ONE-POT BF_3.MeCN CATALYZED SOLVENT FREE SYNTHESIS OF 3,4-DIHYDROPYRIMIDINE-2-ONE ANALOGUES

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Keywords: BF_3.ACN, solvent-free, 3,4-dihydropyrimidine-2-one.

One-pot solvent free three components coupling of aryl aldehydes, β-dicarbonyl compounds, urea or thiourea was performed to afford corresponding 3,4-dihydropyrimidine-2-ones and their sulfur analogs 3,4-dihydro-pyrimidine-2-thiones. It is the first report of BF_3.ACN catalyzed the solvent-free synthesis of pyrimidone analogs.

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INTRODUCTION

The multicomponent reactions (MCRs) are established as a simple, convenient method in synthetic chemistry.[1-3] Furthermore, MCRs are extremely economical, high yielding, less time consuming and with less side reactions.[4-5] Therefore, the design of new MCRs with the green procedure has engaged huge attention, especially in the areas of drug discovery, organic synthesis and material science.

Pyrimidines have extremely biological importance,[6-11] they and their analogs are considered as important bioactive heterocycles [-+]exhibiting interesting biological activities like antiviral,[12] antiprotozoan,[13] anti-proliferative,[14] cytotoxic activity[15] and anti-inflammatory .[16]

As a part of our ongoing efforts to develop new routes for the synthesis of heterocyclic compounds,[17] herein, we like to report a solvent-free single step multicomponent synthesis of 3,4-dihydropyrimidine-2-one and 3,4-dihydropyrimidine-2-thione derivatives.

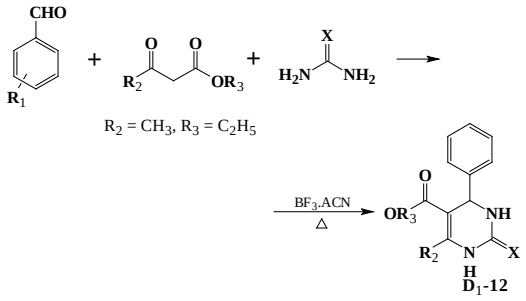

Figure 1. BF_3.ACN catalyzed solvent-free synthesis 3,4-dihydropyrimidine-2-one and 3,4-dihydropyrimidine-2-thione derivatives.

It is the first report of solvent-free condensation of β-keto esters, aryl aldehydes and urea or thiourea in the presence of BF_3.MeCN (BF3*ACN)) as an effective catalyst (**Figure 1)**.

RESULTS AND DISCUSSION

Initially, a mixture of benzaldehyde, ethyl acetoacetate and urea was refluxed in ethanol in the presence of BF_3.ACN (Table 1) to obtain the corresponding 3,4-dihydropyrimidine-2-one derivative. The product was obtained in good yield (90 %). Solvent optimization studies of the above reaction were carried out and are summarized in Table 1. The reaction proceeded very well in solvent-free condition (Table 1, 97%).

Table 1. Solvent optimization for one-pot synthesis 3,4-dihydropyrimidine-2-one in the presence of 10 mol % BF3.MeCN catalyst[a]

Solvent	Condition	Time, min	Yield, %[b]
Ethanol	Reflux	60	90
Water	Reflux	130	85
Water : Ethanol (1:1)	Reflux	120	88
Methanol	Reflux	90	88
Acetonitrile	Reflux	35	92
Solvent Free	90 °C	20	97

a) Experimental conditions: benzaldehyde (2 mmol), urea (3 mmol), ethyl acetoacetate (2 mmol); b) Isolated yield.

Similarly, catalyst optimization studies of the above reaction were also carried out in solvent-free conditions and are summarized in Table 2. When catalyst was used from 5 mol%, 10 mol%, 15 mol% both yield and rate of the reaction was increased. However, the further increment of catalyst amount did not appreciably affect the yield and rate of the reaction. Finally, among all the experimental variations, the 10 mol% BF_3.ACN solvent-free condition at 90 ° C temperature gave the best results with 97% yield (Table 2).

To check the generality and scope of the optimized reaction, different aromatic aldehydes, β-ketoesters, urea and thiourea were used. The resultant 3,4-dihydropyrimidine-2-one (**D_{1-9}**) and 3,4-dihydropyrimidine-2-thione derivatives (**D_{10-12}**) were obtained in good to excellent yields as mentioned in Table 3.

Table 2. Catalyst optimization for one-pot synthesis 3,4-dihydropyrimidine-2-one [a]

Sr. No.	Catalyst, mol %	Time, min	Yield, %[b]
1	5%	35	85
2	10%	20	97
3	15%	15	95
4	20%	15	95
5	25%	15	95

a)Experimental conditions: benzaldehyde (2 mmol), urea (3 mmol), ethyl acetoacetate (2 mmol) at 90◦C; b)Isolated yield.

Table 3. Synthesis of 3,4-dihydropyrimidine-2-ones and 3,4-dihydropyrimidine-2-thiones from aryl aldehydes, β-ketoesters and urea/thiourea[a]

Aldehyde	X	β–keto-ester[c]	Yield[b]	Melting point, ℗C	
				Measured	Reported
C_6H_5	O	EAA	97	203-204	206[18]
m-$NO_2C_6H_4$	O	EAA	94	226-227	227-228[20]
p-HOC_6H_4	O	EAA	99	223-226	227-228[20]
p-ClC_6H_4	O	EAA	95	208-210	209-212[18]
m-ClC_6H_4	O	EAA	98	194-196	193-194[20]
m-HOC_6H_4	O	EAA	97	166-169	167-170[18]
C_6H_5	O	MAA	92	211-213	212-213[18]
p-$MeOC_6H_4$	O	EAA	91	198-199	199-201[19]
p-FC_6H_4	O	EAA	94	175-176	176-178[21]
C_6H_5	S	EAA	99	206-208	207-208[19]
m-$NO_2C_6H_4$	S	MAA	98	273-274	273-275[18]
p-HOC_6H_4	S	EAA	97	201-203	202-203[21]

a) Reaction conditions: Aromatic aldehyde (2 mmol), Urea/Thiourea (3 mmol), MAA or EAA (2 mmol) and catalyst (10 mol%) solvent free at 90^0C; b)Isolated yield, c) MAA-methyl acetoacetate, EAA-ethyl acetoacetate

EXPERIMENTS

All the chemicals were purchased from Sigma Aldrich and used as received without further purification. All compounds were matched with and confirmed by literature data for Melting point, IR, ^{1}H NMR, ^{13}C NMR and mass spectrometry. The melting points were determined on Labstar melting point apparatus and are uncorrected. The IR spectra were taken on a Perkin-Elmer FTIR-1600 spectrophotometer and the data expressed in cm (KBr). ^{1}H and ^{13}C NMR spectra were recorded on Bruker Avance (300 MHz) spectrometer in $CDCl_3$ using TMS as the internal standard. Mass spectra were recorded on an Agilent spectrometer.

General procedure for the preparation of 3,4-dihydropyrimidine-2-one and 3,4-dihydropyrimidine-2-thione derivatives (D_{1-12})

A mixture of β-ketoester (2 mmol), urea/thiourea (3 mmol), aryl aldehyde (2 mmol) and BF_3.ACN (10 mol%) was heated at 90°C till the completion of the reaction, monitored by TLC in Dichloromethane : Methanol (9:1) as a mobile phase. The reaction mixture was cooled and poured in 10 mL ice-water and precipitated solid was filtered out to give the desired crude product. The crude product was recrystallized with ethanol to get pure 3,4-dihydropyrimidine-2-one and 3,4-dihydropyrimidine-2-thione product as shown in (Table 3). The products were analyzed by IR, ^{1}H and ^{13}C NMR.

Ethyl 1,2,3,4-tetrahydro-6-methyl-2-oxo-4-phenylpyrimidine-5-carboxylate

White solid, mp. 203–204 °C; IR (KBr) ν: 3228, 3106, 2936, 1721, 1695, 1604, 1221 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ: 1.23 (t, 3H), 2.35 (s, 3H), 4.10 (m, 2H), 5.25 (s, 1H), 5.98 (s, 1H), 7.88–7.13 (m, 5H), 8.25 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 14.1, 18.3, 54.4, 61.4, 102.3, 126.2, 127.2, 128.7, 143.5, 146.1, 163.6 ppm.

Ethyl 1,2,3,4-tetrahydro-6-methyl-4-(3-nitrophenyl)-2-oxopyrimidine-5-carboxylate (D_2)

Off-white solid, mp. 226-227°C; IR (KBr) ν: 3408, 3106, 2954, 1670, 1605, 1590, 1524, 1348, 1215 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ: 1.21 (t, 3H), 2.54 (s, 3H), 4.37 (q, 2H), 5.21 (s, 1H), 7.18-7.25 (m, 2H), 7.88 (d, 2H, *3J* = 8.7 Hz), 8.17 (s, 1H), 8.81 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 165.7, 158.5, 148.7, 148.4, 131.8, 130.6, 129.5, 125.7, 121.8, 118.8, 61.2, 53.4, 25.4, 17.3 ppm.

Ethyl 1,2,3,4-tetrahydro-4-(4-hydroxyphenyl)-6-methyl-2-oxopyrimidine-5-carboxylate (D_3)

White solid, mp. 223-226°C; IR (KBr) ν: 3510, 3285, 3115, 2968, 1658, 1523, 1466, 1218 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ: 1.14(t, 3H), 2.24 (s, 3H), 3.96 (m, 2H), 5.06 (s, 1H), 6.75 (d, 2H), 7.05 (d, 2H), 9.15 (s, 1H), 9.36 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 166.5, 159.1, 152.8, 147.9, 136.8, 126.3, 124.8, 115.8, 62.8, 49.3, 24.4, 19.4 ppm.

Ethyl 4-(4-chlorophenyl)-1,2,3,4-tetrahydro-6-methyl-2-oxopyrimidine-5-carboxylate (D4)

White solid, mp 208-210°C; IR (KBr) ν: 3239, 3117, 2969, 1715, 1646, 1458, 1225, 1093 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ: 1.21 (t, 3H), 2.38 (s, 3H), 4.11 (m, 2H), 5.85 (s, 1H), 7.31 (d, 2H), 7.30 (d, 2H), 8.06 (s, 1H); ^{13}C NMR (100MHz, $CDCl_3$) δ: 168.2, 158.6, 146.8, 143.3, 145.5, 132.1, 129.2, 117.1, 61.4, 51.2, 22.4, 18.3 ppm.

Ethyl 4-(3-chlorophenyl)-1,2,3,4-tetrahydro-6-methyl-2-oxopyrimidine-5-carboxylate (D_5)

White solid, mp. 194-196°C; IR (KBr) ν:3245, 3110, 2975, 1705, 1655 cm^{-1}; ^{1}H NMR ($CDCl_3$ 300 MHz) δ: 1.21 (t, 3H), 2.43 (s,3H), 4.21 (m, 2H), 5.42 (s, 1H), 7.22 (d, 2H), 7.33 (d, 2H), 7.61 (brs, 1H), 8.12 (brs, 1H). ^{13}C NMR ($CDCl_3$ 100 MHz) δ: 168.2, 158.4, 146.5, 143.2, 145.3, 131.6, 129.2, 117.1, 61.4, 51.4, 22.3, 18.5 ppm.

Ethyl 1,2,3,4-tetrahydro-4-(3-hydroxyphenyl)-6-methyl-2-oxopyrimidine-5-carboxylate (D_6)

White solid, mp. 166-169°C; IR (KBr) ν: 3515, 3310, 3106, 2958, 1724, 1645, 1612, 1466, 1223 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ: 1.14 (t, 3H), 2.25 (s, 3H), 4.06 (m, 2H), 5.06 (s, 1H), 6.62 (d, 1H), 6.68 (d, 2H), 7.10 (t, 2H), 9.11 (s, 1H), 9.31 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 163.7, 157.8, 150.2, 146.4, 133.9, 131.7, 130.2, 124.7, 121.3, 115.8, 60.9, 54.7, 26.2, 18.1 ppm.

Methyl 1,2,3,4-tetrahydro-6-methyl-2-oxo-4-phenylpyrimidine-5-carboxylate (D_7)

White solid, mp. 211-213°C, IR (KBr) ν: 3415, 3320, 3106, 2950, 1728, 1660, 1632, 1475, 1234 cm^{-1}; ^{1}H NMR ($CDCl_3$ 300 MHz) δ: 9.23 (s, 1H), 7.74 (s, 1H), 7.45-7.35 (m, 2H), 7.28-7.26 (m, 3H), 5.18 (d, 1H), 3.55 (s, 3H), 2.26 (s, 3H); ^{13}C NMR ($CDCl_3$ 100 MHz) δ: 166.3, 152.8, 150.1, 145.3, 129.4, 128.4, 127.5, 99.8, 54.6, 51.8, 18.8 ppm.

Ethyl 1,2,3,4-tetrahydro-4-(4-methoxyphenyl)-6-methyl-2-oxopyrimidine-5-carboxylate (D_8)

White solid, mp. 198-199°C; IR (KBr) ν: 3254, 3105, 2955, 1710, 1645, 1515, 1464, 1225 m^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ: 1.13 (t, 3H), 2.24 (s, 3H), 3.38 (s, 3H), 4.1 (m, 2H), 5.11 (s, 1H), 6.90 (d, 2H), 7.16 (d, 2H), 7.71 (s, 1H), 9.14 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 168.0, 158.2, 152.4, 149.5, 136.7, 130.2, 123.3, 118.8, 62.4, 61.8, 49.7, 25.7, 19.7 ppm.

Ethyl 4-(4-fluorophenyl)-1,2,3,4-tetrahydro-6-methyl-2-oxo-pyrimidine-5-carboxylate (D_9)

White solid, mp. 175-176°C; IR (KBr) ν: 3243, 1698, 1638 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ: 9.24 (s, 1H), 7.81 (s, 1H), 7.23 (m, 4H), 5.14 (s, 1H), 4.12 (m, 2H), 2.23 (s, 3H), 1.11 (t, 3H); ^{13}C NMR (100 MHz $CDCl_3$) δ: 165.8, 160.1, 152.2, 148.5, 141.4, 128.3, 115.3, 99.4, 59.4, 53.8, 17.6, 14.8 ppm.

Ethyl 1,2,3,4-tetrahydro-6-methyl-4-phenyl-2-thioxopyrimidine-5-carboxylate (D_{10})

White solid, mp. 206-208°C, IR (KBr) ν: 3236, 3126, 2946, 1728, 1698, 1226 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ: 9.63 (1H, s), 8.94 (1H, s), 6.67-6.54 (m, 5H), 4.53 (d, 1H), 3.37 (m, 2H), 1.61 (3H, s), 0.44 (t, 3H); ^{13}C NMR ($CDCl_3$ 100 MHz) δ: 175.3, 166.3, 145.9, 144.4, 129.3, 128.4, 127.1, 101.7, 60.5, 54.8, 18.1,14.8 ppm.

Ethyl 1,2,3,4-tetrahydro-6-methyl-4-(3-nitrophenyl)-2-thioxopyrimidine-5-carboxylate(D_{11})

White solid, mp. 273-274°C, IR (KBr) ν: 3325, 3215, 3105, 2963, 1715, 1634, 1520 cm^{-1}; ^{1}H NMR (300 MHz,$CDCl_3$) δ: 9.38 (s, 1H), 8.17- 7.69 (m, 4H), 3.88 (m, 2H), 2.24 (s, 3H), 1.13 (t, 3H); ^{13}C NMR ($CDCl_3$ 100 MHz) δ: 165.3, 151.9, 149.6, 147.9, 147.2, 133.2, 130.2, 122.3, 121.4, 98.4, 59.3, 53.7, 17.8, 14.2 ppm.

Ethyl 1,2,3,4-tetrahydro-4-(4-hydroxyphenyl)-6-methyl-2-thioxopyrimidine-5-carboxylate (D_{12})

White solid, mp 201-203 °C; IR (KBr) ν: 3223, 3098, 2980, 1742, 1655, 1459, 1251 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ: 1.24 (t, 3H), 1.89 (s, 3H), 4.16 (m, 2H), 5.87 (s, 1H), 7.32(d, 2H), 7.33 (d, 2H), 8.07 (s, 1H); ^{13}C NMR (100MHz, $CDCl_3$) δ: 168.2, 158.6, 146.8, 143.3, 145.5, 132.1, 129.2, 117.1, 61.4, 51.2, 22.4, 18.3 ppm.

CONCLUSION

In summary, it is the first report of cost-effective, solvent-free mild protocol for the synthesis of 3,4-dihydropyrimidine-2-one and 3,4-dihydropyrimidine-2-thione derivatives using BF_3.ACN as a catalyst. This MCRs protocol offers several significant advantages like operational simplicity, superior atom-economy, shorter reaction time with good to excellent yields.

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SIMPLE CHROMIUM CATALYZED OXIDATIVE SYNTHESIS OF QUINAZOLINONES AND BENZOXAZINONES FROM 2-AMINOBENZAMIDE AND ANTHRANILIC ACID WITH ARYLALDEHYDES

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Keywords: quinazolinones; benzoxazinones; chromium trioxide; catalyst; oxidant.

An easy and efficient protocol for oxidative synthesis of quinazolinones and benzoxazinones using novel catalyst fromed in-situ from chromium trioxide has been developed. Here chromium trioxide acts as an oxidant and its reduction products catalyze the coupling reaction. Newly developed method demonstrates a new alternative to existing method which is a cost effective approach to synthesize important moieties like quinazolinones and benzoxazinones from easily available starting materials in good to excellent yields.

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INTRODUCTION

Nowadays, various heterocyclic compounds have been found with distinguished pharmacological activities in drug design and development.[1] Quinazolinones obtained from natural products form an important skeleton for the synthesis of different therapeutically active drug moieties.[2] Its derivatives are important compounds, and have been widely used in hypnotic,[3] sedative,[4] anticancer,[5-6] anticonvulsant[7] and anti-inflammatory agents.[8] The research interest in the synthesis of 4(3H)-quinazolinone and its derivatives has never faded since the first report of the 4(3H)-quinazolinone.[9] Also, 1-benzoxazin-4-one derivatives are important skeletons due to their proven pharmaceutical activity. For example, some of the drugs which contain 4H-3,1-benzoxazin-4-one as the core structure act as HSV-1 protease inhibitor and human chymase inhibitor[10] along with anti-proliferative activity.[11] Initially, some toxic oxidants like DDQ,[12] $CuCl_2$,[13] MnO_2,[14] $KMnO_4$,[15] $K_2S_2O_8$[16] and $PhI(OAc)_2$[17] were used which yielded the similar quantity of oxidant-derived waste. The use of chromium trioxide as an oxidsant and a catalyst precursor is a promising strategy in organic synthesis which substitutes many expensive transition metal compounds.[18] Especially, the amidation of $C(sp^3)$-H bonds using chromium is very attractive, and it finds the utility in synthesis of a wide range of N and O-heterocycles.[19] Chromium, among transition metals, is particularly attractive in organic synthesis because of its low price.[20] Hence, in continuation to our work,[21-24] we herein tried to report the synthesis of quinazolinones as well as benzoxazinone derivatives using chromium trioxide as the oxidant and catalyst.

MATERIALS AND METHOD

All chemicals and solvents were used from Sigma-aldrich. Melting points were uncorrected and recorded on Optimelt digital melting point apparatus. IR spectra were recorded on Bruker Alpha E FTIR spectrophotometer. ^{1}H NMR was recorded on Varian 300 MHz spectrometer by using TMS as internal standard. Mass spectra were taken with Micromass-QUATTRO-II of WATER mass spectrometer.

General procedure for the synthesis of compound 3a-3m

A mixture of 2-aminobenzamides **1a** (1 mmol), chromium trioxide (20 mol %) and benzaldehyde **2a** (1 mmol) was stirred in dichloroethane (5 mL) and heated at 80 °C for 5 h. After completion of reaction, the resulting solution was cooled to room temperature, and the reaction mixture added to the saturated solution of sodium bisulphate stirred for 10-15 min. Then 10 ml of ethyl acetate was added to the mixture and organic layer was separated, concentrated under vacuum and the resulting residue was purified by column chromatography (hexane /ethyl acetate) to afford the desired product. DCE is very cheap solvents as compared to other solvents, hence we used the same.

Chromium trioxide is explosive with most reactive aldehydes like fluorobenzaldehyde so there is need for precaution.

