160 ml of benzene, and 8 mmole of tert-butyl peroxide was added. Argon was passed through the solution, and the reaction mixture was irradiated with a mercury lamp (150 W) at 20°C for 48 h. The benzene and excess unchanged crown ether were removed by distillation in vacuo in an inert atmosphere. Column chromatography yielded crown ether IV, V, or VI and a mixture of phenyl-substituted crown ethers. Preparative GLC of the latter gave individual mono- (VII, VIII, or IX) and diphenyl-substituted (X, XI, or XII) crown ethers.

1,1'-Bis[2,5,8,11,14-pentaoxacyclopentadecane] (V), 1,1'-Bis[2,5,8,11,14,17-hexaoxacyclooctadecane] (VI), 1-Hydroxy-2,5,8,11,14-pentaoxacyclopentadecane (XIII), 1-Hydroxy-2,5,8,11,14,17-hexaoxacyclooctadecane (XIV), Dihydroxy-2,5,8,11,14-pentaoxacyclopentadecane (XV), and Dihydroxy-2,5,8,11,14,17-hexaoxacyclooctadecane (XVI) (General Method). A 160-mmole sample of crown ether II or III was dissolved in 10 ml of distilled water, one to two drops of concentrated H_2SO_4 were added, and the mixture was cooled to 0°C. An 8-mmole sample of hydrogen peroxide and a solution of 8 mmole of divalent iron sulfate in 10 ml of water were added simultaneously in the course of 20 min with vigorous stirring in an argon atmosphere to the reaction mixture from two dropping funnels while maintaining the temperature at 0°C. Stirring was continued for 1 h. The mixture was then extracted with chloroform (three 50-ml portion), and the extracts were washed with a dilute solution of divalent iron sulfate acidified with H_2SO_4, and dried with anhydrous magnesium sulfate. The chloroform and excess unchanged crown ether were removed by vacuum distillation in an inert atmosphere. The reaction products were isolated by preparative GLC.

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NEW METHODS OF SULFONATION IN THE THIOPHENE SERIES*

T. K. Shustareva

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Simple preparative methods of sulfonation of thiophene derivatives by complexes of sulfur trioxide with ethers, amides, trialkyl phosphates, and sulfoxides under mild conditions were developed.

Up until now, one of the principal methods for obtaining sulfonic acids of thiophene and its homologs was the sulfonation of thiophenes with a threefold excess of the pyridine–sulfur trioxide complex ($Py \cdot SO_3$) at 105-130°C for 8-10 h under pressure in sealed ampuls [1, 2]. This method (Table 1) has a number of substantial drawbacks: low yields and nonhomogeneity of the products obtained, severe conditions (the process is carried out under pressure in sealed ampuls at temperatures above 100°C), excess sulfonating agent (3:1), and the long duration of the process (10-720 h); these drawbacks are due to the low sulfonating activity of the $Py.SO_3$ complex. A sulfonic acid was obtained in 86% yield in the prolonged reaction of thiophene with the more active (as compared with $Py \cdot SO_3$) $Py \cdot 2SO_3$ complex at 25°C [2].

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TABLE 1. Methods for the Sulfonation of Thiophene and Its Derivatives

Substrate	Sulfonating agent	Reaction conditions				Reaction products	Yield, %	Literature cited
		sulfonating agent: substrate ratio	solvent	T, °C	t, h			
Thiophene	H_2SO_4	—	Benzene	25	—	2-SO_3H	45	[3, 4]
	HSO_3Cl	3 : 1		−10	—	2-SO_2Cl	64	[5]
	Py · SO_3	1 : 1	DCE	20—30	720	2-SO_3H	50	[1]
	Py · SO_3	3 : 1	DCE	130	10	2,4-$(SO_3H)_2$	90	[1]
	Py · $2SO_3$	1 : 1	DCE	25	10	2-SO_3H	86	[2]
	DO · SO_3	1 : 1	DCE + 100% DO	25	72	2-SO_3H	75	[2]
2-Cl-Thiophene	Py · SO_3	3 : 1	DCE	125	8	5-SO_3H	95	[2]
	HSO_3Cl	4 : 1		−10	—	5-SO_2Cl	65	[5]
2-Br-Thiophene	Py · SO_3	3 : 1	DCE	105	10	5-SO_3H	90	[2]
	HSO_3Cl	18 : 1		−15	—	5-SO_2Cl	50	[5]
2-I-Thiophene	Py · SO_3	3 : 1	DCE	110	8	5-SO_3H	77	[2]
	HSO_3Cl	18 : 1		−15	—	5-SO_2Cl	57	[5]
2,5-Dimethylthiophene	Py · SO_3	1 : 1	DCE	135	10	3-SO_3H	47	[2]
	33% oleum	—	33% oleum	25	—	3,4-Anhydride	55	[5]
	Py · $2SO_3$	1 : 1	DCE	25	24	3-SO_3H	94	[2]
	DO · SO_3	1 : 1	DCE + 100% DO	25	24	3-SO_3H	95	[2]

