122273) and the Samuel S. Fels Fund for partial support of this research.

Registry No.—**5** picrate, 55975-86-5; **6**, 27691-49-2; **6** picrate, 55871-34-6; **7** picrate, 55871-35-7; **8** picrate, 55871-37-9; **9**, 39159-87-0; **10**, 55871-38-0; **11**, 27691-52-7; **13**, 19397-91-2; **14**, 55259-85-5; **15** trifluoroacetate, 55871-40-4; **16**, 19871-30-8; **17**, 18922-58-2; **18**, 63-74-1; **19**, 68-35-9; **20**, 55871-41-5; **21**, 24194-22-7; **22**, 55871-42-6; **23**, 55871-43-7; **24**, 55871-44-8; **25**, 55871-45-9; **26**, 55871-46-0; **27**, 55871-47-1; DMSO, 67-68-5; TFAA, 407-25-0; *p*-nitrobenzenesulfonamide, 6325-93-5; benzamide, 55-21-0; *p*-nitrobenzamide, 619-80-7; urea, 57-13-6; *p*-nitroaniline, 100-01-6; *o*-fluoroaniline, 348-54-9; benzyl chloroformate, 501-53-1.

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(1) (a) Preliminary communications: *Tetrahedron Lett.*, 1503 (1974); Ninth Middle Atlantic Regional Meeting of the American Chemical Society, Wilkes-Barre, Pa., April 1974, and 169th National Meeting of the American Chemical Society, Philadelphia, Pa., April 1975, Division of Medicinal Chemistry. (b) Part XV: "Iminosulfuranes". Part XIV: . E. Varkey, G. F. Whitfield, and D. Swern, *J. Org. Chem.*, **39**, 3365 (1974).
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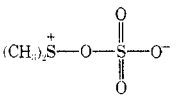
(12) "Activation" of DMSO by sulfur trioxide or phosphorus pentoxide yields a "zwitterionic" intermediate **1**, with a good leaving group. With sulfur trioxide, for example, **1** can be written as A; NMR evidence supports such a formulation.[1b]



A

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(18) Sulfanilamide (**18**) gives a positive ninhydrin test and is soluble in aqueous base.
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(20) J. Pless and W. Bauer, *Angew. Chem., Int. Ed., Engl.*, **85**, 142 (1972).
(21) Infrared spectra were recorded on a Perkin-Elmer 137B or Pye Unicam SP-1000. NMR spectra (hydrogen only) were obtained on Varian Models A-60A or XL-100 with Me_4Si as internal standard. Melting points (uncorrected) were obtained using a Thomas-Hoover capillary apparatus. TLC was conducted on Eastman silica gel chromatograms or coated microscope slides with fluorescent indicator; visualization was effected either with uv light or by development in a chamber containing iodine crystals. All reactants were the purest obtainable; in all cases purity exceeded 97%. Solvents were the best commercial grades and were used as received, except methylene chloride, which was dried and fractionally distilled. DMSO was distilled under reduced pressure from calcium hydride and stored in a nitrogen atmosphere over Linde molecular sieve 4A. Trifluoroacetic anhydride was obtained from various chemical supply houses and was used as received; it contained less than 0.1% free acid. Sulfanilamide and sulfadiazine were the purest grades and were used as received.

Acid-Catalyzed Reactions of Epoxides with Dimethyl Sulfoxide[1a]

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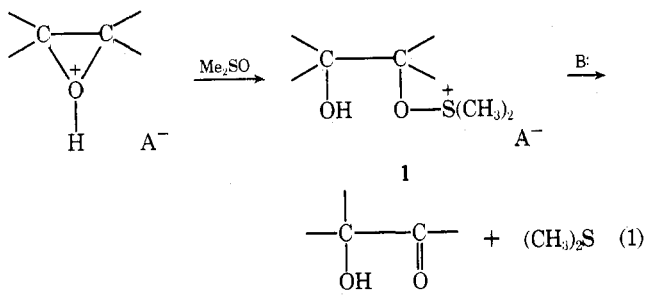
Received April 28, 1975

Ring-opening reactions of styrene oxide, *p*-nitrostyrene oxide, cyclopentene, cyclohexene, and cycloheptene oxides, and *cis*- and *trans*-9,10-epoxystearic acids with Me_2SO in the presence of strong acids have been studied both by NMR and preparatively. In most instances, initial products are vicinal hydroxyalkoxysulfonium salts. Regiospecificity of ring opening is observed with styrene oxide and *p*-nitrostyrene oxide; stereospecificity is observed with cyclohexene oxide and *cis*- and *trans*-9,10-epoxystearic acids. Treatment of selected salts with bases yields mixtures of 1,2-ketols and glycols even in the absence of water, with glycols usually predominating. In contrast with cyclohexene oxide, which reportedly gives fair to good yields of adipoin on treatment with boron fluoride etherate followed by base, cyclopentene and cylcoheptene oxides isomerize largely to the corresponding ketones.

