NEW REACTION OF BENZO[b]THIENO[3,2-b]BENZO[b]THIOPHENE DISULFONE

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A new reaction of benzo[b]thieno[3,2-b]benzo[b]thiophene disulfone with amines that takes place with opening of one of the thiophene rings and nucleophilic substitution in the heteroaromatic ring at the site of cleavage of the S—C bond was observed. The molecular structures of the products of amination of the disulfone were determined by x-ray diffraction analysis. Hydrolysis and dehydration of the amination products gave derivatives of a new heterocyclic system, viz., benzo[b]thieno[3,2-e]benzo[c]-1,2-oxathiin.

In a continuation of our studies of the nucleophilic reactions of heteroaromatic sulfones [1] we studied the reaction of benzo[b]thieno[3,2-b]benzo[b]thiophene disulfone (I) with acyclic and cyclic amines and hydroxy amines. It was found that disulfone I reacts readily with 2 moles of amine in refluxing benzene to give water-soluble compounds (in 70-80% yields). The IR spectra of the products of amination of the disulfone, in which a broad "ammonium band" at 3000 cm^{-1} and absorption bands at 2500 cm^{-1} are present, indicate their saltlike structure. The absence in the PMR spectra of the signal of the proton of an aliphatic hydrogen (δ 5-6 ppm) excludes nucleophilic addition to the central C═C bond. The number and character of the signals in the ^{13}C NMR spectra constitute evidence for the asymmetrical character of the molecules of the resulting compounds. However, we were not able to establish their structures unambiguously by these methods. An x-ray diffraction study of the product of the reaction of disulfone I with ethanolamine showed that it has the 2-hydroxyethylammonium 2-[3-(2-hydroxyethylamino)-1,1-dioxido-2-benzo[b]thieny]benzenesulfinate (IIc) structure* (Fig. 1). A crystal of IIc is made up of molecular ions that are inter-

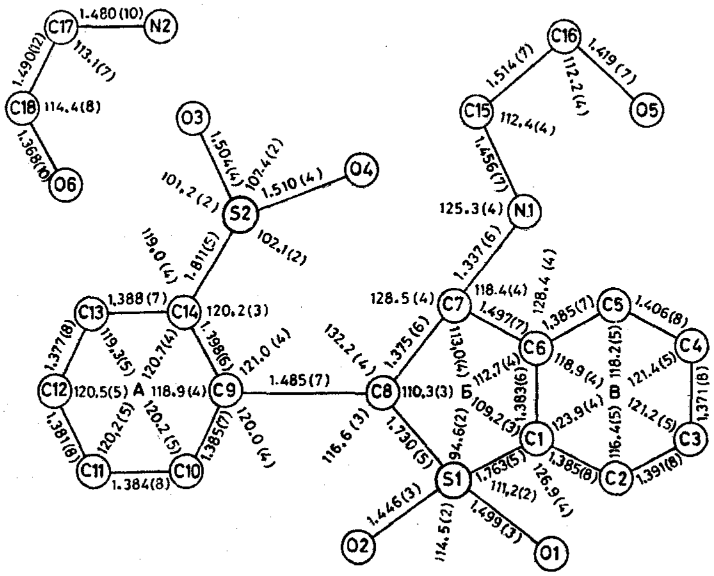

Fig. 1. Geometry of the 2-hydroxyethylammonium 2-[3-(2-hydroxyethylamino)-1,1-dioxido-2-benzo-[b]thienyl]benzenesulfinate molecule.

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*This material will be published separately.

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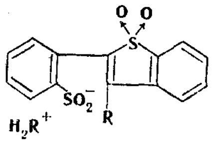
TABLE 1