The results of our quantitative studies of the kinetics and mechanism of the sulfonation of thiophene and its derivatives with complexes of sulfur trioxide with various organic donors [6] made it possible to develop optimal conditions for the synthesis of sulfonic acids in the thiophene series by sulfonation of thiophenes with more active (as compared with Py•SO_3) complexes of sulfur trioxide with ethers [dioxane (DO•SO_3), diethyl ether (DE•SO_3), and tetrahydrofuran (THF•SO_3)], amides [DMF (DMF•SO_3)], trialkyl phosphates [tributyl phosphate (TBF•SO_3)], and sulfoxides [DMSO (DMSO•SO_3)].

The use of more active (as compared with Py•SO_3) sulfonating agents makes it possible to carry out sulfonation under mild conditions (at 20-30°C and atmospheric pressure for 1-2 h with equimolar ratios of the reacting substances). The yields of the desired products range from 90% to 98%. Thiophene, 2-methylthiophene (which is more active than thiophene in electrophilic-substitution reactions), and 2-bromothiophene (which is less active than thiophene) were selected as the starting substrates. Depending on the activity of the substrate and the complex of sulfur trioxide, sulfonation was carried out in an inert solvent [1,2,-dichloroethane (DCE)] without an excess amount of the complexing agent, with an excess of the latter, or in the latter as the reaction medium (Table 2).

A study of the effect of excess complexing agent on the yield of the 2-sulfonic acid of thiophene in the case of sulfonation with the DO•SO_3 complex showed that the highest yield (95-98%) was obtained without an excess of the donor. The yield of the desired product decreased only slightly in the reaction of thiophene with the DO•SO_3 complex in 1,2-dichloroethane with an excess ($\leq$ 20%) of the donor. When the same reaction was carried out in dioxane, the yield of the 2-sulfonic acid of thiophene was 75-78%. More active thiophene derivatives with electron-donor substituents (for example, 2-methylthiophene) were sulfonated by active complexes of sulfur trioxide with ethers (DO•SO_3, E•SO_3, THF•SO_3) either in an inert solvent with excess donor or in the latter as the medium, i.e., under milder conditions, due to a decrease in the reactivity of the sulfonation agent [6]. The sulfonation of such thiophenes by less active complexes of sulfur trioxide (DMF•SO_3, TBP•SO_3, DMSO•SO_3) was carried out in an inert solvent without excess complexing agent. Less active thiophene compounds that contain electron-acceptor substituents (for example, 2-bromothiophene) were sulfonated by complexes of sulfur trioxide in an inert solvent without an excess amount of the donor, i.e., when the sulfonating ability of the complexes was maximal.

Sulfonic acids of thiophene and its derivatives are unstable-in-air, oily, hygroscopic liquids, and they are therefore usually isolated in the form of the barium salts, which are stable during storage. Aqueous solutions of these salts can be readily converted to salts of other metals (sodium, potassium, lead, etc.) by treatment with the corresponding carbonates. The structures of the resulting sulfonic acids were determined by means of the PMR spectra, since the signals of the protons in the α and β positions of the thiophene ring

TABLE 2. New Methods for the Sulfonation of Thiophenes by Complexes of Sulfur Trioxide in the Case of Equimolar Ratios of the Reacting Components

