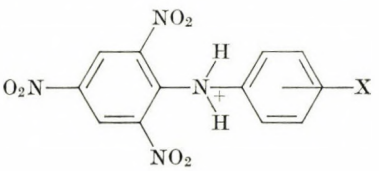


Table I

Some important IR bands of TNT and TNA and their

Acceptor / Compound complexed	TNT								
	m.p.°C	*Colour	ν_{NH_2}		ν_{NO_2} *asym*			ν_{NO_2} *sym*	
A. Condensed ring:									
Anthracene	156	O. R.			1562	1544	1518	1353	—
Naphthalene	—	—			—	—	—	—	—
B. Substituted aniline:									
o-OCH_3	79	O	3450	3125	1558	1545	1525	1362	1343
p-OCH_3	78	R	3150	2860	1562	1545	1532	1358	1342
o-CH_3	76	R	3150	2950	1563	1550	1530	1364	1345
m-CH_3	77	O	3120	2940	1560	1545	1530	1360	1340
p-CH_3	74	R	3100	2900	—	1545	1520	1360	1340
H	69	R	3410	3150	1560	1542	1526	1355	1340
o-Cl	79	Y	3500	3110	1558	1545	1525	1560	1342
m-Cl	77	O	3500	3110	1557	1543	1522	1360	1341
p-Cl	72	R	3150	2950	1560	1542	1522	1358	1340
p-Br	61	O	3110	2900	1560	1550	1523	1360	1339
p-I	69	O	3450	2950	1562	1546	1530	1358	1340
o-COOH	79	Y	3125	2990	1560	1540	1529	1357	1340
p-COOH	85	Y	3500	3100	1560	1545	1525	1365	1345
m-NO_2	—	Y	3500	2950	1560	1545	1530	1360	1346
p-NO_2	71	Y	3495	2990	1560	1545	1530	1362	1342
o-NO_2	75	Y	3500	3125	1560	1545	1525	1360	1342
C. Acceptor	86		—	—	1550	—	1520	1360	—

— = not recorded; ? = not readily identified * Y = yellow; O = orange, R = red

a salt of the type, or a similar sort of bonding. This explanation is accepted on account of the spectral changes observed with some compounds including strong basic amines these can be summarized in the following.

i) The C–Cl band at 710 cm^{-1} in the spectrum of (**III**) is no more apparent.

ii) NH_2 bands are shifted to lower values being those of the $-NH^+-$ structure.

iii) The *asym* $-NO_2$ bands are shifted to higher values due to decreased mesomeric shift from the aromatic ring to the $-NO_2$ groups under the influence of the positive charge on the NH_2-centre.

addition products with aromatic amines

Compound complexed \ Acceptor	TNA								
	m.p. °C	Colour	ν_{NH_2}		ν_{NO_2} *asym*			ν_{NO_2} *sym*	
A. Condensed ring:									
Anthracene	—	—	—	—	—	—	—	—	—
Naphthalene	79	Y			1560	1545	1522	1360	—
B. Substituted aniline:									
o-OCH	84	R	?	3160	1560	1545	1525	1358	1340
p-OCH_3	77	R	3360	3140	1558	1542	1530	1356	1340
o-CH_3	85	Y	3450	3120	?	1538	1520	1355	1320
m-CH_3	79	R	3500	3120	1560	1538	1520	1357	1338
p-CH_3	82	O.Y	3450	3110	1555	1537	1521	1352	?
H	79	O.Y	3150	2950	1560	1542	1522	1355	1320
o-Cl	83	Y	—	2940	1560	1540	1525	1356	1318
m-Cl	74	O	3120	2930	1558	1540	1520	1357	1320
p-Cl	75	O	3450	2980	—	1540	1520	1360	1340
p-Br	85	O	3500	3100	1558	1538	1522	1355	—
p-I	79	O	3400	2950	1560	1540	1518	1350	—
o-COOH	83	Y	3400	3120	1560	1540	—	1357	—
p-CCOH	82	Y	?	3120	1560	1540	1525	1365	1355
m-NO_2	76	Y	3400	3120	—	1540	—	1365	—
p-NO_2	63	Y	3400	3110	1558	1540	—	1357	—
o-NO_2	83	Y	3500	2950	1562	1542	1525	1357	1340
C. Acceptor	68		—	—	1560	1542	1520	1357	—

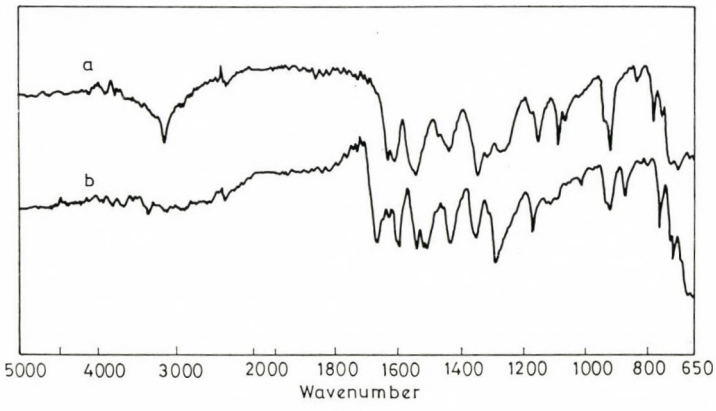
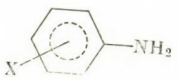


Fig. 3.

Table II

Some IR bands of TNCB and its addition



TNCB III \ X	o-OCH_3	p-OCH_3	o-CH_3	m-CH_3	p-CH_3	H	o-Cl	m-Cl
	3270	3200	2995	3300	3500	2780	3320	3380
	2280	2320	—	2350	2575	2400	3100	2995
1560	—	—	1558	—	—	—	—	—
1556	1520	1543	1540	1540	1535	1550	1545	1545
1545	—	—	—	1520	1520	1520	—	—
1352	1328	1340	1340	1348	1338	1340	1345	1348
788	780	765	760	780	780	760	760	780
83	140	160	156	122	162	178	159	132
Y	O	R	O	R	O	O.Y.	O	Y

— = not recorded; ? = no readily identified; * R = red, Y = yellow; O = orange

ii) Addition compounds involving CT only

This comprises addition compounds formed with the nitro derivatives of aniline. The spectral behaviour of such compounds recalls that observed with molecular complexes of (**I**) and (**II**).

The bands due to the $-NH_2$ groups are still present and the $-NO_2$ bands are splitted as in (**III**) itself. The same trends of colours observed with compounds (**I**) and (**II**) were also formed.

The relatively high m.p's observed for this group of addition compounds which is higher than the parent compound supports the idea of salt formation (Table II).

Solvent effect

To give further supports for the nature of the reaction between picryl chloride and aromatic amines the reaction was carried out in solvents of different polarities. The IR spectra of the resulting compounds were recorded and analysed in the light of the above findings. With *p*-anisidine (high basicity) and *p*-nitro aniline (low basicity) the reaction was found to be the same giving covalent bonding for the former and addition compounds with the latter. On the contrary, aniline gave different products depending on the solvent used. Commonly covalent bonding between aniline and picryl chloride occurs in polar solvents while solvents of low polarities yield molecular complexes.

products with aromatic amines

p-Cl	p-Br	*p*-I	*o*-COOH	*p*-COOH	*m*-NO_2	*p*-NO_2	*o*-NO_2	Assignment
3390	3308	?	3500	3360	3300	3320	3374	νNH_2 (*as*)
3030	3087	2310	2380	3100	2320	2300	3090	νNH_2 (*s*)
1560	—	—	—	—	1560	1555	1565	
1540	1555	1545	1545	1555	1538	1540	1553	$-NO_2$ (*asym*)
—	?	?	—	1540	1520	1510	1517	
1340	1340	1340	1355	1345	1345	1342	1345	$-NO_2$ (*sym*)
765	750	770	770	775	750	760	750	γ-CH (III)
168	186	179	—	—	197	218	78	m.p. °C
R	Y	O	O	Y	Y	Y	O	Colour*

REFERENCES

[1] Issa, R. M., El Essawey, M. M.: Z. phys. Chemie, Leipzig 253 1/2, S. 96—104. (1973)
[2] Briegleb, G., Dalle, H.: Z. Elektrochem. (Ber Bunsengesell. phys. Chemie) **64** (1960) 347; Z. phys. Chemie, N. F. **24** 329 (1960).
[3] Hertel, E., Michant, M.: Liebigs Ann. Chem., **451,** 179 (1926)
[4] Cross, R. D., Fassel, V. A.: J. Amer. Chem. Soc., **79,** 38 (1956)
[5] Mulliken, R. S.: J. Amer. Chem. Soc., **72,** 600 (1950)
[6] Cross, R. D., Nakamoto, K., Fassel, V. A.: Spectrochim. Acta **8,** 142 (1952)
[7] Powel, H. M., Hugse, E. W.: Nature **144,** (1939), 77; J. Chem. Soc., **435** (1943)
[8] Gibson, W. H., Duckham, R., Fairbairn, R.: J. Chem. Soc., **121, 270** (1922)
[9] Chapman, E., Perkin, A. G., Robinson, R.: J. Chem. Soc., **3030** (1927)
[10] Ullmann, F., Nadai, J.: Ber., 1875 (1908).
[11] Manske, R. H.: J. Amer. Chem. Soc., **53,** 1104 (1931)
[12] Vogel, A. I.: "A Text Book of Practical Organic Chemistry", **3**rd edition, Longmans 1961
[13] Rayan, J. J., Humfray, A. A.: J. Chem. Soc. B **1300** (1967)

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MULTILAYER ADSORPTION OF GASES ON HETEROGENEOUS SOLID SURFACES: LOCAL BET BEHAVIOUR OF THE ADSORBED PHASE

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The influence of the surface heterogeneity of the adsorbent on the formation of a multilayer in gas adsorption is discussed, taking into account the full form of the BET equation as the local adsorption isotherm. In numerical calculations, a new method for evaluating the energy distribution function was used.

Introduction

The BET equation is still regarded as the basic equation describing multilayer adsorption of gases on homogeneous solid surfaces. Attempts have made also to use this equation in describing multilayer adsorption on heterogeneous surfaces. MCMILLAN [1], ZETTLEMOYER and WALKER [2], and HILL [3] were the first to introduce the concept of surface heterogeneity into the BET equation. Next, HONIG [4], LEVIN [5], CEROFOLINI [6, 7] and RUDZŃISKI *et al.* [8—10] investigated multilayer adsorption on heterogeneous surfaces, assuming local BET behaviour of the adsorbed phase and some analytical expressions for the energy distribution functions.

The most recent and theoretically most advanced results are those of DORMANT and ADAMSON [11] who used a correct energy distribution evaluated on grounds of the local BET isotherm. They accepted the customary form of the BET equation,

$$\Theta_l(x, \varepsilon) = \frac{c(\varepsilon) \cdot x}{[1 - x] \cdot [1 + c(\varepsilon) \cdot x - x]} \tag{1}$$

where $\Theta_l(x,\varepsilon)$ is the relative surface coverage, $c = (1/c')\exp\left(\frac{\varepsilon}{RT}\right)$ is the BET constant, x is the relative pressure $p/p_{s'}$ ε is the adsorption energy and the constant c' is connected with the molecular partition functions of the molecules adsorbed in the first and subsequent layers. Using Eq. (1) as the local adsorption isotherm in the HALSEY—TAYLOR equation [8], the following expression was obtained for the overall adsorption isotherm

$$\Theta_t(x) = \int_{\varepsilon_{\min}}^{\varepsilon_{\max}} \frac{c(\varepsilon) \cdot x \cdot \chi(\varepsilon) d\varepsilon}{[1 - x] \cdot [1 + c(\varepsilon) \cdot x - x]} \tag{2}$$

where $\chi(\varepsilon)$ is the energy distribution function normalized to unity. If the adsorbed amount $N_l(x)$ is used instead of $\Theta_l(x)$ in Eq. (2), the energy distribution obtained is multiplied by the monolayer capacity N_m, *i.e.* $\chi_1(\varepsilon) = N_m\chi(\varepsilon)$.

The purpose of the paper of DORMANT and ADAMSON [11] was to show how the BET equation can be used to characterize the energetic heterogeneity of the adsorbent, and to provide a detailed example of the error incurred in accepting the parameter c' as giving a correct energy distribution function $\chi(\varepsilon,c')$. Next, this function $\chi(\varepsilon,c')$ was used for evaluating the average adsorption energy according to the following equation:

$$\bar{\varepsilon} = \int_{\varepsilon_{\min}}^{\varepsilon_{\max}} \varepsilon\, \chi(\varepsilon, c')\, d\varepsilon$$

Howver, it is a well known fact that the customary BET equation provides a poor agreement with the experimental data at higher relative adsorbate pressures even in the case of highly homogeneous surfaces. This fact was discussed by a great number of investigators, and numerous modifications of the BET equation were made during the last thirty years [3, 12, 13].

We shall be concerned here with the theories offering improvements of the BET equation, based on more realistic models of the mechanism of multilayer formation. Among the theories concerning the mechanism of secondary adsorption and accepting the BET adsorption model, those of ANDERSON [12] and BRUNAUER *et al.* [13] seem to be most interesting. They have developed, though in different ways, the following modification of the BET equation

$$\Theta_l(x, \varepsilon) = \frac{c(\varepsilon)kx}{[1 - kx][1 + c(\varepsilon) \cdot kx - kx]} \tag{3}$$

where the factor $0 < k \leq 1$ is the correction for a finite number of layers which can be formed on the adsorbent surface. This constant is a measure of the attractive force field of the adsorbent. The basic assumption of the above mentioned theories can be expressed as follows: the thermodynamic properties of the adsorbate in the multilayer differ from those in the bulk liquid, owing to the long-range effect of the adsorbent force field. Thus, it may be expected that the varying force field on a heterogeneous surface will affect the formation of multilayer on heterogeneous surfaces.

The purpose of this paper is to investigate theoretically how far the mechanism of multilayer adsorption is affected by surface heterogeneity. In our studies we shall use a simple numerical method for evaluating the correct energy distribution functions.

Theoretical

In order to investigate the influence of heterogeneity on the formation of the multilayer, we shall use the best-fit procedure. The best-fit procedure is often used in theoretical investigations.

Let us first consider a homogeneous surface and assumed Eq. (3) to hold for this surface. Parameters N_m, c' k can be found by fitting Eq. (3) to the experimental data for an adsorption system investigated.

Now consider Eq. (2) with Eq. (3) as the local adsorption isotherm. Taking some set of the parameters N_m, c', k (parameter c' is practically constant for different patches of the surface [14]; we shall evaluate this value theoretically [11, 15, 16], however, parameter N_m is practically identical with that evaluated for a homogeneous surface [6, 17]), we can evaluate the corresponding energy distributions $\chi(\varepsilon, c', k)$, then the theoretical overall adsorption isotherms $\Theta_t(x, c', k)$ related to the energy distribution obtained. In this way we get a class of the theoretical overall adsorption isotherms determined by all physically significant values of the parameters k and c'. From this class we choose the isotherm which gives the best agreement with the experiment. We assume the values k and c' and the corresponding energy distribution as the correct values for this adsorption system. Later, we shall compare the two k values obtained in the homogeneous and heterogeneous surface approximation. From this comparison we shall deduce information about the influence of heterogeneity on the formation of multilayer on a heterogeneous surface.

There remains to be considered the mathematical problem connected with the evaluation of the energy distribution $\chi(\varepsilon)$ from the experimental data. The problem of finding the energy distribution $\chi(\varepsilon)$ from experimental data has been considered by a number of investigators [11, 15, 16, 18—20]. We used in our calculations a numerical method which seems to be a little simpler than the previous methods. In principle it is similar to the well-known methods for evaluating the function $\chi(\varepsilon)$, *i.e.* those of ADAMSON [11, 21], VAN DONGEN [18] and recently CEROFOLINI [7] and RUDZIŃSKI and JARONIEC [15, 16, 19, 20, 22]. This method is very convenient for the numerical evaluation of parameter k for a heterogeneous surface, which requires multiple calculations of the energy distribution function.

Let us consider the general form of the integral adsorption isotherm

$$\Theta_t(x) = \int_{\Omega} \Theta_l(x, \varepsilon)\, \chi(\varepsilon)\, d\varepsilon \tag{4}$$

where Ω is the range of possible variations in the adsorption energy ε. To this purpose we introduce the following transformation:

$$\varepsilon = f(t) \tag{5}$$

where $f(t)$ is a function defined in the interval $(-1,1)$, which meets the following conditions:

$$f(-1) = \varepsilon_{\min} \text{ and } f(1) = \varepsilon_{\max} \tag{6}$$

In the above $\Omega = (\varepsilon_{\min}, \varepsilon_{\max})$.

Then, Eq. (4) may be rewritten as

$$\Theta_l(x) = \int_{-1}^{1} \Theta_l(x, f(t))\, \chi(f(t)) f'(t)\, dt \tag{7}$$

Let us suppose that the local adsorption isotherm $\Theta_l(x, f(t))$ may be transformed to the following form

$$\Theta_l(x, f(t)) = \frac{H(x)\, S(t)}{B(x) - t} \tag{8}$$

where the functions $B(x)$, $H(x)$ and $S(t)$ satisfy the conditions:

$$| B(x) | > 1;\ H(x) > 0 \text{ and } S(t) > 0 \tag{9}$$

Below we shall show that Langmuir's monolayer adsorption isotherm, and the multilayer adsorption isotherms based on the BET model can be transformed into form (8). As known, these isotherms are most often used in the description of local adsorption [6—11, 15—17, 19—23], therefore, in the mathematical considerations we shall limit ourselves to transform (8).

We expand the function $\chi(f(t))S(t)f'(t)$ into a set of orthogonal Legendre polynomials $P_i(t)$

$$\chi(f(t)) \cdot S(t) \cdot f'(t) = \sum_{i=0}^{\infty} C_i\, P_i(t) \tag{10}$$

where $P_i(t)$ have the form,

$$P_i(t) = \frac{1}{2^i\, i!} \frac{d^i}{dt^i} (t^2 - 1)^i \tag{11}$$

From Eqs (7)—(11) we get

$$\frac{\Theta_l(x)}{H(x)} = \sum_{i=0}^{\infty} C_i \int_{-1}^{1} \frac{P_i(t)\, dt}{B(x) - t} = \sum_{0=0}^{\infty} C_i\, I_i(x) \tag{12}$$

The integrals of Eq. (12) may be evaluated analytically, using the following recursive relation

$$I_i(x) = \frac{-2}{iP_{i-1}(B(x))} + \frac{P_i(B(x))}{P_{i-1}((x))}\, I_{i-1}(x) \quad \text{for } i = 1, 2, \ldots \tag{13}$$

where

$$I_i(x) = \int_{-1}^{1} \frac{P_i(t)\,dt}{B(x) - t} \tag{14}$$

and

$$I_0(x) = \ln \frac{B(x) + 1}{B(x) - 1} \tag{15}$$

Further, we shall replace the sum in Eq. (12) by its N-th partial sum

$$\frac{\Theta_l(x)}{H(x)} = \sum_{i=0}^{N} C_i\, I_i(x) \tag{16}$$

The above equation yields a system of linear equations if we consider the function $\Theta_l(x)$ and $H(x)$ for different values of x_j

$$\frac{\Theta_l(x_j)}{H(x_j)} = \sum_{i=0}^{N} C_i\, I_i(x_j) \quad \text{for} \quad j = 0, 1, \ldots, N \tag{17}$$

The matrix system of the $I_i(x_j)$ $(i, j = 0, 1, \ldots, N)$ is deduced from recursive relation (13)—(15). From Eqs (5) and (10) we obtain the following expression for the adsorption energy distribution

$$\chi(f(t)) = [S(t) f'(t)]^{-1} \sum_{i=0}^{N} C_i\, P_i(t)\,. \tag{18}$$

Coefficients C_i being found from the solution of system (17).

Let us now use transform (8) for the Langmuir and BET adsorption isotherms. For convenience of mathematical notation we shall express the monolayer and multilayer adsorption isotherms in the form of one equation. For this purpose, instead of using the relative pressure $x = p/p_s$ (ranging from 0 to 1) it is much more convenient to define and use an "enhanced pressure"

$$y(x) = \sum_{i=1}^{n} (kx)^i = kx\, \frac{[1 - (kx)^n]}{[1 - kx]} \tag{19}$$

(ranging from 0 to $+\infty$). In the above n is the number of adsorbed layers. In fact, the monolayer and multilayer adsorption isotherms based on the localized adsorption model, expressed in terms of $y(x)$ and ε, assume the particularly simple form

$$\Theta_l(x, \varepsilon) = \frac{\delta \ln y(x)}{\delta \ln x} \cdot \frac{y(x)}{y(x) + c' \exp\left(\dfrac{-\varepsilon}{RT}\right)} \tag{20}$$

The last equation for different parameters n and k gives the Langmuir equation and the well-known BET equations: for $k = 1$ and $n = 1$ Eq. (20) reduces to

the Langmuir equation; for $k = 1$ and $n > 1$ it gives the BET equation for a finite number of layers and for $k = 1$ and $n = \infty$ the customary BET equation. For $k \in (0,1)$, $n = \infty$ the modified BET isotherm (3) is obtained.

Recently, SOKOLOWSKI *et al.* [15, 24] showed that the solution of the integral adsorption equation in the range of average and high pressures is practically independent of the maximum adsorption energy ε_{max}. Thus, we assumed the integration range $\Omega = (\varepsilon_{min}, \infty)$. Using Eq. (20) and the integration range of $(\varepsilon_{min}, +\infty)$, and introducing the notation in Eq. 4

$$\varepsilon = f(t) = -RT \ln\left(\frac{1-t}{2a}\right) \tag{21}$$

where $a = \exp(\varepsilon_{min}/RT)$, we obtain the following expression for the overall adsorption isotherm

$$\Theta_l(x) = \frac{2RTay(x)}{c'} \frac{\delta \ln y(x)}{\delta \ln x} \int_{-1}^{1} \frac{\chi(f(t))\,dt}{\left[\frac{2ay(x)}{c'} + 1 - t\right][1-t]} \tag{22}$$

In the above, transform (21) is the result of transformation of the integration range $(\varepsilon_{min}, +\infty)$ to the interval $(-1,1)$ according to conditions (6). It is known that in the interval $(-1,1)$ the orthogonal Legendre polynomials are definite. These polynomials are very convenient in numerical calculations, because integrals (14) can be obtained analytically.

By comparing Eqs (8) and (20), we find the analytical forms of the functions $B(x)$, $H(x)$ and $S(t)$

$$\begin{aligned} B(x) &= \frac{2ay(x)}{c'} + 1 \qquad & H(x) &= \frac{2ax}{c'} \frac{dy(x)}{dx} \\ f'(t) &= RT(1-t)^{-1} \qquad & S(t) &= 1 \end{aligned} \tag{23}$$

It can be seen that these functions satisfy the requirements of Eq. (9). These functions are used to evaluate the coefficients C_i in linear system (17). Considering Eqs (18) and (21), we obtain the following final expression for the adsorption energy distribution

$$\chi(\varepsilon) = 2a\,RT \exp\left(\frac{-\varepsilon}{RT}\right) \sum_{i=1}^{N} C_i P_i \left(1 - 2a \exp\left[\frac{-\varepsilon}{RT}\right]\right) \tag{24}$$

Results and discussion

The numerical method for evaluating the energy distribution function has been applied to two adsorption systems: argon on rutile at 85 K, and argon on Aerosil at 77.5 K.

The first of these systems has been investigated extensively by a number of authors [11, 15, 16, 25] and its properties are well documented. We have chosen this system to compare the results provided by our numerical method with the results obtained previously by other investigators. Among them, the numerical results of DORMANT and ADAMSON seem to be the most accurate [11]. The DORMANT—ADAMSON method [11] is a method of successive approximations, which has been tested by comparing it with the calorimetric results of DRAIN and MORRISON [25] extrapolated to the zero temperature limit. Unfortunately, there are two limitations of this method. Firstly, it is very time-consuming and secondly, DORMANT and ADAMSON accept the customary form of the BET equation; in other words, they assume that parameter k in Eq. (3) is equal to unity. This is a rather crude assumption and leads to strong disagreement with experiment at higher relative coverages. This was probably the reason why DORMANT and ADAMSON have taken the experimental points from the coverage region corresponding mainly to monolayer adsorption, *i.e.* the points below 1200 cm^3/g at S.T.P. With such limitations on the experimental data, our numerical method yields essentially similar results to those of DORMANT and ADAMSON. This is shown in Fig. 1 where the short-dashed line denotes function $\chi_1(\varepsilon)$ calculated from experimental points below 1200 cm^3/g according to Eq. (24), the long-dashed line corresponds to function $\chi_1(\varepsilon)$ calculated from all the experimental points and the solid line represents the function of DORMANT and ADAMSON. In numerical calculations of these functions the constant was used c' as evaluated by DORMANT and ADAMSON [11].

If all the experimental data, including those in the region of multilayer coverage, are taken into account, the energy distribution takes a form which is slightly different from that shown in Fig. 1.

Now the question arises of which energy distribution is more realistic. For this reason we have evaluated the appropriate theoretical adsorption isotherms for the whole pressure region using both our and the DORMANT—ADAMSON energy distribution. The comparison of the theoretical and experimental isotherms is shown in Fig. 2. It seems that our theoretical isotherm yields the same agreement in the low-pressure region, and a much better one in the region of very high coverages. Therefore, we feel that the energy distribution evaluated from Eq. (24) using all experimental points is more realistic.

For a further illustration of our method, we have chosen the system argon on delta alumina (Aerosil) at 77.5K, investigated experimentally and theoretically by NICOLAON and TEICHNER [26]. The specific surface area of delta alumina, consisting of discrete, spherical, nonporous particles (Aerosil Degussa P 110 C I), measured by nitrogen adsorption, was equal to 98.5 m^2/g.

Thus this system involves the same adsorbate (argon) but a different solid surface. In addition, the system was investigated at very similar temperatures. In the case of this particular system our numerical method is illustrated in more

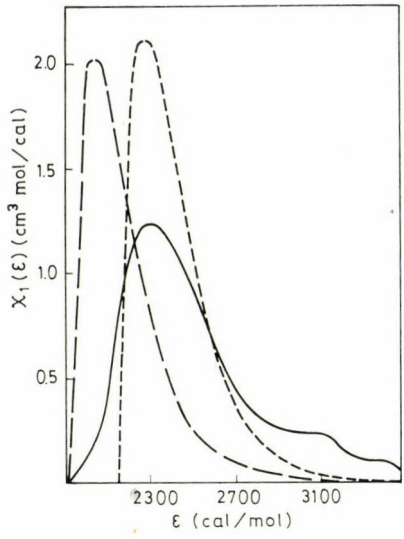

Fig. 1. The energy distribution functions $\chi_1(\varepsilon)$ for the adsorption system argon–rutile at 85 K. Solid line: function $\chi_1(\varepsilon)$ obtained by DORMANT and ADAMSON [11], short-dashed line: function $\chi_1(\varepsilon)$ calculated from the experimental points below 1200 cm³/g at S.T.P., long-dashed line: function $\chi_1(\varepsilon)$ calculated from the whole adsorption isotherm. The two last functions $\chi_1(\varepsilon)$ were calculated according to Eq. (24). All functions $\chi_1(\varepsilon)$ are normalized to monolayer capacity N_m, *i.e.* $\chi_1(\varepsilon) = N_m\chi(\varepsilon)$

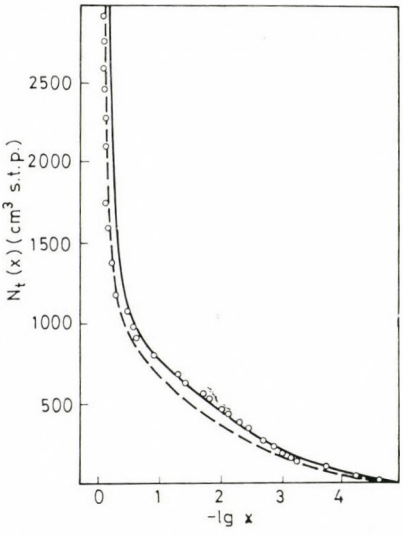

Fig. 2. Theoretical adsorption isotherms $N_t(x)$ *vs.* log x for argon on rutile at 85 K, obtained from our function $\chi_1(\varepsilon)$ (long-dashed line) and from the DORMANT—ADAMSON function $\chi_1(\varepsilon)$ (solid line in Fig. 1).

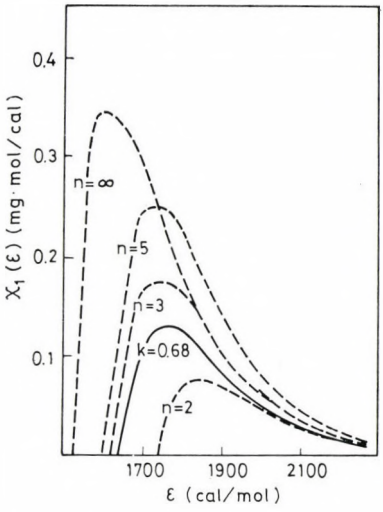

Fig. 3. Energy distribution functions $\chi_1(\varepsilon)$ for the adsorption system argon–aerosil at 77.5 K. Dashed lines: functions $\chi_1(\varepsilon)$ calculated for different numbers of layers formed, *viz.* $n = 2$, 3, 5, ∞; solid line: function $\chi_1(\varepsilon)$ for the best-fit parameter of $k = 0.68$. All functions $\chi_1(\varepsilon)$ are normalized to monolayer capacity and have been calculated according to Eq. (24)

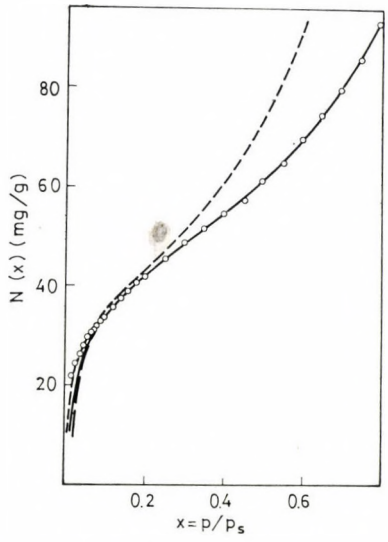

Fig. 4. Theoretical adsorption isotherms for argon on aerosil at 77.5 K, plotted for the whole pressure region. Solid line: $N_l(x)$ calculated from the function $\chi_1(\varepsilon)$ obtained for $k = 0.68$ (see Fig. 3), short-dashed line: theoretical isotherm calculated according to Eq. (1), long-dashed line: theoretical isotherm calculated according to the Eq. (3)

detail. We have accepted the form of the BET equation, assuming a finite number of layers formed on the adsorbent surface, *i.e.* the form where parameter k does not appear. In the numerical procedure k in Eq. (20) is taken to be equal to unity.

