SYNTHESIS OF 3,4-DI(METHYLENE)TETRAHYDROTHIOPHENE-1,1-DIOXIDE AND ITS USE IN ORGANIC SYNTHESIS

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A convenient reaction scheme has been developed for obtaining 3,4-di(methylene)tetrahydrothiophene-1,2-dioxide from the readily available 3,4-dimethyl-2,4-dihydrothiophene-1,1-dioxide through 3,4-di(bromomethyl)-2,5-dihydrothiophene-1,1-dioxide. A feasibility study has been made of the use of the butadiene fragment of the heterocycle in a Diels—Alder reaction with maleic acid derivatives, and the corresponding adducts have been obtained.

Among the publications devoted to derivatives of 2,5-dihydrothiophene-1,1-dioxide [1, 3], only a very few of the studies deal with their use in the synthesis of polycondensed heterocycles. At the same time, they are being used successfully in obtaining derivatives of thiophene and butadiene, including compounds having a natural origin [4, 5]. Among the derivatives of dihydrothiophenedioxide, a number of preparations act in a variety of ways [6-9].

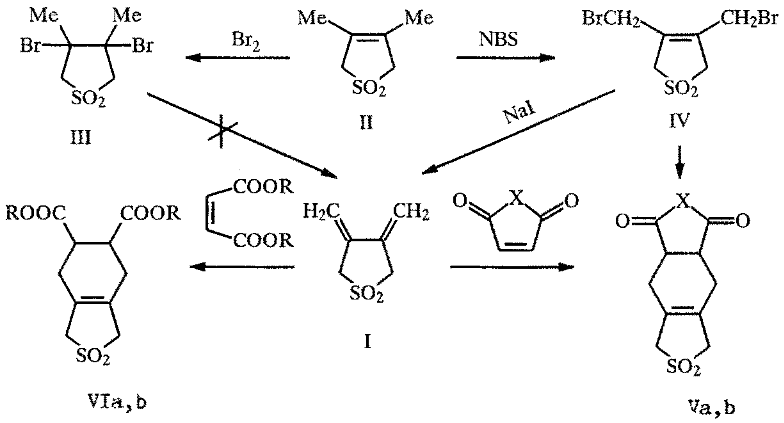
In the light of this background, research on functionalization of these derivatives is undoubtedly a matter of great interest in searching for new physiologically active substances and also new synthons that can be used to obtain organic compounds of various classes.

The work reported here was aimed at developing a preparative method for the synthesis of 3,4-di(methylene)tetrahydrothiophene-1,1-dioxide (I), and also at investigating its physicochemical properties.

The synthesis of the dioxide I that was described by Sadeh and Gaoni [10] is based on construction of the heterocyclic part of the molecule from butadiene. In [10], the compound was obtained by the interaction of 2,3-di(bromomethyl)-1,3-butadiene with sodium sulfide, and subsequent oxidation of the resulting cyclic sulfide. The disadvantage of the method is the low yield of the intermediate dibromide.

We have studied the possibility of synthesizing the dioxide I from products obtained by brominating the readily available 3,4-dimethyl-2,5-dihydrothiophene-1,1-dioxide (II), i.e., the dibromide (III), obtained by addition of molecular bromine in chloroform at the double bond of II, and the dibromide (IV), obtained in moderate yield by free-radical bromination of the dioxide II by N-bromosuccinimide (NBS).

When the dibromide III is dehydrobrominated by the action of a base in alcohol, only a tarry product is formed; this may be the result of splitting out a proton from a methylene group attached to the sulfur atom, followed by polymerization of the thiophenesulfone under the influence of the base.



X = NPh in Va, O in Vb; R = Me in VIa, Et in VIb

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TABLE 1. Characteristics of Compounds I-VI

Compound	Empirical formula	mp, °C	IR spectrum, cm^{-1}	PMR spectrum, ppm	Yield, %
I	$C_6H_8O_2S$	118...119	1640, 1650 (C=CH$_2$); 1130, 1320 (SO$_2$)	5,50 (4H, s, CH$_2$); 3,95 (4H, s, CH$_2$)	60
II	$C_2H_{10}O_2S$	135...137	—	3,62 (4H, s, CH$_2$); 1,65 (6H, s, CH$_3$)	80
III	$C_6H_{10}Br_2O_2S$	214...215	570 (C-Br); 1160, 1375 (CH$_3$); 1315, 1125 (SO$_2$)	—	89
IV	$C_6H_8Br_2O_2S$	125...126	590 (C-Br); 1310, 1135 (SO$_2$);	4,06 (4H, s, CH$_2$); 4,93 (4H s, CH$_2$)	40
Va	$C_{16}H_{15}NO_4S$	175...177	1670 (C=C); 1450 (C-H), 1720 (CONH); 1465 (CH$_2$); 1135 (SO$_2$)	—	89
Vb	$C_{10}H_{10}O_5S$	189...191	1675 (C=C); 1790, 1730 (C=O);1310, 1140 (SO$_2$)	—	91
VIa	$C_{12}H_{16}O_6S$	151...152	1670 (C=C); 1745 (C=O); 1315, 1140 (SO$_2$)	—	87
VIb	$C_{14}H_{20}O_6S$	159...161	1665 (C=C); 1755 (C=O); 1320, 1130 (SO$_2$)	—	84

At 1,4-debromination, dibromide IV was accomodated by means of sodium iodide in acetone at 25°C, we obtained dioxide I with high yields.

