REACTIONS OF AROMATIC AND HETEROAROMATIC COMPOUNDS BEARING ELECTRON-ACCEPTOR SUBSTITUENTS

VIII.* SYNTHESIS AND SOME TRANSFORMATIONS OF DIMETHYL(2-THIENYL) SULFONIUM SALTS

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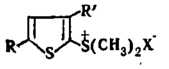
Dimethyl(2-thienyl)sulfonium salts were synthesized for the first time. The corresponding triiodomercurates were obtained by the reaction of methyl 2-thienyl sulfide or its substituted derivatives with methyl iodide and mercuric iodide. Sulfonium perchlorates are formed as a result of the reaction of thiophene compounds with dimethyl sulfoxide in the presence of $POCl_3$ and perchloric acid. The HgI_3^- anion was replaced by NO_3^- by means of an anion-exchange resin. The methods for the dimethylation of sulfonium salts with conversion of them to the corresponding sulfides were studied; the conditions for obtaining quantitative yields from these reactions by means of an anion exchange resin in the acetate form were found.

In the course of our investigations of the specificity of electrophilic substitution of aromatic and heteroaromatic compounds that bear electron-acceptor substituents, it was necessary to study several reactions of dialkyl(2-thienyl)sulfonium salts of the I type:



I–IV

I $R=R'=H$; II $R=Br$, $R'=H$; III $R=R'=Br$; IV $R=CH_3$, $R'=H$

We did not observe any data on such salts in the literature. It therefore became necessary to seek routes for their synthesis. It first seemed expedient to study the action of dimethyl sulfate on methyl 2-thienyl sulfide. However, the necessary salt (I, $X = CH_3OSO_3^-$) could not be obtained when these reagents were heated.

The desired result was achieved only when the method in [2] was used – the corresponding sulfonium triiodomercurates (I-III, $X = HgI_3$) (see Table 1) are formed when a solution of the sulfide and methyl iodide in acetone is stirred in the presence of mercuric iodide. The structure of the salts follows from the method used to synthesize them and is confirmed by the PMR spectra. In particular, the spectrum of salt I ($X = HgI_3$) contains the following signals: singlet for $(CH_3)_2\overset{+}{S}$ at δ 3.42 ppm, quartet for 4-H at 7.40 ppm, $J_{3,4} = 4.5$ Hz, $J_{4,5} = 5$ Hz; quartet at 8.08 for 3-H, $J_{3,4} = 4.5$ Hz, $J_{3,5} = 1.5$ Hz; quartet at 8.21 ppm for 5-H, $J_{4,5} = 5$ Hz, $J_{3,5} = 1.5$ Hz. The salts with the HgI_3^- anion are rather unstable (in particular, they decompose during recrystallization) and, as a consequence of this, are unsuitable for a study of the reactivities. They were converted by a known method [3] by replacement of the HgI_3^- anion by the NO_3^- anion by means of an AV-17 anion-exchange resin in the nitrate form to the corresponding nitrates. Nitrate I ($X = NO_3$) proved to be a

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*See [1] for communication VII.

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TABLE 1. Sulfonium Salts of the Thiophene Series (I-IV)

Sulfonium salt	Prepara. meth.	mp (dec.) °C	Empirical formula	Found, %			Calc., %			Yield, %
				C	H	S	C	H	S	
I, X=HgI_3	A	89—91	$C_6H_9HgI_3S_2$	9,7; 10,0	1,2; 1,3	—	9,9	1,2	—	80
II, X=HgI_3	A	128,5—129,5	$C_6H_8BrHgI_3S_2$	9,0; 8,9	1,0; 1,0	—	8,9	1,0	—	69
III, X=HgI_3	A	94—102	$C_6H_7Br_2HgI_3S_2$[a]	8,3	0,8	7,2	8,2	0,8	7,3	45
I, X=NO_3[b]	B	35—40								97
II, X=NO_3	B	143,5—144,5	$C_6H_8BrNO_3S_2$	24,9; 25,0	3,0; 2,8	—	25,2	2,8	—	96
I, X=ClO_4	C	137—138	$C_6H_9ClO_4S_2$[c]	29,3; 29,5	3,6; 3,7	26,1; 26,0	29,4	3,7	26,2	76
IV, X=ClO_4	C	94—95	$C_7H_{11}ClO_4S_2$[d]	32,7; 32,6	4,5; 4,3	25,1; 25,0	32,5	4,3	24,8	50

