Chemistry

V. G. ZHIRYAKOV and I. I. LEVKOEV

1958

SovietRxiv

reaction scheme

Figure 1: reaction scheme

reaction scheme

Figure 2: reaction scheme

Abstract

Full Text

Chemistry

V. G. ZHIRYAKOV and I. I. LEVKOEV

SYNTHESIS OF 2-METHYL-4,5-THIOPHENO (2′,3′)THIAZOLE

(Presented by Academician I. L. Knunyants, 6 February 1958)

The isosterism of the groups —CH=CH—and —S—is well known for derivatives of thiazole and pyridine. It was of considerable interest to trace the degree of isosterism of these groups in a series of derivatives of benzthiazole and thiophenothiazole, a heterocyclic base containing condensed thiazole and thiophene rings.

In connection with this, it was planned to carry out the synthesis of 2-methyl-4,5-thiopheno (2′,3′) thiazole. To obtain this compound, by analogy with methods for the synthesis of 2-methylbenzthiazole ([1],2), one could start from α-amino-β-mercaptothiophene, with its subsequent interaction with acetic acid or its derivatives, or from a thioacetyl derivative of α-aminothiophene, followed by oxidation with potassium ferricyanide. In view of the low availability of α-amino-β-mercaptothiophene, the second method was chosen:

2-Thioacetylaminothiophene was synthesized by the action of phosphorus pentasulfide on 2-acetylaminothiophene (⌢3) in anhydrous benzene upon heating.

However, the first attempts at synthesizing 2-methyl-4,5-thiopheno (2′,3′) thiazole by oxidizing 2-thioacetylaminothiophene in a 4–8% solution of sodium hydroxide with potassium ferricyanide ended unsuccessfully. In this case a crystalline substance with m.p. 107–108° was obtained, which, as it turned out, was a disulfide of structure (I):

It should be noted that an analogous result was observed at one time in an attempt to oxidize α-thioacetylaminopyridine under the same conditions (⌢4). Only later was 2-methyl-4,5-pyrido-(2′,3′) thiazole obtained in this way, apparently under somewhat modified oxidation conditions (⌢5).

Changing the temperature conditions of oxidation (from −2° to +6°) likewise did not lead to the desired result. It could be thought that lowering the concentration of sodium hydroxide in the reaction mixture would slow the oxidation of the hydrogen of the thioacetamino group, and that the difference in mobility between the hydrogen atom at the β-carbon atom of the thiophene ring and that of the isothioacetamino group would decrease, as a result of which formation of the desired base would occur.

Indeed, when a solution of 2-thioacetylaminothiophene in 2% aqueous sodium hydroxide solution was added to a dilute solution of ferricyanide

potassium ferricyanide—along with the disulfide, we succeeded in obtaining 2-methyl-4,5-thiopheno (2′,3′) thiazole in a yield of 10% of the theoretical.

The base obtained is a colorless oil, gradually turning yellow, with b.p. 102-104°/7 mm. It has the characteristic odor of quinoline bases. It readily forms a picrate, iodomethylate, and iodoethylate.

Table 1

Base	B.p. of base, °C/mm Hg	M.p., °C picrate	M.p., °C iodomethylate	M.p., °C iodoethylate
2-methyl-4,5-thiopheno(2′,3′)thiazole	118-120/14	131-132	221-222	190-191
2-methylbenzthiazole	118/18 (^{6})	153.5 (^{7})	218 (^{8})	196 (^{6})

As can be seen from Table 1, some constants of 2-methyl-4,5-thiopheno (2′,3′) thiazole and 2-methylbenzthiazole, as well as of their derivatives, are quite close to one another.

Experimental Part

2-Acetylaminothiophene was obtained in a yield of 53% of the theoretical by adding a solution of caustic soda to a mixture of an aqueous suspension of the double tin salt of 2-aminothiophene hydrochloride and acetic anhydride. M.p. 159-160° (161-162° (^{3})).

The starting double salt of 2-aminothiophene was obtained by reduction with metallic tin in hydrochloric acid of 2-nitrothiophene (^{3}), which had been synthesized by nitration of thiophene with nitric acid of sp. gr. 1.5 in glacial acetic acid (^{9}).