2-Phenylquinazolin-4(3H)-one (3a)

White solid, mp: 122 °C; ^{1}H NMR (400 MHz, DMSO-d_6): δppm= 7.54 (m, 3H), 7.66-7.94 (m, 4H), 8.10 (d, 2H), 12.11 (1H, NH);^{13}C NMR (100 MHz, DMSO-d_6): δppm = 121.3, 125.4, 128.6, 130.1, 134.5, 148.5, 154.4, 164.6. Anal. calcd. for $C_{14}H_{10}N_2O$: C, 75.66; H, 4.54; N, 12.60; Found: C, 75.62; H, 4.5; N, 12.56.

2-(2,4-Dimethoxyphenyl)quinazolin-4(3H)-one (3b)

White solid, mp: 255 °C; ^{1}H NMR (400 MHz, DMSO-d_6): δppm= 3.80 (s, 3H), 6.63-6.74 (m, 3H), 7.54 (m, 3H), 7.66-7.91 (m, 4H), 12.11 (1H, NH); ^{13}C NMR (100 MHz, DMSO-d_6): δppm = 55.9, 98.4, 106.5, 117.8, 121.8, 124.9, 126.7, 131.8, 134.5, 146.6, 150.7, 160.0, 163.3. Anal. calcd. for$C_{16}H_{14}N_2O_3$: C, 68.07; H, 5.00; N, 9.92; Found: C, 68.11; H, 5.04; N, 9.96.

2-(3-Nitrophenyl)quinazolin-4(3H)-one (3c)

White solid, mp: 147 °C; ^{1}H NMR (400 MHz, DMSO-d_6): δppm= 7.54 (m, 3H), 7.66-7.96 (m, 4H), 8.37-8.72 (d, 2H), 12.11 (1H, NH); ^{13}C NMR (100 MHz, DMSO-d_6): δppm = 121.3, 124.0, 126.7, 130.8, 134.5, 147.8, 153.1, 163.8. Anal. calcd. for $C_{14}H_9N_3O_3$: C, 62.92; H, 3.39; N, 15.72; Found: C, 62.96; H, 3.43; N, 15.76.

2-(4-Methoxyphenyl)quinazolin-4(3H)-one (3d)

White solid, mp: 298 °C; ^{1}H NMR (400 MHz, DMSO-d_6): δppm= 3.78 (s, 3H), 7.54 (m, 3H), 7.66-7.96 (m, 4H), 12.11 (1H, NH); ^{13}C NMR (100 MHz, DMSO-d_6): δppm = 55.3, 114.4, 121.3, 126.5, 129.9, 134.5, 148.5, 154.7, 161.3, 164.6. Anal. calcd. for$C_{15}H_{12}N_2O_2$: C, 71.42; H, 4.79; N, 11.10; Found: C, 71.38; H, 4.75; N, 11.06.

2-(3-Methoxyphenyl)quinazolin-4(3H)-one (3e)

White solid, mp: 198°C; ^{1}H NMR (400 MHz, DMSO-d6): δppm= 3.78 (s, 3H), 7.54 (m, 3H), 7.73 (m, 4H), 12.11 (1H, NH); ^{13}C NMR (100 MHz, DMSO-d_6): δppm = 55.3, 114.4, 121.3, 126.5, 129.9, 134.5, 148.5, 154.7, 161.3, 164.6. Anal. calcd. for$C_{15}H_{12}N_2O_2$: C, 71.42; H, 4.79; N, 11.10; Found: C, 71.38; H, 4.75; N, 11.06.

2-(4-Nitrophenyl)quinazolin-4(3H)-one (3f)

White solid, mp: 209 °C; ^{1}H NMR (400 MHz, DMSO-d_6): δppm= 7.54 (m, 3H), 7.66-7.94 (m, 4H), 8.25-8.37 (d, 2H), 12.11 (1H, NH); ^{13}C NMR (100 MHz, DMSO-d_6): δppm = 121.3, 124.8, 129.2, 134.5, 137.2, 137.2, 149.1, 154.5, 164.6. Anal. calcd. for$C_{14}H_9N_3O_3$: C, 62.92; H, 3.39; N, 15.72; Found: C, 62.96; H, 3.43; N, 15.76.

4-(4-Oxo-3,4-dihydroquinazolin-2-yl)benzonitrile (3g)

White solid, mp: 297 °C; ^{1}H NMR (400 MHz, DMSO-d_6): δppm= 7.54 (m, 3H), 7.65-7.96 (m, 4H), 8.19 (d, 2H), 12.11 (1H, NH); ^{13}C NMR (100 MHz, DMSO-d_6): δppm = 112.2, 118.5, 121.3, 125.4, 128.73, 133.5, 134.5, 148.5, 154.78, 164.6. Anal. calcd. for$C_{15}H_9N_3O$: C, 72.87; H, 3.67; N, 16.99; Found: C, 72.83; H, 3.63; N, 16.95.

2-(4-Hydroxyphenyl)quinazolin-4(3H)-one (3h)

White solid, mp: 292 °C;^{1}H NMR (400 MHz, DMSO-d_6): δppm= 6.94 (m, 3H), 7.54 (m, 3H), 7.65-7.96 (m, 4H), 8.13 (d, 2H), 12.11 (1H, NH); ^{13}C NMR (100 MHz, DMSO-d_6): δppm = 116.8, 121.3, 122.8, 126.5, 130.2, 134.5, 148.5, 151.1, 154.8, 164.6. Anal. calcd. for$C_{14}H_{10}N_2O_2$: C, 70.58; H, 4.23; N, 11.76; Found: C, 70.62; H, 4.27; N, 11.8.

2-(2,3-Dichlorophenyl)quinazolin-4(3H)-one (3i)

White solid, mp: 299 °C; ^{1}H NMR (400 MHz, DMSO-d_6): δppm= 7.38 (m, 3H), 7.54 (m, 3H), 7.65-7.94 (m, 4H), 12.11 (1H, NH); ^{13}C NMR (100 MHz, DMSO-d_6): δppm = 121.8, 124.9, 127.7, 131.0, 132.9, 134.5, 146.9, 149.0, 161.5. Anal. calcd. for$C_{14}H_8Cl_2N_2O$: C, 57.76; H, 2.77; N, 9.62; Found: C, 57.8; H, 2.81; N, 9.66.

2-(2-Phenyl)quinazolin-4(3H)-one (3j)

White solid, mp: 191°C; ^{1}H NMR (400 MHz, DMSO-d_6): δppm= 7.04-7.45 (m, 3H), 7.54 (m, 3H), 7.65-7.94 (m, 4H), 12.11 (1H, NH); ^{13}C NMR (100 MHz, DMSO-d_6): δppm = 116.8, 121.3, 122.8, 126.5, 130.2, 134.5, 148.5, 151.1, 154.8, 164.6. Anal. calcd. for$C_{14}H_{10}N_2O_2$: C, 70.58; H, 4.23; N, 11.76; Found: C, 70.62; H, 4.27; N, 11.8.

2-(2,4-Dichlorophenyl)quinazolin-4(3H)-one (3k)

White solid, mp: 297 °C; ^{1}H NMR (400 MHz, DMSO-d_6): δppm= 7.36 (m, 3H), 7.54 (m, 3H), 7.69-7.94 (m, 4H), 12.11 (1H, NH); ^{13}C NMR (100 MHz, DMSO-d_6): δppm = 121.8, 124.9, 127.7, 131.0, 132.9, 134.5, 146.9, 149.0, 161.5. Anal. calcd. for$C_{14}H_8Cl_2N_2O$: C, 57.76; H, 2.77; N, 9.62; Found: C, 57.8; H, 2.81; N, 9.66.

2-(4-Bromophenyl)quinazolin-4(3H)-one (3l)

White solid, mp: 252 °C; ^{1}H NMR (400 MHz, DMSO-d_6): δppm= 7.55 (m, 3H), 7.66-7.96 (m, 4H), 12.11 (1H, NH); ^{13}C NMR (100 MHz, DMSO-d_6): δppm = 121.3, 123.9, 126.7, 131.3, 134.5, 148.5, 154.6, 164.6. Anal. calcd. for$C_{14}H_8Cl_2N_2O$: C, 55.84; H, 3.01; N, 9.30; Found: C, 55.8; H, 2.97; N, 9.26.

2-(3-Ethoxy-4-hydroxyphenyl)quinazolin-4(3H)-one (3m)

White solid, mp: 315 °C; ^{1}H NMR (400 MHz, DMSO-d_6): δppm= 1.42 (t, 3H, CH_3), 4.14 (q, 2H, CH_2), 5.44 (s, 1H, OH), 6.96 (d, 1H, phenyl ring), 7.46 -7.57 (m, 3H, quinazoline ring), 7.75-7.88 (m, 2H), 7.96 (d, 1H, quinazoline ring), 12.11 (1H, NH); ^{13}C NMR (100 MHz, DMSO-d_6): δppm = 14.7, 64.31, 113.5, 121.0, 122.7, 126.7, 134.5, 147.8, 153.8. Anal. calcd. for$C_{16}H_{14}N_2O_3$: C, 68.07; H, 5.00; N, 9.92; Found: C, 68.11; H, 5.04; N, 9.96.

General procedure for the synthesis of compound 6a-6m

An oven dried three necked round bottom flask was loaded with anthranilic acid (**4**) (1 mmol), benzaldehyde (**5**) (1 mmol), chromium trioxide (20 % mol) in dichloroethane (5 mL). Then, the reaction mixture was heated at 80 °C for 16 h. The completion of the reaction was monitored by TLC. After being cooled at room temperature the reaction mixture was poured in the saturated solution of sodium bisulphate stirred for 10-15 min. Then 10 mL of ethyl acetate was added to the mixture and organic layer was separated, concentrated under vacuum and the resulting residue was purified by column chromatography (hexane/ethyl acetate) to afford the desired product.

2-Phenyl-4H-benzo[*d*][1,3]oxazin-4-one (6a)

White solid, mp: 125°C; ^{1}H NMR (400 MHz, DMSO-d6): δppm= 7.49 -7.53 (m, 3H), 7.68-7.87 (m, 4H), 8.04-8.28 (d, 2H), ^{13}C NMR (100 MHz, DMSO-d6): δppm = 116.0, 126.2, 131.4, 132.2, 136.8, 147.0, 156.8, 159.2. Anal. calcd. for$C_{14}H_9NO_2$: C, 75.33; H, 4.06; N, 6.27; Found: C, 75.37; H, 4.10; N, 6.31.

2-(2-Chlorophenyl)-4H-benzo[*d*][1,3]oxazin-4-one (6b)

White solid, mp: 139 °C; ^{1}H NMR (400 MHz, DMSO-d^6): δppm= 7.28-7.53 (m, 3H, quinazoline ring), 7.68-7.99 (m, 4H, phenyl ring), 8.04 (d, 1H, quinazoline ring); ^{13}C NMR (100 MHz, DMSO-d$_6$): δppm = 116.5, 128.3, 131.9, 132.8, 136.8, 147.2, 156.4, 159.5. Anal. calcd. for$C_{14}H_8ClNO_2$: C, 65.26; H, 3.13; N, 5.44; Found: C, 65.22; H, 3.09; N, 5.40.

2-(3-Chlorophenyl)-4H-benzo[*d*][1,3]oxazin-4-one (6c)

White solid, mp: 128 °C; ^{1}H NMR (400 MHz, DMSO-d$_6$): δppm= 7.43-7.69 (m, 5H), 7.87-8.11 (m, 2H), 8.12 (d, 1H); ^{13}C NMR (100 MHz, DMSO-d$_6$): δppm = 116.5, 128.3, 131.9, 132.8, 136.8, 147.2, 156.4, 159.5. ^{13}C NMR (100 MHz, DMSO-d6): δppm = 116.5, 128.3, 131.9, 132.8, 136.8, 147.2, 156.4, 159.5. Anal. calcd. for$C_{14}H_8ClNO_2$: C, 65.26; H, 3.13; N, 5.44; Found: C, 65.22; H, 3.09; N, 5.40.

2-(4-Chlorophenyl)-4H-benzo[*d*][1,3]oxazin-4-one (6d)

White solid, mp: 191°C; ^{1}H NMR (400 MHz, DMSO-d$_6$): δppm= 7.40-7.41 (m, 3H), 7.69-7.87 (m, 4H), 8.06 (d, 1H); ^{13}C NMR (100 MHz, DMSO-d$_6$): δppm = 116.5, 128.3, 131.9, 132.8, 136.8, 147.2, 156.4, 159.5. Anal. calcd. for$C_{14}H_8ClNO_2$: C, 65.26; H, 3.13; N, 5.44; Found: C, 65.30; H, 3.17; N, 5.48.

2-(4-Ethylphenyl)-4H-benzo[*d*][1,3]oxazin-4-one (6e)

White solid, mp: 98°C; ^{1}H NMR (400 MHz, DMSO-d$_6$): δppm= 1.21 (t, 3H, CH_3), 2.69 (q, 2H, CH_2), 7.42 (d, 2H), 7.68-7.87 (m, 3H), 8.03 (d, 2H), 8.17 (d, 1H); ^{13}C NMR (100 MHz, DMSO-d$_6$): δppm = 15.3, 28.6, 116.0, 126.2 128.4, 131.3, 136.8, 147.0, 157.1, 159.2. Anal. calcd. for$C_{16}H_{13}NO_2$: C, 76.48; H, 5.21; N, 5.57; Found: C, 76.44; H, 5.17; N, 5.53.

7-Chloro-2-phenyl-4H-benzo[*d*][1,3]oxazin-4-one (6f)

White solid, mp: 191 °C; ^{1}H NMR (400 MHz, DMSO-d$_6$): δppm= 7.17 (d, 1H), 7.49-7.87 (m, 5H), 8.19-8.20 (d, 2H); ^{13}C NMR (100 MHz, DMSO-d$_6$): δppm = 113.8, 124.8, 129.8, 131.4, 132.3, 137.9, 147.3, 157.1, 159.5. Anal. calcd. for$C_{14}H_8ClNO_2$: C, 65.26; H, 3.13; N, 5.44; Found: C, 65.30; H, 3.17; N, 5.48.

7-Chloro-2-(3-fluorophenyl)-4H-benzo[*d*][1,3]oxazin-4-one (6g)

White solid, mp: 121°C; ^{1}H NMR (400 MHz, DMSO-d6): δppm==7.43 (d, 1H), 7.60-7.87 (m, 4H), 8.04-8.19 (d, 2H); ^{13}C NMR (100 MHz, DMSO-d6): δppm = 113.8, 115.9, 118.8, 126.3, 129.1, 130.6, 132.8, 137.9, 147.3, 155.6, 159.4, 164.4. Anal. calcd. for$C_{14}H_7ClFNO_2$: C, 61.00; H, 2.56; N, 5.08; Found: C, 61.04; H, 2.6; N, 5.12.

7-Chloro-2-(4-chlorophenyl)-4H-benzo[*d*][1,3]oxazin-4-one (6h)

White solid, mp: 141 °C; ^{1}H NMR (400 MHz, DMSO-d$_6$): δppm=7.41 (d, 1H), 7.70-7.87 (m, 4H), 8.07-8.20 (d, 2H); ^{13}C NMR (100 MHz, DMSO-d$_6$): δppm = 113.8, 124.8, 129.6, 131.7, 138.3, 147.3, 154.5, 159.5. Anal. calcd. for$C_{14}H_7Cl_2NO_2$: C, 57.56; H, 2.42; N, 4.79; Found: C, 57.60; H, 2.46; N, 4.83.

2-(4-Chlorophenyl)-6-nitro-4H-benzo[*d*][1,3]oxazin-4-one (6i)

White solid, mp: 185 °C; ^{1}H NMR (400 MHz, DMSO-d$_6$): δppm=7.41 (d, 1H), 7.93 (m, 4H), 8.04-8.79 (d, 2H); ^{13}C NMR (100 MHz, DMSO-d$_6$): δppm = 118.5, 127.4, 131.0, 131.7, 138.3, 145.8, 150.9, 158.9. Anal. calcd. for$C_{14}H_7ClN_2O_4$: C, 55.56; H, 2.33; N, 9.26; Found: C, 55.52; H, 2.29; N, 9.22.

2-(4-Methoxyphenyl)-6-nitro-4H-benzo[*d*][1,3]oxazin-4-one (6j)

White solid, mp: 177°C; ^{1}H NMR (400 MHz, DMSO-d$_6$): δppm= 3.78 (s, 3H, OCH_3), 7.06 (d, 2H), 7.41 (d, 1H), 7.93 (d, 2H), 8.11-8.79 (d, 2H); ^{13}C NMR (100 MHz, DMSO-d$_6$): δppm = 55.3, 114.2, 118.5, 125.9, 131.0, 145.8, 150.9, 158.9, 163.5. Anal. calcd. for$C_{15}H_{10}N_2O_5$: C, 60.41; H, 3.38; N, 9.39; Found: C, 60.37; H, 3.34; N, 9.35.

6-Nitro-2-(4-nitrophenyl)-4H-benzo[*d*][1,3]oxazin-4-one (6k)

White solid, mp: 185 °C; ^{1}H NMR (400 MHz, DMSO-d$_6$): δppm= 7.92 (m, 4H), 8.26-8.79 (d, 2H), ^{13}C NMR (100 MHz, DMSO-d$_6$): δppm = 118.5, 124.5, 127.4, 130.6, 131.0, 137.4, 145.8, 150.9, 158.9. Anal. calcd. for$C_{14}H_7N_3O_6$: C, 53.68; H, 2.25; N, 13.42; Found: C, 53.72; H, 2.29; N, 13.46.

2-(4-Bromophenyl)-6-nitro-4H-benzo[*d*][1,3]oxazin-4-one (6l)

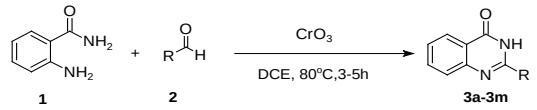
White solid, mp: 150 °C; ^{1}H NMR (400 MHz, DMSO-d$_6$): δppm= 7.70 (d, 1H), 7.93 (m, 4H), 8.02-8.79 (d, 2H); ^{13}C NMR (100 MHz, DMSO-d$_6$): δppm = 118.5, 125.9, 127.4, 131.8, 145.8, 150.9, 158.9. Anal. calcd. for$C_{14}H_7BrN_2O_4$: C, 48.44; H, 2.03; N, 8.07; Found: C, 48.40; H, 1.99; N, 8.03.

2-(4-Fluorophenyl)-6-nitro-4H-benzo[d][1,3]oxazin-4-one (6m)

White solid, mp: 230 °C; ^{1}H NMR (400 MHz, DMSO-d_6): δppm= 7.34 (d, 1H),7.93 (m, 4H), 8.09-8.79 (d, 2H); ^{13}C NMR (100 MHz, DMSO-d_6): δppm = 116.2, 118.5, 127.4, 132.2, 145.8, 150.9, 158.9, 166.8. Anal. calcd. for$C_{14}H_7FN_2O_4$: C, 58.75; H, 2.47; N, 9.79; Found: C, 58.79; H, 2.51; N, 9.83.

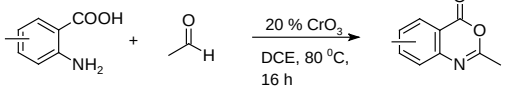
RESULTS AND DISCUSSION

Synthesis of quinazolinones as well as benzoxazinone derivatives using chromium trioxide as the oxidant and catalyst precursor have been performed according to Schemes 1 and 2. The reaction was screened with several copper salts and solvents to enhance the competence of the reactions and the results are summarized in (Table 1).



1 2 3a-3m

Scheme 1.



4 5 6a-6m

Scheme 2.

