SYNTHESIS OF QUINOLYL-SUBSTITUTED 4,7-PHENANTHROLINES

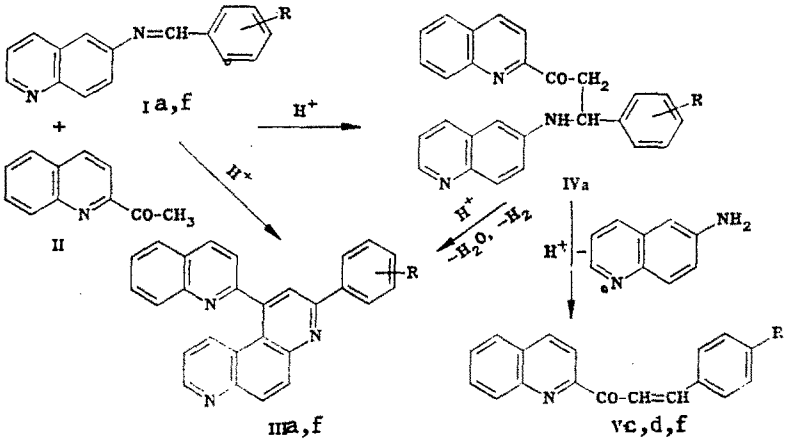
N. S. Kozlov, K. N. Gusak, and V. A. Serzhanina

UDC 547.836.3.7.07:543.422'51

1-(2-Quinolyl)-3-aryl-4,7-phenanthrolines were synthesized by reacting arylidene-6-quinolylamines with 2-acetylquinoline in n-butanol in the presence of hydrochloric acid. It was found that the formation of the 4,7-phenanthroline ring is preceded by the stage of formation of an intermediate aminoketone, 1-(2-quinolyl)-3-phenyl-3-(6-quinolylamino)propan-1-one. The IR, UV, PMR, and mass spectra of the synthesized compounds are discussed.

We have shown in [1-3] that azomethines based on 6-quinolylamine react with CH acids to give 4,7-phenanthroline derivatives. Because of the difficulties involved in their synthesis, the quinolyl derivatives of 4,7-phenanthroline are virtually unknown [4]. To obtain these compounds, we examined the reaction of arylidene-6-quinolylamines with 2-acetylquinoline. The use of 2-acetylquinoline in this reaction opens the possibility of the synthesis of mononuclear derivatives of 4,7-phenanthroline, in the molecules of which the increase in number of nitrogen atoms is combined with an extended conjugation system.

The reaction was carried out by boiling equimolar amounts of the starting reagents in an aliphatic alcohol (C_2, C_4) in the presence of concentrated hydrochloric acid.



a R=H; b R=*p*-F; c R=*p*-Cl; d R=*p*-Br; e R=*m*-NO_2; f R=*p*-OCH_3

1-(2-Quinolyl)-3-aryl-4,7-phenanthrolines IIIa-f (Table 1) were synthesized by condensation of azomethines Ia-f with 2-acetylquinoline II in n-butanol. On carrying out the reaction in ethanol with azomethine If (R = OCH_3), the α,β-unsaturated ketone Vf was isolated together with phenanthroline IIIf; for azomethines Ic, d (R = Cl, Br), the α,β-unsaturated ketones Vc, d were the main condensation products.

The formation of the α,β-unsaturated ketones may occur, on the one hand, as a result of an aldol condensation of 2-acetylquinoline with an aromatic aldehyde separating out as a result of the hydrolysis of the initial azomethine or, on the other hand, due to a hydramic splitting of the intermediate aminoketone (of the IVa type) [5, 6]. In n-butanol both the hydrolysis of azomethines and the splitting of aminoketones are apparently suppressed and, therefore, the condensation proceeds with the preferential formation of 4,7-phenanthrolines.

The intermediate product of the additon of 2-acetylquinoline to a molecule of azomethine, the diquinolyl-substituted β-aminoketone IVa, could be isolated only for benzylidene-6-quinolylamine Ia in ethanol in the presence of concentrated hydro-

Institute of Physical Organic Chemistry, Academy of Sciences of the Belorussian SSR, Minsk 220603. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 6, pp. 796-800, June, 1990. Original article submitted October 17, 1988.