In an earlier study[2] we showed that 2,4,6-trinitrobenzenesulfonic acid is a useful strong acid catalyst for the regio- and stereospecific preparation of crystalline vicinally substituted hydroxyalkoxysulfonium salts (**1**, eq 1) from Me_2SO and epoxides.



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To assess the generality of the acid-catalyzed Me_2SO ring-opening reaction, we had been concurrently exploring other strong acid catalysts (boron trifluoride, fluoroboric, trifluoroacetic, methanesulfonic, sulfuric, and nitric acids) which also provide anions of low nucleophilicity; this paper describes the results of that investigation. Although crystalline salts (**1**) were usually not obtained with the latter group of acids, the course of the reactions and the initial products were readily monitored by NMR. In addition we are reporting (a) the overall oxidation of epoxides to α-hydroxy ketones (ketols) (**2**) via the intermediate salts (**1**) upon treatment with base, (b) the stereospecific conversion of epoxides to 1,2-glycols by hydrolysis of **1** or its attack by nucleophiles, and (c) some miscellaneous reactions of the epoxides and salts (**1**).

The regiospecificity of attack of many nucleophiles on unsymmetrical epoxides under acid conditions has been

Table I
Acid-Catalyzed Ring Opening of Styrene Oxide (3) by Me_2SO[a]

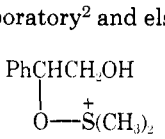
Acid	Products		
	4, %	5, %	Others, %
Trifluoroacetic	52[b]	16[b]	Phenylacetaldehyde (6), 1
Sulfuric	47	c	2-Phenyl-2-hydroxyethanol, 2-sulfonate ester (7), 20[d] 2-Phenyl-2-hydroxyethanol (8), 14
Methanesulfonic	69	c	2-Phenyl-2-hydroxyethanol 2-methanesulfonate ester (9), 25[d]
$Me_2SO \cdot BF_3$	66	c	6, 12
$Me_2SO \cdot HBF_4$[e]	86	c	6, 1
$Me_2SO \cdot HNO_3$	62	c	2-Phenyl-2-hydroxyethanol, 2-nitrate ester (10), 22[d]

[a] Molar ratio Me_2SO:3:acid 5:1:1. [b] After 5 min at 40°, the molar ratio of 4:5 was 6.7 with a total yield of 60%. After 20 min, decomposition of 4 and 5 had occurred, the ratio had decreased to 2.6, and the yield was no longer determinable by NMR. The initial ratio was slightly higher if the acid was added to the Me_2SO–epoxide solution rather than vice versa. [c] 5 could not be detected. [d] Inferred from NMR. [e] We assume that this is the species that predominates in the reaction of Me_2SO with commercial HBF_4 (see Experimental Section).

widely studied and reviewed.[3-6] In contrast, reaction of Me_2SO with epoxides in the presence of acid catalysts has received only limited study. In most cases only the secondary products of the reaction were examined, thereby rendering equivocal conclusions concerning the initial point of attack.[7-12] Direct observation of the intermediate hydroxyalkoxysulfonium salts (1) avoids the problems of earlier approaches to the determination of the regiospecificity of the ring-opening processes, and such observation could confirm the role of the intermediates in the overall reaction.

Results and Discussion

Regiospecificity. Ring Opening of Styrene Oxide (3) (Table I). In Me_2SO solution in the presence of 1 or more equiv of strong acid, the characteristic NMR signals of the oxirane ring of **3**, consisting of three doublets of doublets, rapidly disappear and are replaced by three new sets of signals: a broad triplet centered about δ 5.7; a broad doublet centered about δ 3.9; and two singlets at δ 3.5 and 3.3. On the basis of chemical shift, multiplicity, and integration, and by comparison with the reported spectrum of the corresponding bromo compound,[13] the triplet, doublet, and two singlets can be assigned to the methine, methylene, and *S*-methyl protons,[14] respectively, of the (α-hydroxymethyl)benzyloxydimethylsulfonium cation **4**. This assignment was confirmed by the loss of these signals on treatment of the solution with water or base and also by isolation and further characterization of two salts of this cation in our laboratory[2] and elsewhere.[15]



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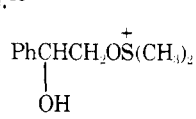