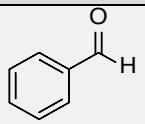
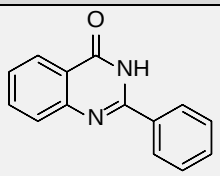
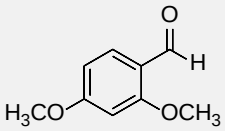
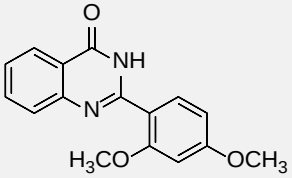
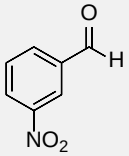
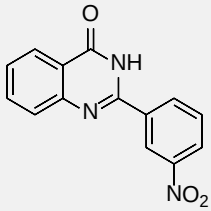
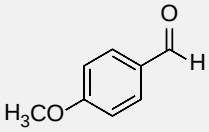
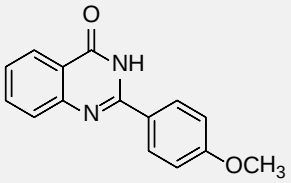
Table 1. Optimization of catalyst and solvent on **3a**

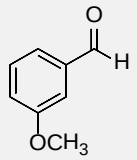
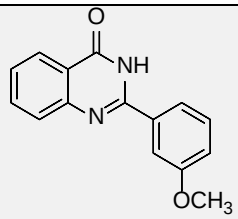
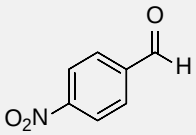
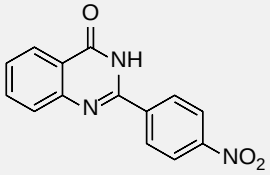
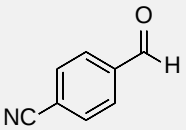
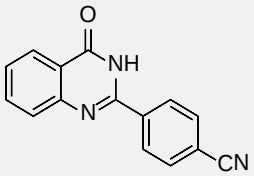
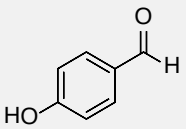
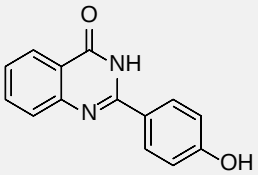
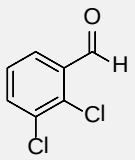
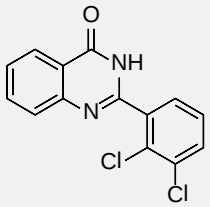
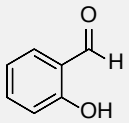
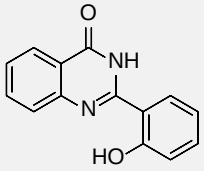
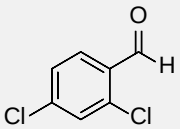
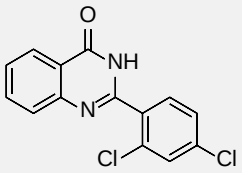
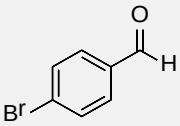
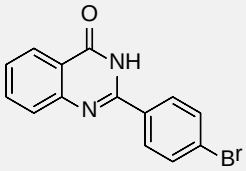
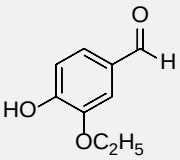
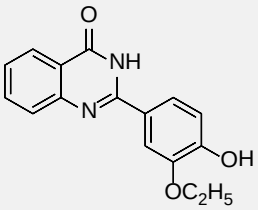
Entry	Catalyst	Solvent	Time, h	Yield,%[a]
1	CuO	DCE	12	10
2	Cu2O	DCE	10	12
3	CuO	DMSO	10	15
4	Cu2O	DMSO	10	21
5	CuO	Dioxane	15	No reaction
6	CuO	DMF	12	26
7	Cu2O	DMF	10	37
8	CrO_3	H_2O	20	No reaction
9	CrO_3	DMF	8	65
10	CrO_3	Toluene	4	80
11	CrO_3	DCE	6	98

It was found that reaction works with each of Cu oxides but there was no reaction with copper(II) oxide in dioxane solvent with reaction time of 15 h (Table 1, Entry 5). Also copper(I) oxide in DMF gave good reaction in 10 h but the yield was considerably low i.e. 37 % (Table 1, Entry 7).

Hence taking into consideration the properties of chromium trioxide, we tried our reactions in the same. Initially we took water as the solvent with chromium trioxide but there was no reaction in 20 h (Table 1, Entry 8). Then we tried taking DMF, toluene and DCE, where DCE turned out to be the best solvent among those examined giving 98% yield (Table 1, Entry 1)

Table 2. Derivatives of quinazolinone compounds **3a-3m**

Entry	R	Product	Yield (%)
3a			90
3b			92
3c			98
3d			97

3e			88
3f			89
3g			80
3h			85
3i			82
3j			81
3k			90
3l			94
3m			88

[a]Isolated yield

This reaction was screened in a number of different Lewis acid catalysts and solvents for its optimization. Using I_2 as a catalyst and DCE as a solvent the obtained yield was 83 % but the reaction time was higher i.e. 16 h (Table 3, Entry 1). Further $AlCl_3$, $ZnCl_2$ and $FeCl_3$ in DCE gave low yield with moderate reaction time (Table 3, Entries 2, 3 and 5). There was no reaction observed with $SnCl_2$ further increasing the reaction time to 20 h (Table 3, Entry 4). Then we choose CrO_3 as the catalyst taking into account our previous quinazolinone reaction. Initially we tried the reaction in

different solvents like toluene, acetonitrile and ethanol but did not observe compatible yields (Table 3, Entries 6-8). Hence, we finally decided to carry out the reaction in DCE as the solvent and got the highest yield of 97 % with the abovementioned combination with comparably less reaction time of 12 h than the other trials (Table 3, Entry 9).

Table 3. Optimization of catalyst and solvent on **6a**

Entry	Catalyst	Solvent	Time, h	Yield, %[a]
1	I_2	DCE	16	83
2	$AlCl_3$	DCE	13	54
3	$ZnCl_2$	DCE	14	12
4	$SnCl_2$	DCE	15	No reaction
5	$FeCl_3$	DCE	12	62
6	CrO_3	Toluene	16	55
7	CrO_3	Acetonitrile	12	26
8	CrO_3	Ethanol	13	46
9	CrO_3	DCE	12	97

[a]Isolated yield

The plausible reaction mechanism of quinazolinone compound is proposed in Fig. 1. Here the aldehyde is reacted with 2-aminobenzamide to give an aminal intermediate. This generated aminal intermediate is oxidized to the corresponding quinazolinone in the presence of $[Cr]^{4+}$ species. Chromium trioxide plays a very important role in the oxidation of aminal intermediate to quinazolinone. $[Cr]^{6+}$ quickly converts to $[Cr]^{4+}$ which forms the most important step in the reaction.

Browsing the literatures related to benzoxazinone synthesis, the following mechanism (Fig. 1) for the oxidative cascade reaction for the synthesis of 2-arylbenzoxazinones using anthranilic acid and benzaldehyde is proposed as an example. First step is the formation of imine **3** from the reaction between anthranilic acid and benzaldehyde catalyzed by chromium trioxide.

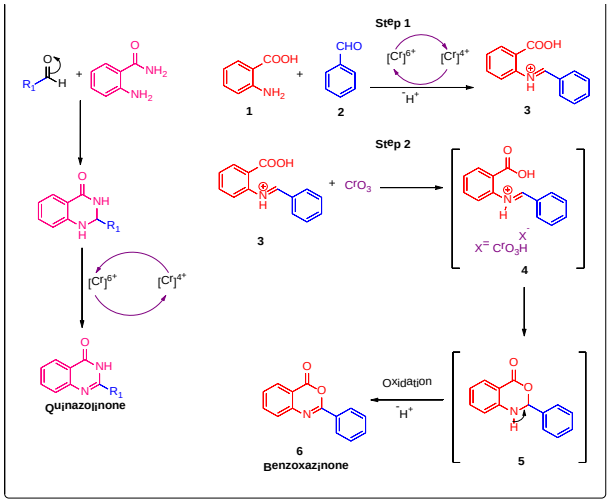


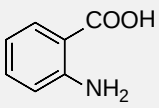
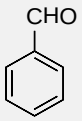
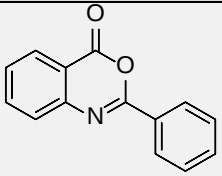
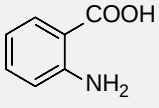
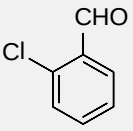
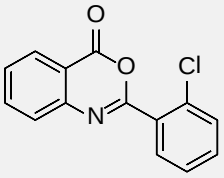
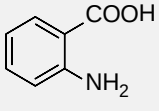
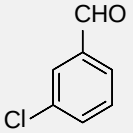
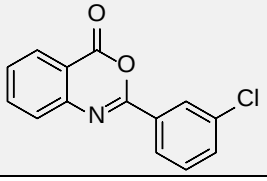
Figure 1. Plausible reaction mechanism for quinazolinone and benzoxazinone compounds

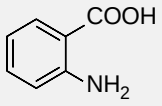
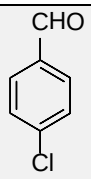
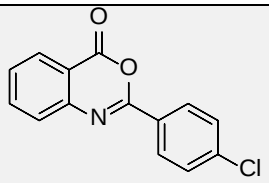
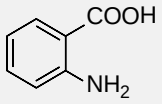
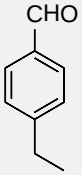
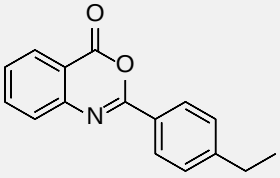
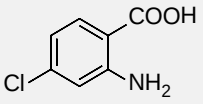
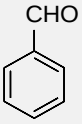
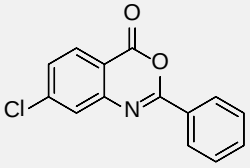
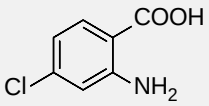
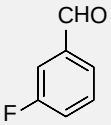
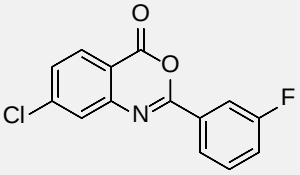
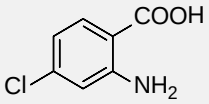
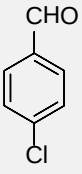
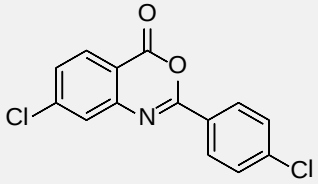
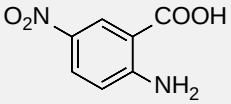
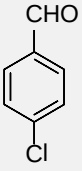
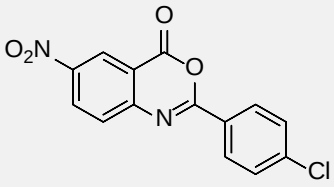
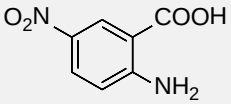
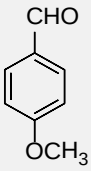
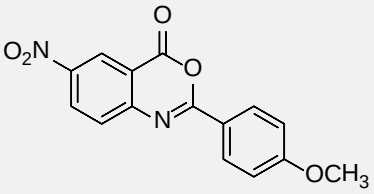
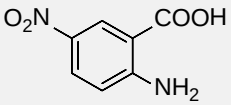
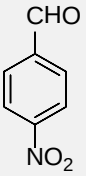
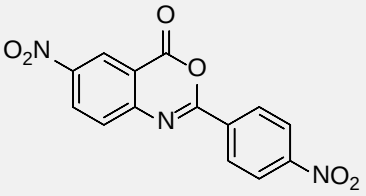
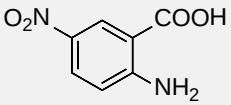
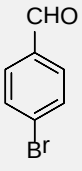
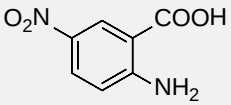
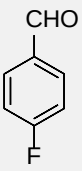
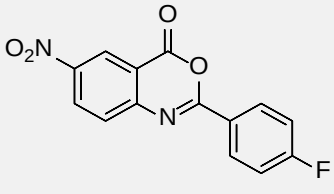
The second step involves the activation of imine group to iminium salt **4** by the active constituent CrO_3H of chromium trioxide (CrO_3). Subsequent cyclization **5** followed by oxidation leads to 2-arylbenzoxazinones **6**.

CONCLUSION

The work illustrates a simple and proficient method for the oxidative synthesis of quinazolinones and benzoxazinones using novel chromium trioxide as the oxidant and catalyst precursor. Also the time required for the completion of reaction is reduced to a great extent. The reaction proceeds very clean and no by-products were observed. Moreover the method is cheap and economical since DCE is used as a solvent. The products were obtained in good to excellent yields.

Table 4. Derivatives of benzoxazinone compounds **6a-6m**

Entry	R1	R_2	Product	Yield(%)
6a				97
6b				87
6c				89

6d				82
6e				86
6f				88
6g				83
6h				92
6i				87
6j				86
6k				89
6l				84
6m				83

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PRODUCING OF InGaAs BULK CRYSTALS BY DIRECT FUSION

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The system of triple $In_{1-x}Ga_xAs$ continuous solid solutions allows the solution of the many problems of modern semiconductor technology as microelectronics, optoelectronics, and nanoelectronics. The remarkable manufactural properties of ternary $In_{1-x}Ga_xAs$ solid solutions make them very useful nanotech performance materials for manufacture nanotech products, such as nanowires, nanotubes, etc. For successful solution of this problem, it is necessary to reveal their intrinsic properties and eliminate the effect of structural imperfections existing in thin films and layers, which is possible by investigating crystals of $In_{1-x}Ga_xAs$ solid solutions in bulk form. The complete miscibility of components in the solid and liquid state and the linear dependence of lattice parameter on the composition of $In_{1-x}Ga_xAs$ solid solutions allow to consider this system as a pseudo-binary alloys system of two components of $(GaAs)_x$ and $(InAs)_{1-x}$ like SiGe alloys system. This feature of the alloys has enabled to apply the comparatively affordable and straightforward method of direct fusion process of InAs and GaAs components for producing of $In_{1-x}Ga_xAs$ alloys with stable chemical composition. Carefully selected conditions of the fusion and processing of crystal growth have allowed obtaining several compositions of InAs-rich $In_{1-x}Ga_xAs$ alloys with uniform distribution of components across the ingot of single crystal by one fusion.

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Introduction

The development of new technologies is impossible without advances in the technology of producing semiconductor materials, among them, III–V binary semiconductor compounds. However, they cannot fully satisfy the requirements of the market of semiconductor materials. Therefore, materials with intermediate properties of binary III–V compounds are required for the development of a number of new ways of semiconductor technology, microelectronics and optoelectronics, among them, nanoelectronics. The solution of this problem is possible by obtaining multicomponent complex compounds, in particular, solid solutions of III–V binary compounds. Although the properties of such materials are not always intermediate between the properties of the original components, nevertheless, the solid solutions of III–V binary compounds enable the monitoring and the combination of the unique physic-chemical properties of their ingredients.

Among semiconductor alloys, the system of continuous solid solutions of $In_{1-x}Ga_xAs$ is of particular interest. High mobility of electrons, direct energy bands, complete miscibility of InAs and GaAs in an arbitrary proportion in solid state enable creation on their base a wide variety of set of fundamental semiconductor devices of the new generation. The remarkable manufactural properties of ternary $In_{1-x}Ga_xAs$ alloys make them truly the best nanotech performance materials and very useful for manufacture nanotech products, such as nanowires, nanotubes, etc.

At the same time due to the unique mutual opposite radiation properties of InAs (radiation increases current carrier concentration) and GaAs (radiation reduces current carriers concentration) $In_{1-x}Ga_xAs$, alloys are potential materials to create devices with the immunity to radiation like InAsP solid solutions.[1] Therefore, the development of improved technology for obtaining $In_{1-x}Ga_xAs$ solid solutions of binary semiconductor compounds is an urgent problem. For successful solution of this problem, it is necessary to reveal their intrinsic properties and eliminate the effect of strains and dislocations existing in thin films and layers, which is possible by investigating single crystals of $In_{1-x}Ga_xAs$ solid solutions in bulk form. Obtained results will be valid for crystals in thin films and layers form too. Therefore, the purpose of the given work is to develop an acceptable efficient**,** simplified method, in comparison with the existing ways of obtaining bulk crystals of $In_{1-x}Ga_xAs$ alloys.

Features of obtaining of InGaAs solid solutions

$In_{1-x}Ga_xAs$ solid solutions may be obtained by different methods. The choice of the technique for obtaining solid solutions of $In_{1-x}Ga_xAs$ depends on the purposes and scales of application. Among these methods of producing solid solutions, there is the growth of epitaxial layers by vacuum evaporation and condensation, and crystallization using a chemical transport reaction through a gaseous phase. However, these methods differ by the small amount of material received and are designed for specific devices. At the same time, the purity of the resulting material is determined by the purity of the original components. Directional crystallization method is also used to produce crystals of $In_{1-x}Ga_xAs$ solid solutions. Several versions of this method for obtaining bulk crystals of semiconductor

decomposed double and triple III–V materials have been developed.[2–6] As a rule, these methods are preceded by synthesis.

The synthesis of solid solutions of III–V binary compounds, as materials with high vapor pressure, requires a method which makes it possible to control the vapor pressure of volatile components. The disadvantage of the majority of existent methods is that they need two stages: synthesis, and then growing the crystal. Growth of ternary single bulk crystals may be carried out by several newly developed industrially important methods such as Bridgman, and zone melting of multicomponent thermal decomposing compounds.

In the given paper, there has been chosen, as a basis, LEC – the liquid encapsulated Czochralski method as a combined process of synthesis and crystal growth method of InGaAs bulk crystals. It has been taken into account that InGaAs alloys have complete miscibility in the solid state and their lattice parameter increases linearly with the fraction of InAs. These properties and the liquid-solid phase diagram of $In_{1-x}Ga_xAs$ solid solutions allows to be limited by a two-component system and consider InGaAs as a pseudo-binary alloys system of two components of III–V semiconductors $(GaAs)_{1-x}$ and $(InAs)_x$, which dissolve continuously in an arbitrary proportion in solid state and form homogeneous system of continuous of solid solutions.[7,8]

The liquid-solid phase diagram shows that crystallization of InGaAs solid solutions is a very complicated process. The whole difficulty is that the pseudo-binary solid solutions crystallize in the temperature range and the process is inclined to internal crystalline liquation. This means that a solid phase is separated in continuous solid solutions, which at gradual cooling retains an elevated concentration of the high-temperature component in comparison with the equilibrium concentration. In the case of $In_{1-x}Ga_xAs$ solid solutions during the crystals growth from the melt, the composition of the primary crystal is enriched by GaAs, while the final part of the ingot is richer in InAs.

This phenomenon has been taken as a basis of our technology of the production of homogenous $In_{1-x}Ga_xAs$ solid solutions for the preparation of crystals with different composition in one ingot. The proposed method is fundamentally different from the methods for obtaining $In_{1-x}Ga_xAs$ crystals with a specific composition in one ingot, and, in turn, requires other conditions of the processing of crystal growth. That is why the aim of the present study is to establish experimentally the limits of the physical possibilities of segregation crystal growth of $In_{1-x}Ga_xAs$ solid solutions, which have favorable components equilibrium segregation coefficients at growing by directional crystallization.

Experimental

The bulk crystals of $In_{1-x}Ga_xAs$ solid solutions have been obtained by direct fusion of their initial components of InAs and GaAs compounds, and then grown by directional crystallization with the known Czochralski method of pulling crystals from melt. The synthesis operation preceding the process of growing of homogeneous InGaAs solid solutions is not fundamentally different from the synthesis of individual InAs and GaAs compounds from the stoichiometric melt. The proposed method makes it possible to avoid the synthesis as a separate process and combine synthesis with the growing of crystal. The obtained $In_{1-x}Ga_xAs$ crystals have been grown in a special chamber. The basic assembly of the technological part of the equipment, which scheme is shown in the Fig.1, presents a high-pressure system of melting camera for growing crystals of semiconductors in the Ar gas atmosphere.

