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

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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, ^{1}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^{-1}) and ^{1}H-NMR spectra in DMSO-d_6 on an EM 390 90 MHz NMR spectrometer using TMS as internal standard (chemical shifts in δ, 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, *m*-nitroaniline, *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

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

Compd. No.	Yield %[a]	m.p. °C	Mol. Form. (mol. wt.)	Analysis: (Calcd./found)%. C	H	N	S	X	IR; $\bar{\nu}$ cm^{-1}	^{1}H NMR δppm
2	68[b]	>300	$C_{14}H_9NO_3$ (255)	70.29 70.10	3.76 3.70	5.85 5.90			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[b]	280-284	$C_{16}H_{14}N_2O_3$ (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[b]	>300	$C_{16}H_{14}N_2O_2$ (266)	72.18 72.20	5.26 5.40	10.52 10.40			3300, 2500 br., 1625 & 1590.	
3c	84[c]	>300	$C_{18}H_{18}N_2O_2$ (294)	73.47 73.20	6.12 6.30	9.52 9.50			3300, 2500 br., 1625 & 1590.	
3d	70[b]	296-299	$C_{20}H_{13}N_3O_4$ (359)	66.85 66.90	3.62 3.80	11.70 11.50			3300, 2500 br., 1625 & 1590.	
3e	80	250-252	$C_{21}H_{16}N_2O_2$ (328)	76.83 76.70	4.88 5.00	8.54 8.40			3300, 2500 br., 1625 & 1590.	3.8 (s, 3H, CH_3), 6.2 (s, 1H, NH), 7.3-9.3 (m, 10H, Ar) & 12.1 (br., 1H, OH).
4	75[b]	>300	$C_{27}H_{21}ClN_2O_2S$ (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	$C_{20}H_{15}N_3O_2$ (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	$C_{20}H_{15}N_3O_2$ (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_2), 5.6(s,1H,CH=N), 7.6-8.5(m,10H,Ar).
6	78	>300	$C_{20}H_{16}N_3O_2Br$ (410)	58.54 58.70	3.90 4.10	10.24 10.30		19.50 20.10		
7	65	>300	$C_{20}H_{13}N_3O$ (311)	77.17 77.10	4.18 4.20	13.50 13.30			3200,3100,1620 & absence of NH_2 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	$C_{34}H_{22}N_4O_4$ (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, continued)

9	80	>300	$C_{38}H_{26}N_4O_6S_2$ (698)	65.33 65.50	3.72 3.90	8.02 8.30		3200, 3100 br., 1720, 1660, 1470 & 1250.	
10a	70	>300	$C_{14}H_{11}N_3O_2$ (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_2), 7.0-7.6 (m, 6H, Ar) & 10.6 (s, 1H, OH)
10b	70	>300	$C_{20}H_{15}N_3O_2$ (329)	72.95 72.80	4.56 4.40	12.77 12.60		3390, 3200, 2500 br., 1630 & 1585.	
10c	65	210-211	$C_{20}H_{13}N_5O_6$ (419)	57.28 57.00	3.10 2.90	16.71 16.80			
11a	85	>300	$C_{14}H_9N_3O$ (235)	71.48 71.80	3.83 4.00	17.87 17.50		3380, 3210, 1640, 1590 & absence of OH band.	
11b	79[b]	200-201	$C_{20}H_{13}N_3O$ (311)	77.17 77.40	4.18 4.30	13.50 13.20		3220, 1630 & 1590.	
12	85[b]	283-285	$C_{14}H_8N_2O_2$ (236)	71.19 71.30	3.39 3.40	11.86 12.20		3500, 3100, 2500, 2215 & 1630.	
13	65	260-262	$C_{14}H_{12}N_4O_2$ (268)	62.69 62.80	4.48 4.40	20.90 20.60		3400–3100, 2500, 1640, 1620 & 1360.	
14	55[b]	243-244	$C_{21}H_{13}N_4O_2Cl$ (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	$C_{14}H_{10}N_2O_3$ (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: oxime and at position-4)

[a]: 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 $CHCl_3$ 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*-phenylene-diamine in gl. acetic acid gave rise to 1,4-diazipin derivative