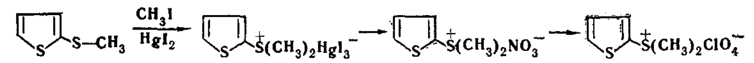
a) Found: Br 17.8; I 42.3%. Calculated: Br 18.1; I 43.0%.

b) The perchlorate obtained from the nitrate (see the experimental section) was identical to the sample obtained via method C.

c) Found: Cl 14.4; 14.4%. Calculated: Cl 14.5%.

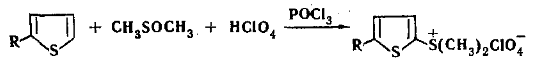
d) Found: Cl 13.8; 13.8%. Calculated: Cl 13.7%.

very hygroscopic substance and was therefore converted to the corresponding perchlorate. Thus the scheme for the synthesis of dimethyl(2-thienyl)sulfonium perchlorate includes the following steps:



In searching for a more convenient method for the synthesis of the sulfonium salts of interest to us, we turned to several other reactions based on the direct electrophilic substitution of hydrogen in activated aromatic compounds by the $(CH_3)_2\overset{+}{S}$ group. This sort of reaction is observed, for example, during the action of chlorodimethylsulfonium hexachloroantimonate on anisole; in this case, the dimethyl (p-methoxyphenyl)sulfonium salt [4] is formed in 85% yield. Considering that thiophene is close to anisole with respect to its activity in electrophilic substitution reactions [5], we attempted to accomplish the analogous transformation with thiophene, but we could not isolate the necessary salt in the pure state.

Another attempt was made in analogy with the known transformation for phenols to sulfonium salts under the influence of sulfoxides (usually dimethyl sulfoxide) and HX acids [6-8]. The intermediate in this reaction is probably the hydroxydialkylsulfonium salt, $(CH_3)_2\overset{+}{S}OHX^-$; i.e., it is analogous to the above-mentioned conversion of chlorodimethylsulfonium hexachloroantimonates [4]. As it turned out, the modification of this reaction using the action of a mixture of dimethyl sulfoxide, $POCl_3$, and perchloric acid [8] makes it possible to obtain readily the necessary salts I and IV (X = ClO_4) from thiophene and methylthiophene.



I R=H; IV R=CH_3

The PMR spectrum of salt I (X = ClO_4) is similar to the spectrum of salt I (X = HgI_3). The spectrum of salt IV – dimethyl(5-methyl-2-thienyl)sulfonium perchlorate – is as follows: a doublet at 2.61 ppm for 5-CH_3, $J_{4,5\text{-}CH_3}$ = 1 Hz; a singlet at 3.45 ppm for $(CH_3)_2S^+$; a quartet at 7.05 ppm for 4-H, $J_{3,4}$ = 4 Hz, $J_{4,5\text{-}CH_3}$ = 1 Hz; a doublet at 7.91 ppm for 3-H, $J_{3,4}$ = 4 Hz.

To prove the structures of the sulfonium salts obtained, it is extremely convenient to convert them to the corresponding known sulfides. This sort of transformation may also be of preparative interest, since one can obtain alkyl 2-thienyl sulfides without using organometallic reagents. There are several methods for the dealkylation of aromatic sulfonium salts. The most widespread of them is treatment with alkali or alkali metal alkoxides [9], but this method proved to be unsuitable in our case because of low yields. The reaction with pyridine [8] or KCl solution [8, 10] is somewhat more convenient for our purposes, but the yields of sulfides under these conditions did not exceed 70%, and, for the most part, were at the 30-50% level, which is clearly inadequate for the determination of the ratio of the isomers that might have been formed in the electrophilic substitution reactions of the sulfonium salts. In searching for a more acceptable method for the demethylation of the sulfonium salts, we turned our attention to the demethylation of ammonium salts by heating their acetates in low-polarity solvents, for example, chloroform or mixtures of chloroform with benzene [11]. We found that this method gives excellent results as applied to sulfonium salts and makes it possible to quantitatively convert the sulfonium salt (for example, as the perchlorate) to the corresponding sulfide, during which the pyrolysis step proves to be superfluous because of the instability of the sulfonium acetates: the perchlorate is converted to the sulfide when a methanol solution of the salt is passed through a column filled with ÉDÉ-10p resin in the acetate form.