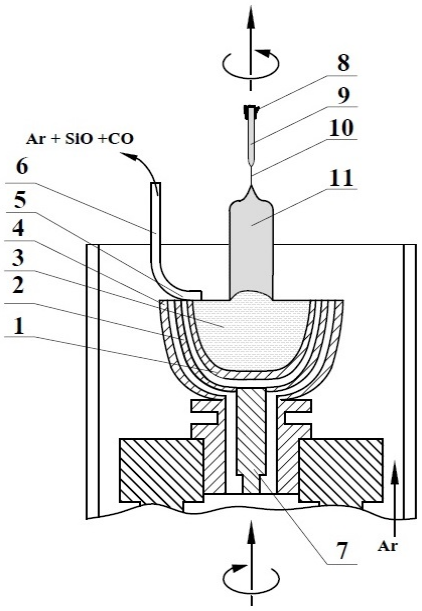

Figure 1. Scheme of vacuum equipment for the production of crystals of $In_{1-x}Ga_xAs$ solid solutions. 1 – quartz crucible, 2 – graphite stand, 3 – melt in the flux capsule, 4 – heater, 5 and 6 – gas-drawing device, 7 – crucible moving axis, 8 – seed moving rod, 9 – seed, 10 – crystal neck, and 11 – crystal of $In_{1-x}Ga_xAs$ solid solution.

The quartz crucible (1) with a charge has been placed on graphite support (2). The graphite supporting block and quartz crucible with the uterine melt of InGaAs are possible to rotate around an axis (7) and move vertically for selection of necessary temperature conditions. Revolving mechanism of graphite supporting block and quartz crucible is placed in the lower part of equipment under the processing chamber. Penetration into an inner space of a chamber is provided by the door, which is closed hermetically and has a viewing window. The lower part of a chamber is connected to the vacuum-gas distributional system.

The fusion of InAs and GaAs, as decomposing semiconductor materials, has been carried out under a protective layer, which prevents intensive evaporation of the volatile As and melt overheating. Best of all, practically unique flux is boron anhydride, which satisfies requirements of chemical stability at the melting points of InGaAs solid solutions (942–1240°C**):** the smaller density than for InAs and GaAs compounds, immiscibility with a melt of InAs and GaAs, As vapor insolubility, transparency allowing controlling the process of seeding a single crystal. However, arsenic, although weakly, dissolves in boron anhydride, which leads to losses of As. Therefore, to reduce losses of As above molten flux, the pressure of the inert gas over the melt has been supported higher than the equilibrium vapor pressure of the volatile component of arsenic at the same

temperature. The flux used softens at a temperature at which the vapor pressure of arsenic is negligible and the mother melt was located in a capsule of boron anhydride.

Pieces of charge are loaded in a quartz crucible (1) an amount to fill crucible volume after melting. At the bottom of the quartz crucible (low-temperature zone), there has been placed a small excess of crushed arsenic, to compensate the evaporation losses, from above a mixture of InAs and GaAs. The mixture has been covered with pieces of B_2O_3, which provide a layer of 20–30mm thick after melting. For compensating of the arsenic losses during melting due to its evaporation, the amount of arsenic has been taken with excess and was calculated by the formula:

$$P_{As}=PVM/RT,$$

where

P = 0.34atm (the equilibrium vapor pressure of the volatile component of arsenic over the melt),

V is the volume of the camera in liters, M is the molecular weight of As_4 steam,

R is the universal gas constant (0.082 atm $mol^{-1}K^{-1}$), and

T is the temperature of the crucible.

The melting process has been carried out in a flowing environment of protective inert argon gas under 0.5atm pressure. The chamber is preliminarily pumped out up to10^{-4} Hgmm pressure. After that, the chamber is washed by a slow flow of argon with equipped special apparatus for gas removing (gas-extracting arrangement – 5 and 6). Finally, the chamber is filled with argon up to appropriate pressure. After delivery electricity to the equipment and reaching a suitable temperature a gas-extracting arrangement is switched on. The delivery and pumping out of inert gas is regulated in such way, that pressure of argon permanently stays on the 0.5 atm level. Then the heater has been turned on and the crucible heated to a temperature of 820–880 °C. First, the flux is melted, then the charge. A liquid mixture of components is formed with heat release, and, as a result, the temperature rises to the melting point of the desired composition in the upper part of the crucible. The melting point varies depending on the composition (x) from 942 °C (for InAs) to 1240 °C (for GaAs) and the temperature slightly exceeded the melting point of the desired composition of solid solution.

Gas release products of a chemical reaction from graphitic details and quartz crucible are typical for the melting process. These chemical agents adjoin closely to the surface of the capsule of boron anhydride, are partly dissolved in it and contaminate it. Therefore gas-extracting arrangement (5 and 6) with pressure relief pipe is included in the processing camera. It removes gas release products of chemical reaction at the same moment as they origin at melting process from the processing chamber.

When the desired melting point has been reached at the top of the crucible, the melt has been maintained at this temperature for 30min to homogenize the melt. The accuracy of the temperature preservation was high because the temperature dependence of the pressure of saturated arsenic vapor has the logarithmic regularity. After the fusion had been completed, pulling of crystal with normal crystallization (heat ejection on all sides) has been performed by the Czochralski method. GaAs crystalline rods oriented in the direction [111] with the length of 50 mm were used as the seeds. A seed crystal has dipped, through flux layer, into the melt. The rotated seed has slowly pulled single crystal from the lower end of the seed. During crystallization along the ingot, a temperature gradient was maintained at which crystallization occurs at the fixed point of the ingot and the crystallization front moves along the ingot by pulling. The obtained crystal has been subjected to slow cooling. During the process of the crystal pulling the crucible with the mother melt revolved with the rate of rotation 45 and 10 revolutions per minute in opposite directions has provided uniformity on the cross section of the bulk crystals. The pulling rate of ~ 0.25–0.30 mm per minute was supported to be equal to the growth rate of crystals to keep the growth temperature constant. Such conditions provide the symmetry of temperature field at the crystallization front into the crucible and compositional uniformity in the crystal of InGaAs. The content of pulled from melt InGaAs crystals after the directional crystallization has been defined by X-ray diffraction method by modernized DRON–4–07 the equipment at Mo-radiation in 0.5 degrees min^{-1}, micro X-ray spectral and emissive spectral analyses. The heterogeneities of experimental samples have been controlled by electrical properties measurements too. Effective segregation coefficient of components has also been calculated.

Results and discussion

The method we used is relatively simple and available compared to other methods. The volatile component of arsenic melts at 800 °C, and the flux at 300 °C softens and melts at 460 °C. The flux forms a thick, viscous liquid which coats the entire melt, including the crucible and in combination with the pressure in the chamber prevents sublimation of As. The flux used softens and melts at a temperature at which the vapor pressure of arsenic is negligible and the mother melt has been located in a capsule of boron anhydride. This allows a direct fusion of the initial components for the production of InGaAs solid solutions.

The method of obtaining a crystal by pulling from the melt does not ensure the uniformity of the composition along the length of the crystal. The crystal has a characteristic gradient in the distribution of the original components along the length. This gradient in the composition of solid solutions, the so-called segregation, depends on the form of the solidus, the difference between solid and liquid phase composition and on the position along the ingot. So at the directional crystallization, the separation of the components of the solid solution depends on the segregation coefficient of a component of InAs and GaAs compounds. The magnitude of equilibrium segregation coefficient of components is determined by the liquid-solid phase diagram of InGaAs and depends on the composition of alloy.[7,8]

So, depending on the value of the segregation coefficient of components gradient along the crystal may be different. The equilibrium segregation coefficient of GaAs in InAs is

much higher than unity. Therefore, the concentration of GaAs near the seed reaches the maximum value and gradually decreases towards the end of the crystal. The solid phase that is released during the crystallization of the InAs–GaAs alloys retains an increased concentration of GaAs at decreasing temperature as compared to the equilibrium composition of the initial melt.

This distinctive attribute of obtaining graded composition distribution along the length of the ingot has been applied to derive benefit from this feature. Carefully selected conditions of fusion and growing of crystal allowed to obtain across the ingot uniformity in the composition of components and chemically stable several compositions of InGaAs solid solutions by one fusion.

The method of direct fusion of InAs and GaAs compounds has been applied in given work for producing crystals at InAs-rich side of InGaAs alloys system. At this, the segregation degree of components is determined by the part of the liquid-solid state diagram of alloys in InAs-rich side of the system, which is shown in the Fig.2**.**

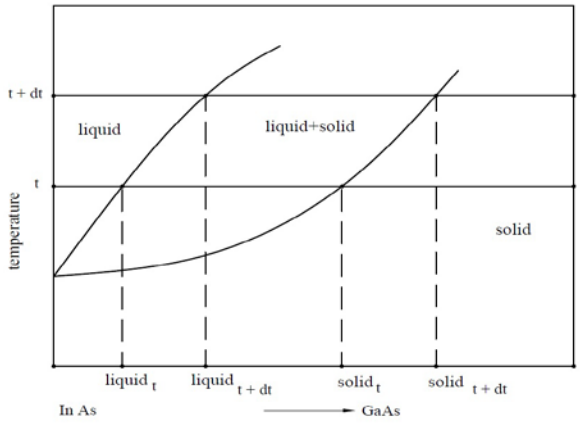

Figure 2. Generalized part of the state diagram of InGaAs continuous solid and liquid solutions in system's InAs-rich side**.**

Crystallization of a solid solution consists of two processes:

(1) The formation of crystals of a solid solution of "solid $_t$" composition, which is in equilibrium with the "liquid $_t$" only at a given temperature *t*: "liquid $_t$" ↔ "solid $_t$." This process assumes diffusion only in the liquid phase and proceeds comparatively easily.

(2) The change in the composition by relatively enriched by GaAs crystals formed at high-temperature *t* + *dt*. This process assumes continuous interaction of the precipitated solid phase with the melt and a change in its composition.

Therefore, only when the rate of cooling of the melt does not exceed the rate of the changes, which occur in the system of the melt-solid phase, a homogeneous solid solution crystallizes. The precise control of the temperature at the growing interface at directional crystallization and crystal pulling speed enabled to achieve uniformity in composition in the cross sections of the ingot. Therefore, it was possible to obtain solid solutions with a uniform composition over a wide range of compositions in InAs-rich InGaAs solid solutions. The crystal composition is determined only by the temperature at the growing interface.

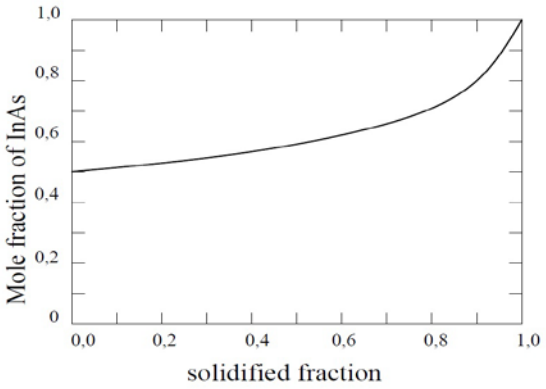

Figure 3. Dependence of InAs composition on a solidified fraction of melt at producing InAs-rich InGaAs solid solutions.

The dependence of InAs content on the solidified fraction of melt at producing the InAs-rich InGaAs solid solutions is shown in the Fig.3. The figure shows the slight change of the solid composition of InGaAs components along the length of the ingot.

The dependence presented in Fig.3 reflects the phenomenon of accumulation of content of InAs little by little in the melt while InGaAs crystal is pulling from melt. So during the process of crystal growth, the melt is slowly enriched by InAs because of worse solubility in the solid phase. GaAs concentration straight at the surface exceeds their concentration in the melt.

InAs content function in InGaAs crystal of the solidified fraction of the GaAs-InAs pseudo-binary growth melt depends on effective segregation coefficient of InAs in GaAs. This process is characterized by the effective segregation coefficient (k_{eff}) of the components, which is the ratio of the concentration of one of the components dissolved in the solid phase to the concentration- in the liquid phase. The effective segregation coefficient of InAs in GaAs for experimental samples has been calculated on the base of experimentally established data of components composition. The effective segregation coefficient of InAs in GaAs has been calculated and found to be 1.025 in presented conditions of melting. That reflects the weak dependence of InAs content on the solidified fraction of growth melt at producing the InAs-rich InGaAs alloys. Therefore the composition of the homogeneous bulk crystals of *n*-type $In_{0.8}Ga_{0.2}As$, $In_{0.7}Ga_{0.3}As$, and $In_{0.6}Ga_{0.4}As$ can be freely selected in one ingot crystals.

Typical X-ray diffraction spectra, X-ray microspectral, emissive spectral analyses, microstructure and electrical properties have shown that obtained single crystals have been single-phase with good uniformity of composition. Fluctuations of components concentration were found to be less than 1 at.%.

Conclusion

There have been obtained ternary $In_{1-x}Ga_xAs$ solid solutions bulk crystals in the InAs-rich side of this system. The method of direct fusion of InAs and GaAs compounds

enable to achieve uniformity in composition in the cross sections of the ingot. The weak dependence of InAs content on the solidified fraction of melt let freely select several compositions in the InAs-rich side of this InGaAs alloys system in one ingot.

Acknowledgment

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ACCESSIBILITY OF ZWITTERIONIC COMPOUNDS FROM PRIMARY AMINES AND 2,5-DIHYDROXY-1,4-BENZOQUINONE

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Keywords: C–N activation; hydrogen bonds; quinones; amination; zwitterions

Following the discovery of an unprecedented transamination reaction between primary alkylamines and a quinonoid molecule of the type $C_6H_2(NHCH_2R)_2(=O)2$ (I), obtained from commercially available diaminoresorcinol.2HCl, we have extended this method to the use of primary arylamines and found that, in contrast, secondary amines led to a different outcome. Whereas functionalized molecules of type **I**, which are best described as 6π +6π zwitterions, were obtained with aniline or 4-methoxyaniline, no transamination was observed with $tBuNH_2$ in ethanol. However, a reaction which afforded salt 2-methylpropan-2-aminium 4-(methylamino)-3,6-dioxocyclohexa-1,4-dien-1-olate (**2b)** took place in water and resulted from hydrolysis of the imine group and deprotonation of 5-hydroxy-2-(methylamino)-4-(methylimino)-cyclohexa-2,5-dienone (**1a)**. Under similar conditions, secondary amines led to comparable results. The cations associated with the anionic quinonoid are readily exchanged in the presence of a primary amine. Whereas for the transamination reaction, basic amines react under mild conditions, slightly harsher conditions are needed for less basic amines such as piperidine, diisopropylamine, or diethylamine. Transamination reactions were also performed with 5-hydroxy-2-(methylamino)-4-(methylimino)-cyclohexa-2,5-dienone (**1a)**, which is more soluble in organic solvents than 2-amino-5-hydroxy-4-iminocyclohexa-2,5-dienone (compound **I**) This led to the first examples of quinonoidal zwitterions functionalized with different alkyl groups on the nitrogen atoms. A number of compounds were characterized by X-ray diffraction, which allowed a better understanding of their electronic situation, and in many cases, the presence of multiple hydrogen-bond donors and acceptors results in crystal packings dominated by these interactions.

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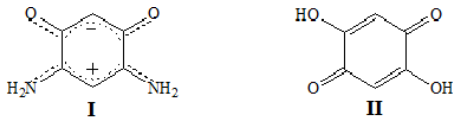
Introduction

Organic compounds containing a quinonoid fragment are of great interest because of their intrinsic properties and their numerous applications in chemistry, physical chemistry and biology.[1-26] In particular, benzoquinonemonoimines have been found to display unique properties in various areas such as coloring,[27] organic,[28,29] supramolecular,[30] coordination, organometallic chemistry[30,31,38,39] and homogeneous catalysis.[32-37] Previous studies have shown that the reactions between alkylamines or arylamines and benzoquinone gave a trans-dialkylaminobenzoquinone or trans-diarylamino-benzoquinone and monoarylamino products.[40-41] Similar reactions with 2,5-dihydroxybenzoquinone have been achieved yielding trans-dialkylaminobenzoquinone and diarylaminobenzoquinone products whose nickel complexes are very active in catalysis.[42] Benzoquinonemonoimines were obtained by transamination reaction of alkyl and arylamines with specific reactants like diaminoresorcinol dihydrochloride or by esterification reaction followed by reduction.[38] The aim of this paper is to show that trans-dialkylaminobenzoquinone and diarylaminobenzoquinones can be obtained with 2,5-dihydroxybenzoquinone at high temperature. Benzoquinonemonoimines products can be obtained by classical condensation reaction followed by nucleophilic substitution of alkylamines with 2,5-dihydroxybenzoquinone.



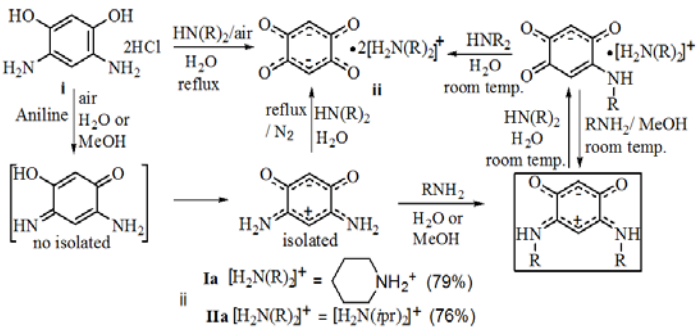
Scheme 1. A zwitterion 6π + 6 π electrons (**I**) and a precursor of zwitterion 12π electrons (2,5-dihydroxy benzoquinone) (**II**).

The first member of this family of 12π-electron quinine was the dianion ligand resulting from deprotonation of compound **II**. The compound **I** is a zwitterion type involving 6π + 6 π electrons chemically not but electronically connected (Scheme 1).

From these reactions, it's possible to convert **I** to **II** by hydrolysis reactions with bulky primary amines or secondary amines in water. The zwitterionic products obtained by reaction of **I** with primary alkylamines were isolated from the reactions of **II** and primary alkylamines at room temperature. The para aminoalkyl-1,4-benzoquinone were obtained after reflux or a long time reaction from **II**.

Result and discussion

The dianionic salts were obtained by hydrolysis reactions of benzoquinonemonoimine in an aqueous solution containing the primary or secondary alkylamine (Scheme 2).



Scheme 2. Amination and hydrolyzed reactions on the parent quinonmonimine zwitterion

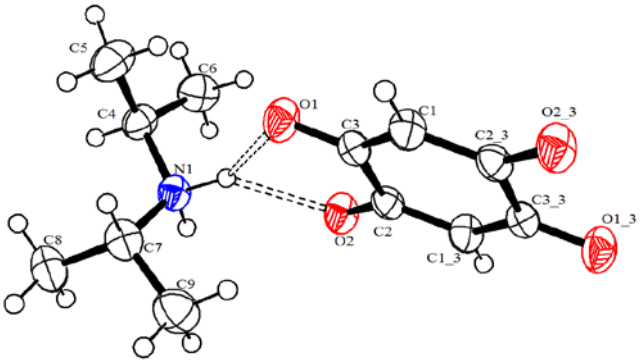
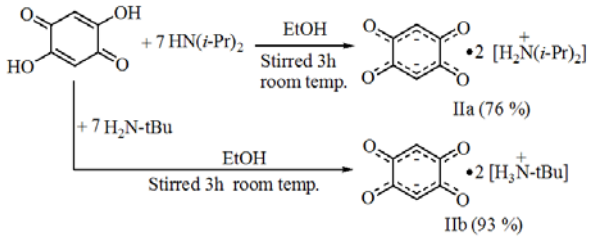


Figure 1. Partially labeled plot of compound **IIa**. Dashed lines indicate H-bonding interactions. The thermal ellipsoids are shown at 50% probability.

The first alkylamine selected for the synthesis of functionalized 2,5-dihydroxy-1,4-benzoquinone was *t*-butylamine. Using a large excess of *t*-butylamine, a dianionic salt was obtained with a yield of 93 % (Scheme 3). The reaction of 2,5-dihydroxy-1,4-benzoquinone **II** with the bulky primary and secondary amine, respectively (NH_2-*t*Bu) and NH(*i*-Pr)$_2$ resulted in the deprotonation of the dihydroxybenzoquinone (Scheme 3).