2-Thioacetylaminothiophene. To 250 ml of anhydrous benzene, a finely ground mixture of 20.3 g of 2-acetylaminothiophene and 10.0 g of phosphorus pentasulfide was gradually added at the boil, after which the liquid was boiled for 2 hours. The benzene layer was decanted, and the resinous residue was boiled with benzene (3 times with 200 ml). The combined benzene solutions were shaken with 4% caustic soda solution (5 times with 230 ml). The resulting aqueous solutions were acidified at 3° with 50% acetic acid to a weakly acidic reaction to litmus. The precipitate was filtered off, washed thoroughly with water, and dried. Yield 6.0 g (26.5%). M.p. 98-100°. After crystallization from ethyl alcohol—slightly yellowish needles with m.p. 111-112°.

Found %: N 8.83,
$C_6H_7NS_2$. Calculated %: N 8.91

2-Methyl-4,5-thiopheno (2′,3′) thiazole. 23.6 g of 2-thioacetylaminothiophene was dissolved at 45° in 700 ml of 2% aqueous caustic soda solution. The solution was added with vigorous stirring over 2 hours at 0° to a solution of 100 g of potassium ferricyanide in 900 ml of water, after which stirring at the same temperature was continued for another 2 hours. On the following day the mixture was thoroughly extracted with ether (2000 ml). The ether was distilled off, and the residue was subjected to steam distillation. The base was extracted from the distillate with 500 ml of ether; the ethereal extract was dried with potash, the ether was distilled off, and the residue was distilled in vacuum. Yield 2.35 g (10.1%). B.p. 102-104°/7 mm (118-120°/14 mm). A colorless oil, slightly yellowing on storage, with a characteristic odor.

Found %: N 8.97,
$C_6H_5NS_2$. Calculated %: N 9.02

Upon cooling the filtered liquid remaining in the flask after distillation of the base, a precipitate of disulfide separated, which was filtered off—

was washed with water and dried. Weight 4.9 g. M.p. 103-105°. After crystallization from water—slightly grayish long needles with m.p. 107-108°. On boiling it with dilute hydrochloric acid, vigorous evolution of hydrogen sulfide and precipitation of sulfur occurred.

Found %: N 8.70,
$C_{12}H_{12}N_2S_4$. Calculated %: N 8.97

Picrate—small greenish-yellow prisms (from ethyl alcohol) with m.p. 131-132°.

Found %: N 14.36,
$C_{12}H_8O_7N_4S_2$. Calculated %: N 14.58

Iodomethylate was obtained by heating the base with 1.25 mol of methyl iodide on a boiling water bath for 5 hours, after which 0.5 mol of methyl iodide was added, and heating was continued for another 6 hours. Yield 75%. Slightly greenish large prisms (from absolute ethyl alcohol) with m.p. 221-222°.

	Found %:	N 4.63,
$C_7H_8NS_2J$.	Calculated %:	N 4.71.

Iodoethylate was obtained by heating the base with 2 mol of ethyl iodide on a boiling water bath for 15 hours, after which 0.5 mol of ethyl iodide was added and the mixture was heated for another 7 hours. Yield 66%. Slightly greenish large prisms (from absolute ethyl alcohol) with m.p. 190–191°.

	Found %:	N 4.47,
$C_8H_{10}NS_2J$.	Calculated %:	N 4.50

The work was carried out at the suggestion of N. N. Sveshnikov, to whom we express our gratitude for participation in the discussion of the results obtained.

All-Union Scientific Research
Cinema-Photo Institute

Received
30 I 1958

CITED LITERATURE

1. A. Hofmann, Ber., **13**, 1236 (1880).
2. P. Jacobson, Ber., **19**, 1072 (1886).
3. W. Steinkopf, Lieb. Ann., **403**, 17 (1914).
4. I. L. Knunyants, D. A. Katrenko, ZhOKh, **10**, 1167 (1940).
5. T. Takahashi, T. Jatsuka, J. Onuma, J. Pharm. Soc. Japan, **64**, 235 (1944); Chem. Abstr., **45**, 4717 (1951).
6. H. Nitzsche, L. Busch, H. Witzel, H. Gansau, Chem. Ber., **85**, 487 (1952).
7. Y. Mizuno, K. Watanabe, J. Pharm. Soc. Japan, **70**, 540 (1950); Chem. Abstr., **45**, 7111 (1951).
8. W. König, W. Meier, J. Prakt. Chem., **109**, 324 (1929).
9. *Syntheses of Organic Preparations*, **2**, IL, 1949, p. 381.

Note: Figure translations are in progress. See original paper for figures.