ACTA CHEMICA SCANDINAVICA 25 (1971) 27–34

Preparation of Some Methyl- and Formylthieno[2,3-b]-thiophenes and Thieno[3,2-b]thiophenes

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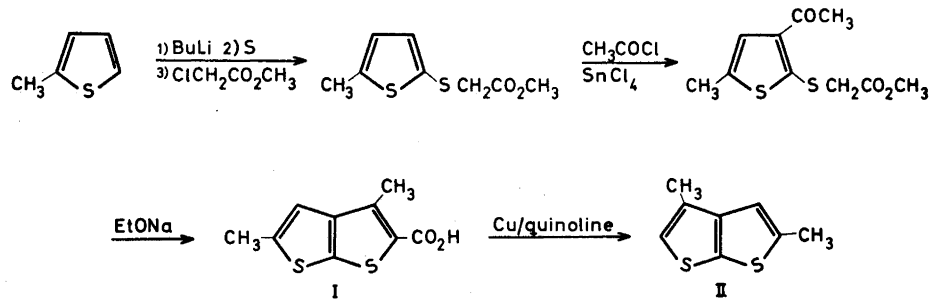
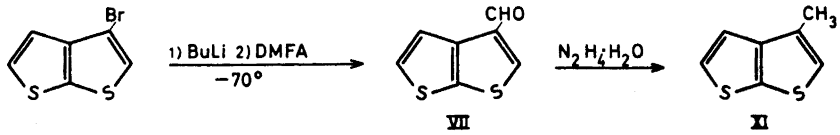
A number of mono- and dimethylthieno[2,3-b]thiophenes and thieno[3,2-b]thiophenes are prepared by condensation of methyl esters of formyl- or acetylthienylthioacetic acid or by Wolff-Kishner reduction of the formylthienothiophenes. The isomeric compositions in the Vilsmeier formylations of the thienothiophenes are reported.

Methyl and ethyl thienothiophenes have been described by Goldfarb *et al.*[1–5] and their synthetic methods have been adapted to the preparation of 2,4-dimethylthieno[2,3-b]thiophene (II) and 2,6-dimethylthieno[3,2-b]thiophene (IV). The starting compounds were 2-methylthiophene and 2-methyl-4-bromothiophene, respectively, which were successively treated with butyllithium, sulphur, and methyl chloroacetate. The methyl thienylthioacetates formed were acetylated with acetyl chloride and stannic chloride, cyclized in ethanolic sodium ethoxide, and the acids decarboxylated with copper in quinoline to give the dimethylsubstituted thienothiophenes.

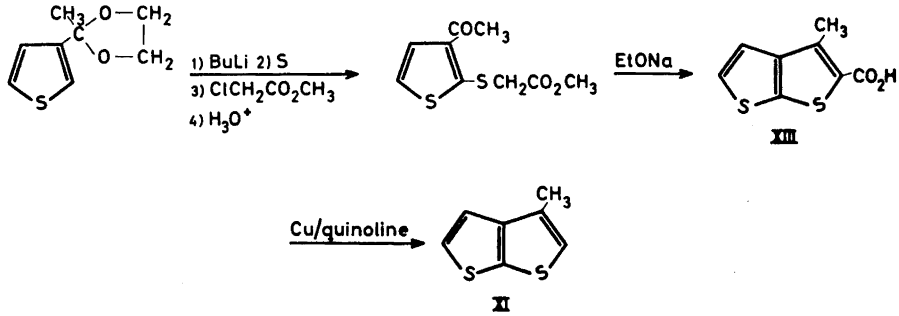


In order to synthesize 3-methylthieno[2,3-b]thiophene (XI), 3-bromothieno[2,3-b]thiophene [6] was treated with ethereal butyllithium at −70°, followed by reaction with *N*,*N*-dimethylformamide (DMFA), to give 3-

formylthieno[2,3-b]thiophene (VII). 3-Formylthieno[3,2-b]thiophene (VIII) was prepared in the same way from 3-bromothieno[3,2-b]thiophene.[6] Wolff-Kishner reduction of the 3-formylthieno[2,3-b]thiophene gave the 3-methylthieno[2,3-b]thiophene (XI). This compound has previously been mentioned by Goldfarb *et al.*,[3,7,8] but no experimental details are given.

