SYNTHESIS OF 2-METHYLTHIENO[3, 2-b]THIENO-[2,3-d]THIAZOLE

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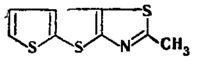
A new heterocyclic base – 2-methylthieno[3,2-b]thieno[2,3-d]thiazole – was synthesized by heating 2-acetamido-3-hydroxythieno[3,2-b]thiophene with phosphorus pentasulfide.

We have previously synthesized [1] 2-methylthieno[2,3-b]thieno[2,3-d]thiazole (1) by oxidation of 2-thioacetamidothieno[2,3-b]thiophene with potassium ferricyanide in aqueous alkaline media. Polymethine dyes of various types were obtained from the quaternary salts of bases I, and their color was discussed in [2].

In the present communication we describe the synthesis of the isomeric base 2-methylthieno[3,2-bthieno-[2,3-d]thiazole (II). We were able to obtain base II by heating 2-acetamido-3-hydroxythieno[3,2-b]thiophene (III) with phosphorus pentasulfide:



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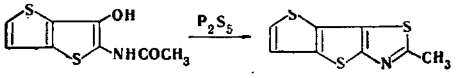
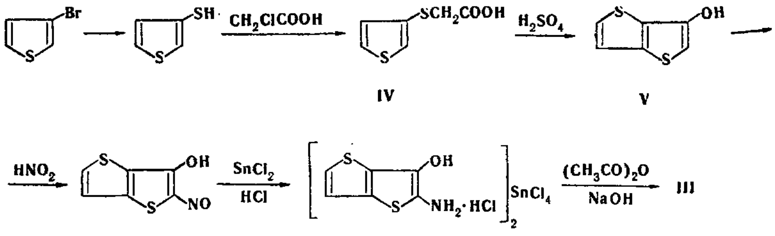


III II

Compound III was synthesized in turn from 3-bromothiophene via the scheme



IV V VI VII

3-Hydroxythieno[3,2-b]thiophene (V) was obtained from 3-thienylthioglycolic acid (IV) by a somewhat modified method [3, 4]. 2-Nitroso-3-hydroxythieno[3,2-b]thiophene (VI) was synthesized in 84% yield by nitrosation of V with sodium nitrite; VI was converted to the double tin salt (VII) of 2-amino-3-hydroxythieno[3,2-b] by reduction with stannous chloride in concentrated hydrochloric acid. Salt VII was converted to III in 63% yield by acetylation with acetic anhydride in aqueous media in the presence of alkali. The yield of II (colorless needles with mp 111-112°) was 30%. The picrate and p-tosylate formed readily. The molecular weight of II determined by mass spectrometry was 211 and was in agreement with structural formula II.

EXPERIMENTAL

Thiophene-3-thiol. A solution of 0.30 mole of 3-bromothiophene in 60 ml of anhydrous ether was added to a solution of 0.308 mole of butyllithium in 150 ml of anhydrous ether at −70° in a stream of nitrogen, after which the mixture was stirred at −70° for 10 min. Sulfur (10 g) was then added at the same temperature in the course of 20 min, and the mixture was stirred while allowing the temperature to rise to room temperature. It was then cooled to 0-5° and treated with 20% ammonium chloride solution. Workup gave a colorless liquid with bp 52-54° (5 mm) [171° [5] and 49-51° (2 mm) [6]] and n_D^{20} 1.6134 in 69% yield.

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3-Thienylthioglycolic Acid (IV). This compound was obtained by the addition of a neutralized (with sodium carbonate) solution of 1.2 moles of chloroacetic acid in 100 ml of water to a solution of sodium thiophene-3-thiolate in 200 ml of water at 40-45° in the course of 30 min with stirring in a stream of nitrogen. The mixture was then heated at 50° for 2 h at 90-95° for 1 h, after which it was cooled and acidified with dilute (1 : 1) hydrochloric acid. The yield was 77%. The colorless oil had bp 130-135° (1-2 mm) and began to crystallize on cooling to give colorless needles (from water) with mp 53° (mp 52-53° [3, 4]).

