PHENANTHROTHIAZOLES

III.* SYNTHESIS OF SOME PHENANTHRO[3,4-d]THIAZOLES AND DETERMINATION OF THE STRUCTURES OF PHENANTHROTHIAZOLES BY MEANS OF PMR SPECTRA

V. P. Bronovitskaya, A. A. Bakhmedova (Kizil'shtein), A. Ya. Berlin, L. M. Alekseeva, and Yu. N. Sheinker

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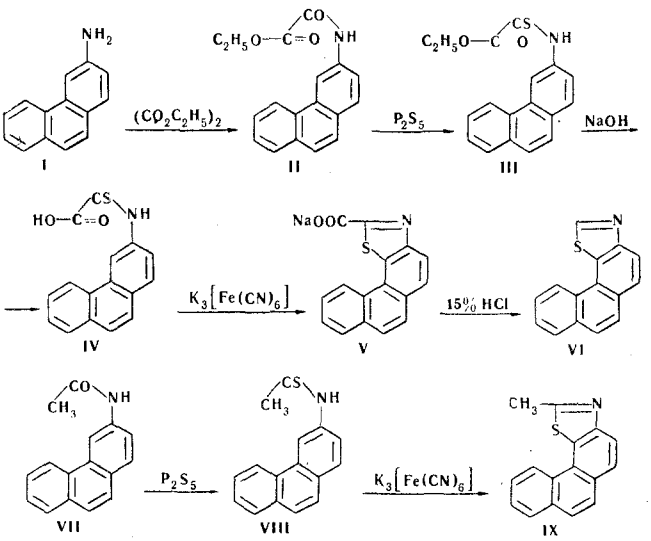
Phenanthro[3,4-d]thiazole and phenanthro[3,4-d]-2'-methylthiazole were synthesized by the oxidative cyclization of 3-phenanthrylthiooxamic acid with subsequent decarboxylation and by the oxidative cyclization of 3-thioacetamidophenanthrene, respectively.

Continuing our study of the relationship between the chemical structure and carcinogenic action of phenanthrothiazoles, we have obtained two new phenanthrothiazoles from 3-aminophenanthrene (I) [2]. Phenanthro[3,4-d]thiazole, which does not contain substituents, was obtained by the same route that we used to synthesize phenanthro[2,1-d]thiazole in [3].

A substituted phenanthro[3,4-d]thiazole with a methyl group in the 2 position of the thiazole ring was obtained by the route previously



*See [1] for communication II.

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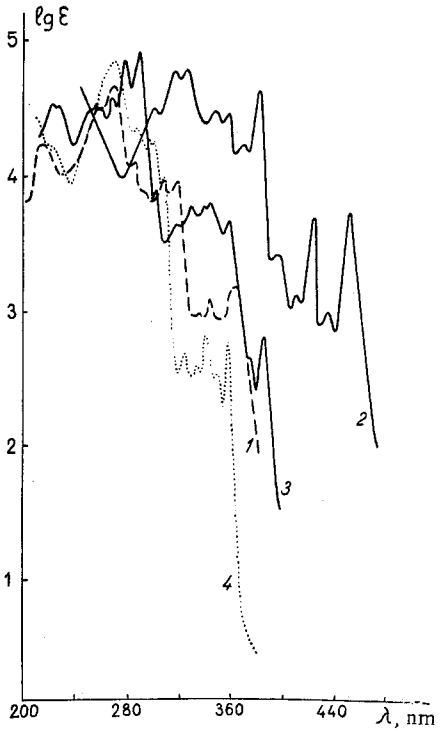


Fig. 1

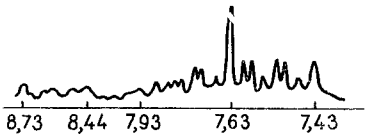


Fig. 2

Fig. 1. UV absorption spectra: 1) phenanthro[3,4-d]thiazole; 2) 3,4-benzophenanthrene; 3) 1,2-benzanthracene; 4) phenanthro[2,1-d]thiazole.

Fig. 2. PMR spectrum of phenanthrene.

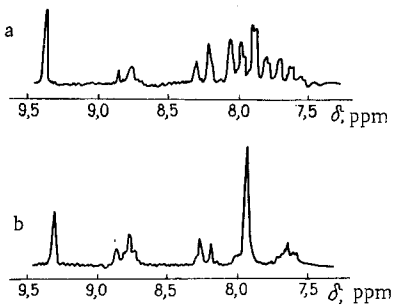
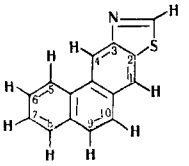


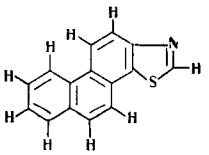
Fig. 3. PMR spectra: a) phenanthro[3,4-d]thiazole (VI); b) phenanthro[2,1-d]thiazole (X).

described for phenanthro[9,10-d]-2'-methylthiazole [4] and for phenanthro[2,1-d]-2'-methylthiazole [1].*

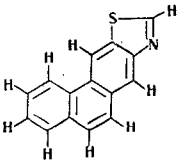
The structures of the phenanthrothiazoles that we obtained required additional confirmation, since, as in the case of the thiooxamic acid (IV), which resulted in the formation of the isomeric phenanthro-[3,2-d]thiazole (VIA), the 2 position of the phenanthrene ring rather than the 4 position might have participated in the cyclization of the thioacetyl derivatives of 3-aminophenanthrene.