 0009-3122/90/2606-0664$12.50

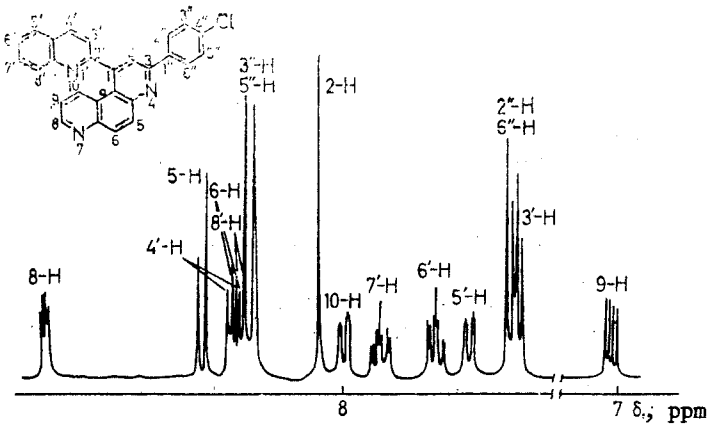


Fig. 1. PMR spectrum of 1-(2-quinolyl)-3-(p-chlorophenyl)-4,7-phenanthroline IIIc.

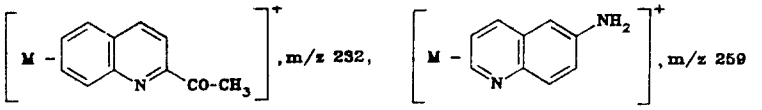
TABLE 1. Characteristics of 1-(2-Quinolyl)-3-aryl-4,7-phenanthrolines (IIIa-f)

Compound	Emperical formula	mp, °C	UV spectrum, λ_{max}, nm (log ε)	Yield, %
IIIa	$C_{27}H_{17}N_3$	194 ... 195	236(4,73), 255(4,72), 297(4,72), 361(3,63)	32
IIIb	$C_{27}H_{16}FN_3$	231 ... 232	235(4,78), 255(4,75), 298(4,76), 360(3,92)	22
IIIc	$C_{27}H_{16}ClN_3$	224 ... 225	232(4,75), 258(4,73), 298((4,78), 359(3,94)	28
IIId	$C_{27}H_{16}BrN_3$	241 ... 242	2,37(4,82), 260(4,76), 297(4,83), 338(4,04), 360(3,92)	26
IIIe	$C_{27}H_{16}N_4O_2$	261 ... 262	236(4,92), 251(4,93), 291(4,96), 340(3,92), 357(3,62)	44
IIIf	$C_{28}H_{19}N_3O$	247 ... 248	234(4,78), 257(4,62), 302(4,62), 366(4,00)	30

chloric acid at 80°C. Aminoketone IVa cyclized into 4,7-phenanthroline IIIa on being boiled in n-butanol with concentrated hydrochloric acid.

The data of the elemental analysis and the spectral investigations confirm the structure of the compounds obtained. In the IR spectrum of aminoketone IVa there are characteristic bands of stretching vibrations of the NH and CO groups (3370 and 1690 cm^{-1}, respectively), which are absent in the spectra of 4,7-phenanthrolines IIIa-f. In the spectra of IIIa-f there is a band of medium intensity at 720-730 cm^{-1}, which is stable to the substitution effect, and which can be assigned to the deformational vibrations of the two ortho-located C–H bonds at the 5- and 6-positions of the phenanthroline skeleton [7].

In the mass spectrum of aminoketone IVa the peak intensity of the molecular ion M^+ is 40%. The most intense are the peaks of



(100 and 88%, respectively). The presence of these fragments indicates the instability of the aminoketone to the action of electron impact.

