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MODE OF OXIDATIONS OF ORGANOSULFUR COMPOUNDS: EXAMPLE OF NUCLEOPHILIC OXYGENATIONS OF THIOLSULFINATES

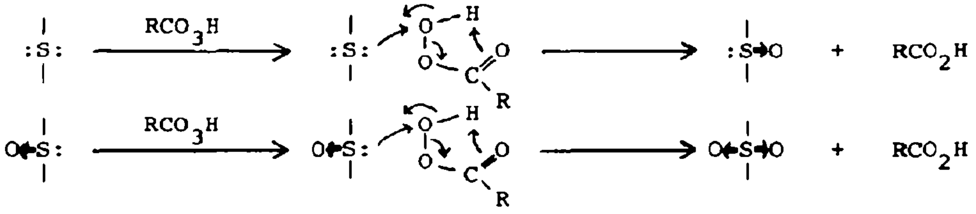
Shigeru Oae* and Toshikazu Takata

Department of Chemistry, University of Tsukuba
Ibaraki 305, Japan

Summary: Two types of oxygenative oxidations(Nucleophilic and Electrophilic Oxidations) of sulfur atom are proposed and a typical mode of nucleophilic oxidation is shown with a few unsymmetrical thiolsulfinates.

During the course of our studies on the oxidations of organic sulfur compounds with various oxidants, we have gradually realized that there are two kinds of mechanistic ways for the oxygenative oxidation on the sulfur atom; namely " Nucleophilic Oxidation " and " Electrophilic Oxidation ".[1] An electrophilic oxygenative oxidation takes place preferentially on an electron-rich sulfenyl sulfur atom, while a nucleophilic oxygenation occurs on such an electron-poor sulfur as sulfinyl sulfur atom. Although the oxidation of divalent sulfur compounds such as sulfides by peracids has been well-established to be initiated by the electrophilic attack of the terminal oxygen of the peracids on the sulfur atom(eq. 1),[2] trivalent sulfur compounds, such as sulfoxide or thiolsulfinate which also has a divalent sulfur atom, may be oxidized via either the nucleophilic or the electrophilic oxidation or both of the sulfinyl sulfur atom(eq. 1' & 2). In fact, two types of oxygenations have already been reported for the oxidation of sulfoxide(eq. 1' & 2).[3,4]

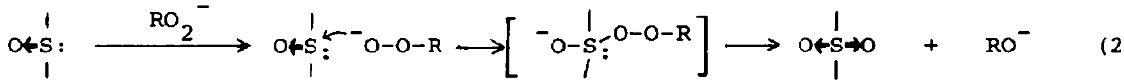
Electrophilic Oxidation;



(1)[2]

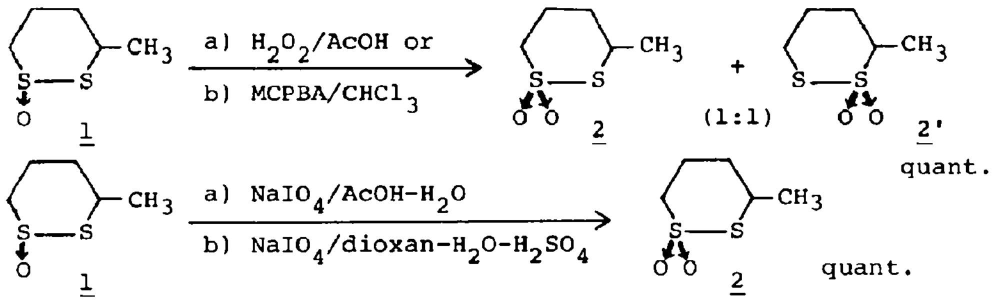
(1')[3]

Nucleophilic Oxidation;



$$O\leftarrow\overset{|}{\underset{|}{S}}: \xrightarrow{RO_2^-} O\leftarrow\overset{|}{\underset{|}{S}}:\leftarrow {}^-O\text{-}O\text{-}R \longrightarrow \left[{}^-O\text{-}\overset{|}{\underset{/}{S}}\!:^{O-O-R} \right] \longrightarrow O\leftarrow\overset{|}{\underset{|}{S}}\rightarrow O \quad + \quad RO^- \qquad (2)^{4)}$$