Assuming $n = 2$, 3, 5 and $n = \infty$, we have evaluated the related energy distribution functions, which are shown in Fig. 3. Using these distributions, we have evaluated the theoretical adsorption isotherms corresponding to the functions $\chi_1(\varepsilon)$ in Fig. 3. It is interesting to note that the best agreement with

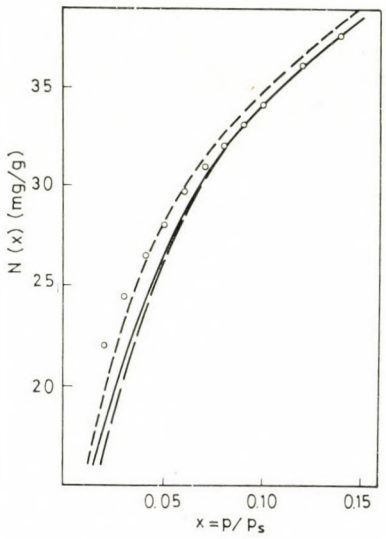

Fig. 5. Theoretical adsorption isotherms from Fig. 4 for the monolayer pressure region

experiment would appear for $2 < n < 3$, if the number of layers were treated statistically. Parameter n was treated in that sense in the paper of NICOLAON and TEICHNER [26], who have found that this number does not exceed 2.52. This fact can be regarded as additional support for the reliability of our method.

Next we used the modified form of the BET equation, which can be obtained from Eq. (20) for $n = \infty$ and $k \in (0.1)$. It is noteworthy that the best distribution function, *i.e.*, function $\chi_1(\varepsilon)$ calculated for $k = 0.68$ (see Fig. 3), lies between those evaluated for $n = 2$ and $n = 3$.

When compared with previous results, this is consistent with the suggestions of NICOLAON and TEICHNER. In a direct way, the reliability of this result can be checked by comparing the appropriate theoretical isotherm with the experimental data. Figures 4 and 5 show that the agreement is satisfactory. The parameters of the theoretical adsorption isotherms shown in Figs 4 and 5 are summarized in Table I.

Table I

Parameters of the theoretical adsorption isotherms shown in Figs 4 and 5

Isotherm equation	N_m (m/g)	k	c or c'
BET, Eq. (1)	37.05	1.00	$c =$ 49
BET, Eq. (3)	41.10	0.71	$c =$ 44
Eq. (22)	41.5	0.68	$c' =$ 4000

The numerical data reported show the importance of the modified BET equation in the investigations of multilayer adsorption on heterogeneous surfaces. The widely used method of DORMANT and ADAMSON does not allow to introduce this improvement. This was the reason why we have developed a simple numerical method for evaluating heterogeneity effects.

The study of argon adsorption on Aerosil, assuming homogeneous and heterogeneous surface approximations, gave but slightly different values of parameters k and n (see Table I, and the discussion referring to Fig. 3). Thus the heterogeneity of the adsorbent surface has no definite effect on the number of adsorption layers formed. The positive aspect of this conclusion is that it may facilitate future theoretical studies of multilayer adsorption on heterogeneous surfaces.

REFERENCES

[1] MCMILLAN, W. G.: J. Chem. Phys., **15,** 390 (1947)
[2] ZETTLEMOYER, A. C., WALKER, W. C.: J. Phys. Chem., **52,** 58 (1948)
[3] HILL, T. L.: Advan. Catalysis, **4,** 232 (1952)
[4] HONIG, J. M.: J. Phys. Chem., **57,** 349 (1953)
[5] LEVIN, W. I.: Zh. Fiz. Khim., **25,** 453 (1951)
[6] CEROFOLINI, G. F.: J. Low Temperature Phys., **6.** 473 (1972)
[7] CEROFOLINI, G. F.: Thin Solid Films, **23,** 129 (1974)
[8] WAKSMUNDZKI, A., RUDZIŃSKI, W., SOKOŁOWSKI, S., JARONIEC, M.: Ann. Soc. Chim. Polon., **48,** 1741 (1974)
[9] RUDZIŃSKI, W., JARONIEC, M., SOKOŁOWSKI, S.: Phys. Lett., **48A,** 171 (1974)
[10] RUDZIŃSKI, W., SOKOŁOWSKI, S., JARONIEC, M., TÓTH, J.: Z. Phys. Chem., **256,** 273 (1975)
[11] DORMANT, L. M., ADAMSON, A. W.: J. Coll. Interface Sci., **38,** 285 (1972)
[12] ANDERSON, R. B.: J. Amer. Chem. Soc., **68,** 686 (1946)
[13] BRUNAUER, S., SKALNY, J., BODOR, E. E.: J. Coll. Interface Sci., **30,** 546 (1969)
[14] HOORY, S. E., PRAUSNITZ, J. M.: Surface Sci., **6,** 377 (1967)
[15] SOKOŁOWSKI, S., JARONIEC, M., CEROFOLINI, G. F.: Surface Sci., **47,** 429 (1975)
[16] RUDZIŃSKI, W., JARONIEC, M., SOKOŁOWSKI, S., CEROFOLINI, G. F.: J. Czech. Phys., **25B,** 891 (1975)
[17] OSCIK, J., DABROWSKI, A., JARONIEC, M., RUDZIŃSKI, W.: J. Coll. Interface Sci., (In press)
[18] VAN DONGEN, R. H.: Surface Sci., **39,** 341 (1973)
[19] JARONIEC, M., RUDZIŃSKI, W., SOKOŁOWSKI, S., SMARZEWSKI, R.: Colloid Polymer Sci., **253,** 164 (1975)

[20] JARONIEC, M., RUDZIŃSKI, W.: Colloid Polymer Sci., **253,** 683 (1975)
[21] ADAMSON, A. W., LING, I.: Advan. Chem., **33,** 51 (1961)
[22] RUDZIŃSKI, E., JARONIEC, M.: Surface Sci., **42,** 553 (1974)
[23] JARONIEC, M.: Surface Sci., **50,** 553 (1975)
[24] SOKOŁOWSKI, S.: Vuoto, **8,** 45 (1975)
[25] DRAIN, L. E., MORRISON, J. A.: Trans. Faraday Soc., **48,** 840 (1952)
[26] NICOLAON, G. A., TEICHNER, S. J.: J. Coll. Interface Sci., **38,** 172 (1972)

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RARE EARTH CHELATES OF N-(2-HYDROXY-1-NAPHTHALIDENE)-β-ALANINE

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N-(2-hydroxy-1-naphthalidene)-β-alanine ($H_2N\beta A$) forms solid chelates with La(III), Ce(III), Pr(III), Nd(III), Sm(III) and Gd(III). The magnetic moments and infrared spectra of these chelates are discussed. Some ligand-exchange reactions of these chelates have been studied.

Introduction

Metal chelates of some tridentate Schiff bases [1] have been studied in this laboratory. A survey of the literature [2] indicates that no systematic study of the chelates of N-(2-hydroxy-1-naphthalidene)-β-alanine with La(III), Ce(III), Pr(III), Nd(III), Sm(III) and Gd(III) has been carried out. It was therefore considered interesting to perform physicochemical investigations on these chelates. The result of these studies are discussed in this communication.

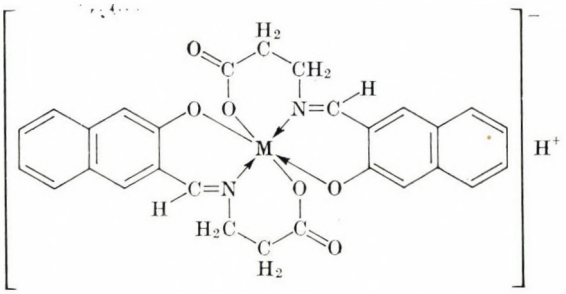

Fig. 1. Where M stands for La(III), Ce(III), Pr(III), Nd(III), Sm(III) and Gd(III)

Experimental

Materials

La(III), Ce(III), Pr(III), Nd(III), Sm(III) and Gd(III) nitrates and EDTA were of analytical reagent grade. 2-hydroxy-1-naphthaldehyde was a Fluka β-alanine (L.R.) a BDH product.

Molecular weights were determined ebulliometrically, using a Gallenkamp semimicro ebulliometer. Magnetic susceptibility measurements were made on a Gouy apparatus, using

Table I

Analyses, yields, molecular weights and values of N-(2-hydroxy-1-naphthalidene)-

Composition of chelate*	Yield %	Analysis Found (%)			
		C	H	N	Metal
H[La $C_{28}H_{22}N_2O_6$]	76	53.92	3.61	4.42	22.22
H[Ce $C_{28}H_{22}N_2O_6$]	74	53.81	3.63	4.44	22.39
H[Pr $C_{28}H_{22}N_2O_6$]	69	53.76	3.59	4.45	22.47
H[Nd $C_{28}H_{22}N_2O_6$]	79	53.49	3.59	4.45	22.88
H[Sm $C_{28}H_{22}N_2O_6$]	77	52.91	3.60	4.39	23.61
H[Gd $C_{28}H_{22}N_2O_6$]	79	52.39	3.52	4.29	24.48

* Bis N-(2-hydroxy-1-naphthalidene)-β-alanine M(III); where M represents La, Ce, Pr, Nd, Sm or Gd.

mercury(II) tetrathiocyanatocobaltate as a reference [3]. Infrared spectra in nujol were recorded on a Perkin Elmer Spectrophotometer using a sodium chloride prism.

Synthesis of $H_2N\beta A$. Equimolar quantities of 2-hydroxy-1-naphthaldehyde (3.4 g) and β-alanine (0.9 g) were dissolved in ethanol and water, respectively, and their solutions were mixed. Two drops of piperidine were added to the mixture, which was then refluxed for 2 hrs. The yellow solution obtained was allowed to stand overnight in a refrigerator for crystallization. The yellow crystals thus separated were recrystallized from ethanol. The yield was found to be quantitative, m.p. 180 °C.

Analysis:
Calcd. for [$C_{14}H_{13}NO_3$] C 69.13; H 5.34; N 5.76.
Found C 68.92; H 5.11; N 5.69%.

Synthesis of rare earth chelates. A solution of the rare earth nitrate (0.02 *M*) in 80% ethanol was slowly added to an ethanolic solution of $H_2N\beta A$ (0.023 *M*) and the mixture was thoroughly mixed. To this mixture, dilute ammonia (1 : 20) was added dropwise till a flocculent yellow mass was formed. Stirring was continued for 5—6 hrs, and after allowing to stand, the solution was filtered, washed with hot ethanol, dried and preserved in a vacuum desiccator. The yields, analyses and magnetic moments are summarized in Table I. The chelates prepared show a 1 : 2 metal-ligand stoichiometry.

Ligand replacement reactions. The Bis N-(2-hydroxy-1-naphthalidene)-β-alaninato-metal chelate (0.01 *M*) thus synthesized was added to a suspension of EDTA (0.01 *M*) in water and the mixture was heated on a water-bath for 3 hrs. On cooling the solution, the $H_2N\beta A$ separated out was extracted into chloroform. On concentrating and cooling the aqueous solution, crystals of the EDTA-chelate were obtained which were separated, dried and preserved in a vacuum desiccator.

On cooling the concentrated chloroform extract, crystals of $H_2N\beta A$ were obtained and the yield was found to be almost quantitative in all cases.

Results and discussion

The metal chelates under investigation do not display sharp melting points but they decompose above 225 °C without melting, giving oxides at 460—490 °C. These compounds are insoluble in water as well as in common organic solvents.

β-alanine chelates of rare earths

Calcd. (%)				Molecular weight		μ_{eff} (B.M. at 303 K)
C	H	N	Metal	Found	Calcd.	
54.11	3.70	4.51	22.37	610	620.9	—
54.01	3.53	4.50	22.52	612	622.1	2.23
53.94	3.53	4.49	22.62	609	622.9	3.33
53.65	3.51	4.47	23.02	615	626.2	3.58
53.13	3.47	4.42	23.77	621	632.3	1.56
52.56	3.44	4.38	24.59	625	639.2	7.90

The broad band present in the IR spectrum of the ligand at 2575 cm^{-1} attributed to the carbonyl group is absent in the spectra of the chelates. Strong bands at 1690 cm^{-1} and 1600 cm^{-1} are due to $\nu C=O$ and $\nu C=C$ respectively. On chelation, the ligand shows no shift in the $\nu C=O$ although a decrease in this frequency on chelation with some transition metals has been reported in the literature. However, in the spectra of the rare earth chelates of salicylaldehyde [4] and acetoacetanilide [5] also, no shift in the carbonyl frequency is observed on chelation.

Bis N-(2-hydroxy-1-naphthalidene)-β-alaninatolanthanum(III)was found to be diamagnetic. The magnetic moments (spin-free values, Table I) obtained experimentally for the remaining rare earth chelates are in fair agreement with the values reported for typical lanthanide sulfates [6]. These values suggest that the lanthanide ion resembles approximately the free ion as far as the *f*-electrons are concerned.

REFERENCES

[1] Mehta, R. K., Gupta, R. K.: Ind. J. Chem., **11**, 56 (1973)
[2] Cotton, F. A.: Progr. Inorg. Chem., **7**, 88 (1966)
[3] Figgis, B. N., Nyholm, R. S.: J. Chem. Soc., **4190** (1958)
[4] Charles, R. G.: J. Inorg. Nucl. Chem., **26**, 2298 (1964)
[5] Budhkar, A. P., Umapathy, P., Sen, D. N.: Ind. J. Chem., **9**, 378 (1971)
[6] Figgis, B. N. Lewis, J.: Techniques of Inorganic Chemistry Vol. **4**, p. 137. Interscience Publishers Inc., New York, 1965

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SINGLE DROP FORMATION ACCOMPANIED BY MASS TRANSFER

(SHORT COMMUNICATION)

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Drop volumes at moderate speed of drop formation measured in non-equilibrium systems were compared with those measured in the equilibrium systems and with data calculated from literature correlations for the case of an equilibrium. The dependence of drop volume upon the concentration of transferring solute was found to be the same in the equilibrium as in the non-equilibrium system under the experimental conditions used.

Drop size is an important factor determining the rate of mass transfer across an interface. Drop formation as a process determining the drop size has been studied experimentally and theoretically by many authors. However, the process is very complex and is not yet fully understood. Almost all data available in the literature relate to systems without mass transfer. It is the purpose of the present work to partly fill this gap.

Experimental

The dependence of drop volume on the concentration of transferred solute was investigated in the system water–acetic acid–benzene (acetic acid as the transferred component, was added to water only; water was the dispersed phase). Water and benzene (originally of analytical grade) used in the experiments have always been twice fractionally redistilled. The second redistillation has been performed no more then two days before the experiment. Of course, both liquids have been mutually saturated. Benzene has been in contact only with glass parts of the apparatus except the external walls of the nozzle. Great care was taken to avoid any contamination of materials and of the apparatus.

The experimental apparatus was of a conventional type. A vertical glass column of 90 mm inner diameter and approximately 400 mm in height was provided with a rectangular jacket for circulating benzene at 25 °C temperature. The drops were formed at stainless steel nozzles made of hypodermic needles sharpened on a watchmaker's lathe. The nozzles were microscopically examined and were rejected if not sharp and free from defects under a 48-fold magnification. The inner diameters of the nozzles were measured in the same way to within 0.003 mm. The nozzle was connected with a glass syringe by polyethylene tubing and it was submerged in the fluid field 9 to 11 mm. The syringe was joined to the apparatus which allows the liquid of dispersed phase to flow at a constant and slow rate.

All drops were formed at the volumetric flow-rate of the dispersed phase of 0.0121 cm^3/s. Concentrations were determined at the instant of drop detachment from the nozzle.

Ten to twelve drops were measured, but it was found that one drop is quite sufficient to obtain reproducible results.

Results and discussion

The measured drop volumes were compared with the data calculated from semi-empirical correlations given by SCHEELE and MEISTER [1] and by CHAZAL and RYAN [2]. Further, the theoretical dependence of drop volume under quasi-static conditions (see HARKINS and BROWN [3]) was included into the comparison. Equilibrium values of physical properties of the system were used when evaluating the drop volumes from the above correlations in spite of the known fact that the interfacial tension of a non-equilibrium system may

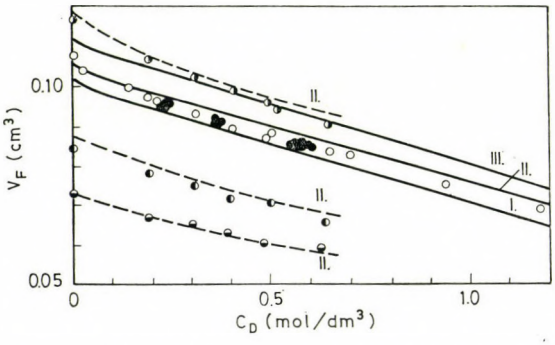

Fig. 1. Comparison of measured and calculated drop volumes. ◑ Volumes given by the nozzle of the wetted inner diameter $d = 0.1527$ cm with negligible concentration in the continuous phase, $c_C = 0$; ○ $d = 0.1375$ cm, system in equilibrium; ● $d = 0.1375$ cm $c_C = 0$; ◐ $d = 0.1068$, $c_C = 0$; ◒ $d = 0.0875$, $c_C = 0$. Line I represents the quasistatic volume, line II the Chazal–Ryan correlation, line III the Scheele–Meister correlation. Full lines correspond to $d = 0.1375$ cm

differ considerably from its equilibrium value. *(cf.* VALENTINE [4]). We have used the values of interfacial tension given by HARKINS and HUMPREY [5] corrected so as their limit should coincide with the value recommended in International Critical Tables [6] for the zero concentration level.

The comparison of measured and calculated data is shown in Fig. 1. It can be seen that surprisingly, under the present experimental conditions the data referring to equilibrium and non-equilibrium systems do not differ from one another. Thus mass transfer has no effect on the volume of a drop formed except in so far as it influences the physical properties of the system. Simultaneously, all three relationships chosen describe the trend of the concentration dependence of the drop volume quite well. Thus it is possible to predict the drop volume in non-equilibrium systems using correlations derived for equilibrium systems. This is important because there are no correlations in the literature dealing with non-equilibrium systems, which frequently occur in chemical engineering practice, while there exist a number of correlations for equilibrium systems.

Symbols

d inside diameter of nozzle,
c_C molar concentration of acetic acid in benzene (continuous phase),
c_D molar concentration of acetic acid in water (dispersed phase),
V_F drop volume

REFERENCES

[1] SCHEELE, G. F., MEISTER, B. J.: AIChE J., **14**, 9 (1968)
[2] CHAZAL, L. E. M., RYAN, J. T.: AIChE J., **17**, 1226 (1971)
[3] HARKINS, W. D., BROWN, F. E.: J. Amer. Chem. Soc., **41**, 499 (1919)
[4] VALENTINE, R. S.: Ph. D. Thesis, University of Washington, Seattle, 1963
[5] HARKINS, W. D., HUMPREY, E. C.: J. Amer. Chem. Soc., **38**, 242 (1916)
[6] International Critical Tables, McGraw Hill, New York 1928

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INVESTIGATION OF MOLECULAR INTERACTIONS IN TWO COMPONENT SYSTEMS: CHLOROFORM–ACETONE AND CHLOROFORM–METHYL ETHYL KETONE

(SHORT COMMUNICATION)

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The molecular interactions in the binary systems chloroform–acetone and chloroform–methyl ethyl ketone were studied on the basis of ultrasound velocity measurements. The adiabatic compressibility, intermolecular free length and available volume variations with the composition of the mixture have been demonstrated. The excess free length and the excess compressibility are found to be negative.

Introduction

Attempts have been made by FORT and MOORE [1], PIOTROWSKA [2], REDDY *et al.* [3], KAULGUD [4] and PRAKASH *et al.* [5] to study the behaviour of binary liquid mixtures by measuring sound velocity and calculating the allied parameters. We report the results of a study of the liquid mixtures chloroform–acetone and chloroform–methyl ethyl ketone. The parameters reported are adiabatic compressibility, intermolecular free length and the available volume.

Experimental

The instrument and the method for the measurement of sound velocity have beeen described previously [6]. The frequency used was 5 MHz and the temperature was maintained at 22 ± 0.1 °C. The liquids were AR grade BDH products and were further purified by standard methods. The densities compared well with the literature values. The liquid mixtures of different mole fractions were prepared by adding the appropriate volumes to dry volumetric flasks. After stabilization, the mixtures were transferred to the ultrasonic cell and the velocity was measured. The densities were measured by the pyknometric technique. The probable error in the measurement of sound velocity was 0.15%.

Results and discussion

The adiabatic compressibility (β), the free length (L_f) and the available volume (V_a) were calculated from the following equations:

$$\beta = \frac{1}{v^2 \varrho}$$

$$L_f = K\beta^{1/2}$$

$$V_a = V\left(1 - \frac{v}{v_\infty}\right)$$

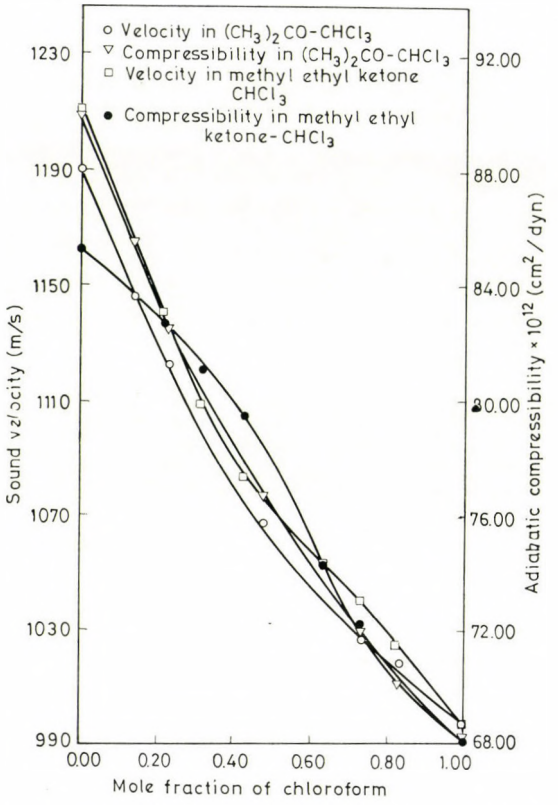

Fig. 1. Velocity and compressibility in the systems $(CH_3)_2CO$–$CHCl_3$ and methyl ethyl ketone–$CHCl_3$

where v is the sound velocity in solution at any concentration, $v_\infty = 1600$ m/sec, V the molar volume and K a known temperature-dependent constant.

The results are shown in the form of graphs. Figure 1 illustrates the variations in velocity and compressibility with the composition of the mixture, while in Fig. 2 the free length and available volume are plotted against the mole fraction of the common liquid chloroform. The nature of the curves is such that it demonstrates the non linear behaviour of the mixtures with regards to the values of v, β, L_f and V_a with changing composition of the mixtures.

The available volume curve is concave to the mole fraction axis, showing that the change is positive. The free length decreases in both cases with increasing mole fraction of chloroform. Whereas in the chloroform–acetone system the excess free length is negative, it is positive in the chloroform–methyl ethyl ketone system. The sign of excess compressibility for the former system is negative, while that for the latter is positive at first and becomes negative later on. According to FORT and MOORE [1], the interaction is stronger if the excess compressibility is negative. This suggests that there is strong interaction

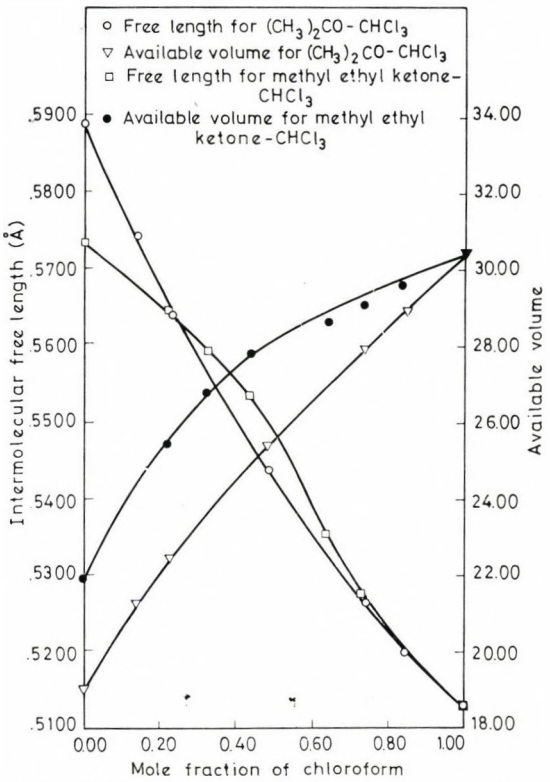

Fig. 2. Free length and available volume in the systems $(CH_3)_2CO$–$CHCl_3$ and methyl ethyl ketone–$CHCl_3$

between chloroform and acetone, through a hydrogen bond, a fact which is supported by the observations of McGLASHAN and RASTOGI [7], NIGAM and MAHL [8]. The latter have, demonstrated the existence of interaction between $CHCl_3$ and $(CH_3)_2CO$ on the basis of interchange energy and viscosity values. There exists some interaction between chloroform and methyl ethyl ketone too and it is stronger when the mole fraction of chloroform is higher.

REFERENCES

[1] FORT, H. J., MOORE, W. H.: Trans. Faraday Soc., **61,** 2102 (1965)
[2] PIOTROWSKA, A.: Rocz. Chem., **39,** 437 (1965)
[3] REDDY, K. C., SUBRAHMANYAM, S. V., BHIMSENACHAR, J.: J. Phys. Soc. Japan, **19,** 559 (1964)
[4] KAULGUD, M. V.: Zeits. Phys. Chem., **36,** 365 (1963)
[5] PRAKASH, S., SRIVASTAV, S. B., PRAKASH, O.: J. Chim. phys. **12,** 115 (1975)
[6] CHATURVEDI, C. V., PRAKASH, S.: Acta Chim. (Budapest) **72,** 289 (1972)
[7] McGLASHAN, M. L., RASTOGI, R. P.: J. Phys. Chem., **65,** 314 (1961)
[8] NIGAM, R. K., MAHL, B. S.: Ind. J. Chem., **9,** 1255 (1971)

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COMPLEX STUDY OF NICKEL SKELETON CATALYSTS, VI.

METALLOGRAPHICAL STUDY OF NOVEL NON-PYROPHORIC NICKEL SKELETON CATALYSTS

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Metallographic, electron microscopic and X-ray diffraction studies were made on Ni–Si, Ni–Al–Si, Ni–Mg and Ni–Zn alloys and on the non-pyrophoric skeleton catalysts prepared from them.

It was found that, in spite of relatively rapid cooling, the phase structures of the alloys correspond to the conditions depicted in the phase diagrams. The alkali used for dissolution purposes first attacks the phases containing the more inactive metals. In the course of catalyst preparation the inactive metal is not leached out completely, and intermetallic compounds too remain in the catalysts. The electron micrographs illustrate the indefinite surface geometries of the catalysts with higher hydroxide contents.

The structure of the skeleton catalyst prepared from the Ni–Mg alloy differs from the other structures. It remains not an intermetallic compound, but unalloyed magnesium unchanged after dissolution, and there is a large amount of crystalline $Mg(OH)_2$ in the catalyst.

Introduction

Apart from the conditions of alkaline leaching the properties of skeleton catalysts depend to a large extent on the structure of the initial alloy and on the distribution of the alloying elements. The activity of catalysts prepared from alloys are affected appreciably by the nature and proportions of the phases constituting the alloy, the compositions and properties of the intermetallic compounds and by the dimensions of the individual crystallites.

For example, in a study of Raney nickel FASMAN and PUSHKARIEVA [1] found that a substantially more active catalyst can be obtained from alloys predominantly containing the intermetallic compound $NiAl_3$ than from those mainly containing Ni_2Al_3: the activity was proportional to the $NiAl_3$ content of the alloy (the activities of the catalysts were determined in the hydrogenation of cinnamic acid and *o*-nitrophenol). The catalyst obtained by leaching an alloy consisting mainly of Ni_2Al_3 sorbed more hydrogen on its surface. The connection between the alloy structure and the catalytic activity has been dealt with by MASON [2] and by SASSOULAS and TRAMBOUZE [3]. In the hydrogenation of acetone, the latter authors found the catalyst prepared from the alloy consisting mainly of Ni_2Al_3 to be more active than that prepared from $NiAl_3$.

Particularly well applicable to the study of skeleton catalysts are those methods which permit examination of both alloys and catalysts: X-ray diffraction, electron microscopy and derivatography. Other methods can be used to study only the initial alloys or the catalysts. While metallography is suitable for discernment of the phase structures of the alloys (and of the different solubilities of the phases in alkali), only the catalysts can be examined with thermodesorption and thermomagnetic measurements.

In earlier papers [4—6] we reported studies by thermal methods on new types of catalysts prepared from Ni–Si, Ni–Al–Si, Ni–Mg and Ni–Zn alloys. We now wish to report a study of these catalysts and of the starting alloys by metallography, electron microscopy and X-ray diffraction. For purposes of comparison, studies were also made on the Degussa B 113 catalyst, and on the Merck Ni–Al alloy, which is suitable for preparation of the traditional, pyrophoric Raney nickel.

Metallographic examination [7] serves to reveal the macrostructures, phase proportions, crystallite dimensions, etc. of alloys. As regards their physical properties (hardness, colour, light reflection, etc.), the phases of a polished piece of metal differ from one another. Depending on the method of examination, lighter and darker, and possibly coloured areas can be observed through a microscope. It may be possible to distinguish the phases more readily after etching in an appropriate solvent.

Numerous authors have dealt with the metallographic examination of Ni–Al alloys containing 40—50 wt % nickel, which are suitable for catalyst preparation. It has been found that the alloy is not homogeneous, but contains phases corresponding to the intermetallic compounds $NiAl_3$ and Ni_2Al_3 and a eutectic containing about 5 wt % nickel [8—10]. An intermetallic compound NiAl also occurs in alloys of higher nickel content, but this cannot be decomposed with alkali [3].

A number of authors have found that the phases with higher aluminium contents are more reactive towards alkali than are those containing less aluminium [3, 10, 11], while the fastest to dissolve is the eutectic Al—$NiAl_3$ [9, 12]. On this basis, FREEL *et al.* were even able to dissolve $NiAl_3$ selectively [10]. However, the view also exists that there is no difference between the rates of dissolution of $NiAl_3$ and Ni_2Al_3 [13].

