Tetrahedron Vol. 37, pp. 37 to 44
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0040-4020/81/0101-0037 $02.00/0

REACTION OF ORGANIC SULFUR COMPOUNDS WITH SUPEROXIDE ANION—III

OXIDATION OF ORGANIC SULFUR COMPOUNDS TO SULFINIC AND SULFONIC ACIDS[1]

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(*Received* 18 *January* 1980)

Abstract Organic sulfur compounds such as disulfide, thiolsulfinate, thiolsulfonate, thiol, sodium thiolate, and sodium sulfinate were readily oxidized to both sulfinic and sulfonic acids with superoxide anion generated from potassium superoxide and 18-crown-6-ether under mild conditions. However, both sulfide and sulfoxide did not react with superoxide anion, O_2^-. Although thiol was easily oxidized to disulfide with O_2^- at room temperature, it was oxidized further with O_2^- at 60 to the corresponding sulfinic and sulfonic acids. Symmetrical disulfide was obtained in the reaction of unsymmetrical thiolsulfinate or thiolsulfonate along with both sulfinic and sulfonic acids. Most reactive was thiolsulfinate which reacted at lower temperature ranging between −40 and 0° to afford the products within 30 min. Relative reactivities fall in the following order: thiolsulfinate > thiolsulfonate > disulfide ≃ sodium thiolate ≃ sodium sulfinate. Polar solvents such as pyridine and acetonitrile were more effective than such a less polar solvent as benzene in the oxidation of the substrate, and increased amount of the crown ether shortened the reaction time. Nucleophilic attack of O_2^- and electron transfer processes are believed to be involved in these oxidations.

Although the role of superoxide anion has been well adovocated in oxygen-metabolizing organisms for the past two decades[2] since the discovery of superoxide dismutase by Fridovich and McCord in 1969,[3] the information on its reactivities with simple organic compounds has been rather scant, especially on the reaction of organic sulfur compounds.[4,5] Superoxide anion is a mild multifunctional reagent which possesses both oxidizing and reducing abilities and also both radical or anionic characters[5b] but generally regarded as a rather weak oxidizing agent.

Only two minor reactions of O_2^- with organic sulfur compounds have been known: one is a reaction of sulfonyl chloride with sodium superoxide to yield sodium sulfonate in a non-crown ether containing system,[6] and the other is a simple oxidation of an alkanethiol to the corresponding disulfide with O_2^- with no experimental detail.[7] These two reactions alone are not enough to understand the fundamental nature of the reactions of O_2^- with organic sulfur compounds. We now have studied the general reactions of organic sulfur compounds bearing S-S linkage, thiols and sulfinates with superoxide anion.

This paper describes general features of the reactions of various organic sulfur compounds with O_2^-.

RESULTS AND DISCUSSION

Superoxide anion generated *in situ* from the system of potassium superoxide and 18-crown-6-ether, as previously reported and usually used,[8] was found to react readily with several organic sulfur compounds (**1**–**5** and **8**) under mild conditions, in an argon atmosphere. However, neither sulfide **6** nor sulfoxide **7** was found to react with O_2^- at all, under the same conditions.

$RSSR$ **1**


$RS(\rightarrow O)SR'$ **2**


$R(O\leftarrow)S(\rightarrow O)SR'$ **3**

$RS^- \cdot {}^+Na$ **4**

$RSO_2^- \cdot {}^+Na$ **5**

RSR' **6**


$RS(\rightarrow O)R'$ **7**

RSH **8**

A solution of one of the substrates and 18-crown-6-ether was added onto potassium superoxide and the heterogeneous mixture was stirred at a set temperature for some periods till the disappearance of the substrate which was monitored by gas or liquid chromatography. After quenching the reaction mixture with a

$$\underset{\mathbf{5},\ \text{or}\ \mathbf{8}}{\mathbf{1},\mathbf{2},\mathbf{3},\mathbf{4},}\ \xrightarrow[\substack{\text{18-crown-6-ether}\\ \text{pyridine}\\ 40 \sim 25}]{KO_2}\ \underset{\mathbf{9}}{R''SO_2} + \underset{\mathbf{10}}{R''SO_3^-} \quad \underset{\mathbf{11}}{(+R'SSR')} \qquad (1)$$