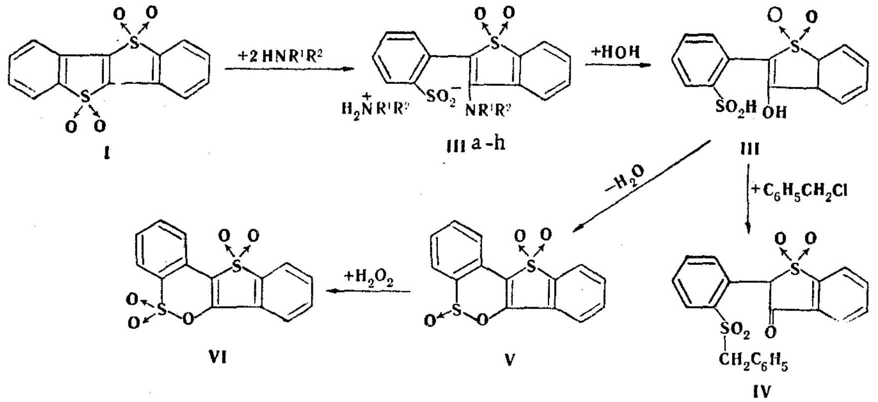


Compound	R	Reaction time, h	mp, °C (from ethanol)	Found, %			Empirical formula	Calc., %			Yield, %
				C	N	H		C	N	H	
IIa	$NH(CH_2)_2CH_3$	1	209—210	56.5	6.1	6.9	$C_{20}H_{26}N_2O_4S_2$	56.8	6.2	6.7	80
IIb	$NH(CH_2)_3CH_3$	1	203—204	58.7	6.7	6.3	$C_{22}H_{30}N_2O_4S_2$	58.6	6.7	6.2	78
IIc	$NHCH_2CH_2OH$	3	199	50.4	5.1	6.6	$C_{18}H_{22}N_2O_6S_2$	50.7	5.2	6.6	72
IId	Pyrrolidino	2	207—208	58.8	5.8	5.9	$C_{22}H_{26}N_2O_4S_2$	59.2	5.9	6.3	74
IIe	Piperidino	5	232	60.8	6.5	5.8	$C_{24}H_{30}N_2O_4S_2$	60.7	6.4	5.8	72
IIf	Perhydro-azepino	2	192	62.3	6.9	5.3	$C_{26}H_{34}N_2O_4S_2$	62.1	6.8	5.6	75
IIg	Morpholino	5	214—215	54.9	5.3	6.2	$C_{22}H_{26}N_2O_6S_2$	55.2	5.5	5.9	72
IIh	N'-(m-Chlorophenyl)-piperazino	8	172—173	58.8	5.0	7.6	$C_{34}H_{34}Cl_2N_4O_4S_2$	58.5	4.9	8.0	76

connected by six hydrogen bonds: HN(1)...O(3), H(1)N(2)...O(3), H(2)N(2)...O(1), H(3)N(2)...O(2), HO(6)...O(4), and HO(5)...O(4). The $\overset{+}{NH_3}$ and OH groups are proton donors, while the oxygen atoms of the sulfonyl group and the sulfinate anion are proton acceptors [2].

The amination of disulfone I consequently takes place with opening of one of the thiophene rings and nucleophilic substitution at the site of cleavage of the C—S bond to give the sulfinate of the corresponding amine (IIa-h) (Table 1).

The sulfonyl group usually undergoes attack by nucleophilic reagents with difficulty. For example, heteroaromatic and aromatic sulfones are cleaved by alkali with subsequent attack on the sulfonyl group by hydroxide ion only on fusion [3, 4]. Only diaryl α-disulfones react readily with nucleophiles with cleavage of the S—S bond [5]. In the case of of disulfone I the direction of the reaction with amines is evidently determined by the relative orientation of two strong electron-acceptor SO_2 groups. Under similar conditions the isomeric benzo[b]thieno[2,3-b]benzo[b]thiophene disulfone adds amines to the central C=C bond without cleavage of the thiophene ring [1].



2-(o-Sulfinophenyl)-3-hydroxybenzo[b]thiophene 1,1-dioxide (III) was obtained by acid hydrolysis of sulfinates II. On the basis of the data from the IR spectra [1070 (S—O), 1160 and 1335 (SO_2), and 3420 cm^{-1} (OH); no carbonyl absorption is present] it may be concluded that III has an enol structure. Sulfinic acid III forms salts and reacts readily with haloalkanes ($C_6H_5CH_2Cl$) to give disulfone IV. The signal of the proton of an aliphatic hydrogen atom in the 2 position [δ 5.56 ppm (1H, s)] is present in the PMR spectrum of the latter; the absorption band of a carbonyl group is observed in the IR spectrum at 1730 cm^{-1}, but the absorption of an OH group is absent, in agreement with ketone structure IV. Under the influence of chlorinating agents ($SOCl_2$ and CH_3COCl) sulfinic acid III undergoes dehydration to give the 5,11,11-trioxide of a new heterocyclic system, viz., benzo[b]thieno-

[3,2-e]benzo[c]-1,2-oxathiin V [IR spectrum: 1070 (S–O); 1160 and 1335 cm^{-1} (SO_2)]. The mass spectrum of V contains a molecular ion peak with m/e 304 and ion peaks with m/e 288 ($[M - O]^+$), 272 ($[M - 2O]^+$), and 240 ($[M - SO_2]^+$). Sulfoxide V is readily converted to disulfone VI by oxidation with hydrogen peroxide.

