SYNTHESIS OF 1,3-DIARYL-4,7-PHENANTHROLINES

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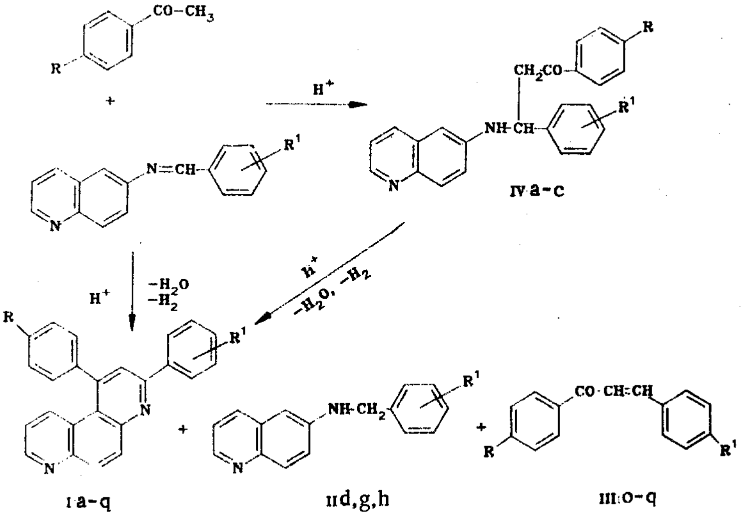
A number of new 1,3-diaryl-4,7-phenanthrolines were synthesized by heterocyclization of arylidene-6-quinolylamines with acetophenones in the presence of an acidic catalyst. Intermediate amino ketones and side products, viz., N-(R^1-benzyl)-6-quinolylamines and α,β-unsaturated ketones, were isolated. The IR, UV, PMR, and mass spectra of the synthesized compounds are discussed.

In the diazaphenanthrene series least study has been devoted to 4,7-phenanthroline derivatives, despite the fact that biologically active and luminescent substances have been found among them [1, 2]. This is explained by the difficulties involved in their synthesis. Methyl- and monophenyl-substituted 4,7-phenanthrolines have been studied most thoroughly [2-4]. Diaryl derivatives of this series have not been described in the literature.

We propose a simple and convenient method for the preparation of 1,3-diaryl-4,7-phenanthrolines by heterocyclization of arylidene-6-quinolylamines with acetophenone and p-substituted acetophenones by refluxing equimolar amounts of them in an aliphatic alcohol (C_2—C_4) in the presence of concentrated HCl.

In some cases, in addition to cyclic products I, we isolated N-(R^1-benzyl)-6-quinolylamines (IId, g, h). Thus for the first time in the 4,7-phenanthroline series we have shown that the hydrogen that is liberated in the formation of the 4,7-phenanthroline ring goes into the reduction of the starting azomethines.

When an electron-acceptor nitro group is present in the para position of the phenyl fragment of the azomethine or the acetophenone, the key reaction products, viz., 4-7-phenanthrolines Io-q, are accompanied by α,β-unsaturated ketones or nitrochalcones IIIo-q, which are evidently formed due to hydrolysis of the starting Schiff bases and subsequent condensation of the liberated aromatic aldehydes with acetophenone or p-nitroacetophenone.



The reaction of acetophenone with azomethines with electron-donor alkylamino groups is hindered as a consequence of a decrease in the activity of the —HC═N— center [5]; prolonged

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(16-17 h) heating of the starting reagents in an ampul is therefore required for the preparation of 4,7-phenanthrolines Ik-m.

It was established that the formation of the 4,7-phenanthroline ring is preceded by a step involving intermediate amino ketones, which are products of the addition of the enolized CH acid to the protonated electrophilic azomethone bond. Amino ketones IVa-c were detected in the reaction mixtures along with the corresponding 4,7-phenanthrolines. They were isolated in the form of individual substances when the reaction was carried out under mild conditions and were converted to 4,7-phenanthrolines by refluxing in n-butanol in the presence of concentrated HCl.

The characteristics of the synthesized compounds are presented in Tables 1 and 2; the structures were confirmed by data from the IR, UV, PMR, and mass spectra.

The IR spectra of I contain absorption bands at 3030-3060 cm^{-1} due to C–H stretching vibrations of the aromatic rings. The bands at 705-720 and 840-855 cm^{-1}, which are indifferent to the effects of substitution, can be ascribed to out-of-plane deformation vibrations of two adjacent C–H bonds of the tetrasubstituted benzene ring [2].

