# **Physical Sciences Section**

Pak. j. sci. ind. res., vol. 36, nos. 6-7, June-July 1993

# BEHAVIOUR OF SOME 3-FORMYL-4-HYDROXY CARBOSTYRILS TOWARDS AMINES, HYDRAZINES AND HYDROXYLAMINE

E. A. MOHAMED, R. M. ABDEL-RAHMAN, A. M. TAWFIK AND M. M. ISMAIL Chemistry Department, Faculty of Education, Ain-Shams University, Roxy, Cairo, Egypt

## (Received June 10, 1990; revised May 12, 1993)

The action of the above titled nucleophiles on 1-hydroxybenzo(f) quinolin -3(4H)-one-2-carbaldehyde has been studied under different conditions and ratios, giving rise to various heterocyclic systems containing carbostyril moiety. The structures of the newly obtained compounds were confirmed by chemical reactions, elemental analysis, <sup>1</sup>H-NMR and IR spectroscopic studies.

Key words: Nitrogen compounds, Formylcarbostyril, Action.

### Introduction

The biological activity and industrial applications of carbostyrils have led to intensive research to synthesize a number of these compounds [1-6]. We have previously reported several approaches to the synthesis of such compounds [7-11].

## Experimental

Melting points are uncorrected - IR spectra (KBr) were recorded on a Beckman IR 4 spectrophotometer ( $V_{max}$  in cm<sup>-1</sup>) and <sup>1</sup>H-NMR spectra in DMSO-d<sub>6</sub> on an EM 390 90 MHz NMR spectrometer using TMS as internal standard (chemical shifts in  $\delta$ , ppm). The starting material 1-hydroxybenzo (f) quinolin-3 (4H) one (1) was prepared according to the method described by E. A. Mohamed [10].

*1-Hydroxybenzo(f) quinolin-3 (4H)one-2-carbaldehyde* (2). 1-Hydroxybenzo (f) quinolin-3(4H)one-2-carbaldehyde was prepared according to the method described by Brown [12].

Condensation with ammonia derivatives. General Procedure. A suspension of compound 2 (0.0025 mole) in ethanol (5 ml) was treated the appropriate ammonia derivative (0.0025 mol); namely: ethanolamine, ethylamine, sec. butylamine, mnitroaniline, p-toluidine, o- and p-phenylenediamine, hydrazine hydrate, phenylhydrazine, 2,4-dinitophenylhydrazine and hydroxylamine hydrochloride), was refluxed for 4 hrs, cooled and poured into water. The solids obtained were filtered off and crystallized from the proper solvent to give the condensation products; 3a-e, 5a,b, 10a-c and 15, respectively (Table 1).

(i) The bis compound 8 was obtained; following the above mentioned general procedure but using *p*-phenylenediamine in a duplicate molar ratio (Table 1).

(ii) The diazipino derivative 7 was obtained also by the same described general method when the reaction of 2 with *o*-phenylenediamine was carried out in gl. acetic acid instead of ethanol; (Table 1). This compound 7 was also obtained when 5a was refluxed in gl. acetic acid for 4 hrs.

(iii) The cyano derivative 12 was obtained by reacting 2 with hydroxylamine hydrochloride in gl. acetic acid in a similar described way (Table 1).

(iv) The pyrazolo derivatives 11a,b were obtained by reacting 2 with hydrazine hydrate and/or phenylhydrazine in gl. acetic acid as a solvent instead of ethanol in the described general procedure (Table 1). These products 11a,b were also obtained by refluxing each of compounds 10a,b (0.1 g) in gl. acetic acid (2 ml) for 3 hrs.

Compound 11b was also obtained by treatment of a hot solution of compound 15 (0.01 mole) in gl. acetic acid (50 ml) with phenyl hydrazine (0.01 mole) and refluxing the reaction mixture for 4 hrs.

Action of p-chlorothiophenol on 3-: Formation of thioether 4. A mixture of 3e (0.01 mole) and p-chlorothiophenol (0.02 mole) was heated at 200° for 5 hrs. The obtained material was washed with pet. ether to afford compound 4 (Table 1).