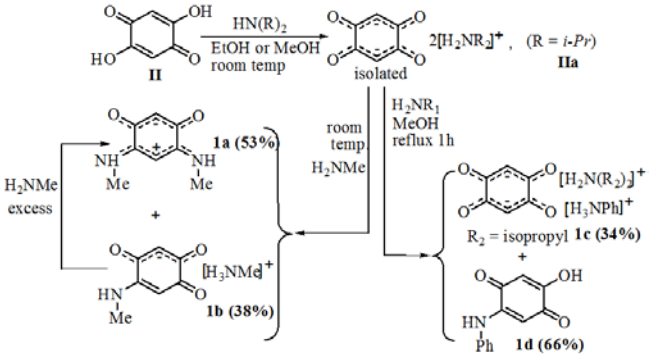


Scheme 3. Encumbered primary amine and secondary amines effect on the 2,5-dihydroxy-1,4-benzoquinone

On the course, except the *t*-butylamine, all primary alkylamines react by transamination on the parent zwitterion **I**. Probably the steric effect of these amines is low. In the alcohol solution, ^{t}BuNH$_2$ react with 2,5-dihydroxy-1,4-benzoquinone to afford an organic salt **IIb**. The NMR data show one singlet for *O···C···CH* group at 5.74 ppm for **IIb**, 5.15 ppm for the first dialkylamine **IIa** (76% yield). The ^{13}C{^{1}H} NMR spectra reveal signals at 115.29 ppm for **IIb** and 101.46 ppm for **IIa** for CH group (*O···C···CH*). The chemical shift of *O···C* group was shown at 181.88 ppm for **IIb** and 181.75 ppm for **IIa**, which was confirmed by single-crystal X-ray diffraction (**Figure 1**). All crystal structures determined in the course of this work are discussed in a separate paragraph (see below).

Surprisingly, when organic salt **IIa** was treated with MeNH$_2$, a complete transamination product **1a** and uncomplete transamination product **1b** was observed. In alcohol or water, **1b** can react with the excess of MeNH$_2$ to afford the product **1a** (see Scheme 2). The NMR spectra of these two products were described in analog reaction in our previous work.[44] In this optic, the organic salt **IIa** was treated by an excess of aniline under reflux in methanol.

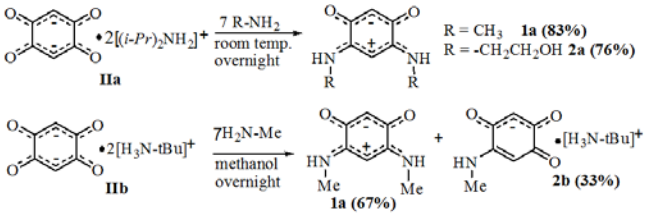
Two products were isolated. The organic diammonium salt [NH$_2$(*i-Pr*)$_2$(PhNH$_3$)(C$_6$H$_2$O$_4$)] (**1c**) was observed as a solid compound while the filtrate solution afforded the monoamino derivative (2-hydroxy-5-(phenylamino)-cyclohexa-2,5-diene-1,4-dione [(PhNHC$_6$H$_3$O$_3$)] (**1d**) (Scheme 4). The ^{1}H NMR spectra contain two signals at 5.74 and 5.84 ppm, which are characteristic of the CH groups of the substituted benzoquinone fragment (N-C=CH and O=CH-C, respectively). ^{13}C{^{1}H} NMR spectroscopic data show two signals for the CH groups, and the one corresponding to N-C=CH shift to 95.80 ppm, downfield with respect to that of the zwitterion. The O=C-**CH**=C-OH resonance was found at 103.97 ppm. The quaternary carbon atoms give rise to five singlets, two of them corresponding to the two O=C carbon atoms with very close chemical shifts to 180.38 and 182.68 ppm. One of the single bond HO-C is shifted to 161.03 ppm. In the aromatic ring, the quaternary carbon atoms give two singlets corresponding to N-C= and =C-N bonds shifted to 146.11 and 137.71 ppm respectively.



Scheme 4. Mono and di-condensation reactions between organic salt and methyl and arylamine

The **IIa** was reacted at room temperature during 3 h with methylamine to form **1a** and with the (2-hydroxyethyl)amine to give **2a**. Both zwitterions **1a** and **2a** have been characterized in the course of previous work.[33] The salt **IIb** reacts with methylamine in methanol solution at room temperature to afford a mixture of **1a** and the organic

salt [(NH_3-tBu)($C_7H_6O_3$)] (**2b**). The **2b** compound can be obtained by hydrolysis reaction of **1a** with tert-butylamine in water from a mixture of **2b** and [(NH_3-Me)($C_7H_6O_3$)] (**1b**) (Scheme 5). In dichloromethane solution, it's possible that the **1b** exchange the methylammonium cation by tert-butylammonium cation yielding **2b**. Surprisingly, **1b** reacts by condensation and transamination reaction with methylamine to afford **1a**. The same compound was obtained by condensation reaction between the organic salt **IIa** or **IIb** and alkyl amines. From the compound **IIa**, it's possible to access the zwitterionic compounds by condensation reactions between **IIa** and primary alkyl amines (methylamine) (**1a**) or (2-aminoethanol) (**2a**). It's an interesting route to access from the quinonemonoimines to products obtained exclusively by transamination reactions or by a more efficient synthesis subsequently developed, which involved the diaminoresorcinol acylation followed by reduction by $LiAlH_4$.[26]



Scheme 5. Reactivity of monoalkylamines on the organic salts by direct condensation reaction

Herein, we report that the scope of this reaction can be extended to primary arylamine. In contrast, secondary amines afforded only organics salts. Gratifyingly, $^tBuNH_2$ reacted at room temperature in methanol, within 1 h, to yield the corresponding salt of type **IIb**, in 93 % yield. Its ^1H and $^{13}C\{^1H\}$ NMR spectroscopic data are consistent with the expected structure, which was confirmed by single-crystal X-ray diffraction (**Figure 2**).

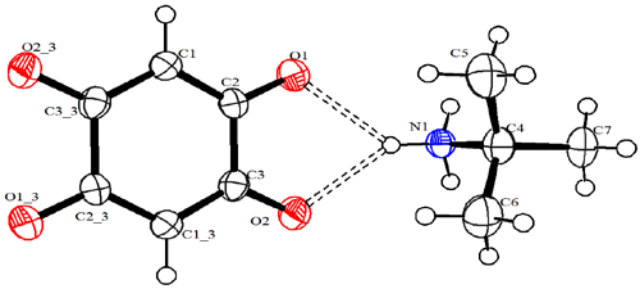
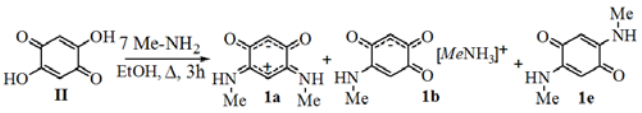


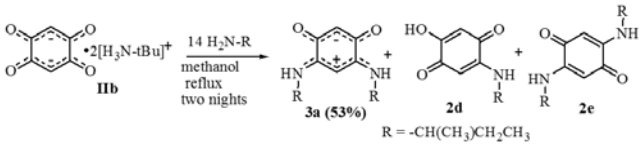
Figure 2. Partially labeled plot of compound **IIb**. Dashed lines indicate H-bonding interactions. The thermal ellipsoids are shown at 50 % probability.

The reaction of **II** with methylamine was performed under reflux within 3 h, whereas the reaction with diisopropylamine afforded **IIa** at room temperature**.** The monoanionic salt **1b** which was previously isolated acts as a reaction intermediate in the conversion of **1a** into **1e** (Scheme 6).



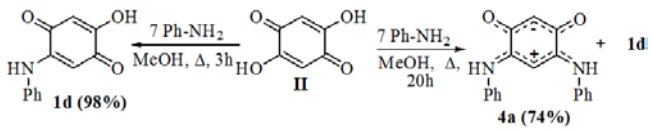
Scheme 6. Reactivity of methylamine on the 2,5-dihydroxy-1,4-benzoquinone giving free different products

Knowing that **1a** reacts with primary amines by transamination reaction, we verified that aniline is not basic enough to perform this transformation. Upon crystallization of the reaction mixture, **1a** was indeed recovered, but the composition of the crystals was found to be [(**1a**)$_2$PhNH$_2$].[44] Another zwitterionic benzoquinonemonoimine was obtained by a condensation reaction between the corresponding alkylamine and the organic salt **IIb** (Scheme 7). The sec-butylamine and organic salt **IIb** react under reflux for overnight to yield three products **3a**, **2d** and **2e**. The main product **3a** was obtained after dissolved the crude product in chloroform solution. The ^1H NMR of **3a** reveal signals of the quinonoid fragment at 5.14 (s, 1H, N···C···C**H**), 5.48 (s, 1H, O···C···C**H**), 8.10 (br s, 2H, 2N**H**). $^{13}C\{^1H\}$ NMR 80.52 (s, N···C···**C**), 98.85 (s, O···C···**C**), 155.73 (s, N···**C**), 172.23 (s, O···**C**). For **2d**, two singlets at 5.42 (s, 1H, N-C=CH) and 5.90 (s, 1H, O=C-CH) were revealed, while one singlet is obtained for the **2e** product at 5.97 (s, 2H, O=C-CH).



Scheme 7. Obtaining symmetrical zwitterionic and two neutrals organics products

The reaction of **II** with excess of aniline yield the monoarylamino derivative **1d** after 3 hours under reflux. Progressively **1d** was converted into the zwitterionic 3-hydroxy-4-(phenylamino)-6-(phenylimino)cyclohexa-2,4-di-enone derivative **4a** (Scheme 8).

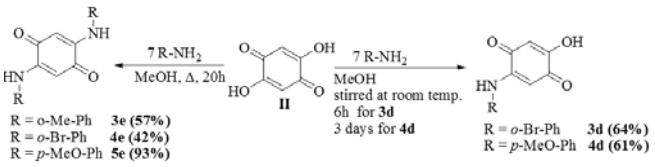


Scheme 8. Effect of reflux time on condensation between aniline and 2,5-dihydroxy-1,4-benzoquinone

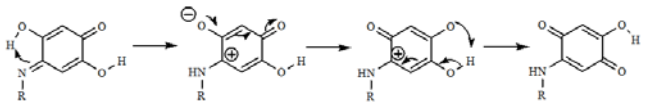
This species **4a** was only observed from **II** and aniline reaction. Other similar reactions give p-diamino-1,4-benzoquinone products. It's observed that the substituted arylamines have high reactivity with the reagent **II**. The product **4a** was obtained[56] from the other transamination reaction between the parent zwitterion **I** and an excess of aniline in the ethanol solution under reflux. The products **1d** (98 %), **3d** (64 %) and **4d** (61 %) were isolated with high purity. The {^1H} NMR spectra of these products contain singlets at 5.13 (s, 1H, N-C=C**H**); 5.87 (s, 1H, O=C-C**H**) for

3d and at 5.57 (s, 1H, N-C=C**H**); 5.81 (s, 1H, O=C-C**H**) for **4d** (Scheme 9).

These monoaminohydroxybenzoquinones products were considered like intermediaries of reactions synthesis between reagent **II** and alkylamines. For a long time or under reflux, these reactions lead only the trans-diarylamino-1,4-benzoquinones. When **II** was reacted with substituted anilines, such as *o*-$MeC_6H_4NH_2$, *o*-$BrC_6H_4NH_2$, *o*-$ClC_6H_4NH_2$, and (*p*-MeO)$C_6H_4NH_2$ the corresponding disubstituted diamino benzoquinones respectively **3e, 4e** and **5e** were isolated. The yield was respectively, 57; 42 and 93 %. We noted from the NMR spectra that the monoamino derivatives **3d** and **4d** were found to be intermediates in the synthesis of **4e** and **5e** respectively. A mechanism of the monocondensation is achieved in Scheme 10.



Scheme 9. Obtaining different products under reflux and at room temperature



Scheme 10. Mechanism of monocondensation with the formation of 2-hydroxy-5-(arylamino)-1,4-benzoquinone

X-ray crystal structure determination for IIa and IIb

The title compounds **IIa** and **IIb** crystallize in the monoclinic space group $P2_1/c$, with one complete zwitterion comprising the asymmetric unit. The two ammonium groups are orientated *trans* with respect to the plane of the central 3,6-dioxocyclohexa-1,4-diene-1,4-bis(olate) ring. Intramolecular interactions within the solid-state structure of the zwitterion are between the two oxygen atoms of each side of the central ring and one H atoms of the nitrogen atom of the ammonium groups. The distances C—O, which are in the range 1.256(2)–1.2667(19) Å are indicative of a bond character slightly different from a double bond (Table 1). In both rings, two moieties of O···C···C···C···O which contain a fully delocalized 6π electrons system are connected by two single bonds with distances of 1.531(3) Å and 1.526(3) Å respectively in **IIa** and **IIb**. These facts show that the non-conjugation of the two 6π electrons systems in the central rings of the zwitterions. As shown by the torsion angles (Table 1) whole atoms of the rings are quasi- coplanar. The torsions angles are slightly different from the ideal angle of 180° and 0° in the planar ring.

Experimental

Chemical reagents in high purity were purchased from Merck and Aldrich and were used without further purification.

Table 1. Selected bond lengths (Å) and torsions angles (°) for the central ring **IIa** and **IIb**

IIa		**IIb**	
O1—C3	1.256(2)	C3—O2	1.259(2)
O2—C2	1.2677(19)	C2—O1	1.261(2)
C1—C2i	1.385(3)	C3—C1i	1.395(2)
C1—C3	1.402(2)	C1—C2	1.394(2)
C2—C3	1.531(3)	C2—C3	1.526(3)
C2i—C1—C3—O1	−178.8 2)	C2i—C1—C3—O2	-179.1(2)
C2i—C1—C3—C2	0.7(3)	C2i—C1—C3—C2	1.0(3)
O2—C2—C3—O1	−1.0(3)	O1—C2—C3—O2	-1.1(3)

The ^1H NMR spectra were recorded at 300 MHz and $^{13}C\{^1H\}$ NMR spectra at 75 MHz on a Bruker AC-300 instrument. Mass spectra were recorded with a Bruker Daltonics microTOF (ESI; positive and/or negative mode; capillary voltage: 4.8 kV; nebulizer pressure: 0.2 bar; desolvation temperature: 180°C; desolvation gas flow rate: 4.5 L/min). Elemental analysis was performed by the Service de Microanalyse, Université de Strasbourg (Strasbourg, France) and the Service Central d'Analyse (Lyon, France).

X-ray data collection, structure determination and refinement

Single crystals of **IIa** and **IIb** were grown by slow evaporation of MeOH solution. A suitable crystal was selected and mounted on a Bruker APEX-II CCD diffractometer with graphite monochromatized MoKα radiation (λ = 0.71073 Å). The crystal was kept at 173(2) K during data collection. Details of the X-ray crystal structure solution and refinement are given in Table 1. The structure was solved with the *SHELXT*[45] structure solution program using direct methods and refined with the *SHELXTL*[46] Software Package. Molecular graphics were generated using *ORTEP-3*.[47]

Synthesis of the compounds

Compound Ia: dipiperidinium 3,6-dioxocyclohexa-1,4-diene-1,4-bis(olate)

Piperidine (0.43 g, 5.07 mmol) was added to a water (30 mL) solution of 2-amino-5-hydroxy-4-iminocyclohexa-2,5-dièнone (0.1 g, 0.724 mmol). The mixture was heated to reflux for five hours. After cooling the solution was washed with dichloromethane solution (3 x 10 mL) then the excess of piperidine was eliminated. The aqueous phase was evaporated and a red solid was obtained (0.178 g, 79 %)

^1H (300 MHz, dmso-d_6) δ(ppm): 8.363 (m, 4H, $2NH_2^+$); 4.969 (s, 2H, N-C=CH-C=O); 2.943 (t, 8H, -CH_2-N-CH_2-); 1.60 (tt, 8H, -CH_2-CH_2-CH_2-); 1.55 (tt, 4H, -CH_2-CH_2-CH_2-)

Table 2. Data collection and refinement parameters for **IIa** and **IIb**

	IIa	**IIb**
Formula	$C_{18}H_{34}N_2O_4$	$C_{14}H_{26}N_2O_4$
M_r	342.47	286.37
Cell setting, Space group	Monoclinic, $P2_1/c$	Monoclinic, $P2_1/c$
a, b, c (Å)	8.7510(6), 9.8940(6), 13.6680	8.4560(10), 7.3850(9), 15.0882(12)
β (°)	122.505(3)	116.893(6)
V (Å^3)	998.02(11)	840.32(6)
Z	2	2
D_x (Mg m^{-3})	1.140	1.132
μ (mm^{-1})	0.08	0.08
Crystal size (mm)	0.18x0.14x0.12	0.22×0.20×0.10
meas.,indep., obs. refl.	3761, 2277, 1073	2517, 1590, 968
R_{int}	0.0579	0.092
θ_{max} (°)	27.485	26.32
$R[F^2 > 2\sigma(F^2)]$, $wR(F^2)$, S	0.0571, 0.1416, 0.94	0.0534, 0.1517, 0.99
Parameters	117	106
$\Delta\rho_{max}$, $\Delta\rho_{min}$ (e Å^{-3})	0.18, –0.212	0.21, –0.23

^{13}C (75 MHz, dmso-d_6), δ(ppm): 179.275 (O···C···CH···C···O); 99.86 (O···C···CH); 43.84(s, CH_2-N-CH_2-); 22.09 (s, CH_2-CH_2-CH_2-); 22.54 (s, CH_2-CH_2-CH_2-). RMN ^{13}C-DEPT 135 (75 MHz, dmso-d_6), δ(ppm): 99.86 (O···C···CH···C···O); 43.84 (s, CH_2-N-CH_2-); 22.09 (s, CH_2-CH_2-CH_2-); 22.54 (s, CH2-CH_2-CH_2-). Anal. Found C, 50.82; H, 6.91; N, 7.26. Calc. for $C_{17}H_{26}N_2O_4 \cdot CH_2Cl_2$ C, 51.65; H, 7.14; N, 7.09.

Compound IIa: diisopropylammonium 3,6-dioxocyclohexa-1,4-diene-1,4-bis(olate)

Diisopropylamine (1.53 g, 15.16 mmol) was added to an ethanol (10 mL) solution of 2,5-dihydroxy-1,4-benzoquinone 1 (0.304 g, 2.17 mmol). Immediately a precipitate appeared in the mixture which is stirred for 3h. The pink solid product was filtered, washed with diethyl ether (2 x 40 mL) and then dried. The product was obtained as a pink solid (0.57 g, 1.66 mmol, 76 %). Suitable crystals for X-ray diffraction were obtained by slow evaporation of an ethanol solution of the product. From the zwitterionic reactant, this product was obtained after reflux in water.

^{1}H NMR (300 MHz, dmso-d_6), δ(ppm): 5.15 (s, 2H, O···C···CH); 3.24-3.25 (m, 4H, -CH-NH_2^+); 1.14 (d, 24H, CH_{3iPr}). ^{13}C{^{1}H} NMR (75 MHz, D_2O), δ(ppm): 18.28 (s, CH_3ipr); 47.22(s, CHipr); 101.46 (s, O···C···CH); 181.75 (s, O···C). These ammonium salts react with primary amines to lead symmetric zwitterionic compounds.

Compounds IIb: 2-methylpropan-2-aminium 3,6-dioxocyclo-hexa-1,4-diene-1,4-bis(olate)

Tert-butylamine (1.096 g, 14.98 mmol) was added to an ethanol (20 mL) solution of 2,5-dihydroxy-1,4-benzoquinone 1 (0.3 g, 2.14 mmol). Red precipitate was immediately formed. The reaction mixture was stirred at room temperature for 3h and then filtered. The red solid was washed with diethyl ether (4 x 20 mL) and air dried (0.57 g, 1.99 mmol, 93 %). Suitable crystals for X-ray diffraction were obtained by slow evaporation of an ethanol solution of the product.

^{1}H NMR (300 MHz, dmso-d_6), δ(ppm): 5.74 (s, 2H, O···C···CH); 1.20 (s, 18H, -CH_3). ^{13}C{^{1}H} NMR (75 MHz, dmso-d_6), δ(ppm: 26.57 (s, CH_3); 51.86 (s, C_{tBu}) 115.29 (s, O···C···CH); 181.88 (s, O···C).

Compound 1a: 5-hydroxy-2-(methylamino)-4-(methylimino)-cyclohexa-2,5-dienone and compound 2b: 2-methylpropan-2-aminium 4-(methylamino)-3,6-dioxocyclohexa-1,4-dien-1-olate from the tert-butylammonium salt (IIb):

Methylamine (0.152 g, 4.89 mmol) was added to an ethanol (20 mL) solution of the salt 2 (0.2 g, 0.698 mmol). The mixture was stirred for 24 hours at room temperature. The mixture was checked by NMR ^{1}H analysis after the solution was evaporated under reduced pressure. A brown solid was analyzed by NMR ^{1}H, which shows the formation of two products 1a (67%) and 1b (33 %). After stirring for three nights, 1a was afforded.

