One Step Synthesis of 4-Hydroxycarbostyrils *VI*[*]

EL-HOSSAIN ALI MOHAMED
Chemistry Department, Faculty of Education, Ain Shams University, Roxy, Cairo, A.R. Egypt

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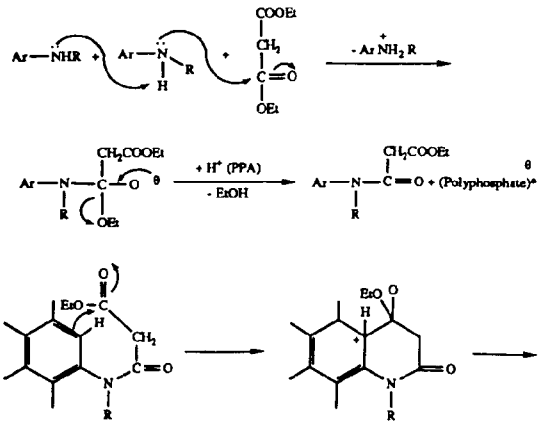
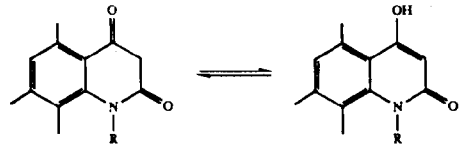
Summary: 4-Hydroxycarbostyril, 4-hydroxy-1-substituted-carbostyrils, 4-hydroxy-6-methylcarbostyril, benzol(f) and benzo(h)-4-hydroxycarbostyrils have been synthesized by one step, simple, short, and effective method. ^{1}H-NMR and IR spectroscopic data are given.

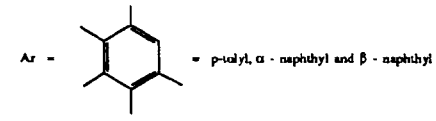
Introduction

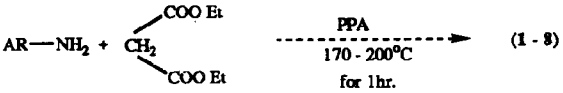
The biological activity and industrial applications of carbostyrils have led to intensive research in methods of synthesis of this class of compounds. Carbostyrils were synthesized from benzoxazine derivatives [1-3], anthranilic acid derivatives [4-5], malonic acid derivatives [6-13]. They can also be prepared by rearrangement ring cleavage of furoquinoline [14], photo- rearrangement reaction of 4-alkoxy-2-methyl-quinoline-1-oxides [15], rearrangement reaction of bi-and monocyclic pyridimidine betaines [16] and from 1,3-indanedione [17]. In fact all these methods mentioned have many difficulties, are of low yields, most of them need unavailable chemical reagents and require severe conditions such as heating for prolonged times at high temperatures. In the present work a series of 4-hydroxycarbostyrils have been synthesized by the action of polyphosphoric acid on a mixture of an appropriate aromatic amine and diethylmalonate. The reaction proceeds quickly and smoothly, giving rise to high yields.

The reaction may proceed *via* the following mechanism:

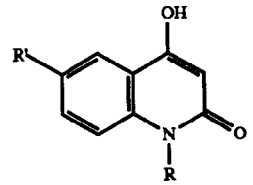






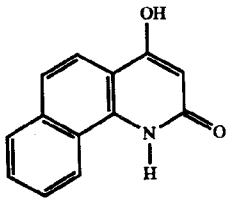


Thus 4-hydroxycarbostyril (1), 4-hydroxy-1-methylcarbostyril (2), 1-ethyl-4-hydroxycarbostyril (3), 4-hydroxy-1-phenylcarbostyril (4), 1-butyl-4-hydroxycarbosyril(5), 4-hydroxy-6-methylcarbostyril (6), benzo(h)-4-hydroxycarbostyril (7) and benzo (f)-4-hydroxycarbostryl (8), have been synthesized starting from the following aromatic amines respectively: aniline, N-methylaniline, N-ethyl aniline, diphenylamine, N-butyla niline, p-toluidine, α-naphthylamine and β-napothylamine.

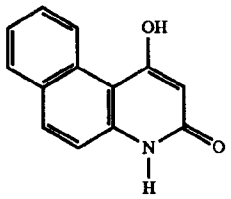


Cpd.	(1)	(2)	(3)	(4)	(5)	(6)
R	H	Me	Et	Ph	Bu	H
R'	H	H	H	H	H	Me

[*]For part (I-V), see [22-26].



