SYNTHESIS OF TWO ISOMERIC DIMETHYLTHIAZOLOPHENOTHIAZINES

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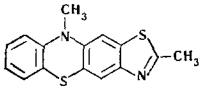
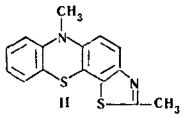
Two condensed four-ringed heterocyclic bases—2, 10-dimethylthiazolo[4, 5-b]phenothiazine and 2, 6-dimethylthiazolo[4, 5-c]phenothiazine—have been synthesized. The structure of the new heterocycles has been confirmed by their IR and UV spectra.

We have previously described condensed three-ringed heterocycles—isomeric thiazolobenzoxazoles [1] and thiazolobenzothiadiazoles [2], from which a number of cyanine dyes were obtained.

The object of the present work was the synthesis of condensed four-ringed bases—dimethylthiazolophenothiazines of structures I and II:

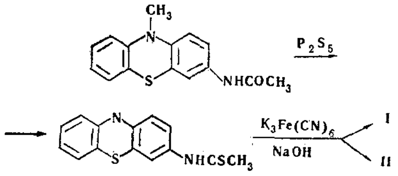


I



II

Both bases were obtained from the known 3-acetylamino-10-methylphenothiazine [3] via the thioacetyl derivative by oxidative condensation:



The mixture of products was chromatographed in chloroform solution on a column of alumina. Two substances containing the same amount of sulfur, corresponding to dimethylthiazolophenothiazines, were isolated. One of them, formed in very low yield, had mp 216–217° C and was sparingly soluble in ethanol, and the other, formed in considerably larger amount, melted at 146° C and was very readily soluble in ethanol. Judging from the yields, it could be assumed that the substance with mp 216–217° C was the linear isomer I and the substance with mp 146° C the angular isomer II.

We made an attempt to obtain the isomer II by independent synthesis, heating a mixture of 6-amino-7-mercapto-2-methylbenzothiazole with catechol in a sealed tube at 220–230° C for 30 hr [4], but we were unable to isolate any individual products from the dark mass so obtained. We were able to obtain convincing information concerning the structure of the dimethylthiazolophenothiazines synthesized by studying their IR and UV spectra.

It is known [5] that the IR spectra of tetrasubstituted benzenes with two hydrogen atoms in the ortho position with respect to one another always have a strong absorption band in the 860–800-cm^{-1} region. In tetrasubstituted benzenes with the hydrogen atoms in the para position with respect to one another, this band is absent, but there is a band in the 900–860-cm^{-1} region. This difference in the IR spectra of the linear and angular isomeric thiazolobenzoxazoles (a case analogous to the present one) was used successfully to establish their structures by Bassignana et al. [6].

Fig. 1 shows the IR spectrum of the compound with mp 216–217° C, which has a strong absorption band at 870 cm^{-1} and no absorption in the 860–800-cm^{-1} region, and the IR spectrum of the compound with mp 146° C, where there is a strong band at 812 cm^{-1} and no absorption in the 900–860-cm^{-1} region.

Thus, it may be concluded from the IR spectra that the higher-melting isomer has the linear structure I and the lower-melting isomer the angular structure II. The same conclusion can be drawn from the UV spectra of the isomers. Figure 2 gives the absorption curves of the compound with mp 216–217° C (1), the compound with mp 146° C (2), and 10-methylphenothiazine (3).

All three curves are similar in shape and in the position of the absorption bands, but the absorption bands of the isomer with mp 216–217° C is shifted considerably towards the long-wave region of the

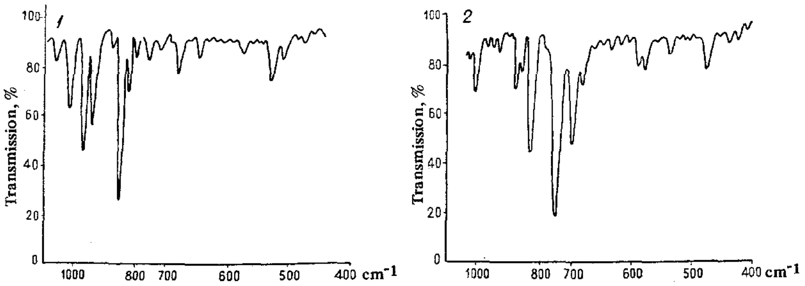


Fig. 1. IR spectra: 1) I; 2) II.