The UV spectra of 4,7-phenanthrolines I have the form that is characteristic for compounds with an angular structure [3, 6] and consist of three principal bands at 330-360, 287-289, and 254-267 nm, which we interpreted as α, p, and β bands, respectively [7].

The mass spectra of I contain maximally intense peaks of molecular ions (M$^+$), rather intense peaks of $[M - H]^+$ and $[M - R]^+$ ions, and low-intensity peaks of $[M - C_6H_5]^+$ ions. The

TABLE 1. Characteristics of 1,3-Diaryl-4,7-phenanthrolines Ia-q

Compound*	R¹	mp, °C	Found, %			Empirical formula	Calc., %			Yield, %
			C	H	N (Hal)		C	H	N (Hal)	
Ia [7]	H	196—197	86,3	4,9	8,4	$C_{24}H_{16}N_2$	86,7	4,9	8,4	44
Ib	p-F	208—209	—	—	7,6	$C_{24}H_{15}FN_2$	—	—	8,0	51
Ic	o-F	183—184	—	—	7,8	$C_{24}H_{15}FN_2$	—	—	8,0	42
Id	p-Cl	228—229	78,8	4,5	8,0 (9,5)	$C_{24}H_{15}ClN_2$	78,6	4,1	7,6 (9,7)	61
Ie	p-Br	227—228	70,0	3,9	6,7 (19,6)	$C_{24}H_{15}BrN_2$	70,1	3,7	6,8 (19,5)	35
If	p-OH	282—283	82,6	5,0	7,9	$C_{24}H_{16}N_2O$	82,7	4,6	8,0	31
Ig	o-OH	227—228	83,0	4,9	8,2	$C_{24}H_{16}N_2O$	82,7	4,6	8,0	50
Ih	o-OH, m-OCH$_3$	231—232	79,8	4,8	7,0	$C_{25}H_{18}N_2O_2$	79,3	4,8	7,4	32
Ii	p-OCH$_3$	156—157	82,6	5,2	7,4	$C_{25}H_{18}N_2O$	82,8	5,0	7,7	35
Ij	o,p-(OCH$_3$)$_2$	174—175	79,2	5,0	7,4	$C_{26}H_{20}N_2O_2$	79,6	5,1	7,1	22
Ik	p-N(CH$_3$)$_2$	213—214	82,7	5,8	10,8	$C_{26}H_{21}N_3$	83,2	5,7	11,2	25
Il	p-N(C$_2$H$_5$)$_2$	182—183	83,9	6,6	10,8	$C_{28}H_{25}N_3$	83,4	6,3	10,4	28
Im	p-N(C$_2$H$_4$Cl)$_2$	151—152	71,0	4,6	9,1 (14,8)	$C_{28}H_{23}Cl_2N_3$	71,2	4,9	8,9 (15,0)	24
In	m-NO$_2$	235—236	75,9	4,4	11,4	$C_{24}H_{15}N_3O_2$	76,4	4,0	11,1	36
Io	p-NO$_2$	253—254	76,2	4,5	10,8	$C_{24}H_{15}N_3O_2$	76,4	4,0	11,1	18
Ip	p-NO$_2$	330—331	68,3	3,6	12,8	$C_{24}H_{14}N_4O_4$	68,2	3,3	13,3	19
Iq	p-Cl	335—336	69,7	3,8	10,3 (8,8)	$C_{24}H_{14}ClN_3O_2$	70,0	3,4	10,2 (8,6)	10

*For Ia-o, R = H; for Ip,q, R = p-NO$_2$.

TABLE 2. Characteristics of the N-(R¹-Benzyl)-6-quinolylamines and 1-Phenyl-3-aryl-3-(6-quinolylamino)-1-propanones