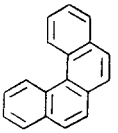
VIa



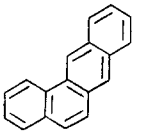
X



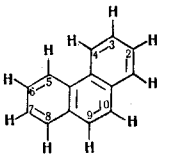
Xa



XI



XII



XIII

A similar problem arose in the synthesis of phenanthrothiazoles from 2-aminophenanthrene [3], when it was necessary to choose between the phenanthro[2,1-d]thiazole (X) and phenanthro[2,3-d]thiazole (Xa) structures. We then decided in favor of the X structure on the basis of the great similarity between the

*In [1], this compound was called 2-methylphenanthro[2,1-d]thiazole.

UV spectrum of the substance obtained and the structure of chrysene as compared with the spectrum of 1,2-benzanthracene, as well as from the close analogy with the cyclization of 2-naphthylthiooxamic acid, which leads exclusively to the angular naphtho]2,1-d]thiazole [5].

However, the slight resemblance between the UV spectrum of VI and the spectra of 3,4-benzophenanthrene (XI) and 1,2-benzanthracene (XII) (Fig. 1) does not provide a basis for choosing between structures VI or VIa.

The structures of phenanthrothiazoles VI and X were established by means of the PMR spectra. The assignment of the signals in the PMR spectra of these compounds was based on a comparison with the spectrum of phenanthrene XIII [6] (Fig. 2). In the latter, the signals of the 1-, 2-, and 3-protons and the equivalent 6-, 7-, and 8-protons are a complex multiplet at 7.4-7.9 ppm. The signals of the 9- and 10-protons are found in the same region but can be isolated as a singlet with an intensity of two proton units at δ 7.63 ppm. The weakest-field signals at 8.4-8.7 ppm were assigned to the 4- and 5-protons in the spectrum of phenanthrene. The reason for this sort of isolation of the signals from the overall group is apparently the effect of the ring currents of the neighboring aromatic rings on the shielding of the 4- and 5-protons.

From its PMR spectrum, the VI structure can be assigned to the phenanthrothiazole synthesized in this study. This is a consequence of the following data (Fig. 3a). In this spectrum, a doublet of broad signals with J 7.5 Hz and an intensity of one proton unit is observed at weak field, and two distinct doublets (8.30 ppm and 8.04 ppm) with J 7.5 Hz, each with an intensity of one proton unit, which are caused by interaction of two protons (an AB system), are observed at stronger field. The presence of such signals corresponds to structure VI, in which the doublet at 8.88 ppm corresponds to $H_{(5)}$, while the other two doublets correspond to $H_{(1)}$ and $H_{(2)}$. The signals of the $H_{(5)}$ proton are broadened due to interaction with the m- and p-protons of its own righ, while the signals of the $H_{(1)}$ and $H_{(2)}$ protons do not undergo broadening because of the absence of other protons in the ring to which they are attached.

The signals of the 6-, 7-, and 8-protons are situated in approximately the same region as in phenanthrene and are displayed as a complex multiplet. The 9- and 10-protons in this system are no longer equivalent, so that a system of AB signals, of which we observe only the central portion – a slightly resolved doublet at 7.91 ppm – corresponds to them in the spectrum.

Structure VIA assumes an entirely different form of spectrum. In this case, two signals – a doublet from $H_{(5)}$ and a singlet from $H_{(4)}$ – should be observed at weak field, and one singlet corresponding to $H_{(1)}$ should be observed at stronger field.

An entirely different picture is observed in the spectrum of X (Fig. 3b): two doublets (just as in the case of phenanthrene) are observed at weak field at 8.78 and 8.83 ppm with J 7.5 Hz. One of the doublets consists of broad signals similar to those for the $H_{(5)}$ proton in structure VI, while the other doublet consists of narrow solitary signals that are probably the A part of the AB system (the symmetrical doublet at 8.17 ppm corresponds to part B). This sort of character of the signals can correspond only to structure X, in which the weak-field doublets can be assigned to $H_{(5)}$ and $H_{(4)}$, while the solitary strong-field signal can be assigned to $H_{(3)}$, which is in the ortho position relative to $H_{(4)}$. The broadening of the lines in the doublets is explained by analogy with the spectrum of structure VI. The signals of the 9- and 10-protons in the spectrum of X prove to be markedly drawn together in terms of their chemical shifts and are displayed in the spectrum as a singlet at 8.05 ppm. The signal of the proton of the thiazole ring in VI and X is a solitary singlet at weakest field at 9.4 and 9.3 ppm, respectively.

Thus a study of the PMR spectra confirmed our initial assumptions regarding the structures of both phenanthro[2,1-d]thiazole (X) and phenanthro[3,4-d]thiazole (VI).