spectrum in comparison with those of the isomer with mp 146° C. It is known that condensed aromatic hydrocarbons with a linear structure, such as anthracene and naphthacene, adsorb at longer wavelengths than their angular isomers—phenanthrene and 1,2-benzanthracene [7, 8, 9]. The UV spectra of the linear and angular three-ringed heterocycles that we synthesized previously (thiazolobenzoxazoles, thiazoloquinolines, etc. [10]) confirm this rule.

All this justifies us in regarding it as established that the compound with mp 216–217° C is 2,10-dimethylthiazolo[5,4-b]phenothiazine and the compound with mp 146° C is 2,6-dimethylthiazolo[4,5-c]phenothiazine.

EXPERIMENTAL

10-Methyl-3-thioacetylaminophenothiazine. Dry pyridine (20 ml) was added to a carefully ground mixture of 5.4 g (0.02 mole) of 3-acetylamino-10-methylphenothiazine and 4.4 g (0.02 mole) of phosphorus pentasulfide, and the reaction mixture was boiled for 45 min. The pyridine was distilled off in vacuum and the residue was dissolved in 80 ml of 10% caustic soda solution; the resulting solution was filtered, and a current of carbon dioxide was passed through the filtrate until precipitation was complete. The light brown precipitate that had deposited was washed with water and dried in a vacuum desiccator. Yield was 4.9 g (87%). The product was used for Yakobson oxidation without further purification (the thioacetyl derivative readily resinifies).

2,10-Dimethylthiazolo[5,4-b]phenothiazine (I) and 2,6-dimethylthiazolo[4,5-c]phenothiazine (II). With stirring and ice water cooling, 45 ml (0.04 mole) of a 20% solution of potassium ferricyanide was added to a solution of 5.72 g (0.02 mole) of 3-thioacetylaminophenothiazine in 80 ml of an 8% solution of caustic soda. Then the mixture was stirred for another 3 hr and was left for a day at room temperature. The oxidation product was extracted with chloroform several times, and after the solvent had been distilled off an oily substance (1.2 g; 20%) remained which crystallized on standing. The crystals were dissolved in a small amount of chloroform, chromatographed on alumina, and eluted with chloroform. After distillation of the solvent, the eluate from the lower zone, light pink, left 0.1 g (8.3%) of a crystalline product with mp 210–211° C. After recrystallization from ethanol, it formed almost colorless needles with mp 216–217° C. Found, %: S 22.37, 22.40. Calculated for $C_{15}H_{12}N_2S_2$, %: S 22.53.

After the distillation of the chloroform, the eluate from the upper zone, light yellow, left 0.78 g (65%) of an oily product which crystallized on standing, mp 142° C. After recrystallization from ethanol, mp 146° C. Found, %: N 9.91, 10.01; S 22.36, 22.38. Calculated for $C_{15}H_{12}N_2S_2$, %: N 9.85; S 22.53.

The IR spectra were recorded on a UR-10 spectrophotometer in tablets of potassium bromide using 2 mg of the substance under investigation to 200 mg of potassium bromide. The UV spectra were recorded on an SF-4 spectrophotometer in ethanolic solutions with a concentration of 2.5 × 10^{-5} M.

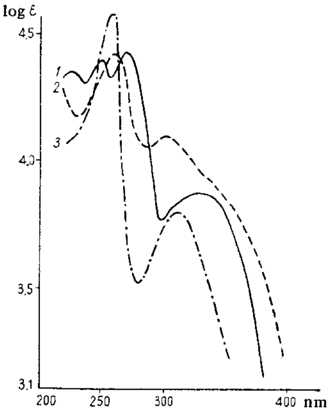


Fig. 2. Absorption spectra: 1) 2,10-dimethylthiazolo-[4,5-b]phenothiazine; 2) 2,6-dimethylthiazolo[4,5-c]phenothiazine; 3) 10-methylphenothiazine.

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