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REACTION OF ORGANIC SULFUR COMPOUNDS WITH SUPEROXIDE ANION: OXIDATION OF DISULFIDES, THIOLSULFINATES AND THIOLSULFONATES TO THEIR SULFINIC AND SULFONIC ACIDS

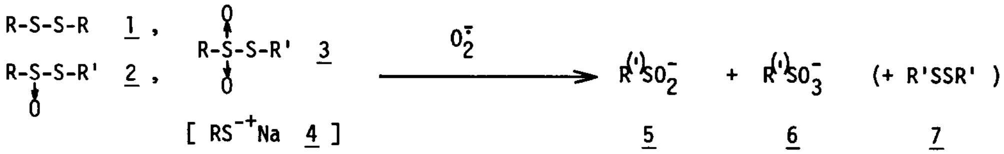
Toshikazu Takata, Yong Hae Kim and Shigeru Oae*

Department of Chemistry, The University of Tsukuba, Ibaraki 300-31, Japan

Although the role of superoxide anion($O_2^{\cdot-}$) has been well advocated in oxygen-metabolizing organisms for the past two decades, the information on its reactivities with simple organic compounds has been rather scant.¹⁾ As to the fundamental reactions of $O_2^{\cdot-}$ with such sulfur compounds as sulfide, disulfide, thiolsulfinate, and thiolsulfonate, there is only a short statement concerning the oxidation of an alkanethiol to the disulfide with $O_2^{\cdot-}$ without any detailed experimental data.²⁾

Superoxide anion posesses multifunctional natures bearing both oxidizing and reducing abilities or radical and anion charactors,¹⁾ and has been regarded as a rather weak oxidizing agent.

We now have found that disulfides 1, thiolsulfinates 2, thiolsulfonates 3, and sodium thiolates 4 are readily oxidized to the corresponding sulfinic and sulfonic acids 5 and 6 with $O_2^{\cdot-}$, generated from KO_2 and 18-crown-6-ether in pyridine under mild conditions.



$$\text{R-S-S-R}\ \mathbf{1},\ \text{R-}\underset{\downarrow\atop O}{\text{S}}\text{-S-R'}\ \mathbf{2},\ \text{R-}\overset{O\atop\uparrow}{\underset{\downarrow\atop O}{\text{S}}}\text{-S-R'}\ \mathbf{3}\ [\ RS^{-+}Na\ \mathbf{4}\ ] \xrightarrow{O_2^{\cdot-}} R^{(\prime)}SO_2^- + R^{(\prime)}SO_3^- \ (+\ R'SSR'\ )$$

A solution of the substrate(1, 2, 3, or 4 : 1.0 mmole, anhydrous 18-crown-6-ether : 1.0 mmole,³⁾ dry pyridine : ca. 7.0 ml) was added onto the potassium superoxide(KO_2 : 3-6 mmole) in a two necked flask which was well dried and argon substituted. The mixture was stirred with magnetic stirrer and quenched into cold water containing ice after the reaction. Upon extracting the mixture three times with chloroform(ca. 100 ml), the combined chloroform layer was washed with water and dried over calcium chloride. After much of chloroform was removed in vacuo, the chloroform soluble organic mixture was subjected to GC assay. The aqueous layer was combined and then concentrated to ca. 10 ml. From the aqueous solution the sulfinic acid was isolated as the corresponding sulfone(RSO_2Me 8) upon treatment with methyl iodide according to the method of Otto[4] or Lindberg.[5] The resulting aqueous solution, after extracting the sulfone with chloroform(ca. 100 ml), was concentrated to ca. 10 ml and then acidified with conc. HCl. Then benzylisothiuronium chloride 10[6][7] was added in excess to form its sulfonic acid salt 9.[8] The benzylisothiuronium salt of the sulfonic acid was isolated as crystal which was purified by recrystallization from acetonitrile or water. All the spectral data and physical properties of these products were identical with those of the authentic samples.