Addition of HBr to compound 5b; Formation of 6. To a suspension of 5b (0.01 mole) in chloroform (10 ml) was added HBr (0.01 mole) with stirring. The reaction mixture was stirred for further 4 hrs. The solid obtained was isolated (Table 1).

*Formation of the thiazolidinone (9).* A mixture of compound 8 (0.01 mole), thioglycollic acid (0.2 mole) in dry benzene (100 ml) and freshly fused anhydrous sodium sulphate (100g), was refluxed for 9 hrs, and filtered off while still hot. Compound (9) was isolated by trituration with sodium carbonate solution, after evaporation of benzene (Table 1).

Addition of hydrazine on compound 12; Formation of the amidrazine derivative 13. Hydrazine hydrate (0.01 mole) was added to a suspention of compound 12 (0.01 mole) in abs. ethanol (100 ml), containing one drop of piperidine. The reaction mixture was then refluxed for 9 hrs and the obtained solid was filtered off (Table 1).

Cyclocondensation of p-chlorobenzoylchloride with compound 13; Formation of the triazolo derivative (14). A mixture

Compd. No.	Yield % <sup>a</sup>	m.p. °C	Mol. Form. (mol. wt.)	Analysis: (Calcd./found)%.					IR; v	<sup>1</sup> H NMR δppm
				C	H	N	S	X	cm <sup>-1</sup>	
2	68 <sup>b</sup>	>300	C <sub>14</sub> H <sub>9</sub> NO <sub>3</sub> (255)	70.29 70.10	3.76 3.70	5.85 5.90		vi, Ano ity of I red june	3400,2500 br., 2840-2720w & 1670-1625,	7.7-8.5 (m, 6H, Ar-H), 9.3 (s, 1H NH) & 10.3 (s, 1H, CHO).
3a	71 <sup>b</sup>	280- 284	C <sub>16</sub> H <sub>14</sub> N <sub>2</sub> O <sub>3</sub> (282)	68.08 68.00	4.97 4.80	9.92 9.70			3600-2800 br., 1590 and absence of C=O; formly.	
3b	66 <sup>ь</sup>	>300	C <sub>16</sub> H <sub>14</sub> N <sub>2</sub> O <sub>2</sub> (266)	72.18 72.20	5.26 5.40	10.52 10.40			3300, 2500 br., 1625 & 1590.	
3c	84°	>300	C <sub>18</sub> H <sub>18</sub> N <sub>2</sub> O <sub>2</sub> (294)	73.47 73.20	6.12 6.30	9.52 9.50			3300, 2500 br., 1625 & 1590.	
3d	70 <sup>b</sup>	296- 299	C <sub>20</sub> H <sub>13</sub> N <sub>3</sub> O <sub>4</sub> (359)	66.85 66.90	3.62 3.80	11.70 11.50			3300, 2500 br., 1625 & 1590,	
1 3e (im 0e)( collocat	80	250- 252	C <sub>21</sub> H <sub>16</sub> N <sub>2</sub> O <sub>2</sub> (328)	76.83 76.70	4.88 5.00	8.54 8.40			3300, 2500 br., 1625 & 1590.	3.8 (s, 3H, CH <sub>3</sub> ), 6.2 (s, 1H, NH), 7.3-9.3 (m, 10H, Ar) & 12.1 (br., 1H, OH).
4 lor	75⁵	>300	C <sub>27</sub> H <sub>21</sub> CIN <sub>2</sub> O <sub>2</sub> S (472.5)	68.57 68.60	4.44 4.60	5.93 6.00	6.77 7.10	7.51 7.30	3500-3300, 2500 br., 1150 & 720.	
5a	85	>300	C <sub>20</sub> H <sub>15</sub> N <sub>3</sub> O <sub>2</sub> (329)	72.95 73.00	4.56 4.50	12.76 12.80			3430, 3340, 1640, 1590 & absence of C=O; formyl band.	
5b	82	>300	C <sub>20</sub> H <sub>15</sub> N <sub>3</sub> O <sub>2</sub> (329)	72.95 72.80	4.56 4.30	12.76 12.50			3430, 3340, 1640, 1590 & absence of C=O; formyl band.	4.0 (s, 2H, NH <sub>2</sub> ), 5.6(s,1H,CH=N), 7.6-8.5(m,10H,Ar).
6	78	>300	C <sub>20</sub> H <sub>16</sub> N <sub>3</sub> O <sub>2</sub> Br (410)	58.54 58.70	3.90 4.10	10.24 10.30		19.50 20.10		
n 7 <sub>0 bon</sub> by (sloa du nu (s di nu (s di nu (s	65	>300	C <sub>20</sub> H <sub>13</sub> N <sub>3</sub> O (311)	77.17 77.10	4.18 4.20	13.50 13.30			3200,3100,1620 & absence of NH <sub>2</sub> and C=O formyl bands	5.8 (s, 1H, NH, azipin), 7-8.1 (m, 11H, Ar + CH=N) & 11.3 (br. 1H, NH).
8	69	>300	C <sub>34</sub> H <sub>22</sub> N <sub>4</sub> O <sub>4</sub> (550)	74.18 74.10	4.00 4.20	10.18 9.90			2500, 1625 & absence of $NH_2$ and C=O; formyl bands.	(Continued)