EXPERIMENTAL

Ethyl 3-Phenanthryloxamate (II). A mixture of 2.93 g (0.015 mole) of 3-aminophenanthrene and 5.86 g (0.038 mole) of dry diethyl oxalate was refluxed for 1 h and cooled. The reaction product was recrystallized from alcohol to give 2.22 g (69%) of II as long, fine, colorless needles with mp 133-135° (from alcohol). Found: C 73.3; H 5.2; N 5.0%. $C_{18}H_{15}NO_3$. Calculated: C 73.7; H 5.1; N 4.8%.

Ethyl 3-Phenanthrylthiooxamate (III). Water (0.1 ml) was added to a solution of 0.1 g of ester II in boiling xylene, and 0.1 g of powdered phosphorus pentasulfide was then added gradually with vigorous stirring. The mixture was refluxed for 1.5 h, and the hot xylene solution was decanted from the small amount of

resinous precipitate. The solvent was removed in vacuo, and the substance was recrystallized from benzene-petroleum ether to give 70% of elongated orange prisms with mp 114-115°. Found: C 69.7; H 5.0; S 10.8%. $C_{18}H_{15}NO_2S$. Calculated: C 69.9; H 4.9; S 10.4%.

3-Phenanthrylthiooxamic Acid (IV). Crude ester III, obtained from 0.1 g of ester II, was treated in the cold with 90 ml of 10% NaOH, and the mixture was allowed to stand overnight. The solution was filtered and acidified with hydrochloric acid to give 84% of orange needles with mp 195-196° (from benzene). Found: C 68.2; H 4.0; N 5.3; S 11.3%. $C_{16}H_{11}NO_2S$. Calculated: C 68.3; H 3.9; N 5.0; S 11.0%.

Phenanthro[3,4-d]thiazole (VI). A solution of 0.78 g (0.0024 mole) of potassium ferricyanide in 4 ml of water was added dropwise with stirring to a solution of 0.12 g of acid IV in 12 ml of 10% NaOH, and the mixture was allowed to stand overnight at room temperature. The resulting precipitate of the sodium salt of V was removed by filtration, washed with a small amount of water, and refluxed for 2 h with 10 ml of 15% HCl. The hot acid solution was filtered and neutralized with ammonium hydroxide, and the base was extracted with ether. The ether was removed and the residue was dissolved in benzene. The solution was decolorized with activated charcoal and diluted with an equal volume of petroleum ether to give 0.09 g (89%) of colorless needles of VI with mp 138-139°. Found: C 76.6; H 4.0; N 6.0; S 13.4%. $C_{15}H_9NS$. Calculated C 76.6; H 3.8; N 6.0; S 13.6%. The picrate was obtained as yellow needles with mp 184-185° (from alcohol). Found: N 11.8%. $C_{15}H_9NS \cdot C_6H_3N_3O_7$. Calculated: N 12.1%.

3-Thioacetamidophenanthrene (VIII). Phosphorus pentasulfide [1.38 g (0.0062 mole)] was added with stirring in the course of 2 h to a refluxing solution of 1.38 g (0.0058 mole) of 3-acetamidophenanthrene (VII) in 100 ml of anhydrous benzene. The hot benzene solution was decanted, concentrated to a small volume, filtered, and diluted with n-hexane until it became turbid. Cooling yielded 0.46 g (31%) of VIII as light-yellow prisms with mp 129-130°. Found: C 76.5; H 5.4; N 5.5; S 12.8%. $C_{16}H_{13}NS$. Calculated: C 76.5; H 5.2; N 5.6; S 12.8%.

Phenanthro[3,4-d]2'-methylthiazole (IX). A total of 1.5 ml of 5% aqueous NaOH was added to a refluxing solution of 0.1 g of VIII in 1 ml of alcohol. The clear solution was cooled to 5°, and a solution of 0.28 g (0.0009 mole) of potassium ferricyanide in 1.5 ml of water was added dropwise to it with stirring. The mixture was allowed to stand overnight at room temperature, and the product was extracted with ether. The ether was removed, and the picrate was obtained from the residue as yellow needles with mp 190-191° (from alcohol). The yield was 0.15 g (79%). Found: C 55.5; H 3.1; N 11.6; S 7.1%. $C_{16}H_{11}NS \cdot C_6H_3N_3O_7$. Calculated: C 55.2; H 2.9; N 11.7; S 6.7%. A suspension of the picrate in benzene was shaken several times with 5% ammonium hydroxide and then washed with water. The benzene was removed, and the residue was decolorized with charcoal and crystallized from methanol to give a quantitative yield of colorless needles of IX with mp 122.5-123.5°. Found: C 77.0; H 4.7; N 6.0%. $C_{16}H_{11}NS$. Calculated: C 77.1; H 4.4; N 5.6%.

The analyses were performed under the supervision of A. D. Chinaeva. The PMR spectra were recorded with a JNM-4H-100 spectrometer with dimethyl sulfoxide as the solvent and tetramethylsilane as the internal standard.

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