Acta Chimica Hungarica

VOLUME 123, NUMBERS 1–2, SEPTEMBER–OCTOBER 1986

Akadémiai Kiadó, Budapest
ACTA CHIM. HUNG. ACHUDC 123 (1–2) 3–67 (1986) HU ISSN 0231–3146

ACTA CHIMICA HUNGARICA

A JOURNAL OF THE HUNGARIAN ACADEMY OF SCIENCES

Acta Chimica publishes original reports on all aspects of chemistry in English.

Acta Chimica is published in three volumes per year, each volume consisting of four issues, by

AKADÉMIAI KIADÓ

Publishing House of the Hungarian Academy of Sciences
H-1054 Budapest, Alkotmány u. 21.

Manuscripts and editorial correspondence should be addressed to

Acta Chimica
H-1450 Budapest P.O. Box 67

Subscription information

Orders should be addressed to

KULTURA Foreign Trading Company
H-1389 Budapest P.O. Box 149

or to its representatives abroad

Acta Chimica is indexed in Current Contents.

NOTICE TO AUTHORS

Acta Chimica publishes original papers on all aspects of chemistry in English. Before preparing a manuscript for submission to this journal authors are advised to consult recent issues.

Form of manuscript

Manuscripts, tables and illustrations should be submitted in triplicate. Manuscripts should be typewritten double spaced (25 lines, 50 characters per line including spaces). The *title page* should include (1) the title of the paper, (2) the full names of the author(s) in the sequence to be published; apply an asterisk to designate the name of the author to whom correspondence should be addressed, (3) name and address of the institution where the work was done. If the paper is part of a series, reference to the previous communication must be given as a footnote.

Abstract

A summary is printed at the head of each paper. This should not exceed 200 words and should state briefly the principal results and major conclusions of the work. It should be suitable for use by abstracting services.

ACTA CHIMICA HUNGARICA

VOLUME 123

AKADÉMIAI KIADÓ, BUDAPEST

1986

Balint, M.-A. s. **Drugarin, C.**
Bánki, J., Billes, F., Gál, M., Grofcsik, A., Jalsovszky, Gy., Sztraka, L.: Complete CNDO force field of *cis*- and *trans*-furan-2-aldehyde 115
Bauer, K. s. **Matolcsy, Gy.**
Bélai, I. s. **Matolcsy, Gy.**
Billes, F. s. **Bánki, J.**
Billes, F., Tóth, A.: A generalized theory of quantitative analysis of multicomponent ampholyte (acid, base) systems by potentiometric titration 3
Burger, K. s. **Csikkel-Szolnoki, A.**
Bushin, S. V. s. **Hardy, Gy.**

Chambers, J. Q. s. **Inzelt, Gy.**
Csáki-Tombácz, E. s. **Csikkel-Szolnoki, A.**
Csányi, L. J., Galbács, Z. M., Nagy, L., Horváth, I.: Osmium-tetroxide as a redox catalyst. Mechanism of OsO_4-catalyzed decomposition of hydrogen peroxide 123
Cser, F. s. **Hardy, Gy.**
Csikkel-Szolnoki, A., Csáki-Tombácz, E., Veres, S., Burger, K.: The chromophore serving as basis for the determination of arsenic with silver diethyldithiocarbamate .. 45

Dancsó, A., Kalaus, Gy., Kajtár-Peredy, M., Szabó, L., Szántay, Cs.: Synthesis of Vinca alkaloids and related compounds, XXIX. Stereochemistry of 1,1-disubstituted-indolo[2,3-*a*]quinolizidines 155
Day, R. W. s. **Inzelt, Gy.**
Drugarin, C., Balint, M.-A.: Determination of the ionization constants of some new *p*-aminohippuric acid derivatives 31
Dvortsák, P. s. **Gál, M.**

Gál, M. s. **Bánki, J.**
Gál, M., Tihanyi, E., Dvortsák, P.: Ring-chain tautomerism of *ortho*-amino-substituted aromatic carboxylic acid hydrazones, I. Formation of 1,2,3,4-tetrahydro-5*H*-1,3,4-benzotriazepin-5-ones and 5,6,7,8-tetrahydro-4*H*-pyrazolo[3,4-*e*][1,2,4]triazepin-4-ones 55
Galbács, Z. M. s. **Csányi, L. J.**
Gerlei, A. s. **Matolcsy, Gy.**
Grofcsik, A. s. **Bánki, J.**

Hardy, Gy., Bushin, S. V., Shtennikova, I. N., Korneeva, E. V., Kolbina, G. F., Cser, F., Nyitrai, K., Smirnov, K. P.: Conformation and optical anisotropy of short-chain molecules with mesogenic side groups 83
Horváth, I. s. **Csányi, L. J.**

Inzelt, Gy., Chambers, J. Q., Day, R. W.: Effect of quinolinium salts on the behaviour of tetracyanoquinodimethane polymer film electrode 137

Jalsovszky, Gy. s. **Bánki, J.**
Jamrógiewicz, Z. s. **Łukasiak, J.**

Kajtár-Peredy, M. s. **Dancsó, A.**
Kalaus, Gy. s. **Dancsó, A.**
Kálmán, A. s. **Körmendy, K.**
Kardos, M. s. **Matolcsy, Gy.**

Kolbina, G. F. s. **Hardy, Gy.**
Koritsánszky, T. s. **Körmendy, K.**
Korneeva, E. V. s. **Hardy, Gy.**
Körmendy, K., Kálmán, A., Koritsánszky, T., Kövesdy, I., Sohár, P., Ruff, F.: Aminophthalazinone derivatives, XI. Chemical properties of imidazo- and pyrimido[2,1-*a*] phthalazinone systems, III. Formation of a new triazaindenoindene skeleton from pyrimidophthalazinone derivatives 15
Kövesdi, I. s. **Körmendy, K.**

Lata, S., Shivahare, G. C.: Spectrophotometric and potentiometric determination of Nb(V) and Ta(V) using barbituric acid 93
Łukasiak, J., Jamrógiewicz, Z.: Studies on 1-aryloxysilatranes, V. Studies on the mechanism hydrolysis of 1-aryloxysilatranes 99

Matolcsy, Gy., Bauer, K., Pál, A., Ujváry, I., Bélai, I., Gerlei, A., Kardos, M., Sohár, P., Pelczer, I.: Phosphane oxides as intermediates in the synthesis of potentially bioactive compounds 145

Nagy, L. s. **Csányi, L. J.**
Narvi, S. S. s. **Sharma, C. L.**
Nyitrai, K. s. **Hardy, Gy.**

Pál, Á. s. **Matolcsy, Gy.**
Pelczer, I. s. **Matolcsy, Gy.**

Ruff, F. s. **Körmendy, K.**

Sharma, C. L., Narvi, S. S.: Physico-chemical studies on the mixed ligand complexes of some diimines with palladium(II), platinum(II), iridium(III), rhodium(III) and platinum(IV) phthalimides 107
Shivahare, G. C. s. **Lata, S.**
Shtennikova, I. N. s. **Hardy, Gy.**
Smirnov, K. P. s. **Hardy, Gy.**
Sohár, P. s. **Körmendy, K.**
Sohár, P. s. **Matolcsy, Gy.**
Szabó, L., s. **Dancsó, A.**
Szántay, Cs. s. **Dancsó, A.**
Szczepek, W. J.: Reactions of 5-hydroxy-6-oxosteroids, VI. Acid-catalyzed isomerization of some 5α-hydroxy-6-oxosteroids 69
Szczepek, W. J.: Reactions of 5-hydroxy-6-oxosteroids, VII. New reagent for the Westphalen-type rearrangement of 5α-hydroxy-6-oxosteroids 77
Sztraka, L. s. **Bánki, J.**

Tihanyi, E. s. **Gál, M.**
Tóth, A. s. **Billes, F.**

Ujváry, I. s. **Matolcsy, Gy.**

Veres, S. s. **Csikkel-Szolnoki, A.**

CONTENTS

PHYSICAL AND INORGANIC CHEMISTRY

A generalized theory of quantitative analysis of multicomponent ampholyte (acid, base) systems by potentiometric titration, **F. Billes, A. Tóth** 3

Determination of the ionization constants of some new *p*-aminohippuric acid derivatives, **C. Drugarin, M.-A. Balint** 31

ORGANIC CHEMISTRY

Aminophthalazinone derivatives, XI. Chemical properties of imidazo- and pyrimido[2,1-*a*]-phthalazinone systems, III. Formation of a new triazaindenoindene skeleton from pyrimidophthalazinone derivatives, **K. Körmendy, A. Kálmán, T. Koritsánszky, I. Kövesdi, P. Sohár, F. Ruff** 15

Ring-chain tautomerism of *ortho*-amino-substituted aromatic carboxylic acid hydrazones, I. Formation of 1,2,3,4-tetrahydro-5*H*-1,3,4-benzotriazepin-5-ones and 5,6,7,8-tetrahydro-4*H*-pyrazolo[3,4-*e*] [1,2,4]triazepin-4-ones, **M. Gál, E. Tihanyi, P. Dvortsák** 55

ANALYTICAL CHEMISTRY

The chromophore serving as basis for the determination of arsenic with silver diethyldithiocarbamate, **A. Csikkel-Szolnoki, E. Csáki-Tombácz, S. Veres, K. Burger** 45

BOOK REVIEWS 63

PRINTED IN HUNGARY

Akadémiai Kiadó és Nyomda, Budapest

Acta Chimica Hungarica 123 (1—2), pp. 3—13 (1986)

A GENERALIZED THEORY OF QUANTITATIVE ANALYSIS OF MULTICOMPONENT AMPHOLYTE (ACID, BASE) SYSTEMS BY POTENTIOMETRIC TITRATION

Ferenc BILLES[1]* and Antal TÓTH[2]

([1]Department of Physical Chemistry, Technical University Budapest, H-1521 Budapest, Budafoki u. 8. and [2]CHINOIN Pharmaceutical and Chemical Works, H-1045 Budapest, Tó u. 1.—5.)

Received June 13, 1985
Accepted for publication October 3, 1985

A relationship is suggested for the quantitative determination of ampholytes in multicomponent systems, by potentiometric titration.

First the one-component case is investigated assuming stepwise titration. The resulting equation is applicable to the determination of ionization or total protonation constants of ampholytes. Generalization of this equation to multicomponent ampholyte systems leads to a relation linear in the initial concentrations.

A further generalization of the method is its application to systems with tautomers. This yields a formula very similar to the above-mentioned, but the interpretations of the constants differ from those.

For the determination of all ionization constants of ampholytes it is often necessary to titrate them both with acids and bases. To have a titration curve without a breakpoint a relation is given for the conversion of the two data types into each other.

All relations are easily programmable in BASIC or Assembler languages and so applicable to processing of titration data by titration controlling computers.

Introduction

Recently several papers have dealt with the shape analysis of potential titration curves, the determination of ionization or protonation constants, the endpoint approximation problem of potentiometric titration and related topics [1—10].

Some attempts have been made for the quantitative determination of several components by potentiometric titration [11, 12].

In this paper we try to develop a more general theory for the quantitative analysis of multicomponent ampholyte systems in amphiprotic solutions.

We think it will be helpful in the evaluation of computer controlled titration data of multicomponent systems.

The following restrictions characterize our model:

1. Each activity coefficient is equal to one,

* To whom correspondence should be addressed.

2. Association and chemical reactions between the components except proton gain or loss are excluded,

3. The first attempt tautomerism is excluded (in Parts 2—4).

Below we use unorthodox notations for some constants to avoid the accumulation of indices. Acidic equilibrium constants (ionization constants) are labelled by K, protonation constants by β. Since this way the notations of indexed ionization constants and ionic product may be confused, for the latter the symbol k is applied.

One-component case

Ampholytes can gain and lose protons. For indexing the forms in protonic equilibria the following convention is chosen: the form without any mobile protons (A) is indexed by zero, all other ones by the number of mobile protons. Ampholytes are of basicity d and acidity e. Equilibria have the form

$$\mathrm{AH}_{i-1}^{(-d+i-1)} + \mathrm{H}^+ \rightleftharpoons \mathrm{AH}_i^{(-d+i)} \tag{1}$$

where electric charges are in parentheses. The equilibrium constants are defined as

$$K_i = \frac{[\mathrm{AH}_{i-1}^{(-d+i-1)}] \cdot [\mathrm{H}^+]}{[\mathrm{AH}_i^{(-d+i)}]} = \frac{c_{i-1} H}{c_i} \tag{2}$$

where c_i stands for $[\mathrm{AH}_i^{-d+i}]$ and H for $[\mathrm{H}^+]$. Since

$$c_i = \frac{1}{K_i} c_{i-1} H \tag{3}$$

$$c_i = \frac{c_0 H^i}{\prod_{r=1}^{i} K_r}$$

Defining the total protonation constants

$$\beta_i = \frac{1}{\prod_{r=1}^{i} K_r} \tag{4}$$

with $\beta_0 = 1$, we have

$$c_i = c_0 \beta_i H^i \tag{5}$$

Taking into account the electric neutrality of the solution

$$\sum_{i=0}^{d+e} (i - e) c_i + H - \frac{k}{H} = 0 \tag{6}$$

where k is the ionic product of the amphiprotic solvent HX

$$k = [H^+]\,[X^-] \tag{7}$$

let c^* be the total ampholyte concentration in the solution. Because of the definition of c_i:

$$c^* = \sum_{i=0}^{d+e} c_i \tag{8}$$

Substituting Eq. 5:

$$c^* = c_0 \sum_{i=0}^{d+e} \beta_i H^i \tag{9}$$

Dividing Eq. (5) by Eq. (9):

$$c_i = c^* \frac{\beta_i H^i}{\sum_{i=0}^{d+e} \beta_i H^i} \tag{10}$$

Using this relation Eq. (6) may be modified to

$$c^* \frac{\sum_{i=0}^{d+e} (i-e)\beta_i H^i}{\sum_{i=0}^{d+e} \beta_i H^i} + H - \frac{k}{H} = 0 \tag{11}$$

Since potentiometric titrations are carried out using mostly univalent strong electrolytes HY, WOH, e.g. in water HCl, NaOH as titrants, the titrant concentration $c^\square$ is practically equal to the concentration of the protons, of the hydroxide ions and of their counter ions Y^- and W^+ in the titrant, respectively.

Using stepwise addition technique in potentiometric titration, the following electric charge balance is formed in the titrate after the addition of the l-th titrant portion

$$c_l^* \frac{\sum_{i=0}^{d+e} (i-e)\beta_i H^i}{\sum_{i=0}^{d+e} \beta_i H^i} + H_l - \frac{k}{H_l} + c_l^\square = 0 \tag{12}$$

where the upper and lower sign applies to titration with bases and acids, respectively, $c_l^\square$ is the Y^- or the W^+ concentration in the titrate and c_l^* is the same for the ampholyte. These concentrations may be expressed by $c^\square$ and c^*, respectively. Let V be the volume of the titrate before the beginning of the titration $l = 0$ and v_l the total added titrant volume after the l-th step. The total titrate volume

$$V_l = V + v_l$$

According to the law of conservation of mass

$$c_l^* \, V_l = c^* \, V$$

e.g.

$$c_l^* = c^* \frac{V}{V_l} \tag{13}$$

and

$$c_l^{\square} \, V_l = c^{\square} \, v_l$$

or

$$c_l^{\square} = c^{\square} \frac{V_l - V}{V_l} \tag{14}$$

substituting Eqs. (13) and (14) into Eq. (12) we have

$$c^* \frac{\sum_{i=0}^{d+e} (i - e) \, \beta_i H_l^i}{\sum_{i=1}^{d+e} \beta_i \, H_l^i} + \frac{V_t}{V} \left(H_l - \frac{k}{H_l} \right) + c^{\square} \frac{V_l - V}{V} = 0 \tag{15}$$

$$l = 0, 1, 2, \ldots, m$$

where m stands for the number of titration steps.

Multicomponent system

Let n be the number of components indexed by j. Applying Eq. (15) for this system

$$\sum_{j=1}^{n} c_j^* \frac{\sum_{i=0}^{d_j+e_j} (i - e_j) \beta_{ij} H_l^i}{\sum_{i=0}^{d_j+e_j} \beta_{ij} \, H_l^i} + \frac{V_l}{V} \left(H_l - \frac{k}{H_l} \right) \pm c^{\square} \frac{V_l - V}{V} = 0 \tag{16}$$

$$l = 0, 1, 2, \ldots, m$$

To solve this equation for the c_j^* concentrations with appropriate accuracy beside the knowledge of the β_{ij} constants and the measurement of the V_l and H_l values the number of steps (m) must be higher than the number of components (n). Labelling the coefficients of the c_j^* concentrations in Eq. (16) by a_j, the sum of the second and third terms by b_l, we have

$$\sum_{j=1}^{n} a_{jl} \, c_j^* = b_l \qquad l = 0, 1, 2, \ldots, m \tag{17}$$

or in matrix notation

$$a\,\mathbf{c}^* = \mathbf{b} \tag{18}$$

where, being $m > n$, a is a general quadratic matrix and is therefore not invertible.

Applying the method of least squares the function to be minimized is

$$F = \sum_{l=0}^{m} \left(\sum_{j=1}^{n} a_{jl}\, c_{jl}^* - b_l \right)^2 \tag{19}$$

Derivating F by c_q^* concentration we have

$$\sum_{j=1}^{n} \left(c_j^* \sum_{l=0}^{m} a_{jl}\, a_{ql} \right) = \sum_{j=0}^{n} a_{ql}\, b_l \quad q = 1, 2, \ldots, n \tag{20}$$

Eq. (20) may be simplified to

$$\sum_{j=1}^{n} c_j^*\, p_{jq} = q_q \tag{21}$$

or in matrix formulation

$$p\,\mathbf{c}^* = \mathbf{g} \tag{22}$$

Since p is a square matrix the linear equation system may be solved by appropriate methods.

Determination of ionization constants

Equation (15) is applicable to the determination of ionization constants. The H_l and V_l values have to be measured and the β's are the unknown quantities. Rewriting Eq. (15) we have

$$\sum_{i=0}^{d+e} \beta_i H_l^i \left[(i-e)\, c^* - \frac{V_l}{V} \left(\frac{k}{H_l} - H_l \right) \pm c^{\square} \frac{V_l - V}{V} \right] = 0 \tag{23}$$

$$l = 0, 1, 2, \ldots, m$$

For the first glance Eq. (23) is a homogeneous linear equation system. With $i = 0$, however, $\beta_0 = 1$ and this term of the sum does not contain unknown quantities, so the true form of Eq. (23) is

$$\sum_{i=0}^{d+e} \beta_i H_l^i \left[(i-a)c^* - \frac{V_l}{V} \left(\frac{k}{H_l} - H_l \right) \pm c^{\square} \frac{V_l - V}{V} \right] = \frac{V_l}{V} \left(\frac{k}{H_l} - H_l \right) \mp c^{\square} \frac{V_l - V}{V} + ec^* \tag{24}$$

In short form

$$\sum_{i=0}^{d+e} \beta_i\, A_{il} = B_l \tag{25}$$

Applying the method of least squares ($m > d + e$) similarly to the case of multicomponent systems the function to be minimized is

$$F = \sum_{l=0}^{m} \gamma_l \left(\sum_{i=1}^{d+e} \beta_i A_{il} - B_l \right)^2$$

where the γ's are weight factors. A recommended weight factor is

$$\gamma_l = \frac{\Delta p V_l}{\Delta V_l}$$

where

$$\Delta \mathrm{pH}_l = \mathrm{pH}_l - \mathrm{pH}_{l-1}$$

and

$$\Delta V_l = V_l - V_{l-1}$$

Derivating F by the β_j's

$$\sum_{i=1}^{d+e} \beta_i \left(\sum_{l=0}^{m} \gamma_l A_{il} A_{ql} \right) = \sum_{l=0}^{m} \gamma_l A_{ql} B_l \tag{26}$$

In short form

$$\sum_{i=1}^{d+e} \beta_i P_{iq} = G_q \tag{27}$$

Determining the total protonation constants the ionization constants can be calculated by Eq. (4):

$$K_i = \frac{\beta_{i-1}}{\beta_i}$$

The numbering of these ionization constants is in accordance with Part 2. for acids as usual, but for bases of opposite meaning.

Conversion of acidic and basic titration curves into each other

It is sometimes advisable to extend the investigated pH range in directions of both acidic and basic titrations. There are pure ampholytes (acids, bases) or multicomponent systems having a pH value in solution near pk. In these cases stepwise titration is needed with both acidic and basic titrant.

Since unified calculations are more profitable, conversion of acidic data to basic ones and vice versa are very useful.

Let V_{lb} be the volume of the titrate after the l-th step in basic titration and V_{la} the same for acidic one. Since the c^* concentration is the same, supposing the identity of the pH values from Eq. (15) we have

$$V_{lb} \left(H_l - \frac{k}{H_l} + c_b^{\square} \right) - c_b^{\square} V = V_{la} \left(H_l - \frac{k}{H_l} - c_a^{\square} \right) + c_a V \tag{28}$$

where $c_b^{\square}$ and $c_a^{\square}$ are the basic and acidic titrant concentrations, respectively.

A similar relation may be derived from Eq. (16) for multicomponent systems.

Effect of tautomerism

Let t_i be the number of tautomers in the ionic state i of an ampholyte. The number of equilibria between these tautomers is $\binom{t_i}{2}$, but only $t_i - 1$ are independent. Since the state with $i = 0$ means the total absence of mobile protons, $t_0 = 1$.

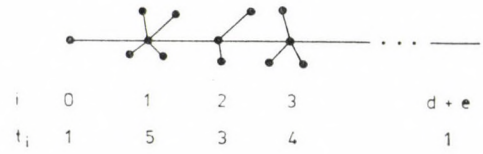


Fig. 1

Fig. 1. shows the graph arbour of the states it is an example. Branching points are arbitrarily selected from the possible t_i's and indexed by one.

Tautometric equilibrium constants are defined as

$$R_{is} = \frac{c_{is}}{c_{i1}} \qquad s = 1, 2, \ldots, t_i \tag{29}$$

where c_{is} is the concentration of the s-th tautomer belonging to the i-th ionization state. Of course $R_{i1} = 1$. According to Eq. (29) the total concentration of tautomers belonging to state i is

$$c_i = c_{i1} \sum_{s=1}^{t_i} R_{is} \tag{30}$$

Ionization constants for the equilibria between the stressed tautomers are

$$K_i' = \frac{c_{i-1,1} H}{c_{i1}} \tag{31}$$

Eq. (31) is the analogue of Eq. (2). Since

$$K_i' = \frac{c_0 H}{c_{11}}$$

similarly to Eq. (5)

$$c_{i1} = c_0 \beta_i H^i \tag{32}$$

with the modified total protonation constant

$$\beta_i' = \frac{1}{\prod_{r=i}^{t} K_r'} \tag{33}$$

Applying Eq. (8) and denoting

$$R_i = \sum_{s=1}^{t_i} R_{is}$$

we have

$$c^* = c_0 \sum_{i=0}^{d+e} H^i \beta_i' R_i \tag{34}$$

Introducing new constants for the virtual total protonation

$$D_i = \beta_i' R_i \tag{35}$$

Equation (34) may be expressed in a shorter form

$$c^* = c_0 \sum_{i=0}^{d+e} D_i H^i$$

Substituting this expression into Eq. (32) and applying Eq. (30)

$$c_i = c^* \frac{D_i H^i}{\sum_{i=0}^{d+e} D_i H^i} \tag{36}$$

which is the total analogue of Eq. (10). The D_i constants replace the total protonation ones. Adopting the method described in Part 1. the final relation for the concentration determination has the form of

$$\sum_{j=1}^{n} c_j^* \frac{\sum_{i=0}^{d_j+e_j} (i-e_j) D_{ij} H_l^i}{\sum_{i=0}^{d_j+e_j} D_{ij} H_l^i} + \frac{V_l}{V}\left(H_l - \frac{k}{H_l}\right) \pm c^{\square} \frac{V_l - V}{V} = 0 \tag{37}$$

All other relations of the former Parts are valid in the presence of tautomers, too, replacing β's by D's.

Virtual total protonation constants, for example, may be calculated similarly to Eq. (24) based on the relation

$$\sum_{i=0}^{d+e} D_i H_l^i \left[(i-e)\, c^* - \frac{V_l}{V}\left(\frac{k}{H_l} - H_l\right) \pm c^{\square} \frac{V_l - V}{V}\right] =$$

$$= \frac{V_l}{V}\left(\frac{k}{H_l} - H_l\right) \mp c^{\square} \frac{V_l - V}{V} + e c^* \tag{38}$$

The ratio of two virtual total protonation constants gives the virtual ionization constant

$$\varkappa_i = \frac{D_{i-1}}{D_i} .$$

These constants have a hardly interpretable physical meaning, they are defined namely as

$$\varkappa_i = K'_i \frac{\sum_{s=1}^{t_i-1} R_{i-1,s}}{\sum_{s=1}^{t_i} R_{is}}$$

Discussion and broader aspects

The outlined theory is easily applicable in the practice of potentiometric titration. Programming in BASIC and practical applications are in progress. Relations (16), (18), (20) and (22) enable one to determine the concentrations in multicomponent systems without tautomerism. When tautomerism also occurs the method of data processing is identical, since Eq. (37) is a full analogue of Eq. (16). The last two equations contain total protonation constants. They are determinable together with the ionization constants from Eqs. (24) and (38), respectively. Eqs. (24)—(27) can be used for those calculations.

All these developed formulae can be easily programmed in Basic or Assembler languages, which are the most frequented ones for mini- and microcomputers. If the titration is computer controlled the data processing can be carried out directly by the controller.

To make data processing easier it is worthwhile to convert the acidic titration data of ampholytes into those of the basic titration ones or vice versa see Eq. (28).

The unit values of activity coefficients cannot be maintained in practice. This is only a more or less acceptable approximation, similarly to the assumption of their constancy during the titration. There is, however, a possible solution to the problem of the activity coefficients by keeping the ionic strength constant. At a high concentration of a neutral component (aid component) it becomes nearly constant. For example, in aqueous solutions this requirement is fulfilled by a higher KCl concentration. Adding always the same aid component in the same concentration to the titrate in the case of determinations of both concentrations and ionization constants, the accuracy of the concentration values increases.

Virtual total protonation constants include both tautomeric equilibrium constants and ionization ones. The independent determination of the β_i' constants allows the determination of the K_i' values [see Eqs (33) and (35)]. If there exists a pH value where the forms of the i-th ionization state build the bulk of all possible forms of the compound in question, the temperature dependence of the spectra serves for distinguishing the spectra of the individual species.

Applying an on-line mini- or microcomputer for the control and data acquisition in the titration process the accuracy of the measurements increases. Namely, by reproduction and data accumulation signal-to-noise ratio and digital resolution improve.

Errors may be determined by recalculating the titration data from the results and by determining the mean square deviation of measured and calculated values.

The pH range of potentiometric measurements is limited by electrodes and titrants. Normally the measurements in water are carried out between pH 1 and 13. It is possible that pK_a values beyond this region are unknown. In this case Eq. (9), is only an approximation and becomes better and better departing from the pH equal to the pK_a in question.

Since protonation equilibria [Eq. (1)] are temperature dependent all the relations derived here hold exactly only under isothermic circumstances. Temperature dependency of pK_a values is of the magnitude of 10^{-2}—10^{-3} pK_a units/Kelvin [13].

List of applied symbols

A: constant in application of the method of least squares
B: constant in application of the method of least squares
D: virtual total protonation constant
F: function to be minimized
G: constant in application of the method of least squares
H: proton concentration
K: acidic equilibrium constant of protonation ionization constant
K': acidic equilibrium constant for protonic equilibrium between tautomers
P: constant in application of the method of least squares
R: tautomeric equilibrium constant
V: titrant volume, without low index: that before the beginning of titration
a: constant in application of the method of least squares
b: constant in application of the method of least squares
c: concentrations excluding that of protons
c': total ampholyte concentration in the titrate, without low index: that before the beginning of titration

$c_1^{\square}$: concentration of the reagent in the titrant
d: basicity of the ampholyte
e: acidity of the ampholyte
g: constant in application of the method of least squares
i: number of mobile protons in the ion or molecule in question
j: serial number of the component in question
k: ion product
l: serial number of added titrant portions
m: total number of added titrant portions
n: number of components
p: constant in application of the method of least squares
s: serial number of the tautomer in question low index
t: number of tautomers
v_1: total volume of added titrant after adding the 1-th portion
β: total protonation constant
β': total protonation constant for protonic equilibria between individual tautomers
γ: weight factor
$\varkappa$: virtual ionization constant

REFERENCES

[1] Ebel, S.: Arch. Pharm., **302,** 856 (1969)
[2] Barry, D. M., Meite, L.: Anal. Chim. Acta, **68,** 435 (1974)
[3] Bates, R. G.: Chem. Non-Aqueous Solvents, **1,** 292 (1966)
[4] Ebel, S., Kroemmelbein, R.: Fresenius' Z. Anal. Chem., **256,** 31 (1971)
[5] Ebel, S., Senning, A.: Angew. Chemie, **89,** 129 (1977)
[6] Mikhailova, D., Chobanova, I.: Probl. Farm., **5,** 93 (1977)
[7] Mosó, I., Seybold, K., Károlyi, L.: Magy. Kém. Lapja, **34,** 394 (1979)
[8] Ben-Yaakov, S., Raviv, R., Guterman, H., Dayan, A., Lazar, B.: Talanta, **29,** 267 (1982)
[9] Garcia, M.-L., Ramis, G., Mongay, C.: Talanta, **29,** 435 (1982)
[10] Zuberbuhler, A. D., Kaden, T. A.: Talanta, **29,** 201 (1982)
[11] Gaizer, F., Puskás, A.: Talanta, **28,** 565 (1981)
[12] Minker, E., Vass, I., Tomka A., Marek, N.: Acta Pharm. Hung., **47,** 90 (1977)
[13] Albert, A., Serjeant, E. P.: The Determination of Ionization Constants, Chapman and Hall, London 1977

Acta Chimica Hungarica 123 (1—2), pp. 15—29 (1986)

AMINOPHTHALAZINONE DERIVATIVES, XI*. CHEMICAL PROPERTIES OF IMIDAZO- AND PYRIMIDO[2,1*a*]PHTHALAZINONE SYSTEMS, III

FORMATION OF A NEW TRIAZAINDENOINDENE SKELETON FROM PYRIMIDOPHTHALAZINONE DERIVATIVES

Károly KÖRMENDY[1]**, Alajos KÁLMÁN[2], Tibor KORITSÁNSZKY[2], István KÖVESDI[1], Pál SOHÁR[3] and Ferenc RUFF[1]

([1] Department of Organic Chemistry, Eötvös Loránd University, H-1088 Budapest, Múzeum krt. 4/b, [2]Central Research Institute of Chemistry, Hungarian Academy of Sciences, H-1525 Budapest, P.O. Box 17. [3]EGIS Pharmaceuticals, Spectroscopic Department, H-1475 Budapest, P.O. Box 100)

Received June 10, 1985
Accepted for publication November 6, 1985

Heterocyclic compounds with the new triazaindenoindene skeleton (**10**, **12**—**16**) have been synthesized by the reactions of pyrimido[2,1-*a*]phthalazinone (**1**), or its derivatives substituted in the benzene ring (**2**, **3**), with acetic or propionic anhydride. The structures were elucidated by preparative and spectroscopic (IR, ^{1}H-NMR, ^{13}C-NMR and X-ray diffraction) methods. The hypothesis suggested as the reaction mechanism of the formation of this skeleton is based on the high reactivity of the zwitter-ionic starting compound to undergo addition reactions.

The isolated main product from the reaction of pyrimido[2,1-*a*]phthalazinone (**1**) with acetic anhydride was a compound of unknown structure; its molecular formula was shown to be $C_{15}H_{15}N_3O_3$ by elementary analysis and mass spectrometry [1]. In this paper the elucidation of the structure of this product is discussed; further, by considering other models, the scope of the reaction is studied. The models selected (**2**, **3**) are derivatives of **1** substituted in the benzene ring, which allow a study of the effect of electron-donating or electron-withdrawing groups on the reactivity of the zwitter-ionic pyrimidopyridazinium-olate part of the molecule.

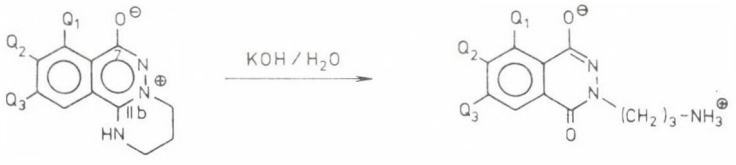
The 9,10-dimethoxy derivative (**2**) was prepared by cyclization of 4-(3-hydroxypropylamino)-6,7-dimethoxy-1(2*H*)-phthalazinone [2] (Fig. 1); the 8-nitro compound (**3**) was synthesized by the reaction sequence **7** → **8** → → **9a** → **3** (Fig. 2), which is a well proved method for the preparation of similar derivatives from 3-bromopropyl-3-nitrophthalimide [3, 4]. (Two isomers, **9a** = 8-NO_2 and **9b** = 5-NO_2, could be formed from the asymmetric nitrophthalimide **8**. The product isolated had structure **9a**, as it will be reported [5] in a next paper of this series. The practically exclusive reactivity with nucleophiles of the imide bond in α-position of 3-nitrophthalimide is in accord

* Part X: Acta Chim. Hung., **117**, 371 (1984).
** To whom correspondence should be addressed.

with the alcoholysis of 3-nitrophthalic anhydride which yields the α-ester as the main product [6].)

The pyrimidine ring of compounds **1**—**3** is readily cleaved by potassium hydroxide solution to give compounds **4**—**6** (cf. Fig. 1). These derivatives were required because in the reaction of **1** with acetic anhydride ring fission to a slight extent was observed (see Fig. 6; **17** [1]), thus the cleavage of the pyrimidine ring could also be expected during the acetolysis of **2** and **3**.

The molecular mass of **10** formed in the reaction of **1** with acetic anhydride (Fig. 3) increases by 84.07 = $C_4H_4O_2$, as compared with the starting compound; this corresponds to the incorporation of two acetyl groups and the



	Q_1	Q_2	Q_3	
1	H	H	H	4
2	H	MeO	MeO	5
3	NO_2	H	H	6

Fig. 1

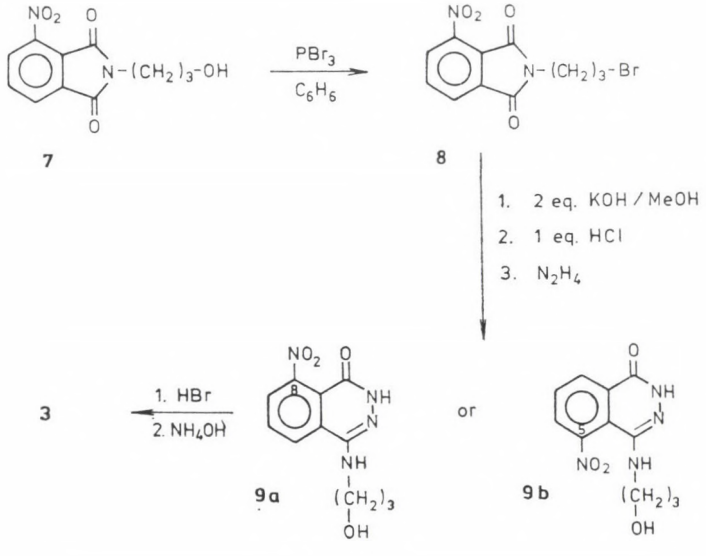


Fig. 2

loss of two hydrogen atoms. According to mass spectrometry the primary principal fragmentation is the loss of ketene, which indicates the presence of a readily detachable acetyl group. Compound **10** remains unchanged in boiling ethanol, but refluxing in sodium hydrogen carbonate solution removes one acetyl group from the molecule (**10** → **11**). With acetic anhydride in pyridine the original compound is recovered (**11** → **10**). There is no unsatura-

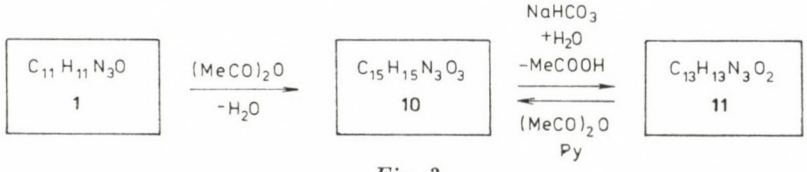


Fig. 3

tion in compound **10**, which should undergo hydrogenation in the presence of Pd/C or PtO_2 catalyst at room temperature and under atmospheric pressure. The infrared spectrum recorded in KBr pellets (Table I) has no band attributable to an NH group; the three carbonyl bands at 1758, 1724 and 1702 cm^{-1} are due to the diacylamide and the amide carbonyl groups in the five-membered ring. In the deacetylated product (**11**) the signal due to amide-NH appears at 3200 cm^{-1}, and the amide I band characteristic of the five-membered ring is found at 1695 cm^{-1}.

No unequivocal conclusion for the structure of **10** could be drawn from the results of the preparative, ^1H- and ^{13}C-NMR, or IR spectral studies; therefore, determination of structure was complemented by X-ray diffraction measurements, which showed compound **10** to have triazaindenoindene skeleton.

Table I

Important bands in the IR *spectra of the triazaindenoindene derivatives* **10**—**16** (in KBr), cm^{-1}

Compound	νNH	νCO diacylamide, isoindolinone	Amide I	νOCH_3	$\nu(C—O—CH_3)$	νNO_2
10		1758, 1724, 1702				
11	3200		1695 (five-membered ring)			
12		1742, 1733, 1707				
13		1748, 1708		2835	1210	
14		1746, 1711		2840	1210	
15		1757, 1713				1538, 1372
16		1748, 1710				1540, 1379

Discussion of the crystal structure of compound 10

A perspective view of the molecular structure of **10** is given in Fig. 4, computed from the final fractional coordinates, which are given with their e.s.d.'s in Tables II and III. The majority of the atomic distances (Table IV) and bond angles (Table V) does not exhibit significant deviations from the expected values. The five-membered hetero-ring *B* of the isoindolinone moiety is not perfectly planar (the mean deviation of the least-squares plane of the five ring atoms is 2.4 pm) and O(1) is out of the plane by 11.8 pm. Nevertheless its best plane makes only a dihedral angle of 2.7(1)° with that of the phenyl *A* ring. Despite the vicinal oxo group separated by a multiple bond [136.4(2) pm], N(6a) at the *B*/*C* ring junction retains some pyramidality ($\lambda_N = 0.36$ rad) [7]. In accordance with the diminished pyramidality of N(6a), ring *C* possessing chair conformation is pseudo-*cis* anellated to ring *B* as shown by the same signs of the endocyclic torsion angles at the junction [6.1(2)° for ring *B* and 48.1(2)° for ring *C*] and the near to zero value of one of them. N(3a) is oriented *pseudoaxially* to ring *B*, whereas C(6) occupies *equatorial* position (see the corresponding torsion angles in Table VI). Rings *C*

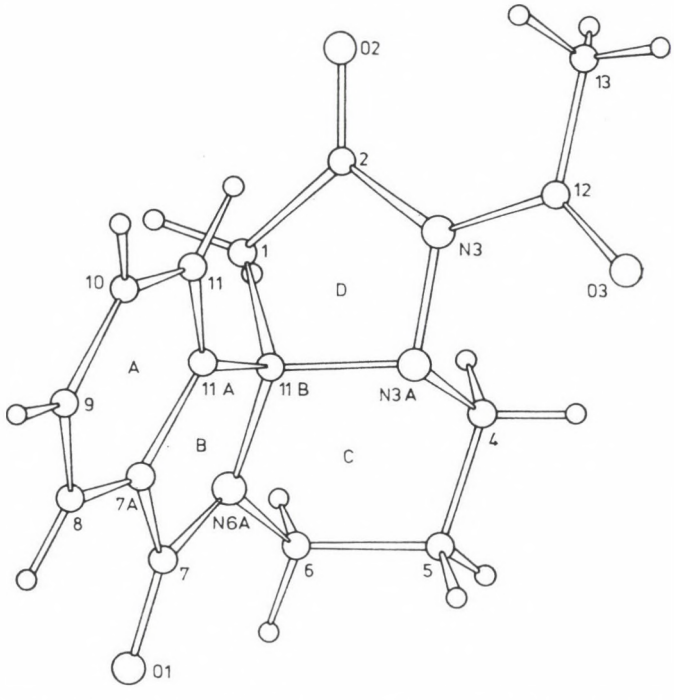


Fig. 4. A perspective view of the molecular geometry of compound 10 with atomic and ring labelling. The bare numbers are for carbon atoms, unless indicated otherwise. The H atoms are shown but not labelled

Table II

Fractional coordinates (10^5 for the x-coordinates of the hetero atoms and 10^4 for the other coordinates) *of* **10** *and equivalent isotropic thermal parameters* (10^{-4} pm^2) *for the non-hydrogen atoms*

Atom	x/a	y/b	z/c	B(eq)
O(1)	10555.5(8)	6383(1)	1658(1)	4.79(4)
O(2)	63169(9)	2717(1)	−62(1)	5.81(5)
O(3)	60874(9)	5500(1)	3032(1)	5.13(5)
N(3)	68357(9)	4302(1)	1582(1)	3.65(4)
N(3a)	77272(8)	4872(1)	2170(1)	3.25(4)
N(6a)	93201(8)	4796(1)	1615(1)	3.59(4)
C(1)	7983(1)	3320(2)	431(1)	4.08(6)
C(2)	6950(1)	3342(1)	575(1)	4.08(6)
C(4)	8045(1)	3947(2)	3300(1)	3.97(6)
C(5)	9069(1)	4244(2)	3797(1)	4.36(6)
C(6)	9685(1)	3962(2)	2745(1)	4.29(6)
C(7)	9751(1)	6011(1)	1254(1)	3.59(5)
C(7a)	9062(1)	6747(1)	307(1)	3.51(5)
C(8)	9167(1)	7976(2)	−400(1)	4.56(6)
C(9)	8399(1)	8428(2)	−1237(1)	5.30(7)
C(10)	7563(1)	7669(2)	−1362(1)	5.29(7)
C(11)	7465(1)	6439(2)	−653(1)	4.44(6)
C(11a)	8220(1)	5999(1)	205(1)	3.37(5)
C(11b)	8329(1)	4713(1)	1090(1)	3.31(5)
C(12)	6025(1)	4693(1)	2123(1)	3.98(5)
C(13)	5101(1)	4069(2)	1567(2)	5.95(8)

$B_{eq} = 4/3^*$ trace (B*G) where G is the direct metric tensor

Table III

Fractional coordinates (10^3) *for the hydrogen atoms of* **10** *with isotropic temperature factor* B_i (10^{-4} pm^2)

Atom	x/a	y/b	z/c	B
H(8)	977(1)	850(2)	−31(1)	5.7(4)
H(9)	843(1)	931(2)	−172(1)	6.3(4)
H(10)	705(1)	800(2)	−194(1)	7.0(4)
H(11)	807(1)	332(1)	−51(1)	5.4(3)
H(12)	829(1)	252(2)	88(1)	5.7(4)
H(41)	797(1)	291(1)	309(1)	5.0(3)
H(42)	764(1)	416(1)	395(1)	4.8(3)
H(51)	925(1)	360(2)	454(1)	6.3(4)
H(52)	914(1)	524(1)	408(1)	5.1(4)
H(61)	969(1)	293(1)	249(1)	4.9(3)
H(62)	1033(1)	426(1)	297(1)	5.1(4)
H(111)	688(1)	587(1)	−74(1)	5.1(3)
H(131)	464(1)	442(2)	202(2)	10.1(6)
H(132)	497(1)	425(2)	68(1)	9.8(6)
H(133)	512(1)	308(2)	164(2)	9.5(6)

Table IV

Bond lengths (pm) *for* **10**. *E.s.d.'s are in parentheses*

O(1) —C(7)	122.0(2)	C(1) —C(11b)	152.6(3)
O(2) —C(2)	120.4(2)	C(4) —C(5)	151.0(2)
O(3) —C(12)	120.7(2)	C(5) —C(6)	150.8(2)
N(3) —N(3a)	144.1(2)	C(7) —C(7a)	147.5(2)
N(3) —C(2)	140.7(2)	C(7a) —C(8)	138.3(3)
N(3) —C(12)	139.2(2)	C(7a) —C(11a)	137.8(2)
N(3a)—C(4)	148.8(2)	C(8) —C(9)	138.0(3)
N(3a)—C(11b)	150.3(2)	C(9) —C(10)	137.6(3)
N(6a)—C(6)	145.6(2)	C(10) —C(11)	138.4(3)
N(6a)—C(7)	136.4(2)	C(11) —C(11a)	137.5(2)
N(6a)—C(11b)	145.1(2)	C(11a)—C(11b)	151.1(2)
C(1) —C(2)	149.5(2)	C(12) —C(13)	148.9(2)

Table V

Bond angles (°) *for* **10**. *E.s.d.'s are in parentheses*

N(3a)	—N(3)	—C(2)	112.2(2)	C(7)	—C(7a)	—C(8)	129.7(3)
N(3a)	—N(3)	—C(12)	117.3(2)	C(7)	—C(7a)	—C(11a)	108.4(2)
C(2)	—N(3)	—C(12)	130.3(2)	C(8)	—C(7a)	—C(11a)	121.9(3)
N(3)	—N(3a)	—C(4)	106.9(2)	C(7a)	—C(8)	—C(9)	117.6(3)
N(3)	—N(3a)	—C(11b)	101.3(2)	C(8)	—C(9)	—C(10)	120.7(3)
C(4)	—N(3a)	—C(11b)	113.0(2)	C(9)	—C(10)	—C(11)	121.2(3)
C(6)	—N(6a)	—C(7)	122.8(2)	C(10)	—C(11)	—C(11a)	118.4(3)
C(6)	—N(6a)	—C(11b)	120.8(2)	C(7a)	—C(11a)	—C(11)	120.0(3)
C(7)	—N(6a)	—C(11b)	112.8(2)	C(7a)	—C(11a)	—C(11b)	109.4(2)
C(2)	—C(1)	—C(11b)	102.1(2)	C(11)	—C(11a)	—C(11b)	130.5(3)
O(2)	—C(2)	—N(3)	125.2(3)	N(3a)	—C(11b)	—N(6a)	109.0(2)
O(2)	—C(2)	—C(1)	128.0(3)	N(3a)	—C(11b)	—C(1)	103.9(2)
N(3)	—C(2)	—C(1)	106.8(2)	N(3a)	—C(11b)	—C(11a)	110.8(2)
N(3a)	—C(4)	—C(5)	110.7(2)	N(6a)	—C(11b)	—C(1)	117.5(2)
C(4)	—C(5)	—C(6)	109.7(2)	N(6a)	—C(11b)	—C(11a)	102.2(2)
N(6a)	—C(6)	—C(5)	108.3(2)	C(1)	—C(11b)	—C(11a)	113.5(2)
O(1)	—C(7)	—N(6a)	125.1(3)	O(3)	—C(12)	—N(3)	119.8(3)
O(1)	—C(7)	—C(7a)	128.1(3)	O(3)	—C(12)	—C(13)	121.9(3)
N(6a)	—C(7)	—C(7a)	106.8(2)	N(3)	—C(12)	—C(13)	118.3(3)

and *D* are fused by a *cis*-junction along a slightly polarized [150.3(2) pm] C(sp^3)—N(sp^3) single bond. N(3a) has pronounced pyramidality ($\lambda_N = 1.15$ rad) while N(3), due to the two neighbouring oxo groups each bound with a multiple bond in the range 139—141 pm, exhibits an sp^2 hybrid state ($\lambda_N = 0.08$ rad). N(3) is bound *equatorially* to ring *C*, whereas C(1) assumes *axial* position to it (Table VI), ring *D* has envelope conformation with C(11b) on the flap. The corresponding puckering parameters [8]: $Q = 35.9(2)$ pm, $\varphi = 147.0(3)°$ and asymmetry factor [9] $fC_s = 1.9$ pm indicating a mirror plane bisecting C(11b). One of the three C=O distances at C(7) is somewhat longer than the others (122.0 vs. 120.6 pm) which may presumably be attributed to the neighbouring C(8) proton.

Table VI

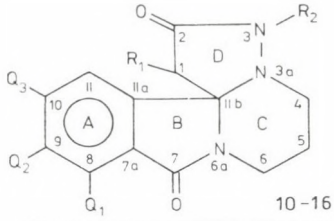
Relevant torsion angles (°) for **10** *E.s.d.'s are in parentheses*

RING *C*	
C(11b)—N(6a)—C(6)—C(5)	—52.2(3)
N(6a)—C(6)—C(5)—C(4)	54.4(2)
C(6)—C(5)—C(4)—N(3a)	—59.5(2)
C(5)—C(4)—N(3a)—C(11b)	56.5(2)
C(4)—N(3a)—C(11b)—N(6a)	—47.8(2)
N(3a)—C(11b)—N(6a)—C(6)	48.1(2)
RING *D*	
C(1)—C(2)—N(3)—N(3a)	—3.0(2)
C(2)—N(3)—N(3a)—C(11b)	24.6(2)
N(3)—N(3a)—C(11b)—C(1)	—35.7(2)
N(3c)—C(11b)—C(1)—C(2)	34.4(2)
C(11b)—C(1)—C(2)—N(3)	—19.7(2)
N(3a)—C(11b)—N(6a)—C(7)	—111.2(2)
N(3a)—C(11b)—C(11a)—C(7a)	112.8(2)
C(6)—N(6a)—C(7)—C(7a)	—165.4(3)
C(6)—N(6a)—C(11b)—C(11a)	165.4(3)
C(6)—N(6a)—C(7)—O(1)	14.7(3)
C(1)—C(11b)—N(3a)—C(4)	78.2(2)
C(1)—C(11b)—N(6a)—C(6)	—69.7(3)
N(3)—N(3a)—C(4)—C(5)	167.1(3)
N(3)—N(3a)—C(11b)—N(6a)	—161.7(2)
C(12)—N(3)—N(3a)—C(11b)	—159.3(3)
C(12)—N(3)—C(2)—C(1)	—178.5(3)

The indeno[3a,4-*a*]indene fundamental skeleton containing no nitrogen, an analogue of compound **10**, is not known; in the literature three other variants are mentioned, viz. the linear [1,2-*a*], [2,1-*a*] types condensed at the five-membered rings, and a type condensed in the [7,1-*cd*] way. Similar ring anellations are to be found in aspidospermidine alkaloids.

Triazaindenoindene compounds are formed also from models **2** and **3** (Fig. 5). The conversion **1** → **10** can be considered as completed after boiling for 3 hours (yield: 71 to 77%). A substantial formation of tar could not be suppressed by the addition of sodium acetate. As a by-product a small amount (9%) of **17** was isolated [1]. The formation of the dimethoxy derivative (**13**) is significantly slower; at least 10 hours of boiling are needed for complete conversion and also the yield is lower (59%). If the reaction is interrupted before completion, unchanged **2** can be isolated from the dark brown mother liquor, containing the tarry by-products.

No acylated product of type **17** indicating ring fission of compound **5** was detected. Reactions which proceed at two different rates were found in the conversion **3** → **15** (Fig. 6), which can be achieved with remarkably high yield (81—91%). About half of compound **3** is converted within 2 hours into the end-product by the more rapid reaction *A*, while the zwitter-ionic **18**



Reaction	Boiling, h	Product	Yield, %	R_1	R_2	Q_1	Q_2	Q_3
1 + *a*	3	**10**	70.8–77.1	H	MeCO	H	H	H
10 + *c*	10 min.	**11**	51.4	H	H	H	H	H
1 + *b*	3	**12**	59.2	Me	EtCO	H	H	H
2 + *a*	10	**13**	59.1	H	MeCO	H	MeO	MeO
2 + *b*	10	**14**	49.6	Me	EtCO	H	MeO	MeO
3 + *a*	10	**15**	80.6	H	MeCO	NO_2	H	H
18 + *a*	10	**15**	90.9					
3 + *b*	10	**16**	53.9	Me	EtCO	NO_2	H	H

Fig. 5. **Synthesis of triazaindenoindene derivatives (Reagent: a = acetic anhydride, b = propionic anhydride, c = 10% $NaHCO_3$ solution)**

Table VII

***^{1}H and ^{13}C chemical shifts of compound* 10**

^{1}H	δ	^{13}C	δ
H—5 *(a, e)*	~ 1.9 (m)	C—5	25.3
H—1 *(syn)*	2.68 (d)*	C—(R_1, CH_3)	26.0
H—1 *(anti)*	3.70 (d)*	C—1	36.4 **
H—4 *(a)*	~ 3.00 (m)	C—4	36.8 **
H—4 *(e)*	3.75 (m)	C—6	53.1
H—6 *(a)*	~ 3.00 (m)	C—11b	78.8
H—6 *(e)*	4.55 (m)	C—8	131.5
H—8	7.85 (m)	C—9	124.9
H—9	~ 7.55 (m)	C—10	134.7
H—10		C—11	122.3
H—11	7.35 (m)	C—7a	131.1
H—(R_1, CH_3)	2.68 (s)	C—11a	148.6
		C—2	167.45 **
		C—7	167.50 **
		C—(R_1, C=O)	173.6

* Based on DNOE tests
** Assignments interchangeable

formed in the side-reaction *B* gives, with acetic anhydride, compound **15** at a much slower rate. Derivatives **12**, **14** and **16** containing a methyl group at position 1 are formed in analogous processes with propionic anhydride.

The signals due to the *equatorial* and *axial* hydrogens of the methylene group vicinal to the nitrogen of the six-membered ring *C* are well separated (Table VII) in the ^{1}H-NMR spectra at 250 MHz of the triazaindenoindene derivatives **10** and **12**. The chemical shifts and spin-spin coupling constants are in accord with the chair conformation, stabilized at room temperature, of the six-membered ring. The diastereotopic geminal protons in ring *D* of compound **10** form an AX spin system with a coupling constant of 21.3 Hz. The assignment of the signals is based on DNOE experiments in the course of which, when the doublet at 3.7 ppm is irradiated, the signals of the two *axial* hydrogens in the N—CH_2 group of ring *C* become more intensive. This observation supports the "*anti*" position to the benzene ring *A*, of the hydrogen with chemical shift 3.7 ppm. The steric position of the methyl group R_1 in

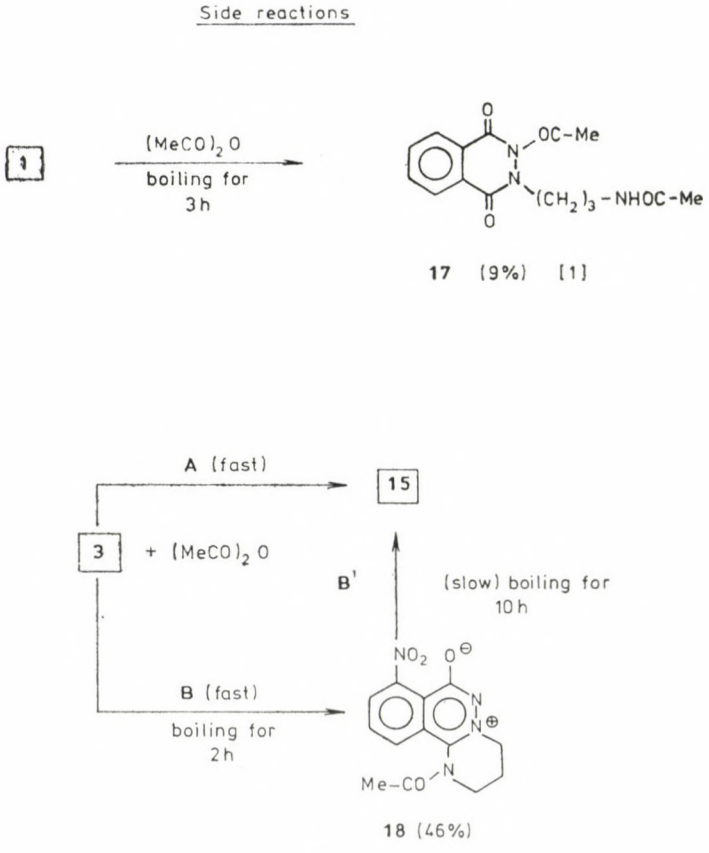


Fig. 6

Table VIII

^1H and ^{13}C chemical shifts of compound **12**

^1H	δ	^{13}C	δ
H—5 (*a*, *e*)	~1.85 (m)	C— (R_1,R_2,CH_3)	8.3***
H—1	3.66 (q)*	C—5	24.0
H— (R_2,CH_3) (*syn*)	0.85 (d)*	C— (R_1,CH_2)	30.3
H—4 (*a*)	~3.00 (m)	C—1	35.5 } **
H—4 (*e*)	3.80 (m)	C—4	37.6 } **
H—6 (*a*)	~3.00 (m)	C—6	51.4
H—6 (*e*)	4.55 (m)	C—11b	81.4
H—8	7.90 (m)	C—8	130.0
H—9 }	~7.55 (m)	C—9	124.4
H—10 }		C—10	131.3
H—11	7.20 (m)	C—11	121.4
H— (R_1,CH_3)	1.25 (t)	C—7a	132.4
H— (R_1,CH_2)	~3.00 (q)	C—11a	143.6
		C—2	170.7
		C—7	166.9
		C— (R_1,C=O)	173.7

* Based on DNOE tests
** Assignments interchangeable
*** Overlapping signals

compound **12** referred to the *axial* hydrogens of ring *C* was also determined by means of DNOE experiments (Table VIII). Irradiation of the methyne quartet at 3.66 ppm intensifies the signals of the two *axial* hydrogens of the N—CH_2-group: this supports the "*syn*" position relative to the aromatic ring *A*, of the methyl group, as expected for steric reasons.

In sum, it may be stated that the formation of triazaindenoindene derivatives is promoted by the electron-withdrawing substituent (NO_2) of the benzene ring, whereas the electron-donating substituent (MeO) has a slight hindering effect. In the latter case diminished reactivity is shown by the fact that the unchanged methoxy compound **2** is detectable in the reaction mixture even after refluxing for 10 hours. The increase of reaction time in the conversion **3** → **15** is due to the side-reaction leading to the formation of substantial amounts of **18**, which has low reactivity.

In the knowledge of the structure of the tetracycle it is obvious that not only acylation reactions occur, but the anhydride, by means of its loose hydrogen in α-position, is bound by 11b-7' addition to the C(11b) atom of the zwitter-ionic initial compounds (**1**—**3**). (Rowe et al. [10, 11] described similar 1,5-addition reactions in the case of several zwitter-ionic phthalazone derivatives.) At present, concerning this rather complicated reaction mechanism (Fig. 7) one may suggest that addition must be the initial step of the process, since the non-zwitter-ionic 6-methylpyrimidophthalazone reacts in a different way: treatment with acetic anhydride results in C(11b)=N(1) → C(3)=C(4)

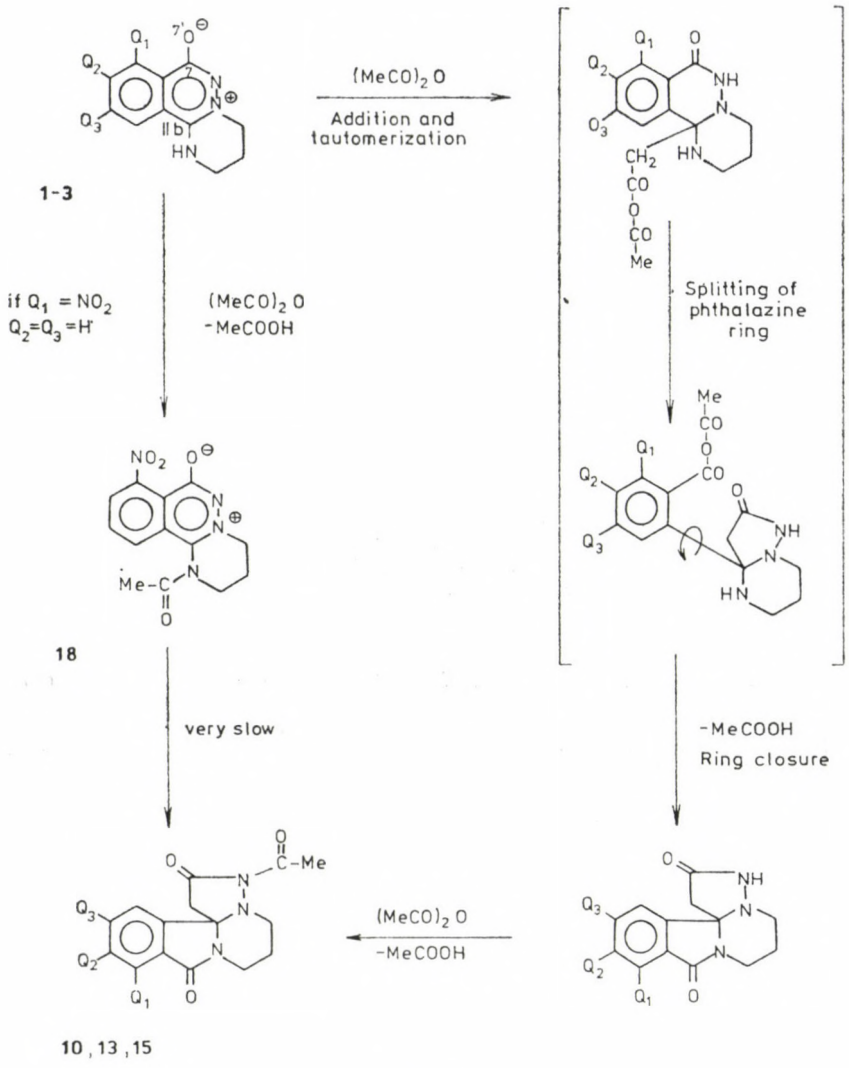


Fig. 7

isomerization [1]. Addition is followed by the fission of the phthalazine ring and the formation of the azaindenone rings. In the conversion an important role may be played by the intramolecular anhydride groups (the intramolecular acylation of N(6) by the anhydride attached to the C(11b) atom may also take place through the strainless bridged ring system), however, considering the great excess of acetic anhydride present, participation of the external anhydride groups cannot be excluded.