TABLE 1. PHYSICAL AND ANALYTICAL DATA OF THE NEW COMPOUNDS.

(Table 1,	continued)								
9 000013	80	>300	C <sub>38</sub> H <sub>26</sub> N <sub>4</sub> O <sub>6</sub> S <sub>2</sub> (698)	65.33 65.50	3.72 3.90	8.02 8.30		3200, 3100 br., 1720, 1660, 1470 & 1250.	
10a 100000 00000 000000 000000	70	>300	C <sub>14</sub> H <sub>11</sub> N <sub>3</sub> O <sub>2</sub> (253)	66.40 66.60	4.35 4.10	16.60 16.90		3390, 3200, 2500 br., 1630 & 1585.	3.4 (br., 1H CH=N), 6.7 (s, 2H NH <sub>2</sub> ), 7.0-7.6 (m, 6H, Ar) & 10.6 (s, 1H, OH)
10b	70	>300	C <sub>20</sub> H <sub>15</sub> N <sub>3</sub> O <sub>2</sub> (329)	72.95 72.80	4.56 4.40	12.77 12.60		3390, 3200, 2500 br., 1630 & 1585.	
10c	65	210- 211	C <sub>20</sub> H <sub>13</sub> N <sub>5</sub> O <sub>6</sub> (419)	57.28 57.00	3.10 2.90	16.71 16.80			
11a	85	>300	C <sub>14</sub> H <sub>9</sub> N <sub>3</sub> O (235)	71.48 71.80	3.83 4.00	17.87 17.50		3380, 3210, 1640, 1590 & absence of OH band.	
11b	79 <sup>ь</sup>	200- 201	C <sub>20</sub> H <sub>13</sub> N <sub>3</sub> O (311)	77.17 77.40	4.18 4.30	13.50 13.20		3220, 1630 & 1590.	
12	85⁵	283- 285	C <sub>14</sub> H <sub>8</sub> N <sub>2</sub> O <sub>2</sub> (236)	71.19 71.30	3.39 3.40	11.86 12.20		3500, 3100, 2500, 2215 & 1630.	
13	65	260- 262	C <sub>14</sub> H <sub>12</sub> N <sub>4</sub> O <sub>2</sub> (268)	62.69 62.80	4.48 4.40	20.90 20.60		3400–3100, 2500, 1640, 1620 & 1360.	
14	55⁵	243- 244	C <sub>21</sub> H <sub>13</sub> N <sub>4</sub> O <sub>2</sub> Cl (388.5)	64.86 64.70	3.35 3.40	14.41 14.50	9.14 9.60	3300, 2500, 1620, 1590 & 1340.	
15	62	>300	C <sub>14</sub> H <sub>10</sub> N <sub>2</sub> O <sub>3</sub> (254)	66.14 65.90	3.94 3.70	11.02 11.20		3600, 2500, 1635 & 1585.	3.4 (br,1H CH=N), 6.7 (s, 1H, NH) 7-7.6 (m, 6H, Ar) & 10.6 (br. 2H, OH: oximo and at position-4)

<sup>a</sup>: Unless otherwise indicated, the crystalin solvent is DMF; b: The crystalin solvent is AcOH; c: The crystalin. solvent is ethanol.

of compound 13 (0.01 mole) and p-chlorobenzoylchloride (0.01 mole), DMF (10 ml) and ethanol (50 ml) was refluxed for 4 hrs. The solid obtained after pouring onto ice was filtered off (Table 1).