Compound*	R¹	mp, °C	IR spectrum, cm^{-1}		Found, %			Empirical formula	Calc., %			M$^+$	Yield, %
			ν_{CO}	ν_{NH}	C	H	N(Cl)		C	H	N(Cl)		
IId	p-Cl	181—182	—	3400	71,5	5,0	10,2 (12,9)	$C_{16}H_{13}ClN_2$	71,5	4,8	10,4 (13,2)	269	23
IIg	o-OH	185—186	—	3410	76,4	5,6	11,0	$C_{16}H_{14}N_2O$	76,9	5,7	11,2	250	23
IIh	o-OH, m-OCH$_3$	187—188	—	3410	72,3	6,0	9,6	$C_{17}H_{16}N_2O_2$	72,8	5,8	10,0	280	20
IVa [7]	H	186—187	1665	3380	81,3	5,7	7,6	$C_{24}H_{20}N_2O$	81,8	5,7	7,9	352	39
IVb	p-F	127—128	1670	3400	—	—	7,7	$C_{24}H_{19}FN_2O$	—	—	7,6	370	48
IVc	o-F	173—174	1670	3370	—	—	7,3	$C_{24}H_{19}FN_2O$	—	—	7,6	370	46

*For these compounds R = H.

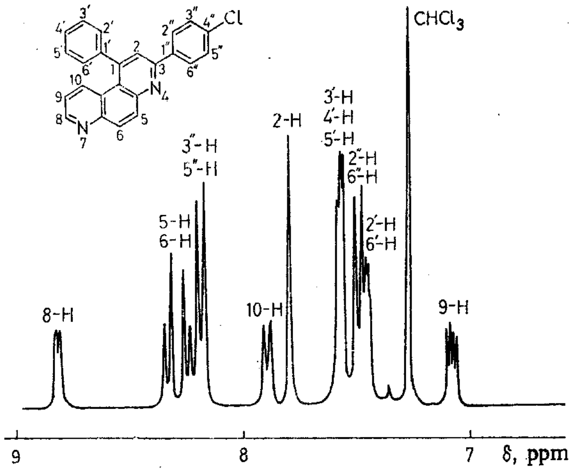

Fig. 1. PMR spectrum of Id.

ejection of neutral HCN molecules in various steps of the fragmentation is also observed. Peaks of doubly charged M^{++} and $[M - CHN]^{++}$ ions are present; this is characteristic for condensed heteroaromatic compounds.

Characteristic doublets of 5-H and 6-H protons of the phenanthroline skeleton at δ 8.33 and 8.24 ppm (J_{56} = 8.9 Hz), respectively, which constitute evidence for the angular structure of the synthesized compounds, are observed in the PMR spectrum of cyclic product Id (Fig. 1). The one-proton singlet at δ 7.80 ppm indicates the presence of substituents in the 1 and 3 positions of the 4,7-phenanthroline system. It is apparent from an analysis of the PMR spectra of the 1,3-diaryl-4,7-phenanthrolines (Table 3) that, depending on its electronic properties, substituent R^1 has an appreciable effect on the chemical shifts of the protons of the substituted benzene ring and virtually no effect on the chemical shifts of the protons of the phenanthroline skeleton. Only a slight change in the position of the signal of the 2-H proton, which is close to the phenyl ring, is observed; the 2-H signal is shifted to weak field to 7.94 ppm when an electron-acceptor nitro group is present in the para position (Io) or when ortho substituents (OH and F, Ic, h) are present.

EXPERIMENTAL

The IR spectra of KBr pellets of the compounds were recorded with a UR-20 spectrometer. The UV spectra of solutions of the compounds in ethanol were recorded with a Specord UV-vis spectrophotometer. The mass spectra were recorded with a Varian MAT-311A spectrometer by direct introduction of the substances into the ion source at an ionizing-electron energy of 70 eV and a vaporization temperature of 130-200°C. The PMR spectra of solutions in $CDCl_3$ were obtained with a Bruker WM-360 spectrometer (360 MHz) with tetramethylsilane as the internal standard. The individuality of the compounds was monitored by thin-layer chromatography (TLC) on activity II Al_2O_3 in a benzene—acetone system (4:1) with development in iodine vapors.

The arylidene-6-quinolylamines were obtained by the method in [8]. The α,β-unsaturated ketones were identified from their melting points [9, 10] and IR and mass spectra.

