NUCLEOPHILIC ADDITION OF DIFUNCTIONAL REAGENTS TO 2,3-DICHLOROBENZO[b]THIOPHENE 1,1-DIOXIDE

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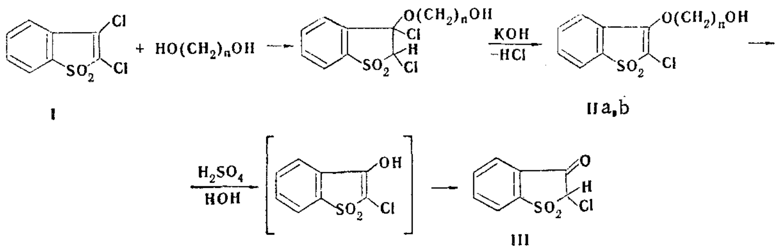
The nucleophilic reactions of 2,3-dichlorobenzo[b]thiophene 1,1-dioxide with α- and β-glycols, α-diamines, and α-amino alcohols proceed with cleavage of hydrogen chloride to give the previously unknown 3-monosubstituted derivatives of 2-chlorobenzo[b]thiophene 1,1-dioxide. The second functional group (the hydroxyl group in amino alcohols) does not enter into the reaction.

The $C_2=C_3$ bond in benzo[b]thiophene 1,1-dioxide is similar to the double bond of divinyl sulfone, which is capable of adding nucleophilic reagents [1-4].

We have investigated the nucleophilic addition of difunctional reagents – glycols, diamines, and amino alcohols – to 2,3-dichlorobenzo[b]thiophene 1,1-dioxide (I). Compound I adds 1,2- and 1,3-glycols in the presence of alkali with splitting out of HCl to give 2-chloro-3-hydroxyalkoxybenzo[b]thiophene 1,1-dioxides (II) (Table 1):



I

IIa,b

III

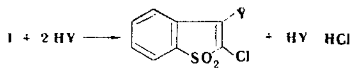
a $n=2$; b $n=3$

Even when a considerable excess of I is present, the second hydroxyl group of the glycol does not enter into the reaction.

The presence of a hydroxyalkoxy group in the 3 position was proved by hydrolysis of compounds of the II type to give 3-oxo-2-chloro-2,3-dihydrobenzo[b]thiophene 1,1-dioxide (III). The IR spectra of II contain absorption maxima at 1265-1270 and 3600 cm^{-1}, which correspond to the vibrations of the $=C-O-C$ and $O-H$ groups, respectively.

Compound I forms the corresponding 3-amino-substituted IVa-c with excess 1,2-diamine (ethylenediamine, piperazine, and N-methylpiperazine) in alcohol or benzene. The second functional group does not enter into the reaction in this case either.

Amino alcohols (ethanolamine and diethanolamine) add to I through the amino group with splitting out of HCl to give amino derivatives IVd,e (Table 1).



IVa - e

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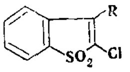
TABLE 1



Comp.	R	Mp, °C (from ethanol)	Empirical formula	Found, %			Calc., %			Yield, %
				C	H	N	C	H	N	
IIa	$O(CH_2)_2OH$	132—133	$C_{10}H_9ClO_4S$	46,1	3,8	—	46,1	3,5	—	65
IIb	$O(CH_2)_3OH$	129—130	$C_{11}H_{11}ClO_4S$	48,3	4,0	—	48,1	4,0	—	61
IVa	$NH(CH_2)_2NH_2$	181—182	$C_{10}H_{11}ClN_2O_2S$	46,3	4,4	10,9	46,4	4,3	10,8	59
IVb	$N(CH_2CH_2)_2NH$†	156—157*	$C_{12}H_{13}ClN_2O_2S$	50,9	4,5	9,8	50,6	4,6	9,8	77
IVc	$N(CH_2CH_2)_2NCH_3$ ‡	168—169	$C_{13}H_{15}ClN_2O_2S$	52,6	5,3	9,0	52,3	5,1	9,4	81
IVd	$NH(CH_2)_2OH$	191—192	$C_{10}H_{10}ClNO_3S$	46,3	3,8	5,2	46,2	3,9	5,4	68
IVe	$N(CH_2CH_2OH)_2$	134—136	$C_{12}H_{14}ClNO_4S$	47,2	4,3	4,9	47,4	4,6	4,6	59

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* From benzene–hexane.