EXPERIMENTAL

The x-ray diffraction study was carried out with a Syntex $P2_1$ diffractometer (with copper emission and a graphite monochromator) with a system for determination of the crystal structures. The mass spectra were recorded with an AEI MS 905 spectrometer at an ionizing voltage of 70 eV with direct introduction of the samples into the source; the input temperature was 160°C, and the ionization chamber temperature was 200°C. The IR spectra were recorded with a UR-20 spectrometer.

Benzo[b]thieno[3,2-b]benzo[b]thiophene Disulfone (I). This compound was obtained by oxidation of benzo[b]thieno[3,2-b]benzo[b]thiophene [6] with H_2O_2 by the method in [7] and decomposed at 330°C. IR spectrum: 1160, 1340 cm^{-1} (SO_2). Found: C 54.9; H 2.6%. $C_{14}H_8O_4S_2$. Calculated: C 55.2; H 2.6%.

2-(3-Amino-1,1-dioxido-2-benzothienyl)benzenesulfinates of Amines (IIa-h). A mixture of 5 mmole of disulfone I and 12 mmole of the corresponding amine in 50 ml of benzene was refluxed until precipitation ceased, and the precipitate was then removed by filtration (in the case of IId,f the solvent was removed by distillation), washed with benzene, and recrystallized from ethanol.

2-(o-Sulfinophenyl)-3-hydroxybenzo[b]thiophene 1,1-Dioxide (III). A solution of 0.85 g (2 mmole) of sulfinate IIa in 30 ml of 5 N H_2SO_4 was heated on a boiling-water bath for 30 min, and the resulting precipitate was removed and washed with water to give 0.51 g (80%) of a product with mp 156-157°C. Found: C 52.0; H 3.0%. $C_{14}H_{10}O_5S_2$. Calculated: C 52.2; H 3.1%.

Potassium 2-(3-Hydroxy-1,1-dioxido-2-benzothienyl)benzenesulfinate (IIIa). A 1.94-g (6 mmole) sample of sulfinic acid III was added to a solution of 0.42 g (3 mmole) of K_2CO_3 in water, and the mixture was heated on a water bath for 30 min. The resulting solution was filtered, and the filtrate was evaporated to dryness to give 2.1 g (97%) of a product with mp 188-190°C. Found: C 46.2; H 2.5%. $C_{14}H_9O_5S_2K$. Calculated: C 46.6; H 2.5%.

2-[o-(Benzylsulfonyl)phenyl]-3-oxo-2,3-dihydrobenzo[b]thiophene 1,1-Dioxide (IV). A mixture of 0.72 g (2 mmole) of salt IIIa and 0.25 g (2 mmole) of benzyl chloride in 50 ml of alcohol was refluxed for 2 h, after which the KCl was removed by filtration, and the solvent was removed by vacuum distillation. The precipitate was washed with water and recrystallized from ethanol to give 0.51 g (62%) of a product with mp 149-150°C. IR spectrum: 1160, 1332 cm^{-1} (SO_2). Found: C 61.4; H 3.9%. $C_{21}H_{16}O_5S_2$. Calculated: C 61.1; H 4.0%.

Benzo[b]thieno[3,2-e]benzo[c]-1,2-oxathiin 5,11,11-Trioxide (V). A mixture of 0.96 g (3 mmole) of sulfinic acid III and 20 ml of thionyl chloride was refluxed for 45 min, after which the thionyl chloride was partially removed by vacuum distillation, and the precipitate was removed by filtration and recrystallized from nitromethane to give 0.78 g (85%) of a product with mp 205-206°C. Found: C 55.0; H 2.6%; M 304 (mass spectrometry). $C_{14}H_8O_4S_2$. Calculated: C 55.2; H 2.6%; M 304.