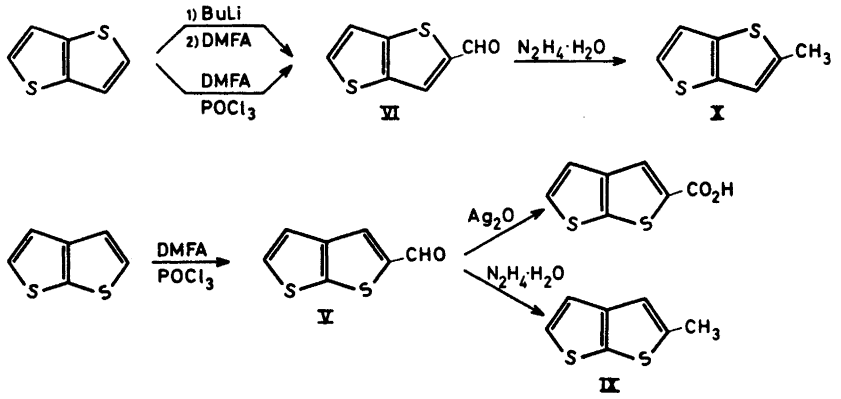


It has also been found that metalation of 3-acetylthiophene ethylene acetal, followed by successive treatment with sulphur and methyl chloroacetate and acid hydrolysis, constitutes a more convenient route to 3-methylthieno-[2,3-b]thiophene (XI). The methyl (3-acetyl-2-thienylthio) acetate was cyclized with ethanolic sodium ethoxide to 2-carboxy-3-methylthieno[2,3-b]thiophene (XIII), which after decarboxylation with copper in quinoline gave the 3-methylthieno[2,3-b]thiophene (XI).



2-Methylthieno[3,2-b]thiophene (X) has been prepared in poor yield by Challenger *et al.*[9] by cyclization of (5-methyl-2-thienylthio)acetic acid with sulphuric acid and subsequent reductive aromatization with sodium borohydride. This reaction has been further studied by Gronowitz *et al.*,[10] who cyclized among others α-(2-thienylthio)propionic acid and obtained X. A better synthetic route to 2-methylthieno[3,2-b]thiophene was found to be Vilsmeier formylation of thieno[3,2-b]thiophene and Wolff-Kishner reduction of the 2-formylthieno[3,2-b]thiophene(VI). The same method was used to prepare 2-methylthieno[2,3-b]thiophene (IX) from thieno[2,3-b]thiophene.

The site of substitution in thieno[3,2-b]thiophene was confirmed by preparing the 2-formylthieno[3,2-b]thiophene (VI) *via* the 2-lithiothieno[3,2-b]-thiophene [11] and treating the lithiated compound with DMFA. To show that the formylation occurs in the 2-position in thieno[2,3-b]thiophene, the 2-formylthieno[2,3-b]thiophene (V) was oxidized with silver oxide. The isolated compound was identified as 2-carboxythieno[2,3-b]thiophene.[11]



A closer look at the crude reaction product after the Vilsmeier formylations of the thienothiophenes showed that the electrophilic reagent attacked predominantly at the α-positions. The crude reaction products were separated by gas chromatography and the peaks identified by means of retention times and their mass spectra and the ratio between the two isomers thus determined. Formylation of thieno[2,3-b]thiophene with one equivalent of phosphorus oxychloride gave only about 0.1 % of the 3-formylthieno[2,3-b]thiophene, that is a ratio of about 1000:1 for the 2-formyl-compound to the 3-formyl-compound. In the case of the thieno[3,2-b]thiophene, the 3-formylated product was present in less than 0.04 %, if present at all. In neither case was any diformylation observed. Gas chromatography after treatment of thieno[3,2-b]thiophene with two equivalents of phosphorus oxychloride showed no sign of diformylation. Thieno[2,3-b]thiophene, however, yielded small amounts of two compounds shown by mass spectroscopy to be diformylated products. No attempts were made to isolate and identify the isomers.

The structures of the compounds are all confirmed by their NMR-spectra. The NMR-data given in the Experimental Part are based on a first order treatment of the spectra. A comprehensive treatment of the NMR-spectra of the thienothiophenes will appear in a paper by Gestblom, Hartmann and the author.