Opinions are even more divided as regards the changes occurring in the course of the alkaline dissolution. PRESNYAKOV *et al.* [9, 12] and ALEIKINA *et al.* [11] found that intermetallic compounds with increasingly higher nickel contents are formed during the leaching process and the pure nickel is produced *via* these. According to MASON [2], FREEL *et al.* [10] and LITTMAN and BLISS [14], however, new intermetallic compounds are not formed; dissolution begins at preferential sites within the phases, progresses with a sharp boundary line, and gradually extends to the entire phase. Depending on the extent of

leaching, the remnants of the original phase can be observed even in the final catalyst.

The scanning electron microscope [15—17] is suitable for investigation of the surfaces of solid substances, *e.g.* the morphology of powders. A resolution equal to the diameter of the electron beam scanning the sample (about 10 nm in the average modern instrument), and pictures with a very high depth of focus can be obtained.

Transmission electron micrographs of traditional Raney nickel were first published by SCHECHTER [18]. The pictures show pock-holed surfaces, with pores 50—100 nm in size. YASAMURA [19] found particles of the freshly prepared catalyst to be pyramidal in shape. According to KNAPPWOST and MADER [20], the sponge-like macroparticles of Raney nickel consist of nickel particles and amorphous aluminium oxide hydroxide.

Systematic studies by scanning electron microscopy were carried out by ROBERTSON *et al.* [21]. Their results show that two crystalline phases can be found in Raney nickel: needle-shaped bayerite ($Al_2O_3 \cdot 3H_2O$), the amount of which depends on the stoichiometric proportion of the alkali used for dissolution, is situated on the nickel particles, which have no characteristic shape. To a certain extent their results are in contradiction with the findings of YASAMURA, and KNAPPWOST and MADER, in their view because changes take place in the structure of the catalyst as a result of the heat involved under the conditions of transmission microscopy.

The most information on the internal structure of the alloys and catalysts, the nature of the individual phases, and the changes taking place during dissolution, can be obtained from X-ray diffraction studies [22].

In this way, LIDORENKO *et al.* [23] found that high-temperature dissolution leads to the formation of fine crystals in which there is a strong distortion of the lattice. At low temperatures, a structure differing considerably from this is produced; the original crystal lattice of the Ni_2Al_3 is retained (in place of the face-centred cubic lattice characteristic for nickel). KLYUCHNIKOV *et al.* [24] followed the alkaline leaching by X-ray diffraction. They found that complete removal of the aluminium from the intermetallic compound Ni_2Al_3 is very difficult, but the presence of $NiAl_3$ promotes the leaching process.

Combined X-ray diffraction and metallographic studies were used by PRESNYAKOV *et al.* [12] to follow the changes occurring during dissolution. They found that the process of leaching consists of two stages. The alkali first attacks the eutectic of high aluminium content and removes it completely from the alloy. The first microdefects and cracks next appear on the crystallites of the phases corresponding to the intermetallic compounds; with the growth of these defects, increasingly more significant lattice defects and distortions are produced, until finally the lattice of nickel atoms in the intermetallic compound collapses completely.

Experimental

Optical micrographs were prepared on a Reichert Me F microscope, at magnifications of 100 and 550 times. Appropriate pieces of the alloys were ground and polished in two, mutually perpendicular planes, and the reflections of the surfaces were then examined. To enhance the differences between the phases and to follow the alkaline leaching, the samples were also photographed after etching with 10 wt % NaOH solution. The samples were kept in alkali solution at about 60 °C for sufficient time for the change to be readily perceptible.

Electron micrographs were taken with a JEOL JSM-U3 scanning electron microscope, at magnifications of 3000 and 10,000 times. An accelerating potential of 25 kV and a current of $(0.2—0.5) \times 10^{-11}$ A were used. The setting angle of the sample holder was 45°. The alloy and catalyst powders were fixed to the sample holder with conducting silver paint, and were examined after coating with a conducting layer of vaporized gold.

The X-ray diffraction patterns were recorded with a Philips PW-1050 large-angle powder diffractometer fitted with a Geiger-Müller counter, in automatic operating mode, with Cu K_α radiation ($\lambda = 0.15418$ nm) filtered with a nickel disc, in the interval of $2\Theta = 5—60°$. More important data on the recordings: scan rate $2\Theta = 0.5°$/min; time constant of the integrator circuit 8 sec; chart paper flow rate 800 mm/hr. Recordings on samples containing zinc and nickel had to be made up to $2\Theta = 100°$ in order to obtain evaluable patterns.

Alloys of the new types of catalysts were prepared by melting the components together in an induction furnace. Technical metals were used as base substances. Alloys containing silicon can simply be melted together without any danger of oxidation, and can be heated well above their melting points. In this way highly fluid alloy melts were obtained, which can be poured into moulds without any danger, or can be dripped into running water and thus cooled rapidly to room temperature.

In the preparation of magnesium- and zinc-containing alloys, the melts were covered with a protective layer because of the low boiling points and ready tendencies of these metals to undergo oxidation. In the case of Ni–Mg alloys a protective salt mixture [25] was used to impede oxidation, while for Ni–Zn alloys finely divided charcoal was employed. These alloys were always cooled down together with the crucible, under running water.

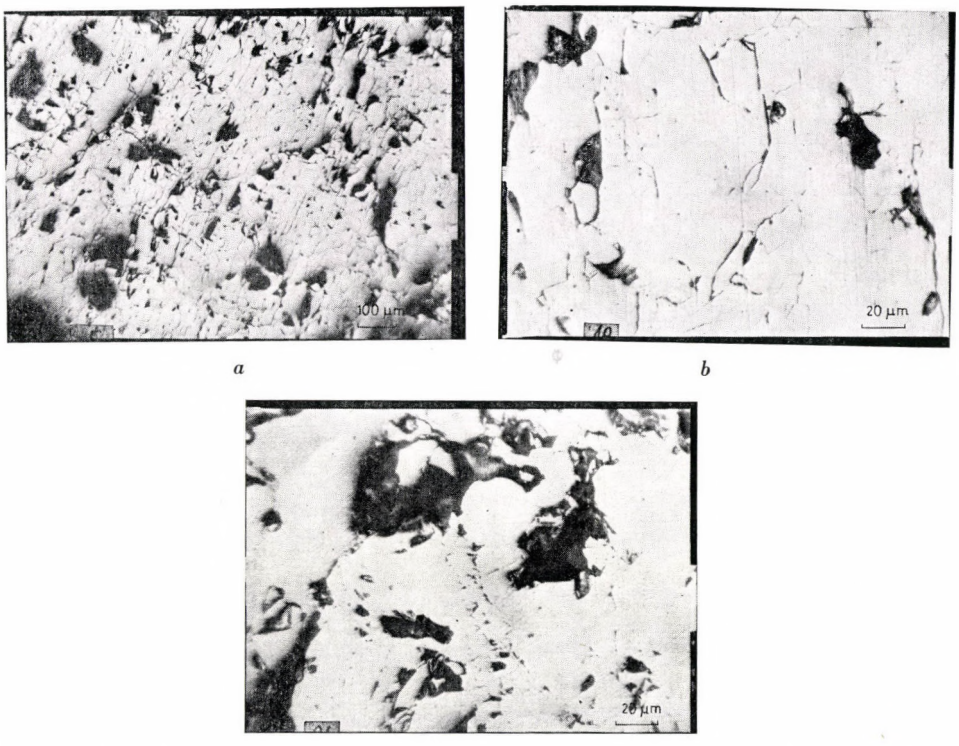
The alloys were ground to the appropriate dispersity in a vibration mill: the fraction with a particle size smaller than 63 μm, separated on a sieve series, was used for catalyst preparation. The inactive component was leached with NaOH solution between 40 and 120 °C, and the catalyst was then washed until neutral, and stored under distilled water. The exact conditions of leaching were determined so that the catalysts should have maximum activity in the hydrogenation of model compounds [26]. The nickel contents of the alloys and catalysts were reported earlier [5].

Prior to measurements, the catalysts were dried at room temperature in air. Because of its pyrophoric nature, the Degussa Raney nickel could not be examined directly, and thus it was freed from hydrogen under silicone oil [6] as described by Csűrös *et al.* [27].

Results and discussion

The starting Ni–Al alloy for the Degussa Raney nickel could not be studied metallographically, as it was available only in the form of powder; accordingly, for comparative purposes the literature data [10] were relied upon.

It can be stated in general of the phase compositions of our alloys that, with the exception of the Ni–Zn alloy, they approximate to the equilibrium structures shown in the phase diagrams [28] (equilibrium could not be established completely during the rapid cooling). The photographs clearly demonstrate that the structures of the two perpendicular sections are the same; the phase proportions agree, and at most the dimensions of the elementary crystals differ a little. Samples taken from different parts of the alloy bulk show the same picture, thus the alloys were homogeneous.

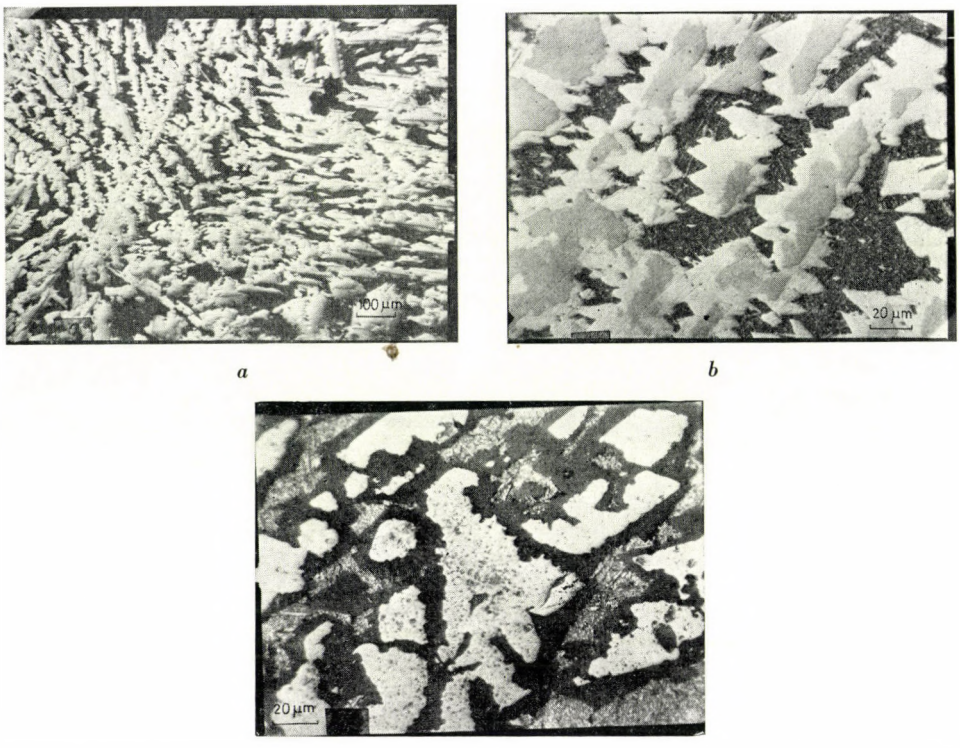


a *b* *c*

Fig. 1. Optical micrographs of a Ni–Si alloy; *a* 100×, *b* 550×, *c* after NaOH etching, 550×

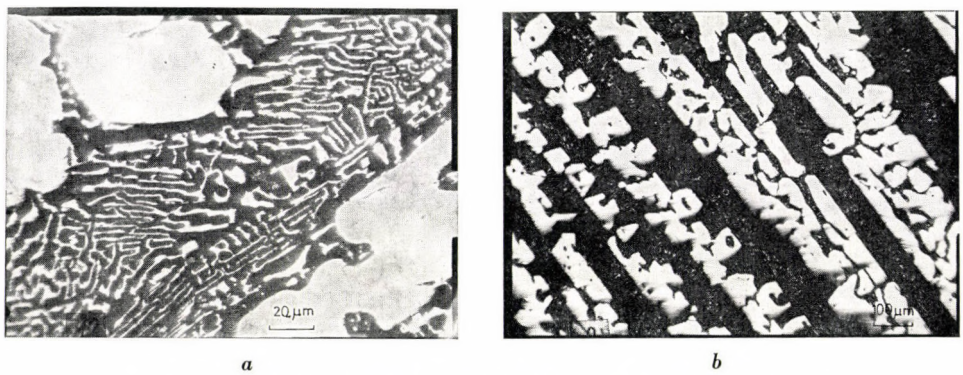
The Ni–Si alloy (Fig. 1) is practically a single, uniform phase; only a little eutectic is present between the large, intergrown crystals, and few holes are visible. The alkali dissolves primarily the dark eutectic; the light, $NiSi_2$-(ξ-) phase is attacked at the edges and at the cracks between the intergrown crystals.

The Ni–Al–Si alloy (with a composition of 40 wt % Ni–55 wt % Al–5 wt % Si) has a characteristically peritectic structure (Fig. 2): a lighter sheath is arranged around a somewhat darker central nucleus (crystals separating out primarily from the melt) in the light phase; this sheath is formed from the crystals with participation of the melt in a solid phase peritectic reaction. The eutectic comprises 15—20% of the alloy. Comparison cannot be made with the equilibrium state, for the phase diagram [29] shows the conditions only above 600 °C. In the course of the etching the eutectic and the peritectic phase dissolve rapidly and strongly, and because of this the light reflections of the phases change and the peritectic part will be darker. The alkali attacks the primary crystals which have become light too (on practically their entire surface), and small holes form on them.



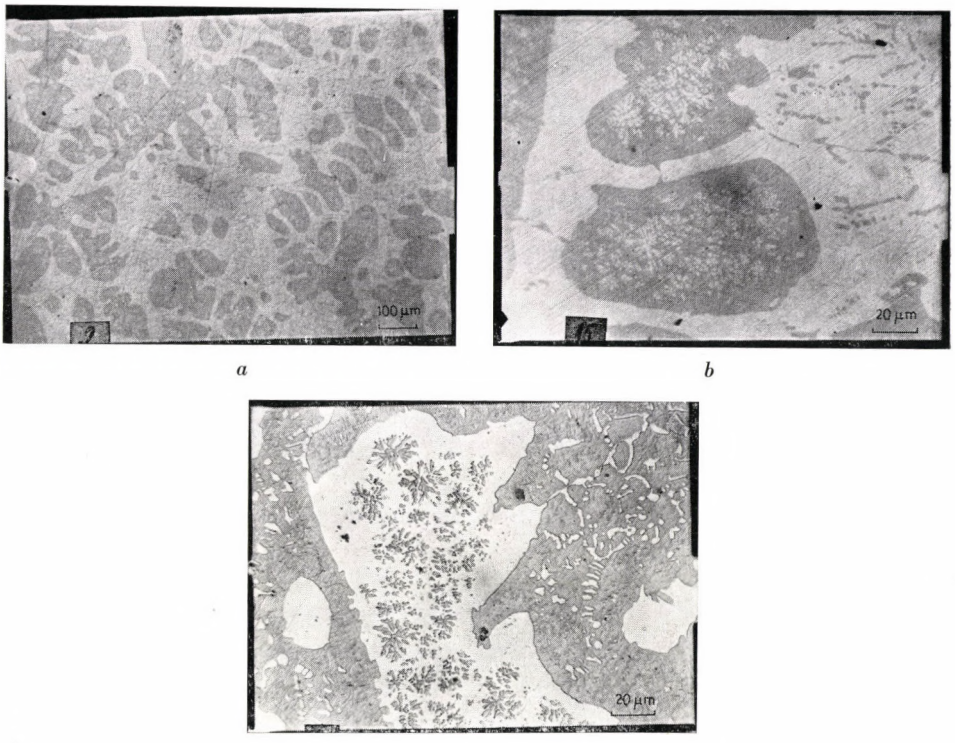
a *b* *c*

Fig. 2. Optical micrographs of a Ni–Al–Si alloy; *a* 100×, *b* 550×, *c* after NaOH etching, 550×



a *b*

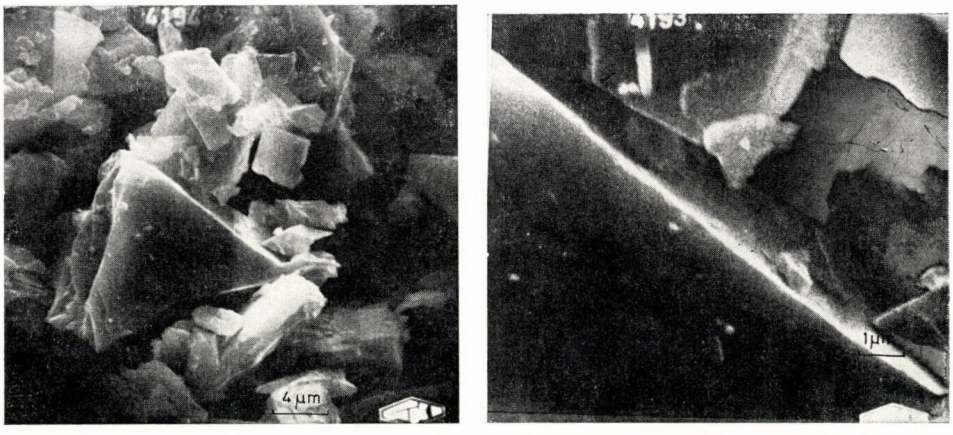
Fig. 3. Optical micrographs of a Ni–Mg alloy; *a* 100×, *b* 550×



a *b*

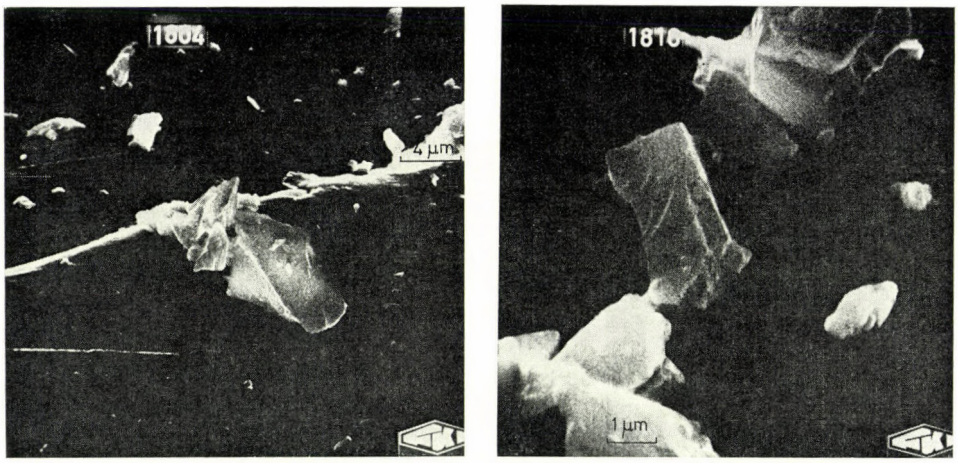
c

Fig. 4. Optical micrographs of a Ni–Zn alloy; *a* 100×, *b* 550×, *c* after NaOH etching, 550×



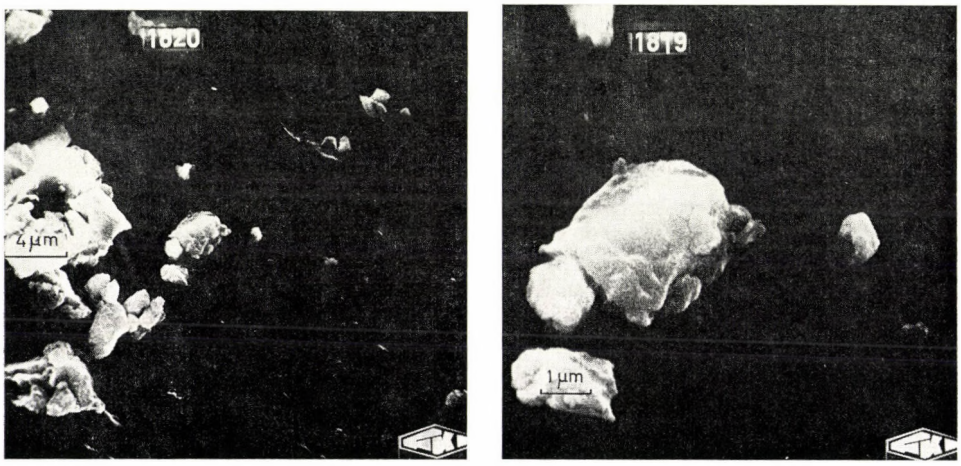
a *b*

Fig. 5. Scanning electron micrographs of Merck Ni–Al alloy powder; *a* 3000×, *b* 10,000×



a *b*

Fig. 6. Scanning electron micrographs of a Ni–Si alloy powder; *a* 3000×, *b* 10,000×

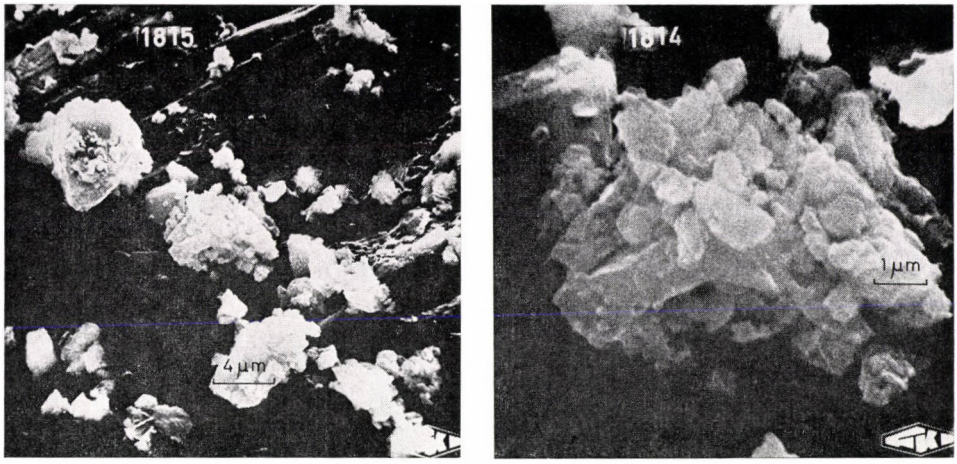


a *b*

Fig. 7. Scanning electron micrographs of a Ni–Al–Si alloy powder; *a* 3000×, *b* 10,000×

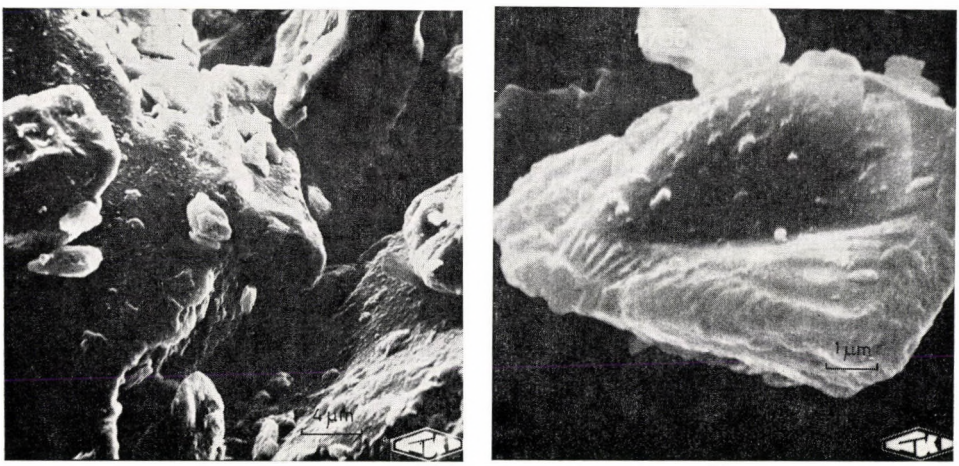
In the Ni–Mg alloy (Fig. 3), the light crystals of $NiMg_2$ are surrounded by approximately the same amount of dark phase, of a typically eutectic nature. The interesting ordering of the light crystals is striking. On alkaline etching the eutectic begins to dissolve; for a long period the large $NiMg_2$ crystals remain unchanged, and the overall picture does not change.

The structure of the Ni–Zn alloy (Fig. 4) differs to the greatest extent from that expected on the basis of the phase diagram. Although the photographs show two phases macroscopically, small inclusions are also present inside both phases. One reason for the formation of the inclusions may be that the melt can



a *b*

Fig. 8. Scanning electron micrographs of a Ni–Mg alloy powder; *a* 3000×, *b* 10,000×

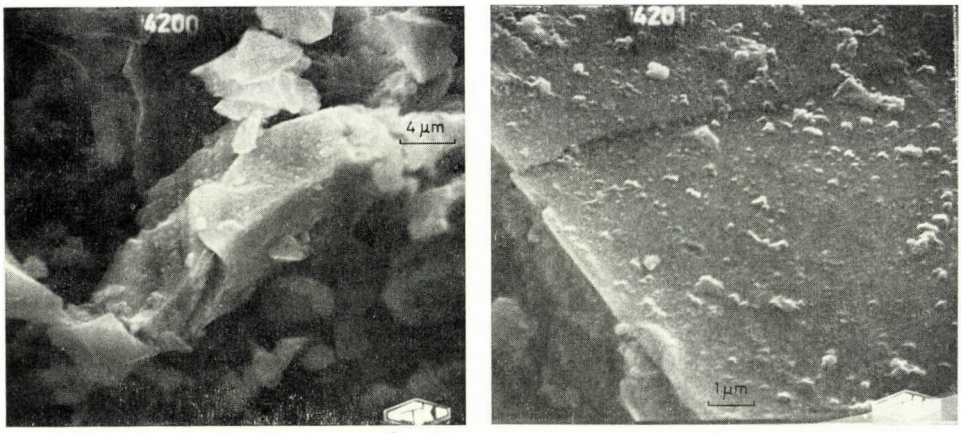


a *b*

Fig. 9. Scanning electron micrographs of a Ni–Zn alloy powder; *a* 3000×, *b* 10,000×

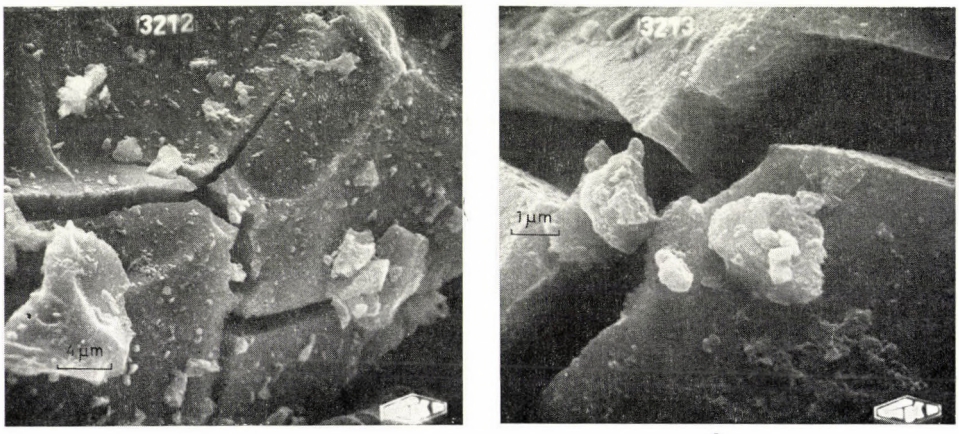
be held only a little above its melting point because of the high vapour pressure of zinc. As the X-ray diffraction results (Fig. 19) indicate the presence of only two intermetallic compounds, it is probable that the inclusions are small units of the other phase. On etching, the alkali dissolves practically only the light phase (thus this is the $NiZn_3$-phase), and the reflections of the phases therefore change: after etching the light phase will be dark, and *vice versa*.

Based on the electron micrographs, it can be said in general of the dispersity of the alloy powders that they are strongly heterogeneous: particles of every size from several ten μm down to below 1 μm can be found in them.



a *b*

Fig. 10. Scanning electron micrographs of Degussa B 113 Ni–Al catalyst; *a* 3000×, *b* 10,000×



a *b*

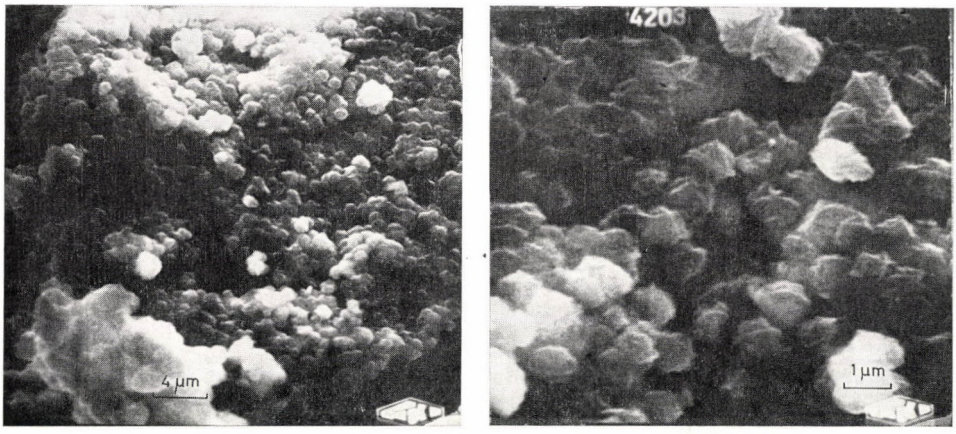
Fig. 11. Scanning electron micrographs of a Ni–Si catalyst; *a* 3000×, *b* 10,000×

The Ni–Mg alloy is comparatively finer, containing particles smaller than 1 μm in a higher proportion.

The shapes of the individual particles and the natures of their surfaces differ in the alloys of different types. The particles of the Merck Ni–Al alloy (Fig. 5) are angular; well-defined apices and edges develop on grinding, and a lamellar structure can be observed at certain sites. These signs of brittle fracture can be seen even more markedly in the very readily grindable Ni–Si alloy (Fig. 6): the particles have glassy, conchoidal, flaked surfaces. The surface of the Ni–Al–Si alloy powder (Fig. 7) is similarly a little conchoidal, but the edges and apices are strongly rounded. The particles of the Ni–Mg alloy (Fig. 8) have irregular shapes; both brittle-fractured and rounded formations are to be ob-

served on them. The small, fine particles tend to adhere together into larger agglomerations. The powder of the Ni–Zn alloy (Fig. 9) contains strongly worn-down particles; the alloy is hard, and its grinding lasts a long time. The surface of the particles is ribbed in places; this may develop from the essentially different hardnesses of the alloy phases.

