Tetrahedron Letters No.40, pp. 4261-4264, 1968. Pergamon Press. Printed in Great Britain.

ON THE MECHANISM OF OXIDATION OF EPOXIDES BY DMSO

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(Received in USA 3 June 1968; received in UK for publication 5 July 1968)

The oxidation of epoxides by dimethylsulfoxide (DMSO) at 90-100° was first reported by Cohen and Tsuji (1), who obtained fair to good yields of α-ketols with boron fluoride as catalyst. Later Tsuji reported (2) that the oxidation can also be effected without boron fluoride if air is passed through the reaction mixture or if a catalytic amount of t-butyl hydroperoxide is present. Tsuji concluded that the boron fluoride catalyzed reaction is ionic but that "free radicals are involved" in the presence of air or hydroperoxide.

We now believe that in all cases previously described, the oxidation is an acid catalyzed ionic process. Oxygen or hydroperoxide does not initiate a free radical chain oxidation, but instead serves to generate an acid catalyst *in situ*.

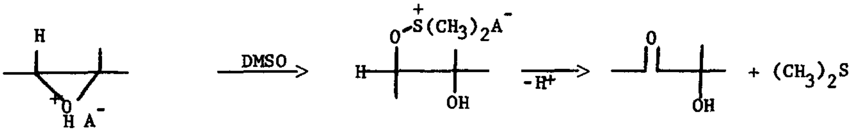
Evidence for the necessity of an acid catalyst is as follows: the "air catalyzed" or "t-butyl hydroperoxide catalyzed" oxidation of styrene oxide by DMSO produces small amounts of a strong acid, determined by titration. When these reactions are attempted in the presence of excess sodium carbonate, oxidation does not take place. If the hydroperoxide and DMSO are heated under the usual conditions of the epoxide oxidation (90-100°) but in the absence of epoxide, the hydroperoxide is consumed and the acid is still formed. If heating is continued until the hydroperoxide is completely decomposed and styrene oxide is then introduced oxidation of the epoxide begins almost immediately. The addition of benzoquinone has no effect.

Thus an acid is required for the oxidation and that with hydroperoxide, it is the acid produced by reaction of hydroperoxide with DMSO that catalyzes the oxidation and <u>not</u> the hydroperoxide itself.

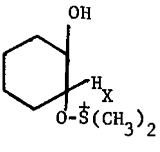
The catalytic activity of oxygen can be explained by suggesting that autoxidation of a small amount of epoxide to a hydroperoxide occurs, which then reacts with DMSO to form the acid catalyst. This explanation is supported by the observation that oxygen, DMSO, and epoxide all together are necessary for the production of an efficient catalyst. Thus, if styrene oxide is heated in air under the usual conditions but in the absence of DMSO, the system purged of oxygen and DMSO then added, no strong acid is produced and essentially no oxidation is noted. Similarly, heating DMSO in air followed by purging the system of oxygen and then adding styrene oxide in the absence of air does not produce the acid catalyst; oxidation is not observed.

Further evidence that the oxidation is not a free radical one is the failure of t-butyl peroxide to catalyze it. This dialkyl peroxide does not form an acid on reaction with DMSO at 100° although the peroxide is largely destroyed. However, it would be expected to initiate a free radical oxidation if such a process were operative. Since the peroxide fails to catalyze the reaction, it seems unlikely that DMSO oxidation of epoxides is a free radical process (3).

In all cases, the reaction course can be rationalized by the following mechanism, in which an alkoxydimethyl sulfonium salt is the key intermediate:



Evidence for the presence of the intermediate has been obtained by detailed examinations of the nmr spectra of styrene oxide and of cyclohexene oxide, respectively, in acidified DMSO. Trifluoroacetic acid was added to DMSO at 0°, followed by epoxide (molar ratio acid: styrene oxide: DMSO, 1:1.4:5; molar ratio acid: cyclohexene oxide: DMSO, 1:1.6:10) The mixture was allowed to stand at room temperature for several minutes, and then the nmr spectrum was determined (~37°). It showed signals consistent with the presence of the alkoxydimethyl sulfonium salts (1 and 2). (Table I) The nmr data closely match those of similar salts (Br in place of OH) isolated and characterized in another investigation (4).



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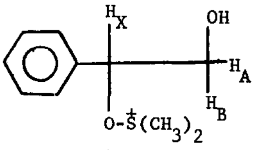

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TABLE I

NMR DATA FOR ALKOXYDIMETHYLSULFONIUM SALTS[a]

$RO\overset{+}{S}(CH_3)_2CF_3CO_2^-$

δ (ppm)	Relative Peak Area	Multiplicity	Peak Separation (cps)	Assignment
~ 4.2	1	broad multiplet	-	1[b]; H_X
3.50, 3.44	6	two singlets	-	1; $(CH_3)_2\overset{+}{S}$
5.76	1	triplet	6.0	2; H_X
3.98	2	doublet	6.0	2; H_A, H_B
3.54, 3.37	6[c]	two singlets	-	2; $(CH_3)_2\overset{+}{S}$

a. Internal standard either TMS or DMSO (δ=2.61)
b. By analogy with other work (4), this is probably trans.
c. Integral of S-methyl protons corrected for small amount of isomer present (sulfoxonium function on β-carbon, OH on α-carbon) whose S-methyl protons apparently absorb in the same region.

Addition of excess pyridine to the solutions of the alkoxydimethyl sulfonium salts produces immediate diminution of the signals due to the salts and an increase in that of dimethyl sulfide, indicating that the salt is decomposing. Simultaneously, the ir spectrum indicates the formation of α-ketol.

These observations are all consistent with the proposed ionic mechanism. Attempts to isolate the sulfonium salts and to demonstrate more fully their role as intermediates in the oxidation are currently in progress.

Acknowledgment: The authors acknowledge with thanks the support of this work by U.S. Public Health Service Grants CA-07803, CA-07174 and CA-10439 of the National Cancer Institute.

References

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2. T. Tsuji, *Tetrahedron Letters*, **1967**, 2975.
3. A preliminary reinvestigation by us of the "air catalyzed" DMSO oxidation of benzyl alcohol at 175° (V. J. Traynelis and W. L. Hergenrother, *J. Amer. Chem. Soc.*, **86**, 298, (1964) shows that this reaction is also acid catalyzed. As with epoxides, a strong acid is formed during oxidation, and the oxidation does not proceed in the presence of sodium carbonate.
4. K. Torssell, *Acta Chem. Scand.*, **21**, 1 (1967).