In the absence of crown ether, the oxidation was very slow, while an increased amount of crown ether accelerated the oxidation, suggesting that superoxide anion must be an oxidizing species.

Disulfides[9] of both aryl and alkyl were oxidized at ca. 25° to afford both sulfinic and sulfonic acids, i.e. 5 and 6. The reaction was sometimes exothermic, however, di-tert-butyl disulfide(Entry No. 2) was not oxidized at all even for 24 h at 25°, due to the large steric hindrance of the bulky tert-butyl group.

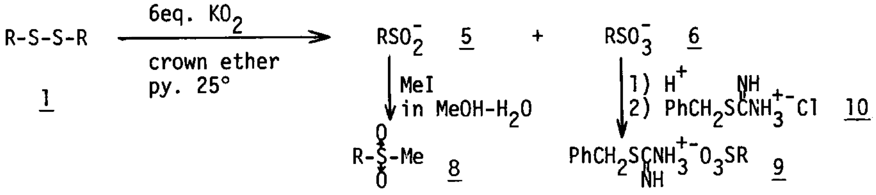


Table I The Reaction of Disulfides with O_2^-

Entry No.,	R	, Reactn. Time[h] ,	RSO_2^- ,	RSO_3^- ,	Recovery[mole %]
1	Me	3.0	0	57	-[a]
2	^tBu	24.0	0	0	100[b]
3	Ph	6.0	trace	81	trace
4	p-Tol	1.0	24	64	12
5	$p-ClC_6H_4$	0.5	46	53	trace

* Yields of RSO_2^- and RSO_3^- are in 1/2 mole %.

a) Recovery was not determined.

b) No reaction.

The oxidation of the thiolsulfinate 2 10)11) proceeded very readily even at -35° and gave the main products, 5 and 6 along with the symmetrical disulfide which is undoubtedly derived from the recombination of the thiyl radical resulted from the nucleophilic attack of superoxide anion at the sulfinyl sulfur atom of thiolsulfinate 2. This fact was supported by the exclusive formation of the acids 5 and 6 from the sulfinyl side of 2.

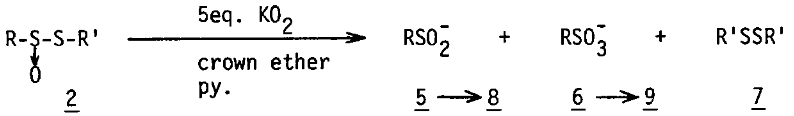
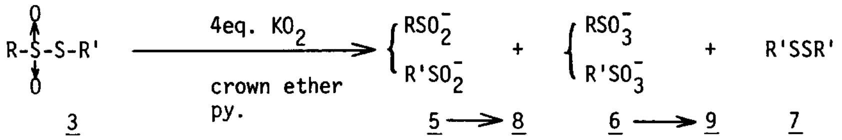


Table II The Reaction of Thiolsulfinates with O_2^-

Entry No.,	R ,	R'	, Temp.[°C],	Time[min],	RSO_2^- ,	RSO_3^-	, R'SSR'[mole %]
1	p-Tol	Ph	-35	90	6	41	34
2	p-Tol	Ph	0	30	trace	45	44
3	Ph	p-Tol	-40 ~ 0	25	trace	48	16
4	Ph	Ph	-40 ~ -20	15	trace	48	35
5	p-Tol	p-Tol	-35	10	trace	40	36

* Yields of RSO_2^- and RSO_3^- are in 1/2 mole %, and small amount of $R'SO_3^-$ was detected by NMR spectrum of 9 in CD_3OD(1/11~2/15 vs. RSO_3^-).

In the case of 3, 12)13) a small amount of the symmetrical disulfide was detected though the main products were RSO_2^-, $R'SO_2^-$, RSO_3^-, and $R'SO_3^-$ under a mild condition(ca. 0°). Formation of these four acids can be explained by assuming concurrent nucleophilic attack of O_2^- at both sulfenyl and sulfonyl sulfur atoms. A further oxidation of the disulfide(R'SSR' 7) formed during the reaction to the acids is also possible. However, this possibility can be ruled out by our observation that the formation of the acids is much faster in the oxidation of 3 than in that of 1.