(7)



(8)

the calculated values: C ± 0.2, H ± 0.18, N ± 0.3. The IR spectra were recorded using Pye-Unicam SP-100 spectrophotometer.

General procedure for preparation of carbostyrils (1-8)

A mixture of the amine (0.1 mole), diethylmalonate (20 ml) and polyphosphoric acid (prepared from 21.4 g of 85% ortho-phosphoric acid and 38.6 g of phosphorus pentoxide) was heated at 170°C for 30 minutes. The temperature was then raised to 200°C for further 30 minutes. The hot oily paste was poured into an aqueous saturated sodium acetate solution (250 ml). The solid formed was collected, washed with water several times, recrystallized from the proper solvent to give compounds (1-4) cf. Table 1). Compounds (1-4) give no melting point depression as admixture with authentic specimen.

Table 1: Spectral data of carboslyrils (1-8)

Cpd	% Yield	m.p.°C	max reported % yield(ref)	reported m.p.°C	Crystn. solvent	Molec. formula	^{1}H-NMR (DMSO- d_6/TMS$_{int}$), δ (ppm), recorded on a Varian A-60 spectrometer.
(1)	96	>300	64 [20]	345-347	EtOH	$C_9H_7NO_2$	10.4(br.,2H,OH and NH, exchangeable with D_2O);7-8(m, 4H,Ar.); 5.8 (s, 1H, =CH at position-3).
(2)	94	268	76 [21]	255-268	MeOH	$C_{10}H_9NO_2$	10.5(s, 1H, OH, exchangeable with D_2O); 7.1-8.1 (m, 4H, Ar); 6(s, 1H, =CH at position-3); 4.2 (s, 3H, CH_3).
(3)	94	264	58 [21]	235-264	MeOH	$C_{11}H_{11}NO_2$	10.5(s, 1H, OH, exchangeable with D_2O); 7.1-8.1 (m, 4H, Ar); 6(s, 1H, = CH at position-3); 4.2(q,2H, CH_2); 1.3(t, 3H, CH_3).
(4)	92	298	60 [22]	297-8	MeOH	$C_{15}H_{11}NO_2$	10.5 (s, 1H, OH, exchangeable with D_2O); 7.2-8.1(m, 9H, Ar); 6(s, 1H, =CH at position-3).
(5)	95	149	--	--	MeOH	$C_{13}H_{15}NO_2$	13.4(s, 1H, OH, exchangeable with D_2O), 7.8-8.3 (m, 4H, Ar); 5.6 (s, 1H, =CH, at position-3); 4.4 (t, 2H, α- CH_2); 1.3-1.8 (m, 4H, $2CH_2$); 0.9 (t, 3H, CH_3).
(6)	92	>300	--	--	DMF	$C_{10}H_9NO_2$	11(br., 2H, OH and NH, exchangeable with D_2O); 7-8 (m, 3H, Ar); 6(s, 1H, -=CH at position-3); 2.1(s, 3H, CH_3).
(7)	93	>300	---	---	DMF	$C_{13}H9NO_2$	11.7(br, 2H, OH and NH, exchangeable with D_2O);
(8)	78	>300	---	---	DMF	$C_{13}H_9NO_2$	7.6-8.2 (m, 6H, Ar); 6(s, 1H, =CH at position-3).

The study of the IR spectra of the compounds (1-8) and related compounds [18,19] showed that they do not display a normal absorption peaks of free O-H vibration, but showed a broad weak band centered at 2500 cm^{-1} due to the formation of intermolecular O-H----O and O-H----N hydrogen bands. The IR spectra revealed also the streching vibration of the C=O group (at the position C-2) at 1625-1650 cm.$^{-1}$ The appearance of other bands between 1500- 1600 cm^{-1} are presumably due to ring vibration involving C=C and C=N bonds. The IR spectra of compounds, (1), (6), (7) and (8) showed the N-H band at 3120-3125 cm.$^{-1}$ The ^{1}H-NMR spectra of the investigated compounds supported the assinged structures.

Experimental

All melting points are uncorrected. The microanalysis were performed by the microanalytical unit at Cairo University. All the new compounds showed the following maxmimum deviations from

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