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Activation of Superoxide. Facile Oxidation of Sulfoxides into Sulfones with a Peroxysulfur Intermediate Generated *in situ* from 2-Nitrobenzenesulfonyl Chloride and Superoxide

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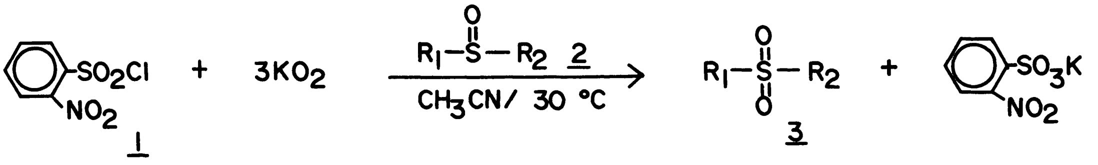
Various sulfoxides, such as dialkyl, alkyl-aryl, and diaryl sulfoxides, were readily oxidized into the corresponding sulfones, in excellent yields under mild conditions, by 2-nitrobenzene peroxysulfur intermediate generated *in situ* from 2-nitrobenzenesulfonyl chloride and potassium superoxide at -30 °C, in dry acetonitrile. Chemoselective oxidation of sulfoxides which contain both double bond and sulfinyl moiety to the sulfones, was observed under the same conditions.

Since the discovery of superoxide dismutase by Fridovich and McCord in 1969,1) intensive investigation of the biology and biochemistry of superoxide anion($O_2^{-\cdot}$) has been made.2) Recently, the accmulation of information on the physical and chemical properties of superoxide has promoted the study of its organic chemistry using superoxide. In the course of our study3-7) of the development of organic synthesis using superoxide, a peroxysulfur intermediate, generated from organosulfur compounds and superoxide, has been found to be a much better oxidizing agent than superoxide itself. Facile and regioselective epoxidations of olefins6), and noble desulfurization of thiocarbonyl substances into their corresponding carbonyl compounds7) using the peroxysulfur intermediate, have been reported.

We have now found that various sulfoxides, such as dialkyl, alkyl-aryl, and diaryl sufoxides, were readily oxidized into the corresponding sulfones, in excellent yields under mild conditions by the 2-nitrobenzene peroxysulfur intermediate, generated *in situ* from 2-nitrobenzenesulfonyl chloride and potassium superoxide at -30 °C in dry acetonitrile, and that chemoselective oxidation of sulfoxides which contain both double bond and sulfinyl moiety, to the sulfones takes place. The yields of sulfones are markedly high when the reaction temperatures are controlled at lower than 0 °C.



The work up is simple and easy: after the reaction mixture was well-stirred at -30 °C for 1.5-6.0 h, simple filtration and concentration gave highly pure sulfones in excellent yields. In the absence of 2-nitrobenzenesulfonyl chloride, no sulfones were obtained and sulfoxides were recovered quantitatively: namely, sulfoxides are not oxidized to the sulfones by superoxide alone without 2-nitrobenzenesulfonyl chloride. The results thus obtained are summarized in Table 1.

Table 1. Oxidation of sulfoxides to the corresponding sulfones with 2-nitrobenzene peroxysulfur intermediate at -30 °C[a)]

Entry	R_1	R_2	Reaction time/h	Yield/%[b)]
1	CH_3	CH_3	1.5	98
2	CH_3CH_2	CH_3CH_2	5.0	89
3	$PhCH_2$	$PhCH_2$	5.5	84
4	Ph	Ph	4.5	88
5	$p\text{-}CH_3\text{-}C_6H_4$	CH_3	6.0	90
6	$p\text{-}CH_3\text{-}C_6H_4$	CH_3CH_2	6.0	82
7	$p\text{-}Br\text{-}C_6H_4$	CH_3	5.5	83
8	$p\text{-}Br\text{-}C_6H_4$	CH_3CH_2	6.5	92
9	2-Naph	CH_3	5.5	83
10	2-Naph	CH_3CH_2	6.0	81

a) Molar ratio; KO_2 : $ArSO_2Cl$: Sulfoxide = 3.0 : 1.0 : 0.6.
b) Isolated yields.