EXPERIMENTAL

Methyl(5-methyl-2-thienylthio)acetate. In the usual nitrogen-swept Grignard apparatus a stirred solution of 34.3 g (0.35 mol) of 2-methylthiophene in 100 ml of dry ether was metalated at 0° by dropwise addition for 1 h of 380 ml of 0.95 N ethereal butyllithium. The mixture was refluxed for 15 min, cooled in ice-water, and 11.6 g (0.36 mol) of sulphur was added in portions over a period of 10 min, followed by stirring at room temperature for about 15 min and reflux for about 1 h. The reaction mixture was again cooled in ice-water, 39.1 g (0.36 mol) of methyl chloroacetate in 50 ml of dry ether was added, with stirring during 15 min and the mixture left overnight at room temperature. The next day 300 ml of a 25 % ammonium chloride solution was added and the pH adjusted to 5 with 1 N hydrochloric acid. The ether layer was treated with 1:10 hydrochloric acid, water and saturated sodium bicarbonate solution and dried with anhydrous magnesium

sulphate. Evaporation of the ether at reduced pressure left 68.8 g of a dark oil which was distilled. The fraction, b.p.$_{0.5}$ 96–99° (50.6 g), was used without further purification. NMR (acetone): τ_3 2.98; τ_4 3.34; τ_{OCH_3} 6.37; τ_{CH_3} 6.49; τ_{CH_3} 7.57. J_{34} = 3.3 cps; J_{CH_3-4} = 1.1 cps.

Methyl (3-acetyl-5-methyl-2-thienylthio)acetate. A solution of 30.3 g (0.15 mol) of methyl (5-methyl-2-thienylthio)acetate and 12.6 g (0.16 mol) of acetyl chloride in 200 ml of dry benzene was cooled to 0°. To this solution was added, dropwise with stirring, a solution of 39.0 g (0.15 mol) of stannic chloride in 45 ml of dry benzene. The temperature in the reaction mixture was not allowed to exceed 3° during the addition. The reaction was stirred at room temperature for 2 h and left overnight, after which 200 ml of 1:10 hydrochloric acid was added and the reaction stirred for 2 h. The benzene layer was washed with water and saturated sodium bicarbonate solution and dried with anhydrous magnesium sulphate. Evaporation of the benzene left 34.9 g of a dark oil, which crystallized on standing. One recrystallization from methanol gave 28.2 g (77 %) of methyl (3-acetyl-5-methyl-2-thienylthio)acetate. The analytic sample was crystallized from methanol to m.p. 68.0–70.5°. NMR (acetone): τ_4 2.84; τ_{CH_3} 6.17; τ_{OCH_3} 6.30; τ_{CH_3} 7.58; τ_{COCH_3} 7.58. J_{CH_3-4} = 1.2 cps. (Found: C 48.87; H 4.90; S 26.29. Calc. for $C_{10}H_{12}O_3S_2$ (244.3): C 49.16; H 4.95; S 26.25.)

2-Carboxy-3,5-dimethylthieno[2,3-b]thiophene (I). To a solution of 5.4 g of sodium in 300 ml of absolute ethanol was added all at once 18.3 g (0.075 mol) of solid methyl (3-acetyl-5-methyl-2-thienylthio)acetate. The reaction was refluxed for 5 h and most of the ethanol removed at reduced pressure. The residue was dissolved in water and 15.6 g (98 %) of 2-carboxy-3,5-dimethyl-thieno[2,3-b]thiophene precipitated upon acidification with dilute hydrochloric acid. The analytical sample was crystallized once from glacial acetic acid. It decomposed without melting at about 252°. NMR (acetone): τ_4 2.92; τ_{3CH_3} 7.33; τ_{5CH_3} 7.42. J_{5CH_3-4} = 1.1 cps. (Found: C 50.71; H 3.80; S 30.54. Calc. for $C_9H_8O_2S_2$ (212.3): C 50.92; H 3.80; S 30.21.)