Compound 1a: ^{1}H NMR (300 MHz, dmso-d_6), δ(ppm): 2.99 (s, br, 6H, CH_3); 4.93 (s, 1H, N···C···C-H); 5.32 (s, 1H, O···C···C-H); The broad signal of NH is not observed near to 9.13 ppm. ^{13}C NMR (75 MHz, dmso-d_6), δ(ppm) = 29.57(s, CH_3); 81.26 (s, N···C···C-H); 97.42(s, O···C···C-H); 156,80(s, C···N); 172,12(s, C···O). Compound 2b: δ(ppm): 1.22 (s, 9H, CH_{3tBu}); 2.70-2.68 (d, 3H, ^{3}J = 4.98 Hz, CH_3); 4.88 (s, 1H, N-C=C-H); 4.90 (s, 1H, O···C···C-H); 7.24 (br s, 1H, NH) ; 7.86 (br s, 3H, NH_3).

Compound 1a: 4-(methylamino)-6-(methylimino)-3-oxocyclohexa-1,4-dien-1-olate and 1b: methylammonium 6-(methylamino)-3,4-dioxocyclohexa-1,5-dien-1-olate from the 2,5-dihydroxy-1,4-benzoquinone (II):

Methylamine (0.31 g, 10 mmol) was added to an ethanol (20 mL) solution of 2,5-dihydroxy-1,4-benzoquinone 1 (0.2 g, 1.43 mmol). Immediately a precipitate was formed (acid-basic reaction). The reaction mixture was stirred under reflux during 3h and a clear red solution is obtained. After cooling, the red solution was reduced by slow evaporation. The product was precipitated in diethyl ether (2x30 mL). The crude brown solid was obtained by filtration then dried under reduced pressure. The crude mixture was composed of two products **1a** and **1b**. The ^{1}HNMR analysis shows results in accordance with those reported above for **1a**.

Compound 1b: ^{1}H NMR (300 MHz, dmso-d_6), δ(ppm): 2.37 (s, 3H, CH_3); 2.69-2.70 (d, 3H, ^{3}J = 4.83 Hz, CH_3); 4.94 (s, 1H, N-C=C-H); 4.99 (s, 1H, O-C=C-H); 7.28 (s, 1H, NH); 7.67 (br s, 3H, NH_3).

The diethyl ether solution was evaporated and a small quantity of product was obtained. The ^{1}H NMR analysis of this product revealed to be a mixture of **1a** and **1e**. The crude product was suspended in dichloromethane (20 mL) and stirred at room temperature during 1 h. The solid obtained after filtration is essentially constituted by **1a** (0.14 g, 0.76 mmol, 53 %). The product **1b** (0.09 g, 0.54 mmol, 38 %) was obtained by evaporation of dichloromethane solution.

Compound 1a: 4-(methylamino)-6-(methyliminio)-3-oxocyclohexa-1,4-dien-1-olate

Methylamine (0.125 g, 4.08 mmol) was added to an ethanol (20 mL) solution of the diisopropylammonium salt of 3,6-dihydroxy-1,4-benzoquinone (**IIa)** (0.2 g, 0.58 mmol). The reaction mixture was stirred at room temperature for two days. The solvent was evaporated and the remaining solid was washed with diethyl ether (2x10 mL). The product was obtained as a brown solid (0.08 g, 0.48 mmol, 83 %). The ^{1}H NMR spectrum analysis revealed that this product contained essentially the compound 1a.

Direct synthesis of compound 1d: 2-hydroxy-5-(phenyl amino) cyclohexa-2, 5-diène-1, 4-dione

Aniline (0.46 g, 4.97 mmol) was added to a methanol (20 mL) solution of 2,5-dihydroxy-1, 4-benzoquinone **II** (0.1 g, 0.71 mmol). The reaction mixture was heated to reflux during 3h. The solvent was removed in vacuum, and the crude solid was washed with pentane (4 x 20 mL). The product was obtained as a purple solid 1d (0.15 g, 0.697 mmol, 98 %).

^{1}H NMR (300 MHz, dmso-d_6), δ(ppm): 5.74 (s, 1H, N-C=C-H); 5.84 (s, 1H, O=C-C-H); 7.20-7.22 (t, 1H,CH) ; 7.36-7.42 (m, 4H, CH_{Ar}) ; 9.24 (s, 1H, NH); 11.21 (s, br 1H, OH). ^{13}C{^{1}H} NMR (75 MHz, dmso-d_6), δ(ppm): 95.80(s, C-C=N) ; 103.97 (s, O=C-C-H) ; 123.49 (s, CH) ; 125.36 (s, CH); 129.14(s, CH); 137.71(s, Cq); 146.11 (s, C-N) ; 161.03 (s, C-O) ; 180.38(s, C=O); 182.68 (s, C=O). The mass spectrum indicates different fragments corresponding to cationic molecules MS (ESI$^+$): m/z = 222.074(15) {[M+Li]$^+$, 15 %, [$C_{12}H_9LiNO_3$]$^+$}; m/z = 228.082 ([{(M-H)+Li}+Li]$^+$, 11 %, {$C_{12}H_9Li_2NO_3$}$^+$); m/z = 238.048 ([M+Na]$^+$, 9 %, {$C_{12}H_9NaNO_3$}$^+$); m/z =244.056 ([{(M-H) + Li} + Na]$^+$, 2 %, {$C_{12}H_9LiNaNO_3$}$^+$). Anal. Calcd. for $C_{12}H_9NO_3$.4/3H_2O: C, 60.25; H, 4.92; N, 5.86; found C, 60.92; H, 4.95; N, 5.65.

Compounds 3a: 4-(butan-2-ylamino)-6-(butan-2-yliminio)-3-oxocyclohexa-1,4-dien-1-olate , 2d: 2-(sec-butylamino)-5-hydroxycyclohexa-2,5-diene-1,4-dione and 2e: 2,5-bis(sec-butylamino)cyclohexa-2,5-diene-1,4-dione

Sec-Butylamine (0.620 g, 8.43 mmol) was added to a methanol (20 mL) suspension of the organic salt **IIb** (0.172 g, 0.602 mmol). The reaction mixture was heated to reflux for two days, allowed to cool to room temperature and after removal of the solvent; the crude red product was obtained and suspended in chloroform (20 mL). The suspension was stirred a room temperature for two hours. The solid was separated by filtration and the red filtrate was evaporated. The product was obtained as a red solid (0.080 g, 0.32 mmol, 53 %). For the NMR analysis, two minor products were detected. ^{1}H NMR (300 MHz, chloroform-d_1), δ(ppm): 5.42 (s, 1H, N-C=CH), 5.90 (s, 1H, O=C-CH) monoalkylamino-hydroxybenzoquinone 2d. ^{1}H NMR (300 MHz, chloroform-d_1), δ(ppm): 5.97 (s, 2H, O=C-CH) trans-dialkylamino-1, 4-benzoquinone 2e.

Compound 3a: ^{1}H NMR (300 MHz, chloroform-d_1), δ(ppm): 0.98 (t, ^{3}J= 7.5 Hz, 6H, CH_2CH_3), 1.31 (d, ^{3}J=6.5Hz, 6H, $CHCH_3$), 1.69 (pent, ^{3}J=7.2 Hz, 4H, CH_2), 3.62 (m, 2H, NCH), 5.14 (s, 1H, N-C-CH), 5.48 (s, 1H, O-C-CH), 8.10 (br s, 2H, NH); ^{13}C NMR (75 MHz, chloroform-d_1), δ(ppm): 10.40 (s, CH_2CH_3), 19.55 (s, $CHCH_3$), 29.16 (s, CH_2), 50.87 (s, NCH), 80.52 (s, N-C-C), 98.85 (s, O-C-C), 155.73 (s, N-C), 172.23 (s, O-C).

Compound 4a: 3-oxo-4-(phenylamino)-6-(phenylimino)cyclohexa-1,4-dienolate

Aniline (4.65 g, 49.96 mmol) was added to a methanol (100 mL) solution of the 2,5-dihydroxy-1,4-benzoquinone **II** (1 g, 7.14 mmol). The reaction mixture was heated to reflux for 19 h. The solvent was partially removed, then the solid product was isolated by precipitation with the addition of pentane (200 mL). The crude solid was obtained as a brown mixture containing two products **4a** and **1d**.

The ^{1}H NMR spectrum indicates that the brown solid was a mixture of two products: the monoaniline **1d** and the bis-aniline **4a** in the respective proportions 26 % and 74 %.

Compound **4a**: ^{1}H NMR (300 MHz, dmso-d_6), δ(ppm: 5.20 (s, 1H, N-C=C-H); 5.81(s, 1H, O-C=C-H); 7.29-7.46 (m, 10H, CH_{Ar}); 10.96 (s, 2H, NH). To complete the assignment of the carbons, those carrying protons H were identified by the sequence ^{13}C{^{1}H} DEPT 135. ^{13}C{^{1}H} NMR (75 MHz, dmso-d_6), δ(ppm: 85.13 (s, N-C-CH) ; 98.07 (s, O-C-CH) ; 124.74 (s, CH) ; 127.39 (s, CH); 129.12 (s, CH); 136.37 (s, Cq); 155.42 (s, C-N) ; 177.76 (s, C-O). MS (ESI$^+$) m/z = 291.11([M+H]$^+$; 70 %). Anal. Cald.

for $C_{18}H_{14}N_2O_2 \cdot 1/6H_2O$: C, 73.71; H, 4.93; N, 9.55; Found: C, 73.72; H, 5.23; N, 9.77.

After several washing with acetonitrile solvent, the compound 4a was obtained with a majority proportion (the estimated percentage of monoamine (**1d**) by ^{1}H NMR was <15 %).

Compound 1d: 2-hydroxy-5-(phenylamino)cyclohexane-1,4-dione and 1c: benzenaminium diisopropylammonium 3,6-dioxocyclohexa-1,4-diene-1,4-bis(olate)

Aniline (0.29 g, 3.08 mmol) was added to a methanol (20 mL) solution of diisopropylammonium salt of 3,6-dihydroxy-1,4-benzoquinone **IIa** (0.077 g, 0.22 mmol). The reaction mixture was heated to reflux during 1 h. The solvent was removed in vacuum and the crude solid was washed with pentane (2x10 mL). The product was obtained as a red solid. The ^{1}H NMR analysis reveals that the crude solid was a mixture of two products. A sample was suspended in the dichloromethane (20 mL) and stirred at room temperature during 1 h, and filtered. The orange solid precipitate is identified as **1d** (0.031 g, 0.14 mmol, 66 %). The remaining solution was evaporated to afford compound **1c** (0.025 g, 0.074 mmol, 34 %).

Compound 1c: ^{1}H NMR (300 MHz, dmso-d_6) δ(ppm): 1.10-1.13 (d, 12H, CH_3isop) ; 3.14-3.23 (m, 2H, CHipr) ; 5,15(s, 2H, O-C-C-H); 6.44-7.0142 (m, 5H, CH_{Ar}); 8.65 (br, 3H, NH); 9.31 (br, 2H, NH) .

Compound 2a: 4-[(2-hydroxyethyl)amino]-6-[(2-hydroxyethyl)iminio]-3-oxocyclohexa-1,4-dien-1-olate

Ethanolamine (0.125 g, 2.04 mmol) was added to an ethanol (10 mL) solution of the diisopropylammonium salt of 2,5-dihydroxy-1,4-benzoquinone 3 (0.1 g, 0.29 mmol). The reaction mixture was stirred during 20 h at room temperature under nitrogen atmosphere. The solvent was removed under vacuum and then the solid product was washed with pentane (2x10 ml) and diethyl ether (10 mL). The product was obtained as a brown solid (0.05 g, 0.22 mmol, 76 %).

^{1}H NMR (300 MHz, dmso-d_6), δ(ppm): 7.70 (s, 2H, 2HN-); 5.59 (s, 1H, CH-C-O); 4.97 (m, 3H, CH-C-N, 2OH); 3.62 (t, 4H CH_2O); 3.46 (t, 4H, CH_2N). ^{1}H NMR (300 MHz, water-d_2): δ(ppm): 5.55 (s, 1H, CH-C-O); 5.28 (s, 1H, CH-C-N); 3.77 (t, 4H, ^3J = 5.2 Hz, CH_2O); 3.56 (t, ^3J = 5.2 Hz, 4H, CH_2N).

Compound 3d: 2-(2-bromophenylamino)-5-hydroxycyclohexa-2,5-diene-1,4-dione

2-Bromoaniline (1.28 g, 7.44 mmol) was added to a methanol (50 mL) solution of 2,5-dihydroxy-1,4-benzoquinone **II** (0.15 g, 1.07 mmol). The reaction mixture was firstly stirred for 6 h but the conversion was very small. Then the reaction mixture was heated to reflux during 1 h and cooled to room temperature. After reduction of the solvent by evaporation, the product was precipitated with addition of diethyl ether (20 mL). The compound 3d was obtained as pink solid (0.2 g, 0.68 mmol, 64%). ^{1}H NMR (300 MHz, dmso-d_6), δ(ppm) : 5.13 (s, 1H, N-C=CH); 5.87 (s, 1H, O=C-CH) ; 7.24-7.30 (m, 1H, CH) ; 7.41-7.51 (m, 2H, CH) ; 7.75-7.78 (m, 1H, CH); 9.05 (s, 1H, NH); 11.56 (br,1H, OH). ^{13}C NMR (75 MHz, dmso-d_6), δ(ppm) = 99.53(s, CH); 104.04 (s, CH); 120.03 (s, Cq_{Ar}); 127.67 (s, CH_{Ar}); 128.63 (s, CH_{Ar}), 128.86 (s, CH_{Ar}); 133.32 (s, CH_{Ar}); 135.97 (s, Cq_{Ar}); 146.61 (s, Cq_{Ar}); 160.78 (s, =C-OH); 180.12 (s, C=O); 182.54 (s, C=O).

Compound 4d: 2-hydroxy-5-(4-methoxyphenylamino)cyclohexa-2,5-diene-1,4-dione

4-Methoxyaniline (0.92 g, 7.49 mmol) was added to a methanol (50 mL) solution of 2,5-dihydroxy-1,4-benzoquinone **II** (0.15 g, 1.07 mmol). The reaction mixture was stirred a room temperature for 3 days. After reduction of the solvent by slow evaporation, the suspension was precipitated by addition of diethyl ether (20 mL), then filtered. The product was obtained is dried into the air, resulting in brown solid (0.16 g, 0.65 mmol, 61 %). The remaining solution obtained after filtration contained essentially 4-methoxyaniline.

^{1}H NMR (300 MHz, dmso-d_6), δ(ppm): 5.57 (s, 1H, N-C=CH); 5.81 (s, 1H, O=C-CH); 6.97 - 6.99 (d, 2H, =CH); 7.25-7.28 (d, 2H, =CH) ; 9.20 (s, 1H, NH); 11.12 (br, 1H, OH). The ^{1}H NMR spectrum further shows a singlet proton signal is observed at 5.61 ppm, this signal is attributed to the protons of the para-substituted product. ^{13}C NMR (75 MHz, dmso-d_6), δ(ppm): 55.23 (s, CH_3); 94.85 (s, CH); 103.79 (s, CH); 114.37 (s, CH); 125.28 (s, CHAr); 130.28 (s, CHAr); 146.83 (s, CHAr); 156.95 (s, CHAr); 179.83 (s, C=O).

Compound 3e: 2,5-bis(methylamino)cyclohexa-2,5-diene-1,4-dione

2-Methylaniline (4.12 g, 38.49 mmol) was added to a methanol (20 mL) solution of 2,5-dihydroxy-1,4-benzoquinone **II** (0.77 g, 5.49 mmol). The reaction mixture was stirred to reflux 20 h, allowed cool to room temperature. The precipitate was recovered by filtration and washed with diethyl ether (2x15 mL) to obtain a brown solid (1g, 3.14 mmol, 57 %). The melting point of the compound 3e is in the range 252-254 °C. ^{1}H NMR (300 MHz, dmso-d_6), δ(ppm): 2.20 (s, 6H, $2CH_3$); 5.01 (s, 2H, N-C=CH); 7.22-7.36 (m, 8H, CH) ; 8.85 (s, 2H, NH). ^{13}C{^{1}H} DEPT (75 MHz, dmso-d_6), δ(ppm): 16.71 (s, CH_3); 94.14(s, O=C-CH C-) ; 125.60 (s, CH_{Ar}) ; 126.32(s, CH_{Ar}); 126.65 (s, CH_{Ar}); 130.51 (s, CH_{Ar}); 133.51 (s, Cq, C_{Ar}); 135.60 (s, Cq, C_{Ar}); 148.95 (s, C-N); 178.48 (s, C=O). MS (ESI$^+$): m/z = 341.13 ([(M+Na)]$^+$, 51%, {$C_{20}H_{18}N_2O_2Na$}$^+$); m/z = 318.14 ([(M)], 28 %, {$C_{20}H_{18}N_2O_2$}$^+$). Anal. Calcd. for $C_{20}H_{18}N_2O_2$: C, 75.45; H, 5.70; N, 8.80: found C, 75.36, H, 5.80; N, 8.78.

Compound 4e: 2,5-bis(2-bromophenylamino)cyclohexa-2,5-diene-1,4-dione

2-Bromoaniline (1.28 g, 7.44 mmol) was added to a methanol (50 mL) solution of 2,5-dihydroxy-1,4-benzoquinone **II** (0.15 g, 1.07 mmol). The reaction mixture was heated to reflux 20 h and allowed to cool to room temperature. The precipitate was recovered by filtration and washed with diethyl ether (2x10 mL). The product was

obtained as pink solid (0.2 g, 0.45 mmol, 42 %). ^{1}H NMR (300 MHz, dmso-d_6), δ(ppm): 5.31 (s, 2H, N-C=CH); 7.32-7.29 (m, 2H, CH) ; 7.50-7.46(m, 4H, CH); 7.80-7.77 (m, 2H, CH); 8.94 (s, 2H, NH). ^{13}C{^{1}H} DEPT (75 MHz, dmso-d), δ(ppm): 95.45 (s, -C=CH-C-) ; 126.80 (s, CH_{Ar}) ; 128.11(s, CH_{Ar}); 128.52 (s, CH_{Ar}); 133.0 (s, CH_{Ar}). ^{13}C{^{1}H} NMR (75 MHz, dmso- d_6), δ(ppm): 95.70 (s, -C=CH-C-); 119.30 (s, Cq , C_{Ar}); 126.80 (s, CH_{Ar}); 128.12 (s, CH_{Ar}); 128.52 (s, CH_{Ar}); 133.0 (s, CH_{Ar}); 135.66 (s, Cq, C_{Ar}); 147.31 (s, Cq, Ar); 178.92 (s, Cq, C=O). MS (ESI$^+$): m/z = 454.94 ([(M+2H) +Li]$^+$, 87 %, [$C_{18}H_{14}Br_2N_2O_2Li$]$^+$). Anal. Calcd. for $C_{18}H_{12}Br_2N_2O_2$: C, 48.25; H, 2.70; N, 6.25: found C, 48.31, H, 2.44; N, 6.18.

