

REACTION OF 3,4-EPOXY-3-METHYL-2,3,4,5-TETRAHYDROTHIOPHENE-1,1-DIOXIDE WITH ALCOHOLS

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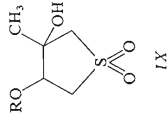
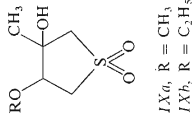
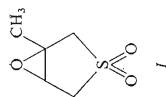
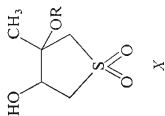
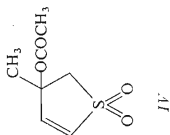
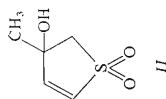
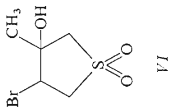
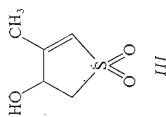
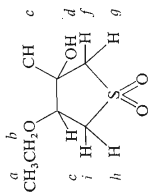
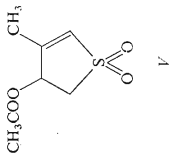
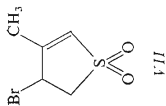
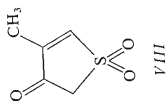
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Isomerisation of 3,4-epoxy-3-methyl-2,3,4,5-tetrahydrothiophene-1,1-dioxide in an alkaline medium afforded a mixture of 4-hydroxy-3-methyl-4,5-dihydrothiophene-1,1-dioxide and 3-hydroxy-3-methyl-2,3-dihydrothiophene-1,1-dioxide. Addition of primary alcohols to 3-hydroxy-3-methyl-2,3-dihydrothiophene-1,1-dioxide in alkaline media afforded 4-alkoxy-3-hydroxy-3-methyl-2,3,4,5-tetrahydrothiophene-1,1-dioxide whereas, under the same conditions, the isomeric 4-hydroxy-3-methyl-4,5-dihydrothiophene-1,1-dioxide did not react with alcohols.

Derivatives of 3,4-epoxy-2,3,4,5-tetrahydrothiophene-1,1-dioxide are isomerised by bases to the corresponding unsaturated alcohols. The rearrangement of the parent 3,4-epoxy-2,3,4,5-tetrahydrothiophene-1,1-dioxide was described by Procházka and Horák¹. Muchamedova and collaborators² found that the reaction of 3,4-epoxy-3-methyl-2,3,4,5-tetrahydrothiophene-1,1-dioxide (*I*) with alcohols in an alkaline medium afforded 3-alkoxy derivatives *X* which arise by addition of the alcohol to the originally formed 4-hydroxy-3-methyl-4,5-dihydrothiophene-1,1-dioxide (*III*). We have studied the isomerisation of the epoxide *I* by sodium hydroxide in aqueous, methanolic and ethanolic solution, or by sodium methoxide or ethoxide in methanol or ethanol.

Action of catalytic amounts of aqueous sodium hydroxide on the epoxide *I* led to an approximately equimolar mixture of 3-hydroxy-3-methyl-2,3-dihydrothiophene-1,1-dioxide (*II*) and 4-hydroxy-3-methyl-4,5-dihydrothiophene-1,1-dioxide (*III*). We separated these isomeric alcohols making use of the fact that acetic anhydride in pyridine reacts substantially faster with the secondary alcohol *III* than with the alcohol *II*. The alcohol *III* was identical with the unsaturated alcohol prepared by hydrolysis of 3,4-dibromo-3-methyl-2,3,4,5-tetrahydrothiophene-1,1-dioxide⁵, as shown by its IR spectra and by the IR spectra and melting point of its acetate *V*. The structure of *III* was further confirmed by its transformation into the known³ bromo derivative *VII* on treatment with phosphorus tribromide and also by its oxidation to the ketone *VIII* (ref.⁷). The alcohol *II* was identical with the dehydrobromination product of the bromohydrin *VI*; this product afforded the identical acetate *IV*. The acetate *IV* arose also directly from the bromohydrin *VI*



by treatment with acetic anhydride in pyridine. The alcohols *II* and *III* were prepared also by lithium chloride-induced isomerisation of the epoxide *I*. The isomerisation product, described in the literature², is probably a mixture of both the isomeric alcohols *II* and *III*; this assumption is supported by the fact that oxidation of this product to the ketone *VIII*, as well as its reaction with sodium ethoxide in ethanol, gave relatively low yields.