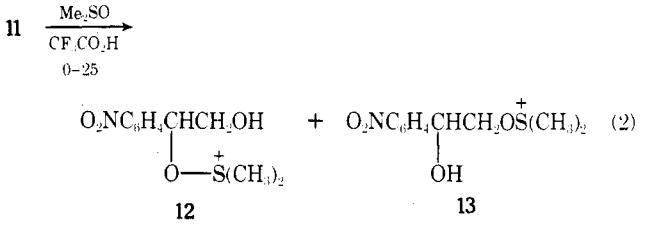
5

With trifluoroacetic acid (Table I), two additional sets of signals are observed: a triplet centered about δ 5.0 and a doublet centered about δ 4.5. These can be assigned to the methine and methylene protons, respectively, of the regioisomer of **4** (α-hydroxybenzyl)methyloxydimethylsulfonium cation **5**. The assignment is a reasonable one from the multiplicity, chemical shifts, and integration, and by comparison with the NMR spectrum of **4**. In addition, the total *S*-methyl signal (**4** + **5**) integrates correctly only if the presence of **5** is accepted. The signals assigned to **5** also disappear upon the addition of water, and the related alkoxydimethylsulfonium salt from *p*-nitrostyrene oxide gives NMR signals closely corresponding to those of **5** as would be expected (see below). Thus, the regioisomers from styrene oxide and Me_2SO can be readily distinguished by NMR.

The results of the ring-opening reaction using various strong acids are summarized in Table I.[16] Other products formed (NMR detection only) are (a) phenylacetaldehyde (**6**) [usually 1% or less except with BF_3 (>10%)], (b) those from reaction of the anions of the strong acids rather than Me_2SO with the protonated epoxide (**7**, **9**, **10**), and (c) 1,2-glycols in the case of sulfuric acid which contains about 4% water.

The main conclusion from Table I is that the acid-catalyzed ring opening of styrene oxide by Me_2SO exhibits the regiospecificity shown by other nucleophiles.[3-5] With the exception of trifluoroacetic acid, complete regiospecificity is obtained and even in that case the expected regioisomer (that of benzylic attack by Me_2SO) predominates (6.7:1). The presumption is that this ratio reflects the products of kinetic control. This conclusion is supported by the stability of cation **4** (with regard to conversion to **5**) under similar conditions with other counterions (Table I). Also, when **4** is isolated as the trinitrobenzenesulfonate and observed by NMR in Me_2SO solution, no conversion to **5** is noted.[2,6b] Similar reasoning applies to the cations formed from *p*-nitrostyrene oxide (see below).

***p*-Nitrostyrene Oxide (11).** Reaction of Me_2SO (5.60 mol) with **11** (0.857 mol) and trifluoroacetic acid (1.00 mol) is not only considerably slower than with **3** but nonbenzylic attack predominates at 0–25° (eq 2). The ratio of **12**:**13** is 0.83–0.87 (1:1.2) and this ratio remains constant for many hours (16 hr at 0° and 4 hr at 25°).



(2)

12 **13**

With the two epoxides examined, acid-catalyzed oxirane ring opening by Me_2SO conforms to the regiospecificity expected from a "borderline SN2" process.

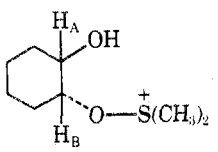
Stereospecificity. Ring Opening of Cyclohexene Oxide (14). To examine the stereospecificity of the Me_2SO–epoxide reaction the cyclohexene oxide–Me_2SO–trifluoroacetic acid system was chosen for initial NMR study. As with styrene oxide (**3**), the signals characteristic of the oxirane ring protons disappear rapidly and three new sets of signals appear: an unresolved multiplet centered about δ 4.4 (4.1–4.7); a multiplet ranging from δ 3.3 to 3.9; and two singlets at δ 3.45 and 3.50. By analogy with **3** and comparison with the NMR spectra of related cations, namely, a bromo compound[13] and a corresponding cation

Table II
Reaction of Intermediate Salts (4 and 5) from Styrene Oxide (3)–Me_2SO–Acids with Various Bases

Acid	Base	Base:cation molar ratio	Phenylacyl alcohol (16), % conversion	2-Phenyl-2-hydroxyethanol (17), % conversion
Trifluoroacetic	Triethylamine	3.4	20	43
Trifluoroacetic	Pyridine-d_5[a]	3.0	18	38
Trifluoroacetic	Pyridine-d_5[b]	2.8	17	80
Trifluoroacetic	$NaHCO_3$[c]	2.8	42	57
Trifluoroacetic	NaH	2.4	None detected	None detected
Sulfonic	Triethylamine	2.9	26	71
Methanesulfonic	Triethylamine	2.4	58	41
$Me_2SO \cdot BF_3$	Triethylamine	2.7	Trace	Trace
$Me_2SO \cdot HBF_4$	Triethylamine	1.8	Trace	Trace
$Me_2SO \cdot HBF_4$	$NaCO_3$[c]	2.0	50[d]	50[d]

[a] Salt (1) solution added to base. [b] Base added to salt solution. [c] Base incompletely soluble in Me_2SO. [d] The spectra were poorly resolved; figures are best estimates.

derived from acid-catalyzed *N*-oxide ring opening,[17] the new signals are assigned to the *trans*-(2-hydroxycyclohexyl)oxydimethylsulfonium cation (**15**). The upfield multiplet



