RESEARCH ON THIOPHENES

X. Synthesis and Some Physical Properties of Thieno-[2,3-b]thiophene*

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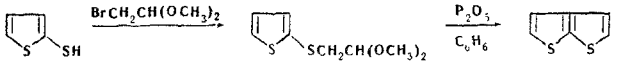
Thieno[2, 3-b]thiophene is prepared in a way similar to that previously described for the synthesis of thieno[3, 2-b]thiophene, the method being based on intramolecular condensation of methyl (3-formyl-2-thienylmercapto) acetate. The IR and PMR spectra of thieno[2, 3-b]-thiophene, 2-ethylthieno[2, 3-b] thiophene and 2-ethylthieno[3, 2-b]-thiophene are investigated.

The literature indicates that attention has been primarily devoted to two methods of synthesizing isomeric thienothiophenes viz. cyclizing (a) aliphatic derivatives, and (b) thiophene derivatives. There are two defects inherent in the first of these, the thienothiophenes are formed as difficulty separable mixtures of isomers, and in very low yields.

A synthesis of thieno[2, 3-b]thiophene, starting from a thiophene derivative, 2-mercaptothiophene, was carried out [1] thus:

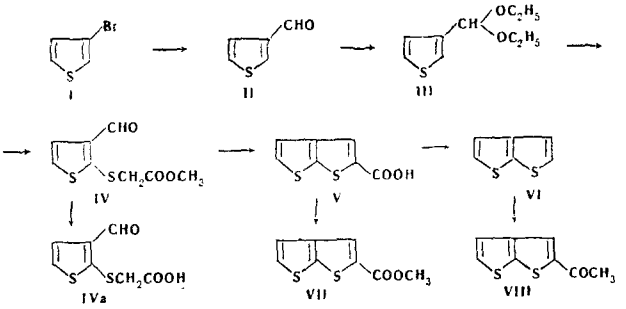


but the yield of thieno[2, 3-b]thiophene is low. It should be mentioned, incidentally, that the cyclization of thienyl-2-mercaptoacetals by acid reagents, used to synthesize thieno[2, 3-b]thiophene, can be accompanied by isomerization.

It is shown in [3, 4], and also in a paper by the present authors [5] that such isomerization can actually take place.

Thus, when using the method of [1, 2], it was impossible to be sure that the resultant thieno[2, 3-b]thiophene was free from traces of isomeric thieno[3, 2-b] thiophene. We have prepared the latter compound by a new method, based on intramolecular condensation of methyl(2-formyl-3-thienylmercapto)acetate [6].

The present paper gives results of our experiments on preparing thieno[2, 3-b]thiophene by an analogous method. Since there is cyclization in alkaline solution, the possibility of isomerization is precluded. Starting from β-bromothiophene, the method of [7] was used to prepare β-thiophenaldehyde, and the appropriate acetal from it. Further, by means of a method developed in our laboratory [8], the acetal was converted to methyl (3-formyl-2-thienylmercapto)acetate, and treatment of the latter with sodium ethoxide gave a carboxylic acid of composition $C_7H_2O_2S_2$. The mere fact that an acid of such composition is formed, as well as an observation [9] indicating that 3-thiophenealdehyde metallizes at position 2, shows that the structure of the acid is V. Thus the sequence of changes leading from β-bromothiophene to the final compound **VI** and its derivative can be represented by:



The last stage, decarboxylation, was effected by heating the thieno[2, 3-b]thiophene-2-carboxylic acid in quinoline. The yield of **VI**, calculated on the starting β-bromothiophene, amounted to about 40%.

It was of interest to determine whether there was a trace of thieno[3, 2-b]thiophene in its isomer **VI**, and for that purpose the IR spectra of these compounds were investigated.* The lots (Figs. 1 and 2) show that the **VI** spectrum contains a larger number of absorption bands than the spectrum of thieno[2, 3-b]thiophene,

*For Part IX see [13].

*This part of the work was done by B. V. Lopatin, to whom we express our thanks.

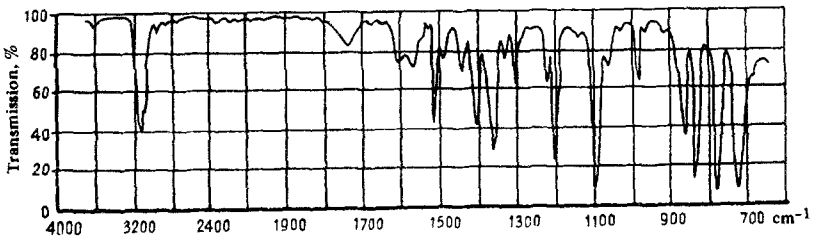


Fig. 1. IR spectrum of thieno[2, 3-b]thiophene (no solvent).