large amount of cold water, the disulfide was isolated from the organic layer and from the aqueous layer sulfinic and sulfonic acids were obtained as oxidation products. The sulfinic acid was isolated as the corresponding methyl sulfone upon treatment of the aqueous layer with methyl iodide according to the method of Otto[9] or Lindberg.[10] The resulting aqueous layer, after extracting the sulfone (**13**), was treated with *S*-benzylisothiuronium chloride (**12**),[11][‡] upon acidification, to obtain its salt of the sulfonic acid as good crystals, according to the known method.[12] Thus, this method of separation is very reliable to

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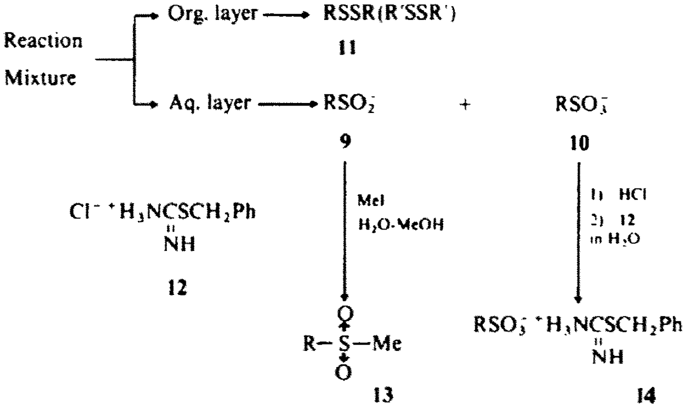
[‡] The melting point of this crystal was very sharp at 139°, and the elemental analysis and spectral data of *S*-benzylisothiuronium *p*-chlorobenzenesulfonate were satisfactory. The melting point previously reported was not constant, at 172 4° and 146–8°; see Ref. 11.



Scheme 1.

determine the amounts of both sulfinic and sulfonic acids which are very difficult to be separated chemically, although estimation of both acids by polarographical determination was reported.[13] Since the *S*-benzylisothiuronium salts of aromatic sulfonic acids can be obtained in better crystalline forms than those of aliphatic sulfonic acids, substrates used in this study were mostly aromatic. In control reactions forming the sulfone and the *S*-benzylisothiuronium salt from the mixture of sulfinic and sulfonic acids under our reaction conditions, isolated yields of the sulfone and the *S*-benzylisothiuronium salt of the sulfonic acid were found to be satisfactory, i.e. ~86 % and ~95 % respectively for any one of phenyl-, *p*-tolyl- and *p*-chlorophenyl derivatives.

The potassium superoxide used was twice the amount required to oxidize each one of the substrates completely to the sulfonic acid, while a half equivalent of the crown ether was used for each of the sulfur atoms of the substrate.

Commercially unobtainable disulfides were synthesised by treatment of thiols with iodine in the presence of pyridine in quantitative yields, according to the method of McAllen *et al.*[14] Both symmetrical and unsymmetrical thiolsulfinates were prepared by treating corresponding sulfinyl chloride[15] with desired thiol in the presence of pyridine, as reported previously.[15a,16] In the same manner, both symmetrical and unsymmetrical thiolsulfonates were prepared by treating corresponding sulfenyl chlorides with proper free sulfinic acids in the presence of pyridine, according to the method reported by Stirling[17] or Klivenyi.[18] Although symmetrical thiolsulfonates can be also prepared by direct oxidation of disulfides with peracid, the yield in this method of condensation is usually higher than that by the peracid oxidation. Sodium sulfinate and thiolate were obtained from the reactions of sulfinic acid and thiol with metallic sodium. Although anhydrous sodium sulfinate may be obtained by removing water in refluxing sodium sulfinate hydrate in benzene or toluene by azeotropic separation, completely anhydrous sulfinate can be prepared more readily by the above mentioned method.