15

is probably due to H_A and the downfield one to H_B. The pair of singlets of the two nonequivalent *S*-methyl groups comprise the third set of signals. To corroborate conclusions from the in situ NMR study, the reaction was repeated on a preparative scale; the trifluoroacetate of **15**, **15a**, mp 82–84°, was isolated in about 40% yield.[18] Its NMR spectrum was identical with that found in the NMR study. Compound **15a** was also obtained independently in about 20% yield from *trans*-1-iodo-2-hydroxycyclohexane, Me_2SO, and silver trifluoroacetate. It would be expected that the trans stereochemistry of the iodohydrin would be preserved in such a displacement by O-3 neighboring group participation.

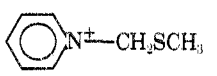
The trans stereochemistry of **15** was confirmed by mild, neutral aqueous hydrolysis of **15a** to *trans*-1,2-cyclohexanediol in almost 50% yield as the sole product. Hydrolysis of secondary alkoxysulfonium salts, such as **15a**, proceeds by exclusive attack at sulfur and the stereochemistry of the salt is preserved in the alcohol produced; this conclusion has ample precedent.[2-5,19]

Reaction of 1 with Bases. Reaction of the intermediate salts (**1**) with bases has been studied in a few cases;[2,7,20] reported products are ketols (α-hydroxy ketones) and dimethyl sulfide. Detailed study of that reaction[20,21] has shown that the reaction is not a simple or general one; yields of ketols are only modest. We have reinvestigated the reaction in NMR tubes with salts formed in situ from Me_2SO, styrene oxide, and strong acids, followed by the immediate addition of various bases; Table II summarizes the results.

The anticipated product, phenacyl alcohol (**16**), was formed in most cases (17–58%) but the major product (38–80%) was 2-phenyl-2-hydroxyethanol (**17**) even though the reactions were run under anhydrous conditions.[22] Other by-products were also formed depending on the base used. In about half the reactions listed in Table II, a good mass balance for the conversion of the cations **4** and **5** to **16** and **17** was obtained. In the other cases, the presence of unidentified substances was indicated by the NMR spectra but they could not be determined quantitatively. Unidentified by-product formation may be associated with failure to control the internal temperature of the base–cation reaction adequately, which was carried out in NMR tubes immersed in an ice–water bath but without monitoring or controlling the internal temperature. The possibility of side reactions, including base-catalyzed condensations of **16**, cannot be excluded.

Mandelaldehyde (or its dimer) could not be detected by NMR even though it is the anticipated product of the reaction of **5** with base. In view of the facile rearrangement of α-hydroxy aldehydes to α-hydroxy ketones,[23,24] failure to observe mandelaldehyde is not too surprising. This result emphasizes the danger in attempting to infer the regiospecificity of Me_2SO attack on the oxirane ring from the final reaction products.

When pyridine was used as the base (Table II) 1-(methylthio)methylpyridinium ion (**18**) was a by-product. With triethylamine, NMR signals consistent with the presence of (methylthiomethyl)trimethylammonium ion (**19**) were observed.



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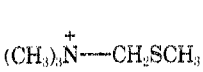

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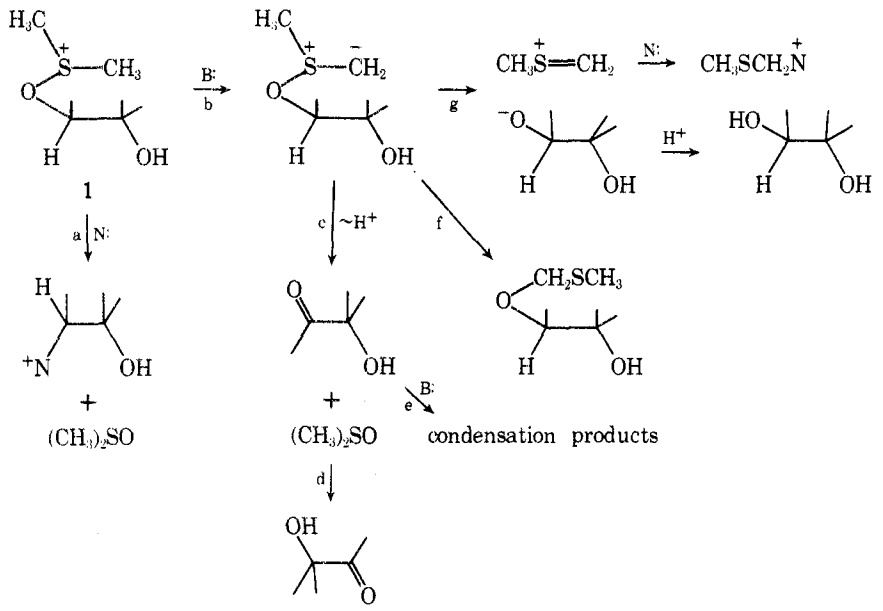
The isolated trifluoroacetate salt of **15** [*trans*-(2-hydroxycyclohexyloxy)dimethylsulfonium trifluoroacetate (**15a**)] was decomposed in neat pyridine or in pyridine–Me_2SO-d_6. The formation of a mixture of products was observed by NMR and the following were isolated in low yield by preparative GLC: *trans*-1,2-cyclohexanediol (**20**), pyridinium trifluoroacetate (**21**), *cis*-(2-hydroxycyclohexyl)pyridinium trifluoroacetate (**22**), in addition to dimethyl sulfide and Me_2SO. 1-(Methylthiomethyl)pyridinium trifluoroacetate (**18**) was tentatively identified also.