EXPERIMENTAL

The PMR spectra of acetone–dimethyl sulfoxide solutions of the sulfonium salts were recorded with an RS-60 spectrometer (Special Design Office, N. D. Zelinskii Institute of Organic Chemistry, Academy of Sciences of the USSR) with hexamethyldisiloxane as the internal standard. The authors thank L. V. Shmelev for recording the spectra.

The chromatographic analyses of the sulfides were performed with an LKhM-8M chromatograph with a thermal-conductivity detector with helium as the gas carrier at a flow rate of 30 ml/min with a stainless steel, 4×2000 mm column filled with 20% polyethylene glycol adipate on Chromosorb W at 150°C.

Preparation of Sulfonium Salts. A) Dimethyl (2-thienyl)sulfonium Triiodomercurate. A 0.011 mole sample of mercuric iodide and 0.048 mole of methyl iodide were added to a solution of 0.01 mole of methyl 2-thienyl sulfide in 20 ml of acetone. The mass was heated and stirred on a water bath for 1 h, during which the mercuric iodide dissolved almost completely. The resulting yellow solution was filtered to remove the excess HgI_2, and the acetone was evaporated to give 5.8 g (80%) of a substance with mp 74-78°. The reaction product was washed with methanol and ether and vacuum dried over paraffin to give a product with mp 89-91°. Dimethyl (5-bromo-2-thienyl)sulfonium and dimethyl(3,5-dibromo-2-thienyl)sulfonium triiodomercurates were also obtained via method A.

B) Dimethyl(2-thienyl)sulfonium Nitrate. A solution of 3.63 g (0.005 mole) of dimethyl(2-thienyl)sulfonium triiodomercurate in a mixture of 55 ml of acetone and 25 ml of water was passed through a column containing 50 g of AV-17 anion exchange resin in the nitrate form.* Another 50 ml of aqueous acetone (1 : 1) was then passed through the same column, and the acetone and water were evaporated. Lyophilic drying gave 1.0 g (97%) of an extremely hygroscopic, dirty-white, crystalline substance with mp 35-40°. Treatment of an aqueous solution of 0.46 g of the nitrate with 70% perchloric acid gave an abundant white precipitate. This precipitate was removed by filtration, washed with methanol and ether, and dried in vacuo over P_2O_5 to give 0.22 g (42%) of dimethyl(2-thienyl)sulfonium perchlorate with mp 135-138°. An analytical sample had mp 137.5-138° (from methanol). Found: C 29.0; 28.8; H 3.5; 3.7; Cl 14.3; 14.4; S 25.9; 26.0%. $C_6H_9ClO_4S_2$. Calculated: C 29.4; H 3.7; Cl 14.5; S 26.2%.

Dimethyl(2-bromo-2-thienyl)sulfonium nitrate was also obtained via method B.

C) Dimethyl(2-thienyl)sulfonium Perchlorate. A 0.25 ml sample of thiophene† was added at 0° to a mixture of 125 ml of 70% perchloric acid and 100 ml of phosphorus oxychloride, the mixture was stirred for 15-20 min, and 0.25 mole of dimethyl sulfoxide was added dropwise to the resulting emulsion while holding the temperature at 5°; in the process, the mixture took on a red-brown color. Stirring was continued for another 1 h at +5° and then for 2 h at room temperature. After this, the contents of the flask were poured over ice, and the resulting light-green precipitate was removed by filtration, washed with methanol and ether, and recrystallized from methanol to give 74% of a product with mp 134-137°. An analytical sample had mp 137-138°. This product did not depress the melting point of a sample of perchlorate obtained through the triiodomercurate and nitrate (see above). Dimethyl(5-methyl-2-thienyl)sulfonium perchlorate was similarly obtained in 50% yield from 2-methylthiophene and had mp 82-85°. An analytical sample had mp 94-95° (from methanol). The physical constants, yields, and results of elementary analysis of the sulfonium salts obtained via methods A, B, and C are presented in Table 1.