This statement is based on the formation of the acetyl derivative **18** appearing in the reaction **3** → **15**. This process is not hindered by this inter-

mediate of reduced reactivity, but the overall rate is significantly affected. Undoubtedly, one cause of the deactivating effect is steric hindrance (addition being impeded), but acetylation of the pyrimidine NH group may also be a retarding factor, since the transacylation reaction leading to the final product may not be a rapid process in the given medium.

Experimental

M.p.'s were measured with a Boetius apparatus. The IR spectra were recorded in KBr pellets with a Zeiss Specord 75 spectrophotometer. The ^{1}H-NMR spectra at 250 MHz and the ^{13}C-NMR spectra at 62.9 MHz were recorded with a Bruker WM-250 spectrometer.

7-Hydroxy-9,10-dimethoxy-1,2,3,4-tetrahydropyrimido[2,1-*a*] phthalazin-5-ium bromide (2. HBr)

A mixture of azeotropic hydrobromic acid (15 mL) and 4-(3-hydroxypropylamino)6,7-dimethoxy-1(2*H*)-phthalazinone [2] (2.79; 0.01 mol) was boiled for 10 min. The mixture, which crystallized to a mass while still hot, was allowed to cool, suspended in ethanol, and filtered off. Yield: 3.18 g (93%) of colourless needles (from water), m.p. 251—253 °C.

$C_{13}H_{16}BrN_3O_3$ (342.2). Calcd. Br 23.4. Found Br 23.2%.

IR (KBr): νOH 3380, νNH$^{\oplus}$ 3300—2600, νC=N 1580, νC—O—C 1221 cm^{-1}.

9,10-Dimethoxy-1,2,3,4-tetrahydropyrimido[2,1-*a*]phthalazin-5-ium-7-olate (2)

The product, which separated from a hot aqueous solution of **2**. HBr with ammonium hydroxide, crystallized as colourless needles from a dilute hot solution of water. M.p. (with sublimation) 253—256 °C.

$C_{13}H_{15}N_3O_3$ (261.3). Calcd. CH_3O 23.8; N 16.1. Found CH_3O 23.5; N 16.2%.

IR (KBr): νNH 3500—2500, νC=N, νCO 1568, 1515, νC—O—C 1214 cm^{-1}.

2-(3-Ammoniumpropyl)-6,7-dimethoxy-2*H*-phthalazin-1-one-4-olate (5)

Compound **2** (0.522 g; 2 mmol) was dissolved in hot 10% KOH (10 mL). After boiling for 1 h, the cooled solution was adjusted to pH 7—8, to give 0.43 g (77.1%) of the product, which was sparely soluble in hot water. For purification the crude product was dissolved in hot, dilute KOH solution and re-precipitated, after filtration, at pH 7—8 to obtain a colourless powder, m.p. 271—273 °C (with decomposition).

$C_{13}H_{17}N_3O_4$ (279.3). Calcd. N 15.0. Found N 15.1%.

IR (KBr): $\nu NH_3^{\oplus}$ 3250—2250, amide I, νC=N 1613, 1564, νC—O—C 1218 cm^{-1}.

3-Bromopropyl-3-nitrophthalimide (8)

To a suspension in chloroform (30 mL) of 3-nitrophthalic anhydride (19.3 g; 0.1 mol) placed into a flask equipped with a reflux condenser and a dropping funnel, a solution of 3-aminopropanol (7.1 g; 0.1 mol) in chloroform (20 mL) was added. After refluxing for a short time, the solvent was evaporated and the residue was fused in an open flask for 1 h in a bath of 160—180 °C. The fused mass was dissolved in hot benzene (150 mL) and phosphorus tribromide (6.4 mL) was added dropwise; the mixture was then boiled, with frequent shaking, until the evolution of hydrogen bromide had ceased (about 30 min). Decomposition by pouring onto ice was followed by evaporation of the benzene. The residual yellow suspension was filtered. Recrystallization from methanol gave light yellow crystals (26 g; 83%), m.p. 111—112 °C.

$C_{11}H_9BrN_2O_4$ (313.1). Calcd. Br 25.5. Found Br 25.3%.

IR (KBr): νCO 1771, 1710, νNO_2 1553, 1364 cm^{-1}.

4-(3-Hydroxypropylamino)-8-nitro-1(2*H*)-phthalazinone (9a)

The bromo compound **8** (31.3 g; 0.1 mol) was refluxed for 30 min in a solution of potassium hydroxide (13.4 g) in methanol (500 mL). After cooling in ice-water, the solution was slightly acidified with *conc.* hydrochloric acid, then 15 mL of 99% hydrazine hydrate was added and the mixture was refluxed for further 60 min. This mixture was diluted with water and the methanol evaporated; the resulting suspension was neutralized with hydrochloric acid, and the crystals which separated were filtered off to yield 11.39 (43.1%) of the product. Yellow crystals from a mixture of dimethylformamide and ethanol, m.p. 211—212 °C.

$C_{11}H_{12}N_4O_4$ (264.3). Calcd. N 21.2. Found N 21.1%.

IR (KBr): νOH, νNH 3320, amide I 1655, νNO_2 1537, 1335, νC—O 995 cm^{-1}.

8-Nitro-1,2,3,4-tetrahydropyrimido[2,1-*a*]phthalazin-5-ium-7-olate (3)

Compound **9a** (5.28 g; 0.02 mol) was dissolved in 48% hydrobromic acid (20 mL) and the mixture was refluxed for 15 min. The residue of evaporation under reduced pressure was taken up in hot water and made alkaline with conc. ammonium hydroxide. The base separated in the form of a yellow powder (4.81 g; 97.8%). It was insoluble in common solvents, but could be recrystallized from a large amount of dimethylsulfoxide. M.p. above 360 °C.

$C_{11}H_{10}N_4O_3$ (246.2). Calcd. N 22.8. Found N 22.8%.

IR (KBr): νNH 3300—2100, νC=N, νCO 1578, 1553, νNO_2 1528, 1362 cm^{-1}.

2-(3-Ammoniumpropyl)-2*H*-5-nitro-phthalazin-1-one-4-olate (6)

Compound **3** (0.492 g; 2 mmol) was dissolved in 10% potassium hydroxide solution (10 mL). After boiling for 30 min, the solution was cooled and adjusted to pH 7—8. The product which separated (0.47 g; 89%) crystallized from water as ochre-yellow elongated plates; m.p. 257—260 °C (evolution of gas).

$C_{11}H_{12}N_4O_4$ (264.3). Calcd. N 21.2. Found N 21.4%.

IR (KBr): $\nu NH_3^{\oplus}$ 3300—2200, νCO, νC=N 1567, νNO_2 1525, 1378 cm^{-1}.

Triazaindenoindene derivatives

3-Acetyl-5,6-dihydro-1*H*,4*H*,7*H*-3,3a,6a-triazaindeno[3a,4-*a*]indene-2(3*H*),7-dione (10)

Pyrimidophthalazinone (**1**) (11.85 g; 0.05 mol) in boiling acetic anhydride (80 mL) gave a rapidly coloured solution. After refluxing for 3 h, the dark brown solution was evaporated under reduced pressure and the crystalline residue suspended in water. After standing for 30 min, this suspension was evaporated to dryness in vacuum. In order to remove the bulk of the tarry by-products, the dry residue was suspended in a 7 : 3 mixture of water and methanol, and poured onto a glass filter where it was thoroughly washed with aqueous methanol. Recrystallization from ethanol in the presence of activated carbon gave well developed columnar crystals (10.1—11.0 g; 70.8—77.1%), m.p. 208—209 °C; it crystallized and melted again at 212—212.5 °C.

$C_{15}H_{15}N_3O_3$ (285.11, as determined by mass spectrometry [1]). For data of elemental analysis, see [1].

IR (KBr): cf. Table I.

^{1}H- and ^{13}C-NMR, cf. Table VII.

5,6-Dihydro-1*H*,4*H*,7*H*-3,3a,6a-triazaindeno[3a,4-*a*]indene-2(3*H*),7-dione (11)

In 20 mL of a 10% aqueous sodium hydrogen carbonate solution, the finely powdered acetyl derivative **10** (1.14 g; 4 mmol) was refluxed, with stirring. Within a few minutes a solution formed, with the evolution of carbon dioxide. Rapid cooling precipitated a hydrate (m.p. 102—105 °C), which lost water over P_2O_5 in vacuum at 78 °C to give a colourless powder (0.50 g; 51.4%), m.p. 173—174 °C. The product could be recrystallized from water.

$C_{13}H_{13}N_3O_2$ (243.3). Calcd. C 64.2; H 5.4; N 17.3. Found C 64.3; H 5.5; N 17.4%.

IR (KBr): cf. Table I.

1-Methyl-3-propionyl-5,6-dihydro-1*H*,4*H*,7*H*-3,3a,6a-triazaindeno[3a,4-*a*] indene-2(3*H*),7-dione (12)

A mixture of propionic anhydride (30 mL) and 4.74 g (0.02 mol) of **1** was refluxed for 3 h to give a dark brown solution. This was evaporated to dryness under reduced pressure (bath temperature 80 °C), and the solid residue was suspended in a 1 : 1 mixture of water and ethanol, and filtered off. Recrystallization from ethanol in the presence of decolourizing carbon gave 3.71 g (59.2%) of a colourless compound. Needles separated first from the solution, which disintegrated on standing to a salt-like powder, m.p. 201—202 °C.

$C_{17}H_{19}N_3O_3$ (313.4). Calcd. C 65.1; H 6.1; N 13.4. Found C 65.0; H 6.1; N 13.5%.

IR (KBr): cf. Table I.

^{1}H- and ^{13}C-NMR: cf. Table VIII.

3-Acetyl-9,10-dimethoxy-5,6-dihydro-1*H*,4*H*,7*H*-3,3a,6a-triazaindeno[3a,4-*a*] indene-2(3*H*),7-dione (13)

A solution of **2** (2.61 g; 0.01 mol) in acetic anhydride (20 mL) was refluxed for 10 h and then evaporated under reduced pressure. The solid residue was suspended in water, allowed to stand for a short time, and then filtered off. The brownish crude product was extracted with chloroform (the small amount of undissolved substance was unchanged **2**), and the extract was treated in hot ethanolic solution with active carbon. Colourless plates from ethanol or from chloroform-petroleum ether mixture (2.04 g; 59.1%); m.p. 245—247 °C.

$C_{17}H_{19}N_3O_5$ (345.4). Calcd. C 51.1; H 5.5.; N 12.2. Found C 51.1; H 5.4; N 12.4%.

IR (KBr): cf. Table I.

1-Methyl-3-propionyl-9,10-dimethoxy-5,6-dihydro-1*H*,4*H*,7*H*-3,3a,6a-triazaindeno [3a,4-*a*]indene-2(3*H*),7-dione (14)

In the way described for the preparation of **13**, compound **2** (2.61 g; 0.01 mol) gave, with propionic anhydride (20 mL), 1.85 g (49.6%) of compound **14**. Colourless crystals from ethanol; m.p. 217—220 °C.

$C_{19}H_{23}N_3O_5$ (373.4). Calcd. C 61.1; H 6.2; N 11.3. Found C 61.0; H 6.1; N 11.4%.

IR (KBr): cf. Table I.

3-Acetyl-8-nitro-5,6-dihydro-1*H*,4*H*,7*H*-3,3a,6a-triazaindeno[3a,4-*a*] indene-2(3*H*),7-dione (15)

(a) Compound **3** (2.46 g; 0.01 mol) was refluxed in acetic anhydride (100 mL) for 2 h to obtain a solution. After further boiling (10 h altogether), the dark brown solution was evaporated under reduced pressure. The solid residue was suspended in water, filtered off, and washed with ethanol. The dichloromethane extract from the crude product was recrystallized from glacial acetic acid in the presence of activated carbon to give colourless crystals (2.66 g; 80.6%); m.p. 270—272 °C.

(b) Compound **18** (288 mg; 1 mmol), isolated during the reaction of **3** with acetic anhydride, was further refluxed in acetic anhydride to convert it into compound **15** in the course of a slow reaction (10 h). Yield: 300 mg (90.9%); m.p. 270—272 °C.

$C_{15}H_{14}N_4O_5$ (330.3). Calcd. C 54.5; H 4.3; N 17.0. Found C 54.6; H 4.4; N 17.1%.

IR (KBr): cf. Table I.

1-Acetyl-8-nitro-1,2,3,4-tetrahydropyrimido[2,1-*a*]phthalazin-5-ium-7-olate (18)

If the **3** → **15** reaction in acetic anhydride was interrupted immediately after the formation of a solution (refluxing for about 2 h), a yellow precipitate separated on cooling (1.32 g; 45.8%), which was insoluble in dichloromethane (in contrast with compound **15**). Yellow needles from a mixture of glacial acetic acid and ethanol; m.p. above 360 °C.

$C_{13}H_{12}N_4O_4$ (288.3). Calcd. N 19.4. Found N 19.6%.

IR (KBr): amide I 1673, νNO_2 1537, 1387 cm^{-1}.

Hydrolysis of **18** in 20% hydrochloric acid gave back compound **3**; prolonged boiling in acetic anhydride resulted in the tetracyclic compound **15** (see there).

1-Methyl-3-propionyl-8-nitro-5,6-dihydro-1*H*,4*H*,7*H*-3,3a,6a-triazaindeno[3a,4-*a*] indene-2(3*H*),7-dione (16)

Proceeding in a similar way as in the synthesis of compound **15**, the reaction **3** → **16** (2.46 g of **3**; 50 mL of propionic anhydride, boiling for 10 h) gave 1.93 g (53.9%) of a product, which was crystallized in the presence of active carbon from ethanol to obtain colourless, salt-like crystals, m.p. 226—228 °C.

$C_{17}H_{18}N_4O_5$ (358.4). Calcd. C 57.0; H 5.1; N 15.6. Found C 57.0; H 5.1; 15.7%.

IR (KBr): cf. Table I.

Crystal and molecular structure of 10

Crystal data. $C_{15}H_{15}N_3O_3$, $M = 285.11$. Monoclinic, $a = 1421.6(3)$, $b = 934.4(2)$, $c = 1043.9(1)$ pm, $\beta = 96.95(1)°$, $V = 1.3765(8)$ nm^3 (by least-squares refinement) on diffractometer angles for 25 automatically centred reflections ($\lambda = 71.073$ pm) space group $P2_1/n$, $Z = 4$, $D_c = 1.337$ Mg.m^{-3}, $F(000) = 600$, $\mu = 0.092$ mm^{-1}.

Data collection, structure determination and refinement were carried out with a CAD-4 diffractometer and a PDP-11/34 minicomputer, $\omega/2\theta$ scan in the range $1.5 \leq \theta \leq 30°$ with scan width $0.5 + 0.4 \tan\theta$ using graphite monochromated Mo—K_α radiation. Three standard reflections were monitored every hour and showed no significant decay of intensities. 2986 unique observations were recorded of which, after data correction for Lorenz and polarization effects (Lp) but not for absorption, 2121 with $F^2 > 1.5\,\sigma(F^2)$ were used for the structure analysis and refinement. The structure was solved by MULTAN [12]. The full matrix least-squares refinement minimized $\Sigma w(\Delta F)^2$. Final $R = 0.043$, $R_w = 0.055$, $R_{tot} = 0.057$, $S = 2.71$, $w = [\sigma^2(F) + 0.25\,(p \cdot F)^2]^{-1}$ where $p = 0.01$. The hydrogen positions were generated from assumed geometries and were refined in the final stage of the least-squares procedure in the isotropic mode. Program system applied: Enraf-Nonius Structure Determination Package with local modifications adapted to PDP-11/34 minicomputer. Atomic scattering factors were taken from standard tables [13]. Lists of structure factors and anisotropic temperature parameters are available from the authors on request.

*

Elemental analyses were made in the Microanalytical Laboratory of the Department (Head: Dr. H. Medzihradszky); the mass spectrum of compound **10** was recorded by Dr. J. Tamás (Central Research Institute of Chemistry, Hungarian Academy of Sciences, Budapest). All this assistance is gratefully acknowledged.

REFERENCES

[1] Körmendy, K., Ruff, F., Kövesdi, I.: Acta Chim. Hung., **117,** 371 (1984)
[2] Körmendy, K.: Acta Chim. Acad. Sci. Hung., **99,** 81 (1979)
[3] Körmendy, K., Ruff, F.: Acta Chim. Hung., **112,** 65 (1983)
[4] Körmendy, K.: Acta Chim. Acad. Sci. Hung., **94,** 373 (1977)
[5] Körmendy, K., Mönh-Ajus, R., Ruff, F., Kövesdi, I.: "Synthesis of hydroxyalkylaminophthalazinone isomers nitrated in the benzene ring" (To be published)
[6] Kahn, R.: Ber., **35,** 3857 (1902)
[7] Dunitz, J. D., Winkler, F. K.: Acta Crystallogr., B**31,** 251 (1975)
[8] Cremer, D., Pople, J. A.: J. Am. Chem. Soc., **97,** 1354 (1975)
[9] Kálmán, A., Czugler, M., Simon, K.: Molecular Structure and Biological Activity (Edited by J. F. Griffin and W. L. Duax), pp. 367—376, Elsevier Biomedical, New York 1982
[10] Rowe, F. M., Cross, E. J.: J. Chem. Soc., **1947,** 461
[11] Simpson, J. C. E.: Condensed Pyridazine and Pyrazine Rings (Weissberger, A.: The Chemistry of Heterocyclic Compounds). Interscience Publishers, Inc., New York—London, 1953 pp. 127, 128
[12] Main, P., Hull, S. E., Lessinger, L., G. Germain, G., Declercq, J. P., Woolfson, M. M.: A System of Computer Programs for Automatic Solution of Crystal Structures from X-ray Diffraction Data (MULTAN), Univ. of York, England and Louvain, Belgium 1978
[13] "International Table for X-ray Crystallography", Vol. III. Birmingham, Kynoch Press 1962

Acta Chimica Hungarica 123 (1—2), pp. 31—44 (1986)

DETERMINATION OF THE IONIZATION CONSTANTS OF SOME NEW *p*-AMINOHIPPURIC ACID DERIVATIVES

Cornel DRUGĂRIN* and M.-Agneta BALINT

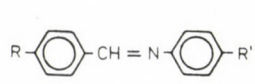
(Laboratorul de Tehnologie Chimica, Universitatea din Timişoara, 1900 Timişoara, str. Pestalozzi 16, Romania)

Received July 18, 1985
Accepted for publication November 27, 1985

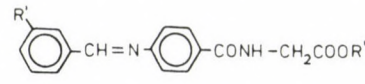
The ionization constants (pK_a) of some new *p*-aminohippuric acid (PAH) derivatives, especially of some Schiff bases, derivatives of PAH, have been determined using the spectrometric (UV-VIS) method. The corresponding pK_a values were calculated either directly from the electronic spectra or by a computer FELIX C256 using a FORTRAN program to separate the overlapping ionization constants.

Introduction

p-Aminohippuric acid (PAH) and its derivatives still present a pharmacological interest [1, 2]. Therefore, in our laboratory some new derivatives were synthesized, aiming at a potentiated pharmacological action [3—5]. There were also synthesized some other structures, derivatives of PAH, having in view properties other than those mentioned above. In this sense, the Schiff bases of PAH present above all a licrystal structure [6—8]:



Schiff bases
(Licrystal structure)



Schiff bases of PAH
(New synthesized structures)

Besides the known licrystal properties, the existence of such new structures of Schiff bases, PAH derivatives, do not offend the known correlation between a potentiated pharmacodynamic effect at phase transitions of licrystals [9].

From this point of view, the determination of the ionization constants of the Schiff bases, derivatives of PAH, presented in this paper, can give important indications regarding the behavior of these compounds in biochemical systems.

* To whom correspondence should be addressed.

The UV-VIS spectrometric method used, though is more time-consuming than the potentiometric or conductometric methods, has the advantage of high accuracy. In addition, the low solubility in water of the compounds studied, required the spectrometric method, which can give in the same time important biochemical information.

In order to clear up some interpretational problems, it was necessary to determine the ionization constants of some other compounds having simpler structures but which are present in the new structures studied.

Experimental

The substances studied, Schiff bases PAH, were synthesized and purified in our laboratory using PAH and the corresponding aldehydes either FLUKA or MERCK.

The experimental procedure applied to determine the ionization constants was generally that indicated by Albert and Serjeant [10].

For all the compounds studied, stock solutions (100 cm^3) in bidistilled water were prepared, with concentrations between 10^{-4}—10^{-5} mol/dm^3, which were diluted (1 : 10) with 0.1 *N* HCl; 0.1 *N* NaOH; C_2H_5OH and water, respectively.

The electronic spectra of these solutions were recorded on a Carl Zeiss spectrophotometer model SPECORD UV VIS, using silica cells of 2 or 1 or 0.1 cm length, jacketed cell holders connected to a thermostatically controlled bath, at a temperature of 20 ± 0.1 °C and, as references, the same solvents were used (1 : 10) diluted with bidistilled water. From these spectra the convenient "analytical" wavelength (λ_{anal}) and the optimal concentrations were selected for the determination of the ionization constants.

The absorbance values, corresponding to different pH's, necessary for calculating the ionization constants, were obtained at the previously selected analytical wavelength from the absorption spectra recorded for a series of solutions prepared from the stock solution diluted (1 : 10) with different 0.1 *M* buffer solutions, viz. chloroacetic acid, formic acid, acetic acid, phosphoric acid, trishydroxymethylaminomethane ("Tris") and sodium carbonate, respectively. When the differences between the absorbance values at λ_{anal} were great for two solutions having close pH values, two buffer solutions were mixed, obtaining intermediate pH values, but maintaining the ionic strength of all the solutions at a constant value (0.09 *M*).

The pH values were measured with a pH-Meter 28 Radiometer (Kopenhagen). The glass and calomel electrodes as well as the standard solutions came from the same supplier.

Results and Discussion

From the UV spectra of the compounds studied in acidic, basic, aqueous and ethanolic medium, as λ_{anal} adequate for the Schiff bases of PAH and their esters, the value of 263.1 nm was selected and the ionization of an existing hydroxy group as substituent was followed at 312.5 nm.

As examples, are given the UV spectra of *p*-[(*p*-hydroxybenzylidene)-amino]hippuric acid in different media searching for λ_{anal} (Fig. 1) and the UV spectra of *p*-(benzylideneamino)hippuric acid at different pH values (Fig. 2).

The ionization constants (pK_a) were calculated in the usual way, using the measured pH values and the registered absorbances (A_i) at λ_{anal}. A typical example of the calculations is given for *p*-[(*p*-methoxybenzilidene)amino]-hippuric acid, methyl ester (Table I).

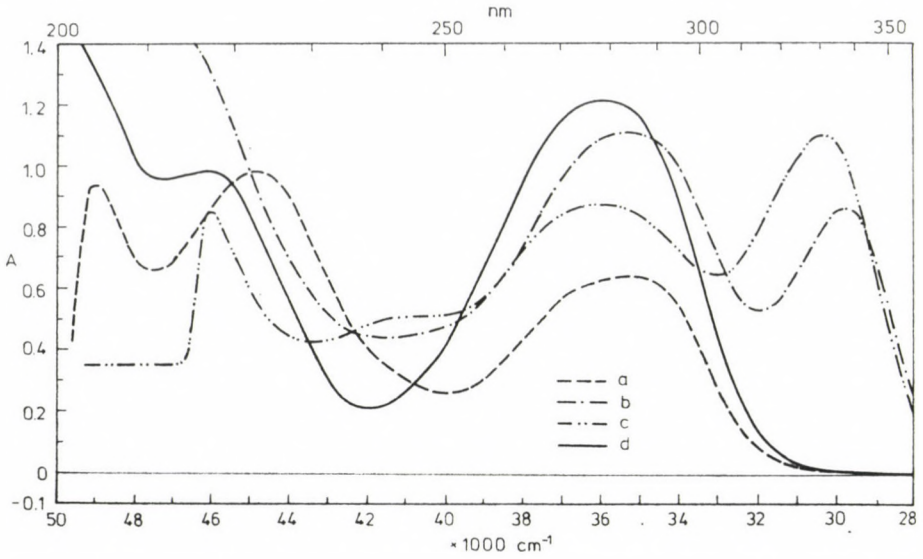
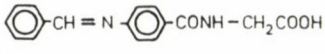


Fig. 1. **The UV spectra of *p*-[(*p*-hydroxybenzylidene)amino]hippuric acid in different solvents. The aqueous stock solution (5×10^{-4} *M*) diluted (1 : 10) in: a — 0.1 *N* HCl; b — Ethanol; c — 0.1 *N* NaOH; d — Water**



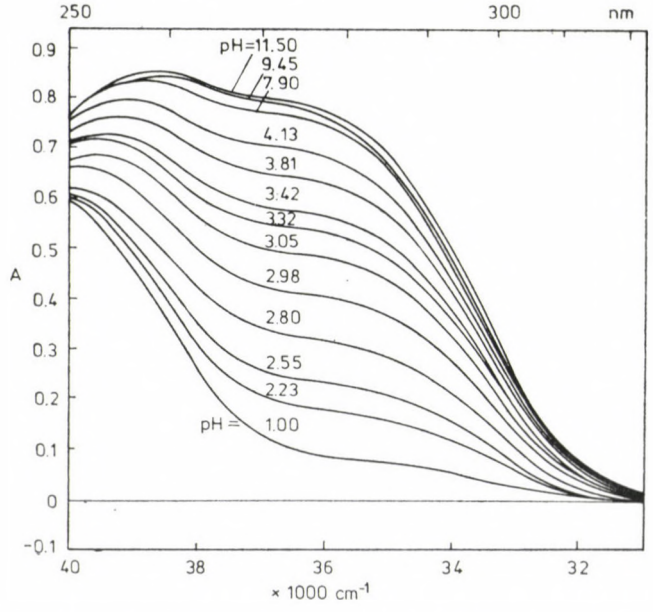


Fig. 2. The UV spectra of *p*-[(*p*-benzylidene)amino]hippuric acid at different pH values. The aqueous stock solution (5×10^{-4} *M*) diluted (1 : 10) in 0.1 *M* buffers

Table I

Determination of the ionization constant (pK_a) *of p-[(p-methoxybenzylidene)amino]hippuric acid methyl ester from spectrometric data*

Concentration : 5×10^{-5} *M*
Cell length : 1 cm
Temperature : 20 °C
Analytical wavelength : 263.1 nm
Absorbance in HCl 0.1 *N* : $(A_{HCl}) = 0.357$
Absorbance in NaOH 0.1 *N* : $(A_{NaOH}) = 1.080$

i	pH_i	Absorbances A_i	$A_i - A_{HCl}$	$A_{NaOH} - A_i$	$\log \frac{A_{NaOH}-A_i}{A_i-A_{HCl}}$	$pK_a = II + VI$
I	II	III	IV	V	VI	VII
1	2.25	0.420	0.390	0.063	+0.790	3.04
2	2.30	0.430	0.380	0.073	+0.710	3.01
3	2.37	0.446	0.364	0.085	+0.630	3.00
4	2.55	0.478	0.332	0.121	+0.440	2.99
5	2.65	0.501	0.309	0.144	+0.330	2.98
6	2.92	0.545	0.265	0.188	+0.150	3.06
7	3.14	0.604	0.206	0.247	−0.078	3.06
8	3.25	0.625	0.185	0.268	−0.160	3.08
9	3.30	0.647	0.163	0.290	−0.250	3.05
10	3.45	0.673	0.137	0.316	−0.360	3.08

$pK_a = 3.03 \pm 0.05$

For some of the substances, the pK_a values calculated, presented a tendency of a continuous increase for the increasing pH values, then the existence of two overlapping ionization constants was supposed. In such cases, for the plot of the absorbance (at λ_{anal}) versus pH, either a jump of the values

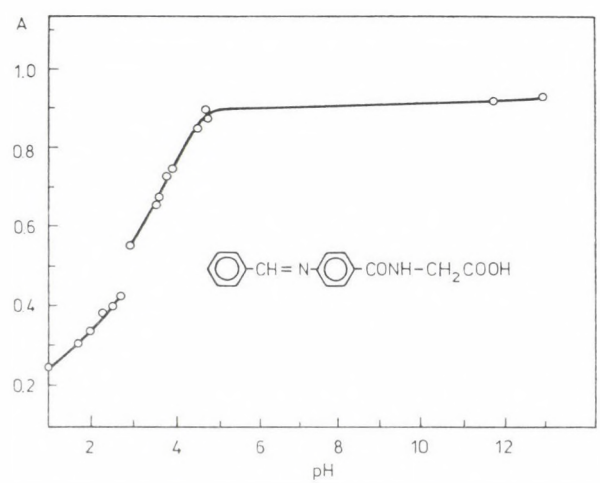


Fig. 3. Variation of the absorbance (at $\lambda_{anal} = 263.1$ nm) as a function of pH. Substance: *p*-[(*p*-benzylidene)amino]hippuric acid Concentration: 5×10^{-5} *M*; cells: 1 cm; temperature: 20 °C

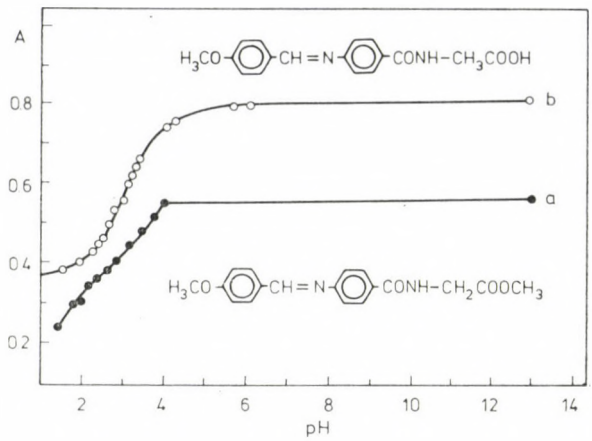


Fig. 4. Variation of the absorbance (at $\lambda_{anal} = 263.1$ nm) as a function of pH. Substances: a. *p*-[(*p*-methoxybenzylidene)amino]hippuric acid, b. *p*-[(*p*-methoxybenzylidene)amino]hippuric acid methyl ester. Concentration: 5×10^{-5} *M*; cells: 1 cm; temperature: 20 °C

of A_i, like in Fig. 3, or a variation in steps like in Fig. 4a, was obtained, instead of a continuous curve which is obtained in case of only one pK_a value, like in Fig. 4b.

The separation of two overlapping constants, which correspond to two ionizing groups in the molecule, implies, firstly, the calculation of the ab-

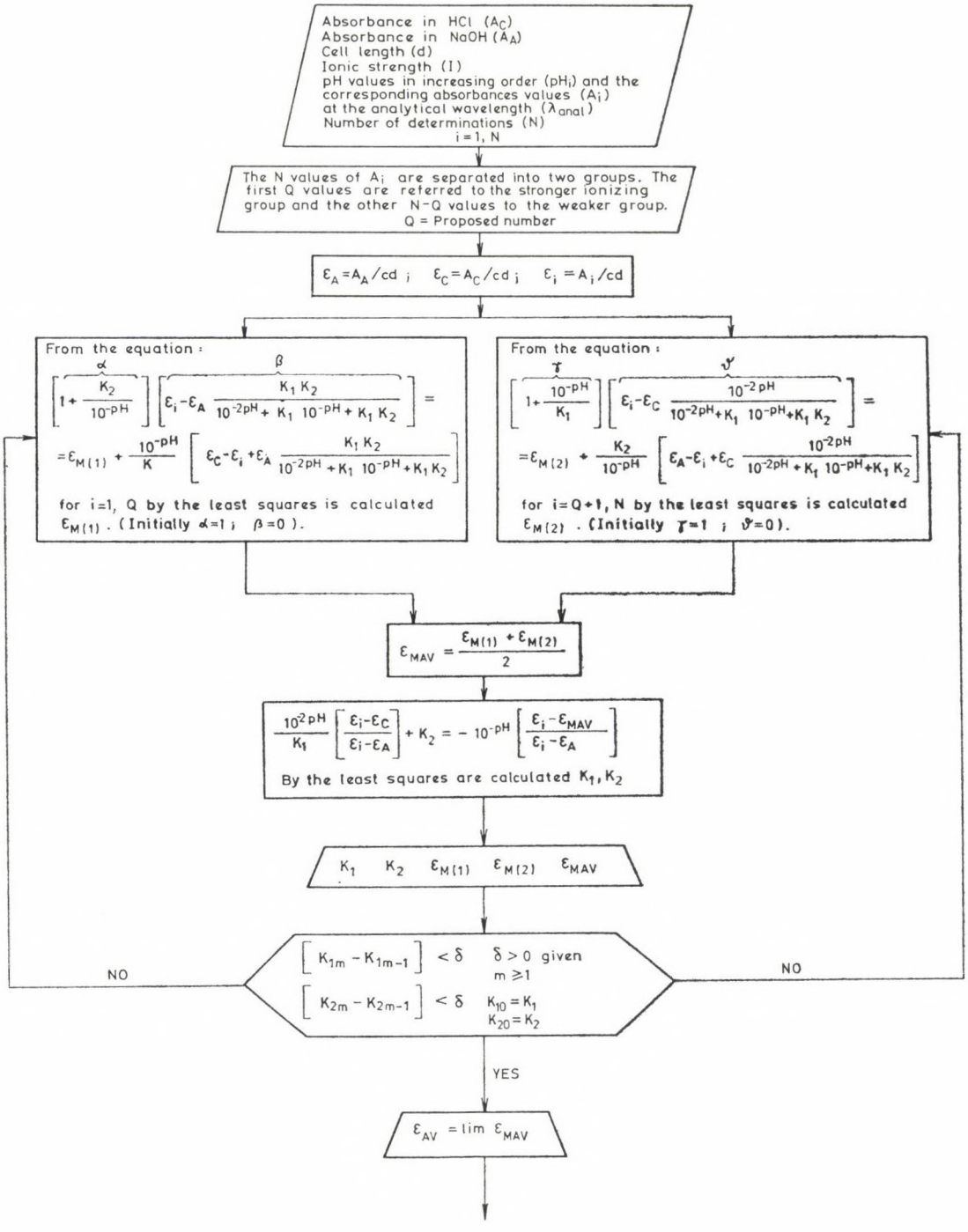
Table II

Calculation by computer FELIX C256 *of the ionization constants from spectrometric data in the case of p-[(p-hydroxybenzylidene)amino]hippuric acid*

Concentration : 5×10^{-5} *M*
Cell length : 1 cm
Ionic strength : 0.09
Analytical wavelength : 263.1 nm
Absorbance in HCl 0.1 *N* : 0.445
Absorbance in NaOH 0.1 *N*: 1.080

STEP I (Computer Program)
(The convergence check is not reproduced here) The result by computer given is: $\varepsilon_M = 15384$
STEP II (Computer Program)

pH	*A*	ε	*X*	*Y*	pK_1	pK_2
1.85	.493	9860.0	—.16316E-04	—.52155E-02	2.501	
2.15	.505	10100.0	—.52298E-05	—.25525E-02	2.681	
2.45	.567	11340.0	—.29938E-05	—.10974E-02	2.547	
2.70	.602	12040.0	—.13076E-05	—.54768E-02	2.587	
2.95	.695	13900.0	—.81749E-06	—.16971E-03		3.990
3.68	.875	17500.0	—.91562E-07	.84602E-04		3.939
4.05	.963	19260.0	—.35168E-07	.11583E-03		3.894
4.75	1.020	20400.0	—.30306E-08	.58325E-04		4.227
5.28	1.040	20800.0	—.40970E-09	.27878E-04		4.553
			AVERAGE VALUES:		2.579	4.121


Absorbance in HCl (A_C)
Absorbance in NaOH (A_A)
Cell length (d)
Ionic strength (I)
pH values in increasing order (pH_i) and the corresponding absorbances values (A_i) at the analytical wavelength (λ_{anal})
Number of determinations (N)
i = 1, N
The N values of A_i are separated into two groups. The first Q values are referred to the stronger ionizing group and the other N-Q values to the weaker group.
Q = Proposed number
$\varepsilon_A = A_A/cd$; $\varepsilon_C = A_C/cd$; $\varepsilon_i = A_i/cd$
From the equation :
$\left[1+\frac{K_2}{10^{-pH}}\right]\left[\varepsilon_i-\varepsilon_A\frac{K_1K_2}{10^{-2pH}+K_1\,10^{-pH}+K_1K_2}\right]=$
$=\varepsilon_{M(1)}+\frac{10^{-pH}}{K}\left[\varepsilon_C-\varepsilon_i+\varepsilon_A\frac{K_1K_2}{10^{-2pH}+K_1\,10^{-pH}+K_1K_2}\right]$
for i=1, Q by the least squares is calculated $\varepsilon_{M(1)}$. (Initially $\alpha=1$; $\beta=0$).
From the equation :
$\left[1+\frac{10^{-pH}}{K_1}\right]\left[\varepsilon_i-\varepsilon_C\frac{10^{-2pH}}{10^{-2pH}+K_1\,10^{-pH}+K_1K_2}\right]=$
$=\varepsilon_{M(2)}+\frac{K_2}{10^{-pH}}\left[\varepsilon_A-\varepsilon_i+\varepsilon_C\frac{10^{-2pH}}{10^{-2pH}+K_1\,10^{-pH}+K_1K_2}\right]$
for i=Q+1, N by the least squares is calculated $\varepsilon_{M(2)}$. (Initially $\gamma=1$; $\vartheta=0$).
$\varepsilon_{MAV}=\frac{\varepsilon_{M(1)}+\varepsilon_{M(2)}}{2}$
$\frac{10^{2pH}}{K_1}\left[\frac{\varepsilon_i-\varepsilon_C}{\varepsilon_i-\varepsilon_A}\right]+K_2=-10^{-pH}\left[\frac{\varepsilon_i-\varepsilon_{MAV}}{\varepsilon_i-\varepsilon_A}\right]$
By the least squares are calculated K_1, K_2
K_1 K_2 $\varepsilon_{M(1)}$ $\varepsilon_{M(2)}$ ε_{MAV}
$\left[K_{1m}-K_{1m-1}\right]<\delta$ $\delta>0$ given
$\left[K_{2m}-K_{2m-1}\right]<\delta$ $m\geq 1$
$K_{10}=K_1$
$K_{20}=K_2$
NO
NO
YES
$\varepsilon_{AV}=\lim \varepsilon_{MAV}$

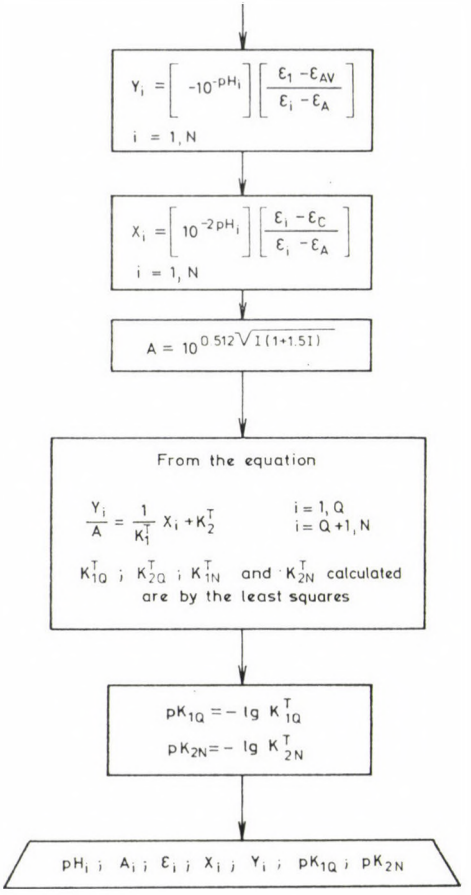


Fig. 5. Determination of the overlapping ionizaton constants from spectrophotometric data in case of substances having an acidic as well a basic group, the ionization process being:

$$\text{diprotonated species} \underset{}{\overset{K_1}{\rightleftharpoons}} \text{monoprotonated species} \overset{K_2}{\rightleftharpoons} \text{nonprotonated species}$$

A; STEP I: Determination of the molar absorptivity of the monoprotonated species
B; STEP II: Determination of the thermodynamic ionization constants

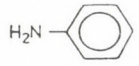
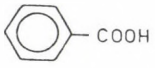
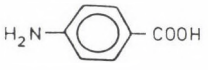
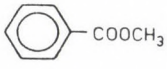
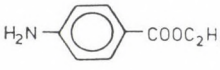
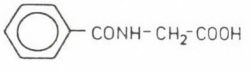
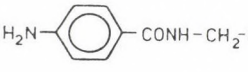
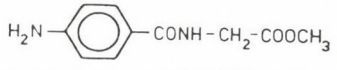
sorbance and the molar absorptivity of the monoprotonated species (ε_M). Both the calculation of ε_M and the separation of the two pK_a values was performed on a computer FELIX C 256 using a FORTRAN program. The scheme of the program is given in Fig. 5.

The separation of two overlapping ionization constants, pK_1 and pK_2 is exemplified for *p*-[(*p*-hydroxybenzylidene)amino]hippuric acid in Table II.

In order to interpret the results obtained for our new synthesized compounds, in Table III are presented the ionization constants of some simpler structures, which contain the main groups of the new moiety studied. These values are literature data for the first three compounds (III/**1**—**3**) and values

Table III

Characterization by UV *spectral data and ionization constants of some basic compounds for interpreting*

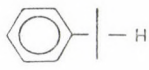
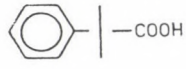
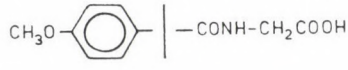
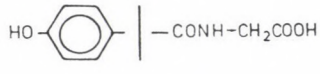
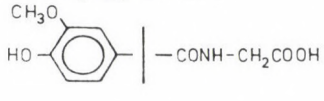
No. Compound	Molar conc. [mol/dm³]	Solvent: I. H_2O II. C_2H_5OH III. HCl IV. NaOH	pH	Maximal molar calculated at the ε_{max} (λ) [(cm mol)$^{-1}$]
LITERATURE DATA				
				
1 Aminobenzene	—	—	—	—
				
2 Benzoic acid	—	—	—	—
				
3 *p*-Aminobenzoic acid	—	—	—	—
EXPERIMENTALLY OBTAINED				
4 Benzoic acid methyl ester	1.25×10^{-3}	I	9.60	—
		II	7.68	—
		III	1.05	—
		IV	13.09	—
5 *p*-(Aminobenzoic)acid ethyl ester	4.50×10^{-5}	I	—	—
		II	—	—
		III	1.05	—
		IV	12.95	—
6 Hippuric acid	5.00×10^{-5}	I	4.45	—
		III	8.30	—
		III	1.05	18800(203)
		IV	12.75	—
7 *p*-Aminohippuric acid	5.00×10^{-5}	I	4.45	—
		II	5.10	19400(207)
		III	1.45	—
		IV	11.55	—
8 *p*-Aminohippuric acid methyl ester		I	4.25	—
		II	—	—
	1.00×10^{-3}	III	1.05	—
		IV	12.75	—

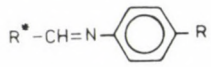
the experimental results

absorptivities wavelength indicated dm³]; [nm]		Molar absorptivities λ_{anal} [nm]	Ionization constants pK_1	pK_2	pK_3	Notes
—	—	—	4.6	—	—	Literature [10]
—	—	—	4.16	—	—	[10]
—	—	—	4.198	—	—	[11]
—	—	—	2.40	4.80	—	[10]
10100(232) 11200(230)	800(275) 936(274) 768(281)		—	—	—	
10100(232) not stable λ_{max}	800(275)					
— — 11600(227) 16200(288)	— — — —	— 263.1	2.76±0.08	—	—	Calculated
13800(230) 12800(232) 14100(230) 13300(233)	— — 960(265) —	263.1	3.61±0.07 —	—	—	$pK_a = 3.59$ [11]
18200(214) 19400(214) 13000(226) 18000(214)	17640(273) 19800(283) 12000(265) 18800(272)	263.1	2.88	4.49		By computer obtained
450(212) 880(215) 360(225) 420(215)	390(278) 980(282) — 525(277)	263.1	2.87±0.07	—	—	Calculated

Table IV

Characterization by UV *spectral data and ionization constants obtained for the compounds studied,*

No. Compound R*	Molar conc. [mol/dm³]	Solvent: I. H_2O II. C_2H_5OH III. HCl IV. NaOH	pH	Maximal molar calculated at the cated [(cm mol)$^{-1}$
1 *p*-(Benzylideneamino)benzene 	5.00×10^{-4}	I II III IV	5.75 8.00 1.45 12.80	16850(245) 23000(242) 15700(252) 16500(245)
2 *p*-(Benzylideneamino)benzoic acid 	500×10^{-5}	I II III IV	— — 1.05 12.95	10000(217) — 15600(231) —
3 *p*-(Benzylideneamino)hippuric acid 	5.00×10^{-5}	I II III IV	— — 1.00 12.82	17200(215) 25600(217) 15400(232) —
4 *p*-[(*p*-Methoxybenzylidene)amino] hippuric acid 	5.00×10^{-5}	I II III IV	4.55 6.35 1.08 12.75	17600(201) 14400(205) 12000(202) —
5 *p*-[(*p*-Methoxybenzylidene)amino] hippuric acid methyl ester 	5.00×10^{-5}	I II III IV	5.65 7.15 1.10 13.00	16400(217) 16000(207) 15540(203) —
6 *p*-[(*p*-Hydroxybenzylidene)amino] hippuric acid 	5.00×10^{-5}	I II III IV	4.62 6.25 0.90 12.85	19600(217) — 19600(223) 10200(245)
7 *p*-(*p*-Hydroxybenzylidene)amino] hippuric acid methyl ester 	1.70×10^{-5}	I II III IV	4.85 4.45 1.02 12.85	14411(220) 33530(224) 14411(224) *14558(242)
8 *p*-[(*p*-Hydroxy-m-methoxybenzylidene)-amino]hippuric acid 	5.00×10^{-5}	— —	— —	— —



absorptivities wavelength indi- ε_{max} (λ) dm³]; [(nm)]		λ_{anal} [nm]	Ionization constants pK₁	pK₂	pK₃	Notes
3200(283) 3600(286) 1640(286) 3200(283)	— — — —	277.7	4.55±0.03	—	—	pK_a value calculated at pH values near to 4.5
18800(255) 19840(252) 14000(250) 21960(257)	15200(266) 16400(268) 2800(278) —	263.1	1.97	4.47		By computer obtained
15000(276) 18740(284) — 18200(265)	— — —	263.1	2.065	3.635		By computer obtained
11600(215) 13000(218) 10800(223) 11600(215)	15200(283) 17000(281) 8000(287) 15200(283)	263.1	2.21	4.08		By computer obtained
22800(280) 17200(218) 14800(223) 16400(217)	— 21000(281) 10760(285) 24000(280)	263.1	3.03±0.05			Calculated
24000(280) 22000(285) 12800(285) 17400(280)	— 17600(377) — 22000(331)	263.1 312.5	2.58	4.12	 7.40±0.07 —	By computer obtained Calculated
19700(284) 24550(287) 10440(284) 14500(285)	— — — 25000(333)	263.1 344.8	2.89±0.15 —		7.69±0.03	Both calculated *Initial values
— —	— —	263.1 344.8	2.21	3.56	 7.22±0.02	By computer obtained Calculated

determined by us for the others, in the same experimental conditions as for the Schiff bases studied (Table IV).

The ionization constants of aminobenzene (III/**1**) $pK_a = 4.60$ and benzoic acid (III/**2**) $pK_a = 4.198$ are very close, due to the inductive and mesomeric effects, which have the same signs in aminobenzene and opposite signs in benzoic acid.

As in the experimental conditions given, for the ester of benzoic acid (III/**4**) no pK_a value can be determined, the hydrolysis does not take place; the relatively small pK_a value (2.76) obtained for the ester (III/**5**) is attributed to the NH_2 group attached to the substituted ring of the esterified benzoic acid. The pK_a (2.87) is in agreement with this value for *p*-aminohippuric acid methyl ester (III/**8**), which is the basic "ring" of the azomethinic compounds studied.

p-Aminobenzoic acid (III/**3**) has two ionization constants (2.40 and 4.80) [11] and these are close to the values (2.88 and 4.49) found for *p*-aminohippuric acid (III/**7**). In the assignment of the pK_a values determined to the acidic and basic group, respectively, we have to take into account the zwitterionic character of these compounds.

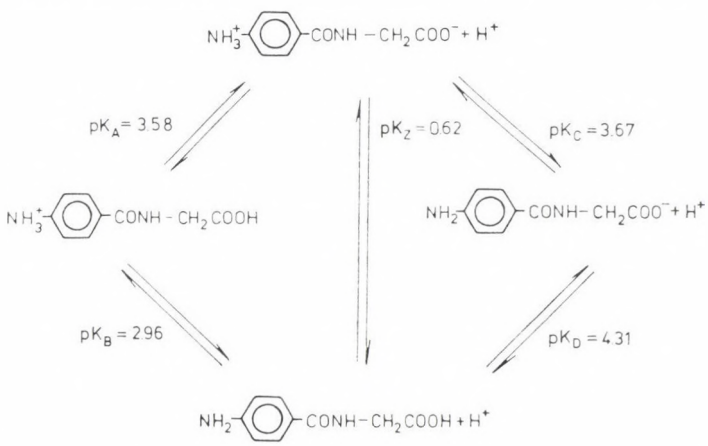
It is well known that zwitterions are defined as molecules which have an acidic pK_a numerically lower than the basic pK_a, in so far as it has acidic and basic groups strong enough to neutralize each other [12].

The test applied to the compounds studied confirm their zwitterionic character, namely:

— one of the pK_a values is markedly different from that of the corresponding ester;

— there is a shift to shorter wavelengths in the long — wave absorption band on adding alkali.

With the two ionization constants of PAH, pK_1 and pK_2 named "macroscopic", using Adam's equations [13] and Bryson's relation [14], the "micro-



scopic" constants pK_A, pK_B, pK_C, pK_D and pK_Z respectively were calculated. The supposed ionization process and the calculated constants are given below.

In order to elucidate some aspects of the results obtained for the synthesized Schiff bases (Table IV), two simpler substances: *p*-(benzylidene)aminobenzene (IV/**1**) and *p*-[(benzylidene)amino]benzoic acid (IV/**2**) were studied.

In aqueous solutions, especially in acidic medium, the —CH=N— bond is broken, the reaction being known and studied in the literature [15, 16].

(IV/1)

(IV/2)

For the first compound (IV/**1**) one pK_a was obtained (4,55), corresponding to the resulting aminobenzene and for the second compound (IV/**2**) two pK_a values (4.47 and 1.97) were obtained corresponding to the zwitterionic *p*-aminobenzoic acid. All these values are in agreement with those obtained for the pure states (III/**1**) and (III/**3**), respectively. The aldehydic part resulting in the reactions mentioned above (even for substituted aldehydes) does not disturb the absorption at λ_{anal}.

The Schiff bases studied in identical hydrolysis conditions, present the same splitting reaction of the azomethinic bond. For the molecular fragment corresponding to the zwitterionic PAH there are two pK_a's obtained (IV/**3**, IV/**4**) and only one for the molecular part corresponding to the methyl ester of PAH (IV/**5**) (provided that the ester bond does not split in the given experimental conditions).

In the case of the compounds containing in the aldehydic ring a *p*-hydroxylic substituent (IV/**6**; IV/**8**) there are three ionization constants obtained: two corresponding to zwitterionic PAH and the third to the hydroxy group of the aldehydic fragment. The determination of the latter constant was made at another λ_{anal}. For the corresponding ester (IV/**7**) the blocking of the carboxy group causes the existence of two ionization constants (2.89 and 7.69), which can be identified and attributed to the NH_2 group from the PAH fragment and to the OH group, respectively.

The position and the nature of the substituents from the aldehydic fragment influence the values of the ionization constants, as can be observed for the compounds presented (IV/**4**—IV/**8**).

REFERENCES

[1] Goodman, L. G., Gilman, A.: Bazele farmacologice ale terapeuticii, Ed. Medicală, Bucureşti 1960
[2] Dreichlinger, O.: Sinteza unor substanţe cu acţiune asupra metabolismului rinichiului, Teză de doctorat, Timişoara 1967
[3] Drugărin, C., Boldea, A.: Die Pharmazie, **31,** 3 (1976)
[4] Drugărin, C., Boldea, A.: Die Pharmazie, **32,** 3 (1976)
[5] Drugărin, C., Boldea, A.: Die Pharmazie, **32,** 2 (1977)
[6] Demus, D.: Textures of Liquid Crystals. VEB Deutscher Verlag für Grundstoffindustrie, Leipzig 1980
[7] Drugărin, C., Geţia, P.: Die Pharmazie, **36,** 4 (1981)
[8] Drugărin, C., Geţia, P.: Die Pharmazie, **36,** 4 (1981)
[9] Meier, G., Sackmann, E., Grabmaier, J. G.: Applications of Liquid Crystals. Springer Verlag, Berlin, Heidelberg, New York 1975
[10] Albert, A., Serjeant, E. P.: The Determination of Ionization Constants. Chapman and Hall 1971
[11] Serjeant, E. P., Dempsey, B.: Ionization Constants for Organic Acids in Aqueous Solution. IUPAC Chemical Data Series, 23, Pergamon Press 1979
[12] Bjerrum, J.: Z. phys. Chem., **104,** 147 (1923)
[13] Adams, J.: J. Am. Chem. Soc., **38,** 1503 (1916)
[14] Bryson, A., Davies, A. G., Serjeant, E. P.: J. Am. Chem. Soc., **85,** 1933 (1963)
[15] Martinet, P., Simonet, J., Tendil, J.: C. R. Acad. Sci. Paris, **268,** Série C (1969)
[16] Nagy, P.: Magy. Kém. Folyóirat, **78,** 213 (1972)

Acta Chimica Hungarica 123 (1—2), pp. 45—54 (1986)

THE CHROMOPHORE SERVING AS BASIS FOR THE DETERMINATION OF ARSENIC WITH SILVER DIETHYLDITHIOCARBAMATE

Anna CSIKKEL-SZOLNOKI[1], Etelka CSÁKI-TOMBÁCZ[2], Sándor VERES[1] and Kálmán BURGER[1]*

([1]József Attila University, Department of Inorganic and Analytical Chemistry, 6720 Szeged, Dóm tér 7., [2]Department of Colloid Chemistry, 6720 Szeged, Aradi vértanúk tere 1.)

Received November 1, 1985
Accepted for publication December 12, 1985

It was shown by preparative model experiments and colloid chemical investigations that the light absorption, serving as basis for the determination of arsenic with silver diethyldithiocarbamate, does not arise from silver colloid, but from a polynuclear dithiocarbamate complex with silver (O) and arsenic(III) central atoms, forming in pyridine a molecular solution.

V. Vasak and V. Sedivec were the first to use the solution of silver diethyldithiocarbamate (AgDDTC) in pyridine for the spectrophotometric determination of trace quantities of arsenic [1]. Our method recently developed is also based on the use of this reagent [2]. Arsine (AsH_3), produced by the reduction of arsenic compounds with sodium tetrahydroborate in hydrochloric acid medium, is absorbed in AgDDTC solution in pyridine, and the light absorption of the red solution formed is determined at 540 nm.

Data in the literature concerning the chemical composition of the chromophore serving as basis of the determination are incomplete or inconsistent. G.W. Powers et al. [3], then W. Fresenius and W. Schneider [4], finally J. Steinke [5] mention the formation of a red complex, but without reference to structure or composition. H. Bode and K. Hachmann [6] attribute the appearance of the red colour to the formation of colloidal silver:

$$AsH_3 + 6\ AgDDTC \rightarrow 6\ Ag + 3\ HDDTC + As(DDTC)_3 \qquad (1)$$

This equation is cited also in two monographs [7, 8]. L. Dubois et al. [9] mention the simultaneous formation of metallic silver and a complex compound, but assign the colour to the complex, and not to silver. The two absorption maxima of the red solution, always present in the visible spectral range, are explained by S. Sandhu and P. Nelson [10] with the following complex forming reaction, however, without an indication of the composition of the complex:

$$AsH_3 + AgDDTC \rightarrow \text{AgDDTC-arsenic complex} + \text{AgDDTC-hydrogen complex} \qquad (2)$$

* To whom correspondence should be addressed.

The aim of our work was to clear inconsistencies in connection with the chemical composition of the red chromophore used as basis of arsenic determination, and to interpret chemical processes proceeding during arsenic determination.

Experimental

Instruments and reagents

Unicam SP 800B ultraviolet spectrophotometer, Pye Unicam SP 1000 infrared spectrophotometer, MOM 3180 analytical ultracentrifuge (with Schlieren optics). Reagents of analytical grade were used for the measurements.

Preparation of AgDDTC

9.0 g of sodium diethyldithiocarbamate (NaDDTC) is dissolved in 400 cm^3 distilled water. The solution is filtered if necessary, then, while stirring, admixed to a solution of 6.8 g silver nitrate in 400 cm^3 water. The yellow precipitate formed is filtered, after settling and decantation, on a separatory funnel in vacuum, washed with distilled water, and dried in a vacuum desiccator.

Preparation of $As(DDTC)_3$

1.97 g As(III) oxide is dissolved in 100 cm^3 0.5 *m* sodium hydroxide, the hydrogen ion concentration of the solution is adjusted with 0.1 *m* hydrochloric acid to about pH 3 and the solution of 10.81 g NaDDTC in 200 cm^3 distilled water is added under continuous stirring. The precipitate formed is filtered, washed and dried as described in the preparation of AgDDTC.

Results and Discussion

Examination of ultraviolet and visible absorption spectra

The red solution formed in the reaction of AsH_3 with AgDDTC has absorption maxima at 410 and 540 nm (Fig. 1). The chromophore is formed in

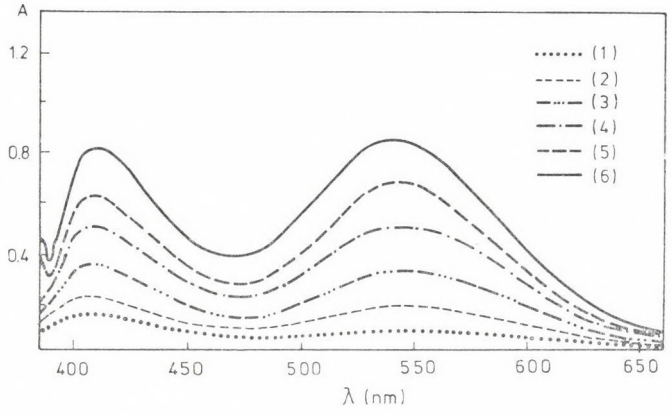


Fig. 1. Light absorption curves of the red chromophore, prepared in solutions of (1) 5; (2) 10; (3) 20; (4) 30; (5) 40; (6) 50 μg As/5 cm^3 content. (d = 5 mm, reference solution: 0.5% AgDDTC in pyridine)

alkaline medium, e.g. in pyridine or in chloroform containing also organic bases (1-ephedrine or brucine) [11]. The location of the first absorption maximum does not depend on the solvent, while the second appears in chloroform at a shorter wavelength than in pyridine. The first absorption bands of the chromophores formed in the determination of both As(III, V) and Sb(III, V)

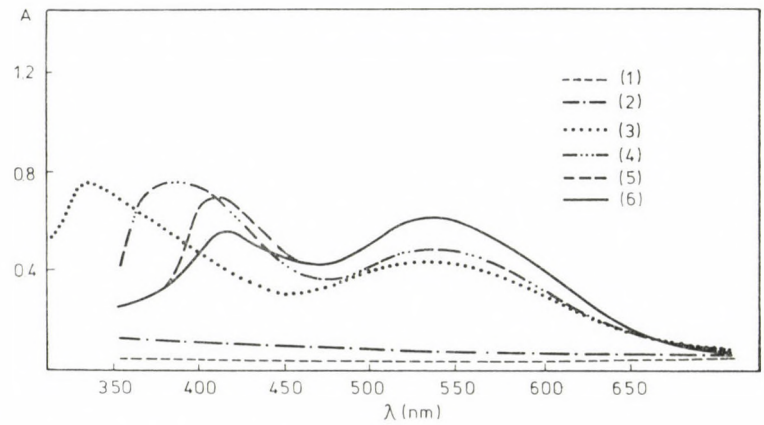


Fig. 2. Light absorption curves of chromophores corresponding to a concentration of 20 μg As/5 cm^3, in pyridine containing AgDDTC solutions of different As : Ag molar ratios; (1) 1 : 1, 1 : 3, 1 : 6; (2) 1 : 12; (3) 1 : 50; (4) 1 : 100; (5) 1 : 300; (6) 1 : 500. (d = 10 mm, pyridine reference solution containing the respective quantities of AgDDTC)

appear at 410 nm, while the nature of ions considerably affects the location of the second absorption maximum (As 540 nm, Sb 500 nm).