Compound 5e: 2,5-bis(4-methoxyphenylamino)cyclohexa-2,5-diene-1,4-dione

4-Methoxyaniline (0.92 g, 7.49 mmol) was added to a methanol (50 mL) solution of 2, 5-dihydroxy-1, 4-benzoquinone **II** (0.15 g, 1.07 mmol). The reaction mixture was heated to reflux 20h. After cooling, the product precipitated and the solvent was slowly evaporated. The precipitate was washed with acetone then dried in air. The product was obtained as a brown solid (0.35 g, 0.99 mmol, 93 %). ^{1}H (300 MHz, dmso-d_6) at room temperature, δ(ppm): 3.67 (s, 6H, OCH_3); 5.61 (s, 2H, N-C=C-H); 6.98-7.01 (d, 4H, $^3J_{HH}$ =9.95 Hz, CH); 7.27-7.29 (d, 4H, $^3J_{HH}$ =9.95 Hz, CH); 9.25 (s, 2H, NH). ^{1}H and ^{13}C NMR was achieved at temperature near (~80 °C). ^{1}H NMR (300 MHz, dmso-d d_6), δ(ppm): 3.80 (s, 6H, -OCH_3); 5.63 (s, 2H, N-C=C-H); 6.99-7.01 (d, 4H, $^3J_{HH}$ =9.95 Hz, CH); 7.27-7.29 (d, 4H, $^3J_{HH}$ =9.95 Hz, CH); 8.89 (s, 2H, NH). ^{13}C{^{1}H} DEPT (75 MHz, dmso-d d_6), δ(ppm) = 54.98 (s, OCH_3); 94.11 (s, -C=CH-C-); 114.23 (s, CH_{Ar}); 124.73 (s, CH_{Ar}). ^{13}C{^{1}H} NMR (75 MHz, dmso-d d_6), δ(ppm) = 54.98 (s, OCH_3); 94.11 (s, -C=CH-C-) ; 114.23 (s, CH_{Ar}) ; 124.73 (s, CH_{Ar}); 130.08 (s, Cq_{Ar}); 147.71 (s, Cq_{Ar}); 156.84 (s, N-C=C) ; 178.72 (s, C=O). The infrared analysis revealed absorption bands around: 1635(s, C=O), 1610(s, C=N) , 1557(s, C=C), 1515(s, C=C), 1481 (s), 1460 (s), 1413 (s) , 1358 (s), 1288 (s), 1257 (s), 1188 (s), 1172 (s), 1110 (m), 1030 (s), 822 (s), 776 (s), 718 (s). MS(ESI$^+$) m/z = 351.13([M+H]$^+$, 62 %). Anal. Calcd. for $C_{20}H_{18}N_2O_4.CH_2Cl_2$: C, 57.94; H, 4.63; N, 6.44; found C, 58.21; H, 4.36; N, 6.67. MS(ESI$^+$) m/z(%) = 351.13(62) ([M+H]$^+$

Conclusions

We have shown that the scope of the reaction leading to the functionalization of the 2,5-dihydroxy-1,4-benzoquinone can be extended from the alkyl to aryl groups. Furthermore, by performing a condensation reaction on the 2,5-dihydroxy-1,4-benzoquinone bearing substituent on the hydroxyl group, the organics salts were obtained. Further extension of the scope of these reactions to secondary amines has proved impossible because 2,5-dihydroxy-1,4-benzoquinone undergoes total acid-base reactions, leading to a series of ionic salts. Finally, we showed that these salts react with primary alkyl amines or aryl amines to generate à zwitterionic structure which can be hydrolyzed, leading to a new series of ionic salts or to give dianionic salts. Two crystals structures have been determined which provide a firm basis for the description of electronic situation in these molecules.

Supplementary material

CCDC 1914357 and 769670 contain the supplementary crystallographic data for the reported complex. These data can be obtained free of charge via http://www.ccdc.cam.ac.uk/conts/retrieving.html, or from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: (+44)-1223-336-033; e-mail: deposit@ccdc.cam.ac.uk. or www: http:// www.ccdc.cam.ac.uk).

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CRYSTAL STRUCTURE OF 2-BROMO-4-HYDROXYPYRIDINE: HYDROGEN AND HALOGEN BONDING

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Keywords: crystal structure; hydrogen bonding; halogen bonding.

The crystal structure of 2-bromo-4-hydroxypyridine **(1)** at 120 K is reported. The compound crystallizes in the monoclinic space group *C*2/c with a = 15.6770(6) Å, b = 3.86471(13) Å, c = 18.0645(7) Å and β = 90.916(3)°. The compound exhibits both the 4-hydroxypyridine and 4-pyridone tautomers as exhibited by the disordered proton which occupies the O-H and N-H positions equally. Hydrogen bonding links the molecules into chains parallel to the *ac*-face diagonal. Halogen bonds [Br … O = 3.0809(15) Å] roughly parallel to the *a*-axis link the chains into layers roughly parallel to the *bc*-face diagonal. π-stacking interactions complete the stabilization of the structure.

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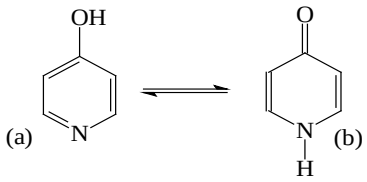
Introduction

2- and 4-Hydroxypyridine molecules are known to be in equilibrium with their tautomeric pyridone forms as shown in Scheme 1.



Scheme 1. The tautomeric forms of (a) 4-hydroxypyridine and (b) 1(H)-4-pyridone.

The crystal structure of the parent compound shows it to be in the 1(H)-4-pyridone form in the solid state, with two polymorphs reported.[1] The tautomerizeable hydrogen atom was located in the lattice and its position refined to clearly demonstrate the tautomer present. The molecules are linked into chains via strong hydrogen bonds ($d_{\text{N-H...O}}$ = 2.66 Å). As a result of the possibility of different tautomers, multiple coordination modes are available to the ligand. Coordination in the pyridone form through the O-atom is clearly preferred and multiple compounds have been reported with the O-coordinated to both transition metal[2] and lanthanide ions.[3] The O-atom is also known to bridge alkali earth metal,[4] transition metal[5] and lanthanide metal ions.[6] Some coordination complexes are known with the molecule N-coordinated in the hydroxypyridine form, but most of these involve 2nd and 3rd row transition metal ions.[7]

We have become interested in the use of hydroxypyridine/pyridone molecules as ligands[8] in particular because of the potential for hydrogen bonding and related intermolecular interactions assisting in the stabilization of extended lattices. One such system is 2-halo-4-hydroxypyridine. An investigation of the literature showed only two reported crystal structures involving such a potential ligand and both are esterified at the O-atom.[9] Here we report the crystal structure of 2-bromo-4-hydroxypyridine.

Experimental

2-Bromo-4-hydroxypyridine was purchased from Ark Pharmaceutical and recrystallized from methanol.

X-Ray structure analysis

Data for **1** were collected using an Agilent Technologies Gemini Eos CC X-ray diffractometer with Mo Kα radiation (λ = 0.71073 Å). Data reduction and correction for Lp and decay were performed using CrysAlisPro.[10] A Gaussian absorption correction was applied via ABSPACK.[Hiba! A könyvjelző nem létezik.] The structure was solved using the SHELXS-97 program[11] and refined via least-squares analysis via SHELXL-2016.[12] Non-hydrogen atoms were refined using anisotropic thermal parameters. Hydrogen atoms bonded to nitrogen and oxygen atoms were located in the difference Fourier maps and their positions refined using fixed isotropic thermal parameters. Antibumping restraints were applied to both N11-H11 and O14-H14 to avoid unrealistically short bond lengths. The remaining hydrogen atoms were placed in geometrically calculated positions and refined using a riding model and fixed isotropic thermal parameters. Crystallographic information and details of the data collection can be found in Table 1.

Results

Compound **1** crystallizes in the monoclinic space group *C*2/*c*. The molecular unit is shown in Figure 1. The tautomerizable proton (H11/H14) is disordered over the two positions. The occupancy was allowed to refine freely and resulted in equal occupancies for the two sites [0.50(3)]. This suggests equal contributions to the structure from the 4-hydroxypyridine and 4-pyridone forms of the molecule.

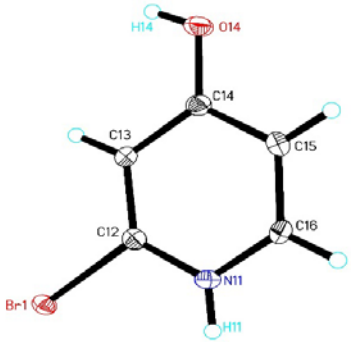


Figure 1. Thermal ellipsoid plot of the molecular unit of **1** showing 50% probability ellipsoids. Only the asymmetric unit and those H-atoms whose positions were refined are labelled.

This is further supported by the packing of the molecules in the lattice. Hydrogen bonding generates chains of molecules parallel to the *ac*-face diagonal in an alternating head-to-head/tail-to-tail fashion (Figure 2). The hydrogen bonding parameters are presented in Table 3.

Table 1. X-ray data of compound 1.

Empirical formula	**C_5H_4BrNO**
Formula weight	174.00
Temperature	120.0(1) K
Wavelength	0.71073 Å
Space group	*C*2/c
a	15.6770(6) Å
b	3.86471(13) Å
c	18.0645(7) Å
α	90°
β	90.916(3) °
γ	90°
Volume	1094.34(7) $Å^3$
Z	8
Density (calculated)	2.112 Mg m^{-3}
Absorption coefficient	7.392 mm^{-1}
F(000)	672
Crystal size	0.21 x 0.10 x 0.06 mm^3
θ range for data collection	5.179 to 26.35°
Index ranges	$-19 \le h \le 19$ $-4 \le k \le 4$ $-22 \le l \le 22$
Reflections collected	5856
Independent reflections	1112 [*R*(int) = 0.0300]
Absorption correction	Gaussian
Max. and min. transmission	0.960 and 0.887
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	1112 / 2 / 80
Goodness-of-fit on F^2	1.059
Final *R* indices [$I>2\sigma(I)$]	R^1 = 0.0172, wR_2 = 0.0396
R indices (all data)	R^1 = 0.0191, wR_2 = 0.0404
Largest diff. peak and hole	0.335 and -0.311 e $Å^{-1}$

Adjacent molecules are related either by an inversion center (O14/O14B) or a two-fold axis (N11/N11A). The apparent double hydrogen bonds seen in Figure 2 are the result of the disorder of the hydrogen atom position.

Table 2. Selected bond lengths [Å] and angles [°] for 1.

Bond	**Distance (Å)**
N11-H11	0.82(2)
O14-H14	0.81(2)
C14-O14	1.296(2)
Bond	**Angle (°)**
C12 N11 C16	117.67(17) 116.94(18)
C15 C14 C13	
O14 C14 C13	122.77(19)
O14 C14 C15	120.29(18)

In each case either H14 or H14B/H11 or H11A are present, but not both. Given the need to have one entire hydrogen atom present in each position to complete the hydrogen bonding, this suggests that in any given chain only one position is occupied, i.e. either H1A and H14, or H1 and H14B and that the chains are then unidirectional with respect to the orientation of the hydrogen atoms.

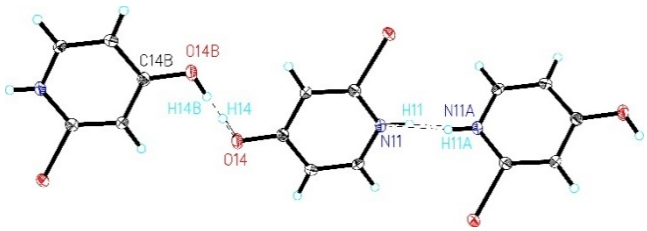


Figure 2. Chain formation via hydrogen bonding in **1**.

However, which chain is oriented in which direction must be random over the lattice, thus generating the disorder. In fact, the structure can be refined by locating the hydrogen atoms on their respective symmetry centers, but that results in unrealistically long O-H and N-H bonds.

Table 3. Hydrogen bonding parameters for 1.

D-H…A	**D-H (Å)**	**H…A(Å)**	**D…A(Å)**	**D-H…A(°)**
N11-H11-N11A	0.82(2)	1.93(2)	2.756(3)	174(5)
O14-H14-O14B	0.81(2)	1.71(2)	2.521(3)	172(7)

Symm. op.: A, -x, y, ½ - z; B, -x -1/2, ½ - y, 1-z.

The molecule itself is nearly planar with a mean deviation of 0.0191Å for the atoms within the ring. The oxygen and bromine atoms are displaced slightly to opposite sides of the plane of the ring (-0.0840 Å and 0.0237 Å respectively). The chains are linked into a complex system of interconnected pleated sheets via halogen bonds between the bromine atoms and adjacent oxygen atoms [$d_{Br1...O14A}$=3.0809(15) Å, $\angle_{C12\text{-}Br1...O14A}$=176.31(7)°, symm. op. A = ½ + x, y - ½, z.]. The resulting layers are further connected into a three-dimensional motif via π-stacking interactions and short Br… Br contacts parallel to the *b*-axis as shown in Figure 4. The interplanar distance between rings is 3.43(1) Å and the slip angle (the angle between the intercentroid axis and the normal to the plane) is 27°. The ring centroids and Br atoms are related by a unit cell translation and are separated by 3.864 Å, corresponding to the *b*-axis length.

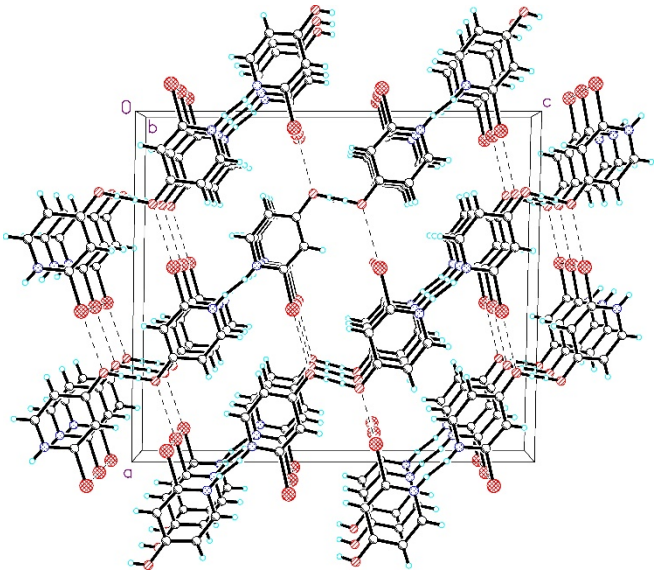


Figure 3. Packing of **1** viewed parallel to the *b*-axis showing the alternating layer structure.

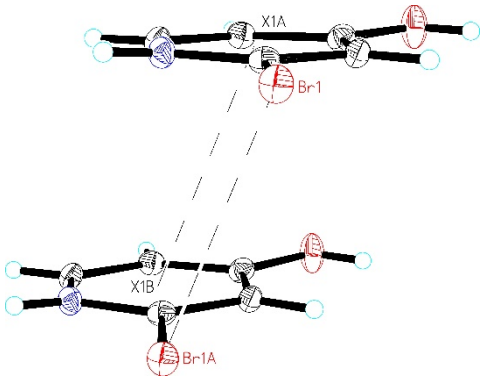


Figure 4. π-stacking between the pyridine rings of **1**. Dashed lines show connections between the ring centroids and short Br…Br contacts.

Discussion

The intermolecular interactions present in the 2-bromo-4-hydroxypyridine molecule make it a strong potential candidate for directing self-assembly of coordination complexes into three-dimensional lattices. The tautomeric forms provide the opportunity for coordination to the metal ions through either the N- or O-atoms. Hydrogen bonding between molecules is strong with D…A distances as short as 2.521(3) Å. The presence of the bromine atom makes distinct changes to the crystal structure. In the parent molecule, strong head-to-tail hydrogen bonding (D…A = 2.657Å)Hiba! A könyvjelző nem létezik. is observed in both polymorphs in contrast to the head-to-head/tail-to-tail form observed in 1. Further, the halogen bonds (Br…O) in 1 form in linkages between the chains resulting in a sheet structure, while the parent molecule exhibits only chains. Halogen bonding is known to compete effectively with hydrogen bonding in several systems.[13]

However, coordination of the N-atom to a metal ion will eliminate that as a potential hydrogen bonding site. Further, the presence of additional hydrogen bonding partners may disrupt the hydrogen bonding between ligand molecules as seen in the structure of 4-hydroxypyridine hydrate.[14] In this structure, there are several crystallographically independent molecules, most of which form the same head-to-tail hydrogen bonded dimers as seen in the parent molecule with additional hydrogen bonds to water molecules via the hydroxypyridine O-atom. In addition, there are 4-hydroxypyridine molecules in the lattice which exhibit only hydrogen bonding to water, generating a distinct chain structure of organic species alternating with pairs of water molecules.

Conclusions

It is clear that substitution of a bromine atom in the 2-position of 4-hydroxypyridine makes a distinct change in the structure of the material in the solid state. In addition to introducing halogen bonding, the conversion of the head-to-tail dimer structure normally seen in 4-hydroxypyridine to the head-to-head/tail-to-tail variety introduces new possibilities for the control of intermolecular forces in complexes of such ligands. Investigations of the corresponding 2-chloro compound are in progress.

Acknowledgements

MMT is grateful for the hospitality of the Chemistry Department at the University of Canterbury, Christchurch, New Zealand.

Supplementary data

CCDC 1921754 contains the supplementary crystallographic data for **1.** This data can be obtained free of charge via http://www.ccdc.cam.ac.uk/con-ts/retrieving.html, or from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: (+44) 1223-336-033; or email: deposit@ccdc.cam.ac.uk.

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ONE-POT SYNTHESIS OF PYRANOPYRAZOLES USING SODIUM LACTATE AS AN EFFICIENT CATALYST

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Keywords: catalyst; green synthesis; one pot; pyranopyrazole; sodium lactate.

An efficient one-pot synthesis of pyranopyrazoles has been achieved by the four-component condensation of hydrazine hydrate, ethyl acetoacetate, aldehydes and malononitrile using sodium lactate as a catalyst in aqueous ethanolic medium under reflux condition. The method is simple and green to afford pyranopyrazoles in a short time. It provides a new base catalyst that readily gives product from moderate to excellent yields.

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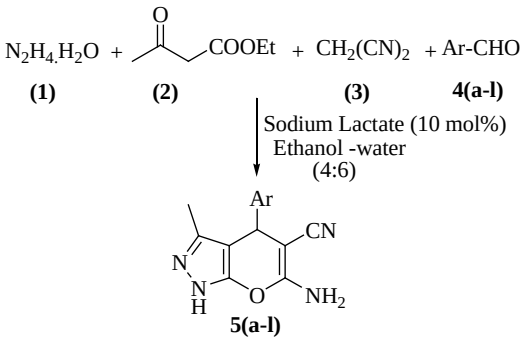
Introduction

Addition of three or more starting materials in one pot and their transformation to final product without isolation of intermediate provides a significant tool for organic synthesis. After the Strecker's amino acid synthesis, many successful attempts were made for organic transformations such as the synthesis of pyranopyrazoles which is one of themost important heterocycles of great biological significance. Pyranopyrazolescaffolds are reported for various biological activities such as analgesic, anti-inflammatory,[1] anti-bacterial,[2] anti-microbial,[3]andantitumor activity.[4]

Many methods are reported for the synthesis of pyranopyrazoles involving the use of three or four component condensation using $CeCl_3$,[5] $InCl_3$,[6] $La(NO_3)_3$,[7] ionic liquids such as $[(CH_2)_4SO_3HMIM][HSO_4]$,[8] [H-NMP][$MeSO_3$],[9] cetyltrimethylammonium chloride,[10] amino acids such as glycine,[11] L-tyrosine,[12] nano-particles such as CuI,[13] Fe_3O_4,[14] Fe_3O_4@SiO_2,[15] 1,3,5-triazine-2,4,6-triamine modified nano rice husk silica,[16] MgO,[17] ZnO,[18,19] and vitamin B_1 on silica coated ferrite (Fe_2O_3@SiO_2) nanoparticles.[20] Some heterogeneous catalysts like cerium (IV) carboxymethylcellulose,[21] acidic montmorillonite K-10 clay[22] are also documented for the one pot synthesis of pyranopyrazoles. Organic acids catalysing the synthesis of these heterocycles include citric acid, [23] and L-Proline.[24] Pyranopyrazoles can also be synthesized by using organic base catalysts like triethyl amine,[25-27] triethanol amine,[28] piperazine, piperidine, pyrrolidine and morpholine,[29] salts like ammonium chloride,[30] and sodium benzoate.[31]

However many of these methods have several drawbacks such as costly catalysts, harsh reaction condition and poor yields. In addition, the problem of waste remains an environmental question. In the present work, we report sodium lactate as a new environmentally benign base catalyst for the four-component synthesis of pyranopyrazoles from hydrazine hydrate, ethyl acetoacetate, malononitrile and various aldehydes (Scheme1).



Scheme 1. Four component pyranopyrazole synthesis.

Experimental

Melting points were recorded in open capillaries and are uncorrected. Structures of the synthesized products were assigned on the basis of spectral analysis. IR spectra were recorded on Shimadzu IR Affinity 1 spectrophotometer using KBr pellets. ^{1}H NMR spectra were recorded in DMSO-d_6 on a BRUKER AVANCE II 400 MHz spectrometer and the chemical shifts were expressed in ppm relative to TMS. Mass spectra were recorded on a Macro mass spectrometer by Electron Spray technique. Sodium lactate (60 %) solution was purchased from Loba Chemicals Pvt. Ltd. Progress of the reaction was monitored on silica pre-coated TLC plates in 40 % ethyl acetate: n-hexane.