Isomerisation of the epoxide *I* by sodium hydroxide in ethanol (or methanol) afforded, in addition to the alcohol *III*, alkoxy derivatives (Table I) which were identical with the products obtained by Muchamedova and coworkers². According to the mentioned authors these products are 3-alkoxy-4-hydroxy-3-methyl-2,3,4,5-tetrahydrothiophene-1,1-dioxides (*X*). Reaction of the epoxide *I* with sodium ethoxide in ethanol afforded also a mixture of the alcohol *III* and the ethoxy derivative *IXb*. The presence of the unsaturated alcohol *III* among the products of the base-catalysed reaction of the epoxide *I* with 2-propanol was observed already earlier², other studies report the formation of both isomeric alkoxy derivatives in the reaction of the epoxide *I* with 2-propanol or benzyl alcohol⁴. 4-Alkoxy derivatives were reported as products of reaction of the epoxide *I* with alcohols in the presence of sulphuric acid².

The fact that in the reaction of the epoxide *I* with alcohols in a basic medium the reaction mixture contained the unreacted alcohol *III* helped us to decide between the alternative structures *IX* and *X* for the obtained alkoxy derivatives. We have proved, particularly on the basis of ¹H-NMR spectra and some reactions, that methoxy and ethoxy derivatives of the structure *IX* are formed preferentially by the reaction of the alcohol *II* with sodium alkoxide in the corresponding alcohol whereas the isomer *III* does not react under the same conditions (Table II). Zimmermanová and Procházka⁵ have described the addition of alcohols to α,β -unsaturated sulphones in an alkaline medium as a synchronous attack of molecules of alcohol and base

TABLE I
Reaction of Epoxide *I* with Bases

Base	Solvent	% <i>IX</i>	% <i>III</i>	Alkoxy derivatives (m.p.), °C
C ₂ H ₅ ONa	ethanol	35	36	78–79
NaOH	ethanol	41	32	78–80
NaOH ^a	ethanol	31	37	78–79
NaOH	methanol	39	37	118–120

^a 0.001 mol of NaOH, reaction time 5 days.

R—O⁽⁻⁾. We can assume that a methyl group can influence unfavourably this addition, both by steric hindrance and by the +I effect which increases the electron density at the reaction center. Analogously, under the same conditions, in the reaction of 3,4-epoxy-3,4-dimethyl-2,3,4,5-tetrahydrothiophene-1,1-dioxide with sodium ethoxide in ethanol no addition to the double bond takes place. Also the isomerisation of 2,3,4,5-tetramethyl-3,4-epoxy-2,3,4,5-tetrahydrothiophene-1,1-dioxide affords only the unsaturated alcohol. On the contrary, the reaction of 3,4-epoxy-2,3,4,5-tetrahydrothiophene-1,1-dioxide with sodium ethoxide in ethanol is facile and leads to the corresponding alkoxy derivative⁶.

The formation of methoxy and ethoxy derivatives from the alcohol *II* supports the structure *IX*, containing the tertiary hydroxyl group, which agrees also with the ¹H-NMR spectrum. Also other facts are in accord with the structure *IX*: the alkoxy derivative *IXb* reacts very slowly with trichloroacetyl isocyanate, and in ¹H-NMR spectrum this reaction causes a great shift of the methyl signal ($\Delta\delta + 0.37$) and a comparable shift of the signal of the hydrogen in the position 4 ($\Delta\delta + 0.38$). For the structure *X* we would expect a great shift of the hydrogen signal (~ 1.0 ppm) and a small shift of the methyl signal. Similar shifts were found for 3- and 4-alkylthio analogues of the compounds *IX* and *X* (ref.⁶). The hydroxyl group in *IX* is not acetylated with acetic anhydride in pyridine, and oxidation of the ethoxy derivative *IXb* with potassium dichromate in dilute sulphuric acid does not afford the ketone *VIII* which should arise from the compound *X*. The methoxy and ethoxy derivatives *IXa* and *IXb* are formed also in the reaction of the acetate *IV* with sodium hydroxide in me-