2,4-Dimethylthieno[2,3-b]thiophene (II). A mixture of 8.48 g (0.04 mol) of 2-carboxy-3,5-dimethylthieno[2,3-b]thiophene (I) and 4.0 g of copper bronze in 150 ml of quinoline was heated in a nitrogen atmosphere with stirring during 1 h to boiling. 150 ml of quinoline was added dropwise during about 2 h to the boiling reaction mixture, while a quinoline/2,4-dimethylthieno[2,3-b]thiophene solution was allowed to distil off at the same rate as the addition took place. The residual quinoline in the reaction vessel was distilled under reduced pressure, and the combined quinoline phases were cooled by the addition of ice, acidified with dilute hydrochloric acid and extracted with ether. The ether was treated with water and with saturated sodium bicarbonate solution, and dried with calcium chloride. Evaporation of the ether left 5.22 g of the crude reaction product as an oil. This oil was distilled at reduced pressure over a small piece of sodium. The fraction, b.p.$_9$ 118–119°, (4.0 g), was redistilled, giving the pure 2,4-dimethylthieno[2,3-b]thiophene (II) in a yield of 2.59 g (38 %), b.p.$_9$ 118.7–119.0°, n_D^{20} 1.6210. NMR (acetone): $\tau_{3,5}$ 3.00, 3.09; τ_{2CH_3} 7.47; τ_{4CH_3} 7.68. J_{CH_3-H} = 1.2 cps. (Found: C 57.04; H 4.74; S 38.40. Calc. for $C_8H_8S_2$ (168.3): C 57.10; H 4.79; S 38.11.)

Methyl (2-methyl-4-thienylthio)acetate. Butyllithium, 34 ml 1.55 N in hexane, was cooled to −70° in the usual Grignard apparatus. A solution of 8.85 g (0.05 mol) of 2-methyl-4-bromothiophene in 20 ml of dry ether was added dropwise with stirring during 10 min, and the reaction mixture stirred for 5 min, after which 1.67 g (0.052 mol) of sulphur was added in one portion. The reaction was stirred for 60 min, the cooling bath removed and the stirring continued for another 120 min. The reaction flask was now cooled in ice-water, a solution of 5.65 g (0.052 mol) of methyl chloroacetate in 20 ml of ether was added during 5 min, and the mixture stirred for 60 min at room temperature. After standing overnight at room temperature, the reaction mixture was cooled to 0°, 125 ml of an ice-cold 25 % ammonium chloride solution was added, and the mixture stirred for 30 min. The ethereal phase was treated with water and saturated sodium bicarbonate solution, and dried with anhydrous magnesium sulphate. Evaporation at reduced pressure left 10.8 g of a dark oil. This oil was distilled, and the fraction b.p.$_{0.1}$ 90–98° (5.25 g) was used without further purification. NMR (acetone): τ_5 2.89; τ_3 3.21; τ_{OCH_3} 6.35; τ_{CH_3} 6.40; τ_{CH_3} 7.57. J_{35} = 1.5 cps; J_{CH_3-3} = 1.2 cps.

Methyl (2-acetyl-5-methyl-3-thienylthio)acetate. To a stirred solution of 18.2 g (0.09 mol) of methyl (2-methyl-4-thienylthio)acetate and 7.8 g (0.10 mol) of acetyl chloride in 140 ml of dry benzene, cooled to 0°, was added dropwise 23.5 g (0.09 mol) of stannic chloride

in 25 ml of dry benzene. The temperature in the reaction vessel was not allowed to exceed 5°. When the reaction was completed, the reaction was stirred for 2 h and left for 48 h, whereafter it was hydrolyzed with 150 ml of 1:10 hydrochloric acid. The aqueous phase was extracted once with benzene, and the combined benzene solutions treated with water and saturated sodium bicarbonate solution. Evaporation of the benzene at reduced pressure left 19.3 g of the crude reaction product. One recrystallization from ethanol gave 14.8 g (76 %) of the title compound. The analytic sample was crystallized twice from methanol. The compound nearly melted between 90 – 92°, but crystallized on further heating and melted at 98.0 – 99.5°. NMR (acetone): τ_4 3.02; τ_{CH_3} 6.15; τ_{OCH_3} 6.30; τ_{CH_3} 7.50; τ_{COCH_3} 7.62. $J_{CH_3-4}=1.0$ cps. (Found: C 49.25; H 5.04; S 26.26. Calc. for $C_{10}H_{12}O_3S_2$ (244.3): C 49.16; H 4.95; S 26.25.)

2-Carboxy-3,5-dimethylthieno[3,2-b]thiophene (III) was prepared, in the manner described above for the preparation of I, from 12.2 g (0.05 mol) of methyl (2-acetyl-5-methyl-3-thienylthio)acetate, 3.6 g of sodium and 200 ml of absolute ethanol. The 2-carboxy-3,5-dimethylthieno[3,2-b]thiophene (III) was obtained in a yield of 8.3 g (78 %) after one recrystallization from glacial acetic acid. It decomposed without melting at 230 – 240°. NMR (acetone): τ_6 2.87; $\tau_{3CH_3,5CH_3}$ 7.38. $J_{5CH_3-6}=1.2$ cps. (Found: C 50.99; H 3.85; S 30.55. Calc. for $C_9H_8O_2S_2$ (212.3): C 50.92; H 3.80; S 30.21.)