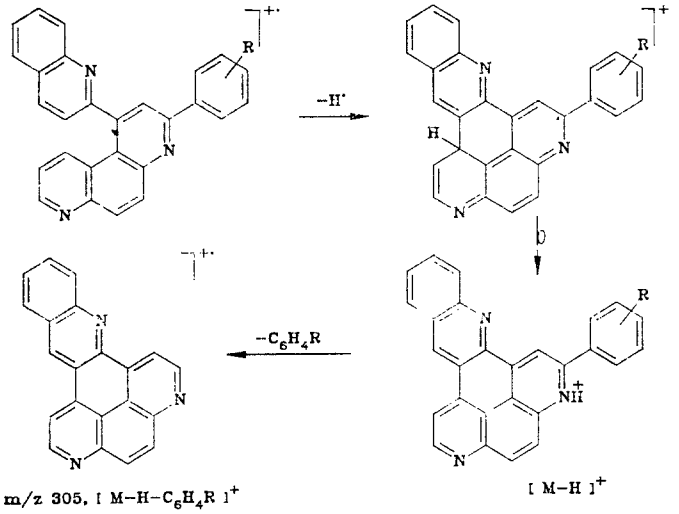
A characteristic feature of the mass spectra of 4,7-phenanthrolines IIIa-f is the small number of the fragmentary ions. The peak of the molecular ion M^+ is most intense, and there are peaks of $[M - H]^+$ ions and low- and medium-intensity peaks (5-25%) with m/z 305 corresponding to the $[M - H - C_6H_4R]^+$ ions. It should be noted that the splitting of the quinolyl substituent at the 1-position is not observed in the spectra of 4,7-phenanthrolines, as in the series of quinolyl-substituted benzo[f]quinolines [8]. It can therefore be assumed that in the 4,7-phenanthroline series the formation of an even-electronic ion $[M - H]^+$ will be accompanied by a cyclization of the molecular ion into an energetically stable system of acridino[1,2,3,4-*lmn*]-4,7-phenanthroline, from which the aromatic substituent is subsequently eliminated.

The UV spectra of 1-(2-quinolyl)-3-aryl-4,7-phenanthrolines IIIa-f (Table 1) consist of three bands: the β-bands at 232-260 nm, p- and 291-302 nm and α- at 340-361 nm. Compared with the spectrum of 1,3-diphenyl-4,7-phenanthroline [9] [225 (4.62), 255 (4.70), 291 (4.78), 337 (3.79), 354 (3.40)], in compounds IIIa-f equalization of intensities of the p- and β-bands

TABLE 2. PMR Spectra of 1-(2-Quinolyl)-3-aryl-4,7-phenanthrolines IIIa-f

Compound	Chemical shifts, δ, ppm													
	2-H, s	5-H, d	6-H,d	8-H, dd	9-H, dd	10-H, d	3'-H, d	4'-H,d	5'-H, dd	6'-H, t.d	7'-H,t.d	8'-H, dd	2''-H, 6''-H	3''-H, 5''-H
IIIa	8,11	8,44	8,30	8,85	7,03	8,03	7,53	8,36	7,65	7,75	7,90	8,27	8,27 . . . 8,36 m	7,47 . . . 7,62 m
IIIb	8,05	8,40	8,29	8,84	7,01	7,99	7,50	8,31	7,62	7,72	7,87	8,26	8,29 d	7,22 t
IIIc	8,07	8,40	8,31	8,84	7,02	7,99	7,50	8,32	7,63	7,73	7,89	8,29	7,51 d	8,26 d
IIId	8,05	8,40	8,28	8,83	7,01	8,00	7,50	8,31	7,63	7,72	7,88	8,24	7,67 d	8,18 d
IIIe*	8,17	8,45	8,35	8,88	7,05	8,03	7,55	8,37	7,68	7,74	7,92	8,35	8,28 d, 9,16 s	7,76 t
IIIf	8,00	8,41	8,29	8,84	7,01	8,01	7,52	8,34	7,63	7,73	7,89	8,28	8,28 d	7,06 d

*4'-H forms a doublet at 8.78 ppm.



and smoothing of the vibrational structure of the α-band with a small bathochromic shift are observed. Substituents R practically do not influence the position and intensity of the bands, and only the electron-donor group OCH_3 slightly shifts the α- and p-bands into the longer-wave region with a simultaneous decrease in the intensity of the p-band.