Basic decomposition of the cations (**12**, **13**) from *p*-nitrostyrene oxide (**11**) yielded only 2-hydroxy-2-*p*-nitrophenylethanol (**23**). No *p*-nitrophenacyl alcohol was observed but it might have undergone rapid condensation in the basic system as it would be expected to be more prone to such condensations than phenacyl alcohol.

In the original work describing the oxidation of epoxides to α-hydroxy ketones,[7] Me_2SO–BF_3–diethyl ether at 100° was employed; cyclohexene oxide was one of the three epoxides studied. When we applied this oxidation technique to cycloheptene (**23**) and cyclopentene oxides (**24**), we obtained mixtures of products which contained the expected ketols, but the major products were cycloheptanone and cyclopentanone, respectively, the BF_3-induced isomeriza-

Scheme I[a]



[a] B: is base, N: nucleophile.

tion products of the epoxides. Furthermore, we have not been able to reproduce the reported yields of ketols from cyclohexene oxide or styrene oxide and Me_2SO using boron fluoride, air or *tert*-butyl hydroperoxide catalysis.[7,11]

Reaction Pathways. The products observed in the decomposition of cations **4, 5, 12, 13,** and **15** can be rationalized on the basis of a series of competing reactions of the cations and intermediate ylides with the nucleophiles present in the system (Scheme I).

Step a accounts for the presence of Me_2SO in the reaction of **15** with pyridine (N:) in DMSO-d_6 and also accounts for the esters formed in the reaction of styrene oxide (**3**) in Me_2SO with the nucleophiles derived from certain strong acids listed in Table I, although esters can also arise by direct attack of the nucleophile on the protonated epoxide. Me_2SO is an effective leaving species; displacements of Me_2SO from alkoxydimethylsulfonium salts of the type **1** have been amply documented.[2,13,25-27]

Step b, the conversion of the cations to carbosulfuranes (ylides), is a well-established one and has been shown to be operative in many base-induced Me_2SO oxidations involving alkoxydimethylsulfonium salts.[13,28,29] Step c is the decomposition of the ylides to complete the redox reaction with the formation of dimethyl sulfide and α-hydroxycarbonyl compounds. This pathway is observed in Me_2SO oxidations; the ylides decompose intramolecularly via a cyclic transition state. Steps d and e are, respectively, the isomerization and condensation of the α-hydroxycarbonyl compounds.

Step f shows the Pummerer rearrangement of the salts (**1**) via the carbosulfuranes to form a methylthiomethyl ether. The formation of Pummerer rearrangement products upon treatment of alkoxysulfonium salts with base is well known.[30,31]

Origin of Diols in the Me_2SO Oxidation of Epoxides. Step g in Scheme I is best rationalized as a competition between nucleophiles for an intermediate sulfur-stabilized carbonium ion from the Pummerer rearrangement[30] to yield glycol and the methylthiomethylated nucleophile. When the nucleophile, N:, is an alcohol a methylthiomethyl ether is formed. With pyridine the product is **18,** as observed with **4, 5,** and **15.** Yields of methylthiomethylated products are consistently lower than those of glycols.

The inclusion of step g in Scheme I is not only consistent with the products observed on treatment of the hydroxysulfonium salts (**1**) with base under mild conditions but can also account for the formation of glycols in other Me_2SO oxidations of epoxides at relatively high temperatures without added base, i.e., under conditions originally described for oxidation of epoxides.[7,9,21,32] In the present study, the formation of glycols from epoxides and Me_2SO under these conditions (no added base) was verified with styrene oxide–boron trifluoride etherate (low yields) and *cis*- and *trans*-9,10-epoxystearic acids (**25, 26**) (no catalyst or water used). The last two epoxides cleanly yielded *threo*- and *erythro*-9,10-dihydroxystearic acids, respectively in 10–30% yields.

The most likely source of these glycols is the ylide–nucleophile reaction (step g, Scheme I). Adventitious hydrolysis of the intermediate sulfonium salts (**1**) was ruled out as a significant source of glycol by a control experiment with *cis*-9,10-epoxystearic acid in which exclusion of water during work-up affected the yield of glycol only slightly.