When a thick suspension of the catalyst stored under liquid was transferred onto the sample holder, no suitable preparation was obtained. Drying of the caked material always yielded a compact, cracked layer, which did not give information on the individual particles. To prevent caking, individual particles were transferred onto the surface of the sample holder by deposition from a highly diluted catalyst suspension.

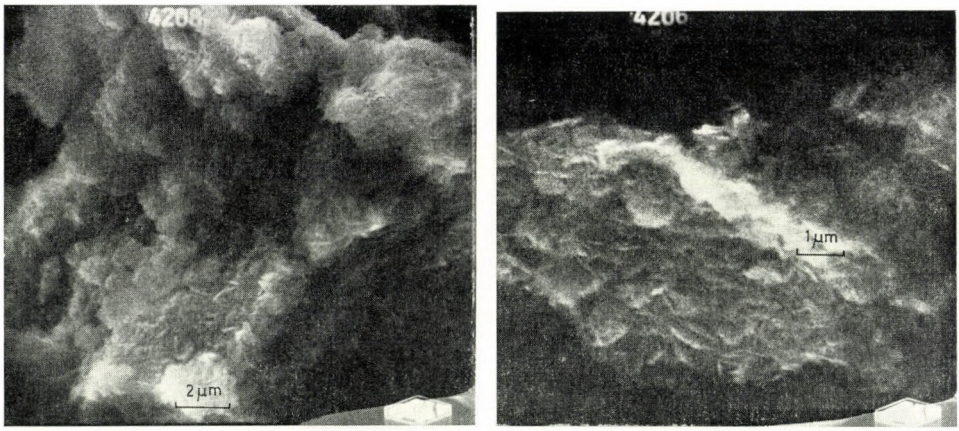


a *b*

Fig. 12. Scanning electron micrographs of a Ni–Al–Si catalyst; *a* 3000×, *b* 10,000×

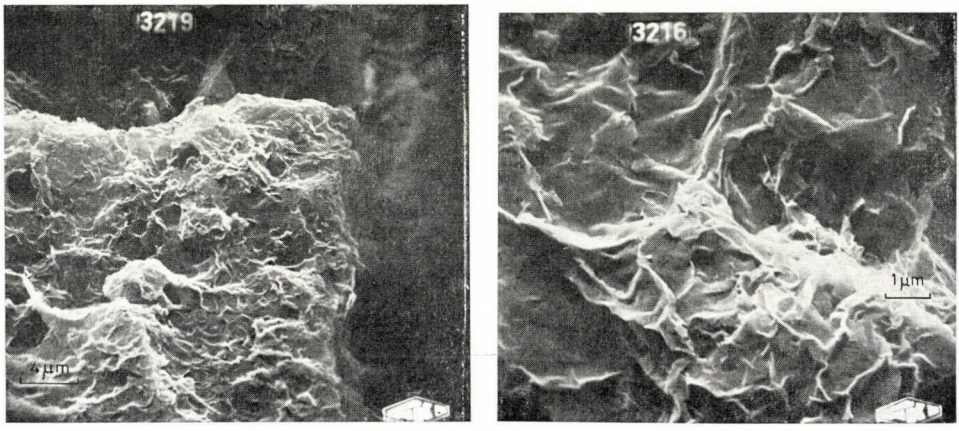
The shape and nature of the particles of the Degussa Raney nickel (Fig. 10) were unchanged compared to those of the alloy, but they were generally smaller. The fine granularity readily discernible on the larger surfaces is characteristic: besides some independent, presumably adherent pieces, there are many small particles which belong to the grain.

Well-defined individual particles could not be separated from the Ni–Si catalyst (Fig. 11) even by sedimentation, it consists of lumps in the suspending liquid too. In spite of this, it can be well seen on the micrograph (*e.g.* at the edges) that the material is an agglomeration of very fine individual particles. The Ni–Al–Si catalyst (Fig. 12) consists of adherent spherical particles with no definite geometry; the metallic part is covered by a mass of hydroxides, the presence of which was also confirmed by derivatographic measurements [6]. The Ni–Mg catalyst (Fig. 13) adheres into larger particles; the surfaces of these are uneven and strongly hydroxidic. Derivatograms show that the cata-



a *b*

Fig. 13. Scanning electron micrographs of a Ni–Mg catalyst; *a* 6000×, *b* 10,000×



a *b*

Fig. 14. Scanning electron micrographs of a Ni–Zn catalyst; *a* 3000×, *b* 10,000×

lyst contains nearly 50% $Mg(OH)_2$ [6], and the X-ray diffraction pattern (Fig. 18b) reveals that a considerable proportion of this is present in the crystalline state.

The Ni–Zn catalyst (Fig. 14) can be readily separated into individual grains by sedimentation. The surfaces of the particles are strongly featured; in the course of the leaching the inactive component was removed to various depths. The plate-like parts formed on the surface of the catalyst grains break down in places owing to mechanical effects during leaching; part of the material consists of fine particles, which sediment out with difficulty. In places cavities of greater depth too can be seen, their size being below 1 µm.

The X-ray diffraction patterns (Figs 15—19) are so arranged that the patterns of an alloy type and the catalyst prepared from it appear side by side.

In the presence of the two intermetallic compounds indicated by the phase diagram ($NiAl_3$ and Ni_2Al_3), the presence of NiAl cannot be detected in the Merck Ni–Al alloy (Fig. 15a), for its reflections coincide with those of Ni_2Al_3. The metallic aluminium in the eutectic is indicated by the weak reflection visible at $2\Theta = 38.50°$ (d = 0.2338 nm).

In general terms, the X-ray diffraction patterns of our own alloys correspond to the phase diagrams. With the exception of the Ni–Zn alloy, in every case there appears a reflection of weak intensity, indicative of the presence of a small amount of residual unalloyed inactive metal. This can be regarded as natural only for the Ni–Al–Si and Ni–Mg alloys, where the inactive component with its lower melting point is one of the components of the eutectic.

In the case of the Ni–Si alloy (Fig. 16a), where we worked with the alloy of composition corresponding practically to the intermetallic compound $NiSi_2$, *i.e.* to the limit of the Si-(χ-) phase, the presence of residual unchanged silicon cannot be established with complete certainty, because of the coincidence with the lines of $NiSi_2$. This is, however, strongly suggested by the double lines (reflection coincidence) to be seen at $2\Theta = 47.3°$ (d = 0.1922 nm) and at $2\Theta = 56.45°$ (d = 0.1630 nm). However, nickel is present in traces in the Ni–Si alloy; this is indicated by the small peak at $2\Theta = 44.32°$ (d = 0.2044 nm).

On the above basis, the conclusion must be drawn that in the case of the Ni–Si alloy, although the highest temperature attained during the alloying is well above the liquidus curve, holding at this maximum temperature for 5—10 min is probably not sufficient for completion of the process. This finding agrees with the observations of OMAROV *et al.* [30]: an alloying time of 10 min is not enough in the preparation of a Ni–Al alloy, it being advisable to keep the material in the molten state for 30—40 min.

It is worth mentioning that there are only Ni–Al compounds ($NiAl_3$ and Ni_2Al_3) in the Ni–Al–Si alloy (Fig. 17a); the diffraction pattern does not contain lines characteristic of either Ni–Si or Ni–Al–Si compounds.

Special attention was paid to the structural examination of the Ni–Zn alloy, for the added reason that on grinding the comparatively hard alloy separated into fractions of different natures. The X-ray diffraction patterns also confirmed our observation that the parts relatively richer in zinc can be ground more easily (Fig. 19a). The fraction which is more difficult to disaggregate (Fig. 20a) is poorer in zinc, and in many cases is completely unsuitable for catalyst preparation.

Only the lines of the NiZn compound appear in such 'residual' Ni–Zn alloys. In contrast with $NiZn_3$, this compound can hardly be decomposed even with strong alkali. For comparison, the diffraction pattern of the alloy containing 45 wt % nickel is also shown (Fig. 20b). This composition corresponds al-

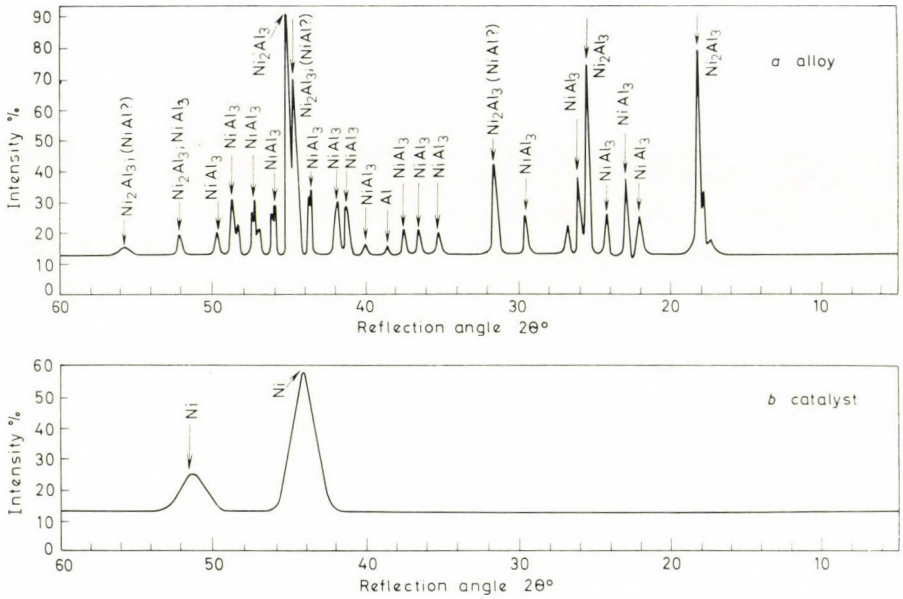


Fig. 15. X-ray diffraction patterns of Merck Ni–Al alloy and Degussa B 113 catalyst

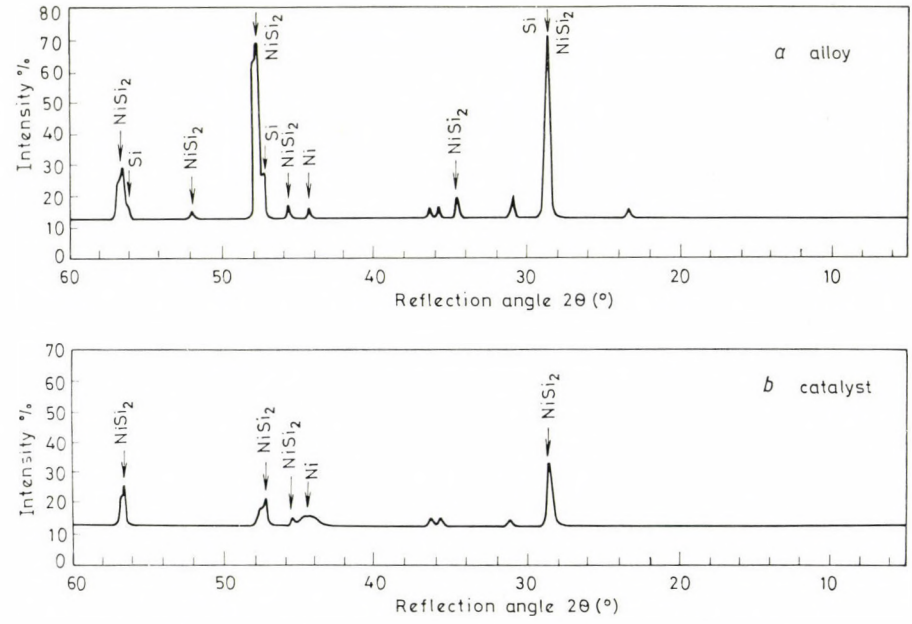


Fig. 16. X-ray diffraction patterns of a Ni–Si alloy and catalyst

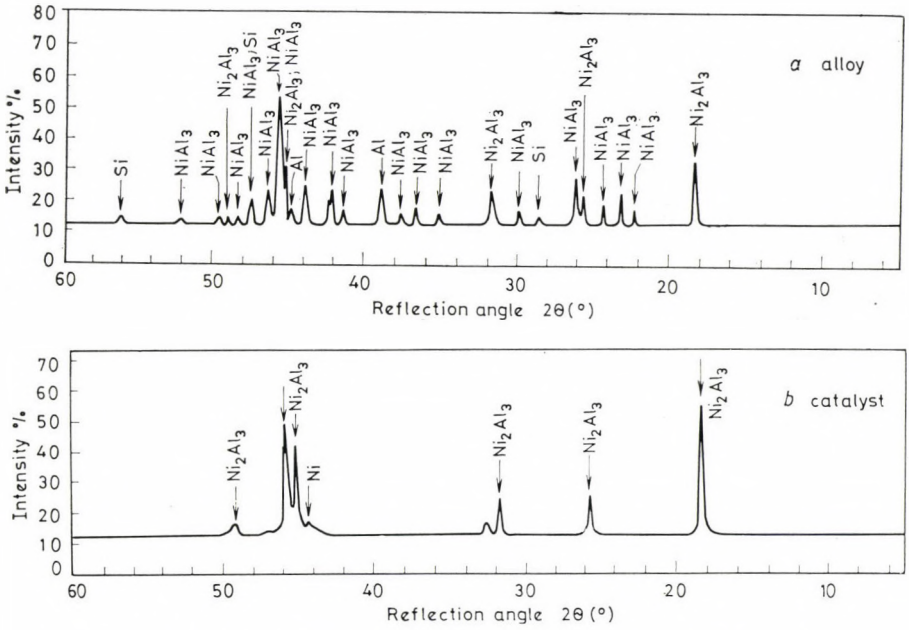


Fig. 17. X-ray diffraction patterns of a Ni–Al–Si alloy and catalyst

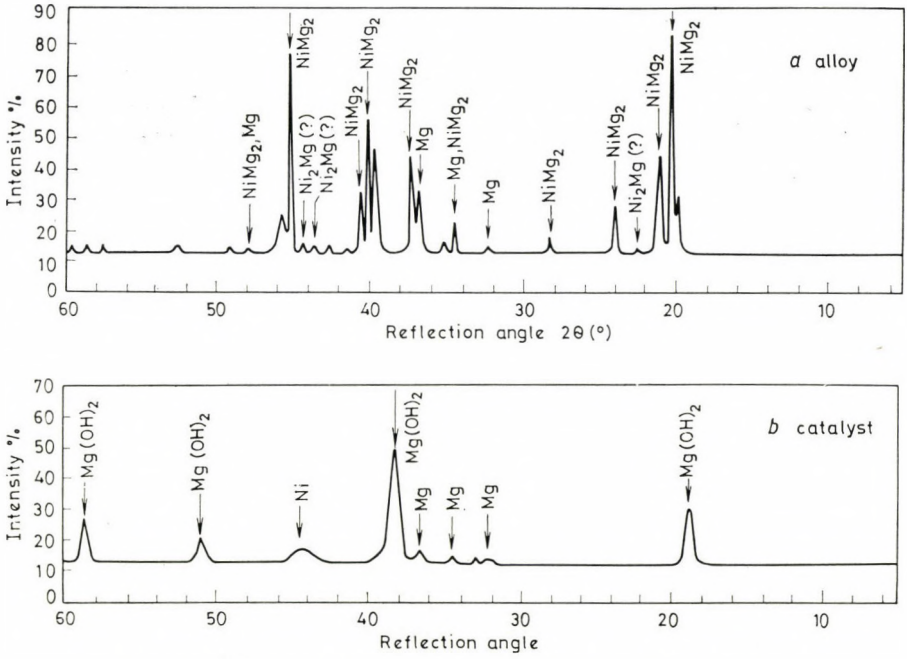


Fig. 18. X-ray diffraction patterns of a Ni–Mg alloy and catalyst

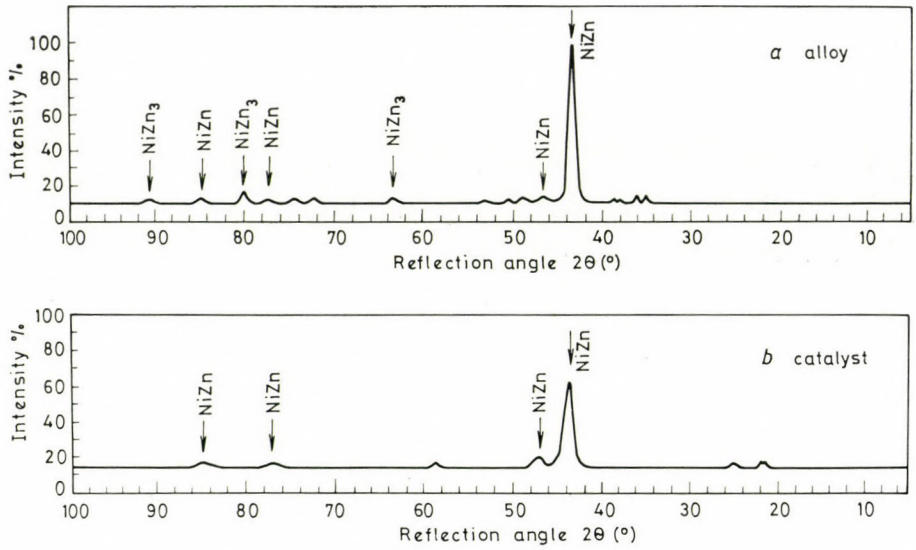


Fig. 19. X-ray diffraction patterns of a Ni–Zn alloy and catalyst

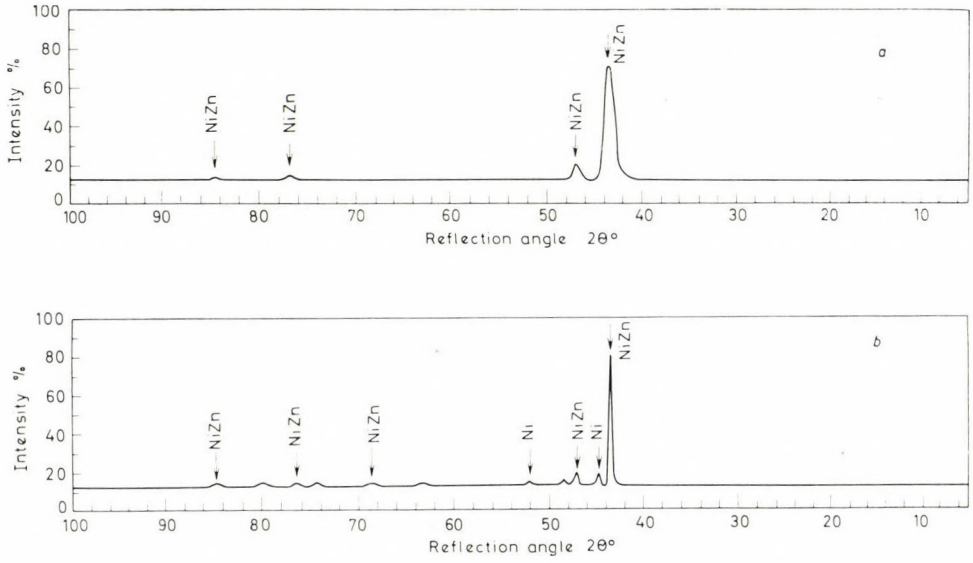


Fig. 20. X-ray diffraction patterns of Ni–Zn alloys; *a* grinding residue of alloy containing 35 wt% nickel (nickel content about 40 wt%), *b* alloy containing 45 wt% nickel

most exactly to the limit of the $\beta_1 =$ phase, and barely differs from the stoichiometric NiZn composition.

In the diffraction pattern of the Degussa Raney nickel (Fig. 15b) only the two strong bands characteristic of nickel can be seen; there is no longer any intermetallic compound in the catalyst.

It is a common feature of our own catalysts that not even the strongest line of nickel appears sharply at $2\Theta = 44.54°$ (d = 0.2034 nm) in the X-ray diffraction pattern. In the majority of cases, only a low-intensity, very broad, diffuse band is indicative of free nickel, while for the catalysts prepared from the Ni–Zn alloy no nickel bands can be seen at all; this is primarily due to strong overlap from the intense, fairly diffuse line of the NiZn compound at $2\Theta = 43.36°$ (d = 0.2087 nm).

Such an uncertain occurrence of the nickel line can be explained in that the size of the nickel crystallites formed on leaching is just on the limit of the X-ray-amorphous range, or below it, and as demonstrated by thermomagnetic measurements [5], their amount is low. Approximate calculations were carried out to establish the size of the crystallites from the broadening of the reflections. For our own catalysts this value lies in the interval of 5—7 nm, while the size of the crystallites of the Degussa Raney nickel is about 5 nm. Literature data [31—34] indicate that the crystallite size of Raney nickel is between 4 and 10 nm.

X-ray diffraction patterns of our catalysts also show that intermetallic compounds also are retained after leaching. In the case of the Ni–Zn catalyst (Fig. 19b) only NiZn, which is poorly soluble in alkali, remains; $NiZn_3$ disappears completely during the leaching.

In the Ni–Si catalyst (Fig. 16b) a part of the $NiSi_2$, which dissolves well in alkali, remains unchanged. Lines of Ni_2Al_3 appear in the diffraction pattern of the catalyst prepared from the Ni–Al–Si alloy (Fig. 17b), whereas the nickel is released completely from the compound richer in aluminium, $NiAl_3$, during leaching. Indirectly, these results also point to the different solubilities in alkali of $NiAl_3$ and Ni_2Al_3.

The inactive components remaining unalloyed were leached completely from these alloys with alkali.

Similarly as with the Degussa Raney nickel, in these three catalysts the X-ray diffraction patterns did not reveal hydroxides formed from the inactive metal, although the derivatograms [6] indicate that there are such hydroxides in the catalysts, in amounts at around the limit of detection by X-ray diffraction.

Results differing from the above were obtained for the catalysts prepared from the Ni–Mg alloy (Fig. 18b). The intermetallic compound $NiMg_2$ in the alloy disappears completely in the course of leaching, while a proportion of the unalloyed magnesium in the eutectic remains present in the catalyst.

The catalyst also contains a significant amount of $Mg(OH)_2$. This is a consequence of the fact that $Mg(OH)_2$ is not an amphoteric substance; it is only weakly soluble in alkali, and on its formation, therefore, the bulk of it remains inside the catalyst or separates out on the surface from the solution. Exactly the same results regarding the structure of the Ni–Mg catalyst were obtained by thermal studies [5, 6].

The results of our investigations show that the alloys suitable for the preparation of skeleton catalysts are not homogeneous systems: various phases develop in them, which may be intermetallic compounds of the catalytically active and inactive components, eutectics, or peritectic formations. The natures and quantities of the phases depend on the nature of the inactive component and, for a given alloy, on the quantitative proportions of the active and inactive component. The structure of the alloy is appreciably affected by the alloying parameters too: the highest temperature attained, the duration of maintenance at the highest temperature, and the rate of cooling.

The different effects of the inactive components aluminium, silicon, magnesium and zinc used together with nickel can be explained in part by the differences in the structures of the alloys. It was found that when different inactive components are used, eutectics and intermetallic compounds of different compositions (*e.g.* $NiAl_3$, $NiSi_2$, $NiMg_2$, $NiZn_3$) are formed, the physical and chemical properties of which also differ. According to the supersaturation theory, one of the sources of the excess free energy accumulating in solid substances on preparation is the presence of different phases, and the supersaturation of the phases. The catalytic activity is frequently proportional to the excess free energy. The different catalytic properties of catalysts prepared from the various alloys can be attributed in part to this reason, and in part to the different degrees of decomposition of the individual phases by alkali.

From the results, a correlation can be demonstrated between the conditions of catalyst preparation and the structure of the initial alloy. The greater the amount of an alkali-resistant intermetallic compound in the initial alloy (*e.g.* Ni_2Al_3), the higher the temperature, the longer the time, and the more concentrated the alkali required for liberation of the total amount of the active component. Our new types of catalysts often contained residual undecomposed intermetallic compound, as a sign of the insufficiency of leaching but this residual alloy plays an important role in the development of the non-pyrophoric properties of the catalysts. It also emerged from our studies that the phase least decomposed by alkali is in the Ni–Zn alloy; the NiZn–phase is practically unsuitable for catalyst preparation.

Analysis of the structure of a given alloy, and of the catalyst prepared from it, in accordance with the above aspects, brings us nearer to an understanding of the processes occurring on preparation of skeleton catalysts, and of the resulting catalytic properties.

REFERENCES

[1] FASMAN, A. B., PUSHKARIEVA, G. A.: Izv. Vyssh. Ucheb. Zaved., Khim. Khim. Technol., **11,** 886 (1968)
[2] MASON, D. M.: in Inst. Gas. Technol. Res. Bull. No. **31,** 1963 (Ed. H. A. Dirksen and H. R. Linden)
[3] SASSOULAS, R., TRAMBOUZE, Y.: Bull. Soc. Chim. France, **5,** 985 (1964)
[4] HEISZMAN, J., BÉKÁSSY, S., PETRÓ, J.: Acta Chim. (Budapest) **86,** 347 (1975); Magy. Kém. Folyóirat, **80,** 411 (1974)
[5] TUNGLER, A., BÉKÁSSY, S., PETRÓ, J.: Acta Chim. (Budapest) **86,** 359 (1975); Magy. Kém. Folyóirat, **80,** 566 (1974)
[6] BÉKÁSSY, S., LIPTAY, G., PETRÓ, J.: Thermochim. Acta, **11,** 45 (1975); Magy. Kém. Folyóirat, **81,** 26 (1975)
[7] VERŐ, J.: Fémtan. Tankönyvkiadó, Budapest, 1969.
[8] ALEXANDER, W. O., VAUGHAN, W. B.: J. Inst. Metals, **61,** 247 (1937)
[9] PRESNYAKOV, A. A., CHERNOUSOVA, K. T., KABIEV, T., FASMAN, A. B., BOCHAROVA, T. T.: Zh. Prikl. Khim., **40,** 958 (1967)
[10] FREEL, J., PIETERS, W. J. M., ANDERSON, R. B.: J. Catal., **16,** 281 (1970)
[11] ALEIKINA, S. M., MARSAKOV, I. K., FASMAN, A. B., VAVRESYUK, I. V.: Elektrokhimiya **6,** 1648 (1970)
[12] PRESNYAKOV, A. A., CHERNOUSOVA, K. T., BOCHAROVA, T. T.: Tr. Inst. Met. i Obogashch., Akad. Nauk Kaz. SSR **15,** 65 (1966)
[13] KABIEV, T., FASMAN, A. B., ISABEKOV, A., CHERNOUSOVA, K. T.: Elektrokhimiya, **1,** 868 (1965)
[14] LITTMAN, H., BLISS, H.: Ind. Eng. Chem., **51,** 662 (1959)
[15] BOOKER, G. R.: Modern Diffraction and Imaging Techniques in Material Science (Ed. S. Amelinckx, R. Gevers, G. Remant and J. van Landuyt), pp. 553—653. North-Holland, Amsterdam—London 1973
[16] THORNTON, P. R.: Scanning Electron Microscopy. Chapman and Hall, London—Paris—New York 1968
[17] CLARKE, D. R.: J. Mater. Sci., **5,** 689 (1970)
[18] SCHECHTER, A. B.: Problemy kinetiki i kataliza, tom. VI. Geterogenny kataliz, p. 137. Izd. Akad. Nauk SSSR 1949
[19] YASAMURA, J.: Nature, **173,** 80 (1954)
[20] KNAPPWOST, A., MADER, K.-H.: Naturwiss., **52,** 590 (1965)
[21] ROBERTSON, S. D., FREEL, J., ANDERSON, R. B.: J. Catal., **24,** 130 (1972)
[22] RUBINSTEIN, A. M.: Ergebnisse röntgenographischer Untersuchungen an heterogenen Katalysatoren. Verlag Technik, Berlin 1955
[23] LIDORENKO, N. S., KAGAN, A. S., KAGAN, N. M., CHIZHIK, S. P., ULYANOVA, G. D., SHISHKINA, A. V.: Dokl. Akad. Nauk SSSR, Khim. Technol., **185,** 1104 (1969)
[24] KLYUCHNIKOV, J. F., FASMAN, A. B., SAPUKOV, I. A., ALMASHEV, B. K., RECHKIN, V. N.: Zh. Prikl. Khim., **44,** 1009 (1971)
[25] HAUGHTON, J. L., PAYNE, R. J. M.: J. Inst. Metals, **54,** 275 (1934)
[26] BÉKÁSSY, S.: Dissertation, Budapest 1974
[27] CSŰRÖS, Z., PETRÓ, J., KÁLMÁN, V., ERDEY, L., PAULIK, F.: Magy. Kém. Folyóirat, **70,** 337 (1964)
[28] HANSEN, M.: Constitution of Binary Alloys, 2nd Ed., McGraw-Hill, New York—Toronto—London 1958
[29] FUSS, V.: Metallographie des Aluminiums und seiner Legierungen. Springer, Berlin 1934
[30] OMAROV, A. K., SHARIPKULOV, R. S., SHKREBKO, K. V.: Vest. Akad. Nauk Kaz. SSSR, **27,** 27 (1971)
[31] DUPONT, G., PIGANIOL, P.: Bull. Soc. Chim. France, **1939,** 322
[32] RUBINSTEIN, A. M.: Usp. Khim., **21,** 1287 (1952)
[33] HOFER, E. M., HINTERMANN, H. E.: Trans. Faraday Soc., **60,** 1457 (1964)
[34] ROBERTSON, S. D., ANDERSON, R. B.: J. Catal., **23,** 286 (1971)

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STUDY OF THE TRANSFORMATIONS OF DIOLS AND CYCLIC ETHERS, XXXVIII

MECHANISM OF THE PLATINUM-CATALYZED ISOMERIZATION OF OXACYCLOALKANES

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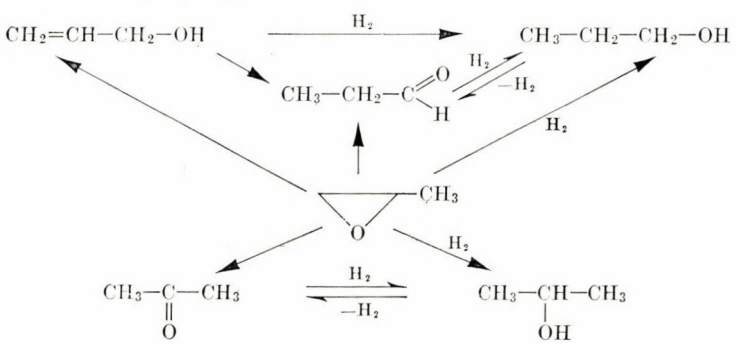
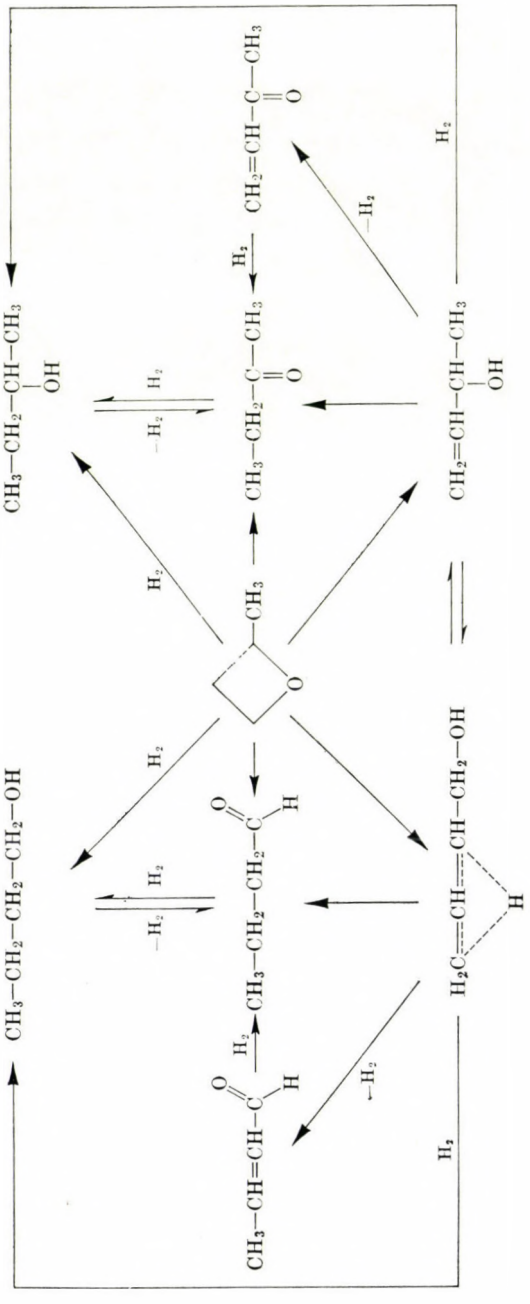
The mechanism of the platinum-catalyzed isomerization of 2-methyloxacycloalkanes (2-methyloxirane, 2-methyloxethane, 2-methyltetrahydrofuran, 2-methyltetrahydropyran) has been studied. A microreactor technique in combination with gas chromatography, a pulse technique, served as the experimental method. The model compounds were studied in a carrier gas stream of hydrogen and helium, on platinum catalysts on thermolite and carbon supports, and also on ammonia-poisoned catalysts. Examinations were further carried out with the reaction products and with a number of compounds assumed as intermediates. The experimental data indicate that the mechanism of isomerization of the oxacycloalkanes depends on the number of atoms in the ring, on the catalyst and on the reaction conditions, and differences exist in the mechanisms of formation of aldehydes and ketones. In the formation of aldehydes a significant role is played by the catalyst sites with electrophilic character. In the formation of ketones the role of the platinum catalyst and the hydrogen chemisorbed on the catalyst as well as the participation of secondary alcohols as intermediates has been experimentally demonstrated.