General procedure

A mixture of ethyl acetoacetate (1 mmol), hydrazine hydrate (1 mmol) and sodium actate solution (10 mol %) was mixed thoroughly. To it 40 % aqueous ethanol (5 mL) was added followed by aldehyde (1 mmol) and malononitrile (1mmol) and the resulting mixture was stirred for a while and then refluxed for appropriate time (Table 1). After completion of reaction, as monitored by TLC, the reaction mixture was allowed to cool and poured onto 50 g

of crushed ice. The solid obtained was then filtered, dried and recrystallized from ethanol.

Table 1. Synthesis of pyranopyrazoles.

Product	Ar	Time (min.)	Yield (%)*	M. P. (°C)
5a	4-OMe-C_6H_4	10	94	210-211
5b	C_6H_5	15	90	244-245
5c	4-Cl-C_6H_4	10	91	233-234
5d	2-Cl-C_6H_4	10	90	245-246
5e	4-OH-C_6H_4	15	84	222-223
5f	4-Br-C_6H_4	10	85	178-180
5g	4-NO_2-C_6H_4	10	86	253-254
5h	3-NO_2-C_6H_4	15	82	190-192
5i	4-Me-C_6H_4	15	83	207-208
5j	3-OMe-4-OH-C_6H_3	20	79	234-235
5k	2-Furyl	20	85	216-218
5l	4-(Piperidin-1-yl)-C_6H_4	15	74	167-169

*Anisaldehyde (1 mmol), ethyl acetoacetate (1 mmol), malononitrile (1 mmol), hydrazine hydrate (1 mmol), 5 mL of 40 % ethanol solution.

Results and Discussion

Commonly, sodium lactate is used for medical applications and is obtained by the treatment of sodium hydroxide with lactic acid. Lactic acid is considered as a green chemical in organic synthesis. Hence we selected its sodium salt for the one pot four component syntheses of pyranopyrazoles. From literature survey, most of the condensation reactions are reported under basic conditions. An aqueous solution of sodium lactate being basic in nature, we used it for the one pot four component condensation purposes.

Table 2. Optimization of reaction conditions for the model reaction.

No.	Ethanol %	Sodium lactate	Temp., °C	Time, min.	Yield, %
1	--	--	RT	60	--
2	--	5	RT	60	31
3	50	5	60	50	65
4	50	5	Reflux	45	73
5	50	10	Reflux	10	92
6	40	10	Reflux	10	94
7	30	10	Reflux	10	81

In order to optimize the reaction conditions, we selected anisaldehyde as a prototype aldehyde. The first attempt was carried out under solvent free condition using anisaldehyde (1 mmol), hydrazine hydrate (1 mmol), malononitrile (1mmol), ethyl acetoacetate (1 mmol) and sodium lactate (5 mol %) at room temperature, which resulted in poor yield of the corresponding product. Then we switched to the use of aqueous ethanol as an environmentally benign and easily available solvent. Ethanol-water system provides an ease for the dissolution for the reactants. To find the effective solvent and optimum catalyst amount, the model reaction was tried with varied solvent proportions and different amounts of sodium lactate. Initially 50 % aqueous-ethanol medium was used under catalyst free condition and a trace product formation was observed at room temperature. Later addition of 5 mol % of sodium lactate improved the yield at but only to a small extent (Table 2, Entry 2).

To improve yield of the model reaction, the reaction mass was heated at 60°C and then to reflux condition. Reflux condition afforded better yield than at 60° C (Table 2, Entry 3 and 4) and thus good yield was obtained under reflux condition. To improve the yield, we increased the amount of sodium lactate to 10 mol % which resulted in an excellent yield of the desired product up to 92 %. To achieve the principles of green chemistry, we tried to reduce percentage of ethanol in the solvent system and found nearly the same efficiency in 40 % ethanol (Table 2, Entry 6). Further decrease in ethanol percentage resulted in decrease in yield of the desired product (Table 2, Entry 7). Hence, 40 % ethanol in water was found to the appropriate and used for further reactions in the presence of 10 mol % sodium lactate.

6-Amino-1,4-dihydro-4-(4-methoxyphenyl)-3-methylpyrano[2,3-c]pyrazole-5-carbonitrile (5a)

IR (KBr, cm^{-1}): 1516, 1600, 2191 (CN), 3117, 3266 (NH_2), 3484 (NH). ^{1}H NMR (400 MHz, DMSO-d_6,) δ = 1.80 (s, 3H, Ar-CH_3), 3.74 (s, 3H, OCH_3), 4.55 (s, 1H, CH), 6.82-6.88 (m, 4H, Ar-H), 7.09 (s, 2H, NH_2), 12.08 (s, 1H, NH); ^{13}C NMR (100 MHz, DMSO-d_6) δ = 9.71, 35.43, 54.95, 57.61, 97.85, 113.72, 120.80, 128.46, 135.54, 136.45, 154.73, 157.93, 160.66. MS (ESI) *m/z* 283.5 (M+1).

6-Amino-1,4-dihydro-3-methyl-4-phenylpyrano[2,3-c]pyrazole-5-carbonitrile (5b)

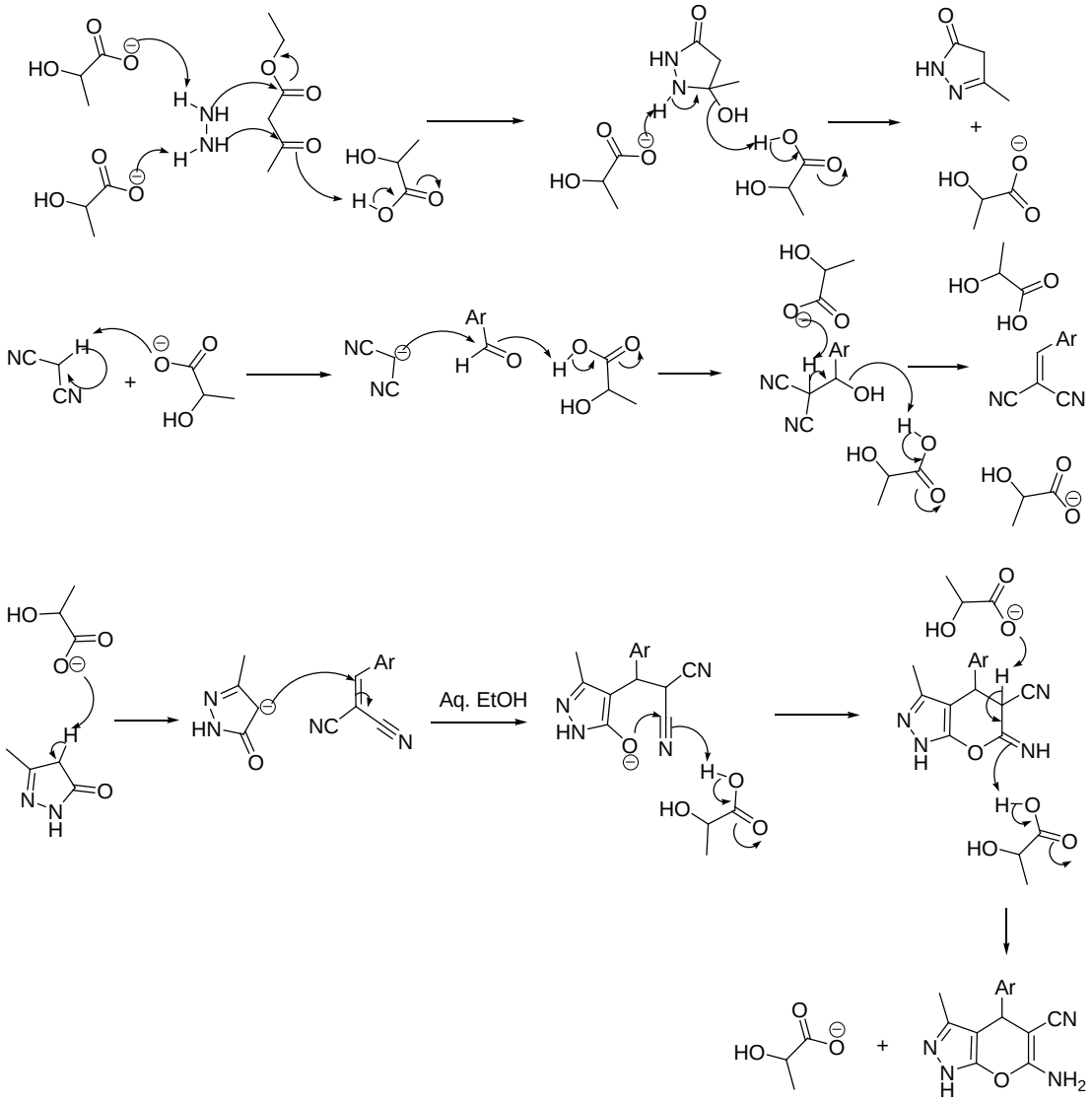
IR (KBr, cm^{-1}): 1512, 1593, 2194 (CN), 3167, 3356 (NH_2), 3410 (NH). ^{1}H NMR (400 MHz, DMSO-d_6) δ = 1.78 (s, 3H, Ar-CH_3), 4.60 (s, 1H, CH), 6.85 (s, 2H, NH_2), 7.10-7.40 (m, 5H, Ar-H), 12.10 (s, 1H, NH); ^{13}C NMR (100 MHz, DMSO-d_6) δ = 9.5, 26.8, 42.4, 48.6, 97.86, 113.1, 126.1, 127.46, 128.5, 138.40, 159.50, 174.1. MS (ESI) *m/z* 253 (M+1).

6-Amino-4-(4-chlorophenyl)-1,4-dihydro-3-methyl pyrano[2,3-c]pyrazole-5-carbonitrile (5c)

IR (KBr, cm^{-1}): 1510, 1595, 2191 (CN), 3117, 3255 (NH_2), 3483 (NH). ^{1}H NMR (400 MHz, DMSO-d_6) δ = 1.80 (s, 3H, Ar-CH_3), 4.64 (s, 1H, CH), 6.94 (s, 2H, NH_2), 7.20 (d, *J=8Hz*, 2Ar-H), 7.37 (d, *J=8Hz*, 2Ar-H), 12.15 (s, 1H, NH); ^{13}C NMR (100 MHz, DMSO-d_6) δ = 9.70, 35.56, 56.79, 97.17, 120.61, 128.42, 129.33, 131.22, 135.67, 143.44, 154.69, 160.89. MS (ESI) *m/z* 287.4 (M+1).

6-Amino-4-(2-chlorophenyl)-1,4-dihydro-3-methylpyrano[2,3-c]pyrazole-5-carbonitrile (5d)

IR (KBr, cm^{-1}): 1523, 1611, 2195 (CN), 3120, 3265 (NH_2), 3480 (NH); ^{1}H NMR (400 MHz, DMSO-d_6,) δ = 1.81 (s, 3H, Ar-CH_3), 4.65 (s, 1H, CH), 6.98 (s, 2H, NH_2), 7.24-7.37 (m, 4H, Ar-H), 13.72 (s, 1H, NH); ^{13}C NMR (100 MHz, DMSO-d_6) δ = 13.42, 56.18, 60.59, 102.20, 119.41, 127.23, 129.10, 129.48, 130.29, 131.35, 132.05, 141.34, 157.90, 160.23. MS (ESI) *m/z* 287.23 (M+1).



Scheme 2. Possible mechanism for the synthesis of pyranopyrazoles using sodium lactate.

6-Amino-1,4-dihydro-4-(4-hydroxyphenyl)-3-methylpyrano[2,3-c]pyrazole-5-carbonitrile (5e)

IR (KBr, cm^{-1}): 1582, 1642, 2220 (CN), 3059, 3340 (NH_2), 3415 (NH). ^{1}H NMR (400 MHz, DMSO-d_6,) δ = 1.99 (s, 3H, Ar-CH_3), 4.50 (s, 1H, CH), 6.10 (d, *J= 8 Hz*, 2H, Ar-H), 6.42 (s, 2H, NH_2), 7.00 (d, *J= 8 Hz*, 2H, Ar-H), 11.12 (s, 1H, OH); 12.07 (s, 1H, NH); ^{13}C NMR (100 MHz, DMSO-d_6) δ = 12.1, 25.43, 71.90, 113.22, 119.5, 127.72, 130.80, 141.40, 144.0, 153.04, 154.44, 159.84. MS (ESI) *m/z* 269.10 (M+1).

6-Amino-4-(4-bromophenyl)-1,4-dihydro-3-methylpyrano[2,3-c]pyrazole-5-carbonitrile (5f)

IR (KBr, cm^{-1}): 1512, 1640, 2220 (CN), 3075, 3280 (NH_2), 3411 (NH).^{1}H NMR (400 MHz, DMSO-d_6) δ = 1.92 (s, 3H, Ar-CH_3), 4.45 (s, 1H, CH), 6.45 (s, 2H, NH_2), 7.04 (d, *J= 8 Hz*, 2H, Ar-H), 7.43 (d, *J= 8 Hz*, 2H, Ar-H), 12.08 (s, 1H, NH); ^{13}C NMR (100 MHz, DMSO-d_6) δ = 11.12, 24.14, 70.76, 112.14, 119.11, 128.39, 120.80, 130.18, 135.01, 143.90, 153.73, 159.10. MS (ESI) *m/z* 331.2 (M+1).

6-Amino-1,4-dihydro-3-methyl-4-(4-nitrophenyl)pyrano[2,3-c]pyrazole-5-carbonitrile (5g)

IR (KBr, cm^{-1}): 1512, 1610, 2198 (CN), 3277, 3380 (NH_2), 3474 (NH). ^{1}H NMR (400 MHz, DMSO-d_6) δ = 2.02 (s, 3H, Ar-CH_3), 4.71 (s, 1H, CH), 6.24 (s, 2H, NH_2), 7.49 (d, *J=8Hz*, 2Ar-H), 8.16 (d, *J=8Hz*, 2Ar-H), 12.18 (s, 1H, NH); ^{13}C NMR (100 MHz, DMSO-d_6) δ = 11.33, 25.50, 56.79, 97.17, 120.61, 128.42, 129.33, 131.22, 135.67, 143.44, 154.69, 160.89. MS (ESI) *m/z* 298.3 (M+1).

6-Amino-1,4-dihydro-3-methyl-4-(3-nitrophenyl)pyrano[2,3-c]pyrazole-5-carbonitrile (5h)

IR (KBr, cm^{-1}): 1509, 1624, 2192 (CN), 3271, 3385 (NH_2), 3470 (NH). ^{1}H NMR (400 MHz, DMSO-d_6) δ=2.02 (s, 3H, Ar-CH_3), 4.74 (s, 1H, CH), 6.37 (s, 2H, NH_2), 7.53-7.63 (m, 2H, 2Ar-H), 8.02-8.07 (m, 1H, Ar-H), 8.11 (s, 1H, Ar-H), 12.19 (s, 1H, NH); ^{13}C NMR (100 MHz, DMSO-d_6): 11.10, 26.3, 72.1, 112.4, 121.2, 127.6, 129.48, 133.11, 135.21,

142.7, 147.1, 151.3, 154.3, 160.67. MS (ESI) *m/z* 298.11 (M+1).

6-Amino-1,4-dihydro-3-methyl-4-p-tolylpyrano[2,3-c]pyrazole-5-carbonitrile (5i)

IR (KBr, cm^{-1}): 1507, 1621, 2184 (CN), 3109, 3260 (NH_2), 3453 (NH); ^{1}H NMR (400 MHz, DMSO-d_6) δ = 2.02 (s, 3H, Ar-CH_3), 2.49 (s, 3H, CH_3), 4.72 (s, 1H, CH), 5.72 (s, 2H, NH_2), 7.24 (d, 2H, *J=8 Hz*, 2Ar-H), 7.61 (d, 2H, *J=8 Hz*, 2Ar-H), 11.92 (s, 1H, NH); ^{13}C NMR (100 MHz, DMSO-d_6) δ = 9.7, 20.4, 35.7, 55.1, 97.7, 117.7, 120.7, 127.6, 128.9, 135.3, 141.6, 154.7, 160.7; MS (ESI) *m/z* 267.1 (M+1).

6-Amino-1,4-dihydro-4-(4-hydroxy-3-methoxyphenyl)-3-methylpyrano[2,3-c]pyrazole-5-carbonitrile (5j)

IR (KBr, cm^{-1}): 1472, 1581, 2154 (CN), 3162, 3370 (NH_2), 3481 (NH). ^{1}H NMR (400 MHz, DMSO-d_6) δ = 1.63 (s, 3H, Ar-CH_3), 3.42 (s, 3H, OCH_3), 4.58 (s, 1H, CH), 6.72 (s, 2H, NH_2), 6.93 (d, 1H, Ar-H), 7.38-7.43 (m, 2H, Ar-H), 10.42 (s, 1H, OH), 12.78 (s, 1H, NH); ^{13}C NMR (100 MHz, DMSO-d_6) δ = 9.7, 34.25, 53.64, 56.64, 97.72, 104.57, 113.61, 115,16, 119.70, 128.12, 134.39, 135.86, 153.62, 157.59, 160.58. MS (ESI) *m/z* 299.12 (M+1).

6-Amino-4-(furan-2-yl)-1,4-dihydro-3-methylpyrano[2,3-c]pyrazole-5-carbonitrile (5k)

IR (KBr, cm^{-1}): 1502, 1613, 2214 (CN), 3221, 3385 (NH_2), 3427 (NH); ^{1}H NMR (400 MHz, DMSO-d_6) δ = 1.88 (s, 3H, Ar-CH_3), 4.56 (s, 1H, CH), 6.52 (s, 2H, NH_2), 6.84 (m, 1H, Ar-H), 7.04 (m, 1H, Ar-H), 7.33(m, 1H, Ar-H), 12.17 (s, 1H, NH); ^{13}C NMR (100 MHz, DMSO-d_6) δ = 9.76, 34.19, 58.92, 57.61, 104.84, 110.63, 117.94, 138.44, 145.52, 155.12, 158.18, 163.70. MS (ESI) *m/z* 243.2 (M+1).

6-Amino-1,4-dihydro-3-methyl-4-(4-(piperidin-1-yl)phenyl)pyrano[2,3-c]pyrazole-5-carbonitrile (5l)

IR (KBr, cm^{-1}): 1540, 1620, 2230 (CN), 3140,3252 (NH_2), 3470 (NH). ^{1}H NMR (400 MHz, DMSO-d_6) δ = 1.51-1.61 (m, 6H, 3CH_2), 1.80 (s, 3H, Ar-CH_3), 3.09 (t, 4H, 2CH_2), 4.47 (s, 1H, CH), 6.76 (s, 2H, NH_2), 6.85 (d, *J= 8Hz*, 2H, Ar-H), 6.98 (d, *J= 8Hz*, 2H, Ar-H), 12.04 (s, 1H, NH); ^{13}C NMR (100 MHz, DMSO-d_6) δ = 9.75, 23.83, 25.33, 35.38, 49.55, 57.73, 98.02, 115.67, 120.91, 127.87, 134.31, 135.45, 150.37, 154.75, 160.63. MS (ESI) *m/z* 336.5 (M+1).

Possible mechanism

The lactate anion helps to accumulate a negative charge on nitrogen to get condensed with ethyl acetoacetate affording pyrazolone (I). Simultaneously, aldehyde and malononitrile undergo Knoevenagel condensation to give arylidine intermediate (II). The reaction of deprotonated pyrazolone with the arylidine intermediate (II), followed by cyclization and tautomerization gives the desired pyranopyrazole product and with regeneration of the lactate anion (Scheme 2).

Conclusion

The present investigation underlines the efficiency of sodium lactate as a base catalyst and the ease of its handling in the experiments. The work up of reaction is quite simple and easy. Sodium lactate acts as a catalyst for the one pot four component syntheses of pyranopyrazoles in aqueous ethanol as an environmentally benign solvent. Thus, this protocol is simples, fast, efficient and serves as a green route for the one pot four component syntheses of pyranopyrazoles.

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