2,6-Dimethylthieno[3,2-b]thiophene (IV) was prepared by decarboxylating 4.24 g (0.02 mol) of 2-carboxy-3,5-dimethylthieno[3,2-b]thiophene (III) in the manner described for the preparation of II, using 12 mg of copper bronze and 100 ml of quinoline. The crude reaction product, 3.21 g, was distilled at reduced pressure, giving 1.98 g (59 %) of the pure 2,6-dimethylthieno[3,2-b]thiophene(IV). B.p.$_{10}$ 116 – 117°, n_D^{20} 1.6202. NMR (acetone): $\tau_{3,5}$ 3.02; τ_{2CH_3} 7.47; τ_{6CH_3} 7.72. $J_{CH_3-H}=1.2$ cps. (Found: C 57.19; H 5.14; S 38.33. Calc. for $C_8H_8S_2$ (168.3); C 57.10; H 4.79; S 38.11.)

2-Formylthieno[2,3-b]thiophene (V). A solution of 14.0 g (0.1 mol) of thieno[2,3-b]-thiophene in 21.9 g (0.3 mol) of *N,N*-dimethylformamide was cooled in ice-water. To the solution was added, during 15 min and with vigorous stirring, 15.3 g (0.1 mol) of phosphorus oxychloride. The temperature in the reaction vessel was not allowed to exceed 20°. The reaction mixture was stirred for 15 min at 0°, 30 min at room temperature, and then heated to 60 – 65°, at which temperature an exothermic reaction started. When the exothermic reaction had ceased, the reaction mixture was heated for 45 min on a steam bath, cooled and poured on ice. The pH was adjusted to 5 – 6 with solid sodium acetate, and the reaction mixture left overnight. The reaction product was taken up in ether and the ether washed with water, then with saturated sodium bicarbonate solution and dried with anhydrous magnesium sulphate. Evaporation of the ether left 15.3 g of the crude reaction product. Recrystallization from ethanol gave the pure 2-formylthieno-[2,3-b]thiophene(V) with m.p. 45.0 – 46.0°. NMR ($CDCl_3$): τ_{CHO} 0.12; τ_3 2.15; τ_5 2.57; τ_4 2.72. $J_{45}=5.3$ cps. (Found: C 50.02; H 2.47; S 38.22. Calc. for $C_7H_4OS_2$ (168.2): C 49.99; H 2.38; S 38.14.)

2-Formylthieno[3,2-b]thiophene (VI). Thieno[3,2-b]thiophene was formylated as described above giving the title compound in a yield of 85 % after recrystallization from ethanol. M.p. 54.5 – 55.0°. NMR ($CDCl_3$): τ_{CHO} 0.03; τ_3 2.07; τ_5 2.31; τ_6 2.68; $J_{56}=5.3$ cps; $J_{36}=0.7$ cps. (Found: C 49.92; H 2.67; S 38.38. Calc. for $C_7H_4OS_2$ (168.2): C 49.99; H 2.38; S 38.14.)

Oxidation of 2-formylthieno[2,3-b]thiophene (V) with silver oxide. To a vigorously stirred and ice-cooled solution of 1.6 g (0.04 mol) of sodium hydroxide in 10 ml of water was added a solution of 3.4 g (0.02 mol) of silver nitrate in 10 ml of water, followed by 1.68 g (0.01 mol) of solid 2-formylthieno[2,3-b]thiophene, added in portions during about 5 min. After stirring for 15 min in the cold, the solid material was filtered off and the filtrate acidified with hydrochloric acid. The precipitated acidic material, 0.8 g, was identified by means of its IR-spectrum to be 2-carboxythieno[2,3-b]thiophene.[11]