Using data published in the literature [6], the effect of the ratio of arsenic hydride and AgDDTC on chromophore formation was investigated (Fig. 2). It was found that at the 1 : 6 AsH_3/AgDDTC molar ratio given in Eq. (1) there is no light absorption yet in the wavelength region from 330 to 650 nm. At a fiftyfold excess of AgDDTC an absorption maximum appears at 330 nm, which is shifted towards longer wavelengths by a further AgDDTC excess. The second maximum (540 nm) too, appears only at a 1 : 50 molar ratio of AsH_3 : AgDDTC, and reaches its maximum value at an about three-hundredfold AgDDTC excess. Our analytical measurements were carried out at several hundred- or thousandfold AgDDTC excess [2].

For the identification of the absorption maxima at 410 and 540 nm the spectra of AgDDTC, of $As(DDTC)_3$ prepared by us and of the decomposition products of NaDDTC (diethylamine and carbon disulfide) were recorded. None of the maxima of the chromophore could be assigned to the substances given above.

Effect of reaction conditions on the chromophore

It was investigated how the magnitude and the location of the two characteristic absorption peaks are influenced by temperature (from —20 °C to 100 °C), various electrolytes (KCl, LiCl, HCl, pyridinium sulfate), oxidizing agents (oxygen, iodine, chlorine) and reducing agents (hydrazine sulfate, hydroxylamine sulfate). The maximum at 540 nm decreases while that at 410 nm increases with increasing temperature (Fig. 3). The maximum at

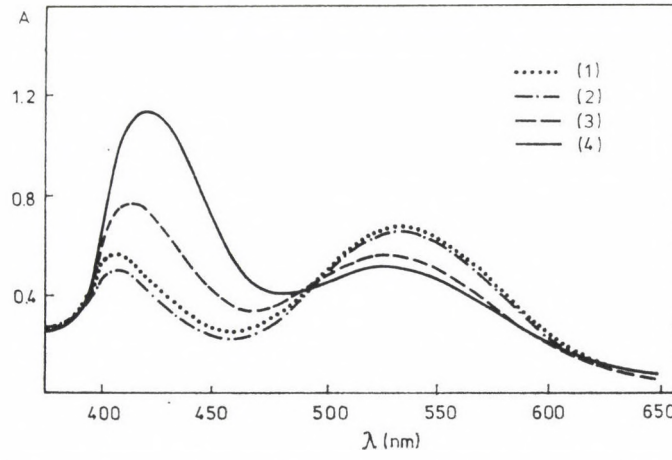


Fig. 3. **Absorption curves of the chromophore, prepared in solutions containing 20 μg As/5 cm^3; (1) measured immediately; (2) after 15 minutes, (3) 1 hour, (4) 2 hours of heating on a water bath at 100 °C. (d = 10 mm, reference solution: 0.5% AgDDTC in pyridine)**

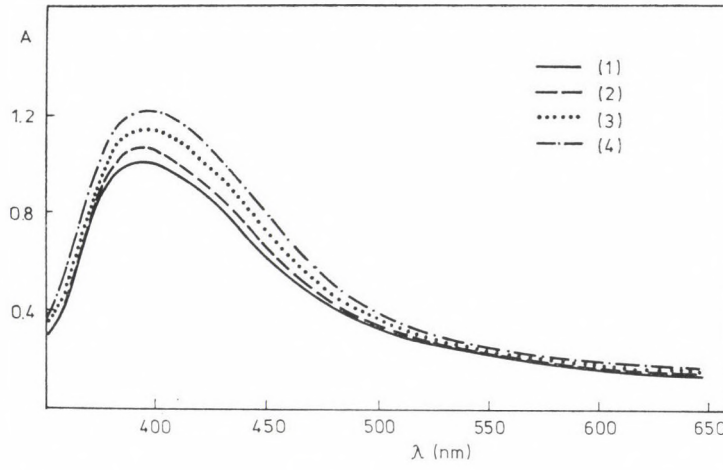


Fig. 4. Absorption curves of silver (0) sol in pyridine-solution (1) 120, (2) 121, (3) 122, (4) 123 hours after preparation. (5 cm^5 0.5% pyridine-containing AgDDTC solution reacted with 6.19×10^{-5} mol hydroxylamine.) (d = 2 mm, reference solution: 0.5% AgDDTC in pyridine)

540 nm disappears by the action of hydroxylamine, and red silver colloid is formed. The other above said investigations of solutions containing the chromophore showed that in the red solutions exposed to various effects the quantity of the compound giving a maximum at 540 nm decreases, while that of the compound giving rise to the maximum at 410 nm scarcely changes. When using higher hydrogen quantities than given in the analytical procedure, the absorption maximum at 410 nm of the red solution formed considerably increases at identical arsenic content, while that at 540 nm does not change.

In the determination of antimony under identical experimental conditions a similar behaviour was found.

These investigations indicate that the absorption maximum at 540 nm is characteristic of the given chromophore used for analytical purposes.

Colloid chemical investigations

Colloid chemical investigations were carried out to clear whether the red chromophore prepared by the analytical process forms a colloidal or molecular solution.

First a silver sol was prepared in pyridine-containing solution by the reduction of AgDDTC with hydroxylamine sulfate. For this purpose, 5 cm^3 of a 0.5% pyridinic AgDDTC (9.7×10^{-5} mol) solution was reduced with 6.19×10^{-5} mol hydroxylamine sulfate. The absorption maximum of this silver sol, red in transmitted light and greyish green in incident light, appeared at 390 nm (Fig. 4), in contrast to the bands of the solution containing the red chromophore prepared according to the analytical prescription, which appear at 410 and 540 nm.

The turbidities of the two kinds of solution were compared on a Spekol photometer, fitted with a turbidity headpiece. The turbidity of the silver sol prepared as described above was found to be 89% ($\lambda = 543$ nm, $d = 1$ cm, 500-fold amplification). The red chromophore prepared according to the analytical prescription does not show turbidity.

H. Bode and K. Hachmann [6] ultracentrifuged the red chromophore for 5 hours at a speed of 50 000 rpm (120 000 g) at 0 °C. They presumed the development of sol (colloidal) state from the concentration distribution obtained.

On centrifuging the pyridine solution of the red chromophore prepared by the analytical procedure (9.34×10^{-8} mol As/5 cm^3 0.5% AgDDTC solution) against pyridine in a two-sector equilibrium cell at a speed of 40 000 rpm ($\sim$ 120 000 g) at 20 °C, a pattern characteristic of regular equilibrium concentration distribution could be observed. The equilibrium of sedimentation and diffusion material flows was established in about 3 hours. The 0.5% AgDDTC reagent showed a completely analogous picture.

On the other hand, silver sol prepared with hydroxylamine reducing agent revealed a fundamentally different behaviour. Centrifuging as described above, the major part of the red substance settled in a brief time and suffered irreversible changes.

The molar mass of the red chromophore prepared according to the analytical prescription cannot be determined with the ultracentrifuging method, because a high (about 300-fold) excess of AgDDTC is needed for the development of the chromophore. The equilibrium concentration distribution described above is characteristic of AgDDTC present in large excess. Centrifuging the red chromophore and the AgDDTC absorbent solutions against one another, patterns completely masking one another are obtained, indicating the establishing of an identical equilibrium concentration distribution.

According to the above said, the pyridine-containing solution of the red chromophore formed during arsenic determination is not a colloidal solution.

Experiments for the preparation of the model of the red chromophore

According to our assumption, silver(0), formed in the arsine reduction of AgDDTC, plays an important part in the formation of the red chromophore. Therefore, experiments were carried out, in which AsH_3, used as reducent in the determination of arsenic, was replaced by other reducing agents.

It became evident during these investigations that the presence of silver(0) and AgDDTC is not sufficient for the formation of the red chromophore, obtained in arsenic determination. Therefore, in our further experiments separately prepared $As(DDTC)_3$ complex was also dissolved in the pyridine-containing solution of AgDDTC. The reduction of silver(I) was carried out in this solution. In the first series of experiments hydroxylamine, then hydrogen was used as reducing agent.

Performing the reduction with hydroxylamine, in solutions containing hydroxylamine and $As(DDTC)_3$ equivalent to 20—1000 μg of arsenic no red chromophore was formed. However, the colour changed from yellow to red, and after two days red silver sol appeared, from which metallic silver precipitated in a few days. Hydroxylamine proved to be a too vigorous reducing agent.

In our reduction experiments with hydrogen produced by sodium tetrahydroborate in the presence of $As(DDTC)_3$, equivalent to 20—20 000 μg arsenic (2.67×10^{-7} to 2.67×10^{-4} mol) dissolved in 5 cm^3 0.5% AgDDTC in pyridine, the reduction resulted in the appearance of the red chromophore. Spectra recorded for solutions of different $As(DDTC)_3$ concentration are shown in Fig. 5 by the series of curves drawn in full.

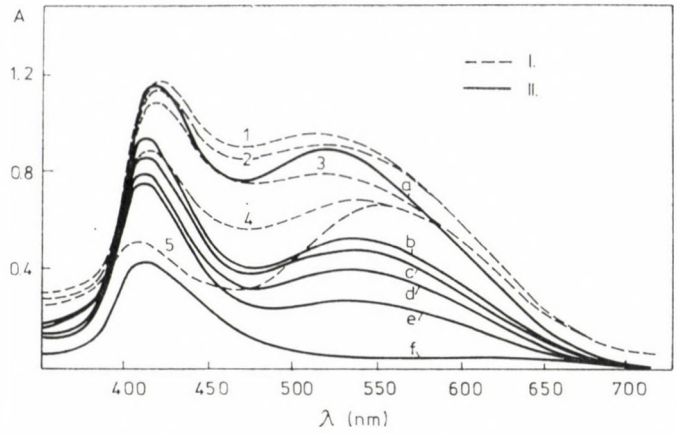


Fig. 5. I. Absorption curves of red chromophore prepared according to the analytical prescription in pyridine containing solutions, at different degrees of hydrogenation: Reduction with: (1) 10; (2) 8; (3) 6; (4) 4; (5) 2 cm³ of 10% $NaBH_4$ solution. (2.67×10^{-7} mol (20 μg) As/5 cm³ 0.5% AgDDTC solution containing pyridine, $d = 10$ mm, reference solution: pyridine-containing 0.5% AgDDTC).

II. Absorption curves of red chromophore formed in the hydrogenation of $As(DDTC)_3$ and AgDDTC, in solutions containing different quantities of $As(DDTC)_3$: (a) 7.70×10^{-6}; (b) 1.54×10^{-5}; (c) 2.30×10^{-5}; (d) 2.69×10^{-5}; (e) 3.40×10^{-5}; (f) 5.50×10^{-4} mol of $As(DDTC)_3$ in 5 cm³ of 0.5% AgDDTC in pyridine. ($d = 10$ mm, 0.5% pyridine-containing AgDDTC reference solution, hydrogen evolved from 20 cm³ of 10% $NaBH_4$)

For comparison the red chromophore was prepared also according to the prescriptions of the analytical procedure [2] in solutions of identical arsenic content, changing the extent of hydrogenation. (Fig. 5, series of curves drawn in dotted lines.) The course of the two series of curves was of identical character.

Investigation of the chromophore, prepared by hydrogenation with sodium tetrahydroborate in a solution containing $As(DDTC)_3$ proved that $As(DDTC)_3$ the central atom of which is As(III), is not reduced by hydrogenation to arsine.

Next, the ultracentrifugal behaviour of the solutions containing red chromophore, prepared in the two different ways, was studied. For comparison solutions of identical absorbance at the location of the absorption maximum (540 nm) were ultracentrifuged.

Solutions containing red chromophore, prepared according to the analytical prescription by reduction with AsH_3, were centrifuged in a capillary cell with a supernatant layer of pyridine. A triple peak appeared on the picture (Fig. 6/b). Since our red solution contains besides the red chromophore a large excess AgDDTC, when centrifuged against pyridine as solvent, the resultant of the concentration gradients of the red chromophore and AgDDTC is obtained. Therefore, we investigated what kinds of gradient curves are

developed, if the solution containing red chromophore, the pyridine solution of AgDDTC and pyridine are centrifuged in the possible variations against one another. Figure 6 shows the gradient curves of samples prepared according to the analytical prescription (9.34×10^{-8} mol As/5 cm^3 0.5% AgDDTC), developed at a speed of 30 000 rpm in a capillary cell at 20 °C, 4 minutes after the pouring on of the reference solution. The red solution gives against the AgDDTC absorbent a peak of negative position (Fig. 6/a), the AgDDTC absorbent against pyridine a peak of positive position (Fig. 6/c). The red solution gives against pyridine the resultant of the two former, the characteristic triple peak (Fig. 6/b). The cause of the peak of negative position is that the red chromophore has a negative refractivity-concentration ($dn/dc < 0$).

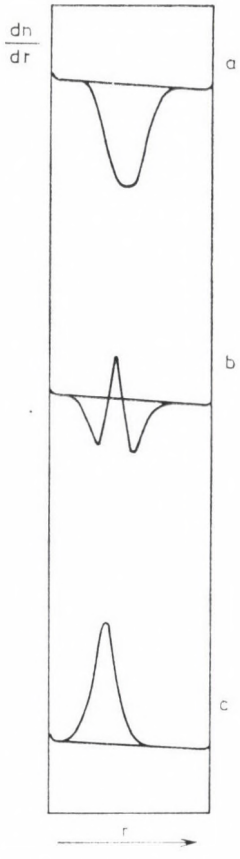


Fig. 6. Gradient curves of red chromophore-containing solution, prepared according to analytical prescription, after 4 minutes of centrifuging. (30000 rpm; 20 °C, capillary cell) a) red chromophore (9.34×10^{-8} mol (7 μg) As/5 cm^3 0.5% AgDDTC solution containing pyridine), against pyridine containing 0.5% AgDDTC reference solution, b) red chromophore in pyridine solution, against pyridine, c) 0.5% AgDDTC solution in pyridine, against pyridine

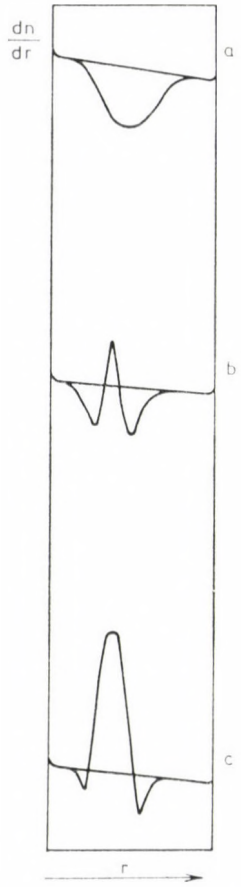


Fig. 7. Gradient curves of solutions containing red chromophore prepared from $As(DDTC)_3$ and AgDDTC by hydrogenation, after 4 minutes of centrifuging (30 000 rpm; 20 °C, capillary cell). Hydrogenation with 20 cm^3 of 10% $NaBH_4$ solution. a) solution containing red chromophore (1.64×10^{-5} mol $As(DDTC)_3$/5 cm^3 0.5% AgDDTC containing pyridine), against non-hydrogenated reference solution of the same composition, b) solution containing red chromophore, against pyridine, c) reference solution used in a), against pyridine

The gradient curve series of red chromophore solutions, prepared from $As(DDTC)_3$ and AgDDTC by hydrogenation (1.64×10^{-5} mol $As(DDTC)_3$/5 cm^3 0.5% AgDDTC), determined under identical conditions as above, is shown in Figs 7/a, b, c. A comparison of Figs 6 and 7 clearly shows that red chromophore solutions prepared by the two different methods behave in the same way during centrifuging.

Sedimentation rate constants could not be determined because of the high diffusion rate of the substances.

Solutions prepared in the two ways, but of identical absorbance at 540 nm, behaved similarly under the effect of changes in temperature, electrolytes, oxidizing and reducing agents.

Conclusions

It becomes evident from all these experiments that a chromophore of identical behaviour with the red chromophore formed during the determination of arsenic with silver diethyldithiocarbamate could be prepared by the reduction with hydrogen of the As(III)$(DDTC)_3$-containing solution of Ag(I)DDTC in pyridine. The ultraviolet and visible spectra of the solutions prepared in the two different ways are identical, chemical effects and ultracentrifuging produce the same changes in both types of systems. According to colloid chemical investigations neither of the solutions is to be considered colloidal.

It was shown that the silver content of AgDDTC can be reduced with hydrogen to metallic silver. However, silver(0) formed in the reaction remains in molecular solution in the presence of an equivalent quantity of As(III) $(DDTC)_3$ and a high excess of AgDDTC. The absence of any of the latter two compounds (as well as a lower than 300-fold AgDDTC excess) results in the precipitation of silver(0) in the form of metallic silver.

All this indicated that the red chromophore formed in the determination of arsenic with AgDDTC is a polynuclear dithiocarbamate complex, containing silver(0) and arsenic(III) as central atoms. The extreme conditions of chromophore formation (high AgDDTC and high reducing agent (hydrogen) excess, further the apolar solvent) made it impossible to determine the composition of the complex by equilibrium analysis.

Similar conclusions were drawn concerning the chromophore formed during antimony determination.

REFERENCES

[1] Vasak, V., Sedivec, V.: Chem. Listy, **46,** 341 (1952)
[2] Veres, S., Nemes-Vetéssy, Zs., Csikkel-Szolnoki, A.: Magy. Kém. Folyóirat, **90,** 351 (1984)
[3] Powers, G. W. Jun., Martin, R. L., Piehl, E. J.: Anal. Chem., **31,** 1589 (1959)
[4] Fresenius, W., Schneider, W.: Z. Anal. Chem., **203,** 417 (1964)
[5] Steinke, J.: Z. Anal. Chem., **240,** 184 (1968)
[6] Bode, H., Hachmann, K.: Z. Anal. Chem., **241,** 18 (1968)
[7] Koch, O. G., Koch-Dedic, G. A.: Handbuch der Spurenanalyse, Part **1,** p. 451. 1974.
[8] Upor, E., Mohai, M., Novák, Gy.: Fotometriás nyomelemzési módszerek (Photometric methods in trace analysis). Műszaki Könyvkiadó, Budapest, p. 143, (1978)
[9] Dubois, L., Teichman, T., Baker, C. J., Zdrojewski, A., Monkman, L. J.: Microchimica Acta, **1969,** 185
[10] Sandhu, S., Nelson, P.: Anal. Chem., **50,** 332 (1978)
[11] Bode, H., Hachmann, K.: Z. Anal. Chem., **229,** 161 (1967)

Acta Chimica Hungarica 123 (1—2), pp. 55—61 (1986)

RING-CHAIN TAUTOMERISM OF *ORTHO*-AMINO-SUBSTITUTED AROMATIC CARBOXYLIC ACID HYDRAZONES*, I

FORMATION OF 1,2,3,4-TETRAHYDRO-5*H*-1,3,4-BENZOTRIAZEPIN-5-ONES AND 5,6,7,8-TETRAHYDRO-4*H*-PYRAZOLO[3,4-*e*] [1,2,4]TRIAZEPIN-4-ONES

Melinda GÁL**, Endre TIHANYI and Péter DVORTSÁK

(Institute for Drug Research, H-1325 Budapest, P.O.B. 82)

Received May 22, 1985

In revised form October 14, 1985

Accepted for publication December 18, 1985

Reactions of *ortho*-amino-substituted aromatic carboxylic acid *N*-methylhydrazides **1a**, **1c** with acetaldehyde and simple ketones gave condensed triazepinones **4**, whereas the *N*-unsubstituted hydrazides **1b** furnished hydrazones **3**. The role of *N*-substitution is discussed and the difference between the aliphatic and aromatic series is pointed out.

The rearrangement of *ortho*-aminobenzoyl-*N*-methylhydrazones of β-dicarbonyl compounds was investigated previously and the existence of a ring-chain equilibrium in solution was observed by NMR spectroscopy [1]. The aim of the present work was to study this ring closure with simple monocarbonyl compounds and to utilize it in the synthesis of new heterocycles.

In ring-chain tautomerism the formation of the cyclic products initiated by nucleophilic attack upon the sp^2 carbon atom can be regarded, according to Baldwin [2], as an *endo*-trigonal process which is favoured in case of six- and seven-membered rings. The ring-chain tautomerism of 2-and 3-amino-aliphatic-hydrazones has been studied and the formation of hexahydro-1,2,4-triazine and imidazolidine rings and/or a ring-chain equilibrium of the hydrazones were demonstrated [3—6]. Interestingly, from 3-aminoalkyl-*N*-alkyl-hydrazones seven-membered rings could not be obtained [6].

Aromatic amino- and heteroaromatic ring NH-groups may also participiate in the ring-chain tautomerism [7—9]. Anthranilic acid hydrazones are known as "open chain" products [10—11], but the β-nitrogen-substituted hydrazides reacted with carbonyl compounds to afford 3-amino-1,2,3,4-tetrahydroquinazolin-4-ones [12—14].

The first example of the formation of a seven-membered ring from an *ortho*-amino-substituted aromatic hydrazide was the reaction of anthranilic

* Presented at the Annual Meeting of the Working Committee for Heterocyclic Chemistry of the Hungarian Academy of Sciences, Balatonfüred, 1984.

** To whom correspondence should be addressed.

acid *N*,*N*'-dimethylhydrazide with carbonyl compounds [15]. As the formation of a Schiff base on the *ortho*-amino groups was ruled out, the only possible direction of this reaction was ring closure.

In the present case the same reaction starting with anthranilic acid *N*-methylhydrazide **1a** is not unambiguous, because it may proceed either on the hydrazide β-nitrogen exclusively (leading to the hydrazone **3**), or with participation of the *ortho*-amino group (ring closure to **4**).

The reaction products of the *ortho*-amino-substituted aromatic carboxylic acid hydrazides **1a—c** with carbonyl compounds are shown in Scheme 1.

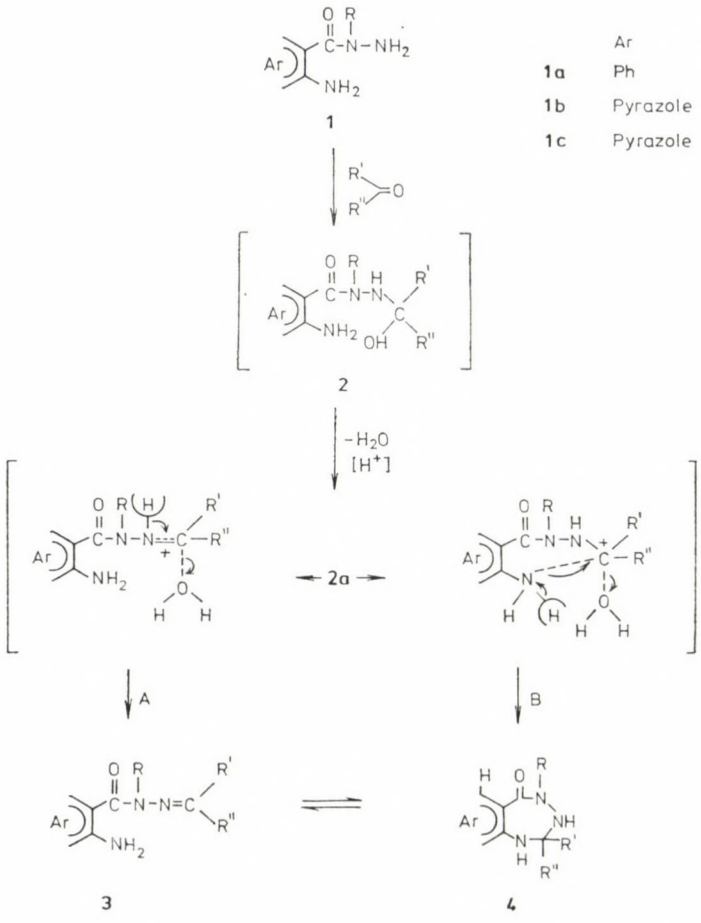
Anthranilic acid and 5-amino-1-phenyl-4-pyrazolecarboxylic acid *N*-methylhydrazides **1a, 1c** gave either cyclic products **4** (with acetaldehyde, acetone and cyclohexanone), or hydrazones **3** (with benzaldehyde), or a ring-chain equilibrium mixture of **3g** $\rightleftharpoons$ **4g** (with acetophenone). Pyrazolecarboxylic acid *N*-unsubstituted hydrazide **1b** gave the hydrazones **3**, similarly to the corresponding anthranilic hydrazide derivatives [10, 11].

The structures of the cyclic products **4** were proved by the NMR and UV spectra. In the case of the acetaldehyde and actone derivatives (**4a, 4b, 4c, 4d**) the ^{1}H-NMR spectra showed methyl signals at $\delta = 1.22$, 1.26, 1.33 and 1.40 ppm, respectively, corresponding to the sp^3 C—CH_3, in contrast to the hydrazone **3e** where the N=C—$(CH_3)_2$ methyl signals appeared at $\delta = 1.9$ and 2.0 ppm. In addition, in the ring closed products **4** there were two different NH signals, further in **4a** and **4c** the phenyl proton in *ortho* position to the carbonyl group appeared at $\delta = 7.61$ and 7.74 ppm, respectively, separately from the multiplet (6.58—6.8 ppm) of the other aromatic protons, thus indicating the fixed position of the carbonyl group. The same type of cyclic structure was established for **4f**, a pyrazole analogue, by its ^{13}C-NMR spectrum; the shift of the spiro carbon ($\delta = 73.3$ ppm) evidenced the ring formation.

There was a significant difference in the UV spectra of the hydrazones **3** and the cyclic products **4**. The characteristic $\pi \rightarrow \pi^*$ band of the hydrazones [11] was missing from the spectra of products **4**.

Hydrazones **3b** and **3c** could be hydrogenated over Pd/C to the corresponding *N*-methyl-*N*'-benzylhydrazides, while the condensed triazepinones **4** remained unaffected by the same procedure. No ring cleavage of the latter occurred either in polar solvents or at higher temperature.

The cyclization seems to be favoured in the interactions of *ortho*-amino-substituted aromatic carboxylic acid *N*-methylhydrazides **1a, 1c** and monocarbonyl compounds, in contrast with the *N*-unsubstituted hydrazides **1b**, also with the corresponding aliphatic analogues, where hydrazone formation [4] or a ring-chain equilibrium [5, 6] was observed (in the latter case even with the *N*-methyl substituted hydrazide derivatives). The difference can be explained by the reaction mechanism (Scheme 1) and by the relative stability of



	Ar	R
1a	Ph	Me
1b	Pyrazole	H
1c	Pyrazole	Me

	Ar	R	R'	R''
3a	Pyrazole	H	H	Me
3b	Ph	Me	H	Ph
3c	Pyrazole	Me	H	Ph
3d	Pyrazole	H	H	Ph
3e	Pyrazole	H	Me	Me
3f	Pyrazole	H	cyclohexyl	
3g	Ph	Me	Me	Ph
3h	Pyrazole	Me	Me	Ph
3i	Pyrazole	H	Me	Ph

	Ar	R	R'	R''
4a	Ph	Me	H	Me
4b	Pyrazole	Me	H	Me
4c	Ph	Me	Me	Me
4d	Pyrazole	Me	Me	Me
4e	Ph	Me	cyclohexyl	
4f	Pyrazole	Me	cyclohexyl	
4g	Ph	Me	Me	Ph

Scheme 1

Table I

Physical and spectral data for **3** *and* **4**

	Ar	R	R'	R''	M.p., °C	Yield, %	IR/KBr cm^{-1} νC=O	νCH$_2$	νNH
3a	Pyrazole	H	H	CH_3	102—105[f]	60	1614	—	3481 3416 3310 3231
3b	Ph	CH_3	H	Ph	131—133[d]	69	1615	—	3470 3360
3c	Pyrazole	CH_3	H	Ph	136—137[a]	97	1600	—	3400 3300
3d	Pyrazole	H	H	Ph	248—249[a]	69	1630	—	3390 3230— —3280b
3e	Pyrazole	H	CH_3	CH_3	202—203[e]	66	1620	—	3470 3290 3185
3f	Pyrazole	H	cyclohexyl		224—226[a]	97	1620	2940 2930 2850	3470 3340
3g	Ph	CH_3	CH_3	Ph	132—134[b]	86	1600	—	3340 3260
4g	Ph	CH_3	CH_3	Ph					
3h	Pyrazole	CH_3	CH_3	Ph	135—137[b]	86	1595	—	3427 3312
3i	Pyrazole	H	CH_3	Ph	173—174[a]	80	1622	—	3460 3377 3333 3167
4a	Ph	CH_3	H	CH_3	157—159[a]	68	1600— —1615b	—	3370 3315 3240
4b	Pyrazole	CH_3	H	CH_3	215—217[a]	76	1593	—	3314 3260
4c	Ph	CH_3	CH_3	CH_3	128—130[c]	64	1600	—	3300 3280
4d	Pyrazole	CH_3	CH_3	CH_3	177—179[e]	75	1580	—	3370 3230
4e	Ph	CH_3	cyclohexyl		132—134[b]	82	1615	2910 2830	3275 3240
4f	Pyrazole	CH_3	cyclohexyl		201—202[a]	97	1615	2920 2850	3280 3230

Solvent of recrystallization: [a]EtOH, [b]EtOH/H_2O, [c]benzene, [d]benzene/petroleum ether, [e]acetone, [f]chromatographed over silica, eluent EtOAc/MeOH 9 : 1

	¹H—NMR					UV/ethanol	
	Ar	R	R'	R"	NH	λ_{max}, nm	ε
g)	8.1 s[i] 7.3—7.55 m	9.7 b	3.48 m	2.03 d	5.78 b	245 268	21 021 18 223
g)	6.1—6.3 m 6.56—7.0 m	3.2 s	7.1 s	6.56—7.0 m	4.26 b	216 289	30 851 21 530
g)	7.75 s[i] 7.25—7.7 m	3.24 s	8.43 s	7.25—7.7 m	5.83 b	233 309	26 510 23 699
h)	8.19 s[i] 7.32—7.7 m	11.4 b	8.19 s	7.32—7.7 m	6.58 b	227 306	24 759 36 086
h)	8.16 s[i] 7.26—7.52 m	9.15 b	1.9 s	2.0 s	6.05 b	242 267	22 282 20 506
h)	8.12 s[i] 7.28—7.52 m	10.0 b	1.4—1.7 m	2.22—2.5 m	6.49 b	243 265 sh	22 840 17 159
g[1])	6.5—7.3 m	3.37 s	2.25 s	6.5—7.3 m	9.8 b		
g[1])	6.5—7.3 m 7.75 dd	3.37 s	1.65 s	6.5—7.3 m	4.2 b 4.5 b	240 321	15 556 2 860
g)	7.63 s[i] 7.38—7.52 m	3.31 s	2.42 s	7.38—7.52 m 7.9—8.0 m	5.98 b	242 313	29 539 4 934
h)	8.3 s[i] 7.4—7.87	10.3 b	2.4 s	7.4—7.87 m	6.77 b	234 299	19 841 20 160
h)	6.58—6.8 m 7.05—7.25 m 7.61 dd	3.1 s	4.43 m	1.22 s	6.15 b 5.9 b	219 328	20 958 2 581
h)	7.65 s[i] 7.35—7.5 m	3.05 s	4.4 m	1.26 d	5.8 d 6.8 b	240	19 451
h)	6.58—6.8 m 6.9—7.3 m 7.74 dd	3.26 s	1.33 s	1.33 s	3.8 b 4.31 b	218 319	21 592 2 216
h)	7.9 s[i] 7.42 s	3.15 s	1.40 s	1.40 s	4.3 b 4.8 b	240	20 456
g)	6.6—6.8 m 6.9—7.4 m 7.76 dd	3.26 s	1.6 b		3.83 b 4.26 b	218 319	20 948 2 158
g)	7.75 s[i] 7.4 s	3.15 s	1.2—1.9 m		4.2 b 4.7 b	240	18 901
j)	143.4 138.5 99.7 } k) 143.1 130.1 128.4 124.4	39.1	73.3 38.0 32.0 25.3 22.5				

Solvent for NMR: g) $CDCl_3$, h) DMSO-d_6 [1]ratio of tautomers 1 : 1 i) pyrazole ring-H, j) [13]C-NMR data, k) pyrazole ring-C shift

the products. Dehydration of the carbinolhydrazine **2** may proceed via the **2a** intermediate, when deprotonation of the β-hydrazino nitrogen leads to hydrazone **3** (route A). This step may be delayed in the presence of a more basic β-hydrazino nitrogen (R=Me). Then intramolecular nucleophilic attack of the *o*-amino group can initiate the ring closure (route B). No "open chain" product was observed in reaction mixtures of **4a—f**, because the aromatic amino character of the *o*-amino group can facilitate its deprotonation during ring formation. The 2-amino aliphatic analogues undergo such a deprotonation less readily, resulting in ring-chain equilibrium [5, 6]. The lack of substitution on the hydrazide moeity (R=H) in the series of 2-amino aliphatic carboxylic acids does not always hinder the ring formation, but in these exceptional cases it is the more nucleophilic 2-amino group which participates in the first attack during the reaction to give a carbinolamine intermediate on the 2-amino group. This intermediate can give rise to the formation of five-membered rings by the nucleophilic attack of the α-hydrazino nitrogen atom [4].

The possibility of conjugation between the azomethine and aromatic ring electrons contributes to the destabilization of the hetero ring in **4**, therefore the hydrazones **3b** and **3c** derived from benzaldehyde do not undergo cyclization. As a result of different effects (ring closure, possibility of conjugation, steric hindrance), the acetophenone derivatives exist in an equilibrium mixture **3g**$\rightleftharpoons$**4g**. The ratio of the **3g**$\rightleftharpoons$**4g** tautomers in chloroform solution changes after dissolution of the samples. The quantity of **3g** increases in time indicating that **4g** predominates in the solid state. The 1 : 1 equilibrium ratio is attained in 8 hours at room temperature.

All m.p.'s are uncorrected. IR spectra were measured using a Perkin Elmer 577 spectrometer. ^{1}H-NMR spectra were obtained at 60 MHz on a Jeol 60 HL spectrometer, using TMS as internal standard. ^{13}C-NMR spectra were recorded on a Varian XL-100 spectrometer (25.16 MHz).

Experimental

Reaction of *ortho*-amino-substituted aromatic carboxylic acid hydrazides 1 with carbonyl compounds

The hydrazides **1** were prepared by known methods [16—18]. The hydrazides **1** (3 mmol) were allowed to react with the carbonyl compounds in the presence of TsOH (0.01 g) under the following conditions:

3.3 mmol of acetaldehyde in ethanol (10 mL) at 0 °C;

3.3 mmol of acetophenone in benzene (15 mL) under reflux conditions; water was removed by azeotropic distillation;

1.5 mL of benzaldehyde at room temperature;

1.5 mL of cyclohexanone at room temperature;

10 mL of acetone, with reflux.

The crystals which precipitated were filtered off, washed with the reaction solvent (3×2 mL) or with petroleum ether (3×5 mL) and recrystallized. Melting points, yields and spectral data are shown in Table I.

*

The authors wish to thank Miss R. Andersen for technical assistance.

REFERENCES

[1] Gál, M., Fehér, Ö., Tihanyi, E., Horváth, Gy., Jerkovich, Gy.: Tetrahedron, **38,** 2933 (1982)
[2] Baldwin, J. E.: J. Chem. Soc., Chem. Commun., **1976,** 734
[3] Golbin, G. C., Balabina, T. A., Usakova, A. N., Ciomo, S. N.: Zh. Org. Khim., **10,** 2218 (1974)
[4] Lobanov, P. S., Poltorak, A. N., Potehin, A. A.: Zh. Org. Khim., **14,** 1086 (1978)
[5] Lobanov, P. S., Poltorak, A. N., Potehin, A. A.: Zh. Org. Khim., **16,** 2297 (1980)
[6] Lobanov, P. S., Solob, O. V., Potehin, A. A.: Zh. Org. Khim., **19,** 2310 (1983)
[7] Tóth, G., Hornyák, Gy., Lempert, K.: Chem. Ber., **110,** 1492 (1977)
[8] Szederkényi, F., Tihanyi, E., Gál, M., Fehér, Ö.: J. Chromatogr., **285,** 91 (1984)
[9] Ger. Offen., DE 3,242,610; Chem. Abstr., **99,** P 105286v (1983)
[10] Beilstein's Handbuch der organischen Chemie, **14,** 323, 334, III 894—895
[11] Grammaticakis, P.: Bull. Soc. Chim. Fr., **1957,** 1242
[12] Hirose, N., Kuriyama, S., Sohda, S., Sakaguchi, K., Yamamoto, H.: Chem. Pharm. Bull., **21,** 1005 (1973)
[13] U. S. Pat., 3,843,654; Chem. Abstr., **82,** 112098n (1975)
[14] U. S. Pat., 3,375,250; Chem. Abstr., **69,** 52170z (1968)
[15] Hromatka, O., Knollmüller, M., Krenmüller, F.: Monatsh. Chem., **100,** 941 (1968)
[16] Dornow, A., Hinz, E.: Chem. Ber., **91,** 1834 (1958)
[17] Smith, R. F., Bates, A. C., Battisi, A. J. Byrnes, P. G., Mroz, C. T., Smearing, T. J., Albrecht, F. X.: J. Org. Chem., **33,** 851 (1968)
[18] Leiby, R. W., Heindel, N. D.: Synth. Commun., **6,** 295 (1976)

Acta Chimica Hungarica 123 (1—2), pp. 63—67 (1986)

BOOK REVIEWS

C. Engelmann, G. Kraft, J. Paulwels, C. Vandercasteele: *Modern Methods for the Determination of Non-Metals in Non-Ferrous Metals*

Walter de Gruyter. Berlin/New York 1985. 410 pages

The book presents recent analytical methods suitable for the quantitative analysis of light non-metallic elements occurring in trace quantities in non-ferrous metals of wide-spread industrial use. The non-metallic elements investigated, O, N, C, B, S and P, are the metal impurities most often met. Non-ferrous metals investigated are: Al, Cu, Ti, Zr, Cr, Ag, Zn, Cd, Ta, Nb, Mo, W, Ni, Na, Be, V, Y, Sn and their more important alloys.

Of the 9 chapters of the book the first three deal with general theoretical and practical problems of analysis, while further chapters describe in detail concrete analytical processes.

The authors discuss first the effects of the presence and concentration of non-metallic elements on the more important technological properties (e.g. corrosion resistance, hardness, ductility, mechanical strength, conductibility, castability, utilizability in nuclear technology) of non-ferrous metals of industrial importance. In the major part of the cases discussed the non-metals are "impurities" of harmful character, but in certain cases they can be considered as useful "additives".

The next chapter deals with nuclear analytical methods, thought of prominent importance in the field investigated, with thermal and fast neutron activation analysis (NAA), charged particle activation analysis (CPAA), and photon activation analysis (PhAA). The ratios of this chapter reflect the intention of the authors to offer directly usable practical information for research and industrial analysis. The concise presentation of the theoretical basis of the processes is followed by the detailed description of the procedures, of the problems of calibration and measuring technique, and of the applicable methods of evaluation and calculation.

In conformity with practical purposes aimed at, and in accordance with wide experimental experiences of the authors, testified by numerous references, a separate chapter deals with problems of sample preparation, considered as the main source of error. In this chapter problems of surface analysis and the elimination of possible inconsistencies of surface and bulk analysis are also discussed.

Further chapters comprise methods of analysis of the selected non-metals, organized according to analytical methods and the more important matrices (pure metals and alloys). The primary commitment of the authors to nuclear analysis is reflected by the fact that all the other methods are discussed under the title "chemical methods"; beginning with titrimetry this includes also emission and absorption optical spectroscopic methods and mass spectrometry. Technical description of measurements, prescriptions of methods requiring chemical separation are given, with the exactness of a handbook, both for "chemical" and nuclear methods (NAA, CPAA, PhAA), discussed separately. Problems of calibration standards and error analysis are dealt with in detail corresponding to their importance. All the chapters are closed by the comparative evaluation of the methods discussed. Where possible, this is based on the results of intercomparisons organized for tests of reference materials circulated by CBR (Community Bureau of References), while less attention is given to analysis results of other, e.g. NBS, reference materials.

The excellently organized book covers a large material, and gives very useful practical information to research and industrial chemists of the given field. It should be emphasized that among the numerous tabulated and separately listed data there is scarcely any clerical error or misprint.

Department of Applied Chemistry,
Technical University, Budapest

Lajos Gy. NAGY

I. Hargittai: *The Structure of Volatile Sulphur Compounds*

Akadémiai Kiadó, Budapest, 1985, 316 pages

This work can be regarded as a special chapter of structural inorganic chemistry written with the purpose to compile accurate S—X, S=X, etc. distances formed by sulphur atoms with X = H, B, C, O, Cl, etc. in different valence states, coordinations and environments described in term of atomic distances, bond angles and internal rotations. The author who has been actively involved in the structure analysis of numerous volatile sulphur compounds since 1967 by the use of the electron diffraction technique, now as an expert of the field guides the reader through these structures with great skill. He is equally at home in the application of microwave spectroscopy, the second powerful technique of molecular studies in the gaseous state. He does not miss to point out convincingly that the majority of the volatile molecules being built up only by a few atoms permit very accurate measurements of atomic distances; e.g. such a simple molecules as SCl_2 enabled scientists to observe difference between the S—Cl distance assumed in the ground state (201.525 pm) and the excited vibrational state (201.538 pm). The author convinces the reader about the advantages of combining electrondiffraction and microwave information in the determination of such structures where there is strong correlation among the parameters (e.g. sulphones. p. 169).

In order to elucidate the structural relationships — whenever it is possible — he tries to present correlations established between the geometrical parameters of the molecules and various physical constants, e.g. electronegativities or spectroscopic data, and to use the results of quantum chemistry (semiempirical and ab initio calculations), as well. Of course, it is admitted that due to their excellent descriptiveless, two simple qualitative models have been mostly used throughout this work: Gillespie's VSEPR theorem and Bartell's atom-atom non-bonded interactions.

After a concise and well-written introduction (10 pages) the compounds of known structures are discussed in five chapters accompanied by a rich bibliography (pp. 275—293) reporting more than 800 publications.

Chapter *1* (pp. 11—39) reports the structures with one-coordinated sulphur, starting with the most frequently observed C=S double bonds formed with C—sp^2 and C—sp atoms.

In Chapter *2* (pp. 40—136) Hargittai presents a great variety of volatile structures with two-coordinated sulphur atom. Starting with symmetrical sulphides, he deals with saturated and aromatic rings incorporating S atom(s) up to the structures with =S= and ≡S— bond systems.

In the short Chapter *3* (pp. 137—162) molecules with three-coordinated sulphur are described. A dozen of vapour-phase sulphoxides (including selenium analogues), three simple thionyl compounds and a few (seven) cyclic sulphites (and selenites) are discussed here.

Chapter *4* (pp. 163—264) offers again a rich collection of structure determinations together with manifold empirical and theoretical investigations. Of the reported molecules with four-coordinated sulphur, sulphones are perhaps the most important. Here the author also summarizes his studies on the correlation between analogous sulphones, sulphoxides. sulphides and related systems.

Since there are only a few volatile compounds with five- and six-coordinated sulphur (the majority of them can be and have already been studied only in crystalline state by X-ray diffraction) their structures (altogether five including SeF_6) are reported together in Chapter *5* (pp. 265—274).

Some remarks: It is misleading if differences in bond lengths, bond angles, etc. smaller than their errors are discussed, as can be seen, e.g., in Fig. 66, where such a small differences as 1.6 pm is regarded as significant versus $\sigma = 2.0$ pm for the two distances compared. No agreement or disagreement between atomic distances, bond angles and internal rotations observed by similar or different techniques can be established without scrutinizing their errors (e.g. 3 σ test, etc.). Consequently, it is rather embarrassing to notice that the standard deviations (or other error parameters) of numerous atomic distances, etc. are missing (cf. Tables 4, 7, 17, 30, 51, 64, 80, etc.).

Question: were they just deliberately omitted as in the case of structure *c* in Table 51, or were they not disclosed in the original sources? Even in the latter case at least their magnitudes ought to have been estimated.

For the same reason, the conclusion that the r (O . . . O) distances measured in crystalline state by X-rays are shorter (presumably due to intermolecular interactions?) than the constant value of 248.4 pm, determined in volatile sulphones by MW spectroscopy, is not convincing. Apart from the fact that the reliability of the structural parameters of 36 randomly selected X-ray analyses (Table 77) cannot be estimated without their e.s.d's, Hargittai's statement is

querried immediately by its own example cited from Sands (p. 219), where the S=O distances are corrected against thermal motions resulting in $r(O \ldots O) = 249.2$ pm! Similarly, if the mean S=O distance of the crystal structures listed in Table 77 (143.6 (10) pm) is increased by the thermal correction given by Sands on a cautious 50% probability level ($\Delta = 1.1$ pm), then — using the mean O=S=O angle of 118.5 (13)° (practically uninfluenced by the thermal correction) — the corresponding $r(O \ldots O)$ distance of 248.7 pm also hardly differs from the mean of the MW and $r(O \ldots O)$ distances listed in Table 76. Further, the sum of the uncorrected mean of the 35 $r(O \ldots O)$ and its mean e.s.d. is also 248.6 pm. Unfortunately, the accuracy of the randomly selected X-ray data (most of them have been transplanted without any revision from an earlier work of Hargittai: *Sulphone Molecular Structures*, Lecture Notes in Chemistry, Springer Verlag, Berlin, 1978) is questionable since 25 of the 36 structures were determined more than 10 years ago mainly on the basis of film technique. Accordingly, if the author wants to discuss such a question as intermolecular effects on the basis of "< 2 pm" difference and if this question has real significance at all, then he must be very precise using a few dozen of new and accurate sulphone structures selected with high criteria (e.g. $R < 0.05$ for no less than 2500 observed reflections, etc.), from the Cambridge Crystallographic Data Base which increases annually by approximately 5000 new crystal structures; among them there are hundreds of organosulphur compounds (since January 1980 598 novel sulphone and sulphoxide structures have been reported by the end of 1985).

This altogether well-written book is a good compillation of the simple structures containing S atom(s) and useful correlations between their parameters. In addition to the workers of the field, spectroscopists (IR, UV, etc.), some of the quantum chemists and others may also use it well.

Alajos KÁLMÁN

Central Research Institute for Chemistry, Hungarian Academy of Sciences, Budapest

Metal Ions in Biological Systems. Vol. 19. Antibiotics and Their Complexes

Ed. H. Sigel, Marcel Dekker, New York and Basel, 1985, XXVI + 429 pp.

Ionophores are substances of moderate molecular weights and are produced by various microorganism. They promote the translocation of metal cations from one side of a lipid bilayer membrane to the other. Some ionophores function as carriers and others as pore- formers or ion channels. Several of these compounds, also termed antibiotics, are used against a variety of bacterial infections. The present volume is devoted to these biologically important compounds, to the more thorough understanding of their coordination chemistry and action, and to stimulate further researches.

The volume opens a historical account of the discovery of ionophores by B. C. Pressman. In the following chapter R. B. Martin describes the properties of tetracyclines and daunorubicin; their structures, and proton- and metal-binding abilities (75 references).

In chapter *1* the author, J. Hajdú, writes on the "Interaction of metal ions with streptonigrin and biological properties of the complexes". Streptonigrin is one of the most effective agents for the treatment of human cancers. The author deals with the structural and chemical properties of streptonigrin and its metal complexes, and with the biological activity and antitumor action of streptonigrin. It appears from the results shown in the chapter, that an approach based on understanding the chemistry involved in the mechanism of action of the drug should be a promising route to improve its chemotherapeutic properties (56 references).

"Bleomycin antibiotics: metal complexes and their biological action" is the title of chapter *4*. The authors (Y. Sugiura, T. Takita and H. Umezawa) write on the structural and synthetic aspects of bleomycin, on its metal complexes, on the redox cycle of the iron-bleomycin complex, on the interaction of DNA of its complexes. They also discuss the molecular mechanism of bleomycin action (65 references).

Chapter *5* authored by K. R. K. Easwaran is entitled: "Interaction between valinomycin and metal ions." Among the neutral ionophores valinomycin has emerged as an extraordinary molecule due to its high specificity for K^+ over Na^+. The monograph deals with the structure and conformation of free valinomycin and its metal ion complexes, and with the role of valinomycin- metal ion complexes in transmembrane ion transport (81 references).

A separate chapter is devoted to beauvericin and the other enniatins (L. K. Steinrauf). These compounds have provided an interesting opportunity to explore some of the aspects of

the membrane transport behaviour of free carriers. The author discusses their ion-binding properties, the mechanism of their transport across the membrane, and deals briefly with the analogs of enniatins (54 references).

Chapter 7 authored by J. F. Hinton and R. E. Koeppe is on the "Complexing properties of gramicidins". Their ion-complexing and transport properties are discussed, and much is reported on the ion selectivity of gramicidin channels (122 references).

"Nactins: their complexes and biological properties" written by Y. Nawata, K. Ando and Y. Iitaka is the title of chapter *8*. Here again emphasize is laid on their molecular structure and complexes (including also ternary complexes). A brief subchapter is devoted to their biological properties (49 references).

G. R. Painter and B. C. Pressman are the authors of chapter *9:* "Cation complexes of the monovalent and polyvalent carboxylic ionophores: lasalocid (X-537A), monensin, A23187 (calcimycin), and related antibiotics." The subchapters have the following titles: Structure of ionophore-cation inclusion complexes; Techniques for measuring equilibrium ionophore — ion affinities; Carboxylic ionophoric — mediated ion transport; Biological test systems; Conformational aspects of ion capture and membrane transport; Biological application of ionophore (130 references).

"Complexes of D-cycloserine and related amino acids with antibiotic properties" (p. O'Brien) is the title of chapter *10*. The author writes on their metal ion coordination properties, mode of action, and organic chemistry (51 references).

In chapter *11* J. B. Neilands and J. R. Valenta deal with "Iron-containing antibiotics". They discuss the mechanisms of antibiosis related to iron, the prospects for chemotherapeutic intervention, the iron(II)- and iron(III)-complexes of a variety of antibioties and finally miscellaneous compounds including among others pulcherrimin, mycelianamide, hadacidin, lipoxamycin, actinonin and thiohydroxamic acids (70 references).

The volume closes with a consideration of factors governing the selective cation — ionophore interactions (H. Gresh and A. Pullman). The author present an approach how to compute on a firmer basis, the main components of the association and their interplay for a certain number of representative ionophore-ligand complexes.

First they outline the methodology, then write on the selective binding of alkali cations by valinomycin, and that of K^+, Na^+ and NH_4^+ by nonactin. They deal also with the selective binding of Mg^{2+} and Ca^{2+} by ionophore A23187, with the structural properties of some ionophores, the energy profiles for single and double occupancy by Na^+ of the gramicidin A channel (131 references).

Volume *19* of this excellent series of books on the role of metal ions in biological system is a source of novel informations, and can be highly recommended to biochemists, biologists, biophysicists and also to chemists interested in life processes.

Endre Kőrös

Institute of Inorganic and
Analytical Chemistry,
L. Eötvös University of Budapest,
Budapest

Chromatography, the state of the art. Volumes I—II

Edited by H. Kalász and L. S. Ettre, Akadémiai Kiadó, Budapest, 1985, 903 pages
ISBN 963 05 4081 9

This two-volumed work, published as Vol. 27 of the series "Symposia Biologica Hungarica", contains the papers presented at the Chromatography Conference held in Budapest, June 1—3, 1983.

The book consists of 62 papers discussing the development and applications of various chromatographic techniques.

The work includes 9 chapters dealing with "Theoretical Aspects", "Stationary Phases for Chromatography", "Chromatography of Amines and Amino Acids", "Separation of Peptides and Proteins", "Separation of Drugs and Metabolites", "Thin-layer Chromatography", "Gas Chromatography", "Calculation and Optimization Methods", as well as a chapter entitled "Various Topics".

Several studies in the volume deal with the most recent theoretical considerations and the development of various chromatographic techniques. Many papers are concerned with the separation and determination of substances having biological activity; other articles report

on the newest results of the investigation of amines, nucleotides, amino acids, peptides, proteins, steroids, various drugs, their metabolites, etc.

Although heterogeneous from the point of view of the chromatographer, the book well illustrates how widely chromatographic techniques have found use in studies of different substances of biological interest.

The book gives an overview of the development and applications of different chromatographic techniques. It should be mentioned, however, that the time of two years which elapsed between the conference and the publication seems to be too long in such a rapidly developing field as chromatographic techniques.

The editors did a remarkable job in the arrangement of the book and in correcting the papers of different quality. The book is well redacted, the printing is well legible. The figures usefully illustrate the topics discussed. The list of contributors and the subject index given at the end of Vol. 2 are of great assistance in finding contributions to various topics.

This book should be welcomed not only by chromatographers, but also by chemists, biochemists and physicians working in different fields of biology and medical research.

Department of Chemical Technology, Technical University, Budapest

László SZEPESY

D. N. Kursanov, Z. N. Parnes, M. I. Kalinkin and N. M. Loim: *Ionic Hydrogenation and Related Reactions*

Harwood Academic Publishers, Chur, London, Paris, New York, 1985. xv + 252 pages

This book is the first volume of the Soviet Scientific Reviews Supplement Series: Chemistry, edited by M. E. Vol'pin. The intention of the new series is to present monographs of Soviet Scientists covering those areas of chemistry in which their contributions have been particularly significant.

Ionic hydrogenation is based on the ability of many organic compounds to undergo protonation with the formation of carbocations which easily abstract a hydride ion from different compounds. As a result hydrogenation of the double bond takes place. The most frequently used combination of proton and hydride donors is the $CF_3COOH + HSiEt_3$ couple.

The book treats this subject in 8 chapters. Four of these are devoted to the hydrogenation of different types of unsaturated organic compounds (unsaturated hydrocarbons, heterocyclic compounds, compounds with a C=O bond and compounds containing other types of multiple bonds). One chapter is concerned with the mechanism of the reaction. The last three chapters contain information on some modified applications of the general principle outlined above: ionic dehydrogenation and disproportionation, ionic hydroalkylation and alkylation, and catalytic ionic hydrogenation. The Appendix gives detailed descriptions of 27 individual applications of ionic hydrogenation for the preparation of organic compounds. About 450 references lead the reader to the original scientific literature.

The most important feature of the book is that it directs attention to this somewhat unusual type of reduction. Not much had been known in this field before the authors started their systematic and broad investigation of ionic hydrogenation. Now it can be seen that this is a convenient preparative method in organic chemistry, with a very distinctive selectivity for internal olefinic double bonds with three substituents — a group of substrates usually difficult to hydrogenate by more conventional means.

In some cases the boundaries between catalytic hydrogenation and ionic hydrogenation seem to be diffuse, as can be clearly seen from the chapter on catalytic ionic hydrogenation. The reader even may have the impression that the authors prefer ionic mechanisms also in such cases where such explanations may be rather disputable. Nevertheless, the unusual view of the authors on several of these examples is stimulative and certainly will initiate new research.

Unfortunately, the book does not contain author or subject indexes, which impairs its use as a handbook. Nevertheless, it is a very useful addition to the organic chemist's bookshelf since — as far as known to the reference — it is the only book available on this special type of hydrogenation.

László MARKÓ

Veszprém University of Chemical Engineering, Department of Organic Chemistry, Veszprém

CHROMATOGRAPHY '84

Proceedings of the Advances in Liquid Chromatography
Szeged, Hungary, September 10-14, 1984

Edited by
H. Kalász and L. S. Ettre

In English. 1986. XII + 612 pages. 17 × 25 cm
Hardcover approx. $59.00
ISBN 963 05 4341 9
Symposia Biologica Hungarica 31

Authors from Canada, Czechoslovakia, Egypt, the German Democratic Republic, Hungary, Poland, Romania, Sweden, the USA and the USSR submitted their results mainly in the field of applied column chromatography. Especially the synthesis and characteristics of stationary phases, chromatographic separation of drugs, metabolites, biologically active and endogenous compounds were the targets of the investigations. At the same time insight into the general and theoretical aspects of chromatography, as computer assisted data evaluation, displacement chromatography, electrochemical detection, etc., are also given in the book.

A total of 54 papers has been divided into 5 chapters: "General topics", "Stationary phases for chromatography and their interactions", "Drugs, metabolites, biologically active compounds and endogenous substances", "Separation of amino acids, polypeptides and nucleotides" and "Separation of substances of various classes" yield 7, 12, 23, 8 and 4 papers, respectively.

This book gives up-to-date papers on the separation of several special and very important substance-groups, in-depth studies on the chromatography of amino acids, peptides, drugs, metabolites, nucleotides, interesting papers on stationary phases. The volume may count on the interest of chemists and biochemists working in theoretical and practical fields alike.

Akadémiai Kiadó, Budapest

Chromatography. The State of the Art Vols 1-2

Proceedings of the Budapest Chromatography Conference June 1–3, 1983 Budapest, Hungary

Symposia Biologica Hungarica Vol. 27
Edited by
H. Kalász and *L. S. Ettre*
In English. 1985. 902 pages. 315 figures. 127 tables.
17×25 cm. Hardcover $75.00/DM 225,—/£52.50
ISBN 963 05 4081 9

The volume containts the papers presented at the different sessions of the Budapest Chromatography Conference, which was held in Budapest, Hungary, through June 1–3, 1983.

The book includes altogether 9 chapters dealing with "Theoretical Aspects", "Stationary Phases for Chromatography", "Chromatography of Amines and Amino Acids", "Separation of Peptides and Proteins", "Separation of Drugs and Metabolites", "Thin-layer Chromatography", "Gas Chromatography", "Calculation and Optimization Methods", as well as "Various Topics".

The papers in the book present the most recent theoretical considerations, practical approaches and results as well as the trends of the latest development. Several papers deal with fields closely connected to biology or medicine (as the fate, action, analysis of drugs and metabolites, isolation of biologically active natural products), some other articles detail such very important theoretical or practical fields as HPLC of nucleotides, amines, amino acids, peptides, proteins, steroids, etc., forced-flow thin-layer chromatography, ion-exchange thin-layer chromatography, capillary liquid chromatography, short and effective columns, etc. These fields may be very interesting to readers who are involved either in chromatography or in separation dealing with any substances with a biological activity.

Since the authors of the papers are either specialists of chromatography or the users of the separation methods in their every-day work, the papers published in the book are up-to-date, and the figures and tables help the understanding of the written text.

AKADÉMIAI KIADÓ
BUDAPEST

Distributors:
KULTURA
Hungarian Foreign Trading Co.
P. O. B. 149.
H-1389 Budapest
Hungary

RECENT PROGRESS IN POLYAMINE RESEARCH

Edited by
L. Selmeci, M. E. Brosnan and *N. Seiler*

In English. 1985. XII + 634 pages, 156 figures. 92 tables.
17×15 cm. Hardcover $65.00/DM 164,—/£45.50
ISBN 963 05 4243 9

This volume provides an overview of current research efforts in the exciting and rapidly expanding field of polyamines. Attention is focussed on aspects considered most up-to-date within the scope of this subject. The book discusses the general and posttranslational regulation of ornithine decarboxylase and related enzymes, the regulation of polyamine levels and control functions of the polyamines, the enzymes and inhibitors of polyamine biosynthesis and catabolism, the roles of the polyamines in cellular differentiation and tissue regeneration, the significance of the polyamines in cancerogenesis and clinical oncology, the metabolism of the polyamines in bacteria, the roles of polyamines in plant physiology, macromolecular polyamine derivatives and methods of polyamine research.

This volume will be of interest to biochemists, molecular biologists, molecular geneticists, cellular physiologists, plant physiologists, pharmacologists, microbiologists and oncologists.