We have also investigated the possibility of using compound I in a Diels—Alder reaction in order to construct polycondensed heterocycles. We found that it reacts readily with derivatives of maleic acid (the anhydride, phenylimide, and esters) to give high yields of products of 1,4-cycloaddition (Va, b, VIa, b). These products can also be formed under conditions of the debromination reaction, i.e., by refluxing the dibromide IV with the maleic acid derivative in acetone in the presence of sodium iodide. By the use of this reaction, the synthesis of this type of compound, starting with the dioxide I, is shortened to a single stage.

The structures of the synthesized compounds I-VI were confirmed by IR and PMR spectroscopic data (Table 1).

EXPERIMENTAL

The IR spectra were taken in a UR-20 instrument (in KBr tablets). The PMR spectra of solutions in deuteroacetone were recorded in a Tesla BS-487 instrument (80 MHz), internal standard HMDS. The melting points were determined on a Boetius microheater stage. The TLC analysis was performed with Silufol plates and iodine vapor development.

The characteristics of the synthesized compounds are listed in Table 1. Elemental analyses of compounds I and II-VI for C, H, and S are in agreement with the calculated analyses.

3,4-Dimethyl-2,5-dihydrothiophene-1,1-dioxide (II). Synthesized by a procedure that has been described previously [11].

3,4-Dibromo-3,4-dimethyltetrahydrothiophene-1,1-dioxide (III). To a solution of 4.38 g (30 mmoles) of the dioxide II in 20 ml of dry chloroform, over a period of 1 h while mixing with a magnetic stirrer, 4.8 g (30 mmoles) of bromine in 20 ml of chloroform was added dropwise, and the mixture was stirred for 1 h longer. The precipitated crystals of the product III were filtered off and recrystallized twice from chloroform.

3,4-Dibromomethyl-2,5-dihydrothiophene-1,1-dioxide (IV). A mixture of 2.92 g (20 mmoles) of the dioxide II, 7.12 g (40 mmoles) of N-bromosuccinimide, and 0.48 g of benzoyl peroxide in 35 ml of dry chloroform was refluxed on a magnetic stirrer for 20 h. After cooling the reaction mixture, the succinimide was filtered off; the filtrate was evaporated down to 2/3 volume and cooled, after which the succinimide was again filtered off, and the solvent was evaporated. To the residue, 25 ml of absolute alcohol was added; the mixture was held at 40°C, and the resulting solution was filtered and allowed to stand in the cold for 30 h. The precipitated crystals of the product V were filtered off and recrystallized from benzene.

3,4-Di(methylene)tetrahydrothiophene-1,1-dioxide (I). To a solution of 2.36 g (15 mmoles) of sodium iodide in 10 ml of dry acetone, while stirring at 25°C, a solution of 2.0 g (6.6 mmoles) of the dibromide IV in 10 ml of dry acetone was added dropwise, and the resulting mixture was stirred for 2 h longer. Then the sodium bromide was filtered off, the reaction mixture was evaporated down to 2/3 volume, and 25 ml of benzene was added; the resulting solution was washed with a 5%

sodium thiosulfate solution and then with water, after which it was dried with anhydrous $CaCl_2$. The solvent was driven off, and the product I was segregated by recrystallization of the residue from a benzene—ether mixture.

N-Phenylimide of 5,6-Dicarboxy-1,3,4,5,6,7-hexahydrobenzo[*c*]thiophene-2,2-dioxide (Va). A. A mixture of 1.44 mg (1 mmole) of the dioxide I and 1.73 mg (1 mmole) of N-phenylmaleimide in 20 ml of xylene was refluxed for 1 h, the solvent was driven off, and the residue was recrystallized from acetone, obtaining the product Va.

Compounds Vb and VIa, b were synthesized analogously.

B. To a stirred mixture of 173 mg (1 mmole) of N-phenylmaleimide, 300 mg (2 mmoles) of sodium iodide, and 20 ml of dry acetone, at 40-50°C, 304 mg (1 mmole) of the dibromide IV in 20 ml of dry acetone was added dropwise over the course of 1 h. The reaction mixture, after stirring for 4 h, was poured into a solution of 1.5 g of sodium thiosulfate in 150 ml of water and allowed to stand in the cold for 8 h. The precipitated crystals of the product Va were filtered off, washed with benzene, and recrystallized from an acetone—DMFA mixture.

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