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PREPARATION AND REACTIONS OF SULFONIUM SALTS FROM EPOXIDES AND DMSO. A STEREOSPECIFIC SYNTHESIS OF 1,2-GLYCOLS

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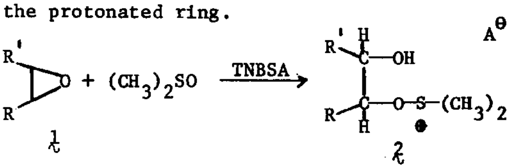
The recent brief communication of Barili *et al.*[1] on the acid-catalyzed hydrolysis of aryl substituted epoxides in dimethyl sulfoxide (DMSO) prompts us to report new aspects of our own work[2] on the acid-catalyzed reactions of epoxides 1 with DMSO which (a) permit the isolation in good yield of pure dimethyl alkoxysulfonium salts 2 which can then be used for a variety of reaction probes; (b) provide rationalizations for certain mechanistic uncertainties in earlier work;[1] (c) define the differences in reactivity between salts 2 derived from epoxides having a benzylic carbon and those that are purely aliphatic; and finally, (d) provide a stereospecific and rapid procedure for conversion of a *cis*- epoxide to a *threo*-glycol and of a *trans*-epoxide to an *erythro*-glycol taking advantage of the clean inversion that occurs when DMSO reacts with the protonated ring.



3, R=ϕ; R'=H
4, R(R')=$-(CH_2)_4-$
5, R=R'=CH_3
6, R=C_2H_5; R'=H
7, R=H; R'=C_2H_5

R = H, alkyl or phenyl
R' = H or alkyl

TNBSA = 2,4,6-trinitrobenzenesulfonic acid
A⊖ = Anion from TNBSA

(a) *Crystalline Dimethyl Alkoxysulfonium Salts*. 2,4,6-Trinitrobenzene sulfonic acid is a convenient and useful strong acid for the preparation of nicely crystalline sulfonium salts. Dimethyl alkoxysulfonium salts 2 are prepared in 60-80% yields, typically, by dissolving anhydrous 2,4,6-trinitrobenzenesulfonic acid (0.0123 moles) in anhydrous DMSO (0.0615 moles) at 60°. The solution is cooled to room temperature and the appropriate epoxide (0.0123-0.0184 moles) is then added dropwise over a period of 10 minutes with constant stirring, followed by stirring for an additional 15 minutes. The viscous, yellow homogenous solution is poured into an excess of cold ethyl acetate with vigorous stirring causing the salts to precipitate. In the case of salts 5,6, 7, ether-ethyl acetate (2:1 by volume) is used as the precipitating solvent. The yields shown in Table I are for salts which have been crystallized once from acetone/ether.[10]

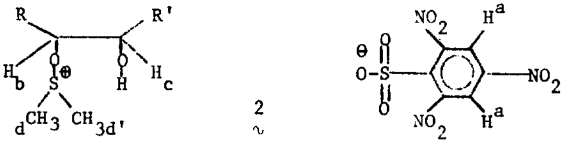
Salts 6 and 7 are obtained as a mixture from 1,2-epoxybutane and are separated by selective solution of 7 in acetone at room temperature; salt 6 is relatively insoluble. Salt 5 is obtained as a mixture of threo- and erythro-isomers from the mixed cis- and trans-2,3-epoxybutanes employed. In the case of styrene oxide, salt 3 is the sole product obtained. The assignment of the structures of 3 and 6 (dimethyl oxysulfonium group on the chiral carbon rather than on the terminal one) and 7 (dimethyl oxysulfonium group on the terminal carbon rather than on the chiral carbon) is made on the basis of nmr spectroscopy. The location of a dimethyl oxysulfonium group on a chiral carbon atom is shown by the S-methyl signals.[3] In the chiral attachment, the $S(CH_3)_2$ group appears as two distinguishable singlets whereas in a nonchiral attachment only one singlet is obtained (see Table II). Yields and melting points of the pure salts are given in Table I; nmr results are given in Table II.

Table I. Dimethyl alkoxysulfonium salts[d] 2

Salt	3		4		5		6		7	
Yield %	65[a]	75[b]	65[a]	83[b]	60[a]	65[b]	12[a]	13[b]	48[a]	53[b]
Mp (°C)	172 - 174[c]		172 - 174		139 - 140		143 - 144		120 - 121	

[a] Epoxide: acid=1 [b] Epoxide:acid=1.5 [c] Starts to decompose at 120° [d] Equivalent wt. was within ± 1% of the calcd. value, elemental analysis agreed with theory.