Intensive studies on the preparation of sulfones have been made. A variety of oxidizing agents, including hydrogen peroxide,[8a)] peracids,[8b,8k)] N-chlorobenzotriazole,[8c)] iodobenzene dichloride,[8d)] organic peroxides,[8e)] sodium hypochlorite,[8e)] aqueous chlorine,[8e)] nitric acid,[8f)] nitronium tetrafluoroborate,[8g)] potassium hydrogen persulfate,[8h)] and metal oxides such as potassium permanganate,[8i)] rutenium tetroxide[8j)] etc., has been utilized for the oxidation of sulfides or sulfoxides to the corresponding sulfones. Most reagents mentioned above require somewhat severe and strong reaction conditions, e.g., heat, acidic, basic, or aqueous media. However, our oxidation system can be conducted in aprotic organic solvent of anhydrous acetonitrile under mild conditions (-30 °C), without using any phase transfer catalyst such as crown ethers which are well used for the superoxide reaction, owing to the poor solubility of metal superoxide in organic solvents. Thus our oxidation system may be applied for the oxidation of sulfoxides which are senstive to temperature or to moisture.

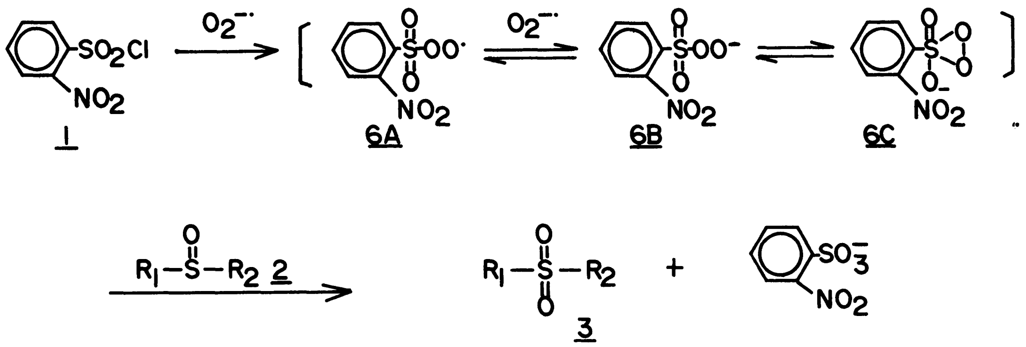
It is noteworthy that chemoselective oxidation of sulfoxides to the sulfones without epoxidation of double bond, was possible as shown in Table 2. Though various oxidizing agents mentioned have been developed, a selective oxidant for the oxidation of sulfoxides to the sulfones without epoxidation nor cleavage of double bond in a molecule which contains both sulfinyl and double bond moiety has not been reported to our knowledge except for one case.[8h)]

Table 2. Chemoselective oxidation of sulfoxides which contain sulfinyl and double bond moiety with 2-nitrobenzene peroxysulfur intermediate at -30 °C[a)]

Substrate	Reaction time/h	Product ratio[b)] Sulfone	Epoxide	Yield/%[c)]
$CH_2=CH-CH_2-\overset{O}{S}-CH_2-CH=CH_2$ (<u>4</u>)	5.5	> 99	-	68
$Ph-CH_2-\overset{O}{S}-CH_2-CH=CH_2$ (<u>5</u>)	5.0	> 99	-	70

a) Molar ratio: KO_2 : $ArSO_2Cl$: Substrate = 3.0 : 1.0 : 0.9.
b) Ratio was determined by ^1H-NMR. c) Isolated yields.

Chemoselective oxidation of sulfide to sulfone without epoxidation using potassium hydrogen persulfate in aqueous methanol was reported by Trost et al.[8h)] But later, Block et al.[9)] argued that potassium hydrogen persulfate in aqueous methanol could oxidize not only sulfide to sulfone but also olefin to the epoxide. Ohtsuka and Oishi[10)] developed an efficient method for the synthesis of macro ketones by intramolecular cyclization of macrolactam sulfones. It is desirable to oxidize sulfoxide moiety only to the sulfone, without epoxidation or cleavage of the double bond moiety, when a macrolactam sufoxide containing double bond is used as a substrate. Thus, we have examined the chemoselectivity of the peroxysulfur intermediate (<u>6</u>) for a substrate containing both the sulfinyl and double bond moiety. Oxidation of allyl sulfoxide (<u>4</u>) and 2-propenyl benzyl sulfoxide (<u>5</u>) with the peroxysulfur intermediate (<u>6</u>) shows highly selective oxidation of sulfoxides to sulfones by giving allyl sulfone and 2-propenyl benzyl sulfone respectively, as shown in Table 2.