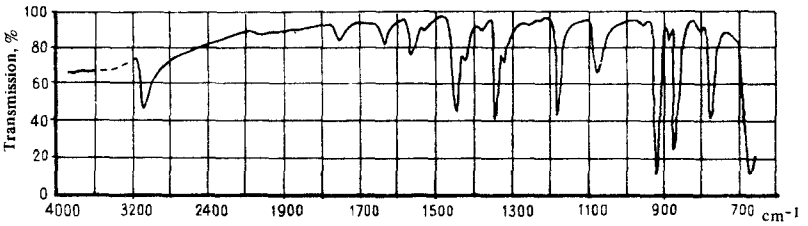


Fig. 2. IR spectrum of thieno[3,2-b]thiophene (tableted with KBr).

and this may be presumed to be connected with lowering of the degree of symmetry of the molecule on passing from the latter to **VI**. Bands with frequencies 676 and 1347 cm^{-1} were selected as analytical bands for quantitative determination. Their high intensities (D = 0.824 and 0.354 respectively), enable the presence of 1–2% (using the 676 cm^{-1} line) or 3–4% (using the 1347 cm^{-1} line) of thieno[3,2-b]thiophene in **VI** to be determined quite confidently. Since the specimen of thiophene prepared by us did not show the 676 and 1347 cm^{-1} absorption bands, it could be concluded that it did not contain any appreciable trace of the isomer.

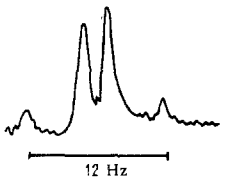


Fig. 3. PMR spectrum of thiophene protons of thieno[3,2-b]thiophene (CCl_4 solvent).

As would be expected, the two isomeric thienothiophenes differed in PMR spectrum (see Table and Figs. 3,4).*

The signals of the C=C double bond protons are in the 6.7–7.3 ppm region. Comparison of ethyl-substituted **IX** and **X** shows the **X** signals to be in a weaker field than the **IX** ones.

Though clear-cut evidence for assigning signals to position 4 or 5 is lacking, however, comparing the spectra of **VI**, **IX**, and **X** with the spectrum of thiophene, the weak field signal can be assigned to a proton in the α position, and the strong field one to one in the β position with respect to sulfur. Not the least spin-spin interaction was observed in the spectra of **VI** and **IX** (in any case it is under 0.3 cps). In **X** the G_{36} constant is somewhat less than in the unsubstituted thieno[3,2-b]thiophene (G_{36} 1.5)[10]. The occurrence of remote interaction between protons 3 and 6 can be regarded as a characteristic of thieno[3,2-b]thiophene.

In **X** the signal from the position 2 proton, and in **X** that from the position 3 have a fine structure due to interaction with CH_2 group protons.

Ethyl group signals are observed separately for CH_2 and CH_3, and have an ordinary fine structure, a quadruplet and a triplet respectively.

EXPERIMENTAL

3-Thiophenealdehyde (II) was prepared as previously described [7], yield 70%, bp 79°–82° (15mm); n_D^{20} 1.5820. 2,4-Dinitrophenylhydrazone mp 235–237° (ex EtOH-AcOEt). The literature [7] gives mp 235°–237°.

3-Thiophenealdehyde diethylacetal (III). A mixture of 54 g (0.48 mole) **II**, 106.8 g (0.68 mole) ethyl orthoformate, 240 ml absolute EtOH, and 5 drops conc. HCl was refluxed for 6 hr. After cooling the solution was poured into 1 *l* water, and the oil that precipitated extracted with ether. The ether extract was washed with water, then dried over $MgSO_4$, yield 64.7 g (73%) acetal bp 96°–102°(12 mm); n_D^{20} 1.4950. Found: C 57.85; 58.06; H 7.43; 7.42; S 17.22; 17.01%, calculated for $C_9H_{14}O_2S$: C 58.06; H 7.59; S 17.20%.

Methyl(3-formyl-2-thienylmercapto)acetate (IV). 110 ml ether solution of BuLi (concentration 0.071 g/ml) was added dropwise to 22g (0.12 mole) acetal III in 50 ml dry ether, cooled to −30° under dry nitrogen, and stirred. When addition was complete and the products had warmed up to room temperature, they were refluxed for 20 min, cooled again to −30°, and 3.9 g (0.12 g-at) dry S added. Then cooling was terminated, and the mixture stirred so long as any S remained unreacted. The products were again cooled to −30°, 13.4 g methyl chloroacetate added dropwise and the mixture refluxed for 2 hr, cooled to between −5° and −10°, and 90 ml 25% ammonium chloride solution added. A white flocculent precipitate formed, and gradually dissolved. The water layer was separated off and extracted with ether, the ether extract combined with the ether layer, and the whole dried over $MgSO_4$. Yield 19.5 g (80%) substance bp 156°–161° (4 mm), which solidified. After recrystallizing from EtOH and washing with heptane it had mp 53–55°. Found: C 44.85; 44.88; H 3.61; 3.62; S 29.04; 29.34%, calculated for $C_8H_8O_3S_2$: C 44.42; H 3.74; S 26.69%.

