SYNTHESIS AND PROPERTIES OF HYDRAZONES OF THE PHENANTHRIDINE SERIES

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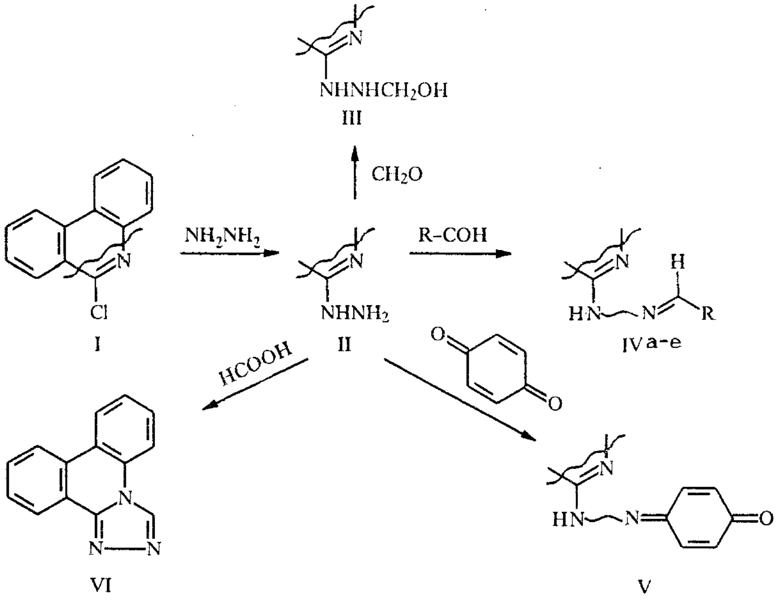
The reaction of 6-hydrazinophenanthridine with carbonyl reagents gave hydrazones, while the reaction with formic acid gave a 1,2,4-triazole derivative.

The research on heteroanalogs of 2-hydrazinopyridine has thus far been extremely limited [1-3], and the phenanthridine ring has not been represented in it. In this connection, 6-hydrazinophenanthridine seems of interest, particularly its reaction with carbonyl reagents, since the resulting hydrazones may serve as synthones for obtaining annelated triazoles [4]. One must also take into account the fact that both phenanthridine [5] and the hydrazone fragment in its side chain [4] are potentially biologically active.

The starting 6-hydrazinophenanthridine (II) is readily obtained from I. Amidrazone II reacts with formaldehyde solution to give alcohol III. The products of the reaction with aldehydes are hydrazones IVa-e, while the product of the reaction with p-benzoquinone is quinoneimine V. Refluxing amidrazone II in formic acid leads to triazole VI.

Signals of an HC=N proton are present in the PMR spectra (Table 1) of hydrazones IV and triazole VI; the location of the signal of this proton in the spectrum of triazole VI is in agreement with the data in [3]. The spectrum of alcohol III contains an OH signal (9.90 ppm), which vanishes when D_2O is added.



IV a R=CCl_3, b R= o-C_6H_4OH, c R= p-$C_6H_4NMe_2$, d R= p-$C_6H_4NO_2$, e R= 1-furyl

To ascertain the structure we compared the spectra of 6-benzylaminophenanthridine (VII) [6], in which the aromatic system of phenanthridine is not disrupted, and amidine VIII, in which the C=N bond is exocyclic. Compound VIII was obtained by quaternization of 6-anilinophenanthridine [7] with dimethyl sulfate, and its structure was proved by alkaline hydrolysis to N-methyl-6-phenanthridone (IX).

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TABLE 1. Characteristics of II-IX