Decomposition of Sulfonium Salts to Sulfides. A) By Refluxing with KCl. A 4 g (0.015 mole) sample of dimethyl(5-methyl-2-thienyl)sulfonium perchlorate was refluxed with 60 ml of saturated potassium chloride solution for 5 h. The resulting oily layer was extracted with ether, and the extract was dried with $MgSO_4$ and evaporated. The residue was vacuum distilled to give 0.32 g (15%) of a transparent, slightly

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*A 250 g sample of resin AV-17 in the chloride form and in the air-dried state was washed with 17 liters of 10% and 15 liters of 5% NaOH solutions until there were no longer Cl^- ions in the filtrate. Distilled water (3 liters) was then added until the wash liquid was weakly alkaline, and 12 liters of 10% sodium nitrate was passed through the resin (see [12]).

†Thiophene–aromatic concentrate containing 30-35% thiophene can be used in place of pure thiophene.

yellowish liquid with n_D^{20} 1.5767 that distilled at 100° (in a bath) and 16 mm [bp 78-79° (10 mm) [3], n_D^{20} 1.5767]. To prove its structure, the product was subjected to the action of acetyl chloride in the presence of $SnCl_4$ to give a ketone with mp 96.5-97.5° (from heptane); this product did not depress the melting point of an authentic sample of 2-methylmercapto-5-methyl-3-acetylthiophene [13].

Methyl 2-Thienyl Sulfide. This compound was similarly obtained from 11 g (0.045 mole) of dimethyl-(2-thienyl)sulfonium perchlorate to give 2.53 g (44%) of a product with bp 72-73° (15 mm) and n_D^{20} 1.5963 (bp 66-67° (10 mm) and n_D^{20} 1.5940 [13]). According to gas-liquid chromatography, the samples of sulfide obtained by the demethylation of the sulfonium salt with KCl solution and a sample obtained via the method in [13] were identical.

B) By Refluxing with Pyridine. A 2.45 g (0.01 mole) sample of dimethyl(2-thienyl)sulfonium perchlorate in 20 ml of pyridine was refluxed for 4 h. The pyridine was removed by distillation, and the residue was extracted with ether. The extract was washed with 5% hydrochloric acid, dried with $CaCl_2$, and distilled at 40 mm and a bath temperature of 150° to give 0.4 g (31%) of methyl 2-thienyl sulfide with n_D^{20} 1.5939; the compound was identified by means of gas-liquid chromatography.

Methyl 5-Methyl-2-thienyl Sulfide. This compound was similarly obtained in 8% yield from dimethyl-(5-methyl-2-thienyl)sulfonium perchlorate and had n_D^{20} 1.5775.

C) On an Anion-Exchange Resin. Anion-exchange resin ÉDÉ-10p [12] in the chloride form was washed with 20% potassium acetate or sodium acetate solution until there were no longer any Cl^- ions in the filtrate (test with $AgNO_3$). The resin was then washed with distilled water until there was no residue after the wash waters were evaporated. The residue was then brought to the air dried state and packed into a column. A solution of 0.3 g (0.0012 mole) of dimethyl(2-thienyl)sulfonium perchlorate in 200 ml of methanol was passed through a column containing 30 g of resin. Evaporation of the methanol gave a light-brown liquid containing methyl 2-thienyl sulfide and acetic acid, according to gas-liquid chromatography. The yield of methyl 2-thienyl sulfide was quantitative, as established by gas-liquid chromatography with an internal standard (acetophenone). The yield of sulfide was ~ 70% when 10 g of resin was used per 0.001 mole of sulfonium salt.

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