Substrate	Sulfonating agent	Process conditions			Reaction product	Yield, %
		solvent	T, °C	t, h		
Thiophene	DO · SO_3	DCE	25	1	2-SO_3H	95—98
	DO · SO_3	DCE + 20% DO	25	2	2-SO_3H	90—93
	DO · SO_3	DO	25	2	2-SO_3H	75—78
	DE · SO_3	DCE	25	1	2-SO_3H	95—98
	DE · SO_3	DCE + 20% DE	25	2	2-SO_3H	92—94
	DE · SO_3	DE	25	2	2-SO_3H	87—89
	THF · SO_3	DCE	25	1	2-SO_3H	96—98
	THF · SO_3	DCE + 20% THF	25	2	2-SO_3H	93—95
	THF · SO_3	THF	25	2	2-SO_3H	73—76
	DMF · SO_3	DCE	35	2	2-SO_3H	92—95
	DMSO · SO_3	DCE	35	2	2-SO_3H	90—91
	TBP · SO_3	DCE	25	1	2-SO_3H	96—98
2-Methylthiophene	DO · SO_3	DCE	25	1	5-SO_3H	95—97
	DO · SO_3	DCE + 20% DO	25	2	5-SO_3H	95—98
	DE · SO_3	DCE + 20% DE	25	1	5-SO_3H	95—97
	THF · SO_3	DCE	25	1	5-SO_3H	96—98
	THF · SO_3	DCE + 20% THF	25	1	5-SO_3H	93—95
	THF · SO_3	THF	25	2	5-SO_3H	95—98
	DMF · SO_3	DCE	25	2	5-SO_3H	94—96
	DMSO · SO_3	DCE	25	2	5-SO_3H	93—97
	TBP · SO_3	DCE	25	1	5-SO_3H	95—98
2-Bromothiophene	DO · SO_3	DCE	25	2	5-SO_3H	92—96
	DE · SO_3	DCE	25	2	5-SO_3H	93—97
	THF · SO_3	DCE	25	2	5-SO_3H	95—97
	DMF · SO_3	DCE	25	3	5-SO_3H	52—55
	DMF · SO_3	DCE	50	2	5-SO_3H	88—92
	DMSO · SO_3	DCE	50	2	5-SO_3H	81—86
	TBP · SO_3	DCE	25	2	5-SO_3H	93—97

have different chemical shifts (CS). According to these data, only α-sulfonic acids were obtained in the sulfonation of thiophenes by complexes of sulfur trioxide. The absence of the β isomers was confirmed by the PMR spectra of the unpurified barium salts with an accuracy of up to 5%.

Thus the developed methods for the sulfonation of thiophenes have a number of advantages as compared with the known methods: high yields of the monosulfonic acids (90-98%) vis-á-vis high selectivity of the process, equimolar ratios of the reacting substances, mild conditions (reaction temperature 20-30°C), and rapidity of the reaction (1-2 h), as well as simplicity of the technological utilization (the reaction was carried out under ordinary conditions rather than under pressure, as in the known method).

The promising character of the use of the developed methods for the sulfonation of other acidophobic compounds must be noted.

EXPERIMENTAL

The UV spectra of solutions of the compounds in water (10^{-4}-10^{-3} mole/liter) were recorded with an SF-16 spectrophotometer. The IR spectra of KBr pellets or solutions in DCE were recorded with a UR-20 spectrophotometer. The PMR spectra were recorded with a Tesla BS-487C spectrometer (80 MHz) using 10-15% solutions of the substances in D_2O with tert-butyl alcohol as the internal standard. The CS found are the values measured relative to tetramethylsilane (TMS).

To illustrate the developed methods of sulfonation in the thiophene series we present several examples of the synthesis of sulfonic acids of thiophene derivatives by means of various complexes of sulfur trioxide. The results are presented in Table 2.

Sulfonation of Thiophene by the DO·SO_3 Complex in DCE. A solution of 1.9 g (24 mmole) of freshly distilled SO_3 dissolved in DCE was added with cooling (5°C) and stirring to a solution of 2.1 g (24 mmole) of dioxane in 30 ml of DCE, after which 2 g (24 mmole) of thiophene was added to the resulting DO·SO_3 complex, and the mixture was maintained at 25°C for 1 h. The workup of the reaction mass was carried out monotypically. It was poured into 50 ml of H_2O, the aqueous mixture was treated with $BaCO_3$ until it gave a neutral reaction and then filtered. The Ba salt of thiophene-2-sulfonic acid (I) was isolated from the evaporated filtrate by the successive addition of 20 ml of ethanol and 20 ml of ether. The white precipitate of I was separated and washed several times with ether. For purification it was reprecipitated from water with a mixture of ethanol and ether and dried in a vacuum desiccator over P_2O_5. The yield of I was 5.37 g (97.5%). For conversion to the sodium salt an aqueous solution of I was treated with Na_2CO_3 and filtered, and the sodium salt of thiophene-2-sulfonic acid was precipitated from the evaporated filtrate with a mixture of ethanol and diethyl ether. The losses in this case were no more than 10% of the expected amount of reaction product.