Benzo[b]thieno[3,2-e]benzo[c]-1,2-oxathiin 5,5,11,11-Tetraoxide (VI). A 0.6-g (2 mmole) sample of V was dissolved by heating in 25 ml of acetic acid; 3 ml of 30% H_2O_2 was added, and the mixture was allowed to stand at room temperature for 12 h. The solvent was partially removed by vacuum distillation, and the precipitate was removed by filtration and recrystallized from acetic acid to give 0.35 g (55%) of a product with mp 261°C. IR spectrum: 1160, 1335 cm^{-1} (SO_2). Found: C 52.7; H 2.6%. $C_{14}H_8O_5S_2$. Calculated: C 52.5; H 2.5%.

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REACTIONS OF POLYSUBSTITUTED THIOPYRANS WITH PROTON ACIDS AND STRUCTURAL STUDIES OF THE RESULTING THIACYCLOHEXANES

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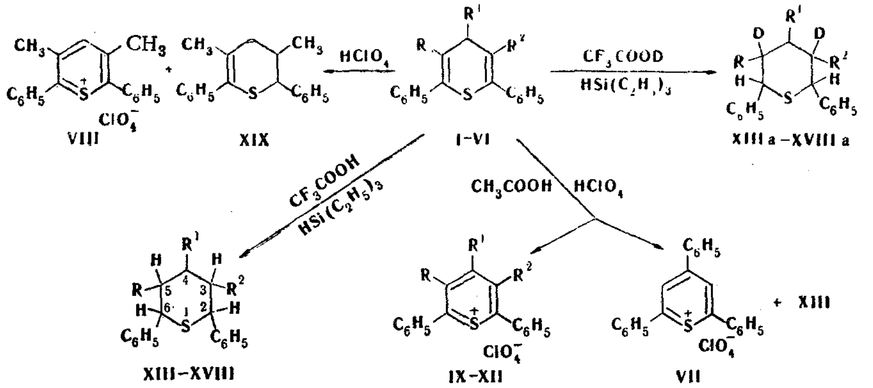
Depending on the number and nature of substituting groups, 4H-thiopyrans under the influence of perchloric and trifluoroacetic acids either undergo disproportionation or form thiapyrylium salts in quantitative yields with the participation of air oxygen; in the case of ionic hydrogenation with $CF_3COOH—SiHEt_3$ they are converted to thiacyclohexanes, regardless of their structure. To ascertain the reason for the difference in the mechanisms of the reaction of polysubstituted thiopyrans with proton acids the structures of the polysubstituted thiacyclohexanes were investigated jointly by NMR spectroscopy and x-ray diffraction analysis; this made it possible to form a judgment regarding the effect of the degree and character of substitution of 4H-thiopyrans on the mechanism of their reaction with proton acids. The tetrahydrothiopyran ring has a chair conformation. The phenyl substituents are equatorially oriented, while the methyl substituents are axially oriented.

We have established the existence of an effect of the degree and character of substitution of 4H-thiopyrans on the mechanism of their reaction with some proton acids. It is known that di- and triaryl-substituted thiopyrans, including sulfide I, react with 70% $HClO_4$ in acetic acid to give thiapyrylium salts and thiacyclohexanes [1], while tetrasubstituted thiopyran II undergoes disproportionation only to perchlorate VIII and dihydrothiopyran XIX [2]. For the first time we have observed that pentasubstituted (III-V) and tetrasubstituted (VI) thiopyrans react with perchloric acid in air to give only thiapyrylium salts IX-XII in quantitative yields, whereas virtually no reaction is observed in a helium atmosphere [3]. Further studies in the case of thiopyran VI made it possible to establish that both thiapyrylium perchlorate XII and thiacyclohexane XVIII are formed in a helium atmosphere when the reaction mixture is allowed to stand for a sufficiently long time (4 months), i.e., thiopyran VI undergoes disproportionation. Thus, in the reaction of thiopyrans with $HClO_4$ in acetic acid the formation of thiapyrylium salts may proceed via two



I, XIII, XIIIa $R=R^2=H$, $R^1=C_6H_5$; II, XIV, XIVa $R=R^2=CH_3$, $R^1=H$; III, IX, XV, XVa $R=R^1=R^2=CH_3$; IV, X, XVI, XVIa $R=R^2=CH_3$, $R^1=C_2H_5$; V, XI, XVII, XVIIa $R=R^2=CH_3$, $R^1=C_6H_5$; VI, XII, XVIII, XVIIIa $R=H$, $R^1=C_6H_5$, $R^2=CH_3$

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