In the absence of the crown ether the reaction was slow or did not occur, while increased amount of the crown ether accelerated the oxidation, suggesting that superoxide anion must be the oxidizing active species.

Reaction of Disulfide **1** *with* O_2^-

Both aryl and alkyl disulfides were oxidized at *ca* 25° with O_2^- to afford both sulfinic and sulfonic acids, i.e. **9** and **10**, generally in good yields (Table 1). Yield of the sulfonic acid is usually larger than that of the sulfinic acid, mainly because the sulfinate is also oxidized further to the corresponding sulfonate with excess superoxide anion present in the reaction system. In general, the reaction was slightly exothermic. However, di-*tert*-butyldisulfide was not oxidized at all, even for 24 hr at 25°, due to the large steric hindrance of the bulky *tert*-butyl group which blocks the S_N2 attack of O_2^- on the sulfur atom. Similarly, 1,2-dithiane, a six-membered cyclic disulfide, was also not oxidized.

$$\underset{\mathbf{1}}{RSSR} \xrightarrow[\text{crown ether, pyridine, } 25^\circ]{6\text{eq } KO_2} \underset{\mathbf{9}}{RSO_2^- \,{}^+K} + \underset{\mathbf{10}}{RSO_3^- \,{}^+K} \qquad (2)$$

Since such a dialkyldisulfide as dibutyldisulfide was generally found to be less reactive than aromatic disulfides, except for dibenzyldisulfide, the conversion of the dialkyldisulfide to the acids is slower than that of the aromatic disulfide and required a prolonged reaction time. Thus the initial step of the oxidation undoubtedly involves a nucleophilic attack of O_2^- on the sulfur atom.

Reaction of thiolsulfinate **2** *with* O_2^-

The oxidation of both symmetrical and unsymmetrical thiolsulfinates **2** proceeded very readily even at −35° within 30 min and gave the sulfinic and sulfonic acids as main products (from the aqueous layer) along with symmetrical disulfides (from the organic layer) which are undoubtedly derived by recombination of the thiyl radicals resulting from nucleophilic attack of O_2^- at the sulfinyl sulfur atom of the thiolsulfinate **2**. These observations are in

Table 1. Reaction of disulfide 1 with O_2

Substrate, (R=)	No.,	Solv.,	Time[h],	RSO_2^-(9),	RSO_3^-(10),	Recovery
Me	1a	Py	3.0	0%a)	57%a)	-b)
Bu	1b	"	1.0	-b)	-b)	69%c)
${}^tBu$	1c	"	24.0	0	0	100
$PhCH_2$	1d	"	0.5	-b)	-b)	5
Ph	1e	"	6.0	trace	81	trace
p-$CH_3C_6H_4$	1f	"	1.0	24	64	12
p-ClC_6H_4	1g	"	0.5	46	53	trace
Ph	1e	CH_3CN	10.0	13	48	7d)
p-$CH_3C_6H_4$	1f	"	6.0	28	56	9d)

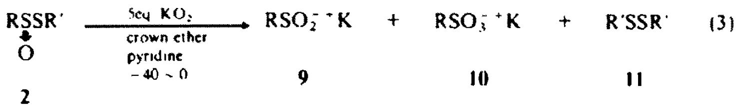
a) Yields of RSO_2^- and RSO_3^- are in 1/2 mole %.

b) Yield was not determined.

c) Yield was in mole%.

d) Side product was obtained in 30%($(PhS)_2CHCN$) for 1c, and 29%($(p\text{-}TolS)_2CHCN$) for 1f, respectively.