## **Results and Discussions**

The starting compound 1-hydroxybenzo (f) quinolin-3(4H) one-2-carbaldehyde (2) was prepared by treatment of 1-hydroxybenzo(f) quinolin-3(4H) one (1) [10] with CHCl<sub>3</sub> in NaOH [12].

Compound 2 on reaction with primary amines in abs. ethanol afforded the imino derivatives 3a-d,, which on fusion with *p*-chlorothiophenol *via* 1,2-addition on the imino bond gave the thioether of the type 4.

On the other hand, compound 2 underwent condensation with diamines such as *o*-and/or *p*-phenylenediamine in abs. ethanol by ratio 1:1 to afford the imino derivatives 5a,b. Compound 5b reacted with HBr to give the bromo derivative 6. Condensation of the formyl derivative 2 with *o*-phenylenediamine in gl. acetic acid gave rise to 1,4-diazipin derivative 7. When the above reaction was carried out with *p*-phenylenediamine in abs. ethanol at the ratio 2:1, the bis dianil compound 8 was isolated.

Thiazolidinone 9 was obtained by the addition cyclization reaction of thioglycolic acid to the bis compound 8; Scheme 1.

Compound 2 condenses with hydrazine hydrate, phenylhydrazine and 2,4-dinitrophenylhydrazine to produce the hydrazones 10 a-c. Compound 10 a-b, on boiling with gl. acetic acid give the pyrazoloderivatives 11 a,b.

Reaction of compound 2 with hydroxylamine in the presence of gl. acetic acid yielded 3-cyano derivative 12 which

on boiling with hydrazine hydrate in ethanol-piperidine gave the amidrazine 13 via nucleophilic attack on C=N group. Structure of 13 was deduced from reaction with *p*-chlorobenzoyl chloride in abs. ethanol-DMF, which gave the triazole 14.

Finally, reaction of compound 2 with hydroxylamine in ethanol gave the monoxime 15, which on refluxing with phenylhydrazine in gl. acetic acid led to the direct formation of the pyrazolo derivative 11b (m.p. and m.m.p. 200°) (Scheme 2). In this reaction the displacement of 3-imino group with hydrazino group occurred [13] followed by loss of one mole of water leading to cyclization, as illustrated in Chart I.





Scheme 2.

(15)

226



#### References

- 1. K. Tomita, J. Pharm. Soc. Japan, 71, 1100 (1951).
- 2. Tatsuo Ohata and Yo Mori, J. Pharm. Soc. Japan, **75**, 1162 (1955).
- 3. K. Matsumoto, M. Suzuki, N. Yoneda and M. Miyoshi, Synthesis, 805 (1976).
- 4. M.G. Coppola and E.G. Hardtmann, J. Heterocyclic Chem.,

accute, diothyl malonate or ethyl cyanotectate (0.02 mole) accute, diothyl malonate or ethyl cyanotectate (0.02 mole) in (40 ml) pyridine was beated under raflux for 12 hrs., the reaction mixture was poured into ice-cold dil. NCI to give product which was crystallized from ethanol (Tables 1 and 2).

Reaction of benzozatione (1) with accept accetant and or malonomitrile. Formation of ( $\beta \neq 9$ ). A mixture of (1) (0.04 mole), sodium athenide and acetyl acetone or malononitrile (0.01 mole) in ( $\beta$ 0 m1) ethanol was beated under reflux for 18 het, the reaction mixture was pouted into ice-cold dif-HEL The product was crystallized from ethanol and acetic acid respectively (Table 1 and 2).

Indeform reaction: Formation of (10). A mixture of (8) (0.01 mole), alkaline solution of methanoi and isslines solution was heated on water bath, the iodoform was separated and the filtrate was acidified by dil-HCI. The product obtained was crystallized form isopropyl alcohol (Tabbles 1 and 2).