With respect to the position and multiplicity of the proton signals of the phenanthroline ring, the PMR spectra of compounds IIIa-f (Fig. 1, Table 2) are identical with the previously reported spectra of 1,3-diaryl-4,7-phenanthrolines [1]. The quinolyl substituent protons form two doublets (3'-H, 4'-H, J = 8.8-8.9 Hz), two doublets of doublets (5'-H, 8'-H, J = 8.8-8.9; J = 2.2-2.4 Hz) and two triplets of doublets (6'-H, 7'-H, J = 7.1-7.4; J = 1.2-1.4 Hz). In several cases, the proton signals of the quinolyl substituents overlap the 6-H signal of the phenanthroline skeleton or the phenyl ring signals (Table 2). In the presence of the electron-accepting nitro group in the molecule of compound IIIf, a small weak-field shift is observed of all of the signals in the spectrum.

EXPERIMENTAL

The IR spectra were run on a UR-20 spectrophotometer in KBr tablets, the UV spectra on a Specord UV-vis spectrophotometer in ethanol. The PMR spectra were obtained on a Bruker WM-360 spectrometer (360 MHz) in $CDCl_3$, using TMS as the internal standard. The mass spectra were recorded on a Varian MAT-311A mass spectrometer by the method of a direct introduction of the material into the ionic source at an energy of ionizing electrons of 70 eV and at an evaporation temperature of 130-200°C.

The data of the elemental analysis of compounds III for C, H, N, and Hal correspond to the calculated values.

Arylidene-6-quinolylamines Ia-f were obtained according to [10].

1-(2-Quinolyl)-3-aryl-4,7-phenanthrolines (IIIa-f). A solution of 5 mmoles of azomethine Ia-f, 5 mmoles (0.85 g) of 2-acetylquinoline and 0.5 ml of a concentrated HCl in 20 ml of n-butanol was boiled for 1 h. The precipitate that separated out was treated with an aqueous solution of NH_4OH, water, dried, and crystallized from an ethanol–benzene (4:1) mixture.

1-(2-Quinolyl)-3-phenyl-3-(6-quinolylamino)propan-1-one (IVa, $C_{27}H_{21}N_3O$) was obtained by boiling 20 ml of an ethanolic solution of 1.2 g (5 mmoles) of azomethine Ia, 0.85 g (5 mmoles) of 2-acetylquinoline, and 5 drops of concentrated HCl for 30 min. After the evaporation of the solvent, the precipitate was treated with an alcoholic NH_4OH solution (1:1) and crystallized from an ethanol–benzene (4:1) mixture. Yield 0.6 g (30%) of aminoketone IVa, mp 174-175°C.

Cyclization of Aminoketone IVa. A mixture of 2.5 mmoles of compound IVa, 0.5 ml of concentrated HCl, and 20 ml of n-butanol was boiled for 2 h. Yield 64% of phenanthroline IIIa.

LITERATURE CITED

1. N. S. Kozlov, K. N. Gusak, V. A. Serzhanina, and N. A. Krot, *Khim. Geterotsikl. Soedin.*, No. 10, 1398 (1985).
2. N. S. Kozlov, K. N. Gusak, V. A. Serzhanina, and G. S. Shmanai, *Dokl. Akad. Nauk Beloruss. SSR* **29**, 336 (1985).