Thermolysis of 15 Trifluoroacetate (15a). Thermolysis of a dimethylalkoxysulfonium salt was carried out to determine the reaction products in the absence of added nucleophiles. Thermolysis of **15a** at 100° yielded numerous products none of which was major: adipoin (2-hydroxycyclohexanone), dimethyl sulfide, trifluoroacetic acid, Me_2SO, 1,2-cyclohexylditrifluoroacetate, *trans*-1,2-cyclohexanediol, bis(methylthio)methane, and many other unidentified compounds. Neither cyclohexene epoxide nor cyclohexanone could be detected.

Experimental Section[33]

Acid-Catalyzed Ring Opening of Epoxides with Me_2SO. Styrene Oxide (3) (Table I). General Procedure. A stock solution of **3** (5.00 g, 0.0416 mol) in anhydrous Me_2SO (15.8 g, 0.202 mol) containing sodium 2,2-dimethyl-2-silapentanesulfonate (DSS, 0.21 g) as an internal NMR standard was prepared in a flask sealed with a serum cap. The appropriate weight of acid was introduced into an NMR tube which was then sealed with a serum cap, evacuated, and immersed in an ice bath, and the stock solution was injected by means of a syringe (molar ratio DMSO:acid:epoxide 5:1:1). The tube was removed from the bath and mixed thoroughly and its NMR spectrum was immediately determined. The molar ratios of the reactants and yields of products were calculated by in-

tegration of the NMR signals using the aromatic proton signals as an internal standard. The results are given in Table I.

p-Nitrostyrene Oxide (11). Compound 11 (0.168 g, 1.02×10^{-3} mol) was similarly treated with a solution (0.655 g) of trifluoroacetic acid (0.469 g, 4.11×10^{-2} mol) in Me_2SO (1.80 g, 2.30×10^{-2} mol) containing DSS (0.053 g). (molar ratio Me_2SO:acid:epoxide 5.60:1.00:0.857.) Initially, the NMR spectrum of the reaction mixture showed only faint signals other than those of 11. The NMR spectrum stabilized after the reaction had been run for 16 hr at 0° and 1 hr at 25°. The epoxide had completely disappeared and the ratio of benzylic to nonbenzylic attack was calculated to be 0.83–0.87 (1:1.2).

Cyclohexene Oxide (14). The NMR experiments were conducted as described above with 3 and 11. Preparative scale ring openings were conducted by slowly adding trifluoroacetic acid (14.4 g, 0.117 mol) to Me_2SO (10 ml) with stirring and cooling to 0° and then allowing the solution to warm to room temperature. A solution of 14 (11.0 g, 0.112 mol) in Me_2SO (5 ml) was added dropwise with stirring over 15 min; the exothermic reaction was controlled at 25–30°. After an additional 15 min the reaction mixture was washed under nitrogen with anhydrous ether (4 × 100 ml). After the last washing, the insoluble liquid residue crystallized spontaneously to give essentially pure **15a**, mp 79–80°. Concentration of the ether washings and storage at −30° for 24 hr gave more product for a total yield of 12.9 g (38.6% based on 14). Recrystallization from chloroform–ether (dissolution at room temperature followed by cooling in the freezer) gave analytical quality material, mp 82–84°, equiv wt calcd 291; found 295. Anal. Calcd for $C_{10}H_{17}F_3O_4S$: C, 41.4; H, 5.90. Found: C, 41.2; H, 5.90.

Alternatively, **15a** could be obtained by treating a solution of *trans*-3-iodocyclohexanol[34] (0.653 g, 0.0029 mol) in chloroform (0.5 ml) with a solution of silver trifluoroacetate (0.668 g, 0.0030 mol) in Me_2SO (1 ml) at room temperature. After the addition of more chloroform (2 ml) the silver iodide was filtered off and ether (25 ml) was added to the residue. Cooling the solution to −20 to −30° yielded **15a** (0.169 g, 20%), mp 83–85°.

***trans*-1,2-Cyclohexanediol (20) from 15a.** The salt (0.657 g, 0.0022 mol) was heated on the steam bath with water (4 ml) for 15 min. The water was then removed azeotropically with benzene and the benzene solution was evaporated to dryness under vacuum. The residual oil was crystallized at 0° from a minimum quantity of ether to yield the trans diol (0.116 g, 46%), mp 101–105°; its ir spectrum was identical with that of an authentic sample.[35]