Thiolsulfinates are quite interesting species to study the mode of the oxidation since they possess both sulfenyl and sulfinyl sulfur atoms, and the attacking site can be readily traced by the use of unsymmetrical thiolsulfinates. For example, in the oxidations of a very stable unsymmetrical thiolsulfinate, 3-methyl-1,2-dithiane-1-oxide 1,[5] these two kinds of oxidations can be clearly seen as shown below equations (3) and (4). While two regio-isomeric unsymmetrical thiolsulfonates(2 & 2') were produced in the same ratio(1:1) nearly quantitatively when 1(0.027 mmole)[5] was oxidized with the system of either 30% H_2O_2-AcOH(0.03 mmole, 0.4 ml, at 27° for 48h)[6b] or MCPBA-$CHCl_3$ (0.03 mmole, 0.4 ml, at 27° for 1h)[6b], the oxidation with either $NaIO_4$-AcOH-H_2O(0.03 mmole, 0.4 ml, 0.15 ml, at 27° for 14h)[6b] or $NaIO_4$-dioxan-H_2O-H_2SO_4 (4.0 mmole, 12 ml, 6.6 ml, a few drops, at 20° for 4h, for 3.33 mmole of 1)[6a] afforded only one isomeric thiolsulfonate 2.



(3)

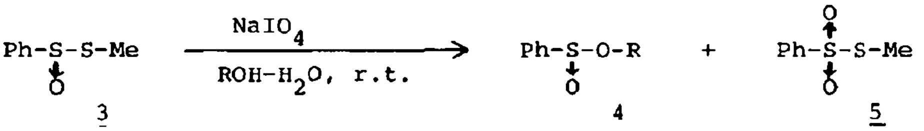
(4)

In the oxidation with peroxide or peracid shown in eq. 3, an electrophilic oxidation is believed to have taken place via the initial formation of the intermediary " α-disulfoxide "[7] which may collapse to yield " only " two isomers 2 & 2' (although four products are obtained generally), since this stable cyclic system tends to keep the original skeletal structure with the sulfur-sulfur linkage. Formation of the two isomeric thiolsulfonates(2 & 2') has undoubtedly been taken place via the intramolecular oxygen transfer from the adjacent sulfinyl group after the initial formation of " α-disulfoxide ", as we have already suggested before.[7a] Thus, this type of oxygenation can be commonly called " Electrophilic Oxidation " of the divalent sulfur atom.

In the reaction shown in eq. 4, only the oxygenation of the sulfinyl sulfur of 1 to form sulfonyl group takes place affording selectively only the corresponding thiolsulfonate 2, as reported in the oxidation of acyclic compounds.[8] We believe this oxidation to be a typical " Nucleophilic Oxidation " of sulfinyl sulfur of 1, because of the following reasons.

1. While the electrophilic oxidation takes place on the sulfenyl sulfur, the sulfinyl sulfur of the thiolsulfinate is more susceptible than the electron-rich sulfenyl sulfur for the nucleophilic attack of the nucleophilic oxidant.

2. In the reaction of 3 with $NaIO_4$ in alcohols the solvent alcohol can compete with the nucleophilic attack on the sulfinyl sulfur atom, thus affording sulfinate 4 together with thiolsulfonate 5,[8] while the amount of the sulfinate 4 decreases with the steric bulkiness of the alkyl group of the alcohol used.

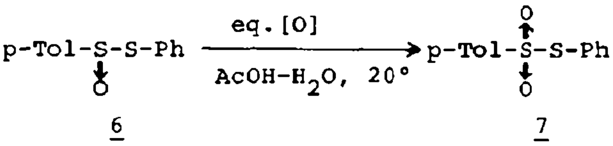


$$\text{Ph-}\underset{O}{\underset{\downarrow}{S}}\text{-S-Me} \xrightarrow[\text{ROH-H}_2\text{O, r.t.}]{NaIO_4} \text{Ph-}\underset{O}{\underset{\downarrow}{S}}\text{-O-R} + \text{Ph-}\overset{O}{\overset{\uparrow}{\underset{O}{\underset{\downarrow}{S}}}}\text{-S-Me} \qquad (5)$$