2-Formylthieno[3,2-b]thiophene (VI) prepared via 2-lithiothieno[3,2-b]thiophene. A solution of 3.5 g (0.025 mol) of thieno[3,2-b]thiophene in 25 ml of dry ether was introduced into the usual nitrogen-swept Grignard apparatus. To this solution was added dropwise with stirring at room temperature 25.3 ml of 0.99 N ethereal butyllithium. The reaction mixture was stirred for 10 min at room temperature. By means of nitrogen the resultant solution was transferred during 10 min into a solution of 2.7 g (0.037 mol) of *N,N*-dimethylformamide in 25 ml of dry ether. The reaction mixture was stirred for 60 min at room temperature and then hydrolyzed by stirring for 30 min with 25 ml

of water. The ethereal layer was treated with 2 N hydrochloric acid until acid reaction of the aqueous layer, washed with water and saturated sodium bicarbonate solution, and dried with anhydrous magnesium sulphate. Evaporation of the ether left 2.9 g of a yellow crystalline product, which turned green on standing. One recrystallization from methanol gave 1.5 g of 2-formylthieno[3,2-b]thiophene with m.p. 52 – 55°. The IR-spectrum of the compound was identical with the spectrum of the 2-formylthieno-[3,2-b]thiophene previously described.

3-Formylthieno[2,3-b]thiophene (VII). In the usual nitrogen-swept Grignard apparatus 49.3 ml of 0.94 N ethereal butyllithium was cooled to −70°. To this solution was added dropwise, with stirring during 10 min, a solution of 10.2 g (0.046 mol) of 3-bromothieno[2,3-b]thiophene [6] in 15 ml of dry ether. The reaction mixture was stirred for 5 min, after which 5.1 g (0.070 mol) of *N,N*-dimethylformamide in 15 ml of dry ether was added all at once, warmed for about 60 min to room temperature and stirred at that temperature for an additional 60 min. The reaction intermediate was hydrolyzed by the addition of 100 ml of water and stirring for about 45 min. The ether layer was treated with 1 N hydrochloric acid until acid reaction, washed with water and saturated sodium bicarbonate solution and dried with anhydrous magnesium sulphate. Evaporation at reduced pressure left 6.85 g of the crude reaction product. Recrystallization from methanol gave 4.3 g (55 %) of 3-formylthieno[2,3-b]thiophene. The analytic sample was recrystallized from hexane to m.p. 66 – 68°. NMR (acetone): τ_{CHO} −0.05; τ_2 1.44; $\tau_{4,5}$ 2.25. (Found: C 49.98; H 2.57; S 38.50. Calc. for $C_7H_4OS_2$ (168.2): C 49.99; H 2.38; S 38.14.)

3-Formylthieno[3,2-b]thiophene (VIII) was prepared from 3-bromothieno[3,2-b]-thiophene [6] in the manner described above in a yield of 57 % after one recrystallization from ethanol. The analytic sample was obtained as colourless prisms by treatment of the compound with charcoal in hexane. M.p. 68 – 69.5°. NMR (acetone): τ_{CHO} −0.08; τ_2 1.32; τ_5 2.23; τ_6 2.50. J_{56} = 5.5 cps; J_{45} = 1.6 cps. (Found: C 50.34; H 2.40; S 38.25. Calc. for $C_7H_4OS_2$ (168.2): C 49.99; H 2.38; S 38.14.)

2-Methylthieno[2,3-b]thiophene (IX). 2-Formylthieno[2,3-b]thiophene, 5.3 g (0.032 mol), was treated with hydrazine according to the method of King and Nord [12] for the preparation of 2-methylthiophene. The reaction mixture was worked up, however, by pouring it into water and extracting it with ether. The ether was washed with water, 2 N hydrochloric acid, and saturated sodium bicarbonate solution and dried over calcium chloride. Evaporation of the ether left 4.6 g of the crude reaction product. Distillation at reduced pressure, over a small piece of sodium, gave 3.6 g (74 %) of the pure 2-methylthieno[2,3-b]thiophene. B.p.$_{10}$ 106.0 – 106.5°. n_D^{20} 1.6407. NMR (acetone): τ_5 2.61; τ_4 2.86; τ_3 3.06; τ_{CH_3} 7.52. J_{CH_3-3} = 1.2 cps; J_{45} = 5.4 cps. (Found: C 54.22; H 3.91; S 41.84. Calc. for $C_7H_6S_2$ (154.3): C 54.50; H 3.92; S 41.57.)

2-Methylthieno[3,2-b]thiophene (X) was prepared from 2-formylthieno[3,2-b]thiophene as described above in a yield of 73 %. B.p.$_9$ 104.5 – 105.0°. n_D^{20} 1.6467 (lit. value [10] n_D^{20} 1.6468). NMR (acetone): τ_5 2.64; τ_6 2.79; τ_3 3.04; τ_{CH_3} 7.52. J_{CH_3-3} = 1.2 cps; J_{56} = 5.4 cps; J_{36} = 0.6 cps.