Meanwhile, we have observed that sodium thiophenolate 4 was directly oxidized with O_2^- to the corresponding benzenesulfonic acid(yield: 86 %, 4 h, 25°). 14) Studies on the mechanisms of all these interesting reactions will be reported shortly.

Table III The Reaction of Thiolsulfonates with O_2^-

Entry No.,	R ,	R' ,	Temp.[°C],	Time[min],	$R^{(')}SO_2^-$,	$R^{(')}SO_3^-$	,R'SSR'[mole %]
1	Ph	Ph	0	58	37	28	25#
2	p-Tol	p-Tol	0	30	14	79	17
3	Ph	p-Tol	0	35	R= 28 R'= 17	R= 36 R'= 9	17
4	p-Tol	Ph	25	8	R= 9 R'= 8	R= 38 R'= 7	9
5	p-ClC_6H_4	p-Tol	0	35	R= 26 R'= 17	R= 25 R'= 23	10
6	p-Tol	p-ClC_6H_4	0	35	R= 14 R'= 3	R= 34 R'= 18	23

* Yields of the acids are in 1/2 mole %, and the ratio of RSO_3^- and $R'SO_3^-$ was determined by NMR spectrum of 9 in CD_3OD.

\# Starting material(11 %) was recovered.

References and Footnotes

1) a) E.Lee-Luff, Chem. Soc. Rev., 6 195(1977). b) T.Matsuura," Oxygen Oxidation Reaction " (Japanease), Maruzen, Tokyo, 1977.

2) There is no detail data, but only a short statement is given: J.S.Filippo Jr., L.J.Romano, C-I.Chern, and J.S.Valentine, J. Org. Chem., 41,586(1976). In addition, a reaction of sulfonyl chloride with sodium superoxide to the sodium sulfonate was reported: A.Le Berre and Y.Berguer, Bull. soc. chim. Fr., 1966, 2368.

3) As for sodium thiolate, 0.5 mmole of crown ether was used. 4) R.Otto, Chem. Ber., 13, 1272 (1880). 5) B.Lindberg, Acta Chem. Scand., 17, 393(1963); C.A., 61, 8149(1964).

6) Benzylisothiuronium chloride was prepared by the reaction of benzyl chloride with thiourea in 95 % alcohol, and then recrystallized from alcohol, mp. 139°(lit.7) 146-8°).

7) E.E.Reid," Organic Chemistry of Bivalent Sulfur ", Vol. V, Chap. 1, p. 27, Chem. Publishing Co., INC., New York, N.Y.

8) a) F.Kurzer and J.P.Powell, J. Chem. Soc., 3728(1952), 4152(1954). b) J.Burdon, I. Farazmand, M.Stacey, and J.C.Tatlow, J. Chem. Soc., 2574(1957). c) J.J.Donleay, J. Am. Chem. Soc., 58, 1004(1936). 9) Commercially unobtainable disulfides were prepared by the reaction of thiols with iodine in the presence of pyridine.

10) Symmetrical and unsymmetrical thiolsulfinates were prepared according to the methods as described previously.11)

11) a) H.J.Backer and H.Kloosterziel, Rec. Trav. Chem., 73, 129(1954). b) M.J.Khosla and N.Anand, J. Sci. Ind. Res. India, 17, 71(1958). c) S.Oae and K.Ikura, Bull. Chem. Soc. Japan, 39, 1306(1966).

12) Symmetrical and unsymmetrical thiolsulfonates were prepared by the reaction of sulfinic acids with sulfenyl chlorides according to Stirling13a) or Klivenyi.13b)

13) a) C.J.M.Stirling, J. Chem. Soc., 3597(1957). b) G.F.Klivenyi, Magy. Hem. Foly., 64, 121 (1958).

14) S.Oae, Y.H.Kim and T.Takata, unpublished results.

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