Earlier, it has been reported that oxygenation of sulfoxide to the sulfone involves either the initial nucleophilic attack of the nucleophilic oxidant,[11)] or the electrophilic attack of electrophilic oxidant.[12,13]

It is worthy of note that the oxidation of p-methylphenyl-, phenyl-, and p-chlorophenyl methyl sulfoxides to the sulfones using 2-nitrobenzene peroxysulfur intermediate(6) appears to be electrophilic: namely, the relative reactivity order was p-methylphenyl- > phenyl- > p-chlorophenyl methyl sulfoxide, for competitive oxidation under the same reaction conditions.[14] Thus, an electrophilic radical species of peroxysulfur intermediate(6A) seems to take an important role. The detailed mechanism is under investigation.

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References

1) J.M. McCord and I. Fridovich, J. Biol. Chem., 244, 6049 (1969).

2) For recent review: E. Lee-Luff, Chem. Soc. Rev., 6, 195 (1977); D.T. Sawyer and J.S. Valentine, Acc. Chem. Res., 14, 393 (1981); A.A. Frimer, "The Chemistry of Functional Group: Peroxide," ed by S. Patai, John Wiley & Sons (1983), Chap. 14.

3) S. Oae, T. Takada, and Y.H. Kim, Tetrahedron, 37, 37 (1981).

4) Y.H. Kim, G.H. Yon, and H.J. Kim, Chem. Lett., 1984, 309.

5) Y.H. Kim and G.H. Yon, J. Chem. Soc., Chem. Commun., 1983, 715.

6) Y.H. Kim and B.C. Chung, J. Org. Chem., 48, 1564 (1983).

7) Y.H. Kim, B.C. Chung, and H.S. Chang, Tetrahedron Lett., 26, 1079 (1985).

8) a) H.S. Schultz, H.B. Freyermuth, and S.R. Buc, J. Org. Chem., 28, 1140 (1963); b) R. Curci, A. Giovine, and G. Modena, Tetrahedron, 22, 1235 (1966); c) W.D. Kingsbury and C.R. Johnson, J. Chem. Soc., Chem. Commun., 1969, 365; d) G. Barbieri, M. Cinquini, S. Colonna, and F. Montanari, J. Chem. Soc., C, 1968, 659; e) C.M. Suter, "The Organic Chemistry of Sulfur," John Wiley, New York (1944), p. 660; f) D.W. Goheen and C.F. Bennet, J. Org. Chem., 26, 1331 (1961); g) G.A. Olah and B.G.B. Gupta, ibid., 48, 3585 (1983); h) B.M. Trost and D.P. Curran, Tetrahedron Lett., 22, 1287 (1981); i) Vogel, "Textbook of Practical Organic Chemistry," 4th ed, Longman Group Limited, London (1978), p. 587; j) C. Djerassi and R.R. Engle, J. Am. Chem. Soc., 75, 3838 (1953); k) C.G. Venier, T.G. Squires, Y.-Y. Chen, G.P. Hussmann, J.C. Shei, and B.F. Smith, J. Org. Chem., 47, 3773 (1982).

9) R. Block, J. Abecassis, and D. Hassan, J. Org. Chem., 50, 1544 (1985).

10) Y. Ohtsuka and T. Oishi, Tetrahedron Lett., 20, 4487 (1979).

11) R. Curci, F.D. Furia, and G. Modena, J. Chem. Soc., Perkin Trans. 2, 1973, 603.

12) R. Curci, A. Giovine, and G. Modena, Tetrahedron, 22, 1235 (1966).

13) S. Oae and T. Takada, Tetrahedron Lett., 21, 3213 (1980).

14) When the oxidations were carried out under the same conditions and stopped after 10 min, the relative reactivity ratio for p-methylphenyl-, phenyl-, and p-chlorophenyl methyl sulfoxides toward the intermediate (6A) was 1.25:1.0:0.54 (ρ = -1.39).

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