Table II. Nmr Data on



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Salt	R	R'	δ ppm (multiplicity)[e]
3[a]	Ø	H	H_a 8.85(s);R7.47(s); H_b 5.58(t);R',H_c 3.90(d); $H_{d,d'}$3.30,3.43 (2s).
4[a]	$-(CH_2)_4-$		H_a 8.89(s); H_b4.15(m); H_c 3.48(m), $H_{d,d'}$3.37,3.32 (2s); R,R' 0.98-2.32 (b).
5[b]	CH_3	CH_3	H_a 8.8(s); H_b 4.35(m); H_c 3.75(m); $H_{d,d'}$3.25, 3.28(2s); R 1.21(d);R'1.04(d).
6[b]	C_2H_5	H	H_a 8.87(s);H_b 4.38(m); H_c, R'3.78(m)[c]; $H_{d,d'}$3.23,3.28(s); R 0.66-1.83(m).
7[b]	H	C_2H_5	H_a 8.83(s);H_b, R 4.28(m); H_c3.66 (m); $H_{d,d'}$3.27[d](s), R' 0.7-1.83 (m).

[a] δ Values are relative to DMSO at 2.6δ [b] TMS at zero δ [c] Multiplet buried under broad OH peak [d] Singlet because oxysulfonium group is not on a chiral carbon [e] DMSO-d_6 used in all cases except 3 in which DMSO was used.

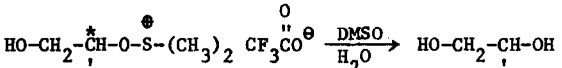
Stirring a suspension of salt 3(from styrene oxide) in acetone with triethylamine for 15 minutes at room temperature yields phenacyl alcohol (60% by nmr; 40% isolated) and triethylammonium 2,4,6-trinitrobenzenesulfonate (100% yield), as well as other unidentified products. (Phenacyl alcohol was characterized by comparison with an authentic sample.) Triethylammonium 2,4,6-trinitrobenzenesulfonate, mp 182-183°, was characterized by its nmr spectrum in acetone-d_6: m, 3.6 δ, 6H, $-CH_2-$; t, 1.25 δ, 9H, CH_3-; s, 8.83 δ, 2H, aromatic.

Although the proton source in the conversion of 1 to 2 is trinitrobenzenesulfonic acid, the actual intermediate that reacts with epoxide may be the acid salt 8, mp 112-114°, a new compound isolated in 80% yield from a solution of 2,4,6-trinitrobenzenesulfonic acid in DMSO by precipitation in ethyl acetate.

The equivalent weight of 8 (calcd. 449, found 454) indicates that the stoichiometry of the crystalline salt corresponds with $[(CH_3)_2SO]_2HA$. The nmr spectrum of 8 in CD_3NO_2 revealed that the four methyl groups are equivalent: s, 8.56 δ, 2H, aromatic; s, 3.00 δ, 12H, CH_3-; s, 10.20δ, 1H, acid proton. One possible rationalization for this is that in solution a proton is bound to an oxygen of one DMSO molecule and strongly hydrogen bonded to another, and the proton rapidly exchanges between the two DMSO molecules (8a ⇄ 8b). A similar explanation has been proposed[12] to rationalize the ir spectrum of CH_3SO_3H in DMSO.

8a $(CH_3)_2\overset{+}{S}\text{-O-H---O=S}(CH_3)_2\ A^- \rightleftharpoons (CH_3)_2S\text{=O---H-O-}\overset{+}{S}(CH_3)_2\ A^-$ 8b

(b) Mechanistic Considerations. Barili and coworkers[1] suggested that in the hydrolysis of aryl substituted epoxides in DMSO, the assumed intermediate salt (not isolated) 9 from optically active styrene oxide racemizes in the presence of excess DMSO at 25° by repeated displacement of the dimethyl oxysulfonium group by a molecule of DMSO. The glycol isolated had an optical purity of only 5%.



$$\underset{\phi}{\text{HO-CH}_2\text{-}\overset{*}{\text{C}}\text{H}}\text{-O-}\overset{\oplus}{\text{S}}\text{-}(CH_3)_2\ CF_3\overset{O}{\overset{\|}{C}}O^{\ominus} \xrightarrow[H_2O]{DMSO} \underset{\phi}{\text{HO-CH}_2\text{-CH}}\text{-OH}$$

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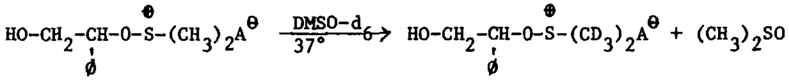
Identity processes of this type (DMSO displacing DMSO) were first reported by Torssell[3] in aliphatic systems at higher temperatures. Our results, the displacement of DMSO by DMSO in salt 3, confirm and lend credence to the conclusion of Barili *et al.*[1] concerning the method of racemization.