TABLE II
Reaction of Alcohols *II* and *III*, and Acetates *IV* and *V* with Bases

Alcohol (acetate)	Base	Solvent	% <i>IX</i>	Alkoxy derivatives m.p., °C
<i>II</i>	C ₂ H ₅ ONa	ethanol	75	79–80
<i>II</i>	CH ₃ ONa	methanol	78	120
<i>II</i> + <i>III</i> ^a	C ₂ H ₅ ONa	ethanol	36	78–79
<i>III</i>	C ₂ H ₅ ONa	ethanol	— ^b	—
<i>IV</i>	NaOH	water	— ^c	—
<i>IV</i>	NaOH	methanol	63	118–120
<i>IV</i>	NaOH	ethanol	46	78–80
<i>V</i>	NaOH	ethanol	— ^c	—

^a A mixture of *II* and *III* ($\sim 1:1$) after isomerisation of *I* with lithium chloride; ^b recovery of *III*;

^c only the corresponding alcohol *II* or *III* was isolated.

thanol and ethanol, respectively; saponification of the acetate *IV* with aqueous sodium hydroxide affords the alcohol *II*. Saponification of the acetate *V* in both cases gives only the alcohol *III* (Table II).

EXPERIMENTAL

Melting points were determined on a Boetius block and are uncorrected. Analytical samples were dried at 0.5 Torr for 8–10 h at appropriate temperatures. IR spectra were taken in chloroform on a UR-10 (Zeiss, Jena) spectrophotometer, $^1\text{H-NMR}$ spectra were measured on a Varian 100 apparatus (chemical shifts are given in ppm, δ scale, internal standard tetramethylsilane).

Isomerisation of the Epoxide *I*

3,4-Epoxy-3-methyl-2,3,4,5-tetrahydrothiophene-1,1-dioxide (*I*) was prepared according to ref.¹, m.p. 90–91°C; ref.² reports m.p. 89–90°C. The epoxide *I* (2.0 g) was heated with water (60 ml) and 0.5M-NaOH (0.3 ml) to 50°C for 2 h. The solution was neutralized with hydrochloric acid, taken down and the residue was treated with a mixture of acetic anhydride (4 ml) and pyridine (10 ml). After 3 h the mixture was diluted with ice-cold water (50 ml), evaporated and the residue was dissolved in chloroform and subjected to chromatography on silica gel (50 g). Elution with chloroform afforded the acetate *V* (1.20 g; 41%), m.p. 94–95°C (ethanol), and the alcohol *II* (0.86 g; 43%), b.p. 135–136°C/0.5 Torr. The alcohol *III* was prepared by saponification of the acetate *V* in ethanolic 1M-NaOH; b.p. 156–157°C/0.2 Torr. For $\text{C}_5\text{H}_8\text{O}_3\text{S}$ (148.1) calculated: 40.54% C, 5.44% H, 21.60% S; found: 40.70% C, 5.52% H, 21.68% S.