Thiophene-2-sulfonic Acid Na Salt. UV Spectrum: λ_{max} 232 nm (log ε 3.90). IR spectrum: 3050 (CH); 1385, 1060 (thiophene ring); 1190-1260 (SO_2); 1010-1080 (SO_2); 700 (thiophene ring); 630 cm^{-1} (SO). PMR spectrum: 7.15 (t, J_{45} = 5, J_{43} = 4 Hz, 4-H), 7.54 (d, J_{35} = 1 Hz, 3-H), 7.65 ppm (d, 5-H). Found: C 25.9; H 1.7; S 34.3%. $C_4H_3NaO_3S_2$. Calculated: C 25.8; H 1.6; S 34.4%.

The S-(α-naphthyl)thiuronium salt had mp 174-175°C, which was in agreement with the value in [2].

Sulfonation of Thiophene with the DO·SO_3 Complex in DCE with Excess Dioxane. A solution of 1.9 g (24 mmole) of freshly distilled SO_3 in DCE was added with stirring and cooling to 5°C to a solution of 2.52 g (28.6 mmole) of dioxane in 30 ml of DCE, after which the reaction was carried out as in the preceding method. The yield was 5.1 g (92.5%). The results of elemental analysis and data from the UV, IR, and PMR spectra of the reaction product were identical to the values for the compound described above.

Sulfonation of Thiophene with the DO·SO_3 Complex in Dioxane. A solution of 1.9 g (24 mmole) of freshly distilled SO_3 in DCE was added with stirring and cooling to 5°C to 30 ml of dioxane, after which the reaction was carried out as described above. The yield was 4.27 g (77.5%). The results of elementary analysis and data UV, IR, and PMR spectra corresponded to the values of the reaction product descrbed above.

Sulfonation of 2-Methylthiophene with the DMSO·SO_3 Complex. A solution of 1.63 g (20.4 mmole) of freshly distilled SO_3 in DCE was added with stirring and cooling to 5°C to a solution of 1.59 g (20.4 mmole) of DMSO in 30 ml of DCE. A 2-g (20.4 mmole) sample of 2-methylthiophene was added to the resulting DMSO·SO_3 complex, and the mixture was maintained at 25°C for 1 h. It was then worked up as indicated for thiophene. The yield of the Ba salt of 2-methylthiophene-5-sulfonic acid (II) was 5.03 g (97.8%).

Na Salt of II. UV spectrum: λ_{max} 239 nm (log ε 3.90). IR spectrum: 3050 (CH); 1465, 1380, 1050 (thiophene ring); 1180-1260 (SO_2); 1010-1105 (SO_2); 690 (thiophene ring); 655 cm^{-1} (SO). PMR spectrum: 2.49 (s, CH_3), 6.74 (J_{43} = 4 Hz, 4-H), 7.3 ppm (d, 3-H). Found: C 30.1; H 2.6; S 32.0%. $C_5H_5NaO_3S_2$. Calculated: C 30.0; H 2.5; S 32.0%.

Sulfonation of Thiophenes with the DMF·SO_3 Complex. This reaction was carried out in the same way as with the DMSO·SO_3 complex.

Sulfonation of 2-Bromothiophene with the TBP·SO_3 Complex. A solution of 0.98 g (12.2 mmole) of freshly distilled SO_3 in DCE was added with stirring and cooling (0-5°C) to a solution of 3.24 g (12.2 mmole) of tributyl phosphate in 30 ml of DCE, 2 g (12.2 mmole) of 2-bromothiophene was added to the resulting TBP·SO_3 complex, and the mixture was maintained at 25°C for 2 h. The reaction mass was worked up as indicated above. The yield of the Ba salt of 2-bromothiophene-5-sulfonic acid (III) was 3.69 g (96.8%).

Na Salt of III. UV spectrum: λ_{max} 247 nm (log ε 3.95). IR spectrum: 3050 (CH); 1410-1470, 1060 (thiophene ring); 1160-1260 (SO_2); 700 (thiophene ring); 640 (CBr); 600 cm^{-1} (SO). PMR spectrum: 7.12 (d, 4-H), 7.31 ppm (d, 3-H). Found: C 18.1; H 0.8; Br 30.2; S 24.0%. $C_4H_2BrNaO_3S_2$. Calculated: C 18.1; H 0.8; Br 30.0; S 24.2%.

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