Compound	Empirical formula	mp,* °C	R_f	IR spectrum,** cm⁻¹			UV spectrum, λ max, nm (log ε)	PMR spectrum, ppm	Yield, %
				C=N	NH	OH			
II	$C_{13}H_{11}N_5$	169...170	0,42		3190		238 (5,48); 332 (4,64)	6,10 (3H, br.s 3NH); 6,90...8,52 (8H, m, Ar)	93
III	$C_{14}H_{13}N_3O$	173...175	0,95		3180	3400	237 (5,05); 335 (4,58)	5,4 (2H, br.sCH_2); 7,10...8,65 (8H, m, Ar and NH—C_6); 9,90 (s, OH); 8,90 (s, NH at CH_2)	68
IV a	$C_{15}H_{10}Cl_3N_3$	185...186	0,77	1625	3100		243 (5,06); 440 (4,19)	7,25...9,00 (8H,m, Ar); 10,20 (s, CH); 11,40 (NH)	51
IV b	$C_{20}H_{15}N_3O$	167...168	0,65	1625	3070	3400	244 (5,16); 394 (4,88)	6,67...8,60 (12H,m, Ar); 8,85 (s, HC–); 10,70 (s, OH)	87
IV c	$C_{22}H_{20}N_4$	220...221	0,84	1620	3085		243 (4,81); 400 (5,93)	2,97 (6H, s, 2CH_3N); 6,57...8,00 (12H, m, Ar); 8,48 (s, HC–)	92
IV d	$C_{20}H_{14}N_4O_2$	230...232	0,79	1620	3090		244 (4,96); 400 (4,62)	6,95...8,60 (12H, m, Ar); 8,75 (s, HC–)	89
IV e	$C_{18}H_{13}N_3O$	148...150	0,87	1630	1350		246 (5,03); 396 (4,78)	6,60 (s, HC); 7,27...8,80 (11H, m, Ar); 10,30 (s, NH)	64
V	$C_{19}H_{13}N_3O$	238...240	0,80	1620	3080		248 (4,04); 338 (4,17)	6,50...8,95 (8H, m Ar)	72
VI	$C_{14}H_9N_3$	216...218	0,85				238 (5,30); 373 (3,95)	7,36...8,70 (8H, m Ar); 9,87 (s, CH)	70
VIII	$C_{20}H_{16}N_2$	123...125	0,84	1630			240 (5,25); 340 (4,67)	3,46 (s, 3H, CH_3N); 6,15...8,60 (m, 13H, Ar)	83

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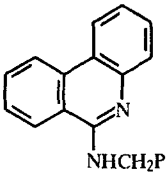
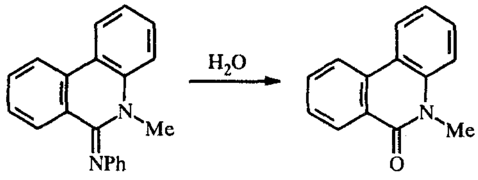
*All of the compounds were recrystallized from isopropyl alcohol.

**Compound V: 1675 cm^{-1} (C=O).



VII



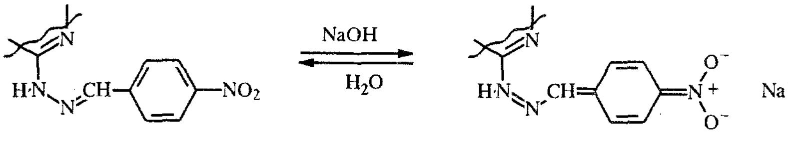
VIII IX

The results obtained in [3] and our data do not make it possible to establish the existence of amidrazone—hydrazineimine tautomerism on the basis of the PMR spectra. In contrast to the spectrum of VII, the characteristic band of an exocyclic C=N bond at 1630 cm^{-1} is present in the IR spectrum of amidine VIII. A comparison of the IR spectra of I-III recorded under the same conditions with the spectra of amidines VII-VIII shows the absence of an azomethine band in the spectra of II and III, which proves the aromatic structure of the phenanthridine. A comparison of the UV spectra of II, III, VII, and VIII shows that the spectra of II, III, and VII are similar to one another, while the spectrum of amidine VIII is distinguished by a broader conjugation band and by a certain degree of bathochromic shift of it (see Table 1), which is associated with disruption of the phenanthridine aromatic system.

In the case of analogous tautomerism for IV and V one should have expected splitting of the signals in the PMR spectrum, but this is not observed. The UV spectra of hydrazone IV, which have a long conjugation chain, differ (see Table 1) from the spectra of II and III, which constitutes evidence for the existence of an overall conjugation chain between the phenanthridine ring and the side chain of the hydrazone. Thus a shoulder of a conjugated NH group (3050-3100 cm^{-1}) is observed in the IR spectrum, while a high-intensity conjugation band at 396-440 nm ($\log\varepsilon$ 4.17-4.93) is observed in the electronic spectrum. In the PMR spectra the signals of the proton of a conjugated NH group are located at weak field: 11.4 ppm for IVa, in the composition of the multiplet of aromatic protons for hydrazones V and IVb-d (in conformity with the overall integral intensity), and at 10.3 ppm for hydrazone IVe. The shift of the singlet of the NH proton in the spectrum of IVe to weaker field as compared with the spectra of hydrazones IVb-d can be explained by the existence of a chelate ring in solution.