AKADÉMIAI KIADÓ
BUDAPEST

Distributors:
KULTURA Hungarian Foreign Trading Co.
P. O. B. 149
H-1389 Budapest
Hungary

Akadémiai Kiadó presents

EUROANALYSIS

Volume V

Reviews on Analytical Chemistry

Edited by
A. HULANICKI

Series Editors:
W. FRESENIUS and **H. MALISSA**

In English. Forthcoming 1986. 192 pages.
17 × 25 cm. Hardcover approx. $ 19.00
ISBN 963 05 4186 6

Euroanalysis is a triennial conference of the Federation of European Chemical Societies (FECS), produced by the Working Party on Analytical Chemistry of FECS.
This volume contains a collection of invited lectures presented at Euroanalysis V, Cracow, Poland, 26–31 August, 1984. The Plenary Lectures dealt with the modern methods of automatic analysis, including electroanalytical techniques, environmental problems, chemical analysis of extraterrestrial materials and the current status and future trends in the application of computer systems in the laboratory.
The problems of trace analysis, qualitative analysis of organic materials, continuous analysis of process streams, speciation in organic surface analysis and the lectures devoted to environmental problems – the topics of the seven Keynote Lectures– indicate that the attention of analytical chemists seems to have been focused on those modern methods of analysis, which were developed from the modern techniques and mathematics.
This volume gives an overview of the present state of European analytical chemistry and will be of great interest to scientists seeking to obtain an insight into the most important techniques and their application in analytical chemistry.

AKADÉMIAI KIADÓ
Budapest

THE PHARMACOLOGY OF BENZOPYRONE DERIVATIVES AND RELATED COMPOUNDS

by

M. Gábor

In English. 1985. appr. 228 pages, 10 figures, 4 tables
17 × 25 cm. Hardcover appr. $25.00
ISBN 963 05 4124 6

Research into benzopyrone derivatives has enjoyed a renaissance during the past twenty years. It has become an increasingly more difficult task to follow the chemical and pharmacological monographs dealing with this subject, not to mention the countless publications in various journals. This new book, therefore, fills a gap, as it discusses the pharmacological effects not only of the benzo-γ-pyrones, but also of benzo-α-pyrone and related benzofuran derivatives.

The monograph consists of three parts:

I. Pharmacokinetics of benzopyrone derivatives and related compounds.
II. Effects of benzopyrone derivatives on various enzyme activities.
III. Pharmacology of benzopyrone derivatives and related compounds.

The monograph is not only an indispensable source-book for those dealing with this topic, but also serves as a guide to research in the future.

Its presentation of the most up-to-date research being carried out throughout the world, together with its compilation of nearly 800 literature references, make this long-needed work of great value for the physician, the chemist, the pharmacist and the clinical pharmacologist.

1828

AKADÉMIAI KIADÓ • BUDAPEST

Text

The text of the paper should be concise. The description of new compounds (in the Experimental) must include the complete analytical data. Special attention must be paid to structural formulas given within the text. Complicated (non-linear) formulas should be drawn on separate sheets of paper and their position in the text should be clearly marked. The numbering of formulas and equations (in parentheses on the right-hand side) is only needed if they are referred to in the text. Units should conform to the International System of Units (SI). In nomenclature the rules of the I.U.P.A.C. are accepted as standard. Symbols for physical quantities are printed in italic type and should, therefore, be underlined in the manuscript.

References

References should be numbered in order of appearance in the text (where the reference number appears in brackets) and listed at the end of the paper. The reference list, too, should by typed double-spaced. Journal titles are to be abbreviated as defined by the Chemical Abstracts Service Source Index.

Examples:

[1] Brossi, A., Lindlar, H., Walter, M., Schneider, O.: Helv. Chim. Acta, **41**, 119 (1958)
[2] Parr, R. G.: Quantum Theory of Molecular Electronic Structure, Benjamin, New York 1964
[3] Warshel, A.: in Modern Theoretical Chemistry, Vol. 7, Part A (Ed. G. A. Segal), Plenum Press, New York 1977

Tables

Each table should be given a Roman number and a brief informative title. Structural formulas should not be used in column headings or in the body of tables.

Figures

Figures should be numbered consecutively with Arabic numerals. Their approximate place should be indicated in the text on the margin. All figures must be identified on the back by the author's name and the figure number in pencil. Standard symbols (such as circles, triangles, squares) are to be used on line-drawings to denote the points determined experimentally. Line-drawings must not contain structural formulas and comments. Spectra or relevant segments thereof, chromatograms, and X-ray diffraction patterns will be reproduced only if concise numerical summaries are inadequate to replace them. Drawings and graphs should be prepared in black ink on good-quality white or tracing paper. Photographs should be submitted on glossy paper as high-contrast copies. Xerox or similar copies are not suitable for reproduction, but may be used for duplicate copies.

Redrawn illustrations will be sent to the authors for checking. No corrections of figures will, therefore, be accepted in the proofs.

Submission of manuscript

After having completed the corrections suggested by the referees and editors, the final manuscript should be submitted in duplicate, in a form ready for publication. If the corrected manuscript is not returned to the editors *within six weeks*, the intended publication of the paper will be regarded as withdrawn by the authors.

Page charge will not be assessed for the publication, however, authors from overseas countries must contribute to the postage of correspondence by sending, together with the manuscript, international postal coupons to the value of U.S. $ 10.—

Proofs and reprints

A set of proofs will be sent to the submitting author. The proofs must be returned within 48 hours of receipt. Late return may cause a delay in the publication of the paper. 100 reprints will be supplied to the authors free of charge.

Periodicals of the Hungarian Academy of Sciences are obtainable at the following addresses:

AUSTRALIA
C.B.D. LIBRARY AND SUBSCRIPTION SERVICE
Box 4886, G.P.O., *Sydney N.S.W. 2001*
COSMOS BOOKSHOP, 145 Ackland Street
St. Kilda (Melbourne), Victoria 3182

AUSTRIA
GLOBUS, Höchstädtplatz 3, *1206 Wien XX*

BELGIUM
OFFICE INTERNATIONAL DE LIBRAIRIE
30 Avenue Marnix, *1050 Bruxelles*
LIBRAIRIE DU MONDE ENTIER
162 rue du Midi, *1000 Bruxelles*

BULGARIA
HEMUS, Bulvar Ruszki 6, *Sofia*

CANADA
PANNONIA BOOKS, P.O. Box 1017
Postal Station "B", *Toronto, Ontario M5T 2T8*

CHINA
CNPICOR, Periodical Department, P.O. Box 50
Peking

CZECHOSLOVAKIA
MAD'ARSKÁ KULTURA, Národní třida 22
115 66 Praha
PNS DOVOZ TISKU, Vinohradská 46, *Praha 2*
PNS DOVOZ TLAČE, *Bratislava 2*

DENMARK
EJNAR MUNKSGAARD, Norregade 6
1165 Copenhagen K

FEDERAL REPUBLIC OF GERMANY
KUNST UND WISSEN ERICH BIEBER
Postfach 46, *7000 Stuttgart 1*

FINLAND
AKATEEMINEN KIRJAKAUPPA, P.O. Box 128
SF-00101 Helsinki 10

FRANCE
DAWSON-FRANCE S. A., B. P. 40, *91121 Palaiseau*
EUROPÉRIODIQUES S. A., 31 Avenue de Versailles, *78170 La Celle St. Cloud*
OFFICE INTERNATIONAL DE DOCUMENTATION ET LIBRAIRIE, 48 rue Gay-Lussac
75240 Paris Cedex 05

GERMAN DEMOCRATIC REPUBLIC
HAUS DER UNGARISCHEN KULTUR
Karl Liebknecht-Straße 9, *DDR-102 Berlin*
DEUTSCHE POST ZEITUNGSVERTRIEBSAMT
Sraße der Pariser Kommüne 3–4, *DDR-104 Berlin*

GREAT BRITAIN
BLACKWELL'S PERIODICALS DIVISION
Hythe Bridge Street, *Oxford OX1 2ET*
BUMPUS, HALDANE AND MAXWELL LTD.
Cowper Works, *Olney, Bucks MK46 4BN*
COLLET'S HOLDINGS LTD., Denington Estate
Wellingborough, Northants NN8 2QT
WM. DAWSON AND SONS LTD., Cannon House
Folkstone, Kent CT19 5EE
H. K. LEWIS AND CO., 136 Gower Street
London WC1E 6BS

GREECE
KOSTARAKIS BROTHERS INTERNATIONAL BOOKSELLERS, 2 Hippokratous Street, *Athens-143*

HOLLAND
MEULENHOFF-BRUNA B.V., Beulingstraat 2,
Amsterdam
MARTINUS NIJHOFF B.V.
Lange Voorhout 9–11, *Den Haag*
SWETS SUBSCRIPTION SERVICE
347b Heereweg, *Lisse*

INDIA
ALLIED PUBLISHING PRIVATE LTD., 13/14
Asaf Ali Road, *New Delhi 110001*
150 B-6 Mount Road, *Madras 600002*
INTERNATIONAL BOOK HOUSE PVT. LTD.
Madame Cama Road, *Bombay 400039*
THE STATE TRADING CORPORATION OF INDIA LTD., Books Import Division, Chandralok
36 Janpath, *New Delhi 110001*

ITALY
INTERSCIENTIA, Via Mazzé 28, *10149 Torino*
LIBRERIA COMMISSIONARIA SANSONI, Via Lamarmora 45, *50121 Firenze*
SANTO VANASIA, Via M. Macchi 58
20124 Milano
D. E. A., Via Lima 28, *00198 Roma*

JAPAN
KINOKUNIYA BOOK-STORE CO. LTD.
17-7 Shinjuku 3 chome, Shinjuku-ku, *Tokyo 160-91*
MARUZEN COMPANY LTD., Book Department, P.O. Box 5050 Tokyo International, *Tokyo 100-31*
NAUKA LTD. IMPORT DEPARTMENT
2-30-19 Minami Ikebukuro, Toshima-ku, *Tokyo 171*

KOREA
CHULPANMUL, *Phenjan*

NORWAY
TANUM-TIDSKRIFT-SENTRALEN A.S., Karl Johansgatan 41–43, *1000 Oslo*

POLAND
WĘGIERSKI INSTYTUT KULTURY, Marszałkowska 80, *00-517 Warszawa*
CKP I W, ul. Towarowa 28, *00-958 Warszawa*

ROUMANIA
D. E. P., *Bucureşti*
ILEXIM, Calea Grivitei 64–66, *Bucureşti*

SOVIET UNION
SOJUZPECHAT — IMPORT, *Moscow*
and the post offices in each town
MEZHDUNARODNAYA KNIGA, *Moscow G-200*

SPAIN
DIAZ DE SANTOS, Lagasca 95, *Madrid 6*

SWEDEN
ALMQVIST AND WIKSELL, Gamla Brogatan 26
101 20 Stockholm
GUMPERTS UNIVERSITETSBOKHANDEL AB
Box 346, *401 25 Göteborg 1*

SWITZERLAND
KARGER LIBRI AG, Petersgraben 31, *4011 Basel*

USA
EBSCO SUBSCRIPTION SERVICES
P.O. Box 1943, *Birmingham, Alabama 35201*
F. W. FAXON COMPANY, INC.
15 Southwest Park, *Westwood Mass. 02090*
THE MOORE-COTTRELL SUBSCRIPTION AGENCIES, *North Cohocton, N. Y. 14868*
READ-MORE PUBLICATIONS, INC.
140 Cedar Street, *New York, N. Y. 10006*
STECHERT-MACMILLAN, INC.
7250 Westfield Avenue, *Pennsauken N. J. 08110*

YUGOSLAVIA
JUGOSLOVENSKA KNJIGA, Terazije 27, *Beograd*
FORUM, Vojvode Mišića 1, *21000 Novi Sad*

Acta Chimica Hungarica

VOLUME 123, NUMBERS 3–4, NOVEMBER–DECEMBER 1986

Akadémiai Kiadó, Budapest
ACTA CHIM. HUNG. ACHUDC 123 (3–4) 69–160 (1986) HU ISSN 0231–3146

ACTA CHIMICA HUNGARICA

A JOURNAL OF THE HUNGARIAN ACADEMY OF SCIENCES

Acta Chimica publishes original reports on all aspects of chemistry in English.

Acta Chimica is published in three volumes per year, each volume consisting of four issues, by

AKADÉMIAI KIADÓ

Publishing House of the Hungarian Academy of Sciences
H-1054 Budapest, Alkotmány u. 21.

Manuscripts and editorial correspondence should be addressed to

Acta Chimica
H-1450 Budapest P.O. Box 67

Subscription information

Orders should be addressed to

KULTURA Foreign Trading Company
H-1389 Budapest P.O. Box 149

or to its representatives abroad

Acta Chimica is indexed in Current Contents.

NOTICE TO AUTHORS

Acta Chimica publishes original papers on all aspects of chemistry in English. Before preparing a manuscript for submission to this journal authors are advised to consult recent issues.

Form of manuscript

Manuscripts, tables and illustrations should be submitted in triplicate. Manuscripts should be typewritten double spaced (25 lines, 50 characters per line including spaces). The *title page* should include (1) the title of the paper, (2) the full names of the author(s) in the sequence to be published; apply an asterisk to designate the name of the author to whom correspondence should be addressed, (3) name and address of the institution where the work was done. If the paper is part of a series, reference to the previous communication must be given as a footnote.

Abstract

A summary is printed at the head of each paper. This should not exceed 200 words and should state briefly the principal results and major conclusions of the work. It should be suitable for use by abstracting services.

CONTENTS

PHYSICAL AND INORGANIC CHEMISTRY

Conformation and optical anisotropy of short-chain molecules with mesogenic side groups, **Gy. Hardy, S. V. Bushin, I. N. Shtennikova, E. V. Korneeva, G. F. Kolbina, F. Cser, K. Nyitrai, K. P. Smirnov** 83

Studies on 1-aryloxysilatranes, V. Studies on the mechanism hydrolysis of 1-aryloxysilatranes, **J. Łukasiak, Z. Jamrógiewicz** 99

Physico-chemical studies on the mixed ligand complexes of some diimines with palladium(II), platinum(II), iridium(III), rhodium(III) and platinum(IV) phthalimides, **C. L. Sharma, S. S. Narvi** 107

Complete CNDO force field of *cis*- and *trans*-furan-2-aldehyde, **J. Bánki, F. Billes, M. Gál, A. Grofcsik, Gy. Jalsovszky, L. Sztraka** 115

Osmium-tetroxide as a redox catalyst. Mechanism of OsO_4-catalyzed decomposition of hydrogen peroxide, **L. J. Csányi, Z. M. Galbács, L. Nagy, I. Horváth** 123

Effect of quinolinium salts on the behaviour of tetracyanoquinodimethane polymer film electrode, **Gy. Inzelt, J. Q. Chambers, R. W. Day** 137

ORGANIC CHEMISTRY

Reactions of 5-hydroxy-6-oxosteroids, VI. Acid catalyzed isomerization of some 5α-hydroxy-6-oxosteroids, **W. J. Szczepek** 69

Reactions of 5-hydroxy-6-oxosteroids, VII. New reagent for the Westphalen-type rearrangement of 5α-hydroxy-6-oxosteroids, **W. J. Szczepek** 77

Phosphane oxides as intermediates in the synthesis of potentially bioactive compounds, **Gy. Matolcsy, K. Bauer, Á. Pál, I. Ujváry, I. Bélai, A. Gerlei, M. Kardos, P. Sohár, I. Pelczer** 145

Synthesis of Vinca alkaloids and related compounds, XXIX. Stereochemistry of 1,1-disubstituted-indolo[2,3-*a*]quinolizidines, **A. Dancsó, Gy. Kalaus, M. Kajtár-Peredy, L. Szabó, Cs. Szántay** 155

ANALYTICAL CHEMISTRY

Spectrophotometric and potentiometric determination of Nb(V) and Ta(V) using barbituric acid, **S. Lata, G. C. Shivahare** 93

Acta Chimica Hungarica 123 (3—4), pp. 69—76 (1986)

REACTIONS OF 5-HYDROXY-6-OXOSTEROIDS, VI*

ACID-CATALYZED ISOMERIZATION OF SOME 5α-HYDROXY-6-OXOSTEROIDS

Wojciech J. Szczepek

(Department of Chemistry, University of Warsaw, 02093 Warszawa, Pasteura 1, Poland)

Received July 17, 1985
Accepted for publication December 18, 1985

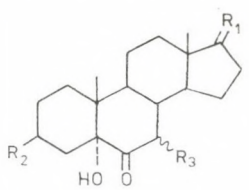
It has been found that a mixture of $KHSO_4$—CF_3COOH is a good reagent for the conversion of some 5α-hydroxy-6-oxosteroids into 5β-hydroxy-6-oxosteroids. The same reaction was also accomplished with $ZnCl_2$—CF_3COOH, $TsOH.H_2O$—CF_3COOH and $BF_3.Et_2O$—CF_3COOH mixtures. These reagents can be used in the case of halogenated and C-7 substituted steroids, when the known basic isomerization cannot be applied. A change in the isomerization mechanism catalyzed by acid and base is proposed.

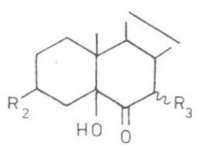
The expected application of $KHSO_4$—$(CF_3CO)_2O$—CF_3COOH mixture, analogous to $KHSO_4$—Ac_2O—AcOH [2], in the Westphalen-type rearrangements required information about the action of strong acid medium ($KHSO_4$—CF_3COOH) on some 5α-hydroxy-6-oxo- and 5β-hydroxy-6-oxosteroids. The starting compounds **1**, **1a**, **2**, **4**, **5**, **6**, **7** and **8** for the isomerizations were readily prepared by known methods (see Experimental). Only conversion of 3β-acetoxy-7α-bromo-5-hydroxy-5α-cholestan-6-one (**2**) to the 7β-bromo epimer **3** was essential. Rowland reported [3] that attempted epimerization of **2** with hydrogen bromide in acetic acid (applied by Cookson [4] for 5α-acetoxy-7α-bromoketone) failed, but treatment with excess lithium bromide in DMF at 75 ± 2 °C for 24 h resulted in the formation of 3β-acetoxy-7β-bromo-5-hydroxy-5α-cholestan-6-one (**3**) in 52% yield. A lower yield (32%) of this 7β-bromo-hydroxyketone was reported by Hanna [5] for epimerization at C-7 with Li_2CO_3 in boiling DMF (8 min). Other 7α-bromo-5α-hydroxyketones were epimerized with LiBr—DMF during an extended period at room temperature [3, 5, 6] or under conditions of precise control of temperature [3].

With regard to the serious difficulties in application of these methods of epimerization, a simplified procedure was wanted. Since it was previously noted [7] that the 7β-bromo-hydroxyketone **3** was formed in 11% yield under dehydrobromination conditions, attempts with DMF—H_2O or DMA—H_2O were carried out. The desired 7β-bromo-hydroxyketone **3** was obtained from 7α-bromo-hydroxyketone in 75% yield by heating under reflux in DMA—H_2O (9 : 1) mixture, or in 62% yield by heating under reflux in DMF—H_2O (9 : 1) mixture.

* Part V: See Ref. [1].

Treatment of the 5α-hydroxyketone **1** with anhydrous $KHSO_4$ in trifluoroacetic acid (TFA) at room temperature for a few days resulted in the formation of less polar products in addition to the main compound, 5β-hydroxyketone **1a**. Chromatography of the crude product (isolated after 14 days) afforded the known [8] 5β-hydroxyketone **1a** in 67% yield. Under the same conditions the 5β-hydroxyketone **1a** gave less polar products and 72% of the recovered starting compound. Similar treatment of the hydroxyketone **5** (17 days) gave the isomeric 5β-hydroxyketone **5a** (52%). The chloroketone **4** (17 days) yielded mainly the product of isomerization (5β-hydroxyketone **4a**, 40%) accompanied by the less polar dichloroketone **4b** (16%). The latter arose from 5α-hydroxyketone **4** and/or 5β-hydroxyketone **4a** and HCl (formed





1 R_1 = β-C_8H_{17}, H; R_2 = OAc; R_3 = H

2 R_1 = β-C_8H_{17}, H; R_2 = OAc; R_3 = α-Br

3 R_1 = β-C_8H_{17}, H; R_2 = OAc; R_3 = β-Br

4 R_1 = β-C_8H_{17}, H; R_2 = Cl; R_3 = H

5 R_1 = O; R_2 = OAc; R_3 = H

5b R_1 = O; R_2 = $OCOCF_3$; R_3 = H

8 R_1 = β-C_8H_{17}, H; R_2 = OH; R_3 = H

9 R_1 = β-C_8H_{17}, H; R_2 = $OCOCF_3$; R_3 = H

1a R_2 = OAc; R_3 = H

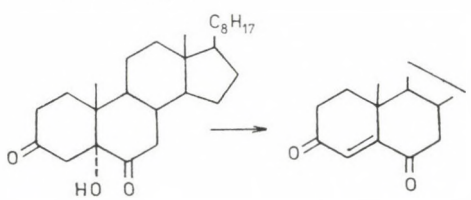
2a R_2 = OAc; R_3 = α-Br

3a R_2 = OAc; R_3 = β-Br

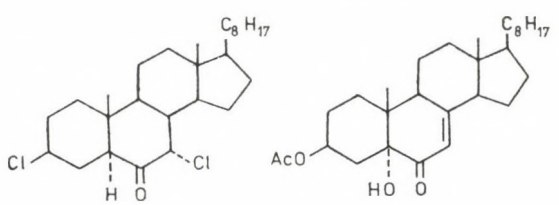
4a R_2 = Cl; R_3 = H

5a R_2 = OAc; R_3 = H

8a R_2 = OH; R_3 = H



6 **6a**



4b **7**

Fig. 1

either in elimination or in substitution reaction at C-3) via substitution at C-7 [9].

In the case of the hydroxy-bromoketones **2** and **3** better results were obtained when commercial anhydrous (without additional drying) $KHSO_4$ was used. Starting from **2** (after 14 days) the known [8] 5β-hydroxy-bromoketone **2a** (22%) was obtained together with the unchanged substrate (68%), while 5α-hydroxy-bromoketone **3** (after 5 days) afforded 5β-hydroxy-bromoketone **3a** (33%). Unexpectedly, the configuration of the bromine substituents at C-7 remained unchanged in the 5β-hydroxyketones **2a** and **3a** and in the recovered substrates **2** and **3**, respectively.

The presence of considerable quantity of water in the reaction mixture caused hydrolysis of an acetate group with the formation of the trifluoroacetate derivative. For example, treatment of the 5α-hydroxyketone **5** with $KHSO_4$ in TFA—H_2O (8 : 2) mixture gave mainly the trifluoroacetate **5b** (20 days, 36%), in addition to the substrate and 5β-hydroxyketone **5a**. The use of 10% of water resulted only in a decrease of the yield of trifluoroacetate **5b**.

A marked difference in the reaction course was observed only in the case of the hydroxy-diketone **6** and hydroxy-enone **7**. The former furnished the known [10] endione **6a** nearly quantitatively. The latter gave a complex mixture of products which was not further investigated. Also the reaction of the dihydroxyketone **8** differed from those described above, leading to the formation of the 3β-trifluoroacetate **9**.

All 5β-hydroxy products were readily identified on the basis of their ^{1}H-NMR data (see Table I). Thus, the 19-H signals of the 5β-hydroxy products appeared at higher field, than those of the corresponding 5α-hydroxy compounds. Furthermore, the half-bandwidths of the 3α-H signals of the 5β-hydroxy compounds were compatible with their equatorial nature. Configurational assignments of the trifluoroacetates **5b** and **9** were based on the comparative ^{1}H-NMR analyses (Table I). In both cases the 7α-H signal appeared as a triplet at low field (δ ca. 2.8) indicating a 5α-hydroxy-6-oxo structure. The magnitudes of half-bandwidths of the 3-H signals proved retention of configuration at C-3.

We have recently shown [9] that the 5β-hydroxyketone **1a** was formed as a by-product when the 5α-hydroxyketone **1** was treated with anhydrous $ZnCl_2$ in boiling acetic acid. Since $KHSO_4$ and $ZnCl_2$, as well as *p*-TsOH.H_2O and BF_3.Et_2O catalyzed the same reaction (formation of 2,4-dien-6-one from 3β-acetoxy-5α-hydroxy-6-ketone [9]), the conclusion was drawn that $ZnCl_2$—TFA, *p*-TsOH.H_2O—TFA and BF_3.Et_2O—TFA mixtures would be also good reagents for the isomerization reaction. Therefore further qualitative (controlled only by TLC) reactions with $KHSO_4$, $ZnCl_2$, *p*-TsOH.H_2O or BF_3.Et_2O in trifluoroacetic acid were performed using the 5α-hydroxy-bromoketone **3**.

Table I

^{1}H-NMR *data for 5α-hydroxy-6-oxo- and 5β-hydroxy-6-oxosteroids*

Compound	18-H	19-H	OAc	5-OH	3α-H	Others	Lit.
1	0.66	0.82	2.00	3.73	5.00[a]	2.76 (t, J = 11.8,7α-H)	—
1a	0.66	0.75	2.06	3.92	5.06[b]		—
	0.67	0.70	1.96	3.76	4.90		[8]
	0.64	0.72	1.94	3.75	4.90		[21]
2	0.68	0.83	2.00	3.47	5.09[a]	4.15 (d, J = 3.8,7β-H)	—
	0.70	0.83	2.01	3.25	5.12	4.20 (7β-H)	[3]
2a	0.70	0.81	2.05	3.64	5.04[b]	3.06 (dd, J = 16 and 3.8,4α-H), 4.40 (d, J = 3.5,7β-H)	—
	0.70	0.77	1.98	3.56	4.92	2.95 (4α-H), 4.35 (7β-H)	[8]
3	0.68	0.79	2.00	3.71	5.01[a]	5.14 (d, J = 9.1,7α-H)	—
	0.70	0.80	2.00	3.93	5.03	5.20 (7α-H)	[3]
3a	0.70	0.74	2.04	3.92	5.05[b]	4.62 (d, J = 9.7,7α-H)	—
4	0.63	0.82	—	—	4.17[a]	2.67 (t, J = 12,7α-H)	—
4a	0.65	0.77	—	—	4.58[b]	2.56 (dd, J = 14.8 and 4.9,4α-H)	—
5	0.85	0.84	2.00	3.85	4.98[a]	2.87 (t, J = 11.5,7α-H)	—
5a	0.86	0.78	2.04	3.84	5.12[b]		—
5b	0.86	0.86	—	3.24	5.24[a]	2.87 (t, J = 12,7α-H)	—
8	0.66	0.80	—	—	3.96[a]	2.72 (t, J = 12,7α-H)	—
8a	0.65	0.74	—	4.42	4.04[c]	4.32 (d, J = 9.9,3β-OH)	—
	0.66	0.74	—	4.42	4.05	4.34 (3β-OH)	[13]
9	0.65	0.83	—	—	5.24[a]	2.73 (t, J = 12.1,7α-H)	—

[a] broad multiplet ($w/2$ = 20—26 Hz)
[b] narrow multiplet ($w/2$ = 7,5—10 Hz)
[c] doublet of multiplets (J = 9.9 Hz), after D_2O exchange: narrow multiplet.

For comparison bromoketones **3** and **3a** were dissolved in neat TFA and kept under the same conditions. In all cases the isomerization reactions leading to an equilibrium mixture of **3** and **3a** were observed and TLC showed that the reaction rates with the different catalysts decreased as follows:

$$BF_3.Et_2O > p\text{-TsOH}.H_2O > KHSO_4 > ZnCl_2 \gg CF_3COOH$$

Apart from isomerization reaction, the formation of less polar products was found. Extension of the reaction time indicated that formation of these products from the 5α-hydroxyketone **3** is faster than from the isomeric 5β-hydroxyketone **3a**.

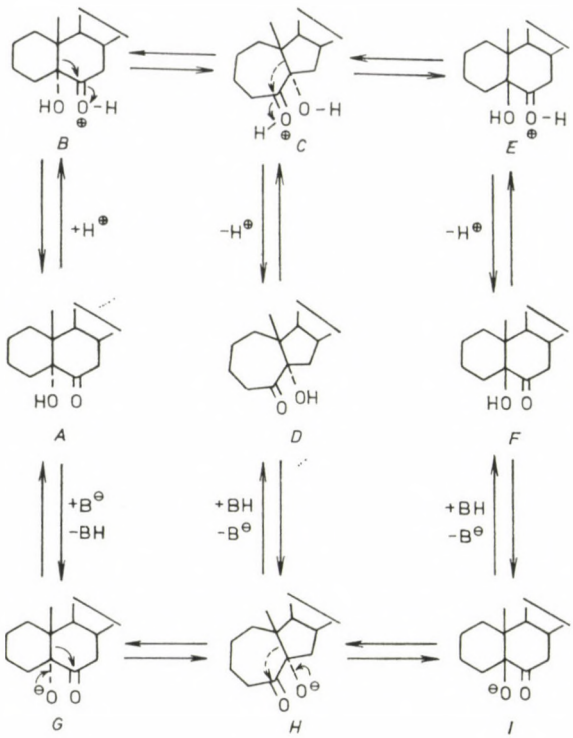


Fig. 2

The catalysts studied may be useful in isomerization reactions of other reactive tertiary α-hydroxyketones, where application of the known basic [11, 1] or acidic [12] conditions is impossible.* The suitable catalyst may be easily selected on the basis of TLC-controlled experiments.** This reaction is the shortest and probably the only way for the preparation of 5β-hydroxy-7β-bromoketones, since epimerization of 5β-hydroxy-7α-bromo-6-ketone at C-7 does not occur [3].

The stereochemical course of equilibration (see Fig. 2) of the 5α-hydroxy-6-oxo *A* and 5β-hydroxy-6-oxo steroids *F*, proposed in our work, is different from that described in the literature [11]. In the present paper it is postulated that isomerization proceeds under both acidic and basic conditions practically

* In the light of our earlier experiments concerned with aromatization processes [9], *p*-TsOH.H_2O, and first of all CF_3SO_3H in boiling acetic acid cannot be used in case of the described 5α-hydroxyketones. The application of basic conditions for halogenated hydroxyketones is similarly impracticable.

** The presence of residual TFA on the TLC plates results in a better separation of the spots of the isomeric hydroxyketones (e.g. 5α-hydroxyketone **1** and 5β-hydroxyketone **1a** have the same R_f values in TLC in the absence of TFA).

via the 5α-hydroxy-4a-oxo-A-homo-B-nor intermediate *D*. Thus, in acidic medium the pathway $A \rightleftarrows B \rightleftarrows C(\rightleftarrows D) \rightleftarrows E \rightleftarrows F$, and under basic conditions the similar route $A \rightleftarrows G \rightleftarrows H(\rightleftarrows D) \rightleftarrows I \rightleftarrows F$ is realized. The solvolysis product of 5-hydroxy-3β-tosyloxy-5β-cholestan-6-one (the 3β-tosyloxy counterpart of **1a**) [13] and products of the Westphalen-type rearrangement of 3β-acetoxy-5-hydroxy-5β-cholestan-6-one (**1a**) [14], which all have the corresponding A-homo-B-nor structure, strongly support the presence of the non-isolable intermediate *D* under equilibrium conditions.

It is noteworthy that the attempted isomerization of 5α-acetoxy- and 5α-methoxy derivatives of the 5α-hydroxyketone **1** failed, proving that the presence of free 5-hydroxyl group is necessary for the conversion of 5α-hydroxy-6-ketone into 5β-hydroxy-6-ketone.

Experimental

IR spectra were taken on a UR-20 spectrophotometer using KBr pellets or $CHCl_3$ solutions. Specific rotations were measured on a Perkin-Elmer 241 polarimeter in $CHCl_3$ solutions at 25 °C, concentrations are expressed in mg per mL. ^{1}H-NMR spectra were recorded on a Jeol INM-4H-100 apparatus (100 MHz) in $CDCl_3$ solutions with TMS as internal standard. The chemical shifts are given in ppm on the δ scale. M.p.'s were determined on a Kofler apparatus of Boetius type, and are uncorrected. For column chromatography Kieselgel (70—230 mesh, Merck) was used.

Syntheses of 3β-acetoxy-5-hydroxy-5α-cholestan-6-one (**1**) [15], 3β-acetoxy-7α-bromo-5-hydroxy-5α-cholestan-6-one (**2**) [15], 3β-acetoxy-5-hydroxy-5α-androstane-6,17-dione (**5**) [16], 3β-acetoxy-5-hydroxy-5α-cholest-7-en-6-one (**7**) [7] and 3β,5-dihydroxy-5α-cholestan-6-one (**8**) [15] were reported earlier from this laboratory. 3β-Acetoxy-5-hydroxy-5β-cholestan-6-one (**1a**) was obtained by a modified procedure [1] of Mazur and Nussim [11]; the product was identical with an authentic sample [9]. 3β-Chloro-5-hydroxy-5α-cholestan-6-one (**4**) was prepared from 3β-chloro-5-cholestene via epoxidation and subsequent oxidation of the mixture of epoxides with CrO_3—H_2O [17] in acetone. The product had m.p. 180—183 °C (Me_2CO) (*lit.* m.p. 182—183 °C [18]). 5-Hydroxy-5α-cholestane-3,6-dione (**6**) was obtained by the known method [19]; it had m.p. 230—233 °C (Me_2CO); δ(Py-d_5): 0.65 (18-H), 1.03 (19-H), 2.72 and 3.10 (AB_q, J = 15.6, 4-H_2), 2.99 (t, J = 12.1, 7α-H) (*lit.* m.p. 232—234 °C [19]).

Modified procedure of the preparation of 3β-acetoxy-7β-bromo-5-hydroxy-5α-cholestan-6-one (3)

(a) A solution of the 7α-bromoketone **2** (19.624 g) in DMA—H_2O (9 : 1) mixture (200 mL) was refluxed for 2 h. The solvent was evaporated under reduced pressure and the residue extracted with benzene and washed with water. The organic layer was dried and evaporated to dryness. The crude product was recrystallized twice from Me_2CO—MeOH (1 : 9) to afford the pure 7β-bromoketone **3** (9.722 g). Chromatography of the residue gave 2.387 g (12%) of recovered starting compound **2** and 5.02 g of 7β-bromoketone **3** (total yield: 14.742 g; 75%). The 7β-bromoketone **3** obtained in this way was identical in all respects with an authentic sample [7].

(b) A solution of the 7α-bromoketone **2** (12.485 g) in DMF—H_2O (9 : 1) mixture (250 mL) was refluxed for 2 h. Isolation of products, as above, and chromatography gave 1.254 g (10%) of unchanged compound **2** and 7.777 g (62%) of the 7β-bromoketone **3**. The fractions of more polar products were not investigated.

Isomerization reactions of the hydroxyketones 1, 1a, 2, 3, 4, 5, 6 and 7 with $KHSO_4$ in trifluoroacetic acid

General procedure: To a solution of the substrate in trifluoroacetic acid (TFA) powdered potassium hydrogen sulfate was added and the mixture was allowed to stand at room temperature for a definite time. It was then evaporated at 35 °C under reduced pressure, diluted

Table II

Substrate (g)	TFA (mL)	$KHSO_4$ (g)	Time (days)	Products (g, %)
1 (5.01)	40	10[a]	14	**1a** (3.357, 67%)
1a (5.046)	40	10[a]	14	**1a** (3.633, 72%)
2 (3.641)	29	3.6[b]	14	**2** (2.486, 68%), **2a** (0.794, 22%)
3 (2.59)	20	1[b]	5	**3** (0.17, 7%), **3a** (0.849, 33%)
4 (0.919)	20	2[a]	17	**4b** (0.15, 16%), **4a** (0.368, 40%)
5 (4.934)	50	5[a]	17	**5a** (2.573, 52%)
6 (5.311)	53	5.3[a]	45 h	**6a** (4.167, 82%)
7 (2.02)	20	2[a]	48 h	a complex mixture of products which was not separated

[a] freshly prepared anhydrous $KHSO_4$
[b] commercial anhydrous $KHSO_4$

with water and ether, and extracted with benzene. The organic layer was washed successively with water, aqueous potassium carbonate and water, and dried over anhydrous Na_2SO_4. After evaporation of the solvent the crude product was chromatographed on silica gel and/or crystallized to give the corresponding pure compounds. The results are summarized in Table II.

The isolated products had the following data: 3β-acetocy-5-hydroxy-5β-cholestan-6-one (**1a**) — m.p. 141—143 °C (Me_2CO), ν_{max}: 3447, 1276, 1703, 1275, 1171 cm^{-1} (*lit.* m.p. 142—143 °C [8]); 3β-acetocy-7α-bromo-5-hydroxy-5β-cholestan-6-one (**2a**) — m.p. 138—140 °C (Me_2CO-hexane), ν_{max}: 3465, 1718, 1287, 1054 cm^{-1} (*lit.* m.p. 137—139 °C [8]); 3β-acetoxy-7β-bromo-5-hydroxy-5β-cholestan-6-one (**3a**) — m.p. 153—156 °C (Et_2O-hexane), $[\alpha]_D$ +47.2° (c = 10.8), ν_{max}: 3476, 1728, 1285, 1191, 1059, 731 cm^{-1} (found: C 64.51; H 8.80; calcd. for $C_{29}H_{47}O_4Br$: C 64.55: H 8.78%); 3β,7α-dichloro-5α-cholestan-6-one (**4b**) — m.p. 116—118 °C (MeOH), $[\alpha]_D$ +25.8° (c = 11.6), ν_{max}: 1730, 759 and 745 (C—Cl_{eq}) cm^{-1} (found: C 71.15; H 9.71; calcd. for $C_{27}H_{44}OCl_2$: C 71.19; H 9.74%); 3β-chloro-5-hydroxy-5β-cholestan-6-one (**4a**) — m.p. 170—173 °C (Me_2CO), $[\alpha]_D$ −5.9° (c = 10.9), ν_{max}: 3438, 1714, 702 (C—Cl_{ax}) cm^{-1} (found: C 74.11; H 10.40; calcd. for $C_{27}H_{45}O_2Cl$: C 74.19; H 10.38%); 3β-acetoxy-5-hydroxy-5β-androstane-6,17-dione (**5a**) — m.p. 194—197 °C (Me_2CO), $[\alpha]_D$ +30.8° (c = 11.4), ν_{max}: 3446, 1737, 1278, 1173 cm^{-1} (found: C 69.51; H 8.30; calcd. for $C_{21}H_{30}O_5$: C 69.59; H 8.34%); 4-cholesten-3,6-dione (**6a**) — m.p. 121—122 °C (Me_2CO-hexane), ν_{max}: 1699, 1612, 1226 cm^{-1}, δ: 0.72 (18-H), 1.17 (19-H), 6.17 (4-H) (*lit.* m.p. 122—123 °C, δ: 0.78 (18-H), 1.20 (19-H), 6.05 (4-H) [10]).

Reactions of 5α-hydroxyketone 5 with $KHSO_4$ in TFA—H_2O mixtures

(a) To a solution of the hydroxyketone **5** (2.681 g) in TFA—H_2O (8 : 2) mixture (55 mL) powdered $KHSO_4$ (5.5 g) was added and the reaction mixture was left stand at room temperature for 20 days. Chromatography of the crude product (isolated as above) afforded 1.094 g (36%) of 5-hydroxy-3β-trifluoroacetoxy-5α-androstane-6,17-dione (**5b**), m.p. 223—226 °C (benzene-hexane), $[\alpha]_D$ −4.2° (c = 11.8), ν_{max}: 3486, 1789, 1728, 1229, 1174 cm^{-1} (found: 60.48; H6.59; calcd. for $C_{21}H_{27}O_5F_3$: C 60.57; H 6.54%). The more polar fractions contained the starting compound **5** and 5β-hydroxyketone **5a**, whose quantities were not determined.

(b) To a solution of the hydroxyketone **5** (2.024 g) in TFA—H_2O (9 : 1) mixture (40 mL) powdered $KHSO_4$ (4 g) was added and the reaction mixture was stored at room temperature for 20 days. The crude product (isolated as above) showed the presence of the trifluoroacetate **5b** (smaller quantity than in the preceding experiment), substrate **5**, the 5β-hydroxyketone **5a** and other by-products. It was not further investigated.

Reaction of the dihydroxyketone 8 with $KHSO_4$ in TFA

To a solution of the dihydroxyketone **8** (5.614 g) in TFA (56 mL) powdered anhydrous $KHSO_4$ (freshly prepared, 5.6. g) was added and the reaction mixture was kept at room temperature for 44 h. Chromatography of the crude product (isolated as above) gave 1.95 g (28%)

of 5-hydroxy-3β-trifluoroacetoxy-5α-cholestan-6-one (**9**), m.p. 182—184 °C (hexane), $[\alpha]_D$ —44° (c = 10.7), ν_{max}: 3467, 1787, 1715, 1227, 1179, 940, 865, 781, 735 cm^{-1} (found: C 67.73; H 8.75; calcd. for $C_{29}H_{45}O_4F_3$: C 67.68; H 8.81%). The residue after crystallization of compound **9** and the remaining fractions were hydrolyzed in the usual manner. Chromatography of the mixture of the obtained alcohols afforded 0.898 g (16%) of 3β,5-dihydroxy-5β-cholestan-6-one (**8a**), m.p. 102—104 °C (hexane), ν_{max}: 3523, 3428, 1709, 1165, 1097 cm^{-1} *(lit.* m.p. 62 °C [20], m.p. 100—101.5 °C [13]). The more polar fractions contained substrate **8**, whose quantity was not determined.

REFERENCES

[1] Szczepek, W. J.: Bull. Pol. Ac. Chem., **34,** 89 (1986)
[2] Kočovský, P., Černý, V., Tureček, F.: Collect. Czech. Chem. Commun., **44,** 234 (1979)
[3] Rowland, A. T., Drawbaugh, R. S., Dalton, J. R.: J. Org. Chem., **42,** 487 (1977)
[4] Cookson, R. C., Dandegaonker, S. H.: J. Chem. Soc., **1955,** 352
[5] Hanna, R., Maalouf, G., Muckensturm, B., Cherry, A.: Tetrahedron, **29,** 2297 (1973)
[6] Hanna, R.: Tetrahedron Lett., **1973,** 3349
[7] Rodewald, W. J., Szczepek, W. J., Gumułka, J.: Polish J. Chem., **53,** 139 (1979)
[8] Rowland, A. T., Bennett, P. J., Shoupe, T. S.: J. Org. Chem., **33,** 2426 (1968)
[9] Jagodziński, J. J., Gumułka, J., Szczepek, W. J.: Tetrahedron, **37,** 1015 (1981)
[10] Jones, J. G. L., Marples, B. A.: J. Chem. Soc. (C), **1968,** 2698
[11] Mazur, Y., Nussim, M.: Tetrahedron Lett., **1961,** 817
[12] Terashima, S., Tamoto, K.: Tetrahedron Lett., **1983,** 2589
[13] Dave, V., Warnhoff, E. W.: J. Org. Chem., **43,** 4622 (1978)
[14] Szczepek, W. J.: to be published (also: Habilitation Thesis, Warszawa, 1982, in Polish)
[15] Rodewald, W. J., Szczepek, W. J., Gumułka, J.: Polish J. Chem., **53,** 797 (1979)
[16] Szczepek, W. J., Gumułka, J., Jagodziński, J. J.: Bull. Acad. Pol. Sci., Ser. Sci. Chim., **28,** 165 (1980)
[17] Knof, L.: Justus Liebigs Ann. Chem., **657,** 171 (1962)
[18] Shoppee, C. W., Bridgwater, R. J., Jones, D. N., Summers, G. H. R.: J. Chem. Soc., **1956,** 2492
[19] Suga, T., Shishibori, T., Matsuura, T.: J. Chem. Soc., Perkin Trans. 1, **1972,** 171
[20] Cookson, R. C., Gandhi, R. P., Southam, R. M.: J. Chem. Soc. (C), **1968,** 2494
[21] Georghiou, P. E., Just, G.: J. Chem. Soc., Perkin Trans. 1, **1973,** 70

Acta Chimica Hungarica 123 (3–4), pp. 77–82 (1986)

REACTIONS OF 5-HYDROXY-6-OXOSTEROIDS, VII*

NEW REAGENT FOR THE WESTPHALEN-TYPE REARRANGEMENT OF 5α-HYDROXY-6-OXOSTEROIDS

Wojciech J. Szczepek

(Department of Chemistry, University of Warsaw, 02093 Warszawa, Pasteura 1, Poland)

Received July 17, 1985
Accepted for publication December 18, 1985

It was found that $KHSO_4$—$(CF_3CO)_2O$ mixture is the best reagent for the Westphalen-type rearrangement of 5α-hydroxy-6-oxosteroids. The reactions can be effected in tetrahydrofuran or in some cases in trifluoroacetic acid as solvents, at room temperature. It seems that this reagent will also be useful in other rearrangements of the same type.

Reactions of 6β-substituted 3β-acetoxy-5α-hydroxysteroids with H_2SO_4—Ac_2O [1] or $KHSO_4$—Ac_2O [2] (except 6β-N_3 [3], 6β-methyl [4], 6β-I [1] and 6β-H [5]) give good yields of the corresponding Westphalen-type products. In contrast to these results, it was found that 6-oxosteroids without a 2β- or 4β-substituent give only ca. 10% yield of the rearranged product [2, 6], or no such product at all [7], whereas introduction of a 2β- or 4β-substituent gives rise to higher the yields of rearranged compound [2, 7, 8].

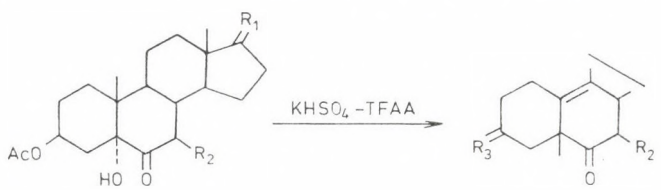
Previous results of the Westphalen-type rearrangement of 3β-acetoxy-5-hydroxy-5α-cholestan-6-one (**1**) with $KHSO_4$—Ac_2O under varying conditions [9] have shown that the use of potassium hydrogen sulfate-trifluoroacetic anhydride in tetrahydrofuran ($KHSO_4$—TFAA/THF) or potassium hydrogen sulfate-trifluoroacetic anhydride in trifluoroacetic acid ($KHSO_4$——TFAA/TFA) is most effective in increasing the yield of the rearranged products.

Reaction of the hydroxyketone **1** with $KHSO_4$—TFAA in THF at room temperature gave the known [2, 10] rearranged acetoxyketone **1a** (62%). It was additionally identified by hydrolysis and subsequent oxidation (CrO_3—H_2O in acetone) to the known hydroxyketone **1b** [11] and diketone **1c** [12]. In the same manner, starting from the hydroxybromoketone **2**, the oily, unstable bromoketone **2a** (25%) was obtained. The low chemical shift of the 5β-methyl signal in the ^{1}H-NMR spectrum of the bromoketone **2a** (δ 1.80) relative to that of ketone **1a** (δ 1.34) supports retention of the configuration of the bromine substituent at C-7 and also proves the conformational mobility of ring B of Westphalen-type compounds, as it has been earlier confirmed [13]. Rearrangement of the hydroxyketone **3**, having the

* Part VI: See preceding paper in this Journal.

polar 17-oxo group, proceeded analogously to give the acetoxyketone **3a** (55%). Hydrolysis of this compound gave hydroxyketone **3b** which, after oxidation, afforded the known [14] triketone **3c**. Further reaction of the hydroxyketone **4**, also containing a polar 17β-acetoxy group, yielded a mixture of products. The main component of this mixture was the rearranged diacetoxyketone **4a**, while the minor one was the simple dehydration product, the diacetoxy-enone **5**. Although the latter was not obtained in the pure state, its presence in the post-reaction mixture was sufficiently evidenced by the ^{1}H-NMR spectrum. The presence of signals due to 19-H, 3α-H and 4-H at δ 1.03, 5.30 and 6.06, respectively, strongly indicated a 3β-acetoxy--4-en-6-oxo structure for this compound [2]. The structure of the diacetoxyketone **4a** was confirmed by chemical transformations. Alkaline hydrolysis of **4a** furnished the dihydroxyketone **4b**, which on oxidation with CrO_3—H_2O in acetone afforded the triketone **3c** described above.

A different reaction course was observed in the case of the hydroxyenone **8**. When treated with $KHSO_4$—TFAA in THF for 28 h it gave the oily ketone **9** (28%) as the major product, but after 46 h afforded ketone **10** and



1 R_1 = β-C_8H_{17}, H; R_2 = H

1a R_3 = β-OAc, H
1b R_3 = β-OH, H
1c R_3 = O

2 R_1 = β-C_8H_{17}, H; R_2 = Br

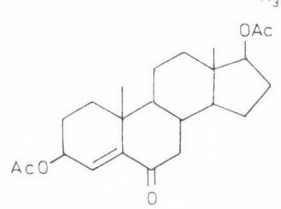
2a R_3 = β-OAc, H

3 R_1 = O; R_2 = H

3a R_3 = β-OAc, H
3b R_3 = β-OH, H
3c R_3 = O

4 R_1 = β-OAc, H; R_2 = H

4a R_3 = β-OAc, H
4b R_1 = R_3 = β-OH, H
1d R_1 = β-C_8H_{17}, H; R_2 = H
R_3 = O; 9α,10α-epoxy



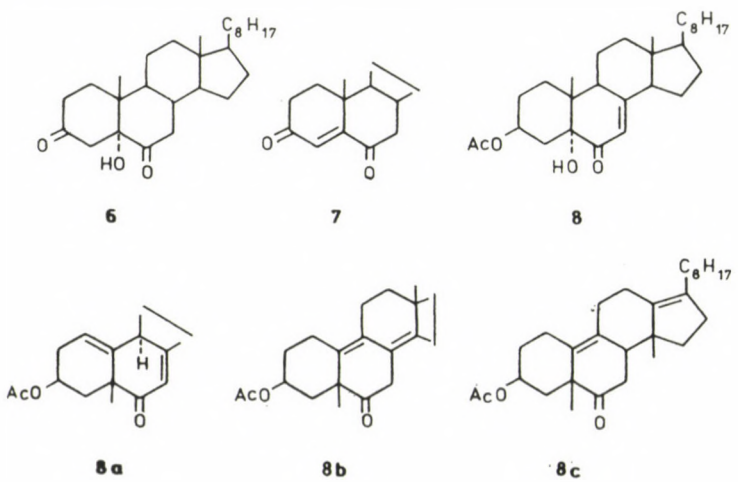
5

Fig. 1

the oily ketone **11** as the main products. The positions of the double bonds in these compounds were deduced from their IR and ^{1}H-NMR spectra. ^{1}H-NMR spectra of compounds **9**, **10** and **11** showed, respectively, the following signals: strongly deshielded signal of 9α-H (δ 2.79) as for ecdysteroids and Δ^7-6-oxosteroids [15, 16], AB quartet of the C-7 methylene group as for $\Delta^{8(14)}$-6-oxosteroids [17], and deshielded doublet of the C-21 methyl group (δ 0.97) as for backbone-rearranged products [18, 19]. The assignments of signals of the 5β-Me and 14β-Me groups agree well with the data reported by Kirk et al. [18] for backbone-rearranged steroids.

The reaction of the hydroxydiketone **6** also differed from those described above. Treatment of this compound with $KHSO_4$—TFAA in THF at 6—10 °C gave a mixture of the rearranged diketone **1c** and enedione **7**. Owing to difficulties in separation of this mixture, it was treated with MCPBA in ethereal solution at room temperature. The reaction was stopped when epoxidation of a control sample of the enedione **7** started (the same result was obtained when epoxidation of a control sample of the diketone **1c** was complete). Separation of the products gave 4-cholesten-3,6-dione (**7**) as the major product and the known [20] α-epoxydiketone **1d** as the minor one (6%).

Application of trifluoroacetic acid (TFA) as the solvent in the rearrangements of hydroxyketones **1** and **2** resulted in no change of the reaction course as compared with the considerably slower reaction of hydroxyketones of this type with $KHSO_4$—TFA [21]. The corresponding rearranged products **1a** and **2a** were isolated in 56% and 50% yield, respectively. However, treatment of the hydroxyketone **4** with $KHSO_4$—TFAA in TFA afforded only the rearranged diacetate **4a**, which was not contaminated by the product of simple 1,2-dehydration, diacetoxy-enone **5**.



6 **7** **8**

8a **8b** **8c**

Fig. 2

In order to shed light on the course of the rearrangement reaction of 5α-hydroxy-7-en-6-oxosteroids, the experiment with hydroxy-enone **8** must be reinvestigated; further the behaviour of the 17β-acetoxy and 17-oxo counterparts of enone **8** will be studied in respect of the backbone product formation.

Experimental

For general experimental directions, see Ref. [21].

Syntheses of 3β-acetoxy-5-hydroxy-5α-cholestan-6-one (**1**) [22], 3β-acetoxy-5-hydroxy-5α-androstane-6,17-dione (**3**) [23], 3β,17β-diacetoxy-5-hydroxy-5α-androstan-6-one (**4**) [23] and 3β-acetoxy-5-hydroxy-5α-cholest-7-en-6-one (**8**) [16] were previously reported from this laboratory. 3β-Acetoxy-7β-bromo-5-hydroxy-5α-cholestan-6-one (**2**) was obtained by a modified method of epimerization at C-7 [21]. 5-Hydroxy-5α-cholestane-3,6-dione (**6**) was prepared according to Suga et al. [24].

Reactions of 5α-hydroxyketones with potassium hydrogen sulfate ($KHSO_4$) and trifluoroacetic anhydride (TFAA) in tetrahydrofuran (THF) or trifluoroacetic acid (TFA)

General procedure: To a solution of the starting compound in THF or TFA powdered anhydrous $KHSO_4$ and TFAA were added. The mixture was stirred and allowed to stand at room temperature for the specified time (TLC control). It was then evaporated at 40 °C (45 °C for TFA) under reduced pressure. The residue was treated with water and ether and shaken until the complete dissolution of $KHSO_4$, then extracted with benzene. Usual work-up and chromatography on silica gel gave the corresponding pure products. Detailed data are summarized in the Table I.

The isolated products had the following data: 3β-acetoxy-5-methyl-19-nor-5β-cholest-9(10)-en-6-one (**1a**), m.p. 94—95.5 °C (MeOH—Me_2CO); ν_{max}: 1745, 1713, 1261, 1245 cm^{-1}; δ: 0.76 (18-H), 1.34 (5β-Me), 2.05 (OAc), 5.18 (m, $w/2$ = 10 Hz, 3α-H) *(lit.* m.p. 94—96 °C: δ: 0.74 (18-H), 1.36 (5β-Me), 2.04 (OAc), 5.10 (3α-H) [2]);

3β-acetoxy-7β-bromo-5-methyl-19-nor-5β-cholest-9(10)-en-6-one (**2a**), an oil; $[\alpha]_D$ +20.9° (c = 11.2); ν_{max}: 1722, 1257 cm^{-1}; δ: 0.84 (18-H), 1.80 (5β-Me), 2.06 (OAc), 4.20 (d, $J \sim 2$ Hz, 7α-H), 5.16 (m, $w/2$ = 12 Hz, 3α-H) (no elemental analysis was made because of the fast decomposition of this compound);

Table I

Compound (g)	$KHSO_4$ (g)	TFAA (mL)	Solvent (mL)	Time (h)	Yield of products (g, %)
1 (5.007)	10	50	THF, 20	66	**1a** (2.983, 62%)
2 (2.046)	4.2	33	THF, 40	24	**2a** (0.5, 25%)
3 (5.114)	10	30	THF, 20	54	**3a** (2.673, 55%)
4 (0.72)	0.4	3.5	THF, 7	43	**4a** and **5** (0.589, 85%)[a]
6 (4.393)	8.8	15	THF, 60	24	crude (3.105)[b]
				6—10 °C	**7** (2.7, 64%), **1d** (0.266, 6%)
8 (2.5)	1	5	THF, 30	28	**8a** (0.679, 28%)
1 (1.463)	3	9	THF, 10	45.5	**8b** (0.164, 12%), **8c** (0.344, 24%)
3 (5.007)	10	20	TFA, 20	48	**1a** (2.694, 56%)
4 (6.055)	12	24	TFA, 24	48	**3a** (2.9, 50%)
(0.785)	0.4	4	TFA, 8	43	**4a** (0.4, 53%)

[a] The ratio of **4a** to **5**, determined from integration of the 4-H signal in **5** and the 17α-H signal in the mixture, was ca. 85 : 15.

[b] A solution of the crude product (3.105 g) in 100 mL of ether was treated with an excess of MCPBA at room temperature. After the complete epoxidation of **1c**, the isolated crude product was chromatographed on silica gel to give the corresponding compounds **7** and **1d**.

3β-acetoxy-5-methyl-19-nor-5β-androst-9(10)-en-6,17-dione (**3a**), m.p. 168—170 °C (Me_2CO); $[\alpha]_D$ +67.0° (c = 12.1); ν_{max}: 1742, 1718, 1244 cm^{-1}; δ: 0.97 (18-H), 1.38 (5β-Me), 2.06 (OAc), 5.13 (m, $w/2$ = 9 Hz, 3α-H) (found: C 73.20; H 8.23; calcd. for $C_{21}H_{28}O_4$: C 73.23; H 8.19%);

3β,17β-diacetoxy-5-methyl-19-nor-5β-androst-9(10)-en-6-one (**4a**), m.p. 118—122 °C (ether-hexane); $[\alpha]_D$ −18.2° (c = 18.2); ν_{max}: 1740, 1715, 1254, 933 cm^{-1}; δ: 0.90 (18-H), 1.37 (5β-Me), 2.06 (2×OAc), 4.61 (t, J = 7.4 Hz, 17α-H), 5.12 (m, $w/2$ = 9 Hz, 3α-H) (found: C 71.16; H 8.32; calcd. for $C_{23}H_{32}O_5$: C 71.11; H 8.30%);

3β,17β-diacetoxy-4-androsten-6-one (**5**), isolated as an impure fraction (contaminated with compound **4a**) showed the following signals corresponding to this compound, δ: 0.83 (18-H), 1.03 (19-H), 5.30 (m, 3α-H), 6.06 (broad s, 4-H);

4-cholesten-3,6-dione (**7**) was identical with an authentic sample [21];

9,10-epoxy-5-methyl-19-nor-5β,9α,10α-cholestane-3,6-dione (**1d**) was identical with an authentic sample [9];

3β-acetoxy-5-methyl-19-nor-5β-cholesta-1(10),7-dien-6-one (**9**), an oil; $[\alpha]_D$ +155.7° (c = 10.8); ν_{max}: 1722, 1665, 1648, 1250 cm^{-1}; δ: 0.64 (18-H), 1.40 (5β-Me), 2.02 (OAc), 2.79 (dd, J = 11 and 6.1 Hz, 9α-H, 4.95 (m, $w/2$ = 14 Hz, 3α-H), 5.48 (t, J = 3.9 Hz, 1-H), 5.65 (broad s, 7-H) (found: C 78.87; H 10.14; calcd. for $C_{29}H_{44}O_3$: C 79.04; H 10.06%);

3β-acetoxy-5-methyl-19-nor-5β-cholesta-8(14),9(10)-dien-6-one (**10**), m.p. 115—117 °C (MeOH); $[\alpha]_D$ +36.5° (c = 12.5); ν_{max}: 1737, 1721, 1263 cm^{-1}; δ: 0.89 (18-H), 1.40 (5β-Me), 2.05 (OAc), 2.99 and 3.31 (AB_q, J = 19.1, 7-H_2), 5.15 (m, $w/2$ = 10 Hz, 3α-H) (found: C 79.01; H 9.97; calcd. for $C_{29}H_{44}O_3$: C 79.04; H 10.06%);

3β-acetoxy-5,14-dimethyl-18,19-di-nor-5β,14β-cholesta-9(10),13(17)-dien-6-one (**11**), an oil; $[\alpha]_D$ −41.2° (c = 12.4); ν_{max}: 1730, 1260 cm^{-1}; δ: 0.97 (d, J = 6.6 Hz, 21-H_3), 1.05 (14β-Me), 1.25 (5β-Me), 2.05 (OAc), 5.19 (m, $w/2$ = 9 Hz, 3α-H) (found: C 78.88; H 10.11; calcd. for $C_{29}H_{44}O_3$: C 79.04; H 10.06%).