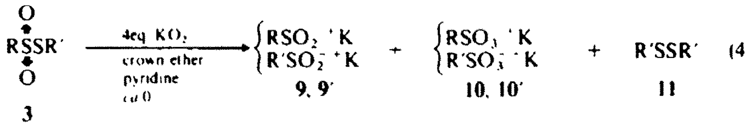
accordance with the exclusive formation of the acids **9** and **10** from the sulfinyl sulfur side of **2** as in the alkaline hydrolysis of unsymmetrical thiolsulfinate,[19b] supporting the nucleophilic attack of O_2^- at the sulfinyl sulfur atom of **2**. The yield of the sulfinic acid was rather low and the main product from the aqueous layer was the sulfonic acid.



$$\underset{\mathbf{2}}{\underset{\displaystyle\overset{\uparrow}{O}}{RS}SR'} \xrightarrow[\text{crown ether, pyridine, } -40\sim 0]{5\text{eq } KO_2} \underset{\mathbf{9}}{RSO_2^-\,{}^+K} + \underset{\mathbf{10}}{RSO_3^-\,{}^+K} + \underset{\mathbf{11}}{R'SSR'} \quad (3)$$

Reaction of thiolsulfonate **3** *with* O_2^-

Symmetrical and unsymmetrical thiolsulfonates **3** were oxidized with O_2 under mild conditions (*ca* 0) to afford four main acids, i.e. two sulfinic acids, RSO_2^- and $R'SO_2^-$, and two sulfonic acids, RSO_3^- and $R'SO_3^-$, from both sides of the S-S linkage, together with a small amount of the symmetrical disulfide derived from the sulfenyl group. The yields of two sulfinic acids from both sides were quantitatively determined by gas chromatography (using a calibration curve) after converting them to their sulfones. The ratio of the sulfonic acids was determined by comparing the integration ratios in the NMR spectrum of a mixture of the *S*-benzylisothiuronium salts of two sulfonic acids.



$$\underset{\mathbf{3}}{\underset{\displaystyle\overset{\uparrow}{O}}{\overset{\displaystyle\overset{O}{\downarrow}}{RS}}SR'} \xrightarrow[\text{crown ether, pyridine, } ca\ 0]{4\text{eq } KO_2} \underset{\mathbf{9},\ \mathbf{9'}}{\left\{\begin{matrix} RSO_2^-\,{}^+K \\ R'SO_2^-\,{}^+K \end{matrix}\right.} + \underset{\mathbf{10},\ \mathbf{10'}}{\left\{\begin{matrix} RSO_3^-\,{}^+K \\ R'SO_3^-\,{}^+K \end{matrix}\right.} + \underset{\mathbf{11}}{R'SSR'} \quad (4)$$

Table 2. Reaction of thiolsulfinate 2 with O_2^-

Substrate, (R=)	(R=)	No.,	Temp.,	Time,	$R^{(\prime)}SO_2^-$(9),	$R^{(\prime)}SO_3^-$(10),c)	R'SSR'
Ph	Ph	3a	0°	58min	37%a)	28%a)	26%a)b)
p-Tol	p-Tol	3b	0	30	14	79	17
Ph	p-Tol	3c	0	35	R= 28 R'= 17	R= 36 R'= 9	17
p-Tol	Ph	3d	25	8	R= 9 R'= 8	R= 38 R'= 7	9
p-ClC_6H_4	p-Tol	3e	0	35	R= 26 R'= 17	R= 25 R'= 23	10
p-Tol	p-ClC_6H_4	3f	0	35	R= 14 R'= 3	R= 34 R'= 18	23

a) Yields of $R^{(\prime)}SO_2^-$ and $R^{(\prime)}SO_3^-$ are in 1/2 mole %, while yield of R'SSR' is in mole %.

b) Starting material(11%) was recovered.

c) The ratio of RSO_3^- and $R'SO_3^-$ was determined from NMR spectrum of the mixture of 14 in CD_3OD.

Table 3. Reaction of thiolsulfonate 3 with $O_2^{\overline{\cdot}}$

Substrate, (R=)	(R=)	No.,	Temp.,	Time,	RSO_2^-(9),	RSO_3^-(10),	R'SSR'
p-Tol	Ph	2a	-35°	90min	6%$^{a)}$	41%$^{a)}$	34%$^{a)}$
"	"	2a	0	30	trace	45	44
Ph	p-Tol	2b	-40 ~ 0	25	"	48	16
Ph	Ph	2c	-40 ~ -20	15	"	48	35
"	"	2c	23	15	"	49	44
p-Tol	p-Tol	2d	-35	10	"	40	36
"	"	2d	-20 ~ 0	30	trace	33	-$^{b)c)}$
"	"	2d	18	10	14	37	50

a) Yields of RSO_2^- and RSO_3^- are in 1/2 mole %, while yield of R'SSR' is in mole %.

b) Solvent used was acetonitrile.

c) Yield of R'SSR' was not determined.