3-Methylthieno[2,3-b]thiophene (XI) prepared from 3-formylthieno[2,3-b]thiophene in the manner described above in a yield of 61 %. B.p.$_{16}$ 119 – 120° (lit. value [7] b.p.$_{760}$ 245°) n_D^{20} 1.6397. NMR (acetone): τ_5 2.44; τ_4 2.70; τ_2 2.86; τ_{CH_3} 7.63. J_{CH_3-2} = 1.2 cps; J_{45} = 5.4 cps; J_{25} = 1.2 cps. (Found: C 54.22; H 3.99; S 41.95. Calc. for $C_7H_6S_2$ (154.3): C 54.50 H 3.92; S 41.57.)

3-Methylthieno[3,2-b]thiophene (XII) was prepared according to Goldfarb *et al.*[5] B.p.$_{16}$ 114.5°; n_D^{20} 1.6390. (lit. value b.p.$_3$ 73 – 74°; n_D^{20} 1.6370). NMR (acetone): τ_5 2.50; τ_6 2.71; τ_2 2.92; τ_{CH_3} 7.68. J_{CH_3-2} = 1.1 cps; J_{56} = 5.3 cps; J_{25} = 1.5 cps.

3-Acetylthiophene was prepared as described by Taft [13] from 3-lithiothiophene and *N,N*-dimethylacetamide in a yield of 67 %. M.p. 58 – 60° (petroleum ether (40 – 60°)), (lit. values m.p. 57.5 – 58.5°,[14] 56 – 57° [13]). NMR (CCl_4): τ_2 2.05; τ_4 2.58; τ_5 2.79; τ_{CH_3} 7.60. J_{45} = 5.0 cps; J_{25} = 2.8 cps; J_{24} = 1.4 cps.

3-Acetylthiophene ethylene ketal. A mixture of 12.6 g (0.10 mol) of 3-acetylthiophene, 9.3 g (0.15 mol) of ethylene glycol and a few crystals of *p*-toluenesulphonic acid in 150 ml of benzene was refluxed for 48 h in a 250 ml flask fitted with a water separator. The reaction mixture was treated with 100 ml of saturated sodium bicarbonate solution, and the benzene layer was washed with water and dried with anhydrous magnesium sulphate. Evaporation of the benzene at reduced pressure left 16.5 g of an oil which partially crystallized on standing in the cold. Filtration gave 12.3 g of a crystal-

line material which after one recrystallization from hexane gave 11.0 g (65 %) of the pure 3-acetylthiophene ethylene ketal. M.p. 34 – 35°. NMR (acetone): $\tau_{arom.}$ 2.50 – 2.98; τ_{CH_2} 6.10; τ_{CH_3} 8.41. (Found: C 56.41; H 5.82; S 18.96. Calc. for $C_8H_{10}O_2S$ (170.2): C 56.44; H 5.92; S 18.84.)

Methyl (3-acetyl-2-thienylthio)acetate. In the usual nitrogen-swept Grignard apparatus 5.10 g (0.03 mol) of 3-acetylthiophene ethylene ketal, dissolved in 30 ml of dry ether, was introduced and the solution cooled to 0°. To the stirred solution, 20 ml of 1.57 N butyllithium in hexane was added during 5 min, and the reaction mixture was refluxed for 30 min and then cooled in ice-water, after which 1.05 g of sulphur was added all at once. The reaction mixture was now refluxed for 90 min and again cooled in ice-water, and 3.58 g (0.033 mol) of methyl chloroacetate in 10 ml of dry ether was added with stirring during 10 min, and the mixture was stirred for 2 h. After standing overnight at room temperature, the reaction mixture was cooled in ice-water, 100 ml of ice-cold 1 N hydrochloric acid was added, and the mixture was stirred for 30 min. 1.90 g of crude methyl (3-acetyl-2-thienylthio)acetate fell out. An additional 0.97 g was obtained from the ether layer by first treating it with water and saturated sodium bicarbonate solution and drying it with anhydrous magnesium sulphate and then, after removing most of the ether, cooling it to −70°. Recrystallization from methanol gave the pure methyl (3-acetyl-2-thienylthio)acetate in a yield of 2.32 g (34 %) with m.p. 81 – 82°. NMR (acetone): $\tau_{4,5}$ 2.46, 2.61; τ_{CH_2} 6.08; τ_{OCH_3} 6.28; τ_{COCH_3} 7.52. $J_{45} = 5.75$ cps. (Found: C 47.03; H 4.37; S 28.06. Cacl. for $C_9H_{10}O_3S_2$ (230.3): C 46.94; H 4.38; S 27.85.)