Hydrolysis of the rearranged acetoxy compounds

A solution of the appropriate acetate (**1a** or **3a** or **4a**) in methanol-THF mixture (9 : 1) was treated with an excess of 20% aqueous NaOH solution at room temperature, until the substrate had disappeared (TLC control). After addition of a saturated aqueous solution of sodium bicarbonate, the product was extracted twice with ether and then twice with benzene. Usual work-up and removal of solvent under reduced pressure gave the corresponding alcohol in nearly quantitative yield. The isolated products had the following data: 3β-hydroxy-5-methyl-19-nor-5β-cholest-9(10)-en-6-one (**1b**), m.p. 100—101.5 °C (hexane); ν_{max}: 3611, 3455, 1710, 1657 cm^{-1}: δ: 0.77 (18-H), 1.43 (5β-Me), 4.19 (m, $w/2$ = 9.5 Hz, 3α-H) *(lit.* m.p. 70—72 °C ($MeOH—Me_2CO—H_2O$); δ: 0.75 (18-H), 1.45 (5β-Me) [11]);

3β-hydroxy-5-methyl-19-nor-5β-androst-9(10)-en-6,17-dione (**3b**), m.p. 213—217 °C ($CHCl_3$—MeOH); $[\alpha]_D$ +70.7° (c = 11.8); ν_{max}: 3450, 1737, 1705 cm^{-1}; δ: 0.98 (18-H), 1.47 (5β-Me), 4.19 (m, $w/2$ = 9 Hz, 3α-H) (found: C 75.54; H 8.59; calcd. for $C_{19}H_{26}O_3$: C 75.46; H 8.67%);

3β,17β-dihydroxy-5-methyl-19-nor-5β-androst-9(10)-en-6-one (**4b**), m.p. 157.5—160 °C (THF-benzene); $[\alpha]_D$ −1.6° (c = 6.2, Py); ν_{max}: 3330 (broad), 1715, 1053, 1023 cm^{-1}; δ(Py): 0.97 (18-H), 1.67 (5β-Me), 3.78 (t, J = 7.4 Hz, 17α-H), 4.30 (m, $w/2$ = 10 Hz, 3α-H) (found: C 75.02; H 9.25; calcd. for $C_{19}H_{28}O_3$: C 74.96; H 9.27%).

Oxidation of the rearranged alcohols

A solution of alcohol **1b** in acetone-ether (10 : 1) was treated with an excess of 43% aqueous CrO_3 solution at room temperature until the starting compound had disappeared (TLC). After addition of water, the product was extracted twice with ether and then twice with benzene. The crude ketone was chromatographed on silica gel to give a nearly quantitative yield of 5β-methyl-19-nor-5β-cholest-9(10)-en-3,6-dione (**1c**), m.p. 100—102 °C (MeOH); ν_{max}: 1716 cm^{-1}; δ: 0.89 (18-H), 1.27 (5β-Me) *(lit.* m.p. 102—103 °C; δ: 0.81 (18-H), 1.22 (5β-Me) [12]).

A solution of the alcohol **3b** or **4b** in acetone-THF (8 : 2) was oxidized as above. The crude product was extracted four times with chloroform and then chromatographed on silica gel to give 5-methyl-19-nor-5β-androst-9(10)-en-3,6,17-trione (**3c**) in nearly quantitative yield m.p. 166—170 °C (Me_2CO-ether); νdss: 1740, 1719 (inflexion) cm^{-1}; δ: 0.99 (18-H), 1.24 (5β-Me) (*lit.* m.p. 175—177 °C [14]; m.p. 175—176 °C; $\nu_{max}^{CCl_4}$ 4: 1740, 1718 cm^{-1} [25]).

*

Support of this work by the Polish Academy of Sciences, Grant No. MR-I.12, is gratefully acknowledged.

REFERENCES

[1] Blunt, J. W., Fischer, A., Hartshorn, M. P., Jones, F. W., Kirk, D. N., Yoong, S. W.: Tetrahedron, **21,** 1567 (1965)
[2] Kočovský, P. Černý, V.: Collect. Czech. Chem. Commun., **42,** 2415 (1977)
[3] Marples, B. A., O'Callaghan, B. M., Scottow, J. L.: J. Chem. Soc., Perkin Trans. 1, **1974,** 1026
[4] Snatzke, G.: Justus Liebigs Ann. Chem., **686,** 167 (1965)
[5] Aebli, H., Grob, C. A., Schumacher, E.: Helv. Chim. Acta, **41,** 774 (1958)
[6] Snatzke, G., Fehlhaber, H.-W.: Justus Liebigs Ann. Chem., **676,** 188 (1964)
[7] Jones, J. G. L., Marples, B. A.: J. Chem. Soc. (C), **1971,** 572
[8] Jones, J. G. L., Marples, B. A.: J. Chem. Soc. (C), **1970,** 2273
[9] Szczepek, W. J.: Bull. Pol. Ac. Chem., **34,** 89 (1986)
[10] Snatzke, G., Fehlhaber, H.-W.: Justus Liebigs Ann. Chem., **676,** 203 (1964)
[11] Kočovský, P., Černy, V., Vašičková, S., Synačková, M.: Collect. Czech. Chem. Commun., **42,** 3339 (1977)
[12] Coxon, J. M., Hartshorn, M. P., Muir, C. N.: Tetrahedron, **25,** 3925 (1969)
[13] Narayanan, C. R., Iyer, K. N.: Tetrahedron Letters, **1966,** 285; Mousseron-Canet, M., Guilleux, J.-C.: C. R. Hebd. Seances Acad. Sci., **262,** 509 (1966); Mousseron-Canet, M., Brial, J. C.: Bull. Soc. Chim. Fr., **1966,** 3867; Brial, J.-C., Mousseron-Canet, M.: Bull. Soc. Chim. Fr., **1968,** 3321
[14] Davis, M., Petrow, V.: J. Chem. Soc., **1949,** 2973
[15] Hikino, H., Hikino, Y., Nomoto, K., Takemoto, T.: Tetrahedron, **24,** 4895 (1968)
[16] Rodewald, W. J., Szczepek, W. J., Gumułka, J.: Polish J. Chem., **53,** 139 (1979)
[17] Lee, E., Liu, Y.-T., Nakanishi, K.: J. Am. Chem. Soc., **98,** 1634 (1976)
[18] Blunt, J. W., Hartshorn, M. P., Kirk, D. N.: Tetrahedron, **22,** 3195 (1966)
[19] Guest, I. G., Marples, B. A.: Tetrahedron Letters, **1969,** 3575
[20] Petrow, V.: J. Chem. Soc., **1939,** 998
[21] Szczepek, W. J.: preceding paper in this Journal
[22] Rodewald, W. J., Szczepek, W. J., Gumułka, J.: Polish J. Chem., **53,** 797 (1979)
[23] Szczepek, W. J., Gumułka, J., Jagodziński, J.: Bull. Acad. Pol. Sci., Ser. Sci. Chim., **28,** 165 (1980)
[24] Suga, T., Shishibori, T., Matsuura, T.: J. Chem. Soc., Perkin Trans. 1, **1972,** 171
[25] Guest, I. G., Marples, B. A.: J. Chem. Soc., Perkin Trans. 1, **1973,** 900

Acta Chimica Hungarica 123 (3—4), pp. 83—92 (1986)

CONFORMATION AND OPTICAL ANISOTROPY OF SHORT-CHAIN MOLECULES WITH MESOGENIC SIDE GROUPS

Gyula HARDY[1], Stanislav Vasiljevits BUSHIN[2], Irina Nikolaevna SHTENNIKOVA[2]*, Evgenija Vasiljevna KORNEEVA[2], Galina Fedorovna KOLBINA[2], Ferenc CSER[1], Károly NYITRAI[1] and Konstantin Pavlovits SMIRNOV[2]

([1]Research Institute for Plastics, H-1950 Budapest, Hungária krt, 114 and [2]Academy of Science. USSR, Institute Macromolecular Compounds, Leningrad, 199004, USSR)

Received June 25, 1985
Accepted for publication February 5, 1986

Translation diffusion D, sedimentation S^*, intrinsic viscosity $[\eta]$ and flow birefringence, the properties of samples and factions of new comb-like polymers of the alkoxyphenyl-acryloyl oxybenzoate series and two samples of alkoxyphenylmethacryloyl oxybenzoates, have been investigated.

The following dependences relating molecular mass M to $[\eta]$, D and S^* were obtained for poly(methylphenyl-*p*-acryloyloxybenzoate): $[\eta] = 0.26\times10^{-3}\ M^{0.40}$, $D = 3.4\times10^{-9}\ M^{-0.46}$ and $S^* = 4.4\times10^{-12}\ M^{0.54}$. The equilibrium rigidity of the molecules of this polymer was determined: the Kuhn segment was determined from diffusion data $A_D = 80 \pm 20$ Å and viscometric data $A_\eta = (65 \pm 15)$ Å and the hydrodynamic diameter of the molecules was also determined: $d_D = (45 \pm 5)$ Å and $d_\eta = (35 \pm 5)$ Å.

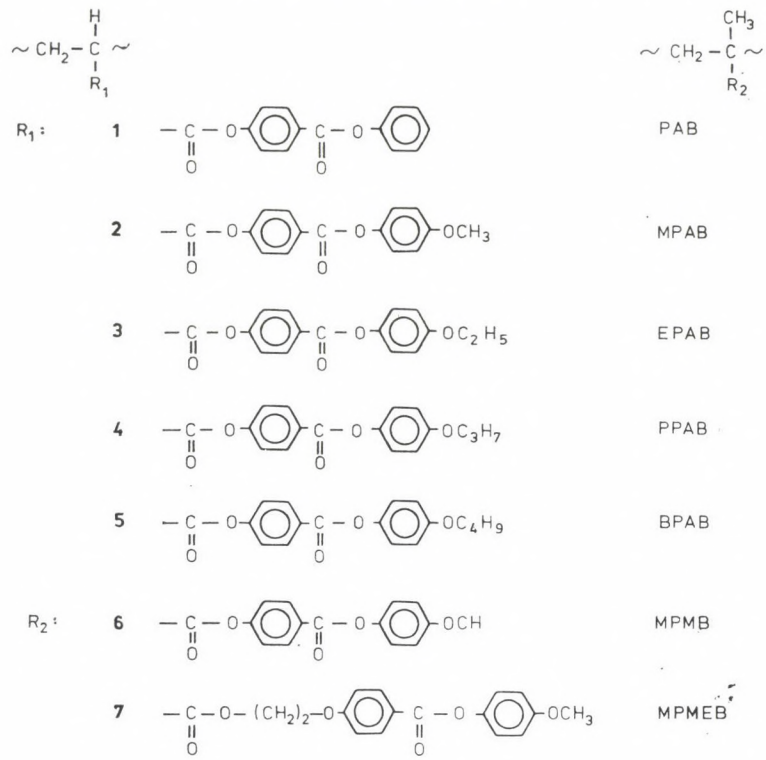
The values of optical anisotropy of the segment of the macromolecules investigated depend on the length of the side-chain group, fall in the range of $(500-850)\times10^{-31}$ m^3 and reflect a high intramolecular orientational order determined by the interaction between mesogenic side groups.

Introduction

The properties of mesomorphic polymers in bulk and in solutions are widely studied by various physical methods [1]. Special investigations have shown [1, 2] that the study of polymers on the molecular level is of considerable importance for the understanding of the nature of generation of polymer mesomorphism.

The present paper deals with the investigation of molecular properties of a number of new comb-like polymers with mesogenic groups in side chains in dilute solutions. These polymers have the following structural formulae:

* To whom correspondence should be addressed.



Experimental

The polymers were obtained by free-radical polymerization from phenyl and *p*-alkoxyphenyl esters of *para*-acryloyloxybenzoic acid [3]. It has been shown [3, 4] that these polymers form anisotropic structures either during the cooling of their melts or when the concentration of their solutions increases. Sample 2 was fractionated into 7 fractions by fractional precipitation from a chloroform solution with hexane. All the samples and fractions of polymer *2* were investigated in one solvent (tetrachloroethane) by flow birefringence (FB), viscometry, sedimentation and translational diffusion. The intrinsic viscosities $[\eta]$ of samples and fractions were determined in a capillary viscometer with the flow time of the solvent = 51.2 s at 21 °C (Tables I and II). The translational diffusion coefficients of samples and fractions were measured with a polarizing diffusometer at 24 °C according to a previously described method [5]. The refractive index increment measured from the areas under the diffusion curves $\Delta_n/\Delta_c = 0.093^{-3}$ m^3/kg. The flotation of non-fractionated samples and that of fractions of polymer 2 in tetrachloroethane was investigated and the buoyancy factor was found to be $(1 - \bar{v}\varrho) = -0.322$ according to pycnometric measurements at 24 °C. Flotation coefficients S^* were measured with a 3170 MOM centrifuge (Hungary) with a polarizing interferometric attachment [5]. The experiments were carried out in a cell with the formation of an artificial boundary at a rotational speed of 60 000 rev/min (for unfranctionated samples at a rotational speed of 40 000 rev/min). Solution concentration c was $\varrho \sim 0.2 \times 10^{-3}$ kg/m^3. The dependences of log x on t (x is the coordinate of the peak top along radial direction and t is the experiment time) are approximated by straight lines (Fig. 1). The values of floration coefficients S^* and molecular masses M of samples and fractions are given in Table I and II.

FB was measured by a visual method [6] in a metal dynamooptimeter with an inner rotor (rotor height was 3×10^{-2} m and the gap between the rotor and the stator ΔR was 2.9×10^{-4} m). All solutions were molecularly disperse, as is confirmed by the type of the dependence of FB on shear stress $g \cdot (\eta - \eta_0)$ for polymer solutions at different concentrations (Figs 2, 3). The values of η and η_0 are the viscosities of the solution investigated and of the solvent, respectively, at 21 °C.

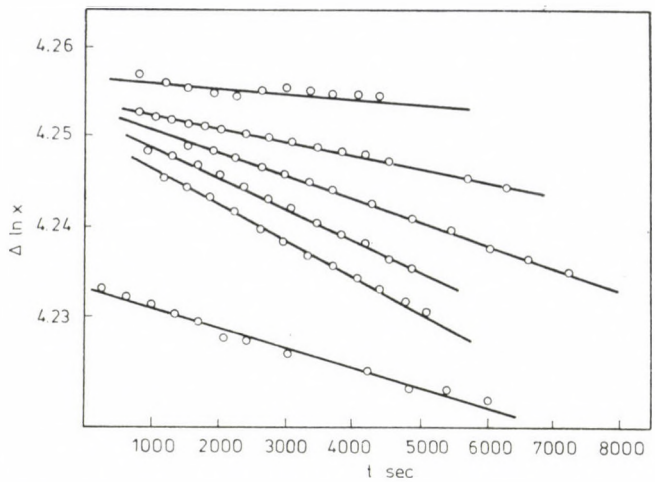


Fig. 1. Dependence of $\Delta \ln x$ on t for the fraction of polymer **2** in tetrachloroethane

Table I

Optical and hydrodynamic characteristics of macromolecules of alkoxy-phenylacryloyl-oxybenzoates in tetrachloroethane

N		$[\eta]\times10^{1}$	$S^{*}\times10^{13}$	$D\times10^{11}$	$M\times10^{-4}$	$\frac{[n]}{[\eta]}\ 10^{9}$	$\alpha_1-\alpha_2\times10^{31}$	$\Delta\alpha\times10^{31}$
1	PAB	0.55	−2.4	1.33	15.5	−42	−510	
2	MPAB	0.14	−1.6	3.6	3.9	−42	−600	−21
3	EPAB	0.49	−2.6	1.4	15.9	−50.54	−600−650	
4	PPAB	0.65	−1.9	1.49	14.9	−65−70	−780−850	
5	BPAB	0.70	−2.4	1.49	16.5	−60−70	−730−850	
6	MPMB	0.13	−1.7	3.5	4.2	−40	−480	
7	MPMEB	0.11	−1.6	3.25	4.2	−10	−120	
	poly(butyl acrylate) (toluene) (for comparison)				30	−0.82	−10	−1.1

Table II

Characteristics of fractions of poly(methylphenyl-n-acryloyloxybenzoate) in tetrachloroethane

N	$[\eta]\times10^{1}$	$D\times10^{11}$	$S^{*}\times10^{13}$	$M_{SD}\times10^{-4}$	$A_0\times10^{16}$	$L\times10^{10}$	$\frac{A_0/A_\infty}{\text{theor.}}$	$A_\infty\times10^{16}$	$\frac{[n]}{[\eta]}\times10^{9}$	$\alpha_1-\alpha_2\times10^{31}$
I*	0.13	3.6	−1.25	2.66	3.06	222	0.822	3.72	−40	−484
II	0.134	3.3	−1.0	2.32	2.65	195	0.814	3.26	−41	−496
III	0.11	3.6	−0.85	1.83	2.50	154	0.800	3.12		
IV	0.10	5.0	−0.65	0.98	2.73	82	0.771	3.54	−33	−390
V	0.07	7.7	−0.35	0.36	2.67	30	0.750	3.56	−25	−300
VI	0.064	7.7	−0.3	0.32	2.49	27	0.750	3.32		
					A_0			A_∞		
					2.68 ± 0.14			3.42 0.22		
VII	0.05	9.5	—	0.25*	2.56**	23	0.750	—		

*$M_{D\eta}$ $A_0 = 2.68\times10^{-16}$ J/K kmol$^{1/3}$; ** $A_0 = A_0/A_{\infty\text{theor.}}$ $(A_\infty)_{av}$.

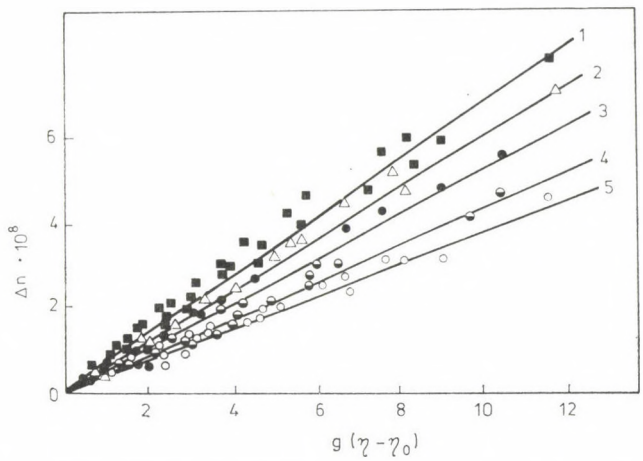


Fig. 2. Dependence of the value of Δn on shear stress $g\ (\eta - \eta_0)$ for solutions of the polymers investigated in tetrachloroethane. Numbers on the curve are polymer numbers is Table I

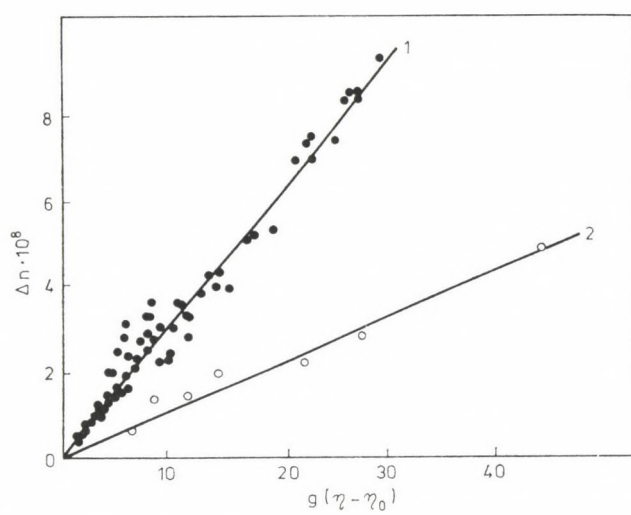


Fig. 3. Dependence of the value of Δn on shear stress $g\ (\eta - \eta_0)$ for the polymers **6** (line 1) and **7** (line 2) in tetrachloroethane

Discussion

Hydrodynamic properties. Table I lists the experimental results for unfractionated samples, and Table II gives those for fractions of sample 2. Analysis of hydrodynamic properties of the polymers under investigation was carried out taking fractions of polymer 2 as example.

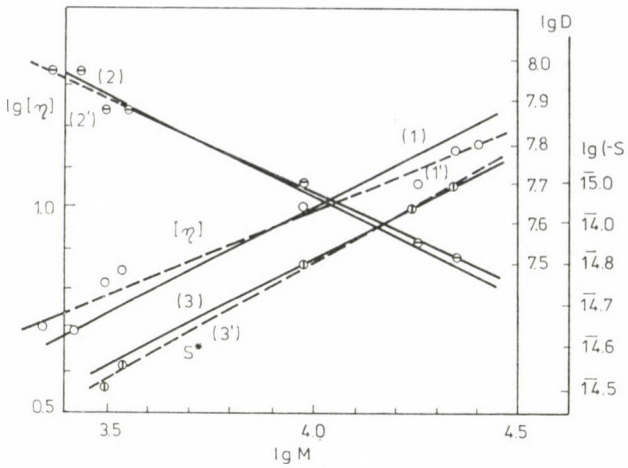


Fig. 4. Dependences of log $[\eta]$ (lines I and I'), log D (lines 2 and 2') and log S^* (lines 3 and 3') on log M for a model of the non-draining Gaussian coil (lines 1, 2 and 3) and a model of a short thick cylinder (broken lings 1', 2' and 3')

The plots in Fig. 4 show the dependences of log $[\eta]$, log D and log S^* on log M for polymer 2. The experimental points fall close to straight lines 1, 2 and 3 described by the equations

$$\begin{aligned} [\eta] &= K_\eta \cdot M^a &&= 9.7\times10^{-5}\, M^{0.5} \\ D &= K_D \cdot M^{-b} &&= 4.7\times10^{-9}\, M^{0.5} \\ S^* &= K_s \cdot M^{1-b} &&= 6.5\times10^{-16}\, M^{0.5} \end{aligned} \qquad (1)$$

The molecular masses of polymer 2 given in Table II correspond to relatively short lengths (L) of molecules since the molecular mass of the monomer unit of polymer $M_0 = 298$ kg/kmol, the degrees of polymerization of fractions, z, range from 90 to 8, which corresponds to the values $L \leq 200$ Å. If it is taken into account that the length of molecules of polymer 2 is small and the polymers investigated exhibit a comb-like structure ($L/d \leq 13$, where d is the geometrical diameter of the molecule), it follows from Eq. (1) that intramolecular hydrodynamic interaction is strong at low coiling of the main chain. Quantitative evaluations of molecular characteristics of polymer 2 according to the data of measurements of $[\eta]$, D, S^* and M were carried out in accordance with low L and the comb-like structure of molecules on the basis of hydrodynamic theories for the model of a weakly bending rodlike spherocylinder [7, 8]. These theories take into account the perturbation of the liquid flow near the ends of the model. Figure 5 shows the experimental dependence of $M^2/[\eta]$ on $\ln L$ (open circles) and of $(3\pi\,\eta_0 LD)/KT$ on $\ln L$ filled circles (k is Boltzmann's constant) and the corresponding theoretical

curves 1, 2, 5, 8 and 3, 4, 6, 7 and the following values fA and d: $A_\eta = 60$ Å, $d_\eta = 40$ Å (curve 1), $A_\eta = 80$ Å, $d_\eta = 30$ Å (curve 2), $A_D = 60$ Å, $d_D = 50$ Å (curve 3), $A_D = 100$ Å, $d_D = 40$ Å (curve 4), $A_\eta = 80$ Å, $d_\eta = 20$ Å (curve 5), $A_D = 100$ Å, $d_D = 20$ Å (curve 6).

It has been previously observed [9] that the values of the Kuhn segment A obtained from the results of measurements of translational friction coefficients and viscometry for polymers with various chemical structures represented by wormlike coils do not coincide. The same discrepancy is observed n this work for polymer 2 the molecules of which are represented by weakly bending thick cylinders. This discrepancy [9] between the values of A_D and A_η is due to the inconsistency between the theories of translational friction and intrinsic viscosity of the wormlike model and, hence, of the wormlike spherocylinder. Another manifestations of this inconsistency [10] is the difference between the average experimental value of hydrodynamic constant $A_0 = 3.4 \times 10^{-16}$ J/K mol$^{1/3}$ obtained for common flexible-chain polymers and the limiting theoretical value $A_\infty = 3.7 \times 10^{-16}$ J/K mol$^{1/3}$ at $L \to \infty$. According to the data of measurements of M, $[\eta]$ and D for fractions of polymer 2, the calculated values of A_0 are $A_0 = \eta_0 D([\eta] \cdot M)^{2/3}$. T $100^{-1/3}$ (Table II). The value of A_0 average over fractions $(A_0)_{av}$ is 2.68×10^{-16} J/K mol$^{1/3}$. No systematic change in A_0 is observed with the change in the molecular mass of the fractions. This value is much lower than the average experimental value of $A_0 = 3.4 \times 10^{-16}$ J/K mol$^{1/3}$ for flexible-chain polymers.

For fractions of polymer 2 at the values of $A = 80$ Å and $d = 40$ Å the ratios A_0/A_∞ relating A_0 to the limiting value A_∞ were calculated according to known theories [7, 8] (Table II). The value of A_∞ for the polymer under investigation obtained from the experimental values of A_0 and the calculated ratios A_0/A_∞ with subsequent averaging over fractions is $(3.4 \pm 0.17) \times 10^{16}$ J/K kmol$^{1/3}$ and coincides with the average experimental value of A_0 for flexible-chain polymers. Moreover, the ratios $(A_\infty$ exp.$/(A_\infty$ theor$)^2$ and $A_\eta/A_D)$ are 0.8. For fraction 7 of polymer 2 the value of A_0 was not determined because the measurements of S^* were absent. This value was, from the average limiting value, $(A_\infty)_{av} = 3.4 \times 10^{-16}$ J/K mol$^{1/3}$ (column 8 in Table II) and the value of $A_0/A_\infty = 0.75$ for fraction 7 (column 3 in Table II). In this case the value of A_0 was $A_0 = 2.55 \times 10^{-16}$ J/K kmol$^{1/3}$ and $M_{D\eta} = 2400$ Kg/kmol. It is noteworthy that the hydrodynamic diameters of molecules of polymer 2 obtained from the data of measurements of translational friction, $d_\eta = (46 \pm 5)$ Å and viscometric data $d = (35 \pm 5)$ Å are high. Both values greatly exceed the length of a completely extended side group of polymer 2, $l \approx 17$ Å, just as the value of the diameter of molecules of polymer 2 obtained from the measurements of polymer density $d\varrho = 15$ Å. However, as can be seen from curves 5 and 6 in Fig. 5, hydrodynamic data cannot be represented on the basis of a wormlike model with a diameter $d \leq 20$ Å. Similar values

of diameters of cylinder-shaped macromolecules were given in [3] based on X-ray and GPC measurements. Here the hydrodynamic molecular volume exceeded that measured in the glassy bulk by X-rays. These high values of the hydrodynamic diameter of macromolecules are probably due to a strong interaction between side chain radicals containing mesogenic groups.

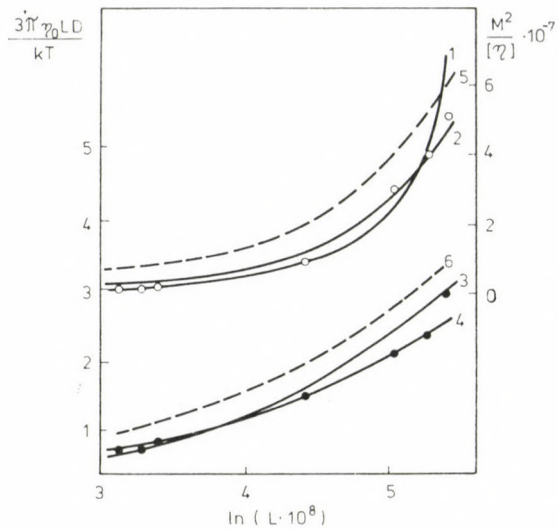


Fig. 5. Experimental dependences of M^2 $[\eta]$ and $3\pi\ \eta^0\ DL/kT$ on $\ln L$ and the corresponding theoretical curves 1, 2, 5 (7) and 3, 4, 6 (6) at the following values of A and d: $A_\eta = 60$ Å, $d_\eta = 40$ Å (curve 1), $A_\eta = 80$ Å, $d_\eta = 30$ Å (curve 2), $A_D = 60$ Å, $d_D = 50$ Å (curve 3), $A_D = 100$ Å, $d_D = 40$ Å (curve 4), $A_\eta = 80$ Å, $d_\eta = 20$ Å (curve 5), $A_D = 100$ Å $d_D = 20$ Å (curve 6)

At this high value of hydrodynamic diameter of molecules $d \approx (30—40)$ Å, the degrees of asymmetry of molecules $p = L/d$ for the fractions investigated are small: they range from (7—5.5) to (1—0.7). In this range of p the dependences of $[\eta]$ and D on M for rodlike particles expressed in the form of the Mark—Kuhn equations are characterized by the values of exponents a and b lower than 0.5 [5]. This makes it possible to consider Eqs (1) approximating the dependences of $[\eta]$, D and S^* on M (Fig. 4, straight lines 1, 2 and 3) only as the first approximation. Straight lines 1', 2' and 3' (broken lines in Fig. 4 plotted by the least-squares method) with slopes less than 0.5 represent the main features of hydrodynamic properties of molecules more closely and are in quantitatively better agreement with the experimental points.

The equations

$$\begin{aligned} [\eta] &= 0.26 \times 10^{-3}\, M^{0.4} \\ D &= 3.4 \times 10^{-3}\, M^{-0.46} \\ S^* &= 4.4 \times 10^{-12}\, M^{0.54} \end{aligned} \qquad (2)$$

are the qualitative and quantitative refinements of Eqs (1). The value of the invariant $\eta_0 K_D K_\eta^{1/3}/100^{1/3}\ T = 2.6\times10^{-16}$ J/K kmol$^{1/3}$ is in agreement with that of $(A_0)_{av} = 2.7\times10^{16}$ kmol$^{1/3}$ is in agreement with that of $(A_0)_{av} = 2.7\times10^{16}$ J/K kmol$^{1/3}$ found for the fractions investigated.

Optical properties

Flow birefringence (FB) observed for polymers listed in Tables I and II and characterized by the value of the shear optical coefficient $[n]/[\eta]$ is negative in sign. This means that the side groups of these polymers exhibit high positive optical anisotropy in a system of their own axes and the optical polarizability of the monomer unit is higher in the direction perpendicular to the axis of the greatest length of the molecule. This experimental fact confirms the comb-like structure of these polymers, and it supports the aperiodic helical model proposed for these polymers in [3], too.

The values of shear optical coefficients of polymers 1—5 in Table I are relatively high, and comparison of polymers with the same molecular mass shows that $[n]/[\eta]$ increases with the module with increasing length of side groups.

It should be noted that since FB was measured in a solvent whose refractive index n_s is not equal to that of the polymers investigated n_k (refractive index increment of the polymer-solvent system $\Delta n/\Delta c \approx 0.093\times10^{-3}$ m^3/kg), the form effect, mainly the microform effect [5], provides a certain contribution to the FB value because the rigidity of the molecules under investigation is relatively high ($A = 70 \pm 10$ Å). The evaluation of contribution of the form anisotropy (always positive) shows that the value of the shear optical coefficient $[n]/[\eta]$ corresponding to the intrinsic anisotropy of these molecules may be 15—20% higher than those listed in Table I.

A certain decrease in the value of $[n]/[\eta]$ observed for fractions of polymer **2** (Table II) with decreasing molecular mass may be due to the non-Gaussian type of the molecules investigated at low M, as has already been mentioned in the discussion of their hydrodynamic properties. For unfractionated samples and for fractions of polymer **2** (from the highest value of $[n]/[\eta]$ the differences between the polarizabilities of the statistical segment $\alpha_1 - \alpha_2$ proportional to the optical anisotropy of the entire molecule $\gamma_1 - \gamma_2$ were determined according to the Kuhn equation [11]

$$\alpha_1 - \alpha_2 = \frac{5}{3}(\gamma_1 - \gamma_2) = \frac{[n]}{[\eta]} \cdot \frac{45\,K\,T_{ns}}{4\pi(n_s^2 + 2)^2} \tag{3}$$

The data listed in Table I and their comparison with the differences between the polarizabilities of comb-like macromolecules without mesogenic groups [12] indicate that the introduction of groups favouring the formation

of the liquid-crystalline structure in low molecular weight liquids (double benzene rings) into the side chain radical leads to a considerable increase in the optical anisotropy of the entire molecule.

The optical anisotropy of poly(butyl acrylate) (PBA) [12] whose side chain is of the same length as that of the polymers investigated but does not contain the mesogenic group, is by a factor of 40—45 lower than that of polymers 1—5. This phenomenon has been observed in a series or comb-like polymer molecules based in methacrylic chains [1]. However, in this case this phenomenon is not so pronounced as, for example, for polymers of the type of phenylmethylacrylic esters of cetyl- or nonyloxybenzoic acids [1, 2] the molecules of which also contain mesogenic side groups but of greater length.

If it is assumed that the equilibrium rigidities of polymers listed in Table I are close to that of polymer **2**, it becomes clear that these polymers are characterized not only by high values of $\alpha_1 - \alpha_2$ but also by relatively high anisotropies of the monomer unit $\Delta\alpha = (\alpha_1 - \alpha_2)/S = (21 \pm 3)\ 10^{-31}\ m^3$ (S is the number of monomer units in a segment). This is also characteristic of macromolecules containing strongly interacting side groups [1]. The data in Table I and Fig. 3 indicate that on passing from polymer **6** to polymer **7** (comparison was carried out in the same solvent) the shear optical coefficient (and, correspondingly, the optical anisotropy) decreases several times. Hence, the contribution provided by the anisotropy of side group to the optical anisotropy of the molecule as a whole decreases although the length of this group increases as a result of the introduction of the aliphatic group —C_2H_4—. This decrease is due to a higher freedom of the mesogenic group, which leads to a decrease in the optical anisotropy of the molecule. Similar experimental facts have been observed in the investigation of a number of flexible-chain polymers containing optically anisotropic side groups.

For polymer **7** in Table I this increase in the distance between the mesogenic group and the main chain and the increase in its freedom of rotation are accompanied by a decrease in the interaction between the mesogenic fragments and the disappearance of high intramolecular orientational order.

In conclusion, it may be said that the hydrodynamic and optical characteristics of the macromolecules investigated show that short chain molecules containing mesogenic groups also exhibit orientational intramolecular order as a result of strong interaction between the side groups. This order is reflected in the relatively high equilibrium rigidity of the main chains, high hydrodynamic diameters of the molecules and high optical anisotropy of the segment and the molecule as a whole.

REFERENCES

[1] Liquid Crystal Order in Polymers (ed. A. Blumstein), Acad. Press, Chap. *2*, *4*, *5*, *6*. New York 1978

[2] Tsvetkov, V. N., Shtennikova, I. N.: Polymer Liquid Crystals. Plenum Press, N. Y. 1984

[3] Hardy, G., Cser, F., Nyitrai, K., Samay, G., Kalló, A.: J. Crystal Growth, **4***B*, 191 (1980) Cser, F.: J. Phys., **40,** 459 (1979)
[4] Cser, F., Nyitrai, K., Hardy, G.: Acta Chim. Acad. Sci. Hung., **100,** 463 (1979)
[5] Tsvetkov, V. N., Eskin, V. E., Frenkel, S. Ya.: Struktura makromolekul v rastvorah, Nauka, Chap. **II**, p. 101, Chap. **V**, p. 396, Chap. **VI**. p. 431. Moscow 1969
[6] Tsvetkov, V. N., Andreeva, L. N.: Adv. Polymer Sci., **39,** 95 (1980)
[7] Norisuye, T., Motowoka, M., Fujita, H.: Macromolecules, **12,** 320 (1979)
[8] Yamakawa, H., Yoshisaki, T.: Macromolecules, **13,** 633 (1980)
[9] Tsvetkov, V. N.: Vysokomol. Soed., ser. *A*, **25,** 1571 (1983)
[10] Tsvetkov, V. N., Lavrenko, P. N., Bushin, S. V.: J. Polymer Sci., **22,** 3447 (1984)
[11] Kuhn, W., Kuhn, H., Buchner, P.: Ergebn. exakten Naturwiss., **25,** I (1951)
[12] Tsvetkov, V. N., Andreeva, L. N., Korneeva, E. V., Lavrenko, P. N.: Dokl. Akad. Nauk SSSR, **205,** 895 (1972)

Acta Chimica Hungarica 123 (3—4), pp. 93—98 (1986)

SPECTROPHOTOMETRIC AND POTENTIOMETRIC DETERMINATION OF Nb(V) AND Ta(V) USING BARBITURIC ACID

Shashi LATA and Girish Chandra SHIVAHARE*

(Department of Chemistry, University of Rajasthan, Jaipur — 302004, India)

Received October 25, 1985
Accepted for publication February 5, 1986

Nb(V) and Ta(V) react with barbituric acid in aqueous media forming pink and reddish coloured soluble complexes having maximum absorbance at 534 nm and 494 nm, respectively. The metal to ligand ratio has been found to be 1 : 2 for the Nb(V) complex and 1 : 1 for the Ta(V) complex. The reaction has been used for spectrophotometric and potentiometric determination of these metals.

Niobium and tantalum have been determined in aqueous media by gravimetric, spectrophotometric and polarographic methods using various reagents [1—4]. There is, however, no reference in the literature regarding potentiometric estimation of these metals together in aqueous media though a few analyses of Nb(V) and Ta(V) in pure solutions in non-aqueous media are reported [5—7]. Estimation of niobium and tantalum in mixture by instrumental methods is of interest since the two metals show close resemblance in their properties. In the present communication barbituric acid (2,4,6-trihydroxy pyrimidine) has been used for spectrophotometric and also potentiometric determination of Nb(V) and Ta(V) together in aqueous media. Barbituric acid gives a pink and reddish colour with Nb(V) and Ta(V) with maximum absorbance at 534 nm and 494 nm, respectively. Estimation of these metals by potentiometric method was also possible since there is a sharp change in potential at the equivalence point which corresponds to 1 : 2 and 1 : 1 (metal : ligand) ratio for Nb(V) and Ta(V) complexes, respectively. Spectrophotometric studies also indicated the same metal to ligand ratio.

Experimental

pH and potential measurements were carried out on a Toshniwal CL 43 pH-meter having a combined glass-calomel electrode. Absorption measurements were carried out on a Beckman DB spectrophotometer using quartz cells of one cm path length.

Preparation of solutions

Solutions of pure Nb_2O_5 and Ta_2O_5 (Fluka) were prepared by fusing them separately with potassium hydrogen sulfate and extracting the melt with 10% aqueous solution of oxalic acid [8]. Nb(V) and Ta(V) were estimated in their respective solutions by precipitating with

* To whom correspondence should be addressed.

tannic acid and finally weighing as pentoxides [1]. These solutions were used as stock solutions and diluted to the required concentration during operation.

0.04 *M* solution of barbituric acid was prepared by dissolving its calculated amount in doubly distilled water and further diluted whenever require.

Results and Discussion

Spectrophotometric determination

Nb(V) and Ta(V) solutions give pink and reddish colour immediately on mixing with barbituric acid solution at pH 4.5 and 6 having maximum absorbance at 534 nm and 494 nm, respectively. The reagent solution did not show any absorbance in these regions.

The systems were found to obey Beer's law within the range of 5 to 68 ppm of Nb(V) and 5 to 130 ppm of Ta(V). Stoichiometry of both complexes has been determined by Job's method of continuous variation [9] and mole ratio method [10]. For the niobium complex the metal to ligand ratio was found to be 1 : 2 whereas for the tantalum complex it was 1 : 1.

Interference by foreign ions

Nb(V) can be estimated in the presence of Mg^{2+}, Al^{3+}, Bi^{3+}, Cr^{3+}, Fe^{3+}, Co^{3+}, $V_5{}^+$, $Ta_5{}^+$, W^{6+} and U^{6+} but Cu^{2+}, Pb^{2+}, Ti^{2+} and Zr^{4+} interfere.

Ta(V) can be estimated by this method in the presence of Mg^{2+}, Al^{3+}, V^{5+}, Nb^{5+}, Mo^{6+}, and U^{6+}, but Cu^{2+}, Pb^{2+}, Ti^{2+}, Co^{3+}, Fe^{3+}, and Zr^{4+} interfere.

Spectrophotometric determination of Nb(V) and Ta(V) can be done directly. Some results of spectrophotometric estimations are given in Tables I and II.

Potentiometric determination

Both direct and reverse titrations were carried out. 1×10^{-2}, 5×10^{-3} and 2.5×10^{-3} *M* solutions of Nb(V) and Ta(V) were used in direct titrations and 1×10^{-3}, 5×10^{-4} and 2.5×10^{-4} *M* solutions in the reverse titrations. In the direct titration the metal solution was added from a micro-burette to the ligand solution in the cell and vice versa in reverse titration. Ligand solutions of similar concentrations were used. Concentration of the solution in the burette was kept 10 times higher than that of the solution in the cell during titration. A sharp change in potential was observed at equivalence point. The end-point was obtained by plotting $\Delta E/\Delta V$ against volume added and it corresponded to 1 : 2 and 1 : 1 metal to ligand ratios for the Nb(V) and Ta(V) complex, respectively.

While titrating the mixture of Nb(V) and Ta(V), the titration curve showed two distinct inflections and two peaks were obtained when $\Delta E/\Delta V$

was plotted against, the volume added. This indicates that the presence of one metal does not interfere with the determination of the other by this method.

Results of some potentiometric estimations are given in Tables III and IV and also represented graphically in Figs 1, 2, 3a and 3b.

Table I

Spectrophotometric estimation of Nb(V) *and* Ta(V) *in pure solutions*

No.	Nb(V) present (μg)	Nb(V) found (μg)	Error (%)	Ta(V) present (μg)	Ta(V) found (μg)	Error (%)
1.	25.34	35.24	0.24	50.68	50.91	0.42
2.	55.75	55.60	0.27	60.34	60.26	0.13
3.	64.70	64.82	0.12	126.70	126.21	0.36

Table II

Spectrophotometric estimation of Nb(V) *and in mixture*

No.	Nb(V) present (μg)	Nb(V) found (μg)	Error (%)	Ta(V) present (μg)	Ta(V) found (μg)	Error (%)
1.	28.28	28.30	0.23	26.98	27.90	0.29
2.	52.50	52.55	0.10	54.82	54.91	0.17
3.	59.18	59.26	0.14	108.42	108.66	0.22

Table III

Potentiometric estimation of Nb(V) *and* Ta(V) *in pure solutions*

No.	Direct Titration			Direct Titration		
	Nb(V) solution vs. barbituric acid solution in cell			Ta(V) solution vs. barbituric acid solution in cell		
	Nb(V) present (μg)	Nb(V) found (μg)	Error (%)	Nb(V) present (μg)	Nb(V) dound (μg)	Error (%)
1.	23.25	23.19	0.26	90.50	90.68	0.19
2.	11.63	11.61	0.17	45.75	45.16	0.20
3.	5.81	5.79	0.34	22.63	22.58	0.22

Table IV

Potentiometric estimation of Nb(V) *and* Ta(V) *in mixture*

No.	Estimation of Nb(V)			Estimation of Ta(V)		
	Nb(V) present (μg)	Nb(V) found (μg)	Error (%)	Ta present (μg)	Ta(V) found (μg)	Error (%)
1.	23.25	23.19	0.26	90.50	90.67	0.21
2.	11.63	11.60	0.26	45.25	45.17	0.18
3.	5.81	5.80	0.17	22.63	22.57	0.27

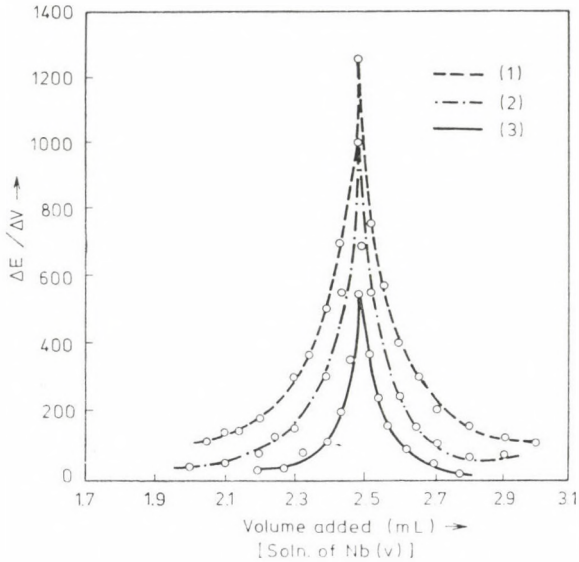


Fig. 1. Direct titration of Nb(V) with barbituric acid; (1) titration of 1.0×10^{-2} *M* soln. of Nb(V) with 50 ml of 1.0×10^{-3} *M* soln. of barbituric acid, (2) titration of 5.0×10^{-3} *M* soln. of Nb(V) with 50 ml of 5.0×10^{-4} *M* soln. of barbituric acid, (3) titration of 2.5×10^{-3} *M* soln. of Nb(V) with 50 ml of 2.5×10^{-4} *M* soln. of barbituric acid

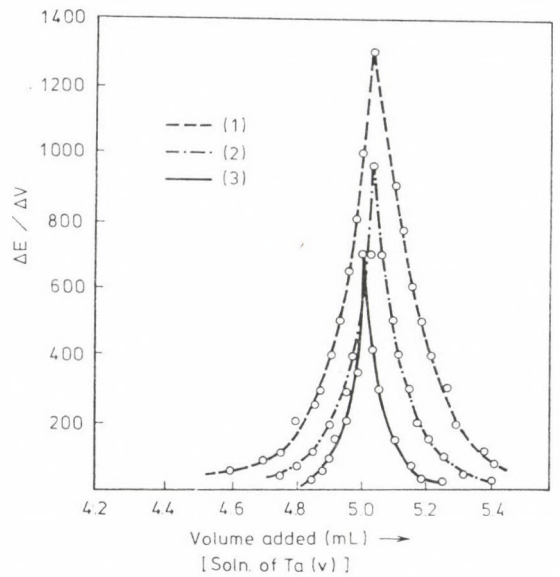


*Fig. 2.*Direct titration of Ta(V) with barbituric acid; (1) titration of 1×10^{-2} *M* soln. of Ta(V) soln. with 50 ml of 1×10^{-3} *M* soln. of barbituric acid, (2) titration of 5×10^{-3} *M* soln. of Ta(V) soln. with of 50 ml of 5×10^{-4} *M* soln. of barbituric acid, (3) titration of 2.5×10^{-3} *M* soln. of Ta(V) soln. with 50 ml of 2.5×10^{-4} *M* soln. of barbituric acid

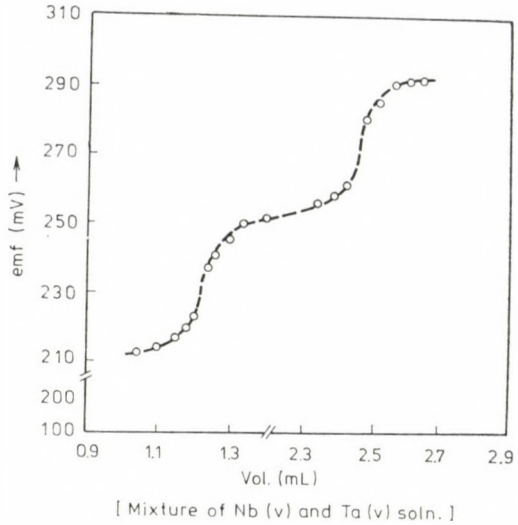


Fig. 3a. Titration of a mixture of 1×10^{-2} *M* Nb(V) and 0.01 *M* Ta(V) soln. with 1×10^{-3} *M* soln of barbituric acid

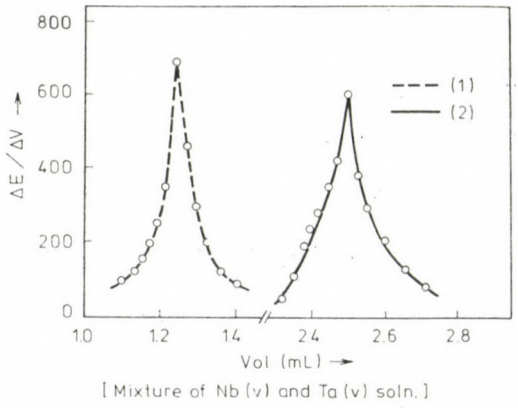


Fig. 3b. Direct titration of a mixture of Nb(V) and Ta(V) with barbituric acid; (1) Nb(V) soln. with ligand soln., (2) Ta(V) soln. with ligand soln.

Interference by foreign ions

Nb(V) can be estimated potentiometrically using barbituric acid in the presence of Mg^{2+}, Co^{2+}, Pb^{2+}, Fe^{3+}, Mo^{6+}, NO_3^-, Cl^-, oxalata but Cd^{2+}, Zr^{4+}, V_5^+, W^{6+}, BO_3^{3-}, I^-, Br^- and citrate interfere.

Ta(V) can be estimated in the presence of Mg^{2+}, Co^{2+}, Fe^{3+}, V^{5+}, Mo^{6+}, NO_3^-, Cl^-, oxalate and citrate but Pb^{2+}, Cd^{2+}, Zr^{4+}, W^{6+}, Br^-, I^- and BO_3^{3-} interfere.

*

One of the authors (s. L.) is grateful to the University Grants Commission, New Delhi for the award of a Research Fellowship.

REFERENCES

[1] Das, M. S., Venkateshwarlu, C. H., Athavale, V. T.: Analyst, **81,** 3 (1956)
[2] Ackermann, G., Koch, S.: Talanta, **9,** 1015 (1962)
[3] Kennedy, J. M.: Anal. Chem., **33,** 943 (1961)
[4] Sherif, M. K., Awadallah, R. M., Mohamed, F. S.: Bull. Rac. Sci. Assint. Univ. Egypt, **7,** 371 (1978)
[5] Sharda, P., Shivahare, G. C.: Indian Chem. Soc., **59,** 904 (1982)
[6] Sharda, P., Shivahare, G. C.: Transactions SAEST, **17,** 47 (1982)
[7] Chomal, S., Shivahare, G. C.: J. Electrochem. Soc., India, **59,** 906 (1985)
[8] Dams, R., Hoste, J.: Talanta, **11,** 1502 (1964)
[9] Job, P.: Ann. Chim., **9,** 113 (1928)
[10] Yoe, J. H., Jones, A. L.: Ind. Engng. Chem., Anal. Ed., **16,** 111 (1944)

Acta Chimica Hungarica 123 (3—4), pp. 99—106 (1986)

STUDIES ON 1-ARYLOXYSILATRANES, V+

STUDIES ON THE MECHANISM HYDROLYSIS OF 1-ARYLOXYSILATRANES

Jerzy ŁUKASIAK* and Zygmunt JAMRÓGIEWICZ

(Laboratory of Instrumental Methods, Chair of Physical Chemistry, Medical Academy, Al. K. Marksa 107, 80—416 Gdańsk, Poland)

Received October 29, 1985
In revised form February 3, 1986
Accepted for publication February 18, 1986

The relationship has been studied between the rate of hydrolysis of 1-aryloxysilatranes — and concentrations of NaOH in aqueous solution as well as in media of different polarity. The results allowed to hypothesize the possibility of operating of the S_N-1-Si mechanism of the reaction parallel to that of S_N-2-Si.

Investigation of the relationship between the rate constant, k, and water concentration in aqueous methanol supported the validity of the hypothesis.

The percentage contribution of the hydrolysis reaction occurring according to the S_N-1-Si mechanism to the overall process has been found to range between 0 and 60 depending on the conditions.

The hitherto reported studies on the mechanism of solvolysis, in particular hydrolysis, of silicon and organosilicon compounds have led to conclusion that the reactions proceed via the S_N-2-Si mechanism [1, 2].

Voronkov and associates have reported [3—5] results showing that as far as the mechanism of the hydrolysis is considered, the compounds can be divided into two groups: 1-alkylsilatranes with R = CH_3, C_2H_5, *n*-C_3H_7, *iso*-C_3H_7 where the constant ϱ calculated from the Hammett's equation, is $\varrho = +4.76$ [3] and 1-alkoxysilatranes (R = CH_3O, C_2H_5O, *n*-C_3H_7O, *iso*-C_3H_7O, *tert*-C_4H_9O, *n*-C_4H_9O, *iso*-C_4H_9O, *sec*-C_4H_9O), where the constant is $\varrho = +2{,}60$ [3]. In another paper [4], the authors classify the compounds using the some criterion into two groups, one embracing alkoxysilatranes, and the other aryloxysilatranes. For the group of alkoxysilatranes (with R = OC_2H_5, *n*-C_3H_7O, *i*-C_3H_7O, *t*-C_4H_9O, *t*-$C_4H_9CH_2O$), the Hammett's constant was $\varrho = -1.26$. Whereas for 1-aryloxysilatranes (with R = C_6H_5O, 2-$CH_3C_6H_4O$, 3-$CH_3C_6H_4O$, 4-$CH_3C_6H_4O$, 4-$CH_3OC_6H_4O$, 4-ClC_6H_4O and $C_6H_5CH_2O$), the constant was $\varrho = -0.23$.

In the group of compounds with positive ϱ values, the rate determining step of the reaction was the nucleophilic attack of the water molecule or of

+ Part IV.: Łukasiak, J., Samet, A., Lipniewicz, I., Nadolski, A.: Studies on 1-aryloxysilatranes. Part IV. Analysis of relationships between the minimal inhibitory concentration and properties of 1-aryloxysilatranes, Farmacja Polska, **41**, 283 (1985).

* To whom correspondence should be addressed.

the hydrated OH^- ion, whilst in the group with negative ϱ values there was the attack of the hydroxonium ion.

Despite the failure of detecting sililenium ion among the hydrolysis products of the compounds [6—11], Bøe [12] suggested that the mechanism of solvolysis of compounds containing the Si—OC bond can be both S_N-2-Si and S_N-1-Si.

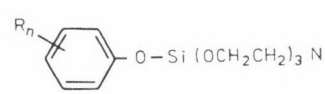
The sililenium ions have yet been observed either in the gas phase or under conditions of mass spectrometry [9, 13]. In [14—16], mass spectra allowed to identify a fragment with $m/e = 174$, assigned to $[N(CH_2CH_2O)_3Si]^+$.

The results of our investigations are concerned with the kinetics of hydrolysis of 1-aryloxysilatranes of the general formula $R_n—C_6H_{5-n}—O—Si(OCH_2CH_2)_3N$, with R = H, Br, I, Cl, CH_3, C_2H_5, NO_2, OCH_3 and $n = 1, 2, 3$ and were published in [17]. The calculated Hammett's constant of the compounds was 0.31. The close to zero value of the constant did not allow to determine the type of the reaction mechanism (as for $|\varrho| < 1$ even the sign of the constant does not provide a sound basis to classify the reaction mechanism) [18].

Experimental

The preparation of the compounds, their identification and the determination of the rate constants were described in the previous reports [16, 17, 19]. The structure of the new compounds 1-(2-phenylphenoxy)silatrane, 1-(4-phenylphenoxy)silatrane and 1-(2-carbonamidophenoxy)silatrane was based on the results of elemental analyses and the IR spectra listed in Table I.

The relationship was determined between the rate constant of hydrolysis and the concentration of NaOH for 1-aryloxysilatranes of the general formula:



where R = H, Br, CH_3, OCH_3, Cl, C_6H_5 and $CONH_2$ with $n = 1$ and 2. The concentration of the silatranes in the solutions was about 10^{-4} *M*, whereas that of NaOH was varied within 0.01—0.06 *M*. For selected compounds, also the relationship between the rate constant and water concentration was studied.

Results

Equations of linear regression of the relationships were computed by the least-squares method. In all equations the regression coefficients were higher than 0.99.

The measurements of the rate constant, k, for eleven 1-aryloxysilatranes for various NaOH concentrations in water allowed the following linear regression equation to be derived.

$$\log k = a \log [\mathrm{NaOH}] + b$$

where numerical values of parameters a and b are shown in Table II.

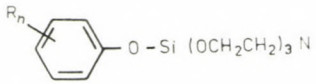
Table I

Results of analysis

Compound	Elemental analysis			Interpretation of IR spectra [20, 21]							
	Calcd. / Found % C	Calcd. / Found % H	Calcd. / Found % Si	$\delta_t(NCH_2)$	$\nu_{as}(NC_3)$ $\delta(CH_2)$	ν_{as}(C—OSi)	ν(C—OSi)	ν(Si—OAr)	$\nu_s(NC_3)$	$\nu_s(SiO_3)$	δ (skel)
1-(2-phenylphenoxy)-silatrane	62.95 / 61.93	6.16 / 6.10	8.18 / 8.01	1270 s	1110 s	1090 s	1020 m	940 m	910 m	650 m	590 s
1-(4-phenylphenoxy)-silatrane	62.95 / 62.05	6.16 / 6.12	8.18 / 7.98	1275 m	1120 s	1100 s	1020 m	940 m	900 s	640 m	580 m
1-(2-carbonamidophenoxy)-silatrane	50.32 / 49.85	5.84 / 5.62	9.04 / 8.99	1270 s	1120 s	1090 s	1020 m	940 m	900 s	630 m	595 m

Table II

Numerical values of the parameters in regression equation,
$\log k = a \log [NaOH] + b$



Parameter \ R_n	2-C_6H_5	4-Br	4-CH_3	4-OCH_3	H	2-$CONH_2$	4-C_6H_5	2-Cl	2-CH_3	2,6-$(CH_3)_2$	2,6-Cl_2
a	0.98	0.97	0.91	0.87	0.87	0.83	0.82	0.80	0.79	0.71	0.66
b	−0.71	−0.67	−0.82	−0.83	−0.89	−0.73	−0.92	−0.77	−1.2	−1.4	−0.99

Table III

Numerical values of the parameters in regression equation,
$\log k = a \log [NaOH] + b$

Compound / Conc. of water % v/v	METHANOL									
	1-phenoxy-silatrane		1-(2,6-dimethyl-phenoxy)silatrane		1-(2-phenylphenoxy)-silatrane		1-(4-phenylphe-noxy)silatrane		1-(2-carbonamido-phenoxy)silatrane	
	a	*b*	*a*	*b*	*a*	*b*	*a*	*b*	*a*	*b*
100	0.87	−0.89	0.73	−1.34	0.98	−0.71	0.82	−0.92	0.83	−0.73
85	0.91	−1.06	0.80	−1.36	0.99	−0.92	0.89	−0.98	0.77	−1.02
70	0.98	−1.16	0.90	−1.48	0.96	−1.12	0.99	−1.03	0.72	−1.27
50	0.97	−1.42	1.04	−1.49	1.04	−1.32	1.07	−1.21	0.89	−1.38

Table IV

Numerical values of the parameters in regression equation,
$\log k = a \log [NaOH] + b$

Solvent / Compound / Conc. of water % v/v	ETHYLENE GLYCOL				ACETONITRILE	
	1-Phenoxysilatrane		1-(2,6-dimethyl-phenoxy)-silatrane		1-Phenoxysilatrane	
	a	*b*	*a*	*b*	*a*	*b*
100	0.87	−0.89	0.73	−1.34	0.87	−0.89
85	0.90	−1.08	0.78	−1.39	0.90	−1.13
70	0.93	−1.18	0.82	−1.57	0.94	−1.22
50	0.99	−1.42	0.92	−1.78	0.98	−1.39
30	—	—	—	—	0.97	−1.51

For all linear regression equations the correlation coefficient $r > 0.995$

A similar equation holds for relationship between the rate constant k and the concentration of NaOH for 1-phenoxysilatrane and 1-(2,6-dimethylphenoxy)silatrane, 1-(2-phenylphenoxy)silatrane, 1-(4-phenylphenoxy)silatrane and 1-(2-carbonamidophenoxy)silatrane in aqueous methanol. Numerical values of a and b are shown in Table III.

For 1-phenoxysilatrane and 1-(2,6-dimethylphenoxy)silatrane similar investigations were also carried out in the water — ethylene glycol and water — acetonitrile solvent systems. The coefficients are shown in Table IV.

It was experimentally verified that in the specified solvent systems, the relationship between the concentration of NaOH and its activity expressed in terms of electrolytic conductivity, λ, was linear:

$$\log \lambda = A \log [NaOH] + B, \text{ where } A = 0.97 - 1.05$$

This allows to ignore the influence of the variations in the activity of NaOH in the solutions on the rate constants occurring in regression equations as the coefficient a.

If the hydrolysis occurred according to the S_N-2-Si mechanism, the rate of the reaction could be expressed by equation

$$v = k_0 \cdot C_s \cdot C_{OH^-}^n$$

where $C_{OH^-} = C_{NaOH}$, C_s — is the silatrane concentration, and n is the order of reaction relative to NaOH. In the case of the S_N-2 mechanism, $n = 1$.

Owing to a large excess of NaOH as compared with the silatrane concentration, the reaction was assumed to be first-order (pseudo-first-order), hence the found k value, $k_f = k_0 \cdot C_{OH^-}^n$. In logarithmic form:

$$\log k_f = \log k_0 + n \log C_{OH^-}$$

where n corresponds to the experimentally found a value (Tables II—IV).

Data in Tables (II—IV) reveal that there is no neat S_N-2 mechanism of the hydrolysis, because the experimentally found order of the reaction relative to NaOH is both fractional and variable. When the solution's polarity decreases, the value of coefficient a approaches unity.

The a value depends primarily on the medium polarity, as evidenced by inspection of the a values for the systems: water — ethylene glycol, water — acetonitrile and water — methanol the dielectric constant of methanol is 31.2, whereas that of ethylene glycol and acetonitrile is 38.8 at 20 °C.

Data in Table II show that *para*-substituents increase the a values and the *ortho*-substituents decrease the value as compared to that of 1-phenoxysilatrane. In di-substituted compounds the effect is stronger that in the monosubstituted ones, with the exception of 1-(2-phenylphenoxy)silatrane and 1-(4-phenylphenoxy)-silatrane where the influence of the position of substitution is just reverse.