Yields of both sulfinic and sulfonic acids from the sulfonyl side are generally larger than those from the sulfenyl side of the thiolsulfonate 3. Formations of these four acids are undoubtedly due to the concurrent nucleophilic attack of $O_2^{\overline{\cdot}}$ at both sulfonyl and sulfenyl sulfur atoms. Further oxidation of the disulfide, R'SSR' **11**, formed during the reaction to the acids is also possible. However, this possibility is quite unlikely in view of our observation that the formation of the acids is much faster in the oxidation of thiolsulfonate 3 than in that of the disulfide 1 (see, Tables 1 and 3).

Thus, the oxidations of all these compounds bearing sulfur-sulfur linkages are considered to be initiated by the nucleophilic attack of $O_2^{\overline{\cdot}}$. The relative reactivities in these three substrates fall in the following order: RS(O)SR′ > RS(O)$_2$SR′ > RSSR, and this order seems to be in accordance with that of the nucleophilic reactions of these compounds with such a hard nucleophile as hydroxide anion, as reported previously.[19] Like the alkaline hydrolysis, $O_2^{\overline{\cdot}}$ apparently attacks only sulfinyl sulfur of thiolsulfinate **2** in view of the predominant formations of the acids from sulfinyl side and the disulfide from the sulfenyl side. Meanwhile, $O_2^{\overline{\cdot}}$, being less basic but more nucleophilic than hydroxide anion, due to the α-effect,[20] would attack competitively both sulfenyl and sulfonyl sulfur atoms of thiolsulfonate 3, unlike hydroxide anion, which is believed to attack exclusively the sulfenyl sulfur of thiolsulfonate in the alkaline hydrolysis,[19c] due mainly to the good leaving ability of the sulfonyl group. However, in view of the formation of the symmetrical disulfide from the sulfenyl side and the larger amount of the acids formed from the sulfonyl side than from the sulfenyl side, the attack of $O_2^{\overline{\cdot}}$ seems to take place preferentially at the hard sulfonyl sulfur rather than at the soft sulfenyl sulfur, despite the stereo-electronic repulsion of two oxygen atoms of the sulfonyl group in the reaction of thiolsulfonate 3 with $O_2^{\overline{\cdot}}$.

Reaction of thiol **8**, *sodium thiolate* **4** *and sodium sulfinate* **5** *with* $O_2^{\overline{\cdot}}$

Oxidation of benzenethiol with $O_2^{\overline{\cdot}}$ gave quantitatively diphenyldisulfide instead of the acids at room temperature, though both sulfinic and sulfonic acids were eventually obtained by heating with excess $O_2^{\overline{\cdot}}$ at 60° for 30 min (eqn 5).

$$\underset{\mathbf{8}}{PhSH} \xrightarrow[\substack{\text{pyridine}\\ 25°,\ 30\ \text{min}}]{3eq\ KO_2 \atop \text{crown ether}} \xrightarrow[30\ \text{min}]{\Delta,\ 60°} \underset{\mathbf{9}}{PhSO_2^-\ {}^+K} + \underset{\mathbf{10}}{PhSO_3^-\ {}^+K} \quad (5)$$

Meanwhile, sodium salt of thiol which was prepared by treating the thiol with metal sodium in dry ether under argon, was directly oxidized with $O_2^{\overline{\cdot}}$ to the corresponding sulfinic and sulfonic acids for 4 h at room temperature (eqn 6). In this reaction a trace amount of the disulfide was obtained along with two acids.

$$\underset{\mathbf{4}}{RS^-\ {}^+Na} \xrightarrow[\substack{\text{crown ether}\\ \text{pyridine } 25°,\ 4h}]{3eq.\ KO_2} \underset{\mathbf{9}}{RSO_2^-} + \underset{\mathbf{10}}{RSO_3^-} \quad (+RSSR) \qquad (6)$$