Reaction of Salts (1) with Base (Table II). To the NMR tubes from the acid-catalyzed ring-opening reaction of 3 with Me_2SO described above under General Procedure, various bases were added in excess by injection through the serum cap while the tube was immersed and shaken in an ice–water bath at 0°. After complete decomposition of the cation, NMR spectra were redetermined and the yields of phenacyl alcohol (16) and 2-phenyl-2-hydroxyethanol (17) were calculated from the ratio of the integral of the aromatic protons to that of the methylene protons of 16 (s, δ 4.98) and the methine (t, δ 4.70) and methylene (d, δ 3.53) protons of 17. (Authentic samples of 16 and 17 were used to give peak enhancement and to confirm the NMR assignments.) Table II summarizes the results. In no case could signals attributable to mandelaldehyde or its dimer be detected.[23]

In most cases, a signal attributable to methyl sulfide (s, δ 2.08) (using peak enhancement) was observed along with one or more singlets in the *S*-methyl region (δ 1.9–2.2). With pyridine, 1-(methylthio)methylpyridinium ion (18) (s, δ 2.28, 5.82) was also present; addition of an authentic sample of 18 (as the chloride) resulted in peak enhancement with the production of no new signals.

When triethylamine was the base in the reactions originally catalyzed by trifluoroacetic, methanesulfonic, and nitric acids, two singlets (δ 5.48 and 2.18) were also observed. These are attributed to the *S*-methylene and *S*-methyl protons of the (methylthiomethyl)trimethylammonium ion (19).

Reaction of 15a with Pyridine. The NMR spectrum of the salt formed in situ from 14, trifluoroacetic acid, and Me_2SO and then treated with excess pyridine was virtually identical with that of a solution of isolated salt (see above) in Me_2SO-d_6 to which excess pyridine was added. The following products also appeared to be present in the solutions: 18, 20, methylthiomethyl ether of 20, adipoin, and methyl sulfide. When the reaction of 15a with pyridine was run on a preparative scale (2 g of salt) and then chromatographed on a 15% Carbowax 20M column at 110° (He flow rate 80 ml/min, injection port 180°, detector 210°) four major fractions were collected and analyzed by ir. In order of increasing retention times, the fractions were identified as 20, 21, 22, and 18.

Reaction of Salts 12 and 13 from p-Nitrostyrene Oxide (11) with Triethylamine. Treatment of the NMR tube (described above) containing 11, trifluoroacetic acid, and Me_2SO with excess triethylamine gave the NMR spectrum of the diol 23 (δ 4.80, t, methine, 1 H, and δ 3.60, d, methylene, 2 H). No signals were found in the region δ 5.5–6.5 (ketol absent).

Boron Trifluoride Etherate Catalyzed Me_2SO Oxidation of Cycloheptene (23) and Cyclopentene (24) Oxides. Epoxide (0.1 mol), Me_2SO (0.5 mol), and boron trifluoride etherate (0.003 mol) were placed in a three-neck flask equipped with a reflux condenser, magnetic stirrer, and thermometer and protected from entry of atmospheric moisture. The flask was immersed in a preheated oil bath maintained at 95° and appearance of dimethyl sulfide and disappearance of epoxide were followed by GLC; 23 had not completely reacted after 24 hr but 24 reacted completely in less than 3 hr. In both cases, the reactions were terminated by pouring the solutions into ice water (100 ml) containing 1% sodium hydroxide. The aqueous solutions were multiply extracted with chloroform or methylene chloride, dried over anhydrous magnesium sulfate, stripped of solvent under vacuum, and then distilled under reduced pressure. All fractions obtained were mixtures (TLC, NMR) with Me_2SO the major contaminant (TLC, NMR). The presence of enolic compounds was demonstrated by the development of green or orange solutions on treatment of the fractions with aqueous ferric chloride. In addition, the fractions were soluble in 10% aqueous sodium hydroxide. The main C=O absorption band, however, was that of the corresponding ketones formed by isomerization of 23 and 24 (cycloheptanone, 1705 cm^{-1}; cyclopentanone, 1745 cm^{-1}) but each spectrum also contained a shoulder at approximately 50 cm^{-1} lower wave number, indicative of the hydrogen bonded carbonyl of an α-ketol.[36] Further attempts at purification of the fractions by preparative GLC or column chromatography gave only mixtures.

Me_2SO Oxidation of *cis*- and *trans*-9,10-Epoxystearic Acids (25, 26). A. The cis epoxy acid 25 (9.0 g, 0.03 mol) and Me_2SO (0.06 mol) were heated at 120–130°. The methyl sulfide formed was condensed in a cold trap and identified as its mercuric chloride complex. After 6.25 hr the reaction mixture was poured into cold water and the gummy mass that separated was dried under vacuum and then digested in hot *n*-heptane. Filtration of the hot solution yielded insoluble *threo*-9,10-dihydroxystearic acid, mp 89–91° (11%); mmp with an authentic sample 90–93°. The filtrate was evaporated to dryness and the residue was recystallized from ethanol to provide the mixed 9,10(10,9)-ketohydroxystearic acids, mp 57–61°, in low yield (identified by ir). Unreacted epoxide was not isolated.