† The hydrochloride (Va) had mp 228-233° (dec.). Found,%: C 44.3; H 4.8; N 8.9. $C_{12}H_{13}ClN_2O_2S \cdot HCl$. Calculated,%: C 44.8; H 4.4; N 8.7.

‡ The hydrochloride (Vb) had mp 223-226° (dec.). Found,%: C 46.3; H 4.6; N 7.9. $C_{13}H_{15}ClN_2O_2S \cdot HCl$. Calculated,%: C 46.6; H 4.8; N 8.3.

a $Y = NH(CH_2)_2NH_2$; b $Y = N(CH_2CH_2)_2NH$; c $Y = N(CH_2CH_2)_2NCH_3$;
d $Y = NHCH_2CH_2OH$; e $Y = N(CH_2CH_2OH)_2$

The structure of amino derivatives IV was confirmed by the presence in their IR spectra of absorption bands of the stretching vibrations of =C−N groups at 1270-1280 cm^{-1} and of the stretching vibrations of a hydroxyl group (for IVd,e) at 3520-3550 cm^{-1}. When amines IV are heated with dilute sulfuric acid, they are hydrolyzed to III; this confirms that the substituent is in the 3 position.

2-Chloro-3-piperazino- (IVb) and 2-chloro-3-(N'-methylpiperazino)benzo[b]thiophene 1,1-dioxide (IVc) can be converted to the corresponding hydrochlorides (V) by the action of alcoholic HCl solution. The remaining amino derivatives are hydrolyzed under similar conditions.

EXPERIMENTAL

2-Chloro-3-(ω-hydroxyalkoxy)benzo[b]thiophene 1,1-Dioxides (II) (Table 1). A 0.01-mole sample of I [5] was added to a solution of 0.01 mole of KOH in 40 ml of the appropriate glycol, and the mixture was heated on a boiling water bath for 4 h and filtered. The excess glycol was removed by vacuum distillation, and the resulting precipitate was separated and washed with water.

2-Chloro-3-aminobenzo[b]thiophene 1,1-Dioxides (IVa-c) (Table 1). A solution of 0.01 mole of I and 0.03 mole of diamine in 40 ml of 85% ethanol was refluxed for 3 h and filtered. The solvent was removed by distillation, and the residue was washed with water and recrystallized.

2-Chloro-3-piperazinobenzo[b]thiophene 1,1-Dioxide Hydrochloride (Va). A 1-ml sample of concentrated hydrochloric acid was added to a solution of 1.42 g (0.05 mole) of IVb in 10 ml of ethanol. The resulting precipitate was washed with alcohol until it was neutral. The yield of Va with mp 228-233° (dec.) was 1.45 g (88%).

2-Chloro-3-(N'-methylpiperazino)benzo[b]thiophene 1,1-Dioxide Hydrochloride (Vb). This compound was similarly obtained in 30% yield from IVc and had mp 223-226° (dec.). Evaporation of the filtrate gave III with mp 154-155° (mp 154-155°, according to [1]) in 56% yield.

2-Chloro-3-(β-hydroxyethylamino)- and 2-Chloro-3-[bis(β-hydroxyethyl)amino]benzo[b]thiophene 1,1-Dioxides (IVd,e). A solution of 0.051 mole of I and 0.15 mole of amino alcohol in 25 ml of 85% ethanol was refluxed for 5 h. Compounds IVd,e were isolated and purified by the procedure used for IVa-c.

3-Oxo-2,3-dihydrobenzo[b]thiophene 1,1-Dioxide (III). A solution of 1.42 g (0.005 mole) of IVb in 5 ml of 6 N H_2SO_4 was heated on a boiling-water bath for 40 min. The solid material was washed with water and recrystallized from ethanol to give 0.8 g (73%) of III with mp 154-155°; $\nu_{C=O}$ 1740 cm^{-1}. The 2,4-dinitrophenylhydrazone had mp 259-262° (dec.). Found,%: N 13.9. $C_{14}H_{10}ClN_4O_6S$. Calculated,%: N 14.1. Compound III was similarly obtained by hydrolysis of the remaining compounds.

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