R =	9	10	(+RSSR)
Ph	9%	86%	trace
p-Tol	10	66	trace

Filippo *et al.*[7] have also reported to have obtained the disulfide in the reaction of an alkanethiol with $O_2^{\overline{\cdot}}$, though no experimental detail was given. Wallace and Shriesheim[21a] also reported that thiols were oxidized to the disulfides in the presence of a catalytic amount of alkali under an oxygen atomsphere, where superoxide anion is considered to be formed as an active oxidant by one electron transfer. Thus, the initial reaction of the thiol with $O_2^{\overline{\cdot}}$ would be the base-catalysed formation of the disulfide and further oxidation to the sulfinic and sulfonic acids upon heating would follow the same reaction path as the reaction of disulfide with $O_2^{\overline{\cdot}}$. The reaction of sodium thiolate with $O_2^{\overline{\cdot}}$ would proceed by the initial one electron transfer from the thiolate anion to $O_2^{\overline{\cdot}}$. A behavior of $O_2^{\overline{\cdot}}$ as an oxidizing agent to accept one electron has been reported.[5b] This appears to be supported by the formation of a small amount of the disulfide in the reaction of **4** with O_2^-, where the disulfide is derived from the recombination of thiyl radicals thus formed. On the other hand, the thiyl radical would also react with O_2^- to afford the sulfinic and sulfonic acids.

$$\underset{\mathbf{1}}{\text{ArSSAr}} \xrightarrow[\text{CH}_3\text{CN}]{O_2^-} \underset{\mathbf{15}\ \ \sim 40\%}{(\text{ArS})_2\text{CHCN}} \quad (+\text{ArSO}_x^-\ {}^+\text{K},\ x = 2, 3) \qquad (8)$$

Ar = Ph, p-Tol

When the reaction was carried out for somewhat a longer time, the amount of the sulfinic acid decreased while the amount of sulfonic acid increased; apparently the sulfinic acid was oxidized further with O_2^- to the corresponding sulfonic acid at room temperature. This result is supported by the fact that anhydrous sodium sulfinate prepared independently was oxidized to the corresponding sulfonate with O_2^- at 25° (2.5 h) in considerable yield (eqn 7). Since nucleophilic attack of O_2^- is not conceivable in this reaction, only the one electron transfer process may explain the formation of the sulfonic acid. The sulfonyl radical thus resulted by one electron transfer from the sulfinate anion, has already been postulated as an intermediate in the photoreaction of hydrocarbon with sulfur dioxide[22] and in the autoxidation of sulfinic acid in the presence of molecular oxygen.[23]

Solvent effect

Although nearly a complete conversion of the substrate (disulfide **1**) to the acids was achieved in such a solvent as pyridine or acetonitrile for *ca* 4 h at *ca* 25°, the conversion was lower in such a solvent as chloroform or benzene even when the amount of the crown ether was increased (× 1.5) and the reaction time was pronlonged. In chloroform, the conversion of di-*p*-tolyldisulfide to the corresponding sulfinic and sulfonic acids with O_2^- was 76% with a half amount excess of the crown ether for 4 h at 25°, while the conversion in dry benzene was only 32% in the same reaction even for 6 h at 25°. This result indicates that the reaction in a more polar solvent is faster than that in a less polar solvent such as benzene. Therefore, these reactions with O_2^- must involve the ionic processes at the rate determining step. The best solvent, among those we used, was pyridine, perhaps because it can dissolve not only disulfide **1**, thiolsulfinate **2** and thiolsulfonate **3** but also sodium thiolate **4**.

Meanwhile, the reaction of disulfide **1** with O_2^- in acetonitrile, gave a considerable amount of a side product which seems to be derived from the radical reaction between the solvent and the disulfide (eqn 8).