An analysis of the phenomena allowed to hypothesize that during the hydrolysis of 1-aryloxysilatranes two parallel mechanisms are operating, S_N-2 and S_N-1, the contribution of either of them depending on the conditions of experiment, in particular on the medium polarity.

In order to verify the hypothesis, a relationship was investigated between the water concentration and the rate constant of hydrolysis, k, for 1-phenoxysilatrane, 1-(2,6-dimethylphenoxy)silatrane, 1-(2-phenylphenoxy)silatrane, 1-(4-phenylphenoxy)silatrane and 1-(2-carbonamidophenoxy)silatrane in aqueous methanol. The results allowed to derive equations of linear regression

$$\ln k = \alpha [H_2O] + \beta$$

Coefficients α and β for two concentrations of NaOH are listed in Table V.

Investigation of the effect of NaOH activity expressed by its electrical conductivity, λ, in relation to water concentration in aqueous methanol

Table V

Numerical values of the parameters in regression equation,
$\ln k = \alpha [H_2O] + \beta$

NaOH *M*	1-Phenoxysilatrane		1-(2,6-dimethylphenoxy)-silatrane		1-(2-phenylphenoxy)-silatrane		1-(4-phenylphenoxy)-silatrane		1-(2-carbonamido-phenoxy)silatrane	
	α	β	α	β	α	β	α	β	α	β
0.01	0.063	−9.5	0.071	−10.2	0.062	−9.45	0.066	−9.52	0.063	−8.9
0.05	0.050	−7.4	0.048	−8.1	0.058	−7.68	0.051	−7.34	0.057	−7.3

Table VI

Rate constants, k_1 and k_2 for the hydrolysis reactions occurring via S_N1 and S_N2 mechanisms, respectively

	SOLVENT									
	Methanol				Ethylene glycol				Acetonitrile	
	1-Phenoxysilatrane		1-(2,6-dimethylphenoxy)-silatrane		1-Phenoxysilatrane		1-(2,6-dimethylphenoxy)-silatrane		1-Phenoxysilatrane	
% H_2O	10^4k_1 s^{-1}	10^4k_2 $s^{-1}dm^3mol^{-1}$	10^4k_1 s^{-1}	10^4k_2 $s^{-1}dm^3mol^{-1}$	10^4k_1 s^{-1}	10^4k_2 $s^{-1}dm^3mol^{-1}$	10^4k_1 s^{-1}	10^4k_2 $s^{-1}dm^3mol^{-1}$	10^4k_1 s^{-1}	10^4k_2 $s^{-1}dm^3mol^{-1}$
100	8.0	1700	9.6	800	8.0	1700	9.6	800	8.0	1700
85	3.0	1100	5.3	700	3.6	1050	3.9	690	3.6	950
70	0.4	700	1.1	450	1.8	800	2.8	400	1.3	500
50	—	400	0.1	400	0.1	400	0.5	200	0.3	400
30	—	—	—	—	—	—	—	—	0.3	250

allowed to derive the following equation:

$$\ln \lambda = \alpha [H_2O] + \beta$$

Coefficient α amounted to 0.027 and was independent of the NaOH concentration over the range 0.01—0.05 M, thus indicating that the variations in α values in Table V cannot be ascribed to variation in the activity of NaOH, but to the nature of the compound studied.

As expected the α values decrease with increasing NaOH concentration (Table V), thus supporting the hypothesis.

Starting from the relationship between constant k for the process involving parallel reactions and k_1 constants of partial processes, one can write:

$$k = k_1 + k_2 \cdot C_{OH^-},$$

where k is the constant of the hydrolysis reaction: k_1 is the rate constant of a reaction following the S_N-1 mechanism and k_2 is the rate constant of a reaction proceeding according to the S_N-2 mechanism, and C_{OH^-} is constant.

On the basis of the k values calculated from the regression equation for two different NaOH concentrations (Tables II and IV) rate constants k_1 and k_2 were estimated for particular hydrolysis conditions of 1-phenoxysilatrane and 1-(2,6-dimethylphenoxy)silatrane. The results are shown in Table VI.

Data in Table VI show a decrease of k_1 with decreasing polarity of the mechanism and a weak relationship between conformation of the compounds and k_1 for the given medium polarity.

On the other hand, k_2 values are clearly dependent on the conformation of the compounds and only slightly on the medium polarity.

The results suggest that the effect of ortho-substituents on the rate of hydrolysis consists mainly on hampering the S_N-2 reaction, whereas variations in the medium polarity affect predominantly the S_N-1 reaction.

Depending on conditions, the percentage contribution of the S_N-1 reaction to the overall process has been estimated to range between 0 and 60.

Conclusions

A comparison of the linear regression lines by using the parallelity test showed that statistically significant differences between coefficients a occur:

(i) for the $\ln k = f(c_{H_2O})$ curves for 0.01 and 0.05 M NaOH concentrations in the case of 1-phenoxysilatrane at a significance level $\alpha < 0.001$, whereas in the case of 1-(2,6-dimethylphenoxy)silatrane at $\alpha < 0.01$.

(ii) for curves described by the equation

$$\log k = a \log c_{OH-} + b$$

in the case of 1-phenoxysilatrane in water and aqueous methanol (1 : 1) at $\alpha = 0.15$ as well as for 1-(2,6-dimethylphenoxy)silatrane at $\alpha < 0.002$. For 1-phenoxysilatrane and 1-(2,6-dimethylphenoxy)silatrane in water and water—ethylene glycol mixture.

(iii) statistically significant differences were noted at $\alpha < 0.05$ and $\alpha < 0.02$, respectively. For 1-phenoxysilatrane in water and water—acetonitrile (1 : 1) the differences were noted at $\alpha < 0.05$.

The differences are justified by our hypothesis admitting the occurrence of parallel S_N-1-Si and S_N-2-Si mechanisms of the hydrolysis of 1-aryloxysilatranes.

The complexity of the reaction is further supported by the deviation from linearity of the plots of the Eyring and Arrhenius equations for 1-(2-methylphenoxy)silatrane and 1-(2,5-dimethylphenoxy)silatrane [17].

REFERENCES

[1] Eaborn, C.: Organosilicon Compounds, Butterworths, London 1960
[2] Sommer, H. L.: Stereochemistry, Mechanism and Silicon, McGraw-Hill, New York 1965
[3] Voronkov, M. G., Zelchan, G. I.: Khim. Geterotsikl. Soedin., **1969,** 450
[4] Voronkov, M. G., Emelyanow, S. I., Zelchan, G. I., Dyakov, M., Kuznetsov, G. I.: Khim. Geterotsikl. Soedin., **1975,** 35
[5] Voronkov, M. G., Emelyanov, S. I., Dyakov, V. M., Vitkovskii, V. Ju., Kapranova, L. V., Baryshok, V. P.: Khim. Geterotsikl. Soedin., **1976,** 1344
[6] Sommer, L. H., Homer, G. D., Messing, A. W., Kutschinski, J. L., Stark, F. O., Michael, K. W.: J. Am. Chem. Soc., **93,** 2093 (1971)
[7] Carre, F., Corriu, R., Leard, M.: J. Organomet. Chem., **24,** 101 (1970)
[8] Carre, F., Corriu, R., Henner, B.: J. Organomet. Chem., **22,** 589 (1970)
[9] Sommer, L. H., Fujimoto, H.: J. Am. Chem. Soc., **91,** 7040 (1969)
[10] Olah, G. A., O'Brien, D. H., Lui, Ch. Y.: J. Am. Chem. Soc., **91,** 701 (1969)
[11] Popkow, K. K.: Zhurn. Obsh. Khim., **39,** 2791 (1969)
[12] Bøe, B.: Mechanism of Solvolysis of Organosilicon Compounds, Bergen Universitet Norway 1975
[13] Odiorne, T. J., Harvey, D. J., Vauros, P.: J. Org. Chem., **38,** 4274 (1973)
[14] Voronkov, M. G., Emelyanov, I. S., Vitkovskii, Ju., Kapranova, L. V., Dyakov, W. M., Baryshok, W. P.: Khim. Geterotsikl. Soed., **1976,** 1344
[15] Müller, T., Hencsei, P., Bihátsi, L.: Periodica Polytechnica, **25,** 181 (1981)
[16] Łukasiak, J.: Acta Chim. Hung., **117,** 271 (1984)
[17] Łukasiak, J., Jamrógiewicz, Z.: Acta Chim. Hung., **115,** 167 (1984)
[18] Schwetlick, K.: Kinetyczene metody badania mechanizmów reakcji-PWN, Warszawa 1975
[19] Łukasiak, J., Jamrógiewicz, Z.: Acta Chim. Acad. Sci. Hung., **105,** 19 (1980)
[20] Voronkov, M. G., Schevchenko, S. G., Brodskaja E. I., Baryshok, W. P., Reich, P., Kunat, D., Frolov, Iu. L.: Izv. Sibirsk. Otd. Akad. Nauk SSSR, Ser. Khim., **5,** 135 (1981)
[21] Hencsei, P., Bihátsi, L., Kovács, I., Szalay, E., Karsai, É. B., Szöllősy, Á., Gál, M.: Acta Chim. Hung., **112,** 261 (1983)

Acta Chimica Hungarica 123 (3—4), pp. 107—114 (1986)

PHYSICO-CHEMICAL STUDIES ON THE MIXED LIGAND COMPLEXES OF SOME DIIMINES WITH PALLADIUM(II), PLATINUM(II), IRIDIUM(III), RHODIUM(III) AND PLATINUM(IV) PHTHALIMIDES

Chokhe Lal SHARMA* and Shahid Suhel NARVI

(Chemistry Department, University of Roorkee, Roorkee-247667, U. P., India)

Received December 13, 1985
Accepted for publication February 18, 1986

The mixed ligand complexes of palladium(II), platinum(II), iridium(III), rhodium(III) and platinum(IV) with phthalimide as primary and diimines (dipyridyl and *o*-phenanthroline) as secondary ligands have been synthesized and characterized on the basis of elemental analysis, electrical conductance, magnetic measurements and spectral (electronic and infrared) data. $[M(P)_2(AM)]$ where M = Pt(II), Pd(II); P = deprotonated phthalimide and Am = amines were planar and $[Pt(P)_4(Am)]$ and $[M(P)_3(Am)(H_2O)]$ were M = Ir(III), Rh(III) were of octahedral structure, various ligand field nephelauxetic parameters have also been evaluated.

The antitumor activity of bis-(amine) platinum(II) complexes with two *cis* anionic leaving groups is by far one of the most ouststanding results in the field of the bioactivity of metal complexes, the *cis*-platin, i.e. *cis* $[Pt(NH_3)_2Cl_2]$ according to the recent reports is the largest selling anticancer drug. This class of complexe exhibits activity, ehrlich ascites, carcinoma and leukemeas [1, 2]. The complexes of platinum metal ions with *o*-phenanthroline and related bases have been shown to be lethal to many bacteria and pathogenic fungi [3]. Beside this the utility of platinum metal complexes as homogeneous catalyst in the reactions of industrial importance is an established fact. Keeping in view the above facts and the pharmacological [4—8] and industrial [9, 10] importance of phthalimide and heterocyclic bases [11—15], it is, therefore, of interest to synthesize such complexes. Activity of these class of organic compounds is reported to have generally been enhanced when they are allowed to form complexes with metals [16, 17]. Hence in this paper we report the preparation and characterization of mixed ligand complexes of Pt(II), Pd(II), Pt(IV), Ir(III) and Rh(III) with phthalimide as primary and 1,10-phenanthroline and 2,2-dipyridyl as secondary ligands.

* Correspondence to be made at: Vikas Nagar, 134/3, University of Roorkee, Roorkee-247667, U. P., India.

Experimental

Reagents and solutions

The platinum metal salts used were obtained from Johnson Mathey Products, London. Phthalimide and amines used were of A. R. (B. D. H.) grade. Palladium(II) chloride was dissolved in dilute HCl while the solutions of all other reagents were prepared in distilled water.

Physical measurements

The infrared spectra were recorded on Beckman IR-20 spectrophotometer using KBr film technique. The electronic spectra (in solutions and solid states) were recorded on a Carl Zeiss 'SPECORD' UV-VIS' fitted with a reflectance attachment of the Rd/O. Conductance measurements were carried out with a Systronics conductivity bridge type 302, in DMSO. The cell constant was 0.69. Magnetic studies were made on a Princeton Applied Research Model 155 VSM at room temperature. Calibration was made with a pure nickel pellet.

Preparation of complexes

Palladium(II) phthalimide

The solutions of palladium(II) chloride in dilute HCl and of potassium phthalimide (prepared by mixing the solutions of alcoholic phthalimide and alcoholic potassium hydroxide in the ratio of 1 : 1) in distilled water were mixed in 1 : 2 ratio and stirred with a magnetic stirrer which gave a thick precipitate of light yellow colour. They were filtered, washed several times with distilled water and finally with methanol and dried in a vacuum desiccator over silica gel.

Diphthalimido-diimine palladium(II); (diimino = dipyridyl or *o*-phenanthroline)

The palladium(II) phthalimide and amine were mixed in 1 : 1 ratio and the mixture was then refluxed in absolute alcohol for about eight hours which gave blackish precipitates. They were filtered, washed several times with alcohol and then dried in a vacuum desiccator.

Potassium dipththalimidodichloroplatinate(II)

Potassium tetrachloroplatinate(II) was obtained by reducing of potassium hexachloroplatinate(IV) with sulphur oxide [19]. The solutions of $K_2[PtCl_4]$ so obtained and potassium phthalimide were mixed in 1 : 3 ratio. The pH of the mixture was adjusted to about 7 by the addition of KOH. The solution was evaporated on a water bath. The complex was dissolved in a 1 : 1 mixture of acetone and alcohol. After filtration, the solvent was evaporated and the solid product was collected which corresponded to the formula $K_2[Pt(C_8H_4O_2N)_2Cl_2]$.

Diphthalimidodiiminoplatinum(II)

The alcoholic solutions of $K_2[Pt(C_8H_4O_2N_2)Cl_2]$ and amine were mixed in a 1 : 1 ratio and the mixture was refluxed on a water bath for about ten hours which gave brown coloured precipitates. They were filtered, washed several times with water and alcohol and then dried in a desiccator over silica gel.

Platinum(IV) phthalimide

All efforts to prepare the imido complex with $K_2[PtCl_6]$ as starting material were unsuccessful. Metal perchlorate was prepared by adding required amount of $PtCl_4$ (obtained from K_2PtCl_4[20]) and silver perchlorate $AgClO_4$ in a small amount of water. On digestion for about an hour a white precipitates (AgCl) separated. An aqueous solution containing $Pt(ClO_4)_4$ and that of potassium phthalimide were mixed in 1 : 6 ratio raising the pH of the mixture to about 8.0 with KOH and then refluxing on a water bath for more than ten hours. The yellow precipitate was filtered, washed several times with water and alcohol and then dried in a vacuum desiccator over silica gel.

Tetraphthalimidodiiminoplatinum(IV)

$[Pt(C_8H_4O_2N)_4(amine)]$ were similarly prepared as the complexes of Pt(II).

M(III) phthalimide ; [M=rhodium(III) crisidium(III)]

Metal perchlorate were prepared by mixing the aqueous solutions of MCl_3 and $AgClO_4$ in the required ratio, the mixture was heated on a water bath for about an hour and AgCl was removed by centrifugation. Small amount of KCl was added to ensure the complete precipitation of silver as silver chloride.

$[M(C_8H_4O_2N)_3]$ were prepared by mixing the aqueous solutions of metal perchlorate and potassium phthalimide in 1 : 6 ratio and then heating the mixture in water bath for about half an hour. The yellow precipitate was filtered, washed with distilled water and dried in a vacuum desiccator.

Triphthalimidoaquodiimine metal(III)]

$[M(C_8H_4O_2N)_3(H_2O)(amine)]$ were also similarly prepared.

All complexes are soluble in dimethylsulphoxide (DMSO). The results of chemical analysis, conductance and magnetic measurements are given in Table I. All complexes are nonelectrolytes.

Results and Discussion

Magnetic and electronic spectral studies

The palladium(II) and platinum(II) complexes were diamagnetic, consistent with the square planar structure of the d^8 metal complexes. The electronic spectra of palladium(II) complexes gave three spin allowed d—d bands corresponding to the transitions $^1A_{1g} \rightarrow {}^1A_{2g}$; $^1A_{1g} \rightarrow {}^1B_{1g}$ and $^1A_{1g} \rightarrow {}^1E_g$ and two charge-transfer bands while platinum(II) complexe gave only three charge-transfer bands (Table III). The d—d bands were obscured by these charge-transfer bands. The charge-transfer band of lowest energy involves transitions from the highest filled metal orbitals to the most stable empty ligand molecular orbital, i.e. $a_{2u}(\pi^*)$. The first charge-transfer transition $b_{2g}(\pi^*) \rightarrow a_{2u}(\pi^*)$ $(^1A_{1g} \rightarrow {}^1B_{1u})$ is orbitally forbidden and has low intensity. The second and third charge-transfer transitions correspond to $a_{1g}(\sigma^*) \rightarrow a_{2g}(\pi^*)$ $(^1A_{1g} \rightarrow {}^1A_{2u})$ and $eg(\pi^*) \rightarrow a_{2u}(\pi^*)$ $(^1A_{1g} \rightarrow {}^1E_u)$, respectively. The values of Δ_1, Δ_2 and Δ_3 are given in Table III for comparison purposes. For these complexes Δ_1 was the largest, indicating thereby more stronger antibonding character of $d_{x^2-y^2}$ than other d orbital. Δ_3 for platinum(II) complexes is less than for the corresponding palladium(II) complexes. Thus d_{z^2} in the case of platinum(II) was more stable than d_{xy}, d_{yz}. This was compatible with the idea that the axial interaction of the solvent molecules in the case of Pd(II) is greater than in the case of Pt(II). The complexes of Ir(III), Rh(III) and Pt(IV) are also diamagnetic as expected. This is consistent with an octahedral arrangement of the donor atoms around the metal ions, producing a stronge field [21, 22].

Acta Chim. Hung. 123, 1986

Table I

Analytical data of complexes

S. No.	Complexes	Colour	M % Calc. (Found)	C % Calc. (Found)	H % Calc. (Found)	N % Calc. (Found)	μ_{eff} (B. M.)	Conductance in DMSO(ohm^{-1} cm^{2}mol^{-1})
1.	$[Pt(C_8H_4O_2N)_2(C_{10}H_8N_2)]$	Brown	30.32 (29.90)	48.52 (48.46)	2.48 (2.40)	8.70 (8.62)	0.00	10.20
2.	$[Pt(C_8H_4O_2N)_2(C_{12}H_8N_2)]$	Brown	28.46 (27.95)	49.05 (48.96)	2.33 (2.25)	8.39 (8.22)	0.00	10.34
3.	$[Pd(C_8H_4O_2N)_2(C_{10}H_8N_2)]$	Bluish Black	19.13 (18.85)	56.31 (56.25)	2.88 (2.82)	10.10 (10.82)	0.00	10.26
4.	$[Pd(C_8H_4O_2N)_2(C_{12}H_8N_2)]$	Bluish Black	17.78 (17.50)	56.37 56.30	2.68 (2.52)	9.68 (9.60)	+0.12	11.20
5.	$[Pt(C_8H_4O_2N)_4(C_{10}H_8N_2)]$	Green	20.86 (20.40)	53.90 (53.75)	2.56 (2.40)	8.98 (8.84)	+0.46	10.00
6.	$[Pt(C_8H_4O_2N)_4(C_{12}H_8N_2)]$	Yellowich Green	19.95 (19.70)	54.04 (53.92)	2.45 (2.30)	8.76 (8.60)	+0.32	10.21
7.	$[Rh(C_8H_4O_2N)_3(C_{10}H_8N_2)H_2O]$	Black	14.40 (14.29)	57.06 (56.90)	3.07 (3.10)	9.79 (9.68)	0.00	10.80
8.	$[Rh(C_8H_4O_2N)_3(H_2O)(C_{12}H_8N_2)]$	Black	13.94 (13.48)	58.45 (58.20)	2.97 (2.80)	9.47 (9.33)	−0.14	10.68
9.	$[Ir(C_8H_4O_2N)_3(H_2O)(C_{10}H_8N_2)]$	Pale Yellow	23.90 (23.72)	50.75 (50.70)	2.74 (2.66)	8.70 (8.66)	−0.18	11.24
10.	$[Ir(C_8H_4O_2N)_3(H_2O)(C_{12}H_8N_2)]$	White	23.21 (23.00)	52.17 (52.08)	2.66 (2.56)	8.45 (8.38)	−0.22	11.18

The ground state of a low spin d^6 metal ion is $^1A_{1g}$. The ligand field transition $t_{2g}^6 \rightarrow t_{2g}^5 eg^1$ gives to two spin allowed $^1T_{1g}$ and $^1T_{2g}$ and two spin forbidden $^3T_{1g}$ and $^3T_{2g}$ excited states. Accordingly four bands can be expected. Bands corresponding to charge-transfer from ligand to metal generally do not appear in visible region in these systems [23]. However, each complex gave two spin allowed bands involving transitions $^1A_{1g} \rightarrow {}^1T_{1g}$ and $^1A_{1g} \rightarrow {}^1T_{2g}$ and one very weak spin forbidden a band due to $^1A_{1g} \rightarrow {}^3T_{1g}$. The bands

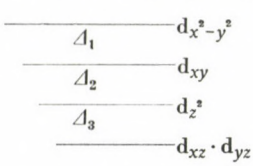
Table II

Spectral properties of the d^8 *complexes*

Complexes	λ_{max}	ε_{max}	Assignment
[Pd(Phth)$_2$(dipy)]	40000	28500	$^1A_{1g} \rightarrow {}^1E_u$
	34500	8500	$^1A_{1g} \rightarrow {}^1A_{2u}$
	31000		$^1A_{1g} \rightarrow {}^1E_g$
	28400		$^1A_{1g} \rightarrow {}^1B_{1g}$
	23100		$^1A_{1g} \rightarrow {}^1A_{2g}$
[Pd(Phth)$_2$(Phen)]	40000	28500	$^1A_{1g} \rightarrow {}^1E_u$
	34500	8500	$^1A_{1g} \rightarrow {}^1A_{2u}$
	31000		$^1A_{1g} \rightarrow {}^1E_g$
	28400		$^1A_{1g} \rightarrow {}^1B_{1g}$
	23100		$^1A_{1g} \rightarrow {}^1A_{2g}$
[Pt(Phth)$_2$(dipy)]	41000	1850	$^1A_{1g} \rightarrow {}^1A_{2u}$
	39500	29000	$^1A_{1g} \rightarrow {}^1E_u$
	36000	2000	$^1A_{1g} \rightarrow {}^1B_{1u}$
[Pt(Phth)$_2$(Phen)]	41000	1850	$^1A_{1g} \rightarrow {}^1A_{2u}$
	39500	29000	$^1A_{1g} \rightarrow {}^1E_u$
	36000	2000	$^1A_{1g} \rightarrow {}^1B_{1u}$

Table III

Metal d*-orbital energies for square planar complexes*



Orbital energy differences (cm^{-1}) for $F_2 = 10F_4 = 700$ cm^{-1}

Complexes	Δ_1	Δ_2	Δ'
[Pd(Phth)$_2$(dipy)]	25550	6700	2250
[Pd(Phth)$_2$(Phen)]	25550	6700	2250
[Pt(Phth)$_2$(dipy)]	—	12000	−3250
[Pt(Phth)$_2$(Phen)]	—	12000	−3250

Phth = deprotonated phthalimide
dipy = dipyridyl
Phen = o_{2g}^5-phenanthroline

Table IV

Electronic spectral data (cm^{-1}) *of platinum*(IV), *iridium*(IV), *and rhodium*(III) *complexes*

S. No.	Complexes	$^1A_{1g} \rightarrow {}^3T_{1g}$	$^1A_{1g} \rightarrow {}^1T_{1g}$	$^1A_{1g} \rightarrow {}^1T_{2g}$ (cm^{-1})	$10Dq$	B	β	C	C/B	L.F.S.E. Kcals/mole
1.	$[Pt(Phth)_4(dipy)]$	19000	27000	35250	31000	515.6	0.72	4000	7.76	35.42
2.	$[Pt(Phth)_4(Phen)]$	19000	27000	35250	31000	515.6	0.72	4000	7.76	35.42
3.	$[Ir(Phth)_3(dipy)H_2O]$	18000	23500	29500	26250	375.0	0.57	2750	7.33	29.99
4.	$[Ir(Phth)_3(Phen)H_2O]$	18000	23500	29500	26250	375.0	0.57	2750	7.33	29.99
5.	$[Rh(Phth)_3(dipy)H_2O]$	15000	19500	26250	21750	421.8	0.58	2250	5.33	24.85
6.	$[Rh(Phth)_3(Phen)H_2O]$	15000	19500	26250	21750	421.8	0.58	2250	5.33	24.85

observed, their assignments, B, β, C, C/B and the values of L. F. S. E. are listed in Table IV. These spectra resemble those of other six coordinated d^6 complexes [22, 24]. The electronic spectra of these d^6 complexes can be used [25] to evaluate ligand field and nephelauxetic parameters. The B value obtained in the range 57—72% of the free ion values suggest considerable orbital overlap with strong covalency in the metal-ligand σ bond. In addition to d—d transition, platinum(IV) complexes have two charge-transfer bands at 39 000 and 48 500 $cm^{-}{}_1$, iridium(III) complexes also have two charge-transfer bands at 37 500 and 45 000 cm^{-1} whereas only one charge-transfer band at 45 000 cm^{-1} was observed in the spectra of rhodium(III) complexes. These may be assigned as ligand too metal charge-transfer bands since empty ligand orbitals are expected at too high energy too participate to any extent in bonding. The values of 10 Dq and hence the stability of these complexes decrease in the order Pt(IV) > Ir(III) > Rg(III) which is in agrement with the spectrochemical series of the metal ions.

The reflectance spectra gave the bands at nearly the same frequency as were obtained in their solution spectra indicating no dissociation of the complexes in solutions.

Infrared studies

The general appearance of the spectra of all the complexes were of the same type because of the presence of same constituents inside the coordination sphere i.e. phthalimide and diimine (dipyridyl or *o*-phenanthroline) except the complexes 7—10 (Table I) which gave two extra bands at around 860 and 650 cm^{-1} due to wagging and rocking modes of coordinated water [26]. A band due to coordinated water molecule was also obtained at around 3400 cm^{-1}.

Phthalimide has two important (NH and CO strecthing) frequency regions. These frequencies, however, can not make a sharp distinction whether coordination is through imido nitrogen or carbonyl oxygen because any change in the imido nitrogen which is directly linked to the carbonyl group, alters

the environment of the molecule and hence the frequency of the later even if it is not coordinated [27]. However, on the basis of Lewis acid concept, coordination through negatively charged phthalimide nitrogen is more probable than that through oxygen [28]. Secondly, there is steric hindrance if the ligand is coordinated through oxygen. There is a shift of carbonyl stretching frequency from 1750 to 1700 $\pm$ 10 cm^{-1} in the spectra of complexes. This negative shift may be due to mass effect [29]. Further the filled orbital of phthalimide nitrogen is made available quasi-aromatic delocalisation which gives lower bond order to C=O and thus a low frequency. There is also a shift in the C—N stretching frequency from 1470 cm^{-1} in free phthalimide to 1485—90 cm^{-1} in the spectra of complexes, thereby provides information about coordination of imido group through nitrogen. The absence of the sharp characteristic peaks in the region 3500 to 3300 cm^{-1} due to ν_{N-H} means the deprotonation of the primary ligand. The possibility of simultaneous coordination of oxygen of C=O group and that of imide nitrogen to the same or two neighbouring metal ions ruled out in the light of steric hindrance and small shift ($\approx$50 cm^{-1}) in the carbonyl stretching frequency. In the spectra of dipyridyl and *o*-phenanthroline complexes two bands observed generally at around 755 cm^{-1} and 905 cm^{-1} in the spectra of free ligand due to out of plane bending (δ_{Ar-H}) modes have been suggested most useful diagnostic in their complexes where these bands shift towards higher side [30]. In our case the former band shifted to 775 cm^{-1} in the spectra of Rh(III) and Ir(III) complexes and to 785—88 cm^{-1} in the spectra of others. The second band shifted to 920 cm^{-1} in the spectra of Ir(III) and Rh(III) and to 935—45 cm^{-1} in the case of others. A sharp band at 1600—1606 cm^{-1} in the spectra of mixed ligand complexes was assigned to characteristic heterocyclic ring vibration. These band confirm the coordination of diimines through nitrogen. Other ring vibrations in the ante 1600—1320 cm^{-1} could not be distinguished because of the mixing or overlapping with the imide vibrations. All these bands increased in intensity in the spectra of complexes which is also a characteristic feature of dipyridyl and *o*-phenanthroline complexes [26, 30].

In the far i.r. region all the complexes gave a broad band at 400—425 cm^{-1} due to M—N frequencies of coordinated imide and diimine and could not be separately assigned due to the overlap of these frequencies. While a very weak band at around 350 cm^{-1} assignable to ν_{M-O} was observed only in the spectra of the complexes 7—10 (Table I).

Thermal analysis

Thermogravimetric and D. T. curves indicate the presence of one coordinated water molecule only in the complexes of Ir(III) and Rh(III).

*

Authors are thankful to Prof. S. N. Tandon, Head, Department of Chemistry for necessary facilities. Award of S. R. F. to one of us (S. S. Narvi) by U. G. C., New Delhi is gratefully acknowledged.

REFERENCES

[1] Harder, H. C., Rosenber, B.: Int. j. Cancer, **6,** 207 (1970)
[2] Welsch, C. W.: j. Nat. Cancer Inst., **47,** 1071 (1971)
[3] Dwyer, F. P., Reid, I. K., Shulman, A., Lycock, G. M., Dixon, S.: Aust. j. Expt. Biol. Med. Sci., **47,** 203 (1969)
[4] Goldman, D. S.: Biochem. Biophys. Acta, **45,** 27 (1960)
[5] Park Devis and Co.: Brit. Patent, 730910 (1955); C. A., **51,** 1255 g (1957)
[6] Keitt, G. W.: Bot. Gaz. (Chicago), **122,** 51 (1960)
[7] Fujimato, K., Hostsuji, T.: japan Patent, 15145 (1966), C. A., **59,** 6933 a (1963)
[8] Thomas, j., Thomas, E., Dubeque, M. T., Chamagnac, A., Melon, j. M., Desgrez, P.: j. Urol. Nephrol. **80,** 789 (1974)
[9] Bairamova, A. G., Mamadov, F. N., Prisadkim, K.: Samazach Mastem, **4,** 111 (1976)
[10] Perveen, V. P., Gordash, Yu. T., Serebridol, S. I. I., Murygina, K. P.: Khim. Tekhnol. Topl. Masel, **11,** 25 (1974)
[11] Kadota, I., Kawachi, Y.: Proc. Soc. Expt. Bio. Med., **101,** 365 (1959)
[12] Albert, A., Rubbo, S. D., Goldacre, R. j., Belfaur, B. G.: Brit. j. Expt. Pathol., **28,** 69 (1974)
[13] Misra, V. S., Saxena, V. K., Shah, P.: j. Ind. Chem. Soc., **58,** 1118 (1981)
[14] Misra, V. S., Saxena, V. K.: Pol. j. Pharmacol. Pharm., **27,** 589 (1975)
[15] Balkrishnan, P. V.: Canad. j. Chem., **56,** 2620 (1978)
[16] Krischner, S., Wei, Y. K. D. Francias, Bergman, F. G.: j. Med. Chem., **9,** 369 (1966)
[17] Thompson, A. J., Williams, R. J. P., Reslova, S.: Structure and Bonding, **11,** 1 (1972)
[18] Brauer, G.: Hand book of Preparative Inorganic Chemistry, Academic Press N. Y. 1968, p. 1572.
[19] Reference [18]: p. 1567.
[20] Lewis, J., Figgis, B. N.: Prog. Inorg. Chem., **6,** 105 (1964)
[21] Preti, C., Tosi, G.: Trans. Metal Chem., **3,** 17 (1978)
[22] Lever, A. B. P.: Inorganic Electronic Spectroscopy, Elsevier, Amsterdam 1968
[23] Gajendragad, M. R., Agarwal, U.: J. Inorg. Nucl. Chem., **37,** 2429 (1975)
[24] Jorgensen, C. K.: Prog. Inorg. Chem., **4,** 73 (1972)
[25] Fujita, J., Nakamoto, K., Kobyashi, M.: J. Am. Chem. Soc., **78,** 3963 (1956)
[26] Srimn, S.: J. Chem. Phys., **1955,** 1371
[27] Bailer, J. C. Jr.: The Chemistry of Coordination Compounds, Reinhold, N. Y. 1956, p. 180.
[28] Svatos, G. F., Curren, C., Quaglino, J. V.: J. Am. Chem. Soc., **77,** 6159 (1955)
[29] Martin, B., Mc Whnnie. W. R., Waind, G. M.: J. Inorg. Nucl. Chem., **23,** 207 (1961)

Acta Chimica Hungarica 123 (3—4), pp 115—122 (1986)

COMPLETE CNDO FORCE FIELD OF *CIS*- AND *TRANS*-FURAN-2-ALDEHYDE

Julius BÁNKI[1], Ferenc BILLES[2]*, Miklós GÁL[3], András GROFCSIK[2], György JALSOVSZKY[4] and Lajos SZTRAKA[2]

([1]Department of Organic Chemistry, Slovak Technical University, CS-81237, Bratislava, Czechoslovakia, [2]Department of Physical Chemistry, Technical University Budapest, H-1521 Budapest, Budafoki út 8, [3]Department of General and Inorganic Chemistry, Eötvös L. University, 1088 Budapest, Múzeum krt. 6—8, [4]Central Research Institute for Chemistry, Hungarian Academy of Sciences, 1525 Budapest, Pusztaszeri út 59—67)

Received January 6, 1986
Accepted for publication February 18, 1986

The complete sets of both O—O *cis* and O—O *trans* furan-2-aldehyde force constants were calculated based on the geometry determined by electron diffraction. The force constant sets were scaled in first approximation by scaling factors of furan, acrolein and glyoxale. A refinement procedure demonstrates the very good transferability of furan scaling factors.

Temperature, solvent and phase dependent infrared spectra and liquid phase Raman spectra were measured.

Total energy distribution and band assignments are given according to the calculations.

Introduction

The infrared and Raman spectra of furan-2-aldehyde were first studied by Allen and Bernstein [1]. They interpreted the observed doublets based on their temperature and solvent dependency by the conformational equilibrium. They found the conformer with higher dipole moment (O—O *cis)* more stable in liquid and solid states. They did not give, however, the assignment for all band pairs because the intensity changes of the weak overlapping band pairs were uncertain.

A series of papers have dealt with the vibrational spectra of furan-2-aldehyde later. Green and Harrison [2] published a full assignment based on infrared and Raman spectra. Katritzky [3], Senechal and Saumagne [4], Claverie et al. [5] have given the characteristic frequencies. Monnig and coworkers [6, 7] and Miller and coworkers [8] have investigated the far infrared spectra.

The approximate normal coordinate analysis of furan-2-aldehyde was carried out by Adamek and coworkers [9]. They applied the same force field for both conformers (O—O *cis* and O—O *trans)* using Scott's [10] force constants for the furan ring and estimated force constants for the aldehyde

* To whom correspondence should be addressed.

group. Adopting this furan force field unchanged, the effect of the aldehyde group on the furan ring force constants was not taken into account. The bulk of the fundamentals were assigned from the vapor phase vibrational spectra but no measurements were carried out in the far infrared.

Sheinker et al. [11] have calculated the normal vibrations of furan-2-aldehyde based on the force fields of furan and acrolein. They have interpreted only two band pairs with the conformational equilibrium. Their fundamentals show a definite difference from those of Adamek [9] (e.g. band pairs at 926—946, and 1146—1154 cm^{-1}, respectively, are two band pairs of conformers according to Adamek and four independent fundamentals in Scheinker's assignment).

In this paper we try to give a coherent view of the force fields and vibrational spectra of furan-2-aldehyde conformers.

Experimental

The infrared spectra of furan-2-aldehyde were recorded in the 400—4000 cm^{-1} region on a Digilab FTS-14 and a Nicolet 7199 Fourier transform infrared spectrometer. The thin layers of liquids and the solids were measured between KBr windows. For temperature depending measurements a SPECAC-Mode-20010 cell was adopted in the temperature interval 210—310 K. The concentrations in the applied solvents (carbon-tetrachloride and carbon-disulfide) were 0.01 mol · dm^{-3} at a cell thickness of 0.1 mm. The vapour spectra were recorded at room temperature in a 10-cm gas cell.

Far infrared spectra were scanned in polyethylene cells in the 20—400 cm^{-1} region by a Grubb Parsons IS3 spectrometer.

Raman spectral data were obtained in liquid phase on a Ramanor HG. 2S spectrometer equipped with an argon ion laser ILA 120, using the 515 nm line for excitation.

Furan-2-aldehyde was freshly distilled before measurements.

The infrared and Raman spectral data are listed in Table I. Since the samples are temperature, solvent and phase dependent mixtures of the two conformers, the recorded spectra contain both spectra in the ratio of their concentrations. In general, the bands of the conformers stand near to each other or overlap each other.

Calculations

The complete set of non-redundant coordinates is based on the internal coordinate set of furan [12] with the addition of coordinates belonging to the aldehyde group (Table II). The transferability of scaling factors requires the separation of stretching and bending motions. Coordinates meeting this requirement were applied.

In our calculations experimental data determined by electron diffraction were used as reference geometry [13] for both O—O *trans* and O—O *cis* conformers. The results of the electron diffraction measurements were evaluated supposing that the geometry during the rotation of the aldehyde group was constant.

According to the CNDO/2 force method the forces were calculated analytically for appropriately distorted nuclear configurations around the reference geometry. The force constants were then evaluated numerically from the changes in forces.

For calculating the in-plane force constants the forces acting on the atoms were determined for both positive and negative displacements. In the case of out-of-plane force constants there is no sense of making a distinction between positive and negative displacements. Therefore four additional displacements were sufficient. The atomic displacements did not exceed 0.5 pm.

Owing to the systematic errors of the force constants obtained from the CNDO/2 calculations, these cannot be directly applied for predicting vibrational frequencies. A great deal of the errors can be corrected by empirical scaling factors [14].

Table I

Vibrational spectral data of furan-2-aldehyde (cm^{-1})

Infrared					Raman		Species	
Vapour[a]		Solution[b]	Liquid	Solid	Liquid		A'	A''
		3150 vw	3150 w	3142 w	3155 w		ν_1	
		3144 vw	3138 m				ν_2	
		3128 vw		3128 m	3128 vw		ν_3	
				3113 s				
		3103 vw	3108 w	3106 w	3108 vw			
		2920 m	2919 w	2916 w				
2841 w	*B*	2838 w	2856 w	2848 m	2858 vw			
2804 w	*B*	2800 m	2816 w	2812 m	2818 vw		ν_4	
2754 vw	*B*	2750 w	2760 vw	2763 vw	2760 vw			
2714 vw	*B*	2712 vw	2720 vw	2715 w	2722 vw			
			2660 vw					
			2540 vw					
			2100 vw					
			2032 vw	2042 vw				
			1900 vw	1900 vw				
				1798 w				
1767 vw		1770 vw	1781 w	1770 vw	1780 vw			
		1733 w		1743 vw				
1718 vs+	*A*	1701 vs	1692 vs	1694 vs	1692 vs		ν_5	
1688 w	*A*	1684 vs	1673 vs	1677 vs	1672 vs			
		1655 w	1643 m		1645 w			
		1637 vw	1630 w	1633 m				
				1627 m				
1577 m+	*A*	1570 s	1571 s	1568 w	1570 m		ν_6	
1508 vw		1520 vw		1511 m	1520 vw			
1479 m	*A*	1477 m	1473 s	1478 s	1475 vs		ν_7	
1473 m	*A*	1465 s	1464 s	1475 sh	1465 vs			
		1447 vw	1442 vw		1444 vw			
1399 vw	*A*	1395 m	1395 s+	1402 m	1396 vs		ν_8	
1394 vw	*B*	1393 sh					ν_9	
1365 vw		1364 w	1370 s	1368 m	1370 vs			
				1365 m				
1277 vw	*A*	1275 m	1277 s	1288 s	1280 vw		ν_{10}	
1272 w		1265 sh		1265 w			ν_{11}	
1242 w	*A*	1245 m	1244 m		1245 vw			
1232 vw	*A*	1237 m	1227 sh	1237 w	1227 sh			
1220 vw	*A*	1218 vw	1222 w	1229 vw	1223 w			
		1207 vw	1210 vw		1208 vw			
1164 w	*A*	1157 m	1158 m+	1167 m	1158 s		ν_{12}	
1155 w	*A*	1148 w		1157 sh	1152 s			
1085 w	*A*	1084 m	1082 m	1081 m	1078 m		ν_{13}	
1018 w	*A*	1015 m	1021 s	1036 vs	1022 m		ν_{14}	
1011 w	*A*	1010 m		1022 vw				
		995 sh		993 vw	995 vw			
947 w	*A*	946 w	949 w	945 sh	947 w		ν_{15}	
933 vw	*B*	929 w	930 s	930 s	930 s			
			900 vw	908 m				
888 w	*A*	887 m	888 s	881 m	885 m		ν_{16}	
882 vw	*C*		872 vw	864 w				ν_{20}
830 w	*C*	830 w	841 w		845 vw			ν_{21}
825 vw	*C*							ν_{22}
759 s	*C*	758 vs	768 s	774 vs	775 vw			ν_{23}
756 s	*C*	754 vs	754 vs	770 vs	755 w		ν_{17}	ν_{24}
746 s	*A*	748 s	748 s		750 sh			ν_{25}
		639 vw	632 sh		633 vw			
		622 vw	623 vw		625 sh			

Table 1 (cotinued)

Infrared				Raman		Species	
Vapour[a]		Solution[b]	Liquid	Solid	Liquid	A'	A''
595 w	C	593 m	593 m	598 vs	596 vw		ν_{25}
		498 sh	501 vw	510 vw	504 vs	ν_{18}	
		495 vw	496 sh	507 vw			
		295 vw	302 vw		303 vw		ν_{26}
		249 vw	256 vw		252 vw		
		211 vw	215 vw		215 w	ν_{19}	
		167 vw	170 vw		170 sh		ν_{27}
		150 vw	152 vw		154 m		

[a] only the wavenumber of the band middle (Q branch) is given
[b] between 400—4000 cm^{-1} the solvent was carbondisulfide, between 20—400 cm^{-1} benzene
+ band structure referring to dublet

In the first attempt an approximate force field was constructed. The in-plane force constants having the same definition as in furan (R_1—R_9 and R_{11}—R_{15}) were corrected by scaling factors obtained for furan by fitting the experimental normal frequencies of furan and its six deuterated derivatives to the calculated frequencies [12]. The in-plane bending force constants of the aldehyde group (R_{10}, R_{18} and R_{19}) were corrected according to the corresponding scaling factors for acrolein and glyoxale [15]. Since the stretching force constant are more sensitive to the chemical environment, they were scaled by estimated factors (R_{16} and R_{17}). Ring and aldehyde OCH force constants were handled separately since in accordance with our experience [16] the CNDO/2 method does not distinguish appropriately these bond types. Most of the force constants of out-of-plane motions (R_{20}—R_{25}) were scaled like the corresponding furan coordinates. The out-of-plane CH bending (R_{27}) force constant of the aldehyde group was corrected by the same factor as the CH bending force constants of furan. Although the torsion of the aldehyde group is a large-amplitude motion, the calculated force constant can be formally scaled. The transferability of such a scaling factor is, however, obviously restricted (R_{26}).

With this scaling factor set the reproduction of the experimental frequencies of furan-2-aldehyde was satisfactory.

As a second level of approximation, a refinement procedure was carried out to fit the force constants (the scaling factors) to the observed normal frequencies of the O—O *trans* and O—O *cis* conformers and also to those of furan and its six deuterated derivatives. During these calculations the scaling factors of the in-plane bending of the aldehyde group (R_{10}, R_{18} and R_{19}) were kept constant.

Results and Discussions

The scaling factors are listed in Table III together with those for furan [12]. The transferability of the furan scaling factors is well demonstrated. When furan scaling factors were used for frequency calculations of furan-2-aldehyde instead of its own ones, the deviations in the calculated values did not exceed 5 cm^{-1}.

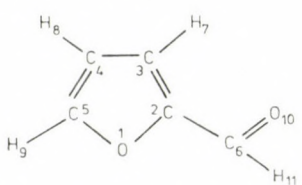
Table IV contains the force constants of the O—O *trans* and O—O *cis* conformers and their deviations. Analyzing these values it is conspicuous that pivot elements of the force constant matrices do not differ essentially. The change in the configuration acts on the electron distribution. This effect is, however, only moderately reflected in the diagonal valence bond force con-

Table II

Internal coordinates of furan-2-aldehyde (for both conformers)

i	Internal coordinate (R_i)
1	$\nu(O_1-C_2)$
2	$\nu(C_2=C_3)$
3	$\nu(C_3-C_4)$
4	$\nu(C_4=C_5)$
5	$\nu(C_5=O_1)$
6	$\nu(C_2-C_6)$
7	$\nu(C_3-H_7)$
8	$\nu(C_4-H_8)$
9	$\nu(C_5-H_9)$
10	$\beta(O_1-C_2-C_6) - \beta(C_3=C_2-C_6)$
11	$\beta(C_2=C_3-H_7) - \beta(C_4-C_3-H_7)$
12	$\beta(C_5=C_4-H_8) - \beta(C_3-C_4-H_8)$
13	$\beta(O_1-C_5-H_9) - \beta(C_4=C_5-H_9)$
14	$\beta(C_2-O_1-C_5) + \cos 144°[\beta(O_1-C_2=C_3) + \beta(O_1-C_5=C_4)] +$ $+ \cos 72°[\beta(C_2=C_3-C_4) + \beta(C_3-C_4=C_5)]$
15	$(1\text{-}\cos 72°\ [\beta(O_1-C_2=C_3) - \beta(O_1-C_5=C_4)] +$ $+ (\cos 144°\text{-}\cos 72°)\ [\beta(C_2=C_3-C_4) - \beta(C_3-C_4=C_5)]$
16	$\nu(C_6=O_{10})$
17	$\nu(C_6-H_{11})$
18	$\beta(C_2-C_6=O_{10}) - \beta(O_{10}=C_6-H_{11})$
19	$\beta(C_2-C_6-H_{11}) - \beta(O_{10}=C_6-H_{11})$
20	$\gamma(C_6-C_3-O_1-C_2)$
21	$\gamma(H_7-C_4-C_2-C_3)$
22	$\gamma(H_8-C_5-C_3-C_4)$
23	$\gamma(H_9-O_1-C_4-C_5)$
24	$\tau(C_2=C_3-C_4=C_5) +$ $+ \cos 144°\ [\tau(C_3-C_4=C_5-O_1) + \tau(O_1-C_2=C_3-C_4)] +$ $+ \cos 72°[\tau(C_4=C_5-O_1-C_2) + \tau(C_5-O_1-C_2=C_3)]$
25	$(1\text{-}\cos 72°)\ [\tau(C_3-C_4=C_5-O_1) - \tau(O_1-C_2=C_3-C_4)] +$ $+ (\cos 144°\text{-}\cos 72°)[\tau(C_4=C_5-O_1-C_2) - \tau(C_5-O_1-C_2=C_3)]$
26	$\tau(C_3=C_2-C_6=O_{10})$
27	$\gamma(H_{11}-C_2-O_{10}-C_6)$

The numbering of atoms is as follows:



ν, stretching: β, in-plane bending; τ, torsion; γ, out-of-plane bending. The normalization factors are not given.

stants. The transition from the O—O *cis* to the O—O *trans* conformer decreases the double bond character of the aldehyde carbonyl bond and increases the same of the O_1—C_2 bond.

There are many interactions very sensitive to the rotation of the aldehyde group. As it was expected, the interactions of coordinates belonging to

Table III

Applied scaling factors for furan and furan-2-aldehyde

Type of coordinate	Scaling factors for furan -2-aldehyde		Serial number of coordinates for
ν(C—C)	0.389	0.388	2, 3, 4, 6
ν(C—H)	0.389	0.388	7, 8, 9
ν(C—O)	0.243	0.242	1, 5
β(C—H)	0.681	0.688	11, 12, 13
β(ring)	1.467	1.445	14, 15
τ(ring)	0.540	0.541	24, 25
γ(C—H)	0.802	0.818	20, 21, 22, 23, 27
$\nu(C-H)_{ald}$		0.344	17
$\nu(C=O)_{ald}$		0.260	16
$\beta(C-H)_{ald}$		0.800	19
$\beta(C=O)_{ald}$		0.800	18
$\beta(C_{irng}-C_{ald})$		0.800	10
τ(ald)		2.500	26

the aldehyde group (in-plane: R_{10}, R_{16}, R_{17}, R_{18}, R_{19} and out-of-plane: R_{20}, R_{26}, R_{27}) show this effect above all. Extremely high deviations are in $F_{10,18}$ and $F_{10,19}$. It is conspicuous, however, that there are also great effects on aldehyde motion interactions with ring angle bending R_{14} (only with this and not with R_{15}) and ring valence bond coordinate R_6 and the CH motion R_8. The behaviour of $F_{8,10}$ is curious, since the corresponding coordinates are very far from each other. In contrast to the in-plane modes the interactions of the out-of-plane aldehyde motions with both ring out-of-plane motions are sensitive to the aldehyde rotation.

The comparison of the ring valence force constants of furan-2-aldehyde and furan [12] shows differences in accordance with the negative electron effect of the aldehyde group. The substitution yields an increase in the force constants in the neighbourhood of the substituent (bond O_1—C_2 and C_2=C_3) and a decrease in the force constants of other bonds.

Experimental and calculated frequencies for both furan-2-aldehyde conformers are presented in Table V together with the elements of the TED (total energy distribution matrix) [17]. Contributions of less than 10% are not included.

In general the calculated and experimental frequencies agree well. There is, however, a relatively great deviation at normal modes 6. and 7. (A similar discrepancy was observed at the corresponding furan vibrations 17. and 3. [12]). The ν(C=C) vibration takes part in both modes in a high percentage. Since the CNDO/2 method underestimates the conjugation between the furan ring and the aldehyde group, the ν(C=C) force constants and consequently the calculated frequencies increase. Deviations at modes 9. and

Table IV

In-plane (lower triangle) *and out-of-plane* (upper triangle) *force constants of* O—O-*trans- and* O—O-*cis furan-2-aldehyde* (stretching force constants in 10^2N.n^{-1}, bending ones in $10^{-1}f$N.m. rad^{-2}, stretching-bending interactions in $10^{-}f$ N.rad^{-2} units) *and their derivatives* (· 10^3)

	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19
	5.242				20	0.376	—0.026	0.006	0.015	—0.095	—0.095	0.125	0.063						
1	5.230					0.384	—0.027	0.006	0.017	—0.097	—0.100	0.154	0.001						
	12					— 8	1	0	2	2	5	— 29	62						
	0.526	8.166				21	0.383	—0.022	0.003	0.166	0.067	0.009	—0.001						
2	0.530	8.167					0.382	—0.022	0.003	0.173	0.067	0.002	0.004						
	— 4	— 1					1	0	0	— 7	0	7	— 5						
	—0.037	0.784	6.283				22	0.383	—0.028	—0.178	0.069	0.006	0.003						
3	—0.040	0.791	6.281					0.383	—0.028	—0.178	0.069	0.007	0.000						
	— 3	— 5	2					0	0	0	0	— 1	3						
	0.136	—0.230	0.770	8.060				23	0.332	0.096	—0.121	—0.014	0.003						
4	0.141	—0.236	0.773	8.057					0.331	0.097	—0.122	—0.013	—0.009						
	— 5	6	— 3	3					1	— 1	1	— 1	12						
	0.271	0.238	—0.148	0.653	5.074	O—O *trans*		24	0.511	—0.004	—0.026	—0.022							
5	0.268	0.241	—0.148	0.656	5.070	O—O *cis*			0.514	—0.004	—0.042	0.008							
	3	— 3	0	— 3	4	deviation			— 3	0	16	— 30							
	0.325	0.458	—0.094	—0.003	—0.071	5.822			25	0.358	0.014	—0.019							
6	0.320	0.455	—0.096	—0.003	—0.067	5.829				0.358	—0.003	0.022							
	5	3	— 2	0	— 4	— 7				0	17	— 41							
	0.008	0.170	0.158	0.014	—0.038	—0.001	5.414			26	0.179	0.026							
7	0.008	0.171	0.160	0.015	—0.039	—0.002	5.413				0.186	0.067							
	0	— 1	— 2	— 1	1	1	1				— 7	— 41							
	—0.037	0.014	0.165	0.171	0.007	0.002	—0.001	5.412			27	0.270							
8	—0.038	0.014	0.165	0.171	0.007	0.002	—0.001	5.412				0.286							
	— 1	0	0	0	0	0	0	0				— 16							
	—0.004	—0.046	0.009	0.176	0.161	0.004	0.002	0.000	5.404										
9	—0.004	—0.045	0.008	0.176	0.161	0.003	0.002	0.000	5.404										
	0	— 1	1	0	0	1	0	0	0										
	0.165	—0.156	—0.016	—0.008	—0.031	0.070	0.001	—0.037	0.004	0.536									
10	0.163	—0.143	—0.026	—0.001	—0.042	0.021	0.001	—0.004	0.004	0.519									
	2	— 13	10	— 7	11	49	0	— 33	0	17									
	0.009	0.145	—0.130	0.013	—0.008	—0.003	—0.012	0.007	—0.003	—0.001	0.394								
11	0.008	0.146	—0.131	0.012	—0.008	—0.003	—0.012	0.007	—0.004	—0.002	0.397								
	1	— 1	1	1	0	0	0	0	1	1	— 3								
	—0.007	0.011	—0.137	0.150	0.007	—0.003	0.007	0.011	—0.004	0.008	—0.008	0.394							
12	—0.007	0.011	—0.137	0.150	0.007	—0.004	0.007	0.011	—0.004	0.009	—0.008	0.394							
	0	0	0	0	0	1	0	0	0	— 1	0	0	0						
	—0.029	—0.014	—0.009	—0.121	0.132	0.009	—0.003	0.003	0.020	0.011	0.008	0.003	0.447						
13	—0.029	—0.014	—0.009	—0.121	0.131	0.007	—0.003	0.003	0.019	0.010	0.008	0.003	0.447						
	0	0	0	0	1	2	0	0	1	1	0	0	0						
	0.109	—0.150	0.222	—0.206	0.064	0.238	—0.063	—0.064	0.191	0.109	—0.057	—0.057	0.092	2.049					
14	0.103	—0.153	0.225	—0.203	0.064	0.221	—0.065	—0.064	0.190	0.101	—0.056	—0.057	0.093	2.048					
	6	3	— 3	— 3	0	17	2	0	1	8	— 1	0	— 1	1					
	0.171	—0.089	—0.016	0.080	—0.194	—0.204	0.214	—0.221	0.148	0.000	—0.006	0.013	0.002	—0.061	1.781				
15	0.175	—0.092	—0.016	0.082	—0.195	—0.199	0.217	—0.222	0.148	0.002	—0.007	0.013	0.002	—0.057	1.784				
	— 4	3	0	— 2	1	— 5	— 3	1	0	— 2	1	0	0	— 4	— 3				
	—0.013	—0.099	0.049	—0.034	0.021	0.586	0.002	0.002	0.001	0.036	0.000	0.000	0.002	0.045	—0.007	10.60			
16	—0.030	—0.077	0.058	—0.040	0.039	0.577	0.000	0.003	0.001	—0.065	—0.001	—0.002	—0.002	0.016	—0.006	10.62			
	17	— 22	— 9	6	— 18	9	2	1	0	101	1	2	4	29	— 1	— 20			
	0.003	0.016	0.005	—0.006	0.007	0.149	0.000	0.001	0.001	—0.034	0.000	—0.002	0.000	0.009	—0.011	0.263	4.402		
17	0.012	0.003	0.003	—0.005	—0.002	0.141	0.000	0.001	0.001	0.034	0.001	0.000	0.002	0.023	—0.009	0.265	4.400		
	— 9	13	2	— 1	9	8	0	0	0	— 68	— 1	— 2	— 2	— 14	— 2	— 2	2		
	0.052	—0.018	0.005	—0.016	0.000	0.206	0.000	—0.001	0.003	0.103	0.001	0.002	—0.004	0.052	—0.005	0.187	—0.196	0.928	
18	—0.055	0.043	0.017	—0.009	0.026	0.201	0.000	0.004	—0.002	—0.130	—0.002	—0.004	0.004	—0.015	—0.009	0.197	—0.191	0.922	
	3	— 61	— 12	— 7	— 26	5	0	— 5	5	233	3	6	— 8	67	4	— 10	— 5	6	
	—0.021	0.048	—0.009	0.009	—0.006	0.055	0.000	0.002	—0.001	—0.097	—0.001	—0.003	—0.002	—0.015	—0.020	—0.273	0.078	—0.375	0.745
19	0.066	—0.007	—0.019	0.004	—0.029	0.052	0.001	—0.002	0.003	0.111	0.002	0.002	0.005	0.040	—0.015	—0.285	0.075	—0.365	0.731
	— 87	55	10	5	23	3	— 1	4	— 4	— 208	— 3	— 5	— 7	— 55	— 5	12	3	— 10	14

Table V

Normal vibrations of furan-2-aldehyde

Species	i	ν_i/cm^{-1} *trans/cis* exper.	calc.	TED % *trans/cis*	Corresponding furan or substituent mode
	1	3150[a]	3146 3146	$\nu CH_{7,8}$ (81/80), νCH_9 (18/19)	1
	2	3144[a]	3137 3136	νCH_7 (57/58), νCH_9 (39/38)	15
	3	3128[a]	3123 3123	$\nu CH_{7,8}$ (57/58), νCH_9 (43/42)	16
	4	2804 2841	2821 2821	νCH_{ald} (100/100)	νCH_{ald}
	5	1694[b]	1705 1721	$\nu C=C$ (60/45), βCC_{ald} (17/19), βCH_{ald} (15/15)	$\nu C=O$
	6	1577	1628 1598	$\nu C=C$ (66/58), $\nu C=O$ (10/24)	17
	7	1473 1479	1552 1549	$\nu C=C$ (61/56), β_{ring} (14/15)	3
	8	1399	1401 1399	$\nu C-C$ (36/36), $\beta CH_{7,8}$ (14/16), βCH_9 (16/18)	4
A'	9	1365 1394	1367 1349	βCH_{ald} (36/54), $\nu C=O$ (20/18)	CH_{ald}
	10	1277	1290 1237	$\nu C-O$ (31/27), νCC_{ald} (11/20), β_{ring} (16/15), βCH_{ald} (20/10)	$2/\nu CC_{ald}$
	11	1242 1272	1237 1232	$\beta CH_{7,8}$ (36/34), βCH_9 (30/27), $\nu C-C$ (14/17), $\nu C=O$ (8/10)	18
	12	1155 1164	1128 1124	$\beta CH_{7,8}$ (33/34), βCH_9 (22/27), $\nu C=C$ (24/21)	20
	13	1085	1065 1075	βCH_7 (26/25), $\nu C-O$ (36/41), $\nu C-C$ (15/14)	6
	14	1011 1018	1007 1018	$\nu C-O$ (29/17), $\nu C-C$ (8/10), $\beta CH_{7,8}$ (54/65)	7
	15	947 933	961 946	$\nu C-O$ (24/23), $\nu C=C$ (18/13), β_{ring} (27/36), βCH_9 (11/11)	5
	16	888	872 868	β_{ring} (67/66), $\nu C-O$ (24/29)	21
	17	746	736 726	β_{ring} (37/25), νCC_{ald} (19/20), $\beta C=O$ (19/18)	8
	18	495[a] 498[a]	467 488	$\beta C=O$ (36/36), βCC_{ald} (18/20), νCC_{ald} (17/17)	$\beta C=O$
	19	213[c]	196 183	βCC_{ald} (68/67), $\beta C=O$ (23/24)	$19/\beta CC_{ald}$
	20	882	880 866	$\gamma CH_{7,8}$ (54/64), γCH_{ald} (34/34)	9
	21	830	851 848	γCH_8 (49/45), γCH_{ald} (35/40), γCH (14/14)	γCH_{ald}
	22	825	809 808	$\gamma CH_{7,8}$ (55/59), γCH_9 (26/25), γCH_{ald} (19/16)	12
	23	756 759	752 750	γCH_9 (60/61), γCH_8 (29/27)	13
A''	24	639[a] 622[a]	637 635	τ_{ring} (82/87)	11
	25	595	578 582	τ_{ring} (100/99)	14
	26	245[c] 280[c]	260 251	γCC_{ald} (62/84), τCC_{ald} (30/12)	$10/\gamma CC_{ald}$
	27	145[c] 134[c]	143 139	τCC_{ald} (67/76), γCC_{ald} (26/5)	τCC_{ald}

Experimental frequencies are take from our vapour spectrum except those marked: a, solution spectrum b, carbonyl stretching frequency unperturbed by Fermi resonance [18]; c, far infrared vapour spectrum [8].