3. N. S. Kozlov, K. N. Gusak, and V. A. Serzhanina, *Dokl. Akad. Nauk Beloruss. SSR* 287, 1142 (1986).
4. N. S. Kozlov, G. S. Shmanai, and K. N. Gusak, *Dokl. Akad. Nauk Beloruss. SSR* 29, 141 (1985).
5. N. S. Kozlov, *5,6-Benzoquinolines* [in Russian], Nauka i Tekhnika, Minsk (1970).
6. N. I. Pavlenko, V. P. Marshtupa, N. A. Klyuev, and B. P. Bashkunov, *Khim. Geterotsikl. Soedin.*, No. 8, 1088 (1981).
7. R. H. Wiley, C. H. Jarboe, and F. N. Hayes, *J. Org. Chem.* 23, 268 (1958).
8. N. S. Kozlov, G. S. Shmanai, V. P. Suboch, and V. I. Vil'chinskaya, *Khim. Geterotsikl. Soedin.*, No. 4, 520 (1979).
9. N. S. Kozlov, K. N. Gusak, V. A. Serzhanina, L. F. Gladchenko, and N. A. Krot, *Khim. Geterotsikl. Soedin.*, No. 12, 1651 (1987).
10. N. S. Kozlov, K. N. Gusak, V. A. Serzhanina, N. A. Krot, and R. D. Sauts, *Dokl. Akad. Nauk Beloruss. SSR* 27, 49 (1983).

SELECTIVE ACID HYDROLYSIS OF 2-SUBSTITUTED-5-DIMETHYLAMINOMETHYLENEAMINOPYRIMIDINES TO 5-AMINO- AND 5-HYDROXYPYRIMIDINES

T. A. Kizner, M. A. Mikhaleva, and E. S. Serebryakova

UDC 547.853.07:542.938

Conditions are described for the selective acid hydrolysis of 2-substituted-5-dimethylaminomethyleneamino-pyrimidines in 0.2-2 M sulfuric acid, to give high yields of the corresponding 5-amino- and difficultly accessible 5-hydroxypyrimidines.

According to a literature report [1], acid hydrolysis of 2-substituted-5-dimethylaminomethyleneaminopyrimidines affords 5-formylamino- or 5-amino-compounds on treatment with 0.2 M acetic acid or 0.02 (0.2) M sulfuric acid, respectively. It has, however, been shown that treatment of 2,4(6)-OH, CH_3,NH_2-substituted 5-aminopyrimidines with 20% sulfuric acid gives the corresponding 5-hydroxypyrimidines [2, p. 236], which forms one method for the preparation of these difficultly accessible pyrimidine derivatives. Information on methods of preparation of 2-aryl-5-amino- or 2-aryl-5-hydroxypyrimidines which do not contain additional substituents in the 4- and 6-positions of the pyrimidine ring are of a fragmentary nature, and are not sufficiently general. For example, the reduction of 2-aryl-5-nitropyrimidines has been reported [3], and the synthesis of 2-phenyl-5-hydroxypyrimidine from 2-phenyl-4-hydroxy-5-methoxypyrimidine [4].

It was therefore desirable to examine the acid hydrolysis of 2-aryl-5-dimethylaminomethyleneaminopyrimidines over a wide pH range, in order to develop a convenient method of synthesis of the corresponding 5-amino- and 5-hydroxypyrimidines. The required 2-aryl compounds (IIIa-e) were obtained by us by reacting the propenylidenamine perchlorate (I) with the amines (IIa-e), as in [5].

It was found that acid hydrolysis of (IIIa, c-e), by boiling in 0.2 M sulfuric acid for 30-110 min, gave, as in [1], the 5-amino-compounds (IVa, c-e) in higher yields than were obtained by reduction of the nitro-compounds [3], and when the acidity of the solution was increased to 1 M sulfuric acid for 30-60 min, the 2-aryl-5-hydroxypyrimidines (Va, c-e) were obtained readily in high yields. The use of 2 M sulfuric acid (~20%; cf. [2]) for the hydrolysis of (IIIa-e) also afforded the 5-hydroxypyrimidines, but after only 15-30 min. In the case of (Va-c), increasing the reaction time resulted in a decrease in the yields of hydrolysis products, and made considerably more difficult their isolation and purification as a result of resinification of the reaction mixture (see, for example, the preparation of (Vb), Table 1).

Novosibirsk Institute of Organic Chemistry, Siberian Section, Academy of Sciences of the USSR, Novosibirsk 630090.
Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 6, pp. 801-803, June, 1990. Original article submitted May 7, 1988.

 0009-3122/90/2606-0668$12.50