Introduction

Earlier investigations confirmed the general character of the isomerization of oxacycloalkanes to oxo compounds [1—3]. It has also been found that of the 2-alkyloxacycloalkanes, oxiranes and oxethanes in the presence of hydrogen and a platinum catalyst give rise to both aldehydes and ketones; in addition, isomerization is observed, leading to the formation of unsaturated alcohols, as is hydrogenolysis, resulting in the formation of saturated alcohols [3]. These processes are shown in the following schemes for the case of 2-methyloxirane and 2-methyloxacyclobutane:





In the five- and six-membered cyclic ethers the isomerization leads mainly to the corresponding ketones.

Examination of the pertinent literature reveals that only the first steps have been made as regards the study of the mechanism of oxacycloalkane isomerization [4, 5].

Investigation of the mechanism of the changes is complicated by the fact that the formation of the products in the transformation of oxacycloalkanes can be explained by various primary and secondary processes, *i.e.*, simultaneous and consecutive changes, as is illustrated by the scheme for 2-methyloxacyclobutane.

In the present paper an account is given of our studies on the mechanism of the platinum-catalyzed isomerization of 2-methyloxacycloalkanes, utilizing the possibilities afforded by the pulse technique. The transformations of four model compounds (**1**, **2**, **3** and **4**) were studied on thermolite as a catalyst support (in the following *T;* this is a support of diatomaceous earth type used in GC (GC = gas chromatography)), on Pt/*T* and Pt/C catalysts (C = active carbon support) in hydrogen and helium as carrier gas, and on ammonia-poisoned catalysts.

1 **2** **3** **4**

Detailed examinations were also performed with a number of compounds assumed as intermediates, under the same experimental conditions as for the model compounds: unsaturated alcohols, saturated alcohols and the end-products. A study was similarly made of the transformation of 2-methylfuran, under the same experimental conditions as for **3**.

Methods

Compounds studied. Of these **1** was a product of BDH, while **2**, **3** and **4** were prepared by known methods [6—8]. Before use, the starting materials were purified by distillation, and their purities were checked by GC and IR.

Catalysts. The catalysts were prepared as described earlier [9]. In the experimental work 1 ml of the Pt/*T* catalyst, containing 10% platinum metal, and 0.2 ml of the Pt/C catalyst containing 18.5% platinum metal, were used. The active metal contents of these two catalysts were approximately the same. Measurements were made between the sixth and thirtieth pulses, where the activities and selectivities of the catalysts were approximately constant. They were next activated [9], and the measurement series repeated.

Experimental method. The examinations were performed by a pulse microreactor technique. The previously described pulse technique [9] was modified only in that rasotherm glass was selected as the material for the construction of the microreactor. The internal diam-

eter of the microreactor was 6 mm. The microreactor was attached to a Carlo Erba GV gas chromatograph. Chromatography conditions:

Column: Two 1 m glass columns, 4 mm in internal diameter, connected in series; the first contained 15% polyethyleneglycol with a molecular weight of 20,000, on thermolite with a grain size of 0.2—0.3 mm; the second contained 15% tris(cyanoethoxy)propane (Fractonitrile III) on the same support.

Carrier gas: 60 ml hydrogen/min, or 60 ml helium/min.

Thermostat temperature: 120 °C.

Detector current: 140 mA.

Injected sample: 0.005 ml.

Peaks were identified using authentic substances, and were evaluated quantitatively *via* calibration curves.

Results

At the beginning of the experimental work it was found that in the temperature interval employed the catalyst supports were practically inactive in the transformations of **3** and **4**. Thermolite, however, was active in the case of **1** and **2**, which at 250 °C underwent a transformation of about 50%, with the formation of mainly the corresponding aldehydes and unsaturated alcohols. On Pt/*T* and Pt/C the conversions were considerably higher, and large differences could also be observed in the directions of the reactions. From this respect there can be no doubt as to the correctness of the conclusions drawn with regard to the isomerizing effects of the supported metal catalysts. The variation in the activity of the Pt/*T* was studied as a function of the number of pulses. From the fifth up to about the thirtieth pulse, the activity and selectivity of the catalyst proved practically constant. Since the activity of the catalyst was relatively constant between two activations, measurements could be carried out with the necessary accuracy. In spite of the fact that the catalysts were activated under similar conditions, it could be observed that effects arising in the activation of the catalysts did have a substantial influence on their surface states, and thus on their activities and selectivities.

In the case of **2** on Pt/*T*, a study was made of the effect of the contact time on the product composition. The contact time was controlled by varying the length of the catalyst bed and the rate of flow of the carrier gas. The experimental data show that the selectivity to butyraldehyde formation is inversely proportional to the contact time (see Table I).

The nature of the active centers responsible for isomerization to aldehydes and ketones was investigated by studying the transformation of oxacycloalkanes on ammonia-poisoned Pt/*T* and Pt/C. The experimental data are given in Tables II—V.

The results show that ammonia does not affect the hydrogenating abilities of the catalysts, and at the same time does not poison those active sites of the catalysts which are responsible for the formation of ketones. Ammonia does have an effect, however, on the formation of the aldehydes. On the basis of these experimental data it can be stated that there is a certain difference

Table I

Transformation of 2-methyloxethane as a function of the length of the catalyst bed

	Selectivity (mol%)[a]			
Catalyst	Pt/T[b]			
Carrier gas	Hydrogen			
Temperature (°C)	230			
Catalyst bed length (mm)	10	6	3	1
Conversion (%)	95	93	65	30
Butyraldehyde	12	12	18	26
Methyl ethyl ketone	9	9	10	12
1-Butanol	19	21	25	21
2-Butanol	5	5	6	8
Crotyl alcohol	0	2	3	0
Allyl carbinol	2	3	5	0
Decomposition products[c]	53	48	33	33

Symbols in the Tables.
a Selectivity is based on 100 mol of the compound reacted
b Pt/T 1 ml; Pt/C 0.2 ml; hydrogen flow 60 ml/min; injection 0.005 ml
c Composition of gaseous decomposition products not examined
d Experimental data before ammonia treatment
e Experimental data after ammonia tratment
f Experimental data after desorption of ammonia

Table II

Transformation of 2-methyloxirane on ammonia-poisoned catalysts[b]

	Selectivity (mol%)[a]				
Catalyst, temp. (°C)	Pt/T, 250			Pt/C, 250	
Carrier gas	Hydrogen			Hydrogen	
	d	e	f	d	e
Conversion (%)	80	70	75	100	100
Propionaldehyde	33	21	30	0	0
Acetone	12	17	14	47	43
1-Propanol	12	10	12	0	0
2-Propanol	3	4	3	9	12
Decompn. products[c]	40	48	41	44	45

between the mechanisms of isomerization of the cyclic ethers to aldehydes and to ketones. In the isomerization to aldehydes a significant role is played by those active sites of the Pt/T which can be poisoned with ammonia.

The above findings are substantiated by the experimental data in Tables VI and VII, which illustrate the roles of the platinum catalyst supports. On

Table III

Transformation of 2-methyloxacyclobutane on ammonia-poisoned catalysts[b]

	Selectivity (mol%)[a]				
Catalyst, temp. (°C)	Pt/*T*, 250			Pt/C, 250	
Carrier gas	Hydrogen			Hydrogen	
	d	e	f	d	e
Conversion (%)	96	90	92	75	78
Butyraldehyde	15	10	16	3	min.
Methyl ethyl ketone	9	9	9	30	26
Crotyl alcohol + allyl carbinol	6	6	6	0	0
1-Butanol	16	19	15	17	20
2-Butanol	4	6	6	3	4
Decompn. products[c]	50	45	48	47	50

Table IV

Transformation of 2-methyltetrahydrofuran on ammonia-poisoned catalysts[b]

	Selectivity (mol%)[a]				
Catalyst, temp. (°C)	Pt/*T*, 300			Pt/*C*, 300	
Carrier gas	Hydrogen			Hydrogen	
	d	e	f	d	e
Conversion (%)	80	76	75	77	87
Methyl propyl ketone	54	54	56	64	66
Decompn. products[c]	46	46	44	36	34

Table V

Transformation of 2-methyltetrahydropyran on ammonia-poisoned catalysts[b]

	Selectivity (mol%)[a]				
Catalyst, temp. (°C)	Pt/*T*, 300			Pt/C, 300	
Carrier gas	Hydrogen			Hydrogen	
	d	e	f	d	e
Conversion (%)	74	80	80	87	92
Methyl butyl ketone	53	50	55	57	50
Decompn. products[c]	47	50	45	43	50

Table VI

Effect of the support on the transformation of 2-methyloxirane

	Selectivity (mol%)[a]									
Catalyst	Pt/T[b]					Pt/C[b]				
Carrier gas	Hydrogen					Hydrogen				
Temperature (°C)	150	200	250	300	350	150	200	250	300	350
Conversion (%)	10	30	64	90	100	15	55	84	100	100
Propionaldehyde	33	30	33	32	7	0	5	0	0	0
Acetone	20	26	12	11	10	54	44	47	36	20
1-Propanol	35	21	12	7	3	0	5	0	0	0
2-Propanol	2	3	3	0	0	33	15	9	0	0
Decompn. product[c]	10	20	40	50	80	13	31	44	64	80

Table VII

Effect of the support on the transformation of 2-methyloxethane

	Selectivity (mol%)[a]					
Catalyst	Pt/T[b]			Pt/C[b]		
Carrier gas	Hydrogen			Hydrogen		
Temperature (°C)	200	250	300	200	250	300
Conversion (%)	60	94	100	45	75	90
Butyraldehyde	13	17	6	11	3	0
Methyl ethyl ketone	8	8	6	33	30	34
1-Butanol	38	17	5	23	17	0
2-Butanol	5	2	0	7	3	0
Crotyl alcohol	5	3	0	0	0	0
Allyl carbinol	8	6	0	0	0	0
Decompn. products[c]	23	47	83	26	47	66

Pt/C not containing centers poisonable with ammonia, the isomerizations of **1** and **2** are shifted towards the formation of the ketones. The essence of this finding is not affected by the experimental fact that the rate of decarbonylation of the aldehydes increases when the temperature is raised.

Experiments on Pt/T and Pt/C were also carried out to isomerize the oxacycloalkanes in the presence of helium as carrier gas in order to establish the effect of the hydrogen used as carrier gas. The main conclusions to be drawn from these investigations, apart from the fact that hydrogenolysis does not proceed in the absence of hydrogen, are as follows.

In the presence of helium as carrier gas, transformation is observed only for **1** and **2**, **3** and **4** are not undergoing isomerization in this temperature

Table VIII

Effect of the carrier gas on the transformation of 2-methyloxirane

	Selectivity (mol%)[a]	
Catalyst, temp. (°C)	Pt/C[b], 250	
Carrier gas	Helium	Hydrogen
Conversion (%)	75	84
Propionaldehyde	5	0
Acetone	65	47
1-Propanol	0	0
2-Propanol	5	9
Decompn. products[c]	25	44

Table IX

Effect of the carrier gas on the transformation of 2-methyloxethane

	Selectivity (mol%)[a]					
Catalyst	Pt/T[b]			Pt/C[b]		
Carrier gas	Helium*			Helium		
Temperature (°C)	200	250	300	250	300	350
Conversion (%)	60	94	100	2	30	90
Butyraldehyde	22	17	8	0	0	0
Methyl ethyl ketone	0	3	1	0	14	15
Crotyl alcohol	10	2	0	0	0	0
Allyl carbinol	30	30	15	0	0	0
1-Butanol	1	4	1	0	0	0
2-Butanol	0	0	0	0	0	0
Methyl vinyl ketone	4	3	2	0	20	15
Decompn. products[c]	33	40	70	100	66	70

* Trace amounts of crotonaledhyde also is formed

range in the absence of hydrogen. Information on the effects of the carrier gas in the case of **1** and **2** is given by the experimental data in Tables VIII and IX.

The absence of hydrogen did not exert an appreciable effect on the rate of transformation of **1**. This experimental observation points to the role of intramolecular processes in the platinum-catalyzed isomerization of **1**.

The experimental data in Tables VII and IX deserve particular attention. In the case of **2** the conversion too is smaller on Pt/C in the absence of hydrogen. Similarly to **3** and **4**, therefore, the presence of hydrogen is the determining factor as regards the formation of the ketones. Although a little methyl ethyl

Table X

Transformation of 2-methylfuran and 2-methyltetrahydrofuran

	Selectivity (mol%)[a]							
Catalyst					Pt/T^b			
Carrier gas					Hydrogen			
Compound	2-methylfuran				2-methyltetrahydrofuran			
Temperature (°C)	200	250	300	350	200	250	300	350
Conversion (%)	46	62	70	74	6	44	67	85
Methyl propyl ketone	54	60	33	13	50	64	70	43
2-Pentanol	9	3	0	0	35	9	0	0
Decompn. products[c]	19	27	63	83	15	27	30	57
2-Methyltetrahydrofuran	18	10	4	4	—	—	—	—

ketone is formed, this is connected with the presence of strongly-bound hydrogen which is not removed from the catalyst. The significance of hydrogen is also supported by the formation of methyl vinyl ketone, which appears in the absence of hydrogen. On Pt/T the conversion does not decrease in the presence of helium, which can be explained by the formation of butyraldehyde and allyl carbinol, catalyzed by the electrophilic centres.

The determining role of the chemisorbed hydrogen in the isomerization of oxacycloalkanes to ketones is further supported by the course of the hydrogenolysis of 2-methylfuran, which is similar to the isomerization of **3** (Table X).

Since the unsaturated and saturated alcohols may well be intermediates, under the experimental conditions used for **2** and on the same catalyst, a study was made of the isomerization of crotyl alcohol, allyl carbinol and methyl vinyl carbinol, and of the dehydrogenation of 1-butanol and 2-butanol to butyraldehyde and methyl ethyl ketone, respectively [10]. The experimental data are

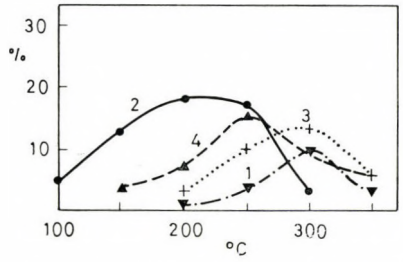


Fig. 1. Variation of the butyraldehyde yield as a function of temperature. (1: % Butyraldehyde from allyl carbinol; 2: % butyraldehyde from crotyl alcohol; 3: % butyraldehyde from 1-butanol; 4: % butyraldehyde from 2-methyloxethane)

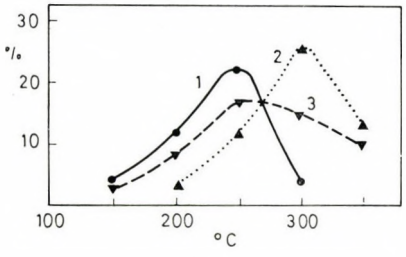


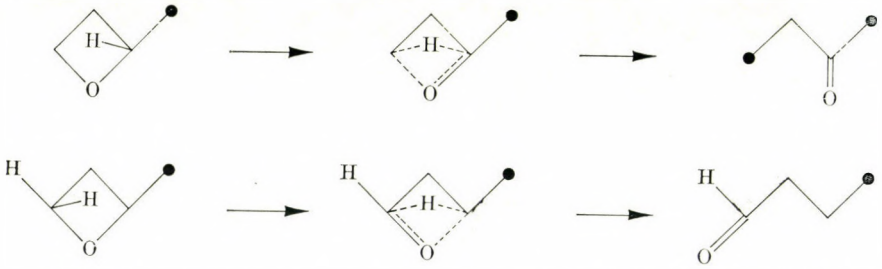
Fig. 2. Variation of the methyl ethyl ketone yield as a function of temperature. (1: % Methyl ethyl ketone from methyl vinyl carbinol; 2: % methyl ethyl ketone from *sec*-butanol; 3: % methyl ethyl ketone from 2-methyloxethane)

presented in Figs 1 and 2, which show the changes in the yields of the two oxo compounds as a function of the temperature.

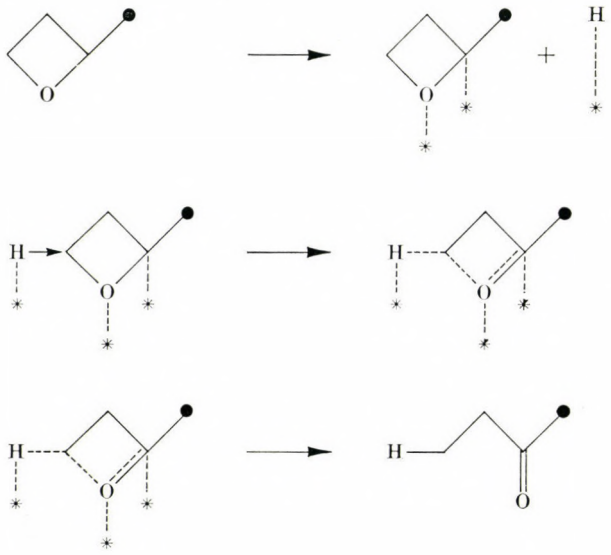
Discussion

An examination was made of the reality of the four routes which can be assumed in principle to explain the isomerization of the oxacycloalkanes to oxo compounds. By way of introduction these four reaction mechanisms are outlined below.

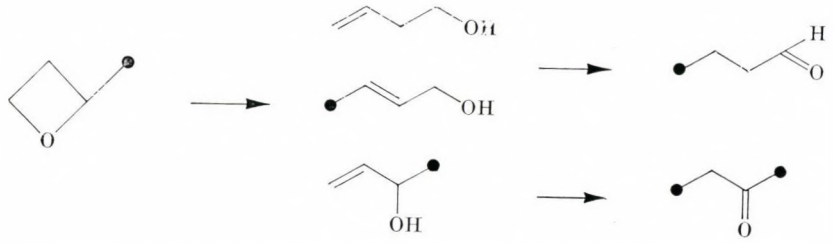
1. The formation of oxo compounds by the intramolecular migration of hydrogen atoms or ions. According to this mechanism, which can be regarded as 1,3-hydrogen migration *via* a four-center transition state, the formation of butyraldehyde and methyl ethyl ketone can be pictured in the following way:



2. The formation of oxo compounds can also be interpreted by means of an intermolecular mechanism, with the participation of chemisorbed hydrogen. In this mechanism the first step is the dissociative chemisorption of the substrate molecule. The transition state is stabilized by the attack of chemisorbed hydrogen on the spatially less shielded carbon atom of the substrate:

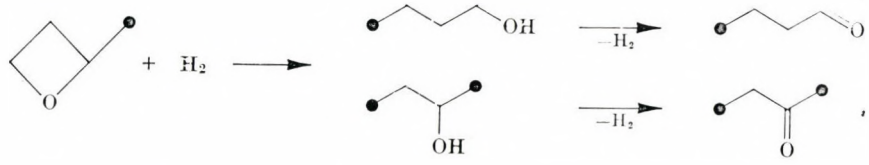


3. The formation of oxo compounds can in principle also be explained by the further isomerization of the unsaturated alcohols produced in the isomerization of the oxacycloalkanes:



It should be noted that the unsaturated alcohols undergo mutual isomerization [10]. This isomerization too can take place according to two main types, intramolecularly with 1,3-hydrogen migration *via* a four-center transition state, and with the participation of sorbed hydrogen [10].

4. The formation of the oxo compounds can further be explained by the catalytic dehydrogenation of the saturated alcohols produced in the hydrogenolysis of the oxacycloalkanes:



On the basis of the experimental results, the isomerization of the oxacycloalkanes on Pt/*T* and on Pt/C can be appropriately interpreted by one or another of the above four reaction mechanisms.

The isomerization of oxiranes and oxethanes to aldehydes can be explained by mechanism 1. Thus, on ammonia-poisoned catalysts, the rate of aldehyde formation decreases. Again, the formation of aldehydes is also observed in the absence of hydrogen. Nor is the possibility of this mechanism excluded in the isomerization of oxiranes to ketones.

According to our earlier experimental work [3], the assumption of mechanism 3 is particularly realistic in the case of 2-methyloxethane. The thermodynamic data indicate that isomerization accompanied by the formation of the corresponding unsaturated alcohols is favoured only in the case of **1** and **2**. Our experimental data show, however, that the formation of unsaturated alcohols can be observed only in the transformation of **2**. It can be seen from the experimental data in Figs 1 and 2 that the oxo compounds are formed at a higher rate by the isomerization of α,β-unsaturated alcohols than by the dehydrogenation of the saturated alcohols. However, comparison of these experimen-

tal data with the data of Figs 1, 6 and 11 of an earlier paper [10] does not prove conclusively the reality of mechanism **3**, for on Pt/*T* in the presence of hydrogen the rate of hydrogenation of the unsaturated alcohols is very high. Further, in the temperature interval favouring the isomerization of **2** the equilibrium unsaturated alcohol $+H_2 \rightleftharpoons$ saturated alcohol is shifted in the direction of formation of the latter.

We have seen that as regards isomerization accompanied by the formation of ketones the presence of hydrogen is favourable and in certain cases is indeed the determining factor. Thus, in the absence of hydrogen the isomerization process does not occur for **3** and **4**, which quite clearly speaks against mechanism 1, while it confirms the reality of mechanisms 2 or 4. The greater probability of this latter mechanism can be explained by the rapid hydrogenolysis of the oxacycloalkanes to give secondary alcohols, and by the thermodynamically favoured dehydrogenation of the secondary alcohols. This latter is proved not only by the experimental data in Table X, but also by the IR data regarding the platinum-catalyzed isomerization of 2-methyltetrahydrofuran [11].

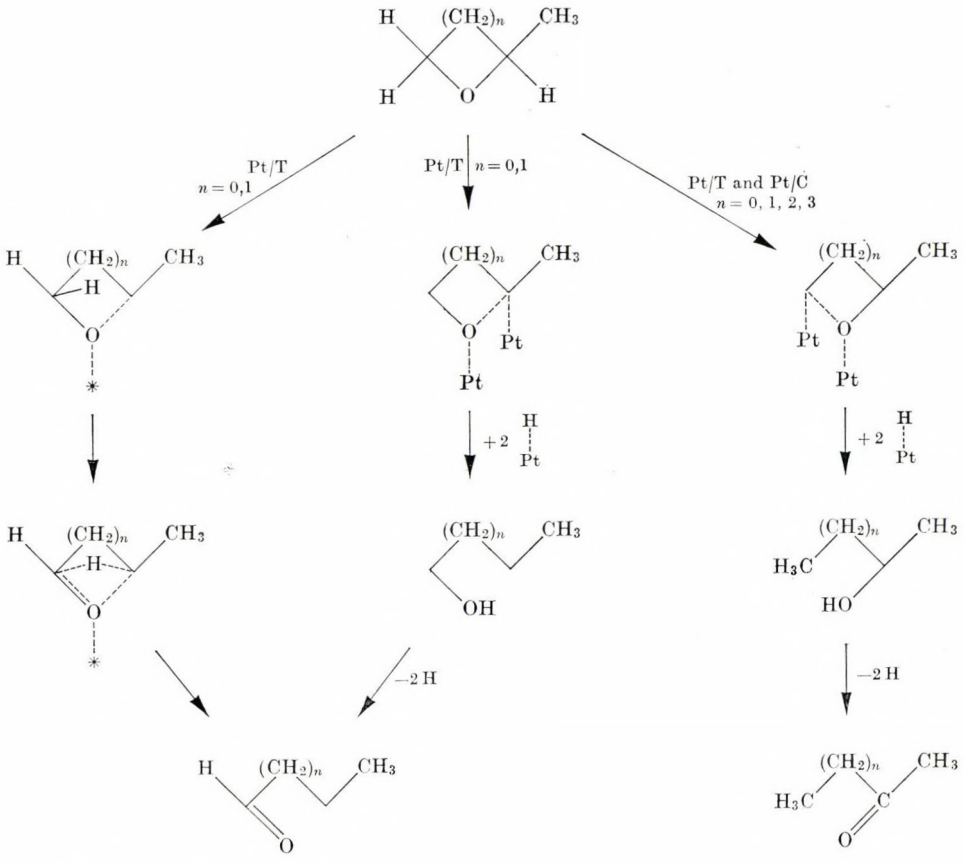
Mechanism 4 is similarly supported by the experimental data of Fig. 24 in Ref. [10]. It can be seen there that on Pt/C the rate of dehydrogenation of 2-butanol is higher than the rate of isomerization of methyl vinyl carbinol.

On the above basis the bulk of our experimental data permit to propose the mechanisms below for the isomerization of the four model compounds.

The formation of the aldehydes can be explained by the participation of the electrophilic centers of the catalyst. Thus, on Pt/C the formation of aldehydes is minimal, while on thermolite, which contains merely electrophilic centers, the formation of ketones is of minor importance in the presence of electrophilic centers the strained three- and four-membered cyclic systems split more easily along the C–O bond adjacent to the substituent, as a consequence of the +I effect of the methyl group. This splitting is accompanied by the formation of the corresponding aldehydes. It should be noted that our experimental data do not invalidate the reality of mechanism 4.

Because of their considerable stability, the five- and six-membered cyclic ethers do not split on chemisorption on the electrophilic centers of the catalyst. These systems can be opened only by chemisorbed hydrogen, with the formation of hydrogenolysis products. This process is accompanied by the formation of secondary alcohols, which for stereochemical reasons are more favoured as a consequence of the attack on the primary carbon atom. In **1** and **2** the formation of the ketone in the presence of hydrogen on both Pt/*T* and Pt/C can in all probability be explained with this same mechanism.

However, our experimental observations do not rule out mechanism 2, especially at higher temperatures. At the same time, it must not be forgotten that in the absence of hydrogen (in the presence of helium as carrier gas) the



*: active center of the catalyst

*: electrophilic center of the Pt/*T* catalyst

rate of isomerization of **1** to acetone is considerable, nor that a certain amount of hydrogen always remains on the catalyst and may facilitate the isomerization by acting as a cocatalyst.

Our experimental results were also analyzed on the basis of the Balandin multiplet theory. In the course of this work many problems arose, and at the present stage it is not possible to draw unambiguous conclusions. In addition, further complex studies are necessary to understand the finer mechanisms catalytic processes and to interpret the catalytic activity.

REFERENCES

[1] SHUIKIN, N. I., BELSKII, L. F.: Dokl. Akad. Nauk SSSR, **120,** 548 (1958); **127,** 91 (1959)
[2] SHUIKIN, N. I., BARTÓK, M., KOVÁCS, Ö., BELSKII, I. F., Izv. Akad. Nauk SSSR, Ser. Khim. 1654 (1962)
[3] BARTÓK, M., TÖRÖK, I., SZABÓ, I.: Acta Chim. (Budapest) **76,** 417 (1973)
[4] BARTÓK, M., NOTHEISZ, F.: III. Internationale Katalyse-Konferenz der DDR, Schloss Reinhardsbrunn, 2—6 April 1974. Tagungsbericht **2,** p. 175.
[5] BARTÓK, M., KARAKHANOV, R. A., NOTHEISZ, F.: Vsesoyuznaya Konferentsiya po Mekhanizmu Geterogenno-Kataliticheskikh Reaktsii, Moscow, 9—13 Sept. 1974. (In Russian). Preprinty dokladov No. 16, p. 8.
[6] BARTÓK, M., GILDE, A. S.: Acta Phys. et Chem. Szeged, **9,** 25 (1963)
[7] SHUIKIN, N. I., BARTÓK, M., KARAKHANOV, R. A., SHOSTAKOVSKII, V. M.: Acta Phys. et Chem. Szeged, **9,** 124 (1963)
[8] SHUIKIN, N. I., BELSKII, I. F., KARAKHANOV, R. A., KOZMA, B., BARTÓK, M.: Acta Phys. et Chem. Szeged, **9,** 37 (1963)
[9] BARTÓK, M., FÉNYI, SZ.: Acta Phys. et Chem. Szeged, **12,** 157 (1966)
[10] BARTÓK, M., TÖRÖK, I.: Acta Chim. (Budapest) **88,** 1 (in press).
[11] RUBINSTEIN, A. M., YAKERSON, V. I., LAFER, L. I., APJOK, J., BARTÓK, M.: Izv. Akad. Nauk SSSR, Ser. Khim. (in press).