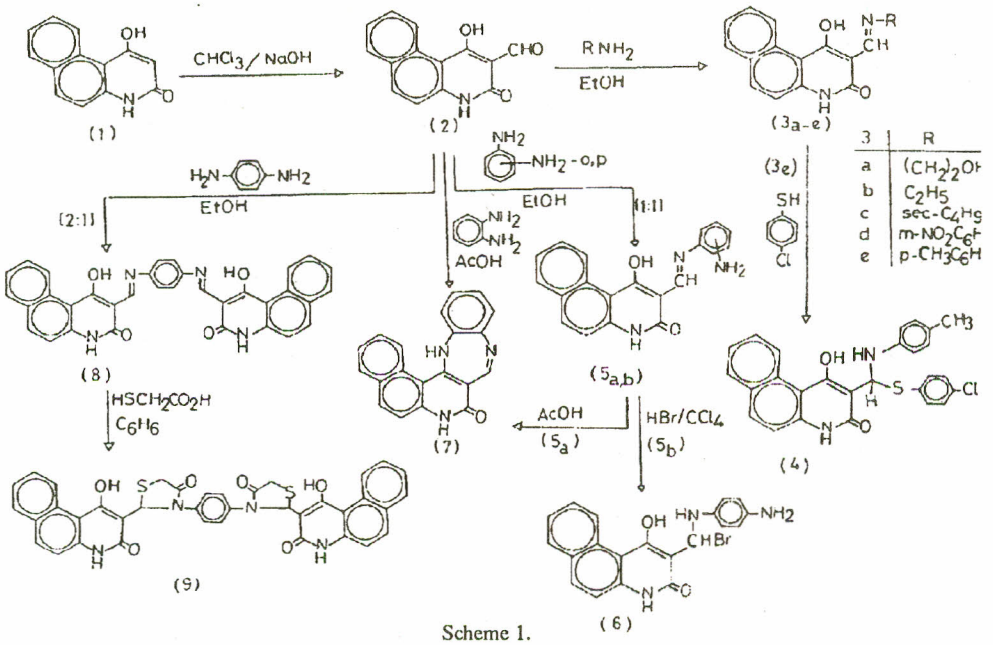
7. When the above reaction was carried out with *p*-phenylenediamine in abs. ethanol at the ratio 2:1, the bis dianil compound 8 was isolated.

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

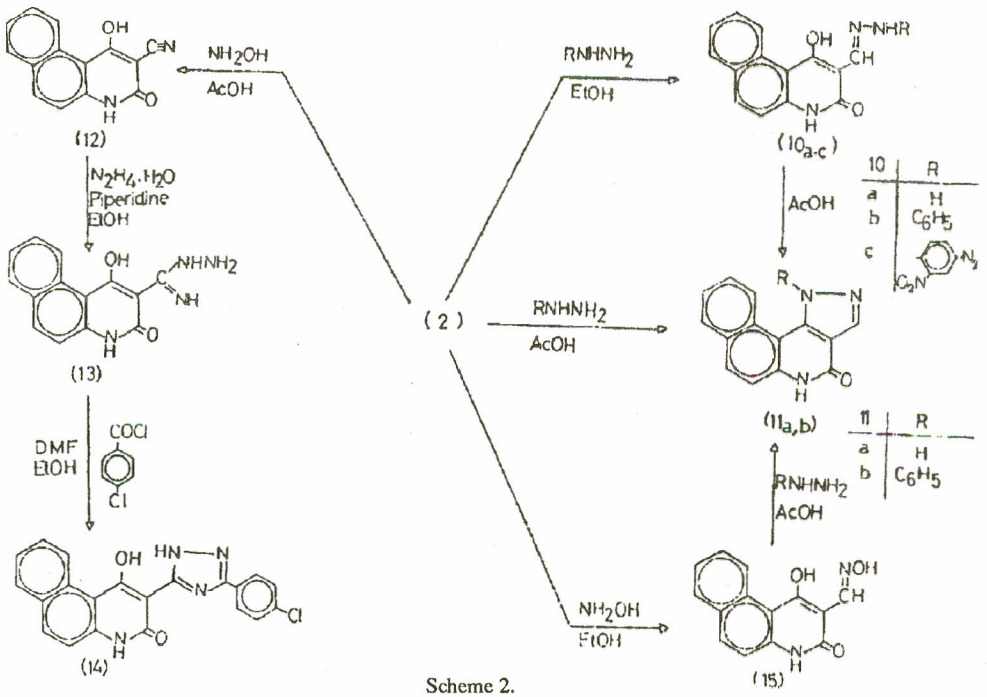
Compound 2 condenses with hydrazine hydrate, phenylhydrazine and 2,4-dinitrophenylhydrazine to produce the hydrazones 10 a-c. Compound 10 a-b, on boiling with gl. acetic acid give the pyrazoloderivatives 11 a,b.

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 1.



Scheme 2.

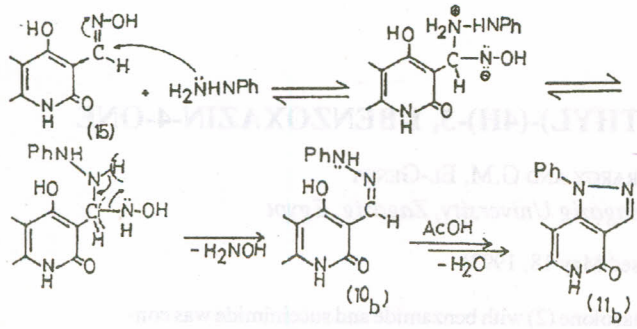


Chart 1

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