10. can be explained by the transferred and unoptimized scaling factors of the bending force constants of the aldehyde group.

The mean deviation of the experimental and calculated frequencies for the O—O *trans* and the O—O *cis* conformers are 24 cm^{-1} and 29 cm^{-1} (in-plane modes), 13 cm^{-1} and 14 cm^{-1} (out-of-plane modes), respectively. The directions of deviations are the same for most of the modes.

The conformational equilibrium does not produce considerable resolutions in furan-2-aldehyde spectra. The calculated frequencies, however, do not reflect this fact. The calculations result in deviations also at modes where no resolution is observed in the spectra (e.g. modes 6., 10., 16., etc.). We can explain this by three reasons:

1. The CNDO/2 method is only a rough approximation and is not able to take into account appropriately the small differences in the force field of the two conformers.

2. The same scaling factors were used for both conformers, i.e. the force fields were not scaled individually.

3. The calculated frequencies are very sensitive to the applied reference geometry (no individual geometries were used).

In our paper on furan force field [12] it was dealt with the substituent effect of the furan fundamentals. Comparing its frequencies to those of furan-2-aldehyde, normal frequencies of modes 11, 14 and 21 were declared as furan skeletal characteristics.

*

The authors are very grateful Dr G. Pongor for the possibility of using his refinement program.

REFERENCES

[1] Allen, G., Bernstein, H. J.: Canad. J. Chem., **33,** 1055 (1955)
[2] Green, J. H. S., Harrison, D. J.: Spectrochim. Acta, **33***A*, 843 (1977)
[3] Katritzky, A. R., Lagowski, J. M.: J. Chem. Soc., **1959,** 657
[4] Senechal, M., Saumagne, P.: J. Chim. Phys. Biol., **69,** 1246 (1972)
[5] Claverie, N., Garrigou-Lagrange, Ch., Domingues dos Santos, J.: J. Chim. Phys., **59,** 1046 (1962)
[6] Monning, F., Dreizler, H., Rudolph, H. D.: Z. Naturforschung, **20a,** 1323 (1965)
[7] Monning, F., Dreizler, H., Rudolph, H. D.: Z. Naturforschung, **21a,** 1633 (1966)
[8] Miller, F. A., Fateley, W. G., Witkowski, R. E.: Spectrochim. Acta, **23A,** 891 (1967)
[9] Adamek, P., Volka, K., Ksandr, Z., Štibor, I.: J. Mol. Spectroscopy, **47,** 252 (1973)
[10] Scott, D. W.: J. Mol. Spectroscopy, **37,** 77 (1971)
[11] Sheinker, V. N., Merinova, E. G., Osipov, O. A.: Zhurn. Obsh. Khim., **46,** 660 (1976)
[12] Bánki, J., Billes, F., Grofcsik, A.: Acta Chim. Hung., **116,** 283 (1984)
[13] Schultz, G., Fellegvári, I., Kolonits, M., Kiss, A. I., Pete, B., Bánki, J.: J. Mol. Struc., **50,** 325 (1978)
[14] Török, F., Hegedüs, A., Kósa, K., Pulay, P.: J. Mol. Struct., **32,** 93 (1976)
[15] Panchenko, Yu. N., Pulay, P., Török, F.: J. Mol. Struct., **34,** 283 (1976)
[16] Grofcsik, A., Billes, F., Fogarasi, G.: J. Mol. Struct., **56,** 277 (1979)
[17] Pulay, P., Török, F.: Acta Chim. Acad. Sci. Hung., **47,** 273 (1966)
[18] Chadwick, D. J., Chambers, J., Meakins, G. D., Snowden, R. L.: J. Chem. Soc. Perkin II, **1975,** 13

Acta Chimica Hungarica 123 (3—4), pp. 123—135 (1986)

OSMIUM-TETROXIDE AS A REDOX CATALYST. MECHANISM OF OsO_4-CATALYSED DECOMPOSITION OF HYDROGEN PEROXIDE

László J. Csányi*, Zoltán M. Galbács, László Nagy and István Horváth

(Institute of Inorganic and Analytical Chemistry, A. József University, H-6701 Szeged, P.O. Box 440)

Received January 6, 1986
Accepted for publication February 18, 1986

A unified mechanism is proposed to describe the OsO_4-catalysed decomposition of hydrogen peroxide. The decomposition is induced by the nucleophilic attack of HO_2^- ion on OsO_4.aq, resulting in a cherry-red transient (absorption maximum at 530 nm) in the range of $9 < pH < 13$. The peroxide adduct of the catalyst undergoes fast intramolecular redox reactions. The first step results in an osmium(VII)—superoxide radical pairs, the second gives dioxygen and osmium(VI). The latter species is then reoxidized by hydrogen peroxide in a two-electron step. This redox cycle represents the molecular component of decomposition with a rate maximum at pH 10.6—10.7, where the concentrations of the osmium(VIII) and osmium(VI) species are just equal. At lower pH, undissociated osmium(VI) acid is formed and peroxidized. The peroxo-osmium(VI) acid undergoes homolysis, and ·OH and osmium(VII) radicals are formed. The latter is reduced by hydrogen peroxide, whereby a radical chain reaction is evolved with the formation of superoxide radicals. The radical chain process involving the ·OH radical depends on the pH, exhibiting a maximum at pH 8.5. At lower pH, the radical component predominates in the decomposition. During the decomposition, the formation of singlet oxygen is also observed in low yield. The proposed reaction scheme proves suitable for simulation the main characteristics of the catalysed decomposition.

Introduction

Due to its advantageous properties, osmium tetroxide is a widely used catalyst. Although OsO_4 is a highly covalent compound, it undergoes strong solvation and therefore dissolves readily both in water and in non-aqueous solvents. Further, it has the great advantage that it can be applied in acidic, neutral and alkaline media. Its general use might be restricted by its relatively high price, but its exceptionally high catalytic activity (it is usually enough to apply it in 10^{-8}—10^{-5} M concentration) means that the price is not a real limiting factor.

Osmium tetroxide catalyses both non-complementary and complementary (in which the partners change their valencies by the same amount) redox reactions. In acidic medium, osmium tetroxide catalyses the oxidation of arsenic(III) by one-electron oxidants such as cerium(IV) or permanganate [1, 2], but it also accelerates the two-electron reduction of hydrogen peroxide and different monoperoxo acids by arsenous acid [3].

* To whom correspondence should be addressed.

The widespread use of hexacyanoferrate(III) as a strong oxidizing agent is made possible by the application of OsO_4 catalysis in alkaline medium. The oxidation of some inorganic [4—6] and organic [7—13] substrates by hexacyanoferrate(III) has been investigated kinetically, and the catalysis was explained by oxidation of the given substrates by osmium(VIII), followed by the fast reoxidation of osmium(VI) by hexacyanoferrate(III). In other cases [14, 15], the formation of an osmium(VII) intermediate has been postulated.

Oxidation with chloramine-T (*N*-chlorotoluenephenylsulphoxide) can be achieved only through OsO_4 catalysis. In the oxidation of some organic substances [16—21] by chloramine-T, the OsO_4-catalysis is similarly explained by the formation of a complex between the catalyst and the substrate, which decomposes into osmium(VI) and products. In these investigations, however, the postulated valence change of the catalyst is supported only by kinetic evidence.

Osmium tetroxide is a widely used reagent in organic syntheses involving the transformation of olefins into α-diols in hydroxylation reactions. The oxidative hydroxylations of aliphatic alicyclic and aromatic olefins are explained in terms of the intermediate formation of osmium(VI) acid esters, the hydrolysis of which yields glycols. Chlorates, hydrogen peroxide or molecular oxygen are used to reoxidize the osmium(VI) formed [22, 23]. A special feature of hydroxylations effected by OsO_4 is that these always result in *cis*-α-diols, in contrast to the other diol-forming catalysts such as Mo, W, Se, etc., which furnish *trans*-α-diols. Details of the kinetics of the hydroxylation reactions are not known.

Based on this short review it can be concluded that in osmium-catalysed redox reactions investigated kinetically without exception a complex formation between the catalyst and the given substrate is postulated followed by the reduction of osmium(VIII) to osmium(VI) and then the reoxidation of osmium(VI) with the oxidizing reagent applied. Experimental evidences, however, do not support the assumed mechanisms.

In this paper an attempt is made to give a unified explanation of experimental facts [24—29] related to the OsO_4-catalysed decomposition of hydrogen peroxide with the hope that further insights and some support would be acquired into the mechanisms of redox catalysis by osmium tetroxide.

General properties of the OsO_4-catalysed decomposition of hydrogen peroxide

When osmium tetroxide or some other osmium species of lower oxidation states solution is added to alkaline hydrogen peroxide ($9 < pH < 13$) solution a transitory cherry-red coloration is observable and the decomposition of

hydrogen peroxide starts immediately [30]. According to the method of Krajlic and Mohsni 0.26 and 0.6% of the total dioxygen evolved appeared as singlet oxygen at pH 8.6 and 10.6, respectively (Fig. 1).

The rate of O_2 evolution was found to depend on the pH of the reaction mixture, with a maximum at pH 10.6 (Fig. 2, upper part, points denoted

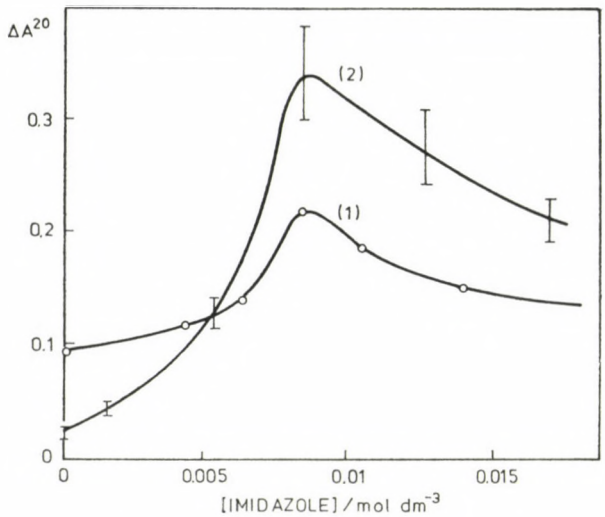


Fig. 1. Detection of singlet oxygen; curve 1: 2.27×10^{-7} *M* OsO_4, 4.54×10^{-2} *M* H_2O_2, $4.35\times$ $\times10^{-5}$ *M* RNO, 0.1 *M* ethanol (to scavenge all of the ·OH radical formed), pH 8.6 (phosphate buffer), cell thickness: 1 cm, curve 2: 1.62×10^{-7} *M* OsO_4, 2.55×10^{-2} *M* H_2O_2, 4.35×10^{-5} *M* RNO, 0.1 *M* ethanol (to scavange all of the ·OH radical formed), pH 10.6 (phosphate buffer), cell thickness: 1 cm

by ·). During the decomposition, hydroxyl and superoxide radicals are formed. The initial rate of formation of ·OH radicals displays a maximum at pH 8.5 as a function of pH (Fig. 2, upper part, points denoted by X). The superoxide radical was measured by e.s.r. method at pH >9.5; its concentration increased monotonously when the pH was raised (points denoted by ■).

The hydroxyl radical is produced mostly in a chain process. This can be concluded from the observation that when ·OH scavengers (2-propanol, ethanol, RNO, etc.) were added to the reaction mixture the overall rate of decomposition was reduced drastically. At pH <9, the contribution of the ·OH radical chain process to the overall decomposition is considerable, but falls to 1—5% at pH >9 (see Fig. 2, lower part, points denoted by Δ and ■).

It was observed that at pH >8.5, osmium(VIII) is progressively reduced with hydrogen peroxide to osmium(VI) [28]. At pH 10.6, where the rate of

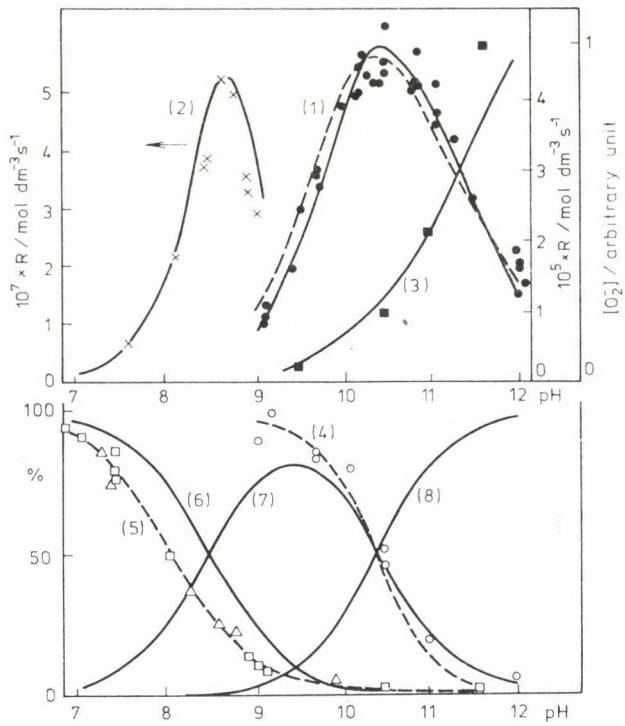


Fig. 2. pH-dependence of catalysed decomposition; curve 1: Initial rate of decomposition of hydrogen peroxide: 3.0×10^{-8} *M* OsO_4, 1.8×10^{-2} *M* H_2O_2, 298 K, pH adjusted by pH-stat. Experimental values: ●; computed values obtained by steady-state treatment: full line; computed values obtained by Gear method: dashed line, curve 2: Initial rate of ·OH radical formation: 1.74×10^{-7} *M* OsO_2, 8.2×10^{-2} *M* H_2O_2, 298 K, pH adjusted by pH-stat. Experimental values: x; computed values by steady-state treatment: full line, curve 3: Change in concentration of superoxide radical: 1.0×10^{-6} *M* OsO_4, 0.1 *M* H_2O_2, 298 K, 0.1 *M* phosphate buffer. Superoxide content measured by e.s.r. method in frozen samples near liquid nitrogen temperature after 2 min conversion. Measured values: ■; computed values obtained by steady-state treatment: full line, curve 4: Change in valency state of catalyst during decomposition. Measured values of $([Os(VIII)]/[Os]_{total})\times100$: ○; computed values by steady-state treatment: dashed line, curve 5: Proportion of rate of formation of ·OH radical to total decomposition rate: $(R^cOH/R_{total})\times100$ values: Δ; Bleaching of RNO during a constant 10% conversion of hydrogen peroxide: 4.0×10^{-7} *M* OsO_4, 2.0×10^{-2} *M* H_2O_2, 2.3×10^{-5} *M* RNO, 298 K, 440 nm, cell thickness: 1 cm $(\Delta A/A_0)\times100$ values denoted by □, curve 6: $([H_2[^6OsO_2(OH)_4]]/[Os(VI)]_{total})\times100$ vs pH, curve 7: $([H[^6OsO_2(OH)_4]^-]/[Os(VI)]_{total})\times100$ vs. pH, curve 8: $([[^6OsO_2(OH)_4]^{2-}]/[Os(VI)]_{total})\times100$ vs pH

decomposition reaches its maximum, the concentration ratio [osmium(VIII)]/[osmium(VI)] is about one (see Fig. 2, lower part, points denoted by o).

The overall rate of decomposition at lower conversions ($< 30\%$) was found to be proportional to the first power of the initial concentration of hydrogen peroxide.

Between pH 9 and 12 the initial rate was proportional to the concentration of the catalyst in the 10^{-9}—10^{-6} *M* interval. At pH < 9 and at higher

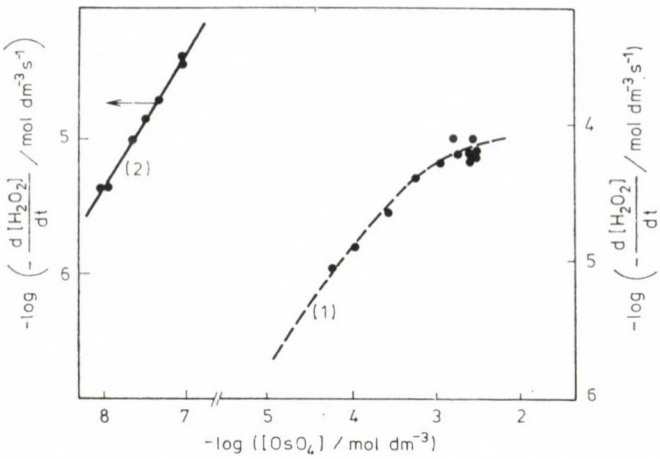


Fig. 3. Dependence of decomposition rate on concentration of catalyst; curve 1: 0.15 *M* H_2O_2, 298 K, pH 5.4 (phosphate buffer), experimental values: ●, computed values by steady-state treatment: dashed line, curve 2: 0.02 *M* H_2O_2, 298 K, pH 10.85 (controlled by pH-stat), experimental values: ●, calculated values: full line

concentrations of osmium tetroxide, the power of the catalyst concentration (m) in rate equation (I)

$$R = k[OsO_4]^m\,[H_2O_2]^n \qquad (I)$$

is less than one. When the concentration of catalyst reaches or exceeds 10^{-3} *M* the rate becomes independent of the catalyst concentration (Fig. 3, curves 1 and 2).

Discussion

It has been shown recently [30] that $OsO_4 \cdot aq$ is attacked by the strongly nucleophilic HO_2^- ion present in the alkaline reaction mixture:

$$H_2O_2 \rightleftarrows H^+ + HO_2^- \qquad (1)$$

$$OsO_4 \cdot aq + HO_2^- \rightleftarrows OsO_2(OH)_3(OO)^- \qquad (2)$$

This intermediate complex is considered to be the cherry-red transient species.

The fate of the cherry-red transient

The complex is composed of an oxidizing (osmium(VIII)) and reducing (HO_2^-) entity. It is therefore plausible to assume that the adduct undergoes a fast intramolecular redox reaction*:

$$^{8}OsO_2(OH)_3(O_2^-) \rightarrow {}^{7}OsO_2(OH)_3(O_2^-) \qquad (3)$$

* For convenience, the oxidation number of osmium is given as a left upper index.

resulting in an osmium(VII) — superoxide radical pair in the solvent cage. With regard to the high electron affinity of the osmium(VII) radical, it seems probable that only a small proportion of the radical pairs escape from the solvent cage:

$$^{7}OsO_2(OH)_3(O_2^{\cdot-}) + H_2O \rightarrow H[^{7}OsO_2(OH)_4] + O_2^{\cdot-} \quad (4)$$

the majority of them reacts within the cage according to step (5):

$$^{7}OsO_2(OH)_3(O_2^{\cdot-}) + H_2O \rightarrow H[^{6}OsO_2(OH)_4]^- + O_2\,. \quad (5)$$

Taking reactions (3) and (5) into consideration, if k_5 does not exceed k_3 considerably and equilibrium (2) is shifted to the right, then the osmium(VII) — superoxide radical pair will accumulate considerably.

The molecular component of the catalysed decomposition

Between pH 9 and 12 hydrogen peroxide decomposes almost entirely to dioxygen, and the radical route is negligible. In this pH range osmium(VIII) is gradually reduced to osmium(VI). At the rate maximum of dioxygen evolution, the concentrations of the two valency states of osmium were found to be equal.

The following may be said concerning the fate of osmium(VI) formed in step (5).

Osmium(VI) formed undergoes protolysis:

$$H[^{6}OsO_2(OH)_4]^- + H_3O^+ \rightleftarrows H_2[^{6}OsO_2(OH)_4] + H_2O \quad (6)$$

$$H[^{6}OsO_2(OH)_4]^- \rightleftarrows [^{6}OsO_2(OH)_4]^{2-} + H^+ \quad (7)$$

and is then peroxidized by H_2O_2:

$$H_2[^{6}OsO_2(OH)_4] + H_2O_2 \rightleftarrows H_2[^{6}OsO_2(OH)_3(OOH)] + H_2O \quad (8)$$

The analogous reactions of the mono and dianionic osmium(VI) species could also take place. At lower pH, peroxoosmium(VI) acid is transformed by O.O bond homolysis into ·OH and an osmium(VI) acid radical, which then rearranges quickly into osmium(VII):

$$H_2[^{6}OsO_2(OH)_3(OOH)] \rightarrow \ldots \rightarrow H[^{7}OsO_2(OH)_4] + \cdot OH \quad (9)$$

At higher pH, the peroxoacid is deprotonated:

$$H_2[^{6}OsO_2(OH)_3(OOH)] \rightleftarrows H^+ + H[^{6}OsO_2(OH)_3(OOH)]^- \quad (10)$$

and then rearranges quickly into osmium(VIII):

$$H[^{6}OsO_2(OH)_3(OOH)]^- \rightarrow {}^{8}OsO_2(OH)_3(O^-) + H_2O \quad (11)$$

The possible peroxide derivatives of osmium(VI) anions, however, can not undergo homolysis as they have free negative charge(s) and the ·OH radical (or its conjugated base, $O^{\cdot-}$) formed take off the electron(s) immediately before escape from the solvent cage, i.e. the osmium(VI) acid radical is oxidized to osmium(VIII) within the cage. Hence, we formulate 2-equivalent steps for osmium(VI) anions:

$$H[^{6}OsO_2(OH)_4]^- + H_2O_2 \rightarrow {}^{8}OsO_2(OH)_3(O^-) + 2H_2O \quad (12)$$

$$[^{6}OsO_2(OH)_4]^{2-} + H_2O_2 \rightarrow {}^{8}OsO_2(OH)_3(O^-) + OH^- + H_2O \quad (13)$$

The experimental fact that the ratio [Os(VIII)]/[Os(VI)] progressively decreases as the pH is increased can easily be explained by assuming that $k_{12} > k_{13}$, i.e. the reoxidation of osmium(VI) slows down with an increase in pH.

In this respect we call attention to the previous observations connected with the formation and decay of peroxosulphurous [32] and peroxonitrous acids [33] in alkaline medium. These derivatives decompose by intramolecular rearrangement of the O.O group, as a results of which the two peroxide O atoms appear within the sulphate and nitrate formed. Further, the rates of decay of these peroxides were found to be indirectly proportional to the pH, which is the case in the present system, too.

The distribution curves of the osmium(VI) acid species (Fig. 2, curves 6—8) reveal that, in the pH range 9—12, the undissociated osmium(VI) acid and its reaction with hydrogen peroxide can be neglected at the discussion of the rate maximum of dioxygen formation.

The overall rate of decomposition of hydrogen peroxide (or twice the rate of dioxygen evolution) is equal to the sum of the rates of the oxidation and reduction of hydrogen peroxide. At any pH, the concentrations of the +8 and +6 valency states of osmium change until the rates of the reduction processes become equal to the rates of the oxidation processes.

If steps (2), (3) and (5) are summed

$$^{8}OsO_4 \cdot aq + HO_2^- \rightarrow H[^{6}OsO_2(OH)_4]^- + O_2 \qquad k_{red}$$

we can write:

$$k_{red}[OsO_4 \cdot aq]\,[HO_2^-] = [H_2O_2]\,\{k_{12}[H[^{6}OsO_2(OH_4]^-] + k_{13}[[^{6}OsO_2(OH)_4]^{2-}]\}$$

As to the pH-dependence of the individual reactions, both the reduction and the oxidation reactions depend on the pH, but in opposite directions, and consequently their resultant rate (the overall rate of decomposition) must pass through a maximum.

The balance equations are:

$$[Os]_{total} = [Os(VIII)]_{total} + [Os(VI)]_{total}$$

$$[H_2O_2]_{total} = [H_2O_2] + [HO_2^-]$$

$$[Os(VIII)]_{total} = [OsO \cdot {}_4aq] + [OsO_4] + [{}^8OsO_2(OH)_4] \approx [OsO_4 \cdot aq]$$

because the concentrations of the latter two species are extremely low.

$$[Os(VI)]_{total} = [H_2[{}^6OsO_2(OH)_4]] + [H[{}^6OsO_2(OH)_4]^-] + [[{}^6OsO_2(OH)_4]^{2-}]$$

Using the appropriate protonation equilibrium constants, we obtain:

$$[Os(VI)]_{total} = \frac{[Os]_{total} k_{red} \frac{1}{1+f}}{k_{red} \frac{1}{1+f} + k_{12} \frac{f}{1+f} \frac{1}{g_1} + k_{13} \frac{f}{1+f} \frac{1}{g_2}} = \frac{[Os]_{total}}{Q} \qquad (A)$$

where

$$f = \frac{[H^+]}{K_1}; \quad g_1 = 1 + \frac{[H^+]}{K_6} + \frac{K_7}{[H^+]};$$

$$g_2 = 1 + \frac{[H^+]}{K_7} + \frac{[H^+]^2}{K_6 K_7}$$

Substituting $[Os(VI)]_{total}$ into the overall rate:

$$-\frac{d[H_2O_2]}{dt} = R_{red} + R_{12} + R_{13} =$$

$$= [H_2O_2]_{total}[Os]_{total} \left\{ k_{red} \frac{Q-1}{Q} + k_{12} \frac{1}{Q} \frac{f}{1+f} + k_{13} \frac{1}{Q} \frac{f}{1+f} \right\} \qquad (B)$$

Equation (B) describes a maximum curve as a function of the pH. For the rate coefficients k_{red}, k_{12} and k_{13}, numerical values were chosen by trial which gave the best fit for the experimentally determined overall decomposition rate vs pH and the [Os(VIII)]/[Os(VI)] vs pH functions. The agreement between the computed and the measured rate values and [Os(VIII)]/[Os(VI)] values as a function of pH is shown in Fig. 2, curves 3 and 4.

The ·OH radical chain component of the catalysed decomposition

The contribution of the rate of the reaction route involving ·OH radicals to the overall rate of decomposition was found to decrease as the pH was increased. Another characteristics of the radical component is that the rate of radical production passes through a maximum as a function of pH, the maximum lying at pH 8.5. Comparison of the pH profile of the relative impor-

tance of the ·OH radical route (Fig. 2, curve 5) with the change in concentration of the osmium(VI) species as a function of pH (Fig. 2, curve 6) suggests that the undissociated osmium(VI) acid species is responsible for ·OH radical production. As mentioned before, homolysis of peroxoosmium(VI) acid results in ·OH and osmium(VII) radicals:

$$H_2[^6OsO_2(OH)_3(OOH)] \rightarrow \ldots \rightarrow H[^7OsO_2(OH)_4] + \cdot OH \qquad (9)$$

The fates of these radicals might be as follows. Osmium(VII), like the intermediate valency state species of most elements (e.g. chromium(V)), can be reduced or oxidized by hydrogen peroxide:

$$H[^7OsO_2(OH)_4] + H_2O_2 \rightarrow H_2[^6OsO_2(OH)_4] + O_2^{\cdot-} + H^+ \qquad (14)$$

$$H[^7OsO_2(OH)_4] + H_2O_2 \rightarrow {}^8OsO_2(OH)_4 + \cdot OH + H_2O \qquad (15)$$

Step (14) results in osmium(VI) acid again, which, through steps (8) and (9), produces, the above radicals and thereby a reaction chain is developed. With respect to the chain propagation, step (15) can be considered a termination reaction. The length of the chain was found to be about 70 at pH 6.8, and about 10 at pH $\geq$ 9.

At higher pH, osmium(VII) dissociates as an acid:

$$H[^7OsO_2(OH)_4] \rightleftharpoons H^+ + [^7OsO_2(OH)_4]^- \qquad (16)$$

and osmium(VII) is oxidized to osmium(VIII):

$$[^7OsO_2(OH)_4]^- + H_2O_2 \rightarrow {}^8OsO_2(OH)_4 + \cdot OH + OH^- \qquad (17)$$

The highly reactive ·OH radical is converted by hydrogen peroxide into the superoxide radical (see later). The rate of initiation of ·OH radicals is:

$$R_{init}^{OH} = k_9[H_2[^6OsO_2(OH)_3(OOH)]] = k_9K_8[H_2[^6OsO_2(OH)_4]]\,[H_2O_2]$$

$$[H_2[^6OsO_2(OH)_3\ (OOH)]] =$$

$$= K_8[Os(VI)]_{total}\,[H_2O_2]_{total}\,\frac{[H^+]}{[H^+] + K_6}\,\frac{[H^+]}{[H^+] + K_{10}}$$

From equation (A):

$$R_{init}^{OH} = k_9K_8\,\frac{[Os]_{total}}{Q}\,[H_2O_2]_{total}\,\frac{[H^+]}{[H^+] + K_6}\,\frac{[H^+]}{[H^+] + K_{10}} \qquad (C)$$

The characteristic pH-dependence of the rate of ·OH radical formation arises from the fact that $[Os(VI)]_{total}$ increases monotonously with increasing pH (see equation (A)), while the concentration of undissociated osmium(VI) acid (together with that of its peroxo derivative) decreases. The agreement between the experimentaland computed values can be seen in Fig. 2, curve 2.

The role and fate of superoxide radicals

Superoxide radicals are produced in different reaction. The ·OH radical formed at lower pH is transformed by the substrate species into the superoxide radical:

$$\cdot OH + H_2O_2 \rightarrow O_2^{\cdot-} + H_3O^+ \tag{18}$$

$$\cdot OH + HO_2^- \rightarrow O_2^{\cdot-} + H_2O \tag{19}$$

It has been mentioned that the superoxide radical is produced in reaction (14), too. Further, reaction (4) is considered a third source, when some of the osmium(VII) and $O_2^{\cdot-}$ radical pairs escape from the solvent cage.

The superoxide radical is a not too reactive species and therefore no decisive role has been attributed to it in the catalysed decomposition scheme. The most important reaction of the superoxide radical is its dismutation. At lower pH, when the protolysis furnishes $HO_2^{\cdot}$ in considerable concentrations:

$$HO_2^{\cdot} \rightleftharpoons H^+ + O_2^{\cdot-} \tag{20}$$

the fastest dismutation step

$$HO_2^{\cdot} + O_2^{\cdot-} \rightarrow HO_2^- + O_2 \tag{21}$$

removes most of the superoxide formed. In this pH range, the superoxide radical can be detected only by the most sensitive means (e.g. with tetranitromethane), and not by the e.s.r. method. At higher pH, the decay of superoxide radicals slows down as step (22)

$$O_2^{\cdot-} + O_2^{\cdot-} + H^+ \rightarrow HO_2^- + O_2 \tag{22}$$

is very slow. As a consequence of this, superoxide radicals progressively accumulate with increasing pH. Under such circumstances, superoxide radicals can easily be detected by the e.s.r. method.

Dependence on the concentration of OsO_4

At lower pH, when the concentration of the catalyst exceeds 10^{-5} *M*, it was found that the order with respect to the catalyst falls below one, and it progressively decreases to zero when the catalyst concentration reaches 10^{-3} *M*. The catalysed decomposition is induced by the peroxidation equilibrium (2), and therefore the overall rate is regulated by the concentrations of catalyst and of HO_2^-. At pH 7 (or below), the concentration of HO_2^- drops well below the concentration of catalyst, HO_2^- being a strong base, and from then on the rate of decomposition is independent of the concentration of

$OsO_4 \cdot aq$. We can write:

$$[HO_2^-]_{total} = [HO_2^-] + [^8OsO_2(OH)_3(O_2^-)] \text{ and}$$
$$[Os(VIII)]_{total} = [OsO_4 \cdot aq] + [OsO_4] + [^8OsO_2(OH)_4] +$$
$$+ [^8OsO_2(OH)_3(O_2^-)] \cong [OsO_4 . aq]$$

for under the reaction conditions pH = 7 and 0.1 M H_2O_2 we have $[HO_2^-] \sim$ $\sim 2.5\ 10^{-6}\ M$, and therefore the concentrations of the adduct and of the other osmium(VIII) species are negligible. Further, from equilibria (1) and (2) we obtain:

$$[^8OsO_2(OH)_3(O_2^-)] = \frac{K_2[OsO_4 . aq]}{1 + K_2[OsO_4 . aq]} \frac{K_1}{[H^+] + K_1} [H_2O_2]_{total} \qquad (D)$$

When $1 < K_2[OsO_4 . aq]$, the term 1 in the denominator can be neglected and therefore the concentration of the adduct (and hence the overall rate of decomposition) is independent of the total concentration of catalyst. This can be seen in Fig. 3, curves 1 and 2.

Formation of singlet oxygen

It has been found that about 0.3 and 0.6% of the total dioxygen evolved appears in the form of singlet oxygen at pH 8.5 and 10.6, respectively. Recent investigations [34—37] have proved convincingly that the proton-induced dismutation of superoxide radicals (step (21)) does not result in singlet oxygen, probably because of the very efficient quenching of singlet oxygen by the superoxide radical in water. The rate coefficient of step

$$O_2^{\cdot-} + {}^1O_2 \rightarrow {}^3O_2 + O_2^{\cdot-}$$

is $1.6 \times 10^9\ M^{-1}s^{-1}$ [35, 36]. If we are not victims of some artifacts and the $^1O_2$ has not arisen from reactions of impurities in the buffers or sodium hydroxide used, we have to look for a redox reaction in which the singlet transition state is favored. Perhaps osmium(VII) can be regarded as such a potential partner, but further investigations are necessary to support this assumption.

pH-*dependence of apparent energy of activation*

The apparent energy of activation of the overall rate of decomposition shows a definite pH-dependence: in the temperature range 278—328 K, values of 105, 75, 47 and 11 kJ mol^{-1} were obtained at pH 7, 8.1, 9 and 10, by measuring the rate of dioxygen evolution. The temperature-dependence of the bleaching rate of RNO (which is indicative of the reaction component involving the OH radical) was different: apparent activation energies of 110, 105, 103 and 39 kJ mol^{-1} were found at pH 7, 8.1, 9 and 10. These observations

are in good agreement with the mechanism proposed. At lower pH, where the radical chain component of decomposition predominates, a considerable activation energy (105—110 kJ mol^{-1}) is required to break the O·O bond of peroxoosmium(VI) acid (see step (9)), while the molecular route of decomposition needs an activation energy of only 11—12 kJ mol^{-1}.

Simulation of OsO_4*-catalysed decomposition*

The useful results of model calculations involving steady-state treatment to characterize the typical features of this catalytic reaction encouraged us to attempt to simulate the system as a whole by solving the differential equation system corresponding to the above reaction steps. With the most reliable rate coefficient and equilibrium constant values from the literature, and with the best estimations obtained by trial for the unknowns, computation by the method of Gear [41] resulted in reasonable agreement with the experimental results. The satisfactory agreement between the observed and computed dependences on the reaction parameters, e.g. the pH profiles of the overall rate and of ·OH and superoxide radical production, as well as the change in valency state of the catalyst, suggests that the proposed series of reactions are all necessary for characterization (see Fig. 3). The assumed mechanism accounts for the transient formation, the reaction orders with respect to the substrate and catalysts, as well as the attainment of a limiting decomposition rate when the catalyst concentration exceeds 10^{-3} M. The rate coefficients [$M^{-1}s^{-1}$ or s^{-1}] and equilibrium constants [M or M^{-1}] used were as follows:

$K_1 = 2.5\times10^{-12}$ [38] $\quad K_2 = 2.0\times10^{3}$ (estimated)
$k_3 = 2.4\times10^{3}$ (estimated) $\quad k_4 = 1.0\times10^{2}$ (estimated)
$k_5 = 2.4\times10^{4}$ (estimated) $\quad K_6 = 3.2\times10^{-9}$ [29]
$K_7 = 4.0\times10^{-11}$ [29] $\quad K_8 = 1.0\times10^{3}$ (estimated)
$k_9 = 1.3\times10^{3}$ (estimated) $\quad K_{10} = 3.3\times10^{-9}$ (estimated)
$k_{11} = 1.1\times10^{4}$ (estimated) $\quad k_{12} = 1.1\times10^{4}$ (estimated)
$k_{13} = 2.3\times10^{3}$ (estimated) $\quad k_{14} = 1.8\times10^{5}$ (estimated)
$k_{15} = 1.3\times10^{5}$ (estimated) $\quad K_{16} = 3.2\times10^{-9}$ (estimated)
$k_{17} = 8.6\times10^{4}$ (estimated) $\quad k_{18} = 2.7\times10^{7}$ [39]
$k_{19} = 7.5\times10^{9}$ [39] $\quad K_{20} = 1.78\times10^{-5}$ [40]
$k_{21} = 1.02\times10^{8}$ [40] $\quad k_{22} = 0.35$ [40]

REFERENCES

[1] Habig, R. L., Pardue, H. L., Worthington, J. B.: Anal. Chem., **39,** 600 (1967)
[2] Gleu, K.: Z. Anal. Chem., **95,** 385 (1933)
[3] Csányi, L. J.: Induced reactions in chemical analysis, in "Treatise on Analytical Chemistry" (Eds. I. M. Kolthoff and P. J. Elving), Part I. Vol **2,** 2nd Ed. Intersci.-Wiley, New York, 1979, pp. 701—787.

[4] Sengupta, K. K., Basu, B.: Indian J. Chem., **16*A***, 808 (1978)
[5] Jindal, V. K., Agrawal, M. C., Mushran, S. P.: J. Chem. Soc. A **1971,** 622
[6] Mohan, D., Gupta, Y. K.: J. Chem. Soc. Dalton, **1977,** 1085
[7] Upadhyay, S. K., Agrawal, M. C.: Indian J. Chem., **15*A***, 416 (1977)
[8] Upadhyay, S. K., Agrawal, M. C.: Indian J. Chem., **16*A***, 39 (1978)
[9] Upadhyay, S. K., Agrawal, M. C.: Indian J. Chem., **15*A***, 709 (1977)
[10] Upadhyay, S. K., Agrawal, M. C.: Monatsh. Chem., **110,** 413 (1979)
[11] Upadhyay, S. K.: Int. J. Chem. Kin., **15,** 669 (1983)
[12] Singh, V. N., Singh, H. S., Saxena, B. B. L.: J. Am. Chem. Soc., **91,** 2643 (1969)
[13] Mehrotra, U. S., Mushran, S. P.: J. Indian Chem. Soc., **45,** 527 (1968)
[14] Neogi, G., Acharya, S., Panda, R. K., Ramaswamy, D.: Int. J. Chem. Kin., **15,** 881 (1983)
[15] Panda, R. K., Neogi, G., Ramaswamy, D.: Int. J. Chem. Kin., **13,** 1001 (1981)
[16] Uma, K. V., Mayanna, S. M.: J. Catal., **61,** 165 (1980)
[17] Mushran, S. P., Mehrotra, R. M., Sanehi, R.: Proc. Nat. Acad. Sci. India, **43*A***, 105 (1973)
[18] Mushran, S. P., Agrawal, M. C., Prased, B.: J. Chem. Soc. B, **1971,** 1712
[19] Mushran, S. P., Sanehi, R., Agrawal, M. C.: Z. Naturforsch., **27*b***, 10 (1972)
[20] Kumar, A., Bose, A. K., Mehrotra, R. M., Mushran, S. P.: Z. Phys. Chem. (Leipzig), **260,** 33 (1979)
[21] Ganapathy, K., Jayagandhi, P.: J. Indian Chem. Soc., **61,** 393 (1984)
[22] Rylander, P. N.: Engelhard Ind. Techn. Bull. Vol. **1,** 90—95 (1968)
[23] Gunstone, F. D.: Hydroxylation Methods in Adv. in Organic Chem. Vol. **1** pp. 103—147, Intersci. New York 1960
[24] Csányi, L. J., Kaszai, S., Molnár, I.: Talanta, **10,** 449 (1963)
[25] Csányi, L. J., Fülöp, K.: Acta. Chim. Acad. Sci. Hung., **38,** 193 (1963)
[26] Csányi, L. J., Galbács, Z. M., Nagy. L.: J. Chem. Soc. Dalton Trans., **1982,** 237
[27] Nagy, L., Galbács, Z. M., Csányi, L. J.: J. Chem. Soc. Dalton Trans., **1982,** 859
[28] Galbács, Z. M., Nagy, L., Csányi, L. J.: Polyhedron, **1,** 175 (1982)
[29] Galbács, Z. M., Zsednai, Á., Csányi, L. J.: Transition Met. Chem., **8,** 328 (1983)
[30] Csányi, L. J., Galbács, Z. M., Marek, N., Nagy, L.: Transition Met. Chem. **11,** 319 (1986)
[31] Krajlić, I., Mohsni, S. El.: Photochem. and Photobiol., **28,** 577 (1978)
[32] Halperin, J., Taube, H.: J. Am. Chem. Soc., **74,** 380 (1952)
[33] Hughes, M. N., Nicklin, H. G.: J. Chem. Soc. A., **1968,** 450
[34] Arudi, R. L., Bielski, B. H. J., Allen, A. O.: Photochem. and Photobiol., **39,** 703 (1984)
[35] Nanni Jr., E. J., Birge, R. R., Hubbard, L. M., Morrison, M. M., Sawyer, D. T.: Inorg. Chem., **20,** 737 (1981)
[36] Aubry, J. M., Rigaudy, J.: J. Am. Chem. Soc., **103,** 4965 (1981)
[37] Foote, C. S., Shook, F. C., Abakerli, R. A.: J. Am. Chem. Soc., **102,** 2503 (1980)
[38] Evans, M. G., Uri, N.: Trans. Faraday Soc., **41,** 138 (1945)
[39] Sehested, K., Holcman, J., Bjergbakke, E., Hart, E. J.: J. Phys. Chem., **86,** 2066 (1982)
[40] Weinstein, J., Bielski, B. H. J.: J. Am. Chem. Soc., **101,** 58 (1979)
[41] Gear, G. W.: Numerical Initial Value Problems in Ordinary Differential Equations, Prentice Hall Inc., Englewood Cliff, New Jersey 1971

Acta Chimica Hungarica 123 (3—4), pp. 137—143 (1986)

EFFECT OF QUINOLINIUM SALTS ON THE BEHAVIOUR OF TETRACYANOQUINODIMETHANE POLYMER FILM ELECTRODE

György INZELT[1]*, James Q. CHAMBERS[2] and Roger W. DAY[2]

([1]Department of Physical-Chemistry and Radiology Eötvös Loránd University, H-1088 Budapest, Puskin u. 11—13. and [2]The University of Tennessee, Department of Chemistry, Knoxville, U. S. A.)

Received July 25, 1985
Accepted for publication February 27, 1986

The behaviour of tetracyanoquinodimethane (TCNQ) polymer film electrode in contact with aqueous quinolinium chloride/quinoline buffer and 1-ethylquinolinium iodide supporting electrolytes has been studied by cyclic voltammetric and spectro-electrochemical methods.

Basically similar behaviour of the Pt-TCNQ electrode was observed in the presence of quinolinium salts relative to supporting electrolyte solutions containing alkali metal ions. However, differences in the interaction and swelling conditions affected the shape of the cyclic voltammetric curve, the stability of the film, and the passivation in acid medium.

Introduction

Tetracyanoquinodimethane (TCNQ), having excellent electron acceptor properties, has been widely studied ever since its preparation [1]. These investigations aim at learning the fundamental chemical, electrochemical and spectroscopical properties of TCNQ and related compounds [2—12]. Interest of the physicists was also aroused by the fact that several salts of this compound (such as tetrahiafulvalene-TCNQ, quinolinium-TCNQ) are quasi-one-dimensional electron conductors with very good conducting properties [13—19].

These interesting features gave motivation to prepare a polymer of the compound [20], and to use this polyester-TCNQ for the preparation of polymer film electrodes [21]. These TCNQ polymer film electrodes in contact with aqueous electrolyte solutions have been studied by means of electrochemical (cyclic voltammetry, chronocoulometry) and spectroscopical (ultraviolet, visible, near infrared and ESR) methods [22—26]. The basic electrochemical and chemical processes occurring in these electrodes and their dependence on the experimental conditions have been elucidated [22—26]. The TCNQ electrode proved to be very stable, both in aqueous solution, or when stored dry over a longer period. This was all the more remarkable, since in aqueous

* To whom correspondence should be addressed.

solution reactions between the reduction products of TCNQ ($TCNQ^{\cdot-}$ and $TCNQ^{2-}$) and oxygen, even if the latter is present in trace quantities, are rapid and irreversible [6]. Its stability and fast colour change accompanying electrochemical reduction make this electrode very suitable for use in electro-optical display. In the case Pt-TCNQ a further possibility of application is offered as a pH indicator [24]. Using supporting electrolytes containing alkali metal, alkali earth metal or tetraalkyl ammonium cations, the TCNQ electrode showed a behaviour fundamentally corresponding to the electrochemistry of dissolved TCNQ electrode; accordingly, it was reduced in two single-electron steps and depending on the pH, this process can be coupled by protonation. In addition to the dimer dianion, $TCNQ_2^{2-}$, observed in the solution [3], the presence of the mixed-valence dimer, TCN_2^{-} can also be detected in the film [22]. Though the mixed-valence dimer has a decisive role in the explanation of the unusually high electric conductivity of solid TCNQ salts, no metal-like behaviour was observed in the case of TCNQ polymer film electrode. The probable reason is that TCNQ is here incorporated in a polymeric chain, and thus no crystallization takes place because of steric hindrance. Hence, the parallel stacking in columns of the planar TCNQ molecules, characteristic of the crystal structure of solid TCNQ salts, cannot occur. Therefore, in the use of quinolinium salts as supporting electrolytes, our aim was not to obtain a polymer film with properties similar to those of the quinolinium-TCNQ crystal, yet it seemed interesting to study the effect of an aromatic, organic cation, as the importance of the nature and concentration of the counter ion on the electrochemical behaviour of the TCNQ electrode had been demonstrated earlier [22, 26].

In the present communication the cyclic voltammetric and the cyclic voltabsorptometric behaviour of the Pt-TCNQ polymer film electrode was studied in the presence of quinolinium chloride/quinoline buffer system and 1-ethylquinolinium iodide supporting electrolytes in aqueous medium.

Experimental

The preparation of the electrode, the electrochemical cells and instruments used have been described previously [21—24]. Freshly vacuum-distilled quinoline was used. The buffer system was prepared by adding a calculated amount of hydrochloric acid. 1-Ethylquinolinium iodide of analytical grade was used without further purification.

Results and Discussion

In the buffer system containing quinolinium chloride and quinoline, the behaviour of the Pt-TCNQ polymer film electrode differed in several respects from the behaviour observed in the presence of alkali metal, alkali

earth metal or tetraalkylammonium ions. This is illustrated by the cyclic voltammogram shown in Fig. 1, obtained in a pH 4.4 quinolinium/quinoline buffer system of 0.5 mol/dm^3 concentration for a Pt-TCNQ electrode of

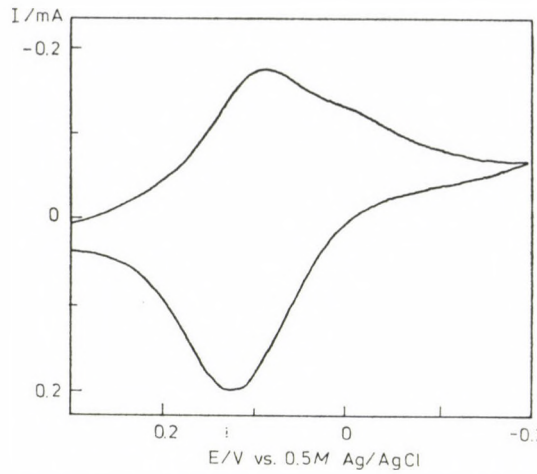


Fig. 1. Cyclic voltammogram of a Pt-TCNQ electrode $\Gamma = 3 \times 10^{-8}$ mol/cm^2 in the presence of 0.5 mol/dm^3 quinolinium chloride and 0.5 mol/dm^3 quinoline, pH = 4.4 at a polarization rate of $v = 0.005$ V/s

$\Gamma = 3 \times 10^{-8}$ mol/cm^2 surface concentration at a polarization rate of v = = 0.005 V/s. According to our experiences gained so far, the first pair of peaks is to be attributed to the reaction

$$TCNQ + e^- + M^+ \rightleftharpoons TCNQ^-M^+, \qquad (1)$$

where M^+ is the counter ion.

Comparison with earlier results [22] shows that in the presence of the quinolinium/quinoline buffer system the peak potentials characteristic of this redox pair are shifted in the direction of more positive potentials. It follows that in the presence of quinolinium ions TCNQ can be more readily reduced (the actual redox potential is more positive), which can be explained by the stronger interaction between quinolinium ion and the $TCNQ^-$ radical anion. This may also be the explanation of the fact that while earlier the passivation of the film was observed at pH 5.5 values [23] in the presence of quinolinium ions a reversible redox behaviour was found even in more acidic media. Passivation was interpreted by presuming that in a moderately or strongly acidic (pH < 6.0) solution the analogous hydroquinone compound, $TCNQH_2$, is formed, and then, similarly to the phenomenon observed in the case of hydroquinone polymer film [27], the rate of charge transport in the film decreases by orders of magnitude.

Since the value of the dissociation constant of the equilibrium

$$TCNQH_2 \rightleftharpoons TCNQH^- + H^+ \qquad (2)$$

was found to be $pK_a = 6.9$ in solution of 0.5 mol/dm^3 alkali metal ion concentration, it follows that even in moderately acid solutions the equilibrium is largely shifted in the direction of the lower arrow, i.e. the formation of $TCNQH_2$. However, the apparent equilibrium constant of reaction (2) depends on the nature and concentration of the M^+ counter ions through the M^+-dependent stability constant of $TCNQH^-M^+$ [28]. Thus, it is not surprising that in the presence of quinolinium ions the value of pK_a may be lower, and even at pH = 4.4 only the formation of the species $TCNQH^-$ is to be taken into account. The cyclic voltammetric peak, corresponding to the reaction

$$TCNQ^-M^+ + e^- + H^+ \rightleftharpoons TCNQH^-M^+ \qquad (3)$$

actually appears, though at pH = 4.4 already strongly merged with the peak of reaction (1). It is a consequence of the shift of the peak potential of reaction (3) by 120 mV per pH unit towards more positive potentials [23], while step (1), in which H^+ ions do not participate, is fundamentally not sensitive to pH changes.

However, cyclic voltammetric results do not provide yet sufficient evidence of the abovesaid, as other products with reversible electrochemical behaviour may also be formed; moreover, they do not give information on the character of the interaction. In order to obtain further data supporting our assumption, a spectroelectrochemical investigation of the system seemed necessary, as this method was found well applicable also earlier in the case of TCNQ electrodes [22]. The spectrum of the reduced film basically corresponded to the absorption curves obtained in the ultraviolet, visible and near infrared regions with the counter ions investigated earlier [22]. Since the maxima characteristic of the reduced species ($TCNQ^-$, $TCNQ_2^{2-}$) appeared at the same wavelengths, and new peaks were not observed, it could be concluded that, under the conditions of our investigation, no π-complex is formed between quinolinium (Q^+) and $TCNQ^{\cdot-}$. This result also means that the reduced species $Q^+TCNQ^{\cdot-}$ is similar in character to those formed in other systems, and is not inconsistent with our assumption that the ion pair or salt formed is more stable than that obtained with the participation of alkali metal ions. The transient behaviour can be readily followed on the cyclic voltabsorptometric curve (CVA), shown in Fig. 2. The curve in Fig. 2 was recorded simultaneously with the cyclic voltammetric curve in Fig. 1, and shows the optical absorption of the film at the wavelength $\lambda = 830$ nm, where the species $TCNQ^{\cdot-}$ has maximal absorption. This curve proves that

in the potential range 0.2—0.0 V vs. 0.5 *M* Ag/AgCl actually $TCNQ^{\cdot-}$ is formed. In the potential range from 0 to —0.2 V second electron transfer with protonation takes place. The product of this reaction is $TCNQH^-$, absorbing in the ultraviolet region; this is evidenced by a decreasing light

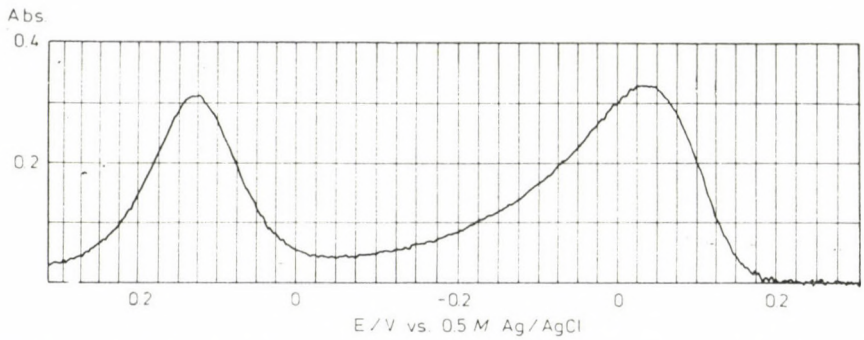


Fig. 2. Change in light absorption at $\lambda = 830$ nm as a function of the potential, recorded simultaneously with the cyclic voltammogram shown in Fig. 1

absorption. During reoxidation, first $TCNQH^-$ is oxidized at about 0.0 V and, in a reversible reaction, $TCNQ^{\cdot-}$ is formed again, which is accompanied by an increased absorption of the film; then at potentials more positive than 0.1 V neutral TCNQ is formed in the process according to reaction (1). (Neutral TCNQ has maximal absorptions at 412 and 432 nm.) Thus, spectroelectrochemical investigations fundamentally supported our conclusions drawn from the cyclic voltammogram.

It is noteworthy that the behaviour of the Pt-TCNQ polymer film electrode does not essentially differ, whether quinolinium or 1-ethylquinolinium salt is used as the supporting electrolyte. The TCNQ film swells better in their presence and is dissolved at higher pH values. By way of example a cyclic voltammogram series obtained for a Pt-TCNQ electrode is shown in Fig. 3. In this case the base electrolyte was 1-ethylquinolinium iodide of 0.5 mol/dm^3 concentration (pH = 7, non-buffered system). On comparing the consecutive curves, a decrease of the peak current (and charge consumed by the film calculated from the integrated area) can be observed, which indicates the slow dissolution of the film. It was shown by investigations in neutral, non-buffered medium that the pH of the film was alkaline [22], thus the second pair of peaks can be attributed here to the formation and the reoxidation of the species $TCNQ^{2-}M^+$. It is interesting that charge transport is faster in the second electron transition, whereas just the opposite effect was observed in the presence of alkali metal ions. This is probably due to the different swelling conditions.

In summary, it can be established that the Pt-TCNQ electrode has basically similar behaviour in the presence of quinolinium salts to the performance observed in solutions of alkali metal base electrolytes. However,

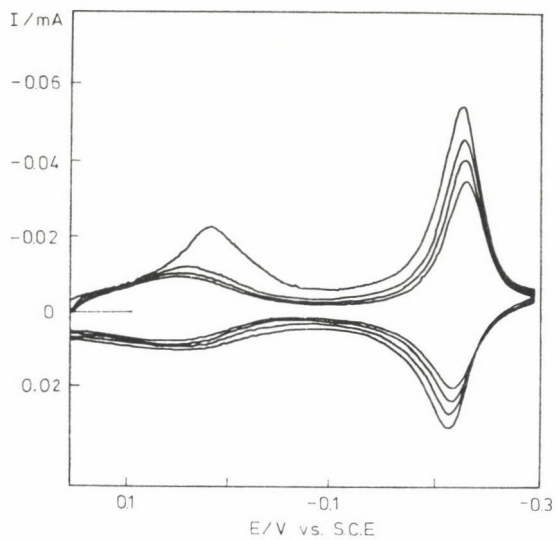


Fig. 3. A cyclic voltammogram series, continuously recorded for a Pt-TCNQ electrode at a polarization rate of $v = 0.02$ V/s, in neutral 0.5 mol/dm^3 1-ethylquinolinium iodide base electrolyte at 20 °C

stronger interaction between the quinolinium ions and the redox sites of reduced TCNQ, further the changed swelling conditions affect the shape of the cyclic voltammetric curve. The change in protonation constants is reflected by the fact that in moderately acid solutions the film is not yet passivated.

*

The present work was sponsored by the U. S. A. R. O. (Project 140. P17715-C).

REFERENCES

[1] Melby, L. R., Harder, R. J., Hertler, W. R., Mahler, W., Benson, R. E., Mochel, W. E.: J. Am. Chem. Soc., **82,** 6408 (1960); **84,** 3374 (1962)
[2] Fisher, P. H. H., McDowell, C. A.: J. Am. Chem. Soc., **85,** 2694 (1963)
[3] Boyd, R. H., Phillips, W. D.: J. Chem. Phys., **43,** 2927 (1965)
[4] Iida, Y.: Bull. Chem. Soc. Japan, **42,** 71 (1969)
[5] Sakai, N.: Bull. Chem. Soc. Japan, **43,** 57 (1970)
[6] Suchanski, M. R., Van Duyne, R. P.: J. Am. Chem. Soc., **98,** 250 (1976)
[7] Jeanmaire, D. L., Van Duyne, R. P.: J. Am. Chem. Soc., **98,** 4029 (1976)
[8] Sharp, M.: Anal. Chim. Acta, **85,** 17 (1976)
[9] Sharp, M.: Electrochim. Acta, **21,** 973 (1976)
[10] Jaeger, C. D., Bard, A. J.: J. Am. Chem. Soc., **102,** 5435 (1980)
[11] Tanaka, J., Tanaka, M., Kawai, T., Takabe, T., Maki, O.: Bull. Chem. Soc. Japan, **49,** 2358 (1976)

[12] Tanaka, J., Tanaka, M., Tanaka, C., Ohno, T., Takabe, T., Anzai, M.: Ann. New York Acad. Sci., **313,** 256 (1978)
[13] Conference on the Physics and Chemistry of Low Dimensional Solids, ed. L. Alcacer, 1980
[14] Menczel, Gy., Kürti, J., Lehőcz, R.: Acta Chim. Hung., **116,** 335 (1984)
[15] Wheland, R. C., Gillson, J. L.: J. Am. Chem. Soc., **98,** 3916 (1976)
[16] Strzelecka, H., Gionis, V., Fugitto, R.: Synth. Metals, **5,** 31 (1982)
[17] Lamache, M., Wuryanto, S., Lequan, M., Lequan, R. M.: Electrochim. Acta, **30,** 455 (1985)
[18] Kathirgamanathan, P., Rosseinsky, D. R.: J. Chem. Soc., Chem. Commun., **356,** 839 (1983)
[19] Carneiro, K., Almeida, H., Alcacer, L.: Solid State Commun., **44,** 959 (1982)
[20] Day, R. W., Karimi, H., Francis, C. V., Kinstle, J. F., Chambers, J. Q.: J. Polym. Sci. (in press)
[21] Day, R. W., Inzelt, G., Kinstle, J. F., Chambers, J. Q.: J. Am. Chem., Soc., **104,** 6804 (1982)
[22] Inzelt, G., Day, R. W., Kinstle, J. F., Chambers, J. Q.: J. Phys. Chem., **87,** 4592 (1983); J. Electroanal. Chem., **161,** 147 (1984)
[23] Inzelt, G., Chambers, J. Q., Kinstle, J. F., Day, R. W.: J. Am. Chem. Soc., **106,** 3396 (1984)
[24] Chambers, J. Q., Inzelt, G.: Anal. Chem., **57,** 1117 (1985)
[25] Inzelt, G., Chambers, J. Q., Kinstle, J. F., Day, R. W., Lange, M. A.: Anal. Chem., **56,** 301 (1984)
[26] Inzelt, G., Chambers, J. Q., Bácskai, J., Day, R. W.: J. Electroanal. Chem., **201,** 301 (1986)
[27] Fukui, M., Kitani, A., Degrand, C., Miller, L. L.: J. Am. Chem. Soc., **104,** 28 (1982)
[28] Inczédy, J.: Analytical Applications of Complex Equilibria, Akadémiai Kiadó, Budapest 1976

Acta Chimica Hungarica 123 (3–4), pp. 145–154 (1986)

PHOSPHANE OXIDES AS INTERMEDIATES IN THE SYNTHESIS OF POTENTIALLY BIOACTIVE COMPOUNDS*

György MATOLCSY[1], Krisztina BAUER[1], Ágnes PÁL[1], István UJVÁRY[1], Iván BÉLAI[1], Anikó GERLEI[1], Mariann KARDOS[1], Pál SOHÁR[2]** and István PELCZER[2]

([1]Plant Protection Institute, Hungarian Academy of Sciences, H-1022 Budapest, Herman O. u. 15. and [2]EGIS Pharmaceuticals, Spectroscopic Department, H-1106 Budapest, Keresztúri út 30–38.)

Received September 5, 1985
Accepted for publication February 27, 1986

New chloromethylphosphane oxides, as well as phosphane oxide-substituted benzyl alcohols, benzaldehydes, aromatic nitro compounds, anilines, and phenols were synthesized as intermediates for the introduction of the phosphane oxide function into bioactive molecules. NMR characteristics of the newly synthesized compounds are discussed in detail.