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CONVERSIONS OF TOSYL AND MESYL DERIVATIVES OF THE MORPHINE GROUP, XIV*

A NEW METHOD FOR THE PREPARATION OF "DEOXYMORPHINE E** AND DIHYDRODEOXYMORPHINE D"

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A new convenient and mild method has been developed for the preparation of deoxymorphine E and dihydrodeoxymorphine D, by the reduction of 3-O-acetyl-6-O-tosylmorphine with $LiAlH_4$ and by further catalytic reduction of the deoxymorphine E thus obtained.

Simple and efficient methods are known for the synthesis of deoxycodeine (Δ^7-deoxycodeine, deoxycodeine E). The lithium aluminium hydride reduction of 6-O-tosylcodeine yields deoxycodeine E in a reaction without allylic rearrangement [1, 2]. On the other hand, the $LiAlH_4$ reduction of halogen derivatives with pseudocodeine structure (β-chlorocodide, bromocodide, iodocodide) involves allylic rearrangement to give deoxycodeine E [3], in accordance with the steric structures of the initial compounds and the stereochemical requirements of reactions of type S_N2'.

In contrast, only one practicable method has been published for the preparation of deoxymorphine E; this consists of the demethylation with pyridinium chloride of deoxycodeine E, prepared by one of the above routes [4].

However, in our experience demethylation reactions attempted in various ways in the case of morphine alkaloids, in general do not proceed satisfactorily.

In the course of our investigations dealing with the synthesis and nucleophilic substitution reactions of the 6-O-tosyl and 6-O-mesyl derivatives of the morphine group, we reported [5] a new method for the preparation of dihydrodeoxymorphine D. This became possible after achieving the synthesis of 3-O-acetyl-6-O-tosyldihydromorphine, unknown up to then, the $LiAlH_4$ reduction of which gave dihydrodeoxymorphine D.

3-O-Acetyl-6-O-tosyl- and 6-O-mesylmorphine have also been synthesized earlier [6], and their nucleophilic substitution reactions have been investigated.

Our present communication reports on the lithium aluminium hydride reduction of 3-O-acetyl-6-O-tosylmorphine, which can be readily effected and affords a mild method of preparing deoxymorphine E (**I**). The latter compound

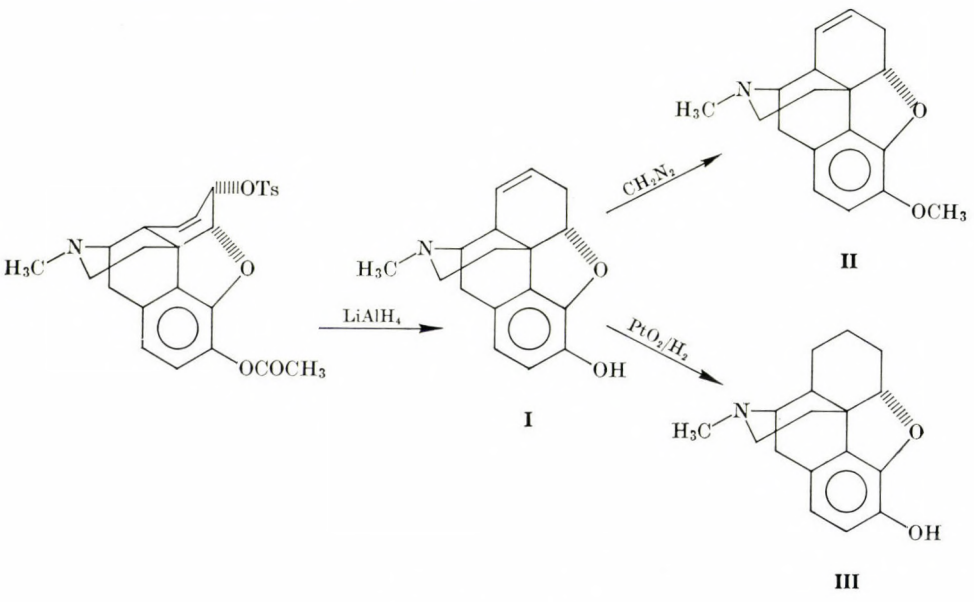
* Part XIII: R. BOGÁR, S. MAKLEIT, J. KNOLL, S. BERÉNYI, G. HORVÁTH: Comm. Dept. Chem. Bulgarian Acad. Sci. **8**, 203 (1975) and Kémiai Közl. **44**, 1 (1975).

** 3-Hydroxy-4,5α-epoxy-7,8-didehydro-17-methylmorphinan.

can be methylated with diazomethane to give deoxycodeine E (**II**), or hydrogenated to yield dihydrodeoxymorphine D (**III**).

The reduction of 3-O-acetyl-6-O-tosylmorphine with $LiAlH_4$, in the present case the elimination of the C-6 hydroxyl group, can be effected easier and thus in a better yield than the similar reaction of 3-O-acetyl-6-O-tosylmorphine also described by us, owing to the presence of the allylic system. In view of the fact that the catalytic reduction of the Δ^7 double bond is quantitative, this method affords at the same time a novel and improved mode of preparation of dihydrodeoxymorphine D (Desomorphine).

The reactions mentioned are shown in the following scheme.



Experimental

Deoxymorphine E (I)

A solution of 3-O-acetyl-6-O-tosylmorphine (4.0 g) in dry THF (40 ml) was added dropwise, with stirring and under nitrogen stream, to a solution of $LiAlH_4$ (0.6 g) in dry THF (40 ml), and the mixture was refluxed for 3 hrs. The excess of $LiAlH_4$ was decomposed first with ether saturated with water, then with water saturated with ether. The organic phase was separated and the aqueous phase extracted with ether (2×30 ml). The combined organic phase was extracted with 7.5% hydrochloric acid solution (3×40 ml). The combined acid solution was made alkaline with ammonium hydroxide and extracted with ether (3×50 ml). The ether extracts were combined, dried, evaporated, and the residue crystallized from a small amount of benzene to obtain 1.0 g (45%) of the product, m.p. 140—142 °C; lit. [4] m.p. 143—144 °C (subl.); $[\alpha]_D$-65° (0.5, ethanol); lit. [4] $[\alpha]_D$-67.2° (1.31, ethanol).

Deoxycodeine E (II)

Deoxymorphine E (100 mg) was dissolved in a small quantity of ether, and an excess of diazomethane in ether was added. The reaction mixture was allowed to stand 48 hrs in refrigerator. It was then evaporated to dryness, the residue was dissolved in chloroform (20 ml),

and washed with 5 ml of a 2% sodium hydroxide solution, then with 2×5 ml of water. After drying, the solution was evaporated to dryness. The gum thus obtained had the same R_f value as authentic deoxycodeine E in TLC. M.p. of hydrochloride: 238 °C; lit. [2] m.p. 239 °C.

Dihydrodeoxymorphine D (III)

Deoxymorphine (**I**) (1.0 g) was hydrogenated in methyl alcohol (30 ml) in the presence of PtO_2 (0.2 g) till saturation (1 hrs). The residue, obtained after the removal of the catalyst by filtration and evaporation of the solution, was crystallized from ether to yield 0.95 g of the product, m.p. 182—185 °C; lit. [5] m.p. 184—185 °C; $[\alpha]_D$-76° (0.5, ethanol); lit. $[\alpha]_D$--75.3° (1.46, ethyl acetate).

*

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REFERENCES

[1] Karrer, P., Widmark, G.: Helv. Chim. Acta **34,** 34 (1951)
[2] Rapoport, H., Bonner, R. M.: J. Am. Chem. Soc., **73,** 2872 (1951)
[3] Stork, G., Clarke, F. H.: J. Am. Chem. Soc., **78,** 4619 (1956)
[4] Rapoport, H., Bonner, R. M.: J. Am. Chem. Soc., **73,** 5485 (1951)
[5] Bognár, R., Makleit, S.: Chem. Ind. **1956,** 1239; Arzneimittel-Forsch., **8,** 323 (1958)
[6] Makleit, S., Bognár, R.: Kémiai Közl. **30,** 289 (1968); Acta Chim. Acad. Sci. Hung. **58,** 203 (1968)

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PYRIMIDINES AND CONDENSED DERIVATIVES, IV* **

N(2)-ACYLISOCYTOSINES, SOME RELATED IMIDAZO[1,2-*a*]PYRIMIDINEDIONES AND AZA ANALOGUES. SYNTHESIS, SPECTRA AND TAUTOMERIC STRUCTURES

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Series of potentially tautomeric and non-tautomeric *N*(2)-acylisocytosines, 1-acyl-2,3-dihydro-5(1*H*)- and -7(1*H*)-imidazo[1,2-*a*]pyrimidinones, imidazo[1,2-*a*]pyrimidinediones and their aza analogues have been synthesized. The sites of acylations of isocytosines, 2,3-dihydro[1,2-*a*]pyrimidinones and their aza analogues have been established by spectroscopic and/or chemical means. The predominant tautomeric forms of the potentially tautomeric compounds have been established.

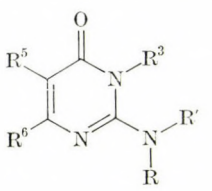
In Part I [2] we have reported on the UV and IR spectra of isocytosines (Types **1**—**3**, R, R′, $R^3 \neq H$), related imidazo[1,2-*a*]pyrimidinones and of some of their aza analogues, all of fixed tautomeric structures, and on the tautomeric structures of potentially tautomeric compounds of the above types (*e.g.* **1**, $R^3 = H$, and **2**, $R^1 = H$). In the present paper we wish to discuss the effects of acyl groups on the spectra of non-tautomeric (R′, R^1, $R^3 \neq H$) compounds of types **1**—**3** (R = ac) as well as on the tautomeric structures of potentially tautomeric compounds of types **1** (R = ac, $R^3 = H$) and **2** (R = ac, $R^1 = H$). Since the site of attachment of acyl groups introduced by acylation into isocytosines and 2,3-dihydro-5(1*H*)- and -7(1*H*)-imidazo[1,2-*a*]pyrimidinones (**4**, **5**, R = H) may be ambiguous (see below), several imidazo[1,2-*a*]-pyrimidinediones (**6**—**8**) and aza analogues **9** (R = Ac), **10** (R = Ac) and **11** have been included into the present study.

Syntheses of non-tautomeric compounds of types 2 (R=ac), 5 (R=ac), 6 (R≠H), 8 ($R^8 \neq H$), 11 and 19 ($R^8 \neq H$)

According to the literature [3], acylation of isocytosines may lead to *O*-acyl derivatives in addition to or instead of the normal *N*(2)-acylation products [4]. The synthesis of compound **2** ($R^1 = R^6 = R' = Me$, R = Ac) by acetylation of the isocytosine **2** ($R^1 = R^6 = R' = Me$, R = H) [1] is therefore, in itself, not structure proving. Since, however, the IR spectrum (KBr) of the product exhibits *two* carbonyl bands (merged into a single very broad band between 1670 and 1640 cm^{-1}), none of them being shifted above 1700 cm^{-1},

* Part III: see [1]

** Partly based on the Diploma Thesis of L. Szőcs, Technical University, Budapest, 1971.



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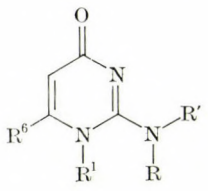

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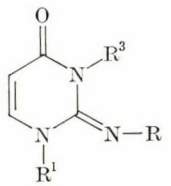

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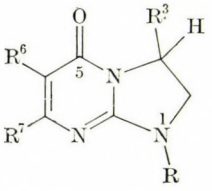

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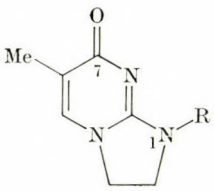

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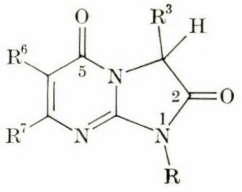

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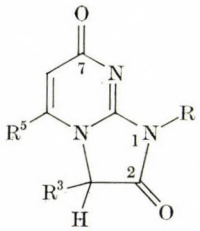

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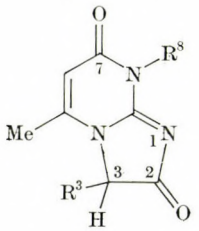

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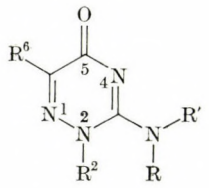

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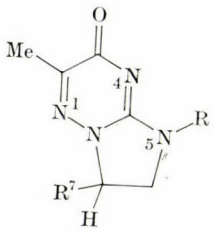

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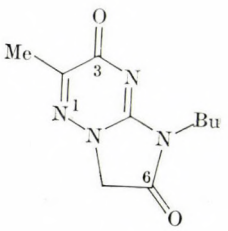

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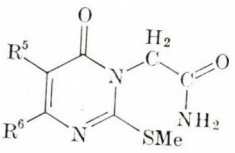

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the product has to be an *N*-acetyl derivative in which the newly introduced acetyl group is *not* attached to *N*(3). The only possible structure for the product is, therefore, **2** ($R^1 = R^6 = R' = Me$, R = Ac).

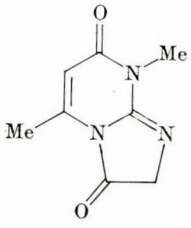
Acetylation of **5** (R = H) [5], mentioned recently by REITER *et al.* [6], does in itself not prove the structure of the product either but, in combination with IR evidence (two carbonyl bands, both below 1700 cm^{-1}), firmly establishes structure **5** (R = Ac), a conclusion reached earlier on the basis of NMR evidence [7].

2,5(1*H*,3*H*)-Imidazopyrimidinediones **6** (R = H) have been synthesized by Russian investigators by three different methods: (1) ammonia-induced [8, 9] or thermal [10] cyclization of *N*(2)-(α-halogenoacyl)-isocytosines (Type

1, $R^3 = R' = H$, R = α-halogenoacyl), (2) base-catalyzed condensation of β-oxo esters with *N-un*substituted glycocyamidines [11, 12], or (3) with *N-un*-substituted α-guanidinoacids [8]. None of these syntheses is structure proving in itself,* nor does any one of them establish the tautomeric structures of the resulting products. When, however, the gross structure **6** is accepted for the products, their tautomeric structures may be deduced from the following observations: (*a*) methylation of **6** (R = H, $R^6 = R^7 =$ Me, $R^6 =$ Et) takes place at *N*(1), as shown by the base-catalyzed degradation of the product [13], and (*b*) the UV spectrum of the non-tautomeric methylation product **6** (R = $R^3 = R^7 =$ Me, $R^6 =$ Et) is practically identical with those of the potentially tautomeric compounds **6** (R = H) [14].

We have devised a structure proving synthesis for Type **6** compounds of fixed tautomeric structures (*i.e.* R ≠ H), based on aminolyses of oxodihydropyrimidylacetamides **12** ($R^5 = H$, $R^6 =$ Me and $R^5 + R^6 = [CH_2]_4$) or the corresponding ethyl esters with primary amines [1].

Synthesis of a 2,7(3*H*,8*H*)-imidazo[1,2-*a*]pyrimidinedione (**8**, $R^3 = H$, $R^8 =$ Me) of fixed tautomeric structure has been achieved by chloroacetylation of **1** (R = R′ = $R^5 = H$, $R^3 = R^6 =$ Me) [15], and ring closure of the resulting *N*(2)-chloroacetyl derivative. An essentially identical synthesis of **8** ($R^3 = H$, $R^8 =$ Me) without isolation of the intermediate chloroacetyl derivative has been earlier performed by Russian authors [10]. None of these syntheses is structure proving in itself, because they could have equally well led to **13.** However, the observation that the ring closure product is converted by acid- or base-catalyzed hydrolysis into the uracil derivative **14** ($R^3 =$ Me) [10], furnishes the required proof of structure both for the end-product and the intermediate chloroacetyl derivative. Additional proof for the attachment of the chloroacetyl group to *N*(2) in the latter comes from the UV spectrum (Table IV, compound No. 6) which is in agreement with the presence of a conjugated chromophore system. Further proof comes from reasoning by analogy: chloro-



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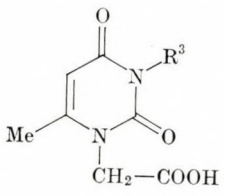

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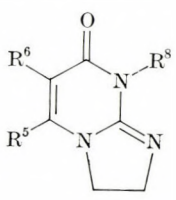

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* For the type (1) syntheses this becomes evident by considering that, in general, not even the site of attachment of the halogenoacyl groups has been rigorously proved. Thermal cyclization of the α-bromoacetyl derivative of 6-methylisocytosine (**1**, R = R′ = $R^3 = R^5 =$ =H, $R^6 =$ Me), however, furnishes two isomeric imidazo[1,2-*a*]pyrimidinediones [10] — obviously one of Type **6** and the other of Type **7**—, whence it follows unequivocally that the α-bromoacetyl group is attached to *N*(2) in the starting compound.

acetylation of **1** (R = R′ = R^3 = R^5 = H, R^6 = Me) also leads to an *N*(2)-chloroacetyl derivative (compound No. 2 of Table IV) in which the site of attachment of the chloroacetyl group has been rigorously proved by chemical means (see below).

Compound **8** (R^3 = R^8 = Me) has been obtained similarly [10].

For the synthesis of compound **11** see Ref. [16].

The synthesis of a 2,5(3*H*,8*H*)-imidazo[1,2-*a*]pyrimidinedione (**19**, R^7 = R^8 = Me) of fixed tautomeric structure has been achieved by chloroacetylation of compound **2** (R^1 = R^6 = Me, R = R′ = H), and ring closure of the resulting *N*(2)-chloroacetyl derivative without isolation of the latter. The alternative structure for the product, with the carbonyl group shifted from position 2 to position 3, is ruled out on the basis of the IR spectrum which exhibits two Amide I bands at comparatively low wave numbers.

UV spectra

The UV spectra of the non-tautomeric compounds mentioned in the previous section belong to four different classes. Fig. 1 shows the characteristic spectra corresponding (1) to the conjugated chromophore system of the Type

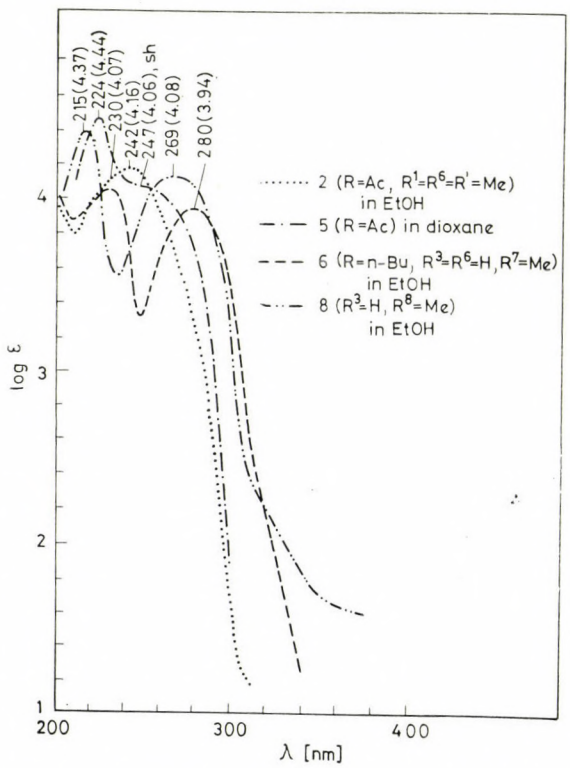


Fig. 1. UV spectra of a Type **2** *N*(2)-acylisocytosine and some imidazo [1,2-a] pyrimidine derivatives of Types **5**, **6** and **8** (non-tautomeric compo

Table I

UV spectra and positions of the νC=O bands of compounds **4** *(R = Ac) and* **6** *(conjugated chromophore)*

No.	Type	R	R^3	R^6	R^7	Solvent	λ_{max} (logε)	Δlogε	IR (KBr) νC=O, cm^{-1}
1 [6]		Ac	H	Me	H	EtOH or dioxane	240 (3.86); 282 (4.04)	+0.18	1690+1675
2 [18]	**4***	Ac	OH	H	Me	EtOH	234 (3.88); 283 (4.00)	+0.12	1695 + 1680
3 [18]		Ac	OH	Br	Me	EtOH	244 (3.92); 296 (4.08)	+0.16	1695 + 1670
4		Ac	H	$-(CH_2)_4-$		EtOH	244 (3.90); 287 (3.98)	+0.08	1665 (b)
5 [1]		H	H	H	Me	EtOH	228 (3.98); 280 (3.83)	−0.15	1780 + 1760 (d) and 1710 (1695, sh); 1765 (1790, sh) and 1710***
						buffer, pH = 6.1	238 (4.03); 278 (3.84) [14]	−0.19	
6 [1]		H	H	$-(CH_2)_4-$		EtOH	244 (4.12); 288 (3.88)	−0.24	1785 + 1765 (d) and 1700 1785 + 1760 (d) and 1690****
7		H	Me	H	Me	buffer, pH = 6.1	237 (4.06); 278 (3.86) [14]	−0.20	
8	**6**	H	Me	Et	Me	buffer, pH = 6.1	246 (4.06); 281 (3.84) [14]	−0.22	
9		Me*	Me	Et	Me	buffer, pH = 2.1—10.30	239 (4.06); 285 (3.92) [14]	−0.14	
10 [1]		*n*—Bu*	H	H	Me	EtOH	230 (4.07); 280 (3.94)**	−0.13	1760 + 1710
11		HOC_2H_4-*	H	$-(CH_2)_4-$		EtOH	236 (4.04); 282 (3.90)	−0.14	1750 + 1675
12		$PhCH_2-$*	H	$-(CH_2)_4-$		EtOH	236 (4.00); 282 (3.92)	−0.08	1750 + 1680

* Fixed tautomeric structure. All other compounds listed are potentially tautomeric, their predominant tautomeric forms corresponding to structure **6** ** Shoulder at 242 (3.74) *** DMSO solution **** $CHCl_3$ solution

Table II

UV spectra and positions of the νC=O bands of some Type **2** *(R=Ac),* **5** *(R=Ac),* **7**, **9** *(R=Ac),* **10** *and* **11** *compounds*
(Cross-conjugated chromophore)

No	Type	Substituents	Solvent	λ_{max} (logε)	νC=O (KBr)
1.	**2**	R=Ac, R^1=R′=R^6=Me	EtOH	242 (4.18)	1650 (b)
			dioxane	242 (4.16)	
2.		1-Methyl-4(1*H*)-pyrimidinone	H_2O (pH 6)	240 (4.17) [17]	
3.	**5**	R=Ac [6]	EtOH	224 251, sh [6]	1695 + 1665
			dioxane	224 (4.41); 247 (4.03), sh	
4.	**7**	R=R^3=H, R^5=Me	EtOH*	217 (4.36); 248 (3.95), sh	1795, w + 1765 (d) and 1715, vw + 1665; 1765 (1795 sh) and 1710***
			dioxane*	211 (4.36); 260 (4.06)	
			buffer (pH 4.1)	** 263 (3.92), sh [14]	
5.		R=H, R^3=R^5=Me	buffer (pH 6.1)	** 257 (3.89), sh [14]	
6.		R=R^5=Me, R^3=H	EtOH	220 (4.39; 258 (3.84)	1760 + 1660
			dioxane	224 (4.26); 253 (3.81)	

Table II, continued

7.		R=Ac, R^2=R′=H, R^6=Me	EtOH	219 (4.41); 236 (4.02), sh	1720 + 1645
8.	**9**	R=Ac, R^2=H, R′= $-C_2H_4OAc$, R^6=Me	EtOH	210 (4.38); 242 (3.90), sh	1740 (ester) + 1730 + 1665
9.		R=Ac, R^2=R′=R^6=Me	dioxane	246 (4.10)	1670 + 1650 (d)
10.		2,6-Dimethyl-5(2*H*)-*as*-triazinone	EtOH	244 (4.07); 265 (3.81), sh [24]	
11.	**10**	R=Ac, R^7=AcO	EtOH	224 (4.44)	1730 (ester) + 1690 + 1660
12.	**26**	5-Acetyl-2-methyl-5,6,7,8-tetrahydro-3*H*-pyrimido[1,2-*b*]-*as*-triazin-3-one	dioxane	239 (4.37)	1695 + 1635
13.	**11**		EtOH	214 (4.35); 233 (4.15); 263 (3.85), sh	1770 + 1665
			dioxane	214 (4.29); 230 (4.10), sh; 265 (3.86), sh	

* The considerable differences between the spectra taken in EtOH and dioxane may be explained by assuming a tautomeric equilibrium **7** (R=H) ⇄ **8** (R^8=H) which is shifted to the left in EtOH and to the right in dioxane *(cf.* Table III)

** The spectra have not been determined below 230 nm, and the compounds have been assigned Type **8** structures in Ref. [14]

*** DMSO solution

6 compounds, (2) to the chromophore system of the Type **8** ($R^8 \neq H$) compounds which contain a semicyclic C=N double bond attached to the pyrimidine ring, and (3) to the two types of cross-conjugated systems, **2** (R = Ac), and **5** (R = Ac) and **11** respectively. (See also Tables I—III). The difference between the latter two types is that, while the carbonyl groups of the five-membered rings in **5** (R = Ac) and **11** are, as a result of ring formation, approximately coplanar with the pyrimidine ring, the acyl group of **2** (R = Ac) is forced by steric interactions into a plane which is almost perpendicular to that of the pyrimidine ring. Conjugation between the double bond system of the ring and the lone pair of the acylamino group is therefore sterically prohibited and, as a result, the spectrum of **2** (R = Ac) is identical — both as to its shape and the λ_{max} (log ε) values — with that of 1-methyl-4(1*H*)-pyrimidinone [17]. The spectra, of **9** (R = Ac, $R^2 = R' = R^6$ = Me) and 2,6-dimethyl-5-(2*H*)-*as*-triazinone [24] are, of course, also identical with the latter (see Table II).

Inspection of the UV spectra of the four Type **6** compounds of fixed tautomeric structures (compounds 9—12 in Table I) reveals that they are extremely similar to those of the non-acylated Type **1** and Type **4** compounds [2] both as to the positions and the intensities of the absorption bands. The Δ log ε rule [2], derived for the non-acylated Type **1** and Type **4** compounds and their analogues, is valid also for the Type **6** compounds demonstrating, on the one hand, once again the unsensitivity of the conjugated chromophore system of the 4(3*H*)-pyrimidinone ring to variations of the nature of the substituents attached to *C*-2 [2], and serving, on the other hand, as a firm tool for establishing the tautomeric structure of potentially tautomeric compounds of Type **6** (compounds 5—8 in Table I; see below) and of the point of attachment of the acetyl group in Type **4** (R = Ac) (compounds 1—3 of Table I) and Type **1** (R = Ac) compounds (Table IV; see below).

The UV spectra of the non-tautomeric compounds of Type **2** (R = Ac), **5** (R = Ac) and **11** ,as well as of 1-methyl-4-(1*H*)-pyrimidinone which serves

Table III

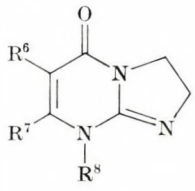
UV spectra and positions of the νC=O bands of Type **8** *(R^8=Me) compounds*

R^8	Solvent	λ_{max} (logε)	Δlogε	νC=O (KBr)
H	EtOH	215 (4.37); 269 (4.08)	—0.29	1745 vw, 1690
	dioxane	214 (4.35); 262 (4.08)	—0.27	(1720 sh) and
	aq. buffer, pH 2—9.85	* 267.5 (4.11) [14]		1635 (1645 sh)**
Me	aq. buffer, pH 2—9.85	* 269 (4.11) [14]		

* The spectra have not been determined below 230 nm
** Same in $CHCl_3$ solution

as the model compound for **2** (R = Ac), are shown in Table II. Both **5** (R = Ac) and **11** have only one well-developed absorption band (around 220 nm); one, respectively two further bands may be recognized as shoulders on the long-wave side of the main band. These spectra are rather similar to the spectra of Type **2** (R ≠ Ac), **5** (R ≠ Ac), **9** (R ≠ Ac) and **10** (R ≠ Ac) compounds reported earlier [2].

The UV spectra of two Type **8** compounds (R^8 = Me) are shown in Table III. Two well separated bands are present as in the spectra of the compounds discussed in Table I and those of the Type **15** and **16** compounds described earlier [2]. Both bands of the compounds **8** (R^8 = Me) are, however, hypsochromically shifted which, on the one hand, permits the Type **8** compounds to be easily distinguished from those listed in Table I and, on the other hand, demonstrates the profound effect of the acyl group attached to the imino nitrogen atom on the electron distribution. The positions of the absorption bands as well as the $\Delta \log \varepsilon$ values of the Type **8** compounds are practically identical with those of compound **17** [19], but the $\Delta \log \varepsilon$ values of these compounds are considerably smaller than those (−0.52 — −0.74) found earlier for the Type **15** and **16** compounds.



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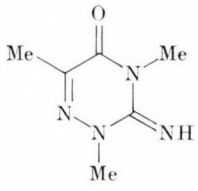

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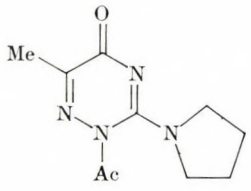

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The UV spectra of the compounds **8** (R^3 = H, R^8 = Me; see Table III) and **19** ($R^7 = R^8$ = Me; see Experimental) differ markedly which demonstrates that, in spite of the apparently identical chromophore systems, the mode of anellation of the two rings has a marked influence on the actual electron distribution. Since the UV spectrum of **19** ($R^7 = R^8$ = Me) has three absorption bands in the near UV region, the $\Delta \log \varepsilon$ rule can not be applied. A similar but less pronounced effect of the mode of anellation on the UV spectra has earlier been observed in the case of the Type **15** and **16** compounds [2].