2-Carboxy-3-methylthieno[2,3-b]thiophene (XIII) was prepared as previously described by cyclizing 2.07 g (0.009 mol) of methyl (3-acetyl-2-thienylthio)acetate with 0.83 g of sodium dissolved in 100 ml of absolute ethanol. 1.73 g (97 %) of the crude 2-carboxy-3-methylthieno[2,3-b]thiophene was isolated. The analytic sample was recrystallized once from ethanol-water. The compound sublimed at about 190° and decomposed without melting in a sealed capillary at 230 – 240°. NMR (acetone): τ_5 2.36; τ_4 2.61; τ_{CH_3} 7.28. $J_{45} = 5.6$ cps. (Found: C 48.34; H 3.17; S 32.62. Calc. for $C_8H_6O_2S_2$ (198.2): C 48.44; H 3.05; S 32.36.)

3-Methylthieno[2,3-b]thiophene (XI) prepared from 2-carboxy-3-methylthieno[2,3-b]-thiophene. The acid XIII, 1.58 g (0.008 mol), was decarboxylated in the manner previously described using 0.8 g of copper bronze and 100 ml of quinoline. The crude reaction product, 1.08 g, was distilled at reduced pressure giving 0.88 g (71 %) of the pure 3-methylthieno-[2,3-b]thiophene. B.p.$_9$ 102.0 – 103.5°, n_D^{20} 1.6401. The IR- and NMR-spectra of the compound were identical with those of the 3-methylthieno[2,3-b]thiophene prepared from VII.

The gas chromatographic analyses were made with an Aerograph 1520 gas chromatograph equipped with a flame ionization detector and a 1/8″ × 8′ column (temp. prog. 50 – 200°, 6°/min, 20 % SE-30 silicone gum on Chromosorb-W HMDS 60 – 80 mesh, 16 ml He/min). Mass spectrometry identifications were performed with an LKB-9000 mass spectrometer with gas chromatograph. The isomeric compositions in the crude reaction products were determined by evaluating the peak areas and comparing them with those from known mixtures of the isomers. The crude reaction product from the formylation of thieno[2,3-b]thiophene showed two completely resolved peaks, ret. times 26.8 and 28.5 min. These were identified as 3- and 2-formylthieno[2,3-b]thiophene, respectively. The isomeric composition was determined to be 2-formylthieno[2,3-b]-thiophene 99 ± 3 % and 3-formylthieno[2,3-b]thiophene 0.1 ± 0.02 %. GLC of the crude reaction product from the formylation of thieno[3,2-b]thiophene also showed two peaks with ret. times 26.4 and 28.6 min consistent with 3-formylthieno[3,2-b]thiophene and 2-formylthieno[3,2-b]thiophene, respectively. The peak with ret. time 26.4 min was, however, too small (less than 0.04 %) to be determined with any accuracy. Also the mass spectrometry identification of the peak was beset with difficulties, even though several attempts on different columns were made. Vilsmeier formylation of the thieno-thiophenes using 1 equiv. of the thienothiophene, 2 equiv. of phosphorus oxychlorid and 5 equiv. of DMFA were performed following the previously described procedure. The crude reaction products were chromatographed on columns packed with 20 % SE-30 and 5 % OV-17, both on Chromosorb-W HMDS. In the case of thieno[3,2-b]thiophene no peak with retention time longer than that for 2-formylthieno[3,2-b]thiophene was observed. The reaction mixture from the formylation of thieno[2,3-b]thiophene, on the other hand, showed on both columns two new not resolved peaks with ret. times 42.3

and 42.6 min (SE-30). The mass spectra showed that both peaks had mass peaks at *m/e* 196 and abundant fragment ions at *m/e* 167, 139, 95, and 69. The total amount of the two compounds is estimated to be less than 1 %.

Acknowledgement. The author is indebted to Professor Salo Gronowitz for his kind interest in this work.

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Received May 12, 1970.