3 4 5

R =	4	5
Et	39%	42%
^{i}Pr	27	67
^{t}Bu	7	82

3. Other metallic oxides such as $KMnO_4$,[9] SeO_2, $NaClO_3$, and $NaIO_3$[10] also found to be nucleophilic oxidants, and oxidize selectively unsymmetrical thilsulfinate 6 in aqueous acetic acid at 20°, to the corresponding thiolsulfonate 7.



$$\text{p-Tol-}\underset{O}{\underset{\downarrow}{S}}\text{-S-Ph} \xrightarrow[\text{AcOH-H}_2\text{O, 20°}]{\text{eq. [O]}} \text{p-Tol-}\overset{O}{\overset{\uparrow}{\underset{O}{\underset{\downarrow}{S}}}}\text{-S-Ph}$$

6 7

Oxidant	Time[h]	Yield[%]^a
$NaIO_4$	1.0	quant.
$NaIO_3$	0.5	quant.
SeO_2	30	80^b
$KMnO_4$	0.5	40^c
$NaClO_3$	30	30^c

a) Yield by HPLC. b) Substrate 6 was recovered(20%). c) Other further oxidized products were formed

4. The oxidation with $NaIO_4$ is an acid-catalyzed reaction. When diphenyl sulfoxide was treated with an equimolar amount of $NaIO_4$ in neutral dioxan-water solution at 20°, diphenyl sulfone was obtained in ca. 30% for 20h, but in the presence of a catalytic amount of hydrogen chloride, the yield of the sulfone increased up to ca. 95% even in 30 min.[6a)]

5. The effect of substituent, observed in the oxidation of a few S-phenyl-p-substituted-benzenethiolsulfinates with $NaIO_3$ in aqueous acetic acid,[6a)] revealed that an electron-reliezing substituent accelerated the rate of the reaction.

Thus, in the nucleophilic oxidation of thiolsulfinate the likely intermediate is the sulfurane which collapses in the rate determining formation of the thiolsulfonate as in the oxidation of the sulfoxide with peroxides and peracid anions(eq. 2).[4)]

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REFERENCES AND FOOTNOTES

1) A review: Oae, S., and Takata, T., Chemistry(Japanease), 34, 756, 891 and 961(1979).

2) For a review see, Barnard, D., Bateman, L., and Cuneen, J.I., " Oxidation of Organic Sulfide ", in " Organic Sulfur Compounds ", ed. by Kharasch, N., Chap. 21, Pergamon Press, 1961.

3) The pH dependency of the oxidation of sulfoxide with peracid in aqueous solvent was observed and discussed: Curci, R., Giovine, A., and Modena, G., Tetrahedron, 22, 1235(1966).

4) Curci, R., DiFuria, F., and Modena, G., J. Chem. Soc., Perkin II, 603(1978), and references cited therein.

5) The compound was first separated by us from the regio-isomeric mixture[5a)] carefully by column chromatography. 5a) Isenberg, N., and Herbrandson, H.F., Int. J. Sulfur Chem., A, 1, 179(1971).

6a) In a typical run,[8)] an aqueous solution of the oxidizing agent was added in a solution of the substrate in an organic solvent and stirred, monitoring the disappearance of the substrate by HPLC.

b) These reactions were carried out in NMR sample tubes, using deuterized solvents.

7a) Oae, S., Kim, Y.H., Takata, T., and Fukushima, D., Tetrahedron,Letters, 119 (1977).

b) Barnard, D., and Percy, E.J., Chem. & Ind., 1332(1960).

c) Chau, M.M., and Kice, J.L., J. Am. Chem. Soc., 98, 7711(1976).

8) Kim, Y.H., Takata, T., and Oae, S., Tetrahedron Letters, 2305(1978).

9) $KMnO_4$ has been reported to oxidize selectively the sulfinyl group to the sulfonyl group when the compound posseses both sulfenyl and sulfinyl groups in the same molecule.[9a)] 9a) For example, Poje, M., and Balenovic, K., Tetrahedron Letters, 1231(1978).

10) So far as we know, $NaIO_3$ has not been reported as an oxidant of any sulfur compound such as sulfide.

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