The nmr spectrum of salt 3 undergoes a drastic change with time in DMSO-d_6 at the nmr probe temperature of 37°. After 2 hrs. the absorption of the $S(CH_3)_2$ group at 3.30 δ and 3.43 δ disappears[4] and a new single peak appears at 2.57 δ, corresponding to liberated DMSO, without any other changes in the remainder of the spectrum.



$$\underset{\phi}{\text{HO-CH}_2\text{-CH}}\text{-O-}\overset{\oplus}{\text{S}}\text{-}(CH_3)_2A^{\ominus} \xrightarrow[37°]{DMSO\text{-}d_6} \underset{\phi}{\text{HO-CH}_2\text{-CH}}\text{-O-}\overset{\oplus}{\text{S}}\text{-}(CD_3)_2A^{\ominus} + (CH_3)_2SO$$

Of special significance is the absence of such exchange in the purely aliphatic salts 4, 5, 6, 7, and 11 under similar conditions.

(c) Methanolysis of Dimethyl Alkoxysulfonium Salts 3. Previous work on the hydrolysis[5,6] and methanolysis,[6,7] of dimethyl alkoxysulfonium salts has shown that H_2O or CH_3OH attacks exclusively at sulfur in both benzylic and non-benzylic systems. In the methanolysis of salt 3, however, using 40 ml of CH_3OH/g of salt, we find that major attack (75%) is not at sulfur but at the benzylic carbon, with displacement of DMSO to form 2-methoxy-2-phenylethanol and the 1:1 acid salt of DMSO and trinitrobenzenesulfonic acid 10, mp 197-198° [nmr (CD_3NO_2) 3.1 δ (6H, s); 8.7δ (2H, s)], and minor attack (25%) is at sulfur to give 1-phenyl-1,2-ethanediol (styrene glycol) and methoxy dimethylsulfonium 2,4,6-trinitrobenzenesulfonate 11, mp 168-170° [nmr (DMSO-d_6) at 3.3δ (6H, s); 8.8 δ (2H, s); 3.98δ (3H,s)].

$(CH_3)_2\text{-}\overset{\oplus}{S}\text{-OH}\ \ A^{\ominus}$ 10

$(CH_3)_2\overset{\oplus}{S}\text{-OCH}_3\ \ A^{\ominus}$ 11

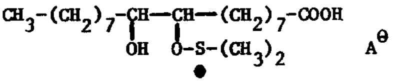
Only in the case of purely aliphatic systems (nonbenzylic) does methanol attack exclusively at sulfur to give glycols and salt 11. Table III compares the results of the reaction of methanol with salts 3, 5, and a mixture of 6 and 7.

Table III. Reaction of Methanol (40 ml) with Alkoxydimethylsulfonium Salts **2** (1g) at Room Temp.

Salt	% Decomposition	Time, hrs.	% Attack on Sulfur	% Attack on Carbon (Displacement of DMSO)
3	100	30	25[a]	75[a]
5	67	14	100(67% yield)[b]	——
6 and **7** mixture	72	14	100(72% yield)[b]	——

[a] Ratio of attack on sulfur and carbon is calculated from the nmr spectrum in DMSO-d_6 of the reaction mixture after evaporation of MeOH. 2-Phenyl-2-methoxyethanol and styrene glycol are characterized by comparison of the resulting spectrum with those of authentic samples. [b] Yields are calculated by actual isolation of glycols and salt **11**.

(d) Stereospecific Preparation of Glycols. Since hydrolysis of alkoxysulfonium salts is reported to proceed exclusively by attack of water at sulfur[5,6,7,8] we examined the reaction of the *cis*- and *trans*-9,10-epoxystearic acids with DMSO-TNBSA followed by hydrolysis to ascertain whether the epoxides are converted stereospecifically to the diastereomeric 9,10-dihydroxystearic acids. If an inversion occurs on opening the oxirane ring with DMSO and hydrolytic attack is then exclusively on the sulfur atom of the salts, the *cis* epoxy acid should yield the *threo* glycol and the *trans* epoxy acid the *erythro* glycol. We prepared dimethyl alkoxysulfonium salts **12** from both the *cis*- and *trans*-epoxystearic acids, using the previously described procedure,[9] but oily precipitates were obtained after addition of the DMSO solution to ether-ethyl acetate (2:1 ratio by volume). After decantation of the solvent layer, the oily lower layer was stirred with water for 12-14 hrs. to give 65-70% yields of *threo*- and *erythro*-9,10-dihydroxystearic acids, respectively, from *cis*- and *trans*-9,10-epoxystearic acids. The crude *threo*- and *erythro*-9,10-dihydroxystearic acids had melting points of 93° and 126°, respectively, which were raised to the anticipated 95° and 130° by one crystallization from ethanol.[11]



$$CH_3-(CH_2)_7-\underset{OH}{CH}-\underset{\overset{\bullet}{O}-S-(CH_3)_2}{CH}-(CH_2)_7-COOH \quad A^{\ominus}$$

(mixture of 9,10 and 10,9 isomers)

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Further research is being conducted into the preparation and properties of sulfonium salts.

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