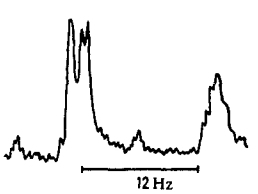
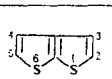
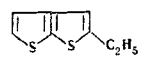
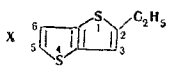


Fig. 4. PMR spectrum of thiophene protons of 2-ethylthieno[3,2-b]-thiophene (CCl_4 solvent).

Thieno[2,3-b]thiophene-2-carboxylic acid (V). 1 g (0.005 mole) IV in 5 ml MeOH was added to a warm stirred solution of 0.32 g (0.013 g-at) Na in 20 ml MeOH, and the mixture stirred and refluxed for 3 hr. A voluminous yellow precipitate formed; most of the MeOH was then distilled off, and the precipitate dissolved in water. The material not dissolved in the water was filtered off, the aqueous solution was cooled with ice water while it was acidified with conc. HCl until acid to Congo Red. A pale yellow precipitate formed, 0.73 g (86%,

*The authors thank V. F. Bystrov for determining and analyzing the PMR spectra of the compounds set out in the table.

Chemical Shifts and Spin-spin Interaction Constants (CCl_4 solutions)
(δ in ppm on TMS)

Compound	δ_2	δ_3	δ_4	δ_5	CH_2	CH_3
VI 	7.27	7.17	7.17	7.27	—	—
			($G_{23}=G_{54}=5.2\pm0.1$ cps)			
IX 	—	6.58	6.77	6.92	2.69	1.27
			($G_{45}=5.3\pm0.3$ cps)			
X 	—	6.76	6.98 (δ_6)	7.05	2.82	1.30
			($G_{36}=0.5\pm0.1$ cps)			
			($G_{56}=5.5\pm0.1$ cps)			

mp 243°–245°). After recrystallizing from EtOH it had mp 249°. The literature [11] gives mp 247°. Found: C 45.69; 45.65; H 2.17; 2.24; S 34.72; 34.55%, calculated for $C_7H_4O_2S_2$: C 45.64; H 2.19; S 34.82%.

(3-Formyl-2-thienylmercapto)acetic acid (IVa). This was synthesized by a method similar to that used for the thiophene-2-carboxylic acid V, the mixture being refluxed for 2 hr. 2.9 g IV gave 2.05 IVa, mp 127°–129° (ex EtOH). Found: C 41.89; 42.04; H 2.82; 2.94; S 31.80; 31.76%, calculated for $C_7H_6O_3S_2$: C 41.56; H 2.99; S 32.21%.

Methyl thieno[2, 3-b]thiophene-2-carboxylate (VII). A saturated ethereal solution of diazomethane containing 0.094 g diazomethane was added dropwise to a boiling EtOH solution of 0.21 g (0.001 mole) V (only part dissolved). Yield of VII 0.2 g. After vacuum distillation it had mp 102.5–103°. The literature gives [12] mp 106.5°. Found: C 48.64; 48.63; H 3.42; 3.10; S 31.81; 32.12%, calculated for $C_8H_6O_2S_2$: C 48.46; H 3.08; S 32.32%.

Thieno[2, 3-b]thiophene (VI). This was prepared by decarboxylating 3.3 g (0.015 mole) thiophene-2-carboxylic acid in 25 ml quinoline in the presence of 0.08 g Cu powder [6]. It was necessary to work up the product carefully to remove all the quinoline. The ether extract was dried over $CaCl_2$, the ether distilled off, and the residue vacuum distilled, yield 1.8 g (92%) material, 68.5° (3 mm); n_D^{20} 1.6675. The literature [11] gives bp 102° (16 mm). Found: C 51.32; 51.75; H 2.98; 3.07; S 45.13; 45.08%, calculated for $C_6H_4S_2$: C 51.40; H 2.87; S 45.75%. The analysis and mp corresponded to thieno[2, 3-b]-thiophene VI, mp 6°–6.5°.

2-Acetylthioeno[2, 3-b]thiophene (VIII). This was synthesized from thieno[2, 3-b]thiophene (0.5 g, 3.6 mM) and AcOCl (0.26 ml) in the presence of $SnCl_4$ (0.35 ml), in 10 ml dry benzene. Yield of VIII 0.6 g, mp 108°–110°. After steam distillation and recrystallization it had mp 113°–114°. The literature [11] gives mp 114°–115°. Found: C 52.68; 52.79; H 3.31; 3.24; S 35.12; 34.96%, calculated for $C_8H_6OS_2$: C 52.71; H 3.35; S 35.17%.

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