Orientation in the acylation of Type 1 (R=H) isocytosines and Type 4 dihydroimidazopyrimidinones (R=H)

Acylation of Type **1** (R = H) isocytosines may, in principle, yield any of three or (if R^3 = H) four isomeric products in which the acyl group is attached to *N*(1), *N*(2), *N*(3) and *O*(4), respectively. The *O*- and 3-acyl derivatives

Table IV

UV spectra and positions of the νC=O bands of N(2)-acylisocytosines **1** *(R=ac)*

No	R	R′	R³	R⁵	R⁶	Solvent	λ_{max}(logε)	Δlogε	νC=O (KBr)
1 [20]	Ac	H	H	H	Me	Dioxane	235 (4.00); 286 (3.88)	−0.12	1650 (b)
2*	$ClCH_2CO$	H	H	H	Me	EtOH	226 (3.94); 286 (3.91)	−0.03	1645 (b)
						Dioxane	238 (3.89); 278 (3.88)	−0.01	
3*	Ac	H	H	n-Bu	Me	**	244 (3.98); 292 (3.90) [3]	−0.09	
4*	$ClCH_2CO$	H	H	*n*-Bu	Me	**	246 (3.95); 291 (3.95) [3]	0	
5 [10]	Ac	H	Me	H	Me	MeOH	274 (3.99) [3]		
						Dioxane	221 (4.18); 270 (4.14)	−0.04	1665 (b)
6	$ClCH_2CO$	H	Me	H	Me	EtOH	218 (4.21); 273 (4.15)	−0.06	1690 + 1645
						Dioxane	224 (4.15); 272 (4.13)	−0.02	
7	Ac	Me	Me	H	Me	EtOH	224 (3.83); 278 (3.70)	−0.13	1650 (b), sh at 1680

* For chemical proof of the site of attachment of the acyl group, see text
** The solvent has not been stated in Ref. [3]

should be easily identifiable on the basis of their UV and IR spectra, since the former contain an aromatic chromophore system and *no* C=O group, while the latter have a diacylamino moiety partly incorporated into the pyrimidine ring. Acylation of Type **4** dihydroimidazopyrimidinones (R = H) can lead only to 1- and 8-acyl derivatives which are the bicyclic analogues of *N*(2)- and 1-acyl derivatives of the Type **1** (R = H) isocytosines. The UV spectra lend themselves as a tool for distinguishing between the two alternatives in both series since, depending on the site of attachment of the acyl group, they should resemble either those of the compounds listed in Table I or that of compound **18** (see below). The latter statement might, in principle, be invalid for potentially tautomeric *N*-acylisocytosines, *e.g.* **1** (R = acyl, R′ and/or R^3 = H), since the latter could exist as the Type **2** (R = acyl) and **3** (R = acyl) tautomers as well. Clearly, the UV spectra should permit ready distinction between the latter three alternatives.

The UV spectra of acyl derivatives of a series of Type **1** (R = H) isocytosines and of Type **4** (R = H) dihydroimidazopyrimidinones are shown in Tables IV and I, respectively. The spectra are essentially identical with those of compounds 9—12 of Table I for which the presence of a conjugated chromophore system has been proved by synthesis (see above), and differ sharply from that of compound **18** (see below). Consequently, acetylation of compounds **1** (R = H) and **4** (R = H) has taken place at *N*(2) and *N*(1),* respectively, and even the potentially tautomeric *N*(2)-acylisocytosines do exist, at least predominantly, as the tautomers of structure **1** (R = acyl). A possible exception to the latter generalization is furnished by compound 6 of Table IV whose absorption bands are shifted hypsochromically as compared with those of the remaining compounds of Tables I and IV to such an extent that their positions almost coincide with those of the compounds **8** (R^8 = Me) (Table III). Moreover, one of the Amide I bands of the compound in question is also shifted towards higher wave numbers which would be difficult to rationalize on the basis of a Type **1** structure. The possibility of compound 6 of Table IV to exist at least in part as the Type **3** tautomer cannot, therefore, be ruled out.

Acetylation may again be seen not to affect the validity of the $\Delta \log \varepsilon$ rule [2] but, in some instances, acetylation appears to cause a slight bathochromic shift of the shorter, or a slight hypsochromic shift of the longer, wavelength absorption band.

Additional evidence for the site of attachment of the acyl groups in compounds 3 and 4 of Table IV comes from the observation that sulfonation of the latter furnishes heteroaromatic *O*-sulfonyl derivatives which can occur only if the acyl groups were attached to *N*(2) [3]. The site of attachment of the chlo-

* A similar conclusion has been derived for compound No. 1 of Table I on the basis of NMR evidence [7].

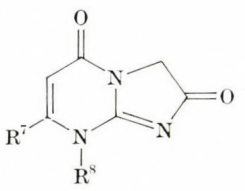
roacetyl group in compound No. 2 of Table IV, on the other hand, follows from the result of ring closure of this compound, which leads to compound **7** (R = = R^3 = H, R^5 = Me) obtained also by structure proving synthesis (see below).

Synthesis and tautomeric structures of further imidazopyrimidinediones

The potentially tautomeric 2,5(1*H*,3*H*)-imidazo[1,2-*a*]pyrimidinediones **6** (R = H) (compounds 5 and 6 of Table I) have been obtained [1] — similarly to their analogues of fixed tautomeric structures (compounds 10—12 of Table I) — by ammonolysis of Type **12** oxodihydropyrimidylacetamides or the corresponding ethyl esters.* The observations that the UV spectra (1) of the products obtained by the ammonolysis method and by ring closure of *N*-chloroacetylisocytosines [8—10], and (2) of the non-tautomeric and potentially tautomeric Type **6** compounds are identical, prove that the *N*-chloroacetylisocytosines are *N*(2)-acyl derivatives, and that the predominant form of the potentially tautomeric 2,5(1*H*,3*H*)-imidazo[1,2-a]pyrimidinones (compounds 5—8 of Table I) are, indeed, of Type **6**.

The IR spectra of the potentially tautomeric and non-tautomeric compounds of Type **6** (Table I) differ in that the latter exhibit two singlet νC=O bands, while in the spectra of the latter at least the higher wave number νC=O band is a doublet. This may indicate that the potentially tautomeric compounds exist partly in the form of the Type **19** tautomers.

The potentially tautomeric 2,7-imidazopyrimidinedione **7** (R = R^3 = H) $\rightleftarrows$ **8** (R^3 = R^8 = H) (compound No. 4 of Table II) has been obtained by ring closure of *N*(2)-chloroacetyl-6-methylisocytosine **1** (R = $ClCH_2CO$, R′ = R^3 = R^5 = H, R^6 = Me; compound No. 2 of Table IV) as well as by ammonolysis of the ethyl oxodihydropyrimidineacetate (**21**). The latter has been obtained by the reaction of ethyl thioureidoacetate [21] with diketene (*cf.* [22]), and methylation of the resulting 2-thiouracil derivative **20**. Since reaction of diketene with monosubstituted thioureas may furnish either 1- or 3-substituted 2-thiouracils



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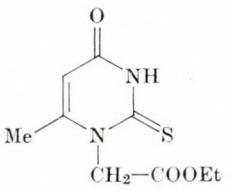

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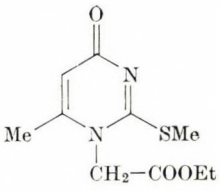

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* For an alternative mode of synthesis of compound No. 5 of Table I, see Ref. [8]; for the syntheses of compounds No's 7—9, see Ref's [8—10, 12, 13].

[1, 22], the orientation in the reaction with ethyl thioureidoacetate had to be established. This was accomplished by hydrolysis of **21** to the uracil derivative **14** (R^3 = H) which proved different from the known isomeric 6-methyl-3-uracil-acetic acid [1].

The UV spectrum of compound No. 4 of Table II is dependent on the nature of the solvent: in ethanol it corresponds to the cross-conjugated form **7**, while in dioxane it exhibits the characteristics of the Type **8** compounds, both as to the positions and the intensities of the absorption bands (and, of course, their $\Delta \log \varepsilon$ values). Since in the KBr- and DMSO—IR spectra both Amide I bands appear as doublets, compound No. 4 of Table II apparently exists as a mixture of the Type **7** and Type **8** tautomers, both in the crystalline state and in DMSO solution.

The 1-methyl derivative **7** (R = R^5 = Me, R^3 = H) (compound No. 6 of Table II) was obtained by allowing to react 6-methyl-2-methylamino-4(3*H*)-pyrimidinone (**1**, R = R^6 = Me, R′ = R^3 = R^5 = H) and chloroacetic anhydride. The structure of the product of this non-structure proving synthesis follows by analogy and from spectral properties (see Table II). In agreement with its fixed structure, the Amide I bands of this compound are not split into doublets, and the UV spectrum remains essentially unchanged when the solvent ethanol is replaced by dioxane.

Aza analogues of the N(2)-acylisocytosines 2 (R = ac) and dihydroimidazopyrimidinones 4 (R = Ac)

The 6-aza analogues of the isocytosines exist predominantly in the cross-conjugated form, with the exception of such cases in which the conjugated or exocyclic form is fixed by substitution of the mobile hydrogen atoms [2]; compound **17** may serve as an example for such an exception. Acylation of the cross-conjugated 6-azaisocytosines or, named more systematically, 3-amino-5-(2*H*)-*as*-triazinones **9** may lead, if R, R^5 = H, in principle to no less than four isomeric derivatives: the *N*(2)-, *N*(3)-, *N*(4)- and *O*-acylation products. The latter two should be easily identifiable on the basis of their IR spectra (*cf.* the analogous acylation of isocytosines discussed above).

Acetylations of **9** (R = R′ = R^2 = H, R^6 = Me) and of **9** (R = R^2 = H, R′ = $-CH_2CH_2OH$, R^6 = Me) furnish acetyl derivatives in which the newly introduced acetyl group is, according to the IR spectra, attached neither to *N*(4), nor to *O*(5). (In the second case acetylation of the side chain hydroxyl group takes place in addition to *N*-acetylation.) The choice between the remaining alternative structures **9** (R = Ac, R^2 = H, R^6 = Me, R′ = H and $-CH_2CH_2OAc$, respectively) and **9** (R^2 = Ac, R = H, R^6 = Me, R' = H and $-CH_2CH_2OAc$, respectively) can be made by comparison of the UV spectra of

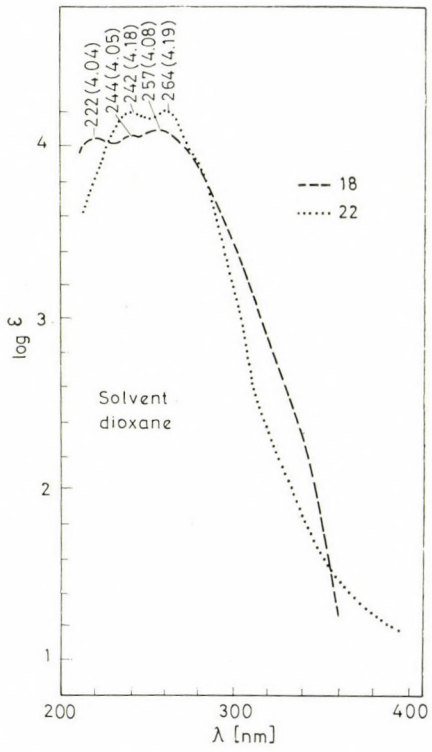


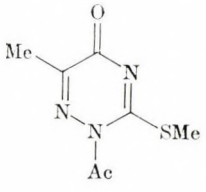
Fig. 2. UV spectra of 2-acyl-5(2*H*)-*as*-triazinones

the products with that of the acetyl derivative of **9** (R + R′ = $[CH_2]_4$, R^2 = H, R^6 = Me). The latter is shown by its IR spectrum to be neither an *N*(4)-, nor an *O*(5)-acetyl derivative, whence **18** follows as the only acceptable structure. Since the UV spectra of the two acetylation products (compounds 7 and 8 of Table II) mentioned above are totally different from that of **18**, they are certainly *N*(3)-acetyl derivatives (**9**, R = Ac, R′, R^2 and R^6 as stated above).

The considerable differences between the UV spectra of **18** and the type **9** (R = Ac) compounds are another indication of the sensitivity of the electron distribution of the cross-conjugated chromophore system to variations of the nature and positions of the ring substituents. The spectra of compounds **18** and **22**—**24** [23] — which, in a broad sense, all are 2-acyl-5(2*H*)-*as*-triazinones — are, on the other hand, quite similar (see Fig. 2).

Acetylation of **10** (R = H, R^8 = OH) furnishes a diacetyl derivative in which one of the acetyl groups is attached to the oxygen atom which has originally been part of the hydroxyl group, while the other is, according to the IR spectrum, *not* attached to the other oxygen atom, nor to *N*(4). As a consequence, **10** (R = Ac, R^8 = OAc) is the only acceptable structure for this compound (No. 11 of Table II), and this structure is in agreement also with the UV spectrum.

10 (R = H, R^8 = OH), the cyclic aminocarbinol form of the aldehyde **9** (R = $-CH_2CHO$, R^2 = R′ = H, R^6 = Me) has been obtained by acid-catalyzed hydrolysis of its dimethyl acetal at room temperature.* No spectroscopic indications are available for the existence of appreciable amounts of the aldehyde form. The aldehyde **9** (R = CH_2CHO, R^2 = R′ = H, R^6 = Me), or its cyclic form, could not be obtained by oxidation of the corresponding **9** (R = $-C_2H_4OH$, R^2 = R′ = H, R^6 = Me) [16], since the latter suffered a glycol type cleavage to **9** (R = R′ = R^2 = H, R^6 = Me) when treated with hot aqueous $KMnO_4$ or the $Pb(OAc)_4$-pyridine complex [27].



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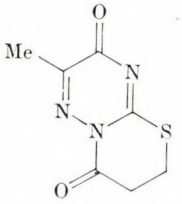

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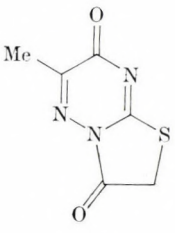

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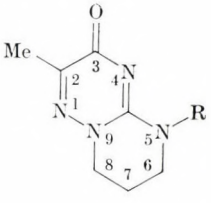

25: R = H
26: R = Ac

The tetrahydropyrimido[1,2-*b*]-*as*-triazinone **25** [16] is also acetylated at *N*(5) since, according to its IR spectrum, the resulting product is *not* an *O*-acetyl derivative, neither does it contain a diacylamine moiety. In agreement with the greater departure from planarity of the hexahydropyrimidine ring as compared with that of the imidazolidine rings of the Type **5** (R = Ac) and Type **11** compounds, the UV spectrum of the acetylated product **26** (compound No. 12 of Table II) resembles those of compounds 1, 2 and 10 of Table II.

Experimental

3,6-Dimethyl-2-methylamino-4(3H)-pyrimidinone(1, R = R^5 = H, R′ = R^3 = R^6 = Me)
A mixture of 3,6-dimethyl-2-methylthio-4(3*H*)-pyrimidinone [29] (1.7 g; 10 mmoles) and methylammonium acetate (4.5 g; 50 mmoles) was kept for 2 hrs at 140—150 °C (bath temperature). On cooling, most of the mixture turned crystalline. The product was filtered off and washed with ether to yield 1.3 g (85%) of the title compound, m.p. 213—214 °C (EtOH).
$C_7H_{11}N_3O$ (153.2). Calcd. C 54.88; H 7.24; N 27.43. Found C 54.85; H 7.25; N 27.05%.

N(2)-Acyl-isocytosines 1 (R = ac) and 2 (R = ac)

(a) A mixture of 6-methylisocytosine **1** (R = R′ = R^3 = R^5 = H, R^6 = Me) [15] (2.5 g; 20 mmoles), anhydrous dioxane (20 ml) and chloroacetyl chloride (5 ml; 63 mmoles) was refluxed for 30 min and evaporated to dryness in vacuum. The residue was dissolved in water (20 ml), and the solution was treated with $NaHCO_3$ until neutral, to yield 2.0 g (50%) of **1** (R = $ClCH_2CO$, R′ = R^3 = R^5 = H, R^6 = Me), m.p. 197 °C (d.) (from DMF; second m.p., after resolidification, above 260 °C (d.).
$C_7H_8ClN_3O_2$ (201.6). Calcd. C 41.70; H 4.00; N 20.84. Found C 41.92; H 4.22; N 20.62%.

* At elevated temperatures the aminocarbinol is readily dehydrated by aqueous HCl to 2-methyl-3(5*H*)-imidazo[1,2-*b*]-*as*-triazinone, see Experimental.

NMR (DMSO-d_6): $\delta \approx 9.5$ (bs, 2H, disappears on addition of D_2O, NH's); 6.0 (s, 1H, 5-H); 4.45 (s, 2H, $COCH_2Cl$); 2.2 (s, 3H, 6-Me).

(b) 3,6-Dimethylisocytosine (**1**, R = R′ = R^5 = H, R^3 = R^6 = Me) [15] (2.8 g; 20 mmoles), $NaHCO_3$ (2.1 g) and chloroacetyl chloride (10 ml) were thoroughly mixed, and the mixture was allowed to stand 2 hrs at room temperature. The excess chloroacetly chloride was distilled off in vacuum. The oily residue turned crystalline when triturated with water (20 ml) and furnished 1.7 g (39%) of **1** (R = $ClCH_2CO$, R′ = R^5 = H, R^3 = R^6 = Me), m.p. 177 °C (from MeOH; second m.p., after resolidification, above 215 °C (d.).

$C_8H_{10}ClN_3O_2$ (215.6). Calcd. C 44.56; H, 4.67; Cl 16.44. Found C 45.18; H 4.38; Cl 16.71%.

The NMR spectrum in DMSO-d_6 is in agreement with the presence of two tautomeric forms (Type **1** ⇄ Type **3**): δ 6.05 + 5.65, (both s, summing up to 1H, 5-H's); 4.4 (s, 2H; $COCH_2Cl$); 3.4 + 3.3 (both s, summing up to 3H, *N*-Me's); 2.3 + 2.1 (both s, summing up to 3H, 6-Me's).

(c) *N*(2)-Acetyl-6-methylisocytosine (R = Ac, R′ = R^3 = R^5 = H, R^6 = Me) has been obtained as described in Ref. [20].

NMR (DMSO-d_6): $\delta \sim 13$ (bs, 2H, disappears on addition of D_2O, NH's); 5.98 (s, 1H, 5-H); 2.2 (s, 6H, 6-Me + Ac).

(d) *N*(2),3,6-Trimethylisocytosine (**1**, R = R^5 = H, R′ = R^3 = R^6 = Me) (1.0 g; 6.5 mmoles) was refluxed for 2 hrs with Ac_2O (10 ml) containing 1 drop of conc. HCl. The mixture was evaporated to dryness in vacuum and the residue recrystallized from CCl_4 to yield 1.1 g (87%) of **1** (R = Ac, R′ = R^3 = R^6 = Me, R^5 = H), m.p. 129—130 °C.

$C_9H_{13}N_3O_2$ (195.2). Calcd. C 55.37; H 6.71; N 21.53. Found C 55.57; H 6.71; N 21.58%.

(e) 1,*N*(2),6-Trimethylisocytosine (**2**, R = H, R^1 = R′ = R^6 = Me) [1] (1.53 g; 10 mmoles) was refluxed for 2 hrs. with acetic anhydride (20 ml). The excess anhydride was distilled off in vacuum and the residue triturated with ether to yield 1.5 g of **2** (R = Ac, R^1 = R′ = R^6 = Me), crystalline powder, m.p. 196 °C (from $CHCl_3$–light petroleum).

$C_9H_{13}N_3O_2$ (195.2). Calcd. C 55.38; H 6.71; N 21.53. Found C 55.43; H 6.79; N 21.39%.

1-Acetyl-2,3,6,7,8,9-hexahydro-5(1H)-imidazo[2,1-b]quinazoline 4 (R = Ac, R^3 = H, R^6 + R^7 = $[CH_2]_4$).

4 (R = R^3 = H, R^6 + R^7 = $[CH_2]_4$) [1] (3.0 g; 13 mmoles) was refluxed for 1 hr with acetic anhydride (10 ml) to yield, after the solution had been allowed to cool, 1.0 g (31%) of the title compound, m.p. 214 °C (from Ac_2O).

$C_{12}H_{15}N_3O_2$ (222.3). Calcd. C 61.79; H 6.48; N 18.02. Found C 61.55, H 6.36, N 18.09%.

3-Acetylamino-6-methyl-5(2H)-as-triazinone (**9**, R = Ac, R^2 = R′ = H, R^6 = Me).

A mixture of acetic anhydride (20 ml) and 3-amino-6-methyl-5(2*H*)-*as*-triazinone [19] (0.5 g; 4 mmoles) was refluxed for 20 min to yield, after the mixture had been allowed to cool, 0.4 g (61.5%) of the title compound, colourless crystals, m.p. 303 °C (from Ac_2O).

$C_6H_8N_4O_2$ (168.15). Calcd. C 42.84; H 4.79; N 33.32. Found C 42.71; H 4.86; N 32.66%.

3-[N-(2-Acetoxyethyl)-N-acetylamino]-6-methyl-5(2H)-as-triazinone (**9**, R = Ac, R^2 = H, R′ = $—C_2H_4OAc$, R^6 = Me).

A mixture of acetic anhydride (5 ml) and 3-(2-hydroxyethylamino)-6-methyl-5(2*H*)-*as*-triazinone [16] (0.34 g; 2 mmoles) was refluxed for 20 min and evaporated to dryness in vacuum. The residue was crystallized from gasoline to yield 0.4 g (78%) of the title compound, m.p. 108—109 °C (from gasoline).

$C_{10}H_{14}N_4O_4$ (254.25). Calcd. C 47.24; H 5.55; N 22.04. Found C 47.14; H 5.61; N 22.48%.

3-(N-Acetyl-N-methylamino)-2,6-dimethyl-5(2H)-as-triazinone (**9**, R = Ac, R^2 = R′ = R^6 = Me).

9 (R = H, R^2 = R′ = R^6 = Me) [26] (0.7 g; 4.5 mmoles) was refluxed for 2.5 hrs with acetic anhydride (5 ml) to which one drop of conc. aq. HCl had been added. The solution was evaporated to dryness in vacuum and the crystalline residue triturated with ether to yield 0.5 g (57%) of the title compound, m.p. 94—96 °C (from CCl_4).

$C_8H_{12}N_4O_2$ (196.2). Calcd. C 48.97; H 6.17; N 28.56. Found C 48.84; H 6.29; N 28.25%.

Ethyl 6-methyl-4-oxo-2-thioxo-3,4-dihydro-1(2H)-pyrimidineacetate (20)

Diketene (9.1 ml; 120 mmoles) was added by drops to a refluxing solution of ethyl thiohydantoate [21] (8.7 g; 54 mmoles) in AcOH (40 ml). The mixture was refluxed for further 10 min and allowed to cool. Water (5 ml) was added by drops to precipitate 7.1 g (58%) of **20**, colourless plates, m.p. 210 °C (from water).

$C_9H_{12}N_2O_3S$ (228.3). Calcd. C 47.35; H 5.30; N 12.28, S 14.05. Found C 47.36; H 5.56; N 12.15; S 14.21%.

UV (EtOH): 219 (4.16); 274 (4.13).

6-Methyl-4-oxo-2-thioxo-3,4-dihydro-1(2H)-pyrimidineacetic acid

The above ethyl ester (1.0 g; 4.4 mmoles) was refluxed for 15 hrs with 20% aq. HCl (40 ml) to yield 0.6 g (68%) of the acid, colourless crystalline powder, m.p. 263—265 °C (from water).

$C_7H_8N_2O_3S$ (200.2). Calcd. C 41.89; H 4.02; N 13.99; S 16.01. Found C 41.97; H 4.31; N 13.67; S 15.51%.

amido-N-Butyl-6-methyl-4-oxo-2-thioxo-3,4-dihydro-1(2H)-pyrimidineacetamide

The ester **20** (1.14 g; 5.0 mmoles) was refluxed for 4 hrs with butylamine (10 ml). The excess amine was distilled off in vacuum and the oily residue crystallized from DMF–H_2O to yield 1.0 g (78%) of the butylamide, m.p. 244—245 °C.

$C_{11}H_{17}N_3O_2S$ (255.3). Calcd. C 51.75; H 6.71; S 12.56. Found C 51.70; H 6.72; N 12.70%.

UV (EtOH): 220 (4.26); 276 (4.18).

IR (KBr): νC=O 1695 and 1665 cm^{-1}.

6-Methyl-2,4-dioxo-3,4-dihydro-1(2H)pyrimidineacetic acid (14, R^3 = H).

A solution of **20** (0.3 g; 1.3 mmole) in a mixture of 1*N* NaOH (1.4 ml) and water (3 ml) was treated with MeI (0.2 ml; 3.2 mmoles) under continuous stirring at room temperature (2 hrs). The mixture was evaporated to dryness, and the residue (a mixture of **21** and NaI) was refluxed with 20% HCl (4 ml) for 8 hrs. The solvent and excess reagent were distilled off in vacuum and the oily residue crystallized from water in the presence of charcoal to yield 0.18 g (75%) of **14** (R^3 = H), colourless needles, m.p. 263—264 °C (d.) (from H_2O).

$C_7H_8N_2O_4$ (184.2). Calcd. C 45.64; H 4.38; N 15.21. Found C 45.72; H 4.24; N 15.65%.

UV (EtOH): 208 (3.91); 264 (4.02).

IR (KBr): νC=O 1745, m, 1700, b vs.

M.p. of the isomeric 1,2-dihydro-4(3*H*) derivative 254—255° [1]; UV (EtOH): 206 (3.94); 260 (3.96).

2,5(1H, 3H)-Imidazo[1,2-a]pyrimidinediones (6)

(a) For the syntheses of compounds 5, 6 and 10 of Table I by ammonolysis and butylaminolysis of the appropriate Type **12** compounds, see Ref. [1]. 2-Hydroxyethyl- and benzylaminolysis of the ethyl ester corresponding to **12** ($R^5 + R^6 = [CH_2]_4$) did not furnish the expected Type **6** compounds; instead, the isocytosine derivatives **1** (R = H; $R^5 + R^6 = [CH_2]_4$, R = HOC_2H_4— and $PhCH_2$—, R^3 = —$CH_2CONHC_2H_4OH$ and —$CH_2CONHCH_2Ph$, respectively) were obtained [1].

(b) The solutions of the above isocytosine derivatives in 20% aq. HCl (10 parts) were refluxed for 30 min and evaporated to dryness in vacuum. The residues were triturated with 10% aq. Na_2CO_3 to yield 90—92% of the corresponding Type **6** compounds.

6, R = HOC_2H_4—, R^3 = H, $R^6 + R^7 = (CH_2)_4$, m.p. 176.5 °C (from water).
$C_{12}H_{15}N_3O_3$ (249.3). Calcd. C 57.82; H 6.07; N 16.86. Found C 57.91; H 6.20; N 17.09%.

6, R = $PhCH_2$—, R^3 = H, $R^6 + R^7 = (CH_2)_4$, m. p. 177 °C (from *i*-PrOH).
$C_{17}H_{17}N_3O_2$ (295.4). Calcd. C 68.66; H 6.44; N 14.13. Found C 68.77; H 6.12; N 14.18%.

5-Methyl-2,7(1H, 3H)-imidazo[1,2-a]pyrimidinedione (7, R = R^3 = H, R^5 = Me)

(a) Sodium (0.46 g; 20 mmoles) and, subsequently, compound **20** (4.56 g; 20 mmoles) were dissolved in anhydrous EtOH (20 ml). MeI (2 ml; 32 mmoles) was added, and the mixture was allowed to stand overnight at room temperature and evaporated to dryness in vacuum. The colourless residue (compound **21** + NaI) was dissolved in anhydrous EtOH, and the solution was saturated at 0 °C with dry NH_3. BF_3-etherate (0.2 ml) was added as a catalyst, and the mixture was heated in a sealed tube for 10 hrs. at 145—150 °C to yield, after being allowed to cool, 2.9 (79%) of **7** (R = R^3 = H, R^5 = Me), colourless crystalline powder, m. p. 305—306 °C (d.; from H_2O).

The product contained one molecule of water of crystallization which was *not* removed even by sublimation at 250 °C/0.1 torr.

$C_7H_7N_3O_2 \cdot H_2O$ (183.2) Calcd. C 45.90; H 4.95; N 22.94. Found C 45.77; H 4.99; N 23.08%.

(b) **1** (R = $ClCH_2CO$, R′ = R^3 = R^5 = H, R^6 = Me; see above) (0.5 g; 2.5 mmoles) was refluxed for 30 min with dry tetraline (10 ml). The solvent was distilled off in vacuum and the crystalline residue triturated with ether to yield 0.2 g (44%) of **7** (R = R^3 = H, R^5 = Me), m.p. 305 °C (d.) which, according the IR spectra, proved identical with the product obtained as described under *(a)*.

1,5-Dimethyl-2,7(1H, 3H)-imidazo[1,2-a]pyrimidinedione (7, R = R^5 = Me, R^3 = H).

A mixture of **1** (R = R^6 = Me, R′ = R^3 = R^5 = H) [15] (1.4 g; 10 mmoles) and chloroacetic anhydride (2.0 g; 12 mmoles) was kept for 3 hrs at 130—140 °C (bath temperature).

The resolidified melt was dissolved in MeOH (20 ml) and treated with ethereal diazomethane solution in order to liberate the product from its HCl salt. The solvents were distilled off in vacuum, and the residue was recrystallized from MeOH to yield 0.6 g (34%) of the title compound, m. p. 322 °C (d.).

$C_8H_9N_3O_2$ (179.2). Calcd. C 53.68; H 5.07; N 23.47. Found C 53.43; H 5.06; N 23.64%.

NMR (DMSO-d_6): δ 2.20 (s, 3H, 5-Me); 3.06 (s, 3H, 1-Me); 4.68 (s, 2H, CH_2CO); 5.74 (s, 1H, 6-H).

5,8-Dimethyl-2,7(3H, 8H)-imidazo[1,2-a]pyrimidinedione (**8**, R^3 = H, R^8 = Me).

1 (R = $ClCH_2CO$—, R′ = R^5 = H, R^3 = R^6 = Me; see above) (0.8 g; 3.7 mmoles) was heated for 5 min at 180 °C (bath temperature). The melt solidified on cooling. It was thoroughly pulverized and sublimed at 200 °C/0.1 torr to yield 0.3 g (45%) of **8** (R^3 = H, R^8 = Me), m.p. 258—260 °C (d.), lit. [10] m.p. 261—262 °C.

$C_8H_9N_3O_2$ (179.2). Calcd. C 53.62; H 5.06; N 23.45. Found C 53.74; H 5.44; N 23.68%.