3-Hydroxy-3-methyl-2,3-dihydrothiophene-1,1-dioxide (*II*)

A solution of the bromohydrin *VI*⁸ (4.60 g; 0.02 mol) in acetone (20 ml) was heated with pyridine (4 ml) for 2 h. The solution was evaporated, the residue dissolved in water, neutralized with sodium hydroxide and again evaporated. The residue was extracted with acetone, the acetone evaporated and the remaining alcohol *II* was distilled at 130–132°C/0.4 Torr; yield 2.51 g (85%). For $\text{C}_5\text{H}_8\text{O}_3\text{S}$ (148.1) calculated: 40.54% C, 5.44% H, 21.60% S; found: 40.82% C, 5.60% H, 21.35% S. The acetate *IV* was prepared by acetylation of the alcohol *II* with acetic anhydride in pyridine for 48 h; m.p. 60–61°C (benzene–light petroleum). For $\text{C}_7\text{H}_{10}\text{O}_4\text{S}$ (191.1) calculated: 43.98% C, 5.27% H, 16.74% S; found: 44.15% C, 5.44% H, 16.45% S. IR spectrum (cm^{-1}): 1110, 1245, 1320, 1610, 1745. The acetate *IV* was also prepared by the reaction of the bromohydrin *VI* (1.15 g; 0.005 mol) with acetic anhydride (3 ml) in pyridine (10 ml). After standing at room temperature for 48 h the solution was worked up, yielding 0.62 g (65%) of the acetate *IV*, m.p. 60–60.5°C, no depression on admixture with the sample prepared above.

3-Methyl-4-oxo-4,5-dihydrothiophene-1,1-dioxide (*VIII*)

This compound was prepared in 63% yield by oxidation of the alcohol *III* according to ref.²; m.p. 162°C (decomposition above 156°C); reported² m.p. 162–163°C (decomposition), 164 to 165°C (ref.⁷). 2,4-Dinitrophenylhydrazone, m.p. 238–239°C (dioxane), ref.² reports 238.5 to 239.5°C.

4-Bromo-3-methyl-4,5-dihydrothiophene-1,1-dioxide (VII)

Phosphorus tribromide (0.84 g; 0.003 mol) was added under cooling with ice to a solution of the alcohol III (1.48 g; 0.01 mol) in chloroform (8 ml). The temperature was kept at 0°C for 30 min, then slowly raised to 20°C, the mixture was decomposed with ice, washed with NaHCO₃, and the solvent evaporated. Crystallisation of the residue from benzene–light petroleum afforded 1.75 g (83%) of the product, m.p. 73–74°C, no depression on admixture with an authentic sample, prepared by dehydrohalogenation of 3,4-dibromo-3-methyl-2,3,4,5-tetrahydrothiophene-1,1-dioxide according to ref.³.

Reaction of Epoxide I, Alcohols II and III and Acetates IV and V with Bases

The epoxide I, alcohol or acetate (0.01 mol) was mixed with a solution of the base (0.03 mol) in the corresponding alcohol (30 ml) and the mixture was allowed to stand at room temperature for 2 days. The solution was neutralized with hydrochloric acid, the precipitated sodium chloride was removed by filtration, the alcohol was distilled off and the residue was dissolved in chloroform and chromatographed on silica gel (30 g).

3-Hydroxy-4-methoxy-3-methyl-2,3,4,5-tetrahydrothiophene-1,1-dioxide (IXa), m.p. 118 to 120°C (benzene–light petroleum); reported² m.p. 114–116°C. IR spectrum (cm⁻¹): 1116, 1325, 2830, 3550.

4-Ethoxy-3-hydroxy-3-methyl-2,3,4,5-tetrahydrothiophene-1,1-dioxide (IXb), m.p. 78–79°C (benzene–light petroleum); reported² m.p. 78–79°C. IR spectrum (cm⁻¹): 1116, 1320, 2970, 3550. ¹H-NMR spectrum: 1.26 t, 3 H (a), $J_{ab} = 7$; 1.475 s, 3 H (c); 3.10 s, 1 H (d); 3.12 d, 1 H (f), $J_{fg} = 13.5$; 3.98 m, 1 H (e); 3.63 m, 2 H (b); ~3.39 m, 2 H (i + h); after addition of trichloroacetyl isocyanate: 1.26 (a), 1.85 (c), 3.33 (f), ~3.64 (b), 4.01 (g), 3.46 (e), ~3.50 (i + h).

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