1,3-Diaryl-4,7-phenanthrolines Ia-q. A mixture of 5 mmole of the azomethine, 20 ml of n-butanol (for Ia-f,h,n-q), isopropyl alcohol (for Ig, j, *l*, m) or ethanol (for Ii, k), 5 mmole of acetophenone (for Ia-o) or p-nitroacetophenone (for Ip, q), and 0.5 ml of concentrated HCl was refluxed for 3-4 h; in the case of Ik-m, the mixture was heated in an ampul for 16-17 h. The resulting precipitate (sometimes after partial evaporation) was removed by filtration, treated with 25% NH_4OH, washed with water until the wash water was neutral, and crystallized from ethanol—benzene (4:1) (for Ia-h, j-*l*), ethanol (Ii, m, n), nitromethane (Io), or dimethylformamide (DMF) (Ip, q). In the case of Io-q nitrochalcones IIIo-q were isolated from the mother liquors after evaporation. The R and R^1 values, melting points, and yields are presented for the following compounds: IIIo, H, NO_2, 158-159°C, 21%; IIIp, NO_2, NO_2, 190-191°C, 48%; IIIq, NO_2, Cl, 148-149°C, 24%.

N-(R^1-Benzyl)-6-quinolylamines IId,g,h. These compounds were obtained from the mother liquors after separation of Id,g,h and were crystallized from isopropyl alcohol—benzene (4:1).

TABLE 3. PMR Spectra of Some 1,3-Diaryl-4,7-phenanthrolines

Compound	δ, ppm										SSCC, Hz				
	2-H, s	5-H, d	6-H, d	8-H, dd	9-H, dd	10-H, d	2'-H, 6'-H, m	3'-H, 4'-H, 5'-H, m	2''-H, 6''-H, d	3''-H, 5''H, d	J_{56}	J_{89}	J_{810}	J_{910}	$J_{2''3''} = J_{5''6''}$
Ia	7,79	8,33	8,22	8,78	7,01	7,85	7,38—7,54 (8H), 8,19 (2H)				9,1	4,3	1,8	8,4	—
Ic*	7,91	8,35	8,25	8,82	7,01	7,93	7,46	7,54	—	—	9,0	4,5	1,7	8,3	11,1 (HF)
Id	7,80	8,33	8,24	8,82	7,07	7,89	7,45	7,58	7,50	8,19	8,9	4,2	1,3	8,3	8,7
Ie	7,77	8,31	8,23	8,82	7,06	7,88	7,43	7,57	7,63	8,10	9,2	4,3	1,6	8,5	8,8
Ih*	7,94	8,26	8,16	8,82	7,06	7,83	7,43	7,57	—	—	9,1	4,3	1,5	8,6	8,6
Ii‡	7,75	8,31	8,20	8,77	7,02	7,84	7,33	7,51	8,16	7,00	9,0	3,2	1,5	8,8	8,8
Il†	7,75	8,36	8,21	8,76	7,03	7,85	7,37	7,55	8,15	6,78	9,2	4,3	1,6	8,8	8,8
Io	7,90	8,35	8,28	8,85	7,12	7,93	7,47	7,60	8,37	8,44	9,0	4,3	1,5	8,8	8,8

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*Signals of the protons of the substituted benzene ring: 8.27 (1H, m, 6''-H), 7.24 (1H, m, 5''-H), 7.34 (1H, t, 4''-H), and 7.19 ppm (1H, dd, 3''-H); $J_{3''4''} = 7.5$ Hz.

†The spectra contain a singlet of the protons of the CH_3O group at 3.95 (Ih) and 3.83 ppm (Ii). Signals of the protons of the substituted benzene ring of Ih: 7.51 (1H, d, 6''-H), 6.95 (1H, d, 4''-H), and 6.84 ppm (1H, t, 5''-H); $J_{5''4''} = J_{5''6''} = 8.6$ Hz.

‡Protons of the $N(C_2H_5)_2$ group: 1.13 (6H, t, $2CH_3$) and 3.35 ppm (4H, q, $2CH_2$); J = 7.2 Hz.

1-Phenyl-3-aryl-3-(6-quinolylamino)-1-propanones IVa-c. A mixture of 5 mmole of the azomethine, 5 mmole of acetophenone, 10 drops of concentrated HCl, and 15 ml of n-butanol was maintained at room temperature for 24 h, after which the solvent was evaporated, and the residue was worked up as in the case of I. Products IVa,c were crystallized from isopropyl alcohol—benzene (4:1), and IVb was crystallized from isopropyl alcohol

Cyclization of Amino Ketones IVa-c. A mixture of 3 mmole of IV, 0.5 ml of concentrated HCl, and 15 ml of n-butanol was refluxed for 2 h. Workup gave Ia-c in 70%, 72%, and 65% yields, respectively.

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