Introduction

Introduction of a phosphane oxide group into biologically active molecules may significantly modify the biological properties. The phosphane oxide group increases hydrophilicity, and as a result influences the pharmacokinetical characteristics of a molecule [1]. Another feature of possible biological impact is the electronic structure of the P=O group. The $4sp^3$ orbitals of the phosphorus atom overlap with the 2p orbitals of P=O oxygen to four σ-bonds, superimposed by a π-bonding system, a fact of probable significance in interacting with the active site on a biological macromolecule. Phosphane oxides as substituents are strongly electronegative, e.g. the dimethylphosphinoyl group has a σ_m value of 0.42 [2]. At the same time, the phosphane oxide group is chemically inert, thus an increased hydrophilicity of the parent compound can be achieved without introducing a reactive moiety, such as hydroxyl, carboxyl or other function.

Only a handful of drugs bearing phosphane oxide substituents has been described. Some of the few examples found in the literature are the dimethylphosphinoylmethyl containing antihistamine [3], analgetic [4, 5], hypotonic [6] and sleep-inducing [7] substances.They were prepared by using chloromethyldimethylphosphane oxide (**3a**, R=R′=Me) as alkylating (phosphinoylmethylating) agent in the final synthetic step.

* This work was performed in the framework of the UNDP/UNIDO/FAO sponsored project "Research on non-toxic insecticides".

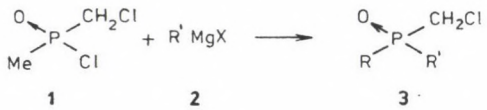
** To whom correspondence should be addressed.

Synthesis

In this paper we report on the preparation of a series of functionalized phosphane oxides, such as chloromethylphosphane oxides, phosphane oxide-substituted benzyl alcohols, benzaldehydes, aromatic nitro compounds, anilines and phenols. These new compounds can be used as intermediates for the introduction of phosphane oxide moiety into the molecule of candidate drugs, pesticides, and other biologically active compounds, whenever their synthesis route includes the use of alkylating agents, benzyl alcohols, benzaldehydes, nitrobenzenes, anilines, or phenols, respectively.

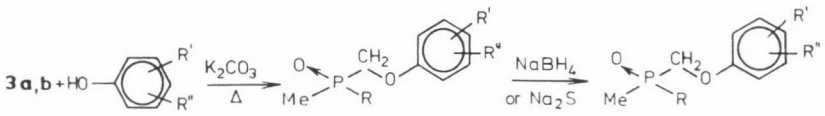
Chloromethylphosphane oxides **3b—e** were prepared by reacting chloromethylmethylphosphinoyl chloride **1** with Grignard reagents **2b—e** (Method *A*). Chloromethyldiphenylphosphane oxide (**3f**) was synthesized from chloromethylphosphonic dichloride (Cl_2POCH_2Cl) and phenylmagnesium bromide (Method *B*).

The (phosphinoylmethoxy)benzaldehydes **5a—c** were obtained by reacting the properly substituted chloromethylphosphane oxide **3a** or **3b** with the corresponding hydroxybenzaldehyde **4a—c** in the presence of anhydrous potassium carbonate under energetic conditions. Reduction of the benzaldehydes **5a—c** with sodium borohydride yielded the corresponding benzyl alcohols **6a—c**.



1 **2** **3**

a: R = R' = Me
b: R = Me, R' = Ph
c: R = Me, R' = 4-Cl-Ph
d: R = Me, R' = 4-MeO-Ph
e: R = Me, R' = CH_2Ph
f: R = R' = Ph



4 **5a,f** **6a,f**

a: R = Me, R' = H, R'' = 3-CHO (**5**) or 3-CH_2OH (**6**)
b: R = Me, R' = 2-MeO, R'' = 4-CHO (**5**) or 4-CH_2OH (**6**)
c: R = Ph, R' = H, R'' = 3-CHO (**5**) or 3-CH_2OH (**6**)
d: R = Me, R' = H, R'' = 2-NO_2 (**5**) or 2-NH_2 (**6**)
e: R = Me, R' = H, R'' = 4-NO_2 (**5**) or 4-NH_2 (**6**)
f: R = Me, R' = 2-Cl, R'' = 4-NO_2 (**5**) or 4-NH_2 (**6**)
g: R = Me, R' = 2-OH, R'' = H
h: R = Me, R' = 4-OH, R'' = H

Reacting the nitrophenols **4d—f** with chloromethyldimethylphosphane oxide **3a** in the presence of potassium carbonate gave crystalline (phosphinoylmethoxy)nitrobenzenes **5d—f**, which on reduction with sodium sulfide [8] yielded the expected phosphane oxide-containing anilines **6d—f**.

The monoethers **5g** and **5h** of pyrocathecol (**4g**) and hydroquinone (**4h**) were obtained in good yields by reacting equimolar quantities of **3a** and the appropriate diphenol in the presence of potassium carbonate.

The compounds described above can be regarded as models for obtaining analogous substances in search for bioactive substances.

Spectroscopic studies

IR *spectra*

The postulated structures of the newly synthesized compounds **3b—f**, **5a—h**, and **6a—f** were proved on the basis of spectroscopic investigations. The most important IR, ^{31}P, ^{1}H and ^{13}C NMR data are given in Tables I, II and III.

The characteristic intensive $\nu P \rightarrow O$ band of the phosphane oxide group [9] appears between 1145 and 1200 cm^{-1}. The absorption bands of the substituents, such as the carbonyl ($\nu C{=}O$) band of **5a—c**, the nitro bands [$\nu_{as}NO_2$, ν_sNO_2, and β_sNO_2] of **5d—f**, the OH band of **5g**, **5h**, and **6a—c** and the $\nu_{as}NH_2$ and ν_sNH_2 bands of **6e—f**, as well as the $\gamma C_{Ar}H$ and $\gamma C_{Ar}C_{Ar}$ bands of the aromatic ring can be found in the expected intervals (see Table I).

^{1}H NMR *spectra*

In the ^{1}H NMR spectra (Table II), the methyl and methylene protons attached to the phosphorus atom have split signals due to $^{2}J(P, H)$-type interactions. In the case of compounds **3b—e**, **5c**, and **6c**, the methylene hydrogens are chemically non-equivalent. Hence the PCH_2 group represents an *ABX* spin system, the *AB* part which (two dd's) appears in the ^{1}H NMR spectrum. The chemical shift of the PCH_2 group differs significantly for the compounds of type **3** and for the other ones (**5a—h** and **6a—f**) because of the presence of the neighbouring oxigen atom in the latter, deshielding the methylene protons.

The ^{1}H NMR signals of the substituents can be identified in all cases (see Table II).

^{13}C NMR *spectra*

The carbon signals of the PCH_3 and PCH_2 groups are doublets due to P, C-interactions (see Table III). The $^{1}J(P, C)$ coupling constant is higher (80—87 Hz) for the latter groups (the corresponding splittings of the methyl

Table I

Characteristic IR *frequencies* (cm^{-1}) *in* KBr *discs and* ^{31}P NMR *chemical shifts in* $CDCl_3$ *solution*[a] [$\delta^{ext.}_{H_3PO_4}$ (85%) = 0 ppm] *at* 101.2 MHz *for compounds* **3a—f, 5a—h** *and* **6a—f**

	$\nu P \rightarrow O$	$\gamma C_{Ar}H$	Other IR bands	δP
3a	1173	—		39.9
3b	1177	764	$\gamma C_{Ar}C_{Ar}$: 696	33.0
		744		
3c	1244	835		32.5
3d	1190	831		
	1177	818		32.8
3e	1180	773	$\gamma C_{Ar}C_{Ar}$: 700	42.2
3f	1196	725	$\gamma C_{Ar}C_{Ar}$: 702	26.1
5a	1186	774	νC=O: 1697, 1680	39.6
	1150	754		
5b	1185	720	νC=O: 1675	37.9
	1165			
5c	1186	731	νC=O: 1697	31.3
5d	1167	750	NO_2: 1522, 1348, 860	39.8
	1148			
5e	1167	850	NO_2: 1514, 1348, 858	38.7
5f	1182	744	NO_2: 1514, 1346, 856	40.1
		723		
5g	1161	756	νOH: ~ 3060	38.5
	1148			
5h	1157	825	νOH: ~ 3130	38.6
6a	1153	786	νOH: ~ 3350	41.7
		692		
6b	1161	775	νOH: ~ 3310	41.3
6c	1169	744	νOH: ~ 3350	33.1
		694		
6d	1171	760	νNH_2: 3460, 3292	39.5
6e	1155	825	νNH_2: 3385, 3234	40.7
6f	1169	758	νNH_2: 3333, 3190	41.2

[a] In DMSO-d_6 for compounds **5b, d, g, h**

carbon signals are 68—71 Hz) in case of compounds **5** and **6**, while for the **3**-type analogues the reversed relation is found (the methyl and methylene carbon signals are split by 71—75 and 65—71 Hz, respectively). This may be explained by the Walsh rule [10], by taking into account that the *s*-character of the phosphorus atom is concentrated in bonds with the most electropositive substituent, as well as that the ^1J(P, C) values increase proportionally with the *s*-character of the P—C bond. The electron density around the methyl carbon is higher in compounds **3** than in derivative **5** and **6**, increasing the *s*-character of the P—C(H_3) bond and, consequently, the ^1J(P, C) values [11]; this is also manifested in higher shielding (in the upfield shift of the methyl carbon signal) in case of compounds **3a—f** relative to the others.

Similarly, the reversed situation is observed for the ^1J(P, CH_2) coupling constants due to the electron-donating character of the phenoxy groups. The chemical shift of the methylene carbon is influenced primarily by the

Table II

^{1}H NMR *data* ($\delta_{TMS} = 0$ ppm, J in Hz) *of compounds* **3a—f, 5a—h** *and* **6a—f** *in* $CDCl_3$ *or* DMSO-d_6 (**5b, d**) *solution at* 250 MHz

Compound	PCH_3, d[a]	PCH_2, d	ArH	CH_{1-3}/OH
3a	1.65 (13.2)	3.61 (8.2)	—	—
3b	1.93 (13.3)	367 and 3.76[b]	7.5—7.7, *m* (3H), 7.8—7.9, *m* (2H)[c]	—
3c	1.92 (13.3)	3.65 and 3.75[b]	7.55 and 7.78, 2×*m* (2×2H)[d]	—
3d	1.89 (13.3)	3.64 and 3.73[b]	7.03 and 7.74, 2×*m* (2×2H)[d]	3.86, *s*, 3H
3e	1.60 (12.9)	3.47 and 3.51[b]	~ 7.33, *s* (5H)	3.32, *d* (14.3), 2H
3f	—	4.05 (6.6)	7.45—7.6 *m* (6H), 7.75—7.9, *m* (4H)[c]	—
5a	1.69 (13.2)	4.32 (8.1)	7.5, *m* (1H)[e]~, 7.45—7.6, *m* (3H)	10.00, *s*, 1H
5b	1.55 (13.5)	4.48 (6.5)	7.25—7.75, *m* (3H)	3.90, *s*, 3H 9.90, *s*, 1H
5c	1.96 (13.5)	4.40 and 4.50[b]	7.2—7.6, *m* (7H), ~ 7.9, *m* (2H)[c]	9.95, *s*, 1H
5d	1.57 (13.7)	4.58 (7.2)	H-4′: 7.22, ~t, H-6′: ~ 7.53, ~*d*, H-5′: 7.74, ~t, H-3′: 7.95, ~*d*	—
5e	1.72 (13.3)	4.38 (7.9)	7.08, 8.22, 2×*m* (2×2H)[f]	—
5f	1.76 (13.3)	4.42 (8.4)	H-6′: 7.14, *d* (9.0), H-5′: 8.21, *dd*,	—
5g	1.68 (13.1)	4.32 (4.6)	H-3′: 8.30, *d* (2.6) 6.8—7.0 *m* (4H)	~4.5, *s*, (1H)[g]
5h	1.66 (13.3)	4.18 (8.0)	6.75, 6.81, 2×*m* (2×2H)[f]	~ 4.5, *s*, (1H)[g]
6a	1.52 (13.3)	4.10 (8.2)	H-6′: 6.72, ~*d*, H-2′, 4′: ~ 6.92, *m*, H-5′: 7.22, *m*	4.57, *s*, 2H ~ 3.2[g], ~ *s*, 1H 3.83, *s*, 3H
6b	1.67 (13.5)	4.27 (7.7)	6.8—7.0, *m* (3H)	4.61, *s*, 2H ~5.85[g], *s*, 1H
6c	1.72 (13.5)	4.14 and 4.21[b]	H-6′: 6.65, *m*, H-2′, 4′: ~ 6.85, *m*, H-5′: 7.10, *m* H-3″,4″,5″: ~ 7.4 *m*, H-2″,6″: ~ 7.7, *m*	4.50, *s*, 2H ~ 4.3, ~ s[b,g], 1H
6d	1.66 (13.3)	4.28 (7.6)	~ 6.75, ~ 6.88, 2×*m* (2×2H)	~ 3.7[g], ~ *s*, 2H
6e	1.62 (13.2)	4.16 (8.1)	~ 6.64, ~ 6.76, 2×*m* (2×2H)[f]	~ 3.5[g], ~ *s*, 2H
6f	1.68 (13.4)	4.20 (8.3)	H-5′: 6.57, *dd*, H-3′: 6.75, *d* (2.6), H-6′: 6.82, *d* (8.7)	~ 3.8[g], ~ *s*, 2H

[a] 3H (**3b, c, d, e, 5c** and **6c**) or 6H (**3a, 5a, b, d—h** and **6a, b, d—f**); [b] In case of **3b, c, d, e, 5c** and **6c** *A* and *B* part (2×*dd*) of an *ABX* multiplet $J(A, B)$, $J(A, X)$ and $J(B, X)$: 13.7, 8.4 and 7.0 (**3b**), 14, 9 and 8 (**3c**), 13.5, 8.2 and 6.7 (**3d**), 13.8, 8.2 and 7.9 (**3e**), 12.2, 8.5 and 6.8 (**5c**), 12.4, 8.6 and 7.1 Hz (**6c**); [c] *ortho*-protons of the phenyl ring; [d] *AA′BB′X* multiplet, $J(A, B) \cong 9$, $J(A, X) \cong 11$, $J(B, X) \cong 2$ Hz; [e] H-6′ signal; [f] *AA′BB′* multiplet, $J(A, B)$: 9.2 Hz; [g] broad signal; [h] overlapped by the PCH_2 multiplet.

attached heteroatom: the chloro-substitution is revealed by a strong shielding (upfield shift due to heavy atom effect [12a]), whereas the oxygen causes a significant downfield shift (decreasing the electronic excitation energies and the radii of p-orbitals); consequently, there are large differences in the methylene shifts of the **3**-type and **5**- or **6**-type compounds: 35—40 ppm for the former, and 66—69 ppm for the latter.

As a rule, the signals of the aromatic carbons, as well as those of the substituents in the ring are identifiable, without exception. The OCH_3 groups give lines at 55.4 (**3d**), 57.5 (**5b**) and 56.0 (**6b**); the carbonyl shifts of **5a—c**

Table III

^{13}C NMR *data* [$\delta_{TMS} = 0$ ppm, ^1J(P, C) in Hz] *for compounds* **3a—f, 5a—h** *and* **6a—f** *in* $CDCl_3$ *solution*[a] *at* 20.14 MHz[b]

Compound	δPCH_3	$^1J(P,CH_3)$	δPCH_2	$^1J(P,CH_2)$	C-1′	C-2′	C-6′	C-3′	C-5′	C-4′	Other lines
3a	13.1	71.9	37.3	67.6	—	—	—	—	—	—	—
3b	13.0	74.5	38.9	69.6		130.6		128.7		132.5	—
3c	13.2	75.0	38.9	70.4		132.3		129.3		139.6	—
3d	13.3	74.8	39.4	70.0	122.1	132.6		114.6		163.3	OCH_3: 55.4
3e	12.0	71.1	35.3	67.1	130.9	129.4		129.3		127.4	—
			35.8	65.6							
3f	—	—	37.5	71.7		130.9		128.2		132.0	—
5a	14.7	69.6	66.6	83.6	159.5	121.3	113.7	138.4	130.5	124.6	C=O: 191.3
5b	15.7	68.4	68.9	80.4	155.9	151.1	112.3	115.0	126.9	132.2	OCH_3: 57.5
											C=O: 192.8
5c	12.7	70.9	66.9	84.3	?[c]	130.2[c]		128.3[c]		131.9[c]	C=O: 191.0
					158.9	121.0	113.4	137.6	129.9	123.7	
5d	15.8	68.6	69.2	80.6	153.2	141.4	117.4	126.9	136.4	123.4	—
5e	14.1	69.7	66.5	82.1	163.1	114.4		125.4		142.1	—
5f	14.9	70.0	67.4	81.7	159.0	124.0	112.6	126.3	124.1	142.7	—
5g	15.8	67.8	69.8	81.3	149.0	148.8	117.1	118.0	124.1	120.8	—
5h	15.8	68.0	69.2	82.4	153.6		117.6[d]			153.9	—
6a	14.3	69.2	66.5	85.3	158.9	112.9	113.5	143.7	129.6	120.4	OCH_2: 64.5
6b	14.2	68.7	68.1	86.2	147.6	150.3	111.8	116.1	119.4	137.2	OCH_3: 56.0
											OCH_2: 64.4
6c	13.3	70.9	66.8	86.2	131.6[c]	130.3[c]		128.5[c]		132.1[c]	
					158.7	112.8	113.3	143.8	129.3	120.2	OCH_2: 64.1
6d	14.8	69.0	67.3	83.5	146.5	136.8	112.8	115.9	118.6	123.0	—
6e	13.6	68.9	66.3	85.0	151.0	114.9		115.4		140.6	—
6f	14.5	69.0	68.4	83.9	147.2	124.3	117.0	116.5	114.3	142.4	—

[a] In case of **5b, d, g, h** the solvent was DMSO-d_6; [b] at 62.89 MHz in case of **3d, 5a** and **6b**; [c] signals of the phenyl substituent R; [d] two overlapping lines.

are at 191.3, 192.8 and 191.0 ppm; the signals of the hydroxymethyl groups in **6a—c** are at 64.5, 64.4 and 64.1 ppm, respectively.

The C-1′ doublet of the p-substituted aromatic carbons (in **3b, c, f, 5c** and **6c**) is not observable. The only exception is **3d**, where the observed C-1′ doublet is at 122.1 ppm, split by 107.4 Hz. The ^2J(P, C-2′, 6′), the ^3J(P, C-3′, 5′) and the ^4J(P, C-4′) coupling constants are 8—10.5, 10—13 and 2—3 Hz for compounds **3b, c, d** and **f**, respectively. The $^3J(P—CH_2—O—C\text{-}1)$ coupling constants of compounds **5** and **6** are between 8 and 13 Hz. Splittings due to $^4J(P—CH_2—O—C—C\text{-}2', 6')$ interactions are not significant.

^{31}P NMR *spectra*

The ^{31}P chemical shifts (Table I) are influenced primarily by the nature of the substituents attached to the phosphorus atom: one aryl substitution causes shielding at about 7 ppm, in accordance with the literature. (The shifts of the molecules $OPPh_3$ and $OPEt_3$ are, e.g. 27 and 48 ppm [12b].)

The signals of the dimethyl-substituted derivatives (**3a**, **5a**, **b**, **d**—**h** and **6a**, **b**, **d**—**f**) appear in the interval 38—45 ppm, while for the aryl-methyl analogues **3b**—**d**, **5c**, **6c** this chemical shift is found between 31 and 33 ppm. In the spectrum of the diphenyl-substituted compound **3f** a further upfield shift of about 7 ppm was observed (the ^{31}P signal is at 26.1 ppm). Consequently, the influence of the substituents is additive.

It is interesting to note that the presence of a benzyl group gives rise to a downfield shift similar to that caused by a methyl substituent (cf. the shift of 42.2 ppm, measured for **3e**), while chloromethyl substitution has a similar effect on the ^{31}P shift to that of a phenyl ring (see the similar shifts of **3a**, on one hand, and of **5a**, **b**, **d**—**h** and **6a**, **b**, **d**—**f**, respectively, on the other), in spite of the isolating methylene group between the phosphorus and chlorine atoms. This fact may be explained by a $d\pi$—$p\pi$ interaction.

*

The authors gratefully acknowledge the financial and organizational support received from the UN organizations UNDP and UNIDO. Thanks are due to Hoechst AG for a gift of chloromethyldimethylphosphane oxide (**3a**), chloromethylmethylphosphinoyl chloride (**1**) and chloromethylphosphonic dichloride. We are indepted to Mr. Gy. Mányai for recording the IR spectra, to Mrs. J. Csákvári and Mr. A. Fürjes for skilled technical assistance.

Experimental

IR spectra were run in KBr pellets on a Bruker IFS-113v FT-IR spectrometer. ^{1}H and ^{13}C NMR spectra were recorded on Bruker WM-250 and WP-80-SY spectrometers at 250.13 MHz and 62.89 or 20.15 MHz, respectively (see Table III). ^{31}P NMR spectra were run at 101.2 MHz on the WM-250 spectrometer.

Typical parameters for ^{1}H measurements were as follows: internal reference: TMS lock signal: the ^{2}H resonance of the solvent; pulse width: 1 μs ($\sim$20° flip angle); acquisition time: 2.05 s for 16 K data points. Lorentzian exponential multiplication was used for signal-to-noise enhancement (line with 0.7 Hz).

Acquisition and data processing parameters for the ^{13}C spectra at 62.89 and 20.15 MHz, respectively: $\sim$25° flip angle; pulse widht: 7.5 and 3.5 μs; BB decoupling, with ca. 2.5 and 1 W power; memory size: 32 and 16 K for 16 and 5 kHz spectral width; exponential multiplications of line width 3.0 and 1.0 Hz; repetition rate 2 s, general number of scans 4—16 K; acquisition time: 0.5 and 1.65 s.

^{31}P NMR experiments were run in power gated mode, using 5 s delays between scans. During the acquisition BB decoupling of about 2.5 W was applied; 16 K data points for 25 kHz spectral width and pulse width of 24.8 μs (90° flip angle) were used. Typical number of scans: 16—64.

General procedure for the preparation of chloromethylphosphane oxides (3b—e)

Method A: 0.06 mol (8.82 g) of chloromethylphosphinoyl chloride (**1**) dissolved in 50 mL of dry ether was added to a stirred solution of the Grignard-reagent prepared from 0.06 mol of magnesium at ambient temperature. (During the preparation of benzyl-magnesium bromide, the reaction temperature was kept below 10 °C to avoid side reactions.) Stirring was continued at reflux temperature for 2 h more. After cooling, the etheral layer was decanted and treated with 50 mL saturated NH_4Cl solution. The crude product was isolated by extracting this mixture with 3×60 mL chloroform. The combined organic solution was dried over Na_2SO_4, filtered, and concentrated in vacuum. The crude product was recrystallized from *n*-hexane (Table IV).

Table IV

Physical and analytical data of compounds **3b—f, 5a—h** *and* **6a—f**

Compound	Yield (%)	Melting point (°C)	Formula	Molecular weight	Elemental analysis (%)			Calculated found	
					C	H	N	P	Cl
3b[a]	37	102—104	$C_8H_{10}ClOP$	188.57	50.95	5.35	—	16.43	18.80
					51.33	5.09		16.86	18.65
3c[a]	32	103—104	$C_8H_9Cl_2OP$	223.04	43.08	4.07	—	13.89	31.79
					43.29	4.40		13.48	31.72
3d[a]	30	94—95	$C_9H_{12}ClO_2P$	218.62	49.44	5.53	—	14.17	16.22
					49.72	5.35		14.41	15.88
3e[a]	26	90—93	$C_9H_{12}ClOP$	202.62	53.35	5.96	—	15.29	17.50
					53.27	5.58		14.90	17.87
3f[b]	24	138—139	$C_{13}H_{12}ClOP$	250.66	62.29	4.83	—	12.36	14.15
					62.48	5.04		12.80	14.33
5a	89	88—90	$C_{10}H_{13}O_3P$	212.18	56.60	6.18	—	14.60	—
					56.28	6.05		14.37	
5b	91	115—117	$C_{11}H_{15}O_4P$	242.21	54.55	6.24	—	12.79	—
					54.95	6.38		13.08	
5c	87	75—77	$C_{15}H_{15}O_3P$	274.25	65.69	5.51	—	11.30	—
					65.80	5.85		11.77	
5d	60	148—153	$C_9H_{12}NO_4P$	229.17	47.17	5.28	6.11	13.52	—
					47.05	5.28	6.02	12.83	
5e	87	152—156	$C_9H_{12}NO_4P$	229.17	47.17	5.28	6.11	13.52	—
					47.37	4.91	5.81	12.93	
5f	67	154—158	$C_9H_{11}ClNO_4P$	263.62	41.00	4.21	5.31	11.75	13.45
					40.71	4.43	5.02	11.64	13.32
5g	75	185—187	$C_9H_{13}O_3P$	200.17	54.00	6.55	—	15.47	—
					53.46	6.76		14.89	
5h	77	114—116	$C_9H_{13}O_3P$	200.17	54.00	6.55	—	15.47	—
					54.34	6.30		15.86	
6a	85	oil[c]	$C_{10}H_{15}O_3P$	214.20	56.07	7.06	—	14.46	—
					56.69	7.34		15.10	
6b	67	103	$C_{11}H_{17}O_4P$	244.22	54.09	7.02	—	12.68	—
					53.76	7.04		12.32	
6c	73	oil[d]	$C_{15}H_{17}O_3P$	276.26	65.21	6.20	—	11.21	—
					64.82	6.51		10.83	
6d	38	148	$C_9H_{14}NO_2P$	199.19	54.27	7.09	7.09	15.55	—
					53.83	6.96	6.76	15.95	
6e	88	113—115	$C_9H_{14}NO_2P$	199.19	54.27	7.09	7.03	15.55	—
					53.64	6.90	6.97	15.15	
6f	47	79—82	$C_9H_{13}ClNO_2P$	233.63	46.27	5.61	6.00	13.26	15.18
					46.01	5.33	5.80	12.82	15.39

[a] Method *A*;
[b] Method *B*;
[c] Viscous oil which crystallizes at 0 °C;
[d] $n_D^{25} = 1.5862$.

Chloromethyldiphenylphosphane oxide (3f)

Method B: Chloromethylphosphonic dichloride in 30 mL dry ether was added at room temperature to the phenylmagnesium bromide solution prepared from 0.06 mol (1.46 g) of magnesium and 0.06 mol (9.4 g) of bromobenzene in 60 mL dry ether. After 2 h at reflux temperature, the reaction mixture was worked up as above to afford **3f** in 24% yield (see Table IV).

General procedure for the preparation of (phosphinoylmethoxy)-bezaldehydes (5a—c)

A mixture of 0.11 mol of the appropriate chloromethylphosphane oxide **3a** or **3b**, 0.10 mol of hydroxybenzaldehyde **4a—c**, and 0.11 mol of finely powdered K_2CO_3 was vigorously stirred at 120—125 °C for 3 h. After cooling, the product was dissolved in 100 mL of chloroform, the inorganic salts were separated by filtration and the filtrate was washed successively with 10% NaOH solution, water and brine (20 mL each). The organic phase was dried over Na_2SO_4, filtered, treated with charcoal, and evaporated to dryness. The crude product was purified by column chromatography using chloroform-methanol (9 : 1) solvent mixture as eluent (Table IV).

General procedure for the preparation of (phosphinoylmethoxy)benzyl alcohols (6a—c)

To a stirred solution of 0.08 mol benzaldehyde derivative **5a—c** in 100 mL ethanol was added 0.05 mol of $NaBH_4$ in small portions at ambient temperature. The reaction mixture, after stirring for 4 h, was carefully acidified with acetic acid. After evaporation of the solvent, the organic residue was dissolved in 60 mL of chloroform, the inorganic salts were removed by filtration, the filtrate was treated with charcoal, and the resulting clear solution was evaporated to dryness to afford the crude product **6a—c**, which was purified either by recrystallization from benzene or by column chromatography using chloroform-methanol (9 : 1) solvent mixture as eluent (Table IV).

General procedure for the preparation of (phosphinoylmethoxy)-nitrobenzenes (5d—f)

A mixture of 0.06 mol of chloromethylphosphane oxide **3a**, 0.06 mol of the appropriate nitrophenol **4d—f**, and 0.07 mol of finely powdered K_2CO_3 was stirred at 150—160 °C for 7 h. After cooling, the product was dissolved in 60 mL of chloroform, the inorganic salts were removed by filtration. The filtrate was evaporated to dryness and the crude product was recrystallized from benzene to give the pure nitro derivatives **5d—f** (Table IV).

General procedure for the preparation of (phosphinoylmethoxy)-anilines (6d—f)

A mixture consisting of 0.051 mol of the appropriate nitro compound **5d—f**, 0.126 mol $Na_2S.9H_2O$, and 4.5 mL of water was stirred at 100—110 °C for 7 h. The cold reaction mixture was then acidified with 10% HCl solution (pH = 1) and left at ambient temperature for 30 min. After filtration from the precipitate, the pH of the filtrate was adjusted to 7.5 with 10% NaOH solution. The resulting solution was extracted with three 100 mL portions of chloroform. The organic extract was dried over Na_2SO_4 and, after evaporation of the solvent, the crude product was purified by repeated rubbing with ether (Table IV).

General procedure for the preparation of (phosphinoylmethoxy)-phenols (5g and 5h)

A mixture of 0.05 mol of the diphenol **4g** or **4h**, 0.05 mol of the chloromethylphosphane oxide **3a**, and 0.05 mol of finely powdered K_2CO_3 was vigorously stirred for 3 h at 120—125 °C. The mixture was cooled to 80 °C, 50 mL of dry ethanol was added, and the suspension was refluxed for 15 min. After cooling, the inorganic salts were filtered off, the filtrate was concentrated and the crude product was purified by column chromatography using ethyl acetate as eluent to obtain the pure monoethers **5g** and **5h** (Table IV).

REFERENCES

[1] Weissermel, K., Kleiner, H.-J., Finke, M., Felcht, U.-H.: Angew. Chem., **93,** 256 (1981); Angew. Chem., Int. Ed. Engl., **20,** 223 (1981)

[2] Hansch, C., Leo, A., Unger, S. H., Ki Hwan Kim, Nikaitani, D., Lien, E. J.: J. Med. Chem., **16,** 1207 (1973)

[3] Söder, A., Weber, R.-O., von Boksa, I., Bollmann, V.: Dtsch. Bundes-Pat., 2, 411, 406 (1974), Farbwerke Hoechst AG; [Chem. Abstr., **84,** 43582 (1967)]; Söder, A., Weber,

R.-O., von Boksa, I., Bollmann, V.: Dtsch. Bundes-Pat., 2,428,625 (1974), Farbwerke Hoechst AG; [Chem. Abstr. **84,** 135272 (1976)]
[4] Söder, A., Perrey, K.: Dtsch. Bundes-Pat., 2, 505, 415 (1975), Farbwerke Hoechst AG; [Chem. Abstr., **85,** 192887 (1976)
[5] Söder, A., Perrey, K.: Polish J. Chem., **54,** 1305 (1980)
[6] Glamkowski, E. J., Strupczewski, J. T., Wolf, E. H.: D.O.S. 2, 322, 851 (1972), Farbwerke Hoechst AG; [Chem. Abstr., **80,** 83240 (1974)]
[7] Wolf, E., Kohl, H., Härtfelder, G.: Dtsch. Bundes-Pat., 2, 022, 503 (1970), Farbwerke Hoechst AG; [Chem. Abstr. **76,** 72570 (1972)]
[8] Price, C. C., Stacy, G. W.: Org. Synth. Coll. Vol. **3,** p. 86., John Wiley and Sons, New York 1955
[9] Holly, S., Sohár, P.: Theoretical and Technical Introduction to the Series: Absorption Spectra in the Infrared Region (L. Láng and W. H. Prichard, Ed's.), p. 131., Akadémiai Kiadó, Budapest 1975
[10] Mavel, C. F. G.: NMR Studies of Phosphorus Compounds (1965—1969). In the series "Annual Reports on NMR Spectroscopy" (E. F. Moon, Ed.), Vol. **5***B*, p. 70., Academic Press, London—New York 1973
[11] Albright, T. A.: Org. Magn. Reson., **8,** 489 (1976)
[12] Sohár, P.: Nuclear Magnetic Resonance Spectroscopy. (a) Vol. **2,** pp. 156. and 158., (b) Vol. **2,** p. 268. CRC Press, Boca Raton, Florida 1983

Acta Chimica Hungarica 123 (3—4), pp. 155—160 (1986)

SYNTHESIS OF VINCA ALKALOIDS AND RELATED COMPOUNDS, XXIX*

STEREOCHEMISTRY OF 1,1-DISUBSTITUTED-INDOLO[2,3-*a*]QUINOLIZIDINES

András DANCSÓ[1], György KALAUS[2], Mária KAJTÁR-PEREDY[1], Lajos SZABÓ[2] and Csaba SZÁNTAY[1, 2]**

([1]Central Research Institute for Chemistry, Hungarian Academy of Sciences, H-1525 Budapest, P.O. Box 17, and [2]Institute of Organic Chemistry, Technical University, H-1521 Budapest, Gellért tér 4.)

Received November 29, 1985
Accepted for publication February 27, 1986

Some 1-benzyl-1-ethyl-indolo[2,3-*a*]quinolizidines (**1a**, **1b**, **2a**, **2b**, **4**) were synthetized and their stereochemistry established. The C/D ring annelation in compounds **2a** and **2b** proved to be *trans*.

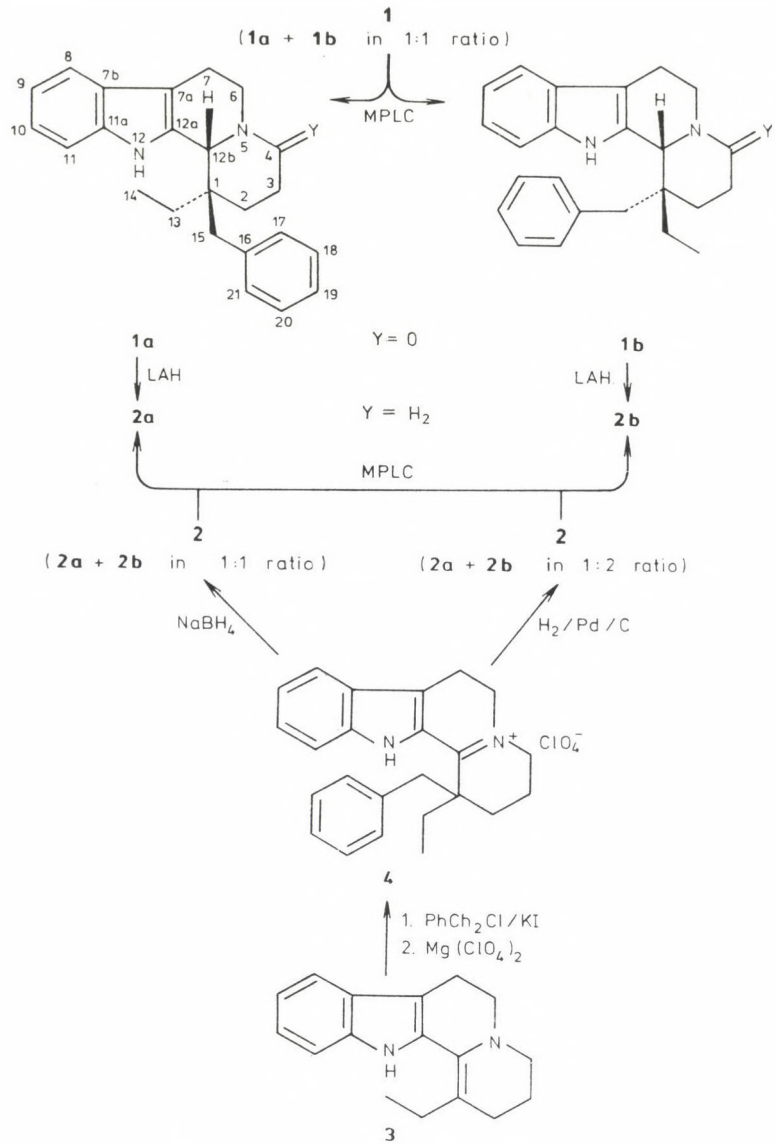
A few years ago the synthesis of the diastereomeric mixture of **1** was reported [2]. Recently **1** was separated by medium pressure liquid chromatography (MPLC) into two components, **1a** and **1b** (Scheme 1).

The stereostructures are suggested on the basis of spectroscopical evidences: i) The chemical shifts in the ^{13}C-NMR spectrum of the *axial* methylene groups are significantly less then of the *equatorial* ones [3] (see Table II). ii) The chemical shift in the ^{1}H-NMR spectrum of the methyl group of **1a** is 0.80 ppm, while this value for **1b** is 1.06 ppm. The difference is due to that the ethyl moiety in **1a** is *axial* and during its rotation the methyl group immerses into the shielding zone of the anisotropic magnetic field of the indole ring (Fig. 1). In **1b** the methyl group is far from the aromatic current.

The two lactams **1a** and **1b** were reduced to the amines **2a** and **2b**, respectively.

There is another, more convenient route to compounds **2**: the direct benzylation of Wenkert's enamine **3** [4] to the iminium salt **4**, followed by reduction. This latter step, when using sodium borohydride as reducing agent, gave rise to **2a** and **2b** in 1 : 1 ratio. On the other hand, catalytic reduction resulted in the mixture of the same compounds in 1 : 2 ratio. The observed stereoselectivity may be explained by the steric difference of the two substituents at position 1. The benzyl group is the bulkier one, therefore, the C=N

* For part XXVIII, see Ref. [1].
** To whom correspondence should be addressed.



Scheme 1

moiety is adsorbed more readily with its opposite side on the surface of the catalyst, and the hydrogen atom becomes attached to the 12b carbon atom in *trans* position with respect to the benzyl group.

The two quinolizidines **2a** and **2b** showed Bohlmann bands in their IR spectra and characteristic C4, C6, C7, C12b chemical shifts in their ^{13}C-NMR spectra, i.e. the C/D ring annelation in these compounds proved to be *trans*.

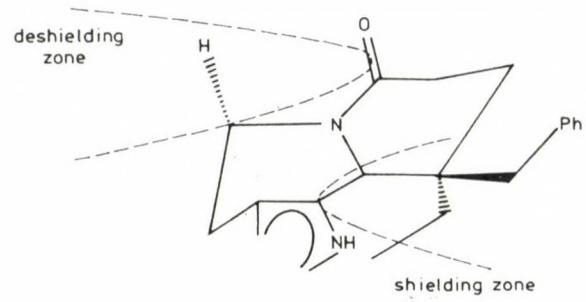


Fig. 1

Experimental

M.p.'s are uncorrected. The IR spectra were recorded with a Karl Zeiss SPECORD 75 IR instrument. ^{1}H- and ^{13}C-NMR spectra were obtained on a Varian XL-100 spectrometer at 100.1 and 25.16 MHz, respectively. Mass spectra were taken on an AEI MS 902 instrument.

Separation of 1a and 1b

A crystalline mixture of **1a** and **1b** (**1**; 0.46 g) [2] was chromatographed on a medium pressure column in two steps. The parameters were the following: column length: 0.3 m, diameter: 0.04 m, pressure: 0.2 MPa, adsorbent: E. Merck Art. 7749 silica gel, eluent: toluene-ethyl acetate 1 : 1. This procedure yielded 0.2 g each of the two products, which were recrystallized from ethyl acetate (11 mL).

Table I

MS *spectra of compounds* **1a**, **1b**, **2a**, *and* **2b**

m/z	%				Remarks	
	1a	**1b**	**2a**	**2b**	**1a** and **1b**	**2a** and **2b**
358	100	30			*M*	
344			90	90		*M*
343			100	100		*M* — 1
328			10	10		*M* — Me
315			5	7		*M* — Et
311			10	3		
267	4	3	5	15	*M* — Bz	*M* — Ph
266	4	3			*M* — 92	
256	3	2				
253			10	20		*M* — Bz
251	4	2				
212	50	50				
197			30	30		
185			15	25		
170	100	100	35	60	tetrahydro-β-carboline fragment	
169	50	60	25	50		
156	4	6				
143	10	10				
91	10	15	10	50	benzyl	

Table II

^{13}C—NMR *spectra of compounds* **1a**, **1b**, **2a**, *and* **2b**.
Chemical shifts, δ, in ppm, relative to TMS

Carbon	1a	1b	2a	2b
1	41.11	40.74	41.21s	40.72
2	27.12	29.47	34.06	31.10
3	28.52	30.12	25.05[c]	29.71
4	169.62	170.06	56.50	57.21
6	39.39	40.51	54.23	54.35
7	21.05	21.16	21.87[c]	21.96
7a	111.91	112.57	111.75	112.12
7b	126.08	126.35	127.7	128.80
8	117.46	117.71	117.86	117.94
9	121.39	121.64	121.44	121.52
10	118.92	119.20	119.32	119.37
11	111.78	111.74	110.69	110.73
11a	131.27	130.95	130.63[a]	130.91[a]
12a	136.75[a]	137.06[a]	137.74	139.25
12b	60.84	60.33	67.76d	66.63
13	24.30	26.42	21.87[c]	22.40
14	7.26	8.41	7.90	7.99
15	41.94	37.95	43.87t	38.84
16	136.86[a]	137.45[a]	130.80[a]	130.80[a]
17 and 21	128.02[b]	127.84[b]	128.11[b]	127.62[b]
18 and 20	131.12[b]	130.53[b]	130.92[b]	130.72[b]
19	126.56	126.13	126.41	125.66

[a] The assignment is interchangeble.
[b] Equivalent carbons, identic lines, double intensity.
[c] Coincidental lines, double intensity.

(±)-1β-Benzyl-1α-ethyl-1,2,3,4,6,7,12,12bβ-octahydroindolo[2,3-*a*]quinolizin-4-one (1a)

First m.p. 230 °C, second m.p. 244 °C.
IR(KBr): 3352 (indole NH), 1620 (lactam) cm^{-1}.
MS (70 eV): see Table I.
^1H-NMR($CDCl_3$ + DMSO-d_6,δ): 9.59 (1H, bs, indole NH); 6.9—7.6 (4H, m, aromatic CH protons); 7.32 (5H, s, Ph); 4.87—5.18 (1H, m, 6αH); 4.85 (1H, s 12bβH); 3.27 (1H, d, $|J| = 14$ Hz) and 3.07 (1H, d, $|J| = 14$ Hz) (benzyl methyelene); 2.6—2.9 (3H, m, 6βH + 7-H_2); 2.30 (2H, t, $J = 6.5$ Hz, 3-H_2); 1.66 (2H, t, $J = 6.5$ Hz, 2-H_2); 1.34 (2H, q, $J = 7.3$ Hz, ethyl methylene); 0.80 (3H, t, $J = 7.3$ Hz, Me) ppm.
^{13}C-NMR($CDCl_3$ + DMSO-d_6): see Table II.

(±)-1α-Benzyl-1β-ethyl-1,2,3,4,6,7,12,12bβ-octahydroindolo[2,3-*a*]quinolizin-4-one (1b)

First m.p. 237 °C, second m.p. 257—258 °C.
IR(KBr): 3358 (indole NH), 1613 (lactam) cm^{-1}.
MS(70 eV): see Table I.
^1H-NMR($CDCl_3$, δ): 8.00 (1H, bs, indole NH); 6.9—7.6 (9H, m, aromatic CH protons); 5.0—5.4 (1H, m, 6αH); 4.95 (1H, s, 12bβH); 1.4—3.1 (11H, m); 1.06 (3H, t, $J = 7.4$ Hz, Me) ppm.
^{13}C-NMR($CDCl_3$ + DMSO-d_6): see Table II.

(±)-1β-Benzyl-1α-ethyl-1,2,3,4,6,7,12,12bβ-octahydroindolo[2,3-*a*]quinolizine (2a)

Compound **1a** (80 mg, 0.223 mmol) was refluxed with lithium aluminium hydride (20 mg) in abs. terahydrofuran (10 mL) for 4 h. The mixture was cooled and a 20% solution of potassium sodium tartrate in water [5] was added dropwise until the mixture became again

homogeneous. The solution was extracted with dichloromethane (4×50 mL), the extract was washed with brine (100 mL) and dried over sodium sulfate. The solvents were removed in vacuum and the crude product was purified by preparative TLC to give **2a** (60mg 75%) as an oil, which was crystallized as the hydrochloride salt, m.p. 203 °C.

IR(10% solution in $CHCl_3$): 3436 (indole NH), 2752 and 2800 (Bohlmann bands) cm^{-1}.

MS(70 eV): see Table I.

^{1}H-NMR($CDCl_3$, δ): 7.97 (1H, bs, indole NH); 6.5—7.7 (9H, m, aromatic CH protons); 2.1—3.5 (9H, m); 0.8—2.1 (6H, m); 0.74 (3H, t, J = 7.4 Hz, Me) ppm.

^{13}C-NMR($CDCl_3$): see Table II.

(±)-1α-Benzyl-1β-ethyl-1,2,3,4,6,7,12,12bβ-octahydroindolo[2,3-*a*]quinolizine (2b)

It was prepared from **1b** in the same way, and crystallized as the hydrochloride salt, m.p. 216 °C.

IR(10% solution in $CHCl_3$): 3431 (indole NH), 2749 and 2802 (Bohlmann bands) cm^{-1}.

MS(70 eV): see Table I.

^{1}H-NMR($CDCl_3$, δ): 7.78 (1H, bs, indole NH); 6.9—7.6 (9H, m, aromatic CH protons); 3.47 (1H, s, 12bβH); 3.36 (1H, d, $|J|$ = 14 Hz) and 2.30 (1H, d, $|J|$ = 14 Hz) (benzyl methylene); 1.3—3.2 (12H, m); 1.04 (3H, t, J = 7.5 Hz, Me) ppm.

^{13}C-NMR($CDCl_3$): see Table II.

1-Benzyl-1-ethyl-1,2,3,4,6,7-hexahydro-12*H*-indolo-[2,3-*a*]quinolizin-5-ium-perchlorate(4)

1-Ethyl-1,2,3,4,6,7-hexahydro-12*H*-indolo[2,3-*a*]quinolizin-5-ium perchlorate (10 g) [3] was distributed between dichloromethane (100 mL) and 10% sodium hydroxide solution (100 mL). The organic phase was filtered through potassium carbonate, the solvent was removed in vacuum and the resulting Wenkert's enamine **3** was refluxed with benzyl chloride (5 mL) and potassium iodide (0.5 g) in dry acetonitrile (100 mL) for 5 days under an inert atmosphere. The mixture was cooled, filtered and a solution of anhydrous magnesium perchlorate in acetonitrile (3.16 g in 30 mL) was added. The mixture was then filtered, the solvent evaporated in vacuum and the residue crystallized from methanol to give yellow crystalls of **4** (1.56 g; 12.5%), m.p. 215°C.

IR(KBr): 3364 (indole NH), 1614 (C=N), 1585 (Ph), 1092 and 1054 (ClO_4^-) cm^{-1}.

MS(70 eV, m/z(%)): 341(10) (*M*), 340(20), 313(15), 312(35) (*M*-Et), 311(**100**), 251(20), 250(20) (*M*-Bz), 249(95), 221(10), 220(10), 219(20), 206(20), 197(15), 171(10), 170(20), 169(16) (dihydro-β-carboline fragment), 91(20) (Bz).

^{1}H-NMR($CDCl_3$ + DMSO-d_6,δ): 10.8 (1H, bs, indole NH); 6.9—7.8 (9H, m, aromatic CH protons); 3.0—4.2 (6H, m); 3.56 (1H, d, $|J|$ = 14 Hz) and 3.16 (1H, d, $|J|$ = 14 Hz) (benzyl methylene); 1.6—2.9 (6H, m); 0.81 (3H, t, J = 7.2 Hz, Me) ppm.

$C_{24}H_{27}ClN_2O_4$ (442.95). Calcd. C 65.08; H 6.14; N 6.32. Found C 65.13; H 6.21; N 6.18%.

Reduction of 4 with sodium borohydride

Compound **4** (1.56 g; 3.52 mmol) was dissolved in methanol (100 mL) and treated with sodium borohydride (0.2 g) for 1 h. The methanol was removed in vacuum, the residue dissolved in dichloromethane (100 mL), washed with saturated sodium hydrogen carbonate solution and dried over magnesium sulfate, then filtered. The filtrate was saturated with hydrogen chloride gas, the solvent removed in vacuum, and the product crystallized from methanol to give a white crystalline mixture of the hydrochloride salts of **2a** and **2b** (in 1 : 1 ratio; 0.93 g; 69%, m.p. 189—192 °C.

$C_{24}H_{28}N_2$. HCl (380.97). Calcd. C 75.67; H 7.67; N 7.35. Found C 75.58; H 7.77; N 7.17%.

Catalytic reduction of 4

10% Palladium-on-charcoal catalyst (about 50 mg) was prehydrogenated in some methanol, then a solution of the perchlorate salt **4** in methanol (50 mg; $1.13 \cdot 10^{-4}$ mol in 25 mL) was added. Hydrogenation was carried out at room temperature and atmospheric pressure. After the absorption of the calculated amount of hydrogen (2.7 mL) (about 15 min) the catalyst

was filtered off and the methanol was removed in vacuum. The residue was distributed between chloroform and 10% sodium hydroxide solution, the organic phase was dried and the chloroform removed in vacuum to give a mixture of **2a** and **2b** (in 1 : 2 ratio; 35 mg; 89%).

Separation of 2a and 2b

A mixture of **2a** and **2b** (0.5 g) was chromatographed in two steps under the following conditions: column length: 0.5 m, diameter: 0.056 m, adsorbent: Reanal Kieselgelt 60 GF_{254} No 0772, $\Delta p = 0.3$ MPa, eluent: toluene-ethyl acetate-chloroform 7 : 2 : 1. The retention of **2a** was the greater. From a 1 : 1 mixture 0.2 g of **2a** and **2b** each was isolated.

*

The authors wish to express their thanks to Dr J. Tamás for the MS measurments, and to the Chemical Works of Gedeon Richter Ltd. for financial support of this research.

REFERENCES

[1] Kardos-Balogh, Zs., Sóti, F., Incze, M., Kajtár-Peredy, M., Szántay, Cs.: Heterocycles, **24,** 63 (1986)
[2] Kalaus, Gy., Győry, P., Szabó, L., Szántay, Cs.: J. Org. Chem., **43,** 5017 (1978)
[3] Kalaus, Gy., Győry, P., Kajtár-Peredy, M., Radics, L., Szabó, L., Szántay, Cs.: Chem. Ber., **114,** 1476 (1981)
[4] Wenkert, E., Wickberg, B.: J. Am. Chem. Soc., **87,** 1580 (1965)
[5] Dreiding, A. S., Hartmann, J. A.: J. Am. Chem. Soc., **75,** 939 (1953)

CONFERENCES OF THE HUNGARIAN PHARMACEUTICAL SOCIETY IN 1987

VIth Conference on Hospital Pharmacy
New ways of drug control and preparation
26—28 March, Zalaegerszeg
In Hungarian, German and English

VIth National Conference on the History of Pharmacy
April, Kecskemét
In Hungarian

XIXth Colloquium of Drug Analysis
8—10 April, Sárospatak
Drug Analysis
In Hungarian

XXIInd "Rozsnyay Mátyás" Memorial Competition for Young Pharmacists
May, Zalaegerszeg
In Hungarian

IVth National Colloquium of Young Pharmacists
Current problems of pharmacy and professional policy
27—28 August, Kaposvár
In Hungarian

Conference on Social Pharmacy
Current problems of pharmaceutical organization
20—23 September, Pécs
In Hungarian

Congressus Pharmaceutics VIII
Main topic: natural products
October, 1988, Budapest
In Hungarian, German and English

All inquiries are to be addressed to:

Secretariat of the Hungarian Pharmaceutical Society
(Magyar Gyógyszerészeti Társaság Titkársága)
H-1092 Budapest, Hőgyes u. 4.
Tel: 36-1-181-573

PRINTED IN HUNGARY

Akadémiai Kiadó és Nyomda, Budapest

Text

The text of the paper should be concise. The description of new compounds (in the Experimental) must include the complete analytical data. Special attention must be paid to structural formulas given within the text. Complicated (non-linear) formulas should be drawn on separate sheets of paper and their position in the text should be clearly marked. The numbering of formulas and equations (in parentheses on the right-hand side) is only needed if they are referred to in the text. Units should conform to the International System of Units (SI). In nomenclature the rules of the I.U.P.A.C. are accepted as standard. Symbols for physical quantities are printed in italic type and should, therefore, be underlined in the manuscript.

References

References should be numbered in order of appearance in the text (where the reference number appears in brackets) and listed at the end of the paper. The reference list, too, should by typed double-spaced. Journal titles are to be abbreviated as defined by the Chemical Abstracts Service Source Index.

Examples:

[1] Brossi, A., Lindlar, H., Walter, M., Schneider, O.: Helv. Chim. Acta, **41**, 119 (1958)
[2] Parr, R. G.: Quantum Theory of Molecular Electronic Structure, Benjamin, New York 1964
[3] Warshel, A.: in Modern Theoretical Chemistry, Vol. 7, Part A (Ed. G. A. Segal), Plenum Press, New York 1977

Tables

Each table should be given a Roman number and a brief informative title. Structural formulas should not be used in column headings or in the body of tables.

Figures

Figures should be numbered consecutively with Arabic numerals. Their approximate place should be indicated in the text on the margin. All figures must be identified on the back by the author's name and the figure number in pencil. Standard symbols (such as circles, triangles, squares) are to be used on line-drawings to denote the points determined experimentally. Line-drawings must not contain structural formulas and comments. Spectra or relevant segments thereof, chromatograms, and X-ray diffraction patterns will be reproduced only if concise numerical summaries are inadequate to replace them. Drawings and graphs should be prepared in black ink on good-quality white or tracing paper. Photographs should be submitted on glossy paper as high-contrast copies. Xerox or similar copies are not suitable for reproduction, but may be used for duplicate copies.

Redrawn illustrations will be sent to the authors for checking. No corrections of figures will, therefore, be accepted in the proofs.

Submission of manuscript

After having completed the corrections suggested by the referees and editors, the final manuscript should be submitted in duplicate, in a form ready for publication. If the corrected manuscript is not returned to the editors *within six weeks*, the intended publication of the paper will be regarded as withdrawn by the authors.

Page charge will not be assessed for the publication, however, authors from overseas countries must contribute to the postage of correspondence by sending, together with the manuscript, international postal coupons to the value of U.S. $ 10.—

Proofs and reprints

A set of proofs will be sent to the submitting author. The proofs must be returned within 48 hours of receipt. Late return may cause a delay in the publication of the paper. 100 reprints will be supplied to the authors free of charge.

Periodicals of the Hungarian Academy of Sciences are obtainable at the following addresses:

AUSTRALIA
C.B.D. LIBRARY AND SUBSCRIPTION SERVICE
Box 4886, G.P.O., *Sydney N.S.W. 2001*
COSMOS BOOKSHOP, 145 Ackland Street
St. Kilda (Melbourne), Victoria 3182

AUSTRIA
GLOBUS, Höchstädtplatz 3, *1206 Wien XX*

BELGIUM
OFFICE INTERNATIONAL DE LIBRAIRIE
30 Avenue Marnix, *1050 Bruxelles*
LIBRAIRIE DU MONDE ENTIER
162 rue du Midi, *1000 Bruxelles*

BULGARIA
HEMUS, Bulvar Ruszki 6, *Sofia*

CANADA
PANNONIA BOOKS, P.O. Box 1017
Postal Station "B", *Toronto, Ontario M5T 2T8*

CHINA
CNPICOR, Periodical Department, P.O. Box 50
Peking

CZECHOSLOVAKIA
MAD'ARSKÁ KULTURA, Národní třida 22
115 66 Praha
PNS DOVOZ TISKU, Vinohradská 46, *Praha 2*
PNS DOVOZ TLAČE, *Bratislava 2*

DENMARK
EJNAR MUNKSGAARD, Norregade 6
1165 Copenhagen K

FEDERAL REPUBLIC OF GERMANY
KUNST UND WISSEN ERICH BIEBER
Postfach 46, *7000 Stuttgart 1*

FINLAND
AKATEEMINEN KIRJAKAUPPA, P.O. Box 128
SF-00101 Helsinki 10

FRANCE
DAWSON-FRANCE S. A., B. P. 40, *91121 Palaiseau*
EUROPÉRIODIQUES S. A., 31 Avenue de Versailles, *78170 La Celle St. Cloud*
OFFICE INTERNATIONAL DE DOCUMENTATION ET LIBRAIRIE, 48 rue Gay-Lussac
75240 Paris Cedex 05

GERMAN DEMOCRATIC REPUBLIC
HAUS DER UNGARISCHEN KULTUR
Karl Liebknecht-Straße 9, *DDR-102 Berlin*
DEUTSCHE POST ZEITUNGSVERTRIEBSAMT
Sraße der Pariser Kommüne 3–4, *DDR-104 Berlin*

GREAT BRITAIN
BLACKWELL'S PERIODICALS DIVISION
Hythe Bridge Street, *Oxford OX1 2ET*
BUMPUS, HALDANE AND MAXWELL LTD.
Cowper Works, *Olney, Bucks MK46 4BN*
COLLET'S HOLDINGS LTD., Denington Estate
Wellingborough, Northants NN8 2QT
WM. DAWSON AND SONS LTD., Cannon House
Folkstone, Kent CT19 5EE
H. K. LEWIS AND CO., 136 Gower Street
London WC1E 6BS

GREECE
KOSTARAKIS BROTHERS INTERNATIONAL BOOKSELLERS, 2 Hippokratous Street, *Athens-143*

HOLLAND
MEULENHOFF-BRUNA B.V., Beulingstraat 2,
Amsterdam
MARTINUS NIJHOFF B.V.
Lange Voorhout 9–11, *Den Haag*

SWETS SUBSCRIPTION SERVICE
347b Heereweg, *Lisse*

INDIA
ALLIED PUBLISHING PRIVATE LTD., 13/14 Asaf Ali Road, *New Delhi 110001*
150 B-6 Mount Road, *Madras 600002*
INTERNATIONAL BOOK HOUSE PVT. LTD.
Madame Cama Road, *Bombay 400039*
THE STATE TRADING CORPORATION OF INDIA LTD., Books Import Division, Chandralok 36 Janpath, *New Delhi 110001*

ITALY
INTERSCIENTIA, Via Mazzé 28, *10149 Torino*
LIBRERIA COMMISSIONARIA SANSONI, Via Lamarmora 45, *50121 Firenze*
SANTO VANASIA, Via M. Macchi 58
20124 Milano
D. E. A., Via Lima 28, *00198 Roma*

JAPAN
KINOKUNIYA BOOK-STORE CO. LTD.
17-7 Shinjuku 3 chome, Shinjuku-ku, *Tokyo 160-91*
MARUZEN COMPANY LTD., Book Department, P.O. Box 5050 Tokyo International, *Tokyo 100-31*
NAUKA LTD. IMPORT DEPARTMENT
2-30-19 Minami Ikebukuro, Toshima-ku, *Tokyo 171*

KOREA
CHULPANMUL, *Phenjan*

NORWAY
TANUM-TIDSKRIFT-SENTRALEN A.S., Karl Johansgatan 41–43, *1000 Oslo*

POLAND
WĘGIERSKI INSTYTUT KULTURY, Marszałkowska 80, *00-517 Warszawa*
CKP I W, ul. Towarowa 28, *00-958 Warszawa*

ROUMANIA
D. E. P., *Bucureşti*
ILEXIM, Calea Grivitei 64–66, *Bucureşti*

SOVIET UNION
SOJUZPECHAT — IMPORT, *Moscow*
and the post offices in each town
MEZHDUNARODNAYA KNIGA, *Moscow G-200*

SPAIN
DIAZ DE SANTOS, Lagasca 95, *Madrid 6*

SWEDEN
ALMQVIST AND WIKSELL, Gamla Brogatan 26
101 20 Stockholm
GUMPERTS UNIVERSITETSBOKHANDEL AB
Box 346, *401 25 Göteborg 1*

SWITZERLAND
KARGER LIBRI AG, Petersgraben 31, *4011 Basel*

USA
EBSCO SUBSCRIPTION SERVICES
P.O. Box 1943, *Birmingham, Alabama 35201*
F. W. FAXON COMPANY, INC.
15 Southwest Park, *Westwood Mass. 02090*
THE MOORE-COTTRELL SUBSCRIPTION AGENCIES, *North Cohocton, N. Y. 14868*
READ-MORE PUBLICATIONS, INC.
140 Cedar Street, *New York, N. Y. 10006*
STECHERT-MACMILLAN, INC.
7250 Westfield Avenue, *Pennsauken N. J. 08110*

YUGOSLAVIA
JUGOSLOVENSKA KNJIGA, Terazije 27, *Beograd*
FORUM, Vojvode Mišića 1, *21000 Novi Sad*

Index: 26.007