7,8-Dimethyl-2,5(3H, 8H)-imidazo[1,2-a]pyrimidinedione (**19**, R^7 = R^8 = Me).

(a) 1,6-Dimethyl-2-methylthio-4(1*H*)-pyrimidinone [1] (1.7 g; 10 mmoles) was added to ammonium acetate (3.85g; 50 mmoles) preheated to 120 °C, and the mixture was kept at 160—170 °C (bath temperature) until the evolution of methanethiol ceased (about 2 hrs). The melt gradually solidified during this period. The product was pulverized and washed with acetone to yield 1.1 g (85%) of the title compound, colourless crystals, m.p. above 350 °C (d.; aqueous acetone), lit. [30] m.p. 329 °C (d.). (The synthesis described in the literature was not structure-proving.)

(b) A mixture of the above product (1.0 g; 7 mmoles) and chloroacetic anhydride (1.3 g; 7.5 mmoles) was heated for 3 hrs at 130—140 °C (bath temperature). The resulting crystalline product was dissolved in methanol (60 ml). Freshly prepared ethereal diazomethane was added in portions until the total amount of the title compound was liberated from its hydrochloride. Part of the solvent was evaporated, and the mixture was filtered to yield 0.7 g (56%) of the title compound, colourless crystals, m.p. 275—277 °C (d.; DMF).

$C_8H_9N_3O$ (197.2). Calcd. C 53.62; H 5.06; N 23.45. Found C 53.64; H 5.09; N 23.53%.

IR (KBr): 1745 and 1700 cm^{-1} (b). UV (dioxane): 242 (4.08); 274 (3.71). UV (EtOH): 210 (3.91); 246 (3.96); 272 (3.66).

7-Acetoxy-5-acetyl-2-methyl-6,7-dihydro-3(5H)-imidazo[1,2-b]-as-triazinone (**10**, R = Ac, R^7 = AcO).

(a) A mixture of 6-methyl-3-methylthio-5(2*H*)-*as*-triazinone (1.57 g; 10 mmoles), anhydrous ethanol (10 ml) and 2,2-dimethoxyethylamine (1.2 g; 11.4 mmoles) was refluxed for 4 hrs and evaporated to dryness in vacuum. The oily residue was triturated with light petroleum to yield 2.6 g (99%) of *2,2-dimethoxyethylammonium 6-methyl-3-methylthio-as-triazin-5-olate*,* colourless needles, m.p. 112—120° (d. (from EtOH–light petroleum).

$C_9H_{18}N_4O_3S$ (262.3). Calcd. C 41.21; H 6.92. Found C 41.32; H 6.25%.

(b) When the above product (or the original oily residue) was heated at 150 °C (bath temperature) for 1 hr, vigorous evolution of methanethiol took place. The solid product was recrystallized from a small amount of methanol to yield 1.1 g (52%) of *3-(2,2-dimethoxyethylamino)-6-methyl-5(2H)-as-triazinone* (**9**, R^2 = R′ = H, R = $[MeO]_2CH_2CH_2$—, R^6 = Me) colourless crystalline powder m.p. 220—222 °C.

$C_8H_{14}N_4O_3S$ (214.2). Calcd. C 44.86; H 6.59; N 26.16. Found C 44.98; H 6.42; N 26.09%.

UV (EtOH): 210 (4.38); 244 (3.84).

IR (KBr): νC=O 1660 cm^{-1}.

(c) The above product (2.0 g; 9.4 mmoles) was stirred with *N* aq. HCl (25 ml) for 10 hrs room temperature. The mixture was evaporated to dryness in vacuum, and the brownish oily residue was triturated with acetone until it turned crystalline. The resulting hydrochloride was triturated with 10% aq. Na_2CO_3 to yield 0.6 g (77%) of *7-hydroxy-2-methyl-6,7-dihydro-3(5H)-imidazo [1,2-b]-as-triazinone* (**10**, R = H, R^7 = OH), colourless crystalline powder, m.p. 240—241 °C (d.) (DMF–acetone).

$C_6H_8N_4O_2$ (168.15). Calcd. C. 42.85; H 4.79; 33.32. N Found C 42.96; H 4.82; N 33.18%.

UV (EtOH): 208 (4.38); 250 (3.84).

(d) The above product (0.3 g; 1.8 mmole) was refluxed for 30 min with a mixture of AcOH and Ac_2O (3 ml, each). The resulting brown solution was evaporated to dryness in vacuum, and the residue was recrystallized from a small amount of water to yield 0.17 g (37%) of **10** (R = Ac, R^7 = AcO), colourless crystalline powder, m.p. 180—181 °C.

$C_{10}H_{12}N_4O_4$ (252.23). Calcd. C 47.61; H 4.79; N 22.21. Found C 47.49; H 4.87; N 22.07%.

* *Cf.* Ref. [16].

2-Methyl-3(5H)-imidazo[1,2-b]-as-triazinone

(a) 3-(2,2-Dimethoxyethylamino)-6-methyl-5(2*H*)-*as*-triazinone (1.0 g; 4.7 mmoles) was refluxed for 10 hrs with 20% aq. HCl (15 ml). The mixture was evaporated to dryness in vacuum to yield 0.45 g (64%) of the title compound, colourless crystalline powder, m.p. above 300 °C (from water).

$C_6H_6N_4O$ (150.14). Calcd. C 47.99; H 4.03. Found C 47.52; H 4.00%.

UV (EtOH): 212 (4.22); 246 (3.82); 308 (3.69).

IR (KBr): ν >C—H (five-membered ring) 3100, νC=O 1630 cm^{-1}.

(b) **10** (R = H, R^7 = OH) (0.3 g; 1.8 mmole) was refluxed for 1.5 hr with 20% aq. HCl (10 ml). The mixture was evaporated to dryness in vacuum. The residue was triturated with a small amount of 10% aq. Na_2CO_3 and slightly acidified with AcOH to yield. 0.2 g (75%) of a product which, according to m.p's and IR spectra, proved identical with the substance obtained as described under *(a)*.

2-Acetyl-6-methyl-3-pyrrolidino-5(2H)-as-triazinone (18)

(a) A mixture of 6-methyl-3-methylthio-5(2*H*)-*as*-triazinone (1.57 g; 10 mmoles) and pyrrolidine (10 ml) was refluxed for 20 hrs and allowed to stand overnight to yield 1.6 g (89%) of **9** (R^2 = H, R + R′ = $[CH_2]_4$, R^6 = Me), m.p. 298—300 °C (d.) (from $MeNO_2$).

$C_8H_{12}N_4O$ (180.2). Calcd. C 53.32; H 6.72; N 31.09. Found C 53.52; H 6.63; N 31.20%.

(b) The above product (1.5 g) was refluxed for 1 hr with a mixture of Ac_2O (20 ml) and pyridine (0.5 ml). 1.1 g of unchanged starting compound was recovered when the mixture was allowed to cool. The filtrate was evaporated to dryness in vacuum and the resulting yellow gum was extracted with boiling gasoline (20 ml). The product, 0.1 g (20%, based on unrecovered starting material), crystalline needles, m.p. 104—105 °C (from gasoline), separated on cooling.

$C_{10}H_{14}N_4O_2$ (222.2). Calcd. C 54.05; H 6.35; N 25.22. Found C 54.11; H 6.44; N 25.66; 24.95%.

UV (anhydrous dioxane): 222 (4.04); 244 (4.05); 257 (4.08).

IR (KBr): νC=O 1725 + 1708/1700, d.

For comparison [23]:

22, UV (anhydrous dioxane): 242 (4.18); 264 (4.19).
IR (KBr): νC=O 1745 + 1685.

23, UV (anhydrous dioxane): 238 (4.14); 264 (4.24).
IR (KBr): νC=O 1765 + 1675.

24, UV (anhydrous dioxane): 232 (4.18); 255 (4.06).
IR (KBr): νC=O 1760 + 1690.

5-Acetyl-2-methyl-5,6,7,8-tetrahydro-3H-pyrimido[1,2-b]-as-triazin-3-one (26)

A mixture of **25** [16] (0.32 g; 2 mmoles), acetic anhydride (5 ml) and one drop of conc. HCl was refluxed for 1 hr and evaporated to dryness in vacuum. The crystalline residue was triturated with ether to yield 0.25 g (62%) of **26**, m.p. 127—128 °C (from CCl_4).

$C_9H_{12}N_4O_2$ (208.2). Calcd. C 51.92; H 5.81; N 26.91. Found C 51.81; H 6.04; N 27.07%.

*

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REFERENCES

[1] Ágai, B., Hornyák, Gy., Lempert, K.: Periodica Polytechn. [Budapest], Ser. Chem. Engng. **18,** 47 (1974)
[2] Ágai, B., Hornyák, Gy., Láng, L., Lempert, K., Sohár, P.: Periodica Polytechn. [Budapest], Ser. Chem. Engng. **15,** 43 (1971)
[3] Snell, B. K.: J. Chem. Soc. (C) **1968,** 2358
[4] Phillips, A. P., Mentha, J.: J. Am. Chem. Soc. **76,** 6200 (1954)
[5] Reiter, J., Sohár, P., Toldy, L.: Tetrahedron Letters **1970,** 1411

* The latter have been published in full in Ref. [28]

[6] REITER, J., SOHÁR, P., TOLDY, L.: Tetrahedron Letters **1970,** 1417
[7] SOHÁR, P., REITER, J., TOLDY, L.: Org. Magnetic Resonance **3,** 689 (1971)
[8] PROKOF'EV, M. A., ANTONOVICH, E. G., SHVACHKIN, YU. P.: Doklady Akad. Nauk SSSR **87,** 783 (1952); Chem. Abstr. **48,** 169 (1954)
[9] PROKOF'EV, M. A., SHABAROVA, Z. A., ANTONOVICH, E. G.: Zh. Obshch. Khim. **25,** 397 (1955)
[10] ANTONOVICH, E. G., PROKOF'EV, M. A.: Vestnik Moskov. Univ. **10,** No. 3, Ser. Fiz.-Mat. i Estestven. Nauk No. 2, 57 (1955); Chem. Abstr. **49,** 10972 (1955)
[11] PROKOF'EV, M. A., SHVACHKIN, YU. P.: Zh. Obshch. Khim. **24,** 1046 (1954)
[12] PROKOF'EV, M. A., SHVACHKIN, YU. P.: Zh. Obshch. Khim. **25,** 975 (1955)
[13] SHVACHKIN, YU. P., PROKOF'EV, M. A.: Zh. Obshch. Khim. **26,** 3416 (1956)
[14] PROKOF'EV, M. A., ANTONOVICH, E. G., SHVACHKIN, YU. P.: Vestnik Moskov. Univ. **12,** Ser. Mat., Mekh., Astron., Fiz. Khim. No. 3, 199 (1957); Chem. Abstr. **52,** 9145 (1958)
[15] MAJIMA, R.: Ber. **41,** 176 (1908)
[16] HORNYÁK, GY., LEMPERT, K., ZAUER, K.: Acta Chim. Acad. Sci. Hung. **61,** 181 (1969)
[17] BROWN, D. J., HOERGER, E., MASON, S. F.: J. Chem. Soc. **1955,** 211
[18] HORNYÁK, GY., LEMPERT, K.: Acta Chim. Acad. Sci. Hung. **68,** 277 (1971)
[19] PITHA, J., FIEDLER, P., GUT, J.: Coll. Czechoslov. Chem. Commun. **31,** 1864 (1966)
[20] PARNELL, E. W.: J. Chem. Soc. **1962,** 2856
[21] ELMORE, D. T., TOSELAND, P. A., TYRRELL, H. J. V.: J. Chem. Soc. **1955,** 4388
[22] LACEY, R. N.: J. Chem. Soc. **1954,** 839
[23] DOLESCHALL, G., HORNYÁK, GY., LÁNG, L., LEMPERT, K., ZAUER, K.: Acta Chim. Acad. Sci. Hung. **57,** 191 (1968)
[24] LEE, J., PAUDLER, W. W.: J. Heterocyclic Chem. **9,** 995 (1972)
[25] BEHREND, R.: Ber **19,** 220 (1886)
[26] GUT, J., HESOUN, D., NOVÁČEK, A.: Coll. Czechoslov. Chem. Commun. **31,** 2014 (1966)
[27] PARTCH, R. E.: Tetrahedron Letters **1964,** 3071
[28] Absorption Spectra in the UV and Visible Regions (Edited by L. Láng), Vol's 1—19, Publishing House of the Hungarian Academy of Sciences, Budapest 1959—1974.
[29] WHEELER, H. L., MCFARLAND, D. F.: Am. Chem. J. **42,** 101 (1909)
[30] STACEY, G. J., (Imperial Chemical Industries, Ltd.): Brit. Pat. 679637 (June 18, 1952); Chem. Abstr. **47,** P 4920 (1953)

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THE SYNTHESIS OF ISOFLAVONE GLYCOSIDES, XIII*

THE SYNTHESIS OF FORMONONETIN-7-β-GENTIOBIOSIDE AND -7-β-SOPHOROSIDE

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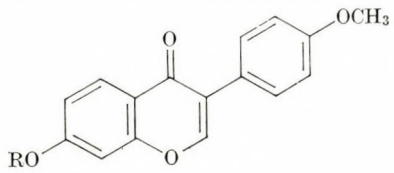
The 7-0-β-gentiobioside and 7-0-β-sophoroside of formononetin have been synthesized and found to be different from a formononetin-7-0-glucosyl-glucoside isolated from *Cladrastis platycarpa*.

From the bark of *Cladrastis platycarpa*, a tree growing in Japan, IMAMURA *et al.* recently isolated a glucosyl-glucoside of formononetin (**1**) with the structure of the disaccharide unspecified [2]. Since among the numerous possible glucosyl-glucoses only gentiobiose (6-O-β-D-glucopyranosyl-glucose) and sophorose (2-O-β-D-glucopyranosyl-glucose) have been reported to be associated with flavonoids [3], it was plausible that one of these may be the sugar moiety of the above mentioned glycoside.

In order to verify this assumption, we have prepared formononetin-7-O-β-gentiobioside (**2**) and -7-O-sophoroside (**3**) by coupling formononetin (**1**) with the corresponding α-acetobromosugars, followed by saponification of the resulting glycoside acetates (**4** and **5**, respectively). Both **2** and **3** were clearly distinct from the natural product both by m.p., IR and chromatographic mobility. Dr. H. IMAMURA kindly provided us with the information that he had obtained evidence showing the sugar component of the natural product to be laminaribiose (3-O-β-D-glucopyranosyl-glucose). Since he also informed us that a synthesis of formononetin-7-O-β-laminaribioside was in progress, we did not pursue our investigations any further.



1 : R = H
2 : R = β-gentiobiosyl
3 : R = β-sophorosyl
4 : R = hepta-0-acetylgentiobiosyl
5 : R = hepta-0-acetylsophorosyl

* For Part XII, see Ref. [1]

Experimental

7-Hydroxy-4'-methoxyisoflavon-7-0-β-gentiobioseheptaacetate (4)

A solution of 1 [4] (0.30 g) and α-acetobromogentiobiose [5] (0.5 g) in anhydrous pyridine (610 ml) was stirred with silver oxide (0.20 g) and anhydrous calcium sulfate (Drierite) at room temperature for 3 hrs. The reaction mixture was filtered into 15% aqueous acetic acid (30 ml). The precipitate was collected, dried and triturated with chloroform (20 ml). The undissolved aglycon was separated, the chloroform evaporated, and the residue crystallized first from ethanol and then from ethanol–chloroform to afford the product (0.17 g; 17%) as colourless prisms, m.p. 215—215.5 °C.

$C_{42}H_{46}O_{21}$ (886.8). Calcd. C 56.77; H 5.23. Found C 56.72; H 5.25%.

7-Hydroxy-4'-methoxyisoflavone-7-0-β-gentiobioside, Formononetin-7-0-β-gentiobioside (2)

Compound **4** (123 mg) was boiled with 0.01 *N* sodium methoxide (5 ml) for 10 min. After neutralization with acetic acid the solution was filtered and evaporated to about 1/3 of its original volume. The product was collected and recrystallized from methanol to afford **2** (12 mg) as small, colourless needles, m.p. 188—191 °C.

$C_{28}H_{32}O_{14} \cdot 2H_2O$ (628.57). Calcd. C 53.50; H 5.77. Found C 53.86; H 5.59%.

6-Hydrox-4'-methoxyisoflavone-7-0-β-sophoroside heptaacetate (5)

Coupling of **1** (0.3 g) with α-acetobromosophorose [6] (0.5 g), as described for **4**, afforded **5**; after repeated recrystallizations from ethanol the product was colourless needles, m.p. 199—201°.

$C_{42}H_{46}O_{21}$ (886.8). Calcd. C 56.77; H 5.23. Found C 56.70; H 5.34%.

7-Hydroxy-4'-methoxyisoflavone-7-0-β-sophoroside (3)

Deacetylation of **5**, as described for **2**, gave **3** as colourless needles (from MeOH), m.p. 213—216 °C.

$C_{28}H_{32}O_{14} \cdot 2H_2O$ (628.57). Calcd. C 53.50; H 5.77. Found C 53.24: H 5.47%

*

We are indebted to Dr. IMAMURA for a sample of the the natural product and for communicating his unpublished results.

REFERENCES

[1] FARKAS, L., WOLFNER, A.: Acta Chim. Acad. Sci. Hung., **67,** 109 (1971)
[2] IMAMURA, H., HIBINO, Y., OHASHI, H.: Phytochemistry **13,** 757 (1974)
[3] WAGNER, H.: in "Progress in the Chemistry of Natural Products", **31,** 159 (1974)
[4] FARKAS, L., MAJOR, Á., PALLOS, L., VÁRADY, J.: Chem. Ber., **91,** 2858 (1958)
[5] TAKIURA, K., HONDA, S., ENDO, K., KAKEHI, K.: Chem. Pharm. Bull., **20,** 438 (1972)
[6] FREUDENBERG, K., SOFF, K.: Chem. Ber., **69,** 1245 (1936)

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NOVEL TYPE PHOTOISOMERS FROM *N*-(4-METHYL-3-QUINAZOLINIO)-AMIDATES*

(PRELIMINARY COMMUNICATION)

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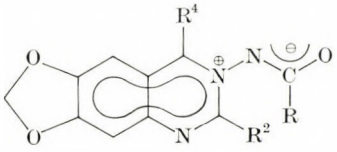
([a]Department of Organic Chemistry, Technical University, Budapest, Hungary and [b]Department of Chemistry, Odense University, Odense, Denmark)

Received January 2, 1976

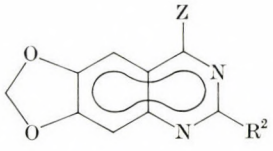
Irradiation in ethanol of the title compounds gives rise to the formation of isomers by formal 1,3-shifts of the acylnitrene groups from nitrogen to carbon.

The photochemistry of *N*-(3-quinazolinio)-amidates (**I**), such as compound **IA** (= **I**, $R^2 = R^4 = Me$, R = OEt), has been described in Ref. [1]. We have now isolated a photoisomer **IIIA** (III; $R^2 = Me$), m. p. 160—162°C, in 5% yield in addition to **IIA** (II; $R^2 = Me$) on irradiation of Ar purged ethanol solutions of **IA** with a high pressure Hg immersion lamp through Pyrex. Analogous products, *viz.* **IIB** (**II**; $R^2 = H$) (23%, m. p. 165°C) and **IIIB** (**III**; $R^2 = H$) (7%, m. p. 176—177°C) have been obtained on irradiation of **IB** (**I**; $R^2 = H$, $R^4 = Me$, R = OEt).

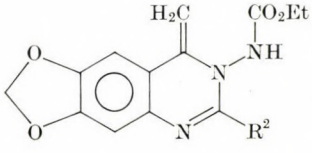
The structure assignment of compounds **IIIA** and **B** is based (1) on the presence of bands at 3420, 1730, 1225 and 1035 cm^{-1}, and 3400, 1725, 1215 and 1035 cm^{-1}, respectively, in the KBr IR spectra; (2) on the virtual identity of the EtOH UV spectra of compounds **IIA**, **IIB**, **IIIA** and **IIIB**; (3) on the NMR and (4) mass spectra.



I



II: Z = Me



IV

III: Z = CH_2—NH—COOEt

NMR spectra. **IIIA** ($CDCl_3$): δ 7.35, s, 5-H + 8-H; 6.45, bs, exchangeable, NH; 6.25, s, OCH_2O; 4.87, d, $J = 4.5$ Hz (s, after addition of D_2O), 4-CH_2N; 4.30, q, + 1.35, t, $J = 7$ Hz, COOEt; 2.85, s, 2-Me. **IIIB** (DMSO—d_6 + $CDCl_3$):

* Part XI of Electron Deficient Heterocyclic Ammonioamidates, and Part III of *N*-(3-Quinazolinio)-amidates. For Parts X and II, respectively, see Ref. [1].

δ 8.97, s, 2-H; 7.60, s, 5-H; 7.30, s, 8-H; 6.25, s, OCH_2O; 4.75, s + d, $J = 3.5$ Hz, 4-CH_2N (with NH partially deuterated); 4.07, q, + 1.2, t, $J = 7$ Hz, COOEt.

Mass spectra (70 eV, 100 °C). **IIIA**: *m/e* 289: 93% (M), *m/e* 288: 6% (**a**), *m/e* 260: 8% (**b**), *m/e* 244: 12%, *m/e* 242: 6% (**c**), *m/e* 216: 100% (**d**), *m/e* 202: 79% (**e**), *m/e* 189: 13% (**f**), *m/e* 188: 20%, *m/e* 187: 25%, *m/e* 174: 2%, *m/e*: 161: 3%. **IIIB**: *m/e* 275: 78% (M), *m/e* 274: 6% (**a**), *m/e* 246: 8% (**b**), *m/e* 230, 14%, *m/e* 228: 10% (**c**), *m/e* 202: 100% (**d**), *m/e* 188: 32% (**e**), *m/e* 175: 16% (**f**), *m/e* 174: 24%, *m/e* 173: 12%, *m/e* 160: 13%, *m/e* 147: 12%; with metastable peaks corresponding to the processes $M^{+\cdot} \rightarrow$**a**, $M^{+\cdot} \rightarrow$**d**, $M^{+\cdot} \rightarrow$**e**, **a**→**b**, **b**→**c**, **b**→**d** and **d**→**f** in both series.

The formation of the type **III** photolysis products is without precedence in the photochemistry of heterocyclic ammonioamidates, and only a single comparable reaction is known in the related *N*-oxide series, *i.e.* the gas phase photoisomerization of 2-picoline-*N*-oxide into 2-pyridinemethanol induced by irradiation with 3261 Å light [2]. Two mechanisms may be considered in order to rationalize the formation of the type **III** products: (a) photolysis of the N—N bond of the starting compounds **I** (R^4 = Me), and insertion of the resulting excited singlet nitrene into a C—H bond of the 4-methyl group of the quinazoline fragment **II** (Z=Me); (b) tautomerization of the starting compound (the hydrogen atoms of the 4-methyl group of **IIIA** are rapidly exchanged in CD_3OD solution at room temperature [3]), and subsequent sigmatropic [1, 3] shift of the ethoxycarbonylamino group of the resulting type **IV** tautomers.

REFERENCES

[1] Fetter, J., Lempert, K., Møller, J., Szalai, G.: Tetrahedron Letters **1975**, 2775
[2] Hata, N.: Bull. Chem. Soc. Japan **34**, 1440 (1961)
[3] Fetter, J., Lempert, K., Moller, J.: Tetrahedron **31**, 2559 (1975)

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INDEX

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A kiadásért felel az Akadémiai Kiadó igazgatója. Műszaki szerkesztő: Zacsik Annamária
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РЕЗЮМЕ

Газовохроматографический анализ смеси N_2, CO, CO_2, Cl_2, HCl и $COCl_2$, используя детектор газовой плотности

Г. АЛЕКСАНДЕР и Г. ГАРЗО

Было описано разделение заглавных соединений подачей двух образцов на две колонны. Обсуждаются условия разделения и детектирования, предъявляемые вследствие корродирующей природы смеси.

pH-Метрическое исследование тройных систем: оксованадий(IV)— 8-гидроксихинолин-5-сульфоновая кислота – дигидрофенольные соединения

С. П. СИНГ и ДЖ. П. ТАНДОН

Образование смешанного хелата в системе, содержащей ванадильный ион, 8-гидроксихинолин-5-сульфоновую кислоту и тирон или соль хромотроповой кислоты, было исследовано pH-метрически при ионной силе, равной 0,1 (KNO_3) и $30 \pm 0{,}5°C$. Были определены константы стабильности образующегося комплекса со смешанными лигандами, с составом 1 : 1 : 1. Было найдено, что, с точки зрения вторичных лигандов, стабильность уменьшается в следующем ряду: хромотроповая кислота > тирон.

ИК спектрофотометрическое исследование комплексов с переносом заряда некоторых производных симметричного тринитробензола с ароматическими соединениями

А. М. ХИНДАВЕЙ, А. М. Г. НАССАР и Р. М. ИССА

ИК спектры продуктов присоединения некоторых производных симм. тринитробензола с ароматическими соединениями анализируются с целью выясения типа взаимодействия. Сдвиги полос NH_2 ароматических аминов и асимметричных полос NO_2 производных симм. тринитробензола позволяют отличить кпз от молекулярных комплексов. Был исследован также эффект растворителя для выяснения природы реакции между пикрилхлоридом и ароматическими аминами.

Многослойная адсорбция газов на гетерогенных твердых поверхностях: местное БЭТ поведение адсорбированной фазы

М. ЯРОНЕЦ и В. РУДЗИНСКИ

Было обсуждено влияние гетерогенности поверхности адсорбента на образование многомолекулярного слоя в газовой адсорбции, используя полную форму уравнения БЭТ в качестве местной адсорбционной изотермы. В численных расчетах был использован новый метод определения зависимости распределения энергии.

Хелаты редкоземельных металлов с N-(2-гидрокси-1-нафталиден)-β-аланином

Д. Д. ОЗА, Б. Р. СИНГВИ и Р. К. МЕХТА

N-(2-Гидрокси-1-нафталиден)-β-аланин образует твердые хелаты с La(III), Ce(III), Pr(III), Nd(III), Sm(III) и Gd(III). Обуждаются величины магнитных моментов и ИК-спектры этих хелатов. Были исследованы также некоторые реакции лигандного замещения этих хелатов.

Комплексное исследование никелевых катализаторов, VI

Исследование металлической структуры непирофорных никелевых катализаторов нового типа

Ш. БЕКАШШИ, Й. ПЕТРО, Э. КРИШТЬЯК, А. ЧАНАДИ и А. КАЛЬМАН

Металлографическим, электронно-микроскопическим и рентгено-дифракционным методами были изучены сплавы Ni—Si, Ni—Al—Si, Ni—Mg и Ni—Zn и приготовленные из них непирофорные катализаторы.

Несмотря на относительно быстрое охлаждение, фазовая структура сплавов соответствует условиям, указанным на диаграмме состояний. Щелочь сначала атакует фазы, содержащие большие количества неактивного металла. При приготовлении катализаторов неактивный металл не выщелачивается полностью, так что в нем остаются и интерметаллические соединения. Электронно-микроскопические съемки наглядно показывают неопределенную поверхностную геометрию катализаторов, содержащих большие количества гидроокиси.

Структура катализатора из сплава Ni—Mg отклоняется от остальных. После выщелачивания остается неизменным не интерметаллическое соединение, а нелегированный магний, и в катализаторе находится большое количество $Mg(OH)_2$ кристаллической структуры.

Исследование превращений диолов и циклических эфиров, XXXVIII

Механизм изомеризации оксациклоалканов, катализированной платиной

М. БАРТОК

Был исследовани механизм изомеризации 2-метилоксациклоалканов (2-метилоксиран, 2-метилоксетан, 2-метилтетрагидрофуран, 2-метилтетрагидропиран), катализированной платиной. В качестве экспериментального метода была использована микрореакторная техника, комбинированная с газовой хроматографией, техника импульса. Модельные соединения были исследованы в токе газа-носителя водорода и гелия, в присутствии платиновых катализаторов на термолитном и угольном носителях, а также в присутствии катализаторов, отравленных аммиаком. Были проведены исследования продуктов реакции, а также ряда соединений, полагаемых промежуточными продуктами. Экспериментальные данные указывают на то, что механизм изомеризации оксациклоалканов зависит от числа атомов в кольце, от используемого катализатора и от условий проведения реакции. Было также установлено, что в механизмах образования альдегидов и кетонов существуют различия. Важную роль в образовании альдегидов играют такие центры на катализаторе, которые обладают электрофильным характером. Экспериментально также была подтверждена важная роль платинового катализатора, водорода, хемисорбированного на катализаторе, а также участия вторичных спиртов в качестве промежуточных продуктов в процессе образования кетонов.

Исследование тозильных и мезильных производных в морфиновом ряду, XIV

Новый метод получения дезоксикодеина-E

Ш. МАКЛЕЙТ, Ш. БЕРЕНИ и Р. БОГНАР

Был разработан новый, легко осуществимый метод получения дезоксиморфина-E и дигидродезоксиморфина-D путем восстановления 3-O-ацетил-6-O-тозилморфина $LiAlH_4$ и дальнейшим каталитическим восстановлением полученного дезоксиморфина-E.

Пиримидины и их конденсированные производные, IV

N(2)-ацилизоцитозины, некоторые родственные имидазо [1,2-a]-пиримидиндионы и аза-аналоги. Синтез, спектры и таутомерные структуры

ДЬ. ХОРНЯК, Б. АГАИ, Л. СЁЧ и К. ЛЕМПЕРТ

Были синтезированы серии потенциально таутомерных и нетаутомерных N(2)-ацилизоцитозинов, 1-ацил-2,3-дигидро-5(1*H*)- и -7(1*H*)-имидазо [1,2-a] пиримидинонов, имидазо [1,2-a] пиримидиндианов и их аза-аналогов. На основе спектроскопических данных и/или химическим путем были определены места ацилирования изоцитозинов, 2,3-дигидро [1,2-a] пиримидинонов и их аза-аналогов. Была определена также доминирующая таутомерная форма потенциально таутомерных соединений.

Синтез изофлавонглюкозидов, XIII

Синтез формононетин-7-β-генциобиозида и -7-β-софорозида

Л. ФАРКАШ, А. КАЛЬМАН и А. ВОЛЬФНЕР

Были синтезированы 7-O-β-генциобиозид и 7-O-β-софорозид формононетина. Было найдено, что они отличаются от формононетин-7-O-глюкозилглюкозида, изолированного из *Cladrastis platycarpa*.

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