Attention is directed to the fact that the absorption bands of the NH groups in the IR spectra of the above-indicated solutions of II and III are broadened and located in the long-wave region (3190 and 3180 cm^{-1}, respectively), while the signals of the protons of the NH group in the PMR spectra lie at weak field (all three protons at 6.1 ppm for II [3] and one of the NH protons at 8.9 ppm for alcohol III), which constitutes evidence for intramolecular association; for II the location of the hydrogen bond is determined unambiguously. Additional confirmation of this sort of interaction is the absence of a relationship between ν_s and ν_{as} of the NH_2 group in the spectrum of this compound.

Compound IVd undergoes a change in its structure under the influence of 10% NaOH in DMSO; the color of the solution changes from yellow [λ_{max} 425 nm ($\log\varepsilon$ 4.75)] to crimson [λ_{max} 537 nm ($\log\varepsilon$ 4.47)]. Doubling of the signal of the HC=N group occurs in the PMR spectrum of this solution in d_6-DMSO; the integral ratio indicates the existence of approximately equal amounts of two forms:



EXPERIMENTAL

The PMR spectra of solutions in d_6-DMSO were recorded with an RYa-2310 spectrometer (60 MHz) with hexamethyldisiloxane (HMDS) as the internal standard. The IR spectra of suspensions in fluorinated mineral oil (or of solutions in CCl_4 in the case of I-III, VIII, and IX) were obtained with a UR-20 spectrometer. The UV spectra of solutions in ethanol were recorded with an SF-26 spectrophotometer. Thin-layer chromatography was realized on Silufol UV-254 plates in an acetone—ethanol—chloroform (1:3:6) system with development by bromine vapors.

The results of elementary analysis of C, H, N, and Cl were in agreement with the calculated values.

6-Hydrazinophenanthridine (II). A solution of 2.13 g (10 mmole) of 6-chlorophenanthridine [9] in 50 ml of ethanol was refluxed for 3 h with 4.5 ml (100 mmole) of 70% hydrazine hydrate, after which the mixture was cooled to room temperature and diluted with 100 ml of water. The resulting precipitate was removed by filtration, dried, and recrystallized.

6-Hydroxymethylhydrazophenanthridine (III). A solution of 2.09 g (10 mmole) of II was refluxed for 4 h in 50 ml of ethanol with 2.7 ml (100 mmole) of 40% formaldehyde solution, after which the solvent was removed by distillation in vacuo. The III that precipitated when ether was added to the residue was removed by filtration, dried, and recrystallized.

Hydrazones IV and V (General Method). A solution of 2.09 g (10 mmole) of hydrazine II was refluxed for 3 h in 50 ml of ethanol with 10 mmole of the corresponding carbonyl compound, after which it was cooled to room temperature and diluted with 100 ml of water. The resulting precipitate was removed by filtration, dried, and recrystallized.

1,2,4-Triazolo[4,3-f]phenanthridine (VI). A solution of 1.05 g (5 mmole) of amidrazone II was refluxed in 15 ml of 99% HCOOH for 2 h, after which it was cooled and diluted with 10% NaOH until the mixture was alkaline. The resulting precipitate was removed by filtration, dried, and recrystallized.

5-Methyl-6-phenylamino-5,6-dihydrophenanthridine (VIII). A solution of 2.70 g (10 mmole) of VIII [7] in 30 ml of absolute benzene was refluxed with 2.23 ml (15 mmole) of freshly distilled dimethyl sulfate for 2 h. The resulting precipitate was removed by filtration, dried, and dissolved in water. The addition of 10% NH_4OH gave base VIII, which was removed by filtration, dried, and recrystallized.

N-Methyl-6-phenanthridone (IX). A solution of 2.84 g (10 mmole) of amidine VIII was refluxed in a mixture of 30 ml of a solution of ethylene glycol, 10% water, and 20% NaOH for 10 h, after which the mixture was cooled and diluted with 300 ml of water, and the resulting precipitate was removed by filtration, dried, and recrystallized from ethanol to give 0.2 g of IX [10].

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