Action of hydrazine hydrate on (8): Formation of (11). A solution of (8) (0.91 mole) and hydrazin hydrazic (0.02 mole) in (30 ml) isoproponal was heated under reflux for 6 hrs. The product obtained after cooling was crystallized from isopropyl alcohol (Tables 1 and 2).

Friedel-Crafts reaction with benzoutmone (1): formation of (12). A solution of (1) (0.01 mole) in toluene, mayieoe or cumone (50 ml), AICl, (0.04 mole) was added with stirting, a vigorous evolution of hydrogen chloride took place. Stirting was continued for 8 hrs. at room temperature acid ice-cold dil-HCl was added. The organic layer was washed with HQO, dred by anhydroas MgSO, and excess noivent was removed by steam distillation. The solid obtained was crystallized from soluence (Tables 1 and 2). 16(8), 1605 (1979).

- Y. Kawase, S. Yamaguchi, M. Morita and T. Uesugi, Bull. Chem. Soc. Japan, 53(4), 1057 (1980).
- A. Knierzinger, O.S. Wolfbeis, J. Heterocyclic Chem., 17(2), 225 (1980).
- A.A. Sayed, S.M. Sami, A. El-Fayomi and E.A. Mohamed, Egypt J. Chem., 19(5), 811 (1976).
- A.A. Sayed, S.M. Sami, A. El-Fayomi and E.A. Mohamed, Acta Chem. Hung., 94(2), 131 (1977).
- S.M. Abu-El-Wafa, E.A. Mohamed, R.M. Issa and M. Gaber, Indian J. Chem., 24(A), 407 (1985).
- 10. E.A. Mohamed, J. Chem. Soc. Pak., 13(3), 166 (1991).
- 11. E.A. Mohamed, R.M. Abdel-Rahman, A.A. Sayed and M.M. Ismail, J. Indian Chem. Soc., **69**, 472 (1992).
- 12. R.F.C. Brown, J.J. Hobbs, G.K. Hughes and E. Ritchie, Australian J. Chem., 7, 348 (1954).
- R.S. Varma and P.K. Garg., J. Indian Chem. Soc., 53, 980 (1981).

nand + (34), quintervoites have over apprect to internation biological and pharmacological purposes such as dimetic [3] antihistaminic [4], anticonvulsant [5] and long active sedative agent [6]. This promoted us to prepare and study the reaction of these compounds.

#### Experimental

Melting points reported are uncorrected. It spectra we have not a Pyc-Unicam No. 641749 spectraphotome

ter and PMR spectra on a Bittmberg No. 4032 instrument. Action of formanide on 1; Formation of 2. A mixture of (E) (0.01 mole) and formanide (0.015 mole) was heated at

1367 in out bath for 3 ars, 1 ne product outained area crosing was crystallized from othanol (Tables 1 and 2).

Formatiza of manutch bases (3  $a \approx 0$ ). A mixture of (4) (0.01 mole), formatiza of manutch bases (3  $a \approx 0$ ). A mixture of (2) and (0.01 mole), formatich years and excinimide in (30 ml) amide or inside namely benzamide and succinimide in (30 ml) esthanol was heated moder reflux for 3 hrs. The product obtained after cooling was crystallized from ethanol (Tables 1 and 2).

Action of ethyl chloroac etate on quinazolinose 2: Pornution of (4). A solution of (2) (0.01 mole and ethyl chloroacetate (0.01 mole) in (30 ml) ethanol was heated under reflux for 6 hrs. The product obtained after cooling was crystalized from othanol (Tables 1 and 2).

Benroylation of quinazolinone (2), Formation of (3), A mixture of (2) (0.01 mole) and benzoyl chloride (0.01 mole) in (30 ml) dry benzette was heated under rollux for 3 hrs. The product obtained after cooling was crystalized from isoprepyl alcohol (Tables 1 and 2).

Action of phosphorus pennasulphide on (2): Formation of (5) A mixture of (2) (0.01 mote) and phosphorous penusulphide (0.03 mole) in (40 ml) dry exylence was licented