3-Hydroxythieno[3,2-b]thiophene (V). This compound was obtained by cyclization of IV at 95-100° in concentrated sulfuric acid. Workup gave light-yellow prisms (from aqueous ethanol) with mp 98.5-99° (mp 98-98.5° [4]) in 14.2% yield.

2-Nitroso-3-hydroxythieno[3,2-b]thiophene (VI). A 15.6-g (0.1 mole) sample of V was added to a solution of 4 g (0.1 mole) of sodium hydroxide in 100 ml of water, after which the solution was filtered, and 7.6 g (0.11 mole) of sodium nitrite was added to the filtrate. The resulting solution was cooled to 0-5° and added dropwise with vigorous stirring to 200 ml of dilute (1 : 1) hydrochloric acid. The mixture was stirred at 0-5° for 2 h, and the resulting precipitate was removed by filtration, washed with water, and dried to give 15.5 g (84%) of a product with mp 195-196°. Recyrstallization from benzene gave light-yellow prisms with mp 204-205°. Found: N 7.4; S 34.5%. $C_6H_3NO_2S_2$. Calculated: N 7.5; S 34.6%.

2-Acetamido-3-hydroxythieno[3,2-b]thiophene (III). An 18.5-g (0.1 mole) sample of IV was added with stirring at 35-40° to a solution of 100 g of stannous chloride in 170 ml of concentrated hydrochloric acid, and the mixture was stirred at 38-42° for 3 h. It was then cooled, and the precipitated VII was removed by filtration, washed with ether, and dried to give 34.5 g (51%) of colorless prisms (from aqueous ethanol) of VII. A solution of 22 g of acetic anhydride in 36 ml of ether was added with vigorous stirring at 0-5° to a suspension of 34.0 g (0.05 mole) of VII in 200 ml of water, after which a solution of 50 g of sodium hydroxide in 100 ml of water was added dropwise in the course of 10-15 min. The mixture was then stirred at 0-5° for 40 min and at room temperature for 30 min. The ether was removed in vacuo, and the solution was acidified with respect to Congo red with dilute (1 : 1) hydrochloric acid. Workup gave 13.5 g (63.4%) of pinkish prisms (from 50% ethanol in the presence of activated charcoal) of III with mp 163-164°. Found: C 45.0; H 3.2%. $C_6H_7NO_2S_2$. Calculated: C 45.1; H 3.3%.

2-Methylthieno[3,2-b]thieno[2,3-d]thiazole (II). A mixture of 4.26 g (0.02 mole) of III and 4 g of phosphorus pentasulfide was heated at 140-145° for 5 min, after which it was cooled to 100°, treated with hot water, and neutralized with 8% sodium hydroxide solution. The base was removed by steam distillation and extracted from the distillate with ether. Workup of the extract gave 1.3 g (30.8%) of a product with mp 106-107°. Recrystallization from petroleum ether gave colorless needles with mp 111-112°. Found: C 45.4; H 2.3; N 6.6%. $C_8H_5NS_2$. Calculated: C 45.5; H 2.4; N 6.7%. The picrate was obtained as yellow needles (from ethanol) with mp 140-141°. Found: N 12.6%. $C_8H_5NS_3 \cdot C_6H_3N_3O_7$. Calculated: N 12.66%.

Ethyl p-Tosylate. A mixture of 2.11 g (0.01 mole) of II and 2.2 g (0.011 mole) of ethyl p-toluenesulfonate was heated at 140-150° for 6 h, after which it was cooled and treated with anhydrous acetone. The precipitate was removed by filtration, washed with anhydrous acetone and anhydrous ether, and vacuum dried to give grayish prisms (from anhydrous ethanol), with mp 214-215°, in 70% yield. Found: C 49.5; H 4.3%. $C_{17}H_{18}NO_3S_4$. Calculated: C 49.5; H 4.4%.

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