To ensure that the diol was *not* formed by hydrolysis during the work-up procedure the following pair of experiments was conducted. The cis epoxy acid and Me_2SO (mole ratio 25:Me_2SO 1:5) were heated at 120° for 24 hr. Me_2SO was removed by vacuum distillation (pot temperature 94–107°), care being taken to exclude moisture, and the reaction flask was sealed and removed to a drybox, where two samples were taken. The first was washed with *n*-heptane under anhydrous conditions to give the insoluble threo diol, mp 88–92° (15%). The second sample was removed from the drybox and allowed to stand in water overnight. Water was drained from the resultant slurry, ethanol was added, and the solution was stripped under vacuum to remove ethanol and water. The remaining solid was washed with *n*-heptane to give the insoluble threo diol (18%).

B. The oxidation of 26 (0.01 mol) was carried out in the same way as that of 25 except that more Me_2SO (0.035 mol) was used and the reaction time was 68 hr at 85° because the reaction proceeded slowly. Work-up as described above gave *erythro*-9,10-dihydroxystearic acid, mp 129–133° (lit.[37] mp 131°) (32%). Its ir spectrum was identical with that of an authentic sample. No ketohydroxystearic acids could be isolated. Unreacted epoxide was recovered (37% yield).

Miscellaneous Compounds. Cyclopentene (24) and cycloheptene (23) epoxides were prepared by peroxyacetic acid oxidation at 0° of the corresponding olefins in CH_2Cl_2 solution containing a large excess of powdered sodium carbonate;[38] GLC was used to monitor olefin consumption. The crude epoxides were then fractionally distilled through a Vigreux column: 23, bp 160–161°, and 24, bp 99–99.5°. *cis*- and *trans*-9,10-epoxystearic acids (25 and 26, respectively) were prepared by peroxyacetic acid epoxidation of oleic and elaidic acids, respectively, following a literature procedure.[39]

Me_2SO–Acid Salts. The Me_2SO–BF_3 adduct was prepared by the dropwise addition of boron trifluoride etherate to Me_2SO in

CCl_4 at room temperature. The adduct precipitated as it formed; it was filtered and triturated with several portions of dry ether. Drying under vacuum yielded hygroscopic white crystals, mp 59–63° (lit.[40] mp 60°). It is unnecessary and undesirable to heat the reaction mixture to 175° in the preparation of this adduct as reported.[40] Me_2SO–HNO_3 was prepared by adding nitric acid (9.23 g of 70%, 0.1 mol) dropwise with stirring to a solution of Me_2SO (8.0 g, 0.103 mol) in ethanol (50 ml of 95%) at 10°. The mixture was allowed to warm to room temperature and then evaporated to dryness under vacuum. The residual oil slowly crystallized on storage in a freezer (ca. −20°). The solid was recrystallized from absolute ethanol (8.9 g, 61%); it had mp 43–44° and equiv wt 141 (calcd 141). Its ir spectrum was identical with that reported.[41] The Me_2SO–HBF_4 adduct was similarly prepared from Me_2SO and 50% aqueous HBF_4 but the adduct, mp 71–72°, could not be obtained in analytical purity. Attempts to determine its equivalent weight by titration gave anomalous results owing to fading endpoints.

1-(Methylthio)methylpyridinium Chloride. Dry pyridine (40 ml, 0.5 mol) was added to chloromethyl methyl sulfide (4.83 g, 0.05 mol) in a round-bottom flask protected from atmospheric moisture. The turbid mixture was heated at 50° for 1 hr and ether (20 ml) was added to the solid reaction mixture. The insoluble solid was filtered, washed with ether, and dried under vacuum (7.8 g, 88%), mp 149–158°. Recrystallization from acetone–ethanol (10:1 v/v) and thorough drying over P_2O_5 gave the pure compound (5.8 g, 67%), mp 155–160° (lit.[42] mp 158–160°). It is an extremely hygroscopic compound: NMR (D_2O, DSS internal standard) δ 2.28, s, 3 H; 5.82, s, 2 H; 8.0–9.3, m, 5 H.

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Registry No.—**3,** 96-09-3; **11,** 6388-74-5; **14,** 286-20-4; **15a,** 55913-50-3; **16,** 582-24-1; **17,** 93-56-1; **20,** 931-17-9; **23,** 286-45-3; **24,** 285-67-6; **25,** 24560-98-3; **26,** 13980-07-9; dimethyl sulfoxide, 67-68-5; *trans*-3-iodocyclohexanol, 55913-51-4; *threo*-9,10-dihydoxystearic acid, 2391-05-1; 9,10-ketohydroxystearic acid, 13985-42-7; 10,9-ketohydroxystearic acid, 13985-41-6; *erythro*-9,10-dihydroxystearic acid, 3639-32-5; 1-(methylthio)methylpyridinium chloride, 5983-12-0.

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