Bis(arylthio)-acetonitrile **15**, a side product, was isolated as a viscous oil by column chromatography of the residue of the organic extract (eluent; hexane:chloroform:ethyl acetate = 4:1:1, on silica gel). This product, however, could not be obtained in the oxidation of thiolsulfinate **2** with O_2^- in acetonitrile, presumably due to the low temperature (−20°) and a short reaction time (15–30 min). The structure of the product was determined by various spectral data and the elemental analysis also supported it.

$$\underset{\mathbf{5}}{\text{RSO}_2^-\ {}^+\text{Na}} \xrightarrow[\substack{\text{crown ether}\\ \text{pyridine}\\ 25^\circ,\ 2.5\text{h}}]{\text{eq KO}_2} \underset{\mathbf{10}}{\text{RSO}_3^-} \quad (+\text{RSO}_2^-:\ \text{recovery}) \qquad (7)$$

R = Ph 80% trace

p-tol 74 17%

It is obvious that the products formed in the superoxide oxidation closely resemble those of the alkaline autoxidation of thiol[13,24] and disulfide,[21,24] in which Berger[13] indicated that the main product was sulfinic acid and sulfonic acid was a minor product. Wallace *et al.*, however, reported that the only product formed in the alkaline autoxidation of thiol[21] and disulfide[21b,25] was sulfonic acid. Our recent detailed investigation 24 (lit.) on the alkaline autoxidations of thiol and disulfide indicated that the main product was sulfinic acid while the amount of sulfonic acid was small, in accordance with the result of Berger. If such a substrate as disulfide **1** would remain in the reaction with superoxide anion, the alkaline autoxidation of the disulfide could also take place even after quenching the reaction mixture into cold water, because the quenched solution is alkaline and molecular oxygen also exists under these conditions. However, the autoxidation of the disulfide even in higher concentrations of the substrate, alkali and crown ether (more than 7–10 times) and even under pure oxygen atmosphere, was found to require more than 20 h at room temperature till the starting material disappeared completely, in pyridine-water (2:1) (eqn 9). Therefore, the alkaline

$$\underset{\mathbf{1}}{\text{PhSSPh}} \xrightarrow[\substack{\text{crown ether}\\ \text{pyridine-water (2:1)}\\ 25^\circ,\ >20\text{h}}]{\text{KOH O}_2} \underset{\substack{\mathbf{9}\\ 50\%}}{\text{PhSO}_2^-} + \underset{\substack{\mathbf{10}\\ 41\%}}{\text{PhSO}_3^-} \qquad (9)$$

autoxidation during the subsequent work-up of the reaction with O_2^- should be negligible, since the autoxidation is considerably slower than the reaction with O_2^-.

Thus, in this study, organic sulfur compounds such as disulfide **1**, thiolsulfinate **2**, thiolsulfonate **3**, sodium thiolate **4**, and sodium sulfinate **5** were found to be oxidized easily with O_2^- to afford the corresponding sulfinic and sulfonic acids, though O_2^- is regarded to be a rather weak oxidizing agent. When disulfide **1** is oxidized to the sulfonic acid with a common peracid a markedly long reaction time is usually required. Meanwhile, both sulfide **6** and sulfoxide **7** were inert to O_2^-. Although thiol was easily oxidized to the corresponding disulfide with O_2^- at room temperature, it was oxidized further with O_2^- by heating at *ca* 60° to the sulfinic and sulfonic acids. These reactions with O_2^- resemble the alkaline autoxidation in which thiol, sodium thiolate and disulfide are known to be similarly oxidized to afford both sulfinic and sulfonic acids.[13,24] In the autoxidation, however, the main product was sulfinic acid and not sulfonic acid, unlike the reaction with O_2^- in which sulfinate is oxidized further to sulfonate with excess O_2^- present in the reaction system. In the reaction of these organic sulfur compounds with O_2^- the ionic process appears to be more important than the radical process, since the reaction took place faster in a more polar solvent such as pyridine than in a less polar solvent such as benzene. Initial nucleophilic attack of O_2^- on the sulfur atom of disulfide **1**, thiolsulfinate **2** or thiolsulfonate **3** is undoubtedly involved in view of the product distributions in the reactions with unsymmetrical thiolsulfinate **2** and thiolsulfonate **3**. Meanwhile, the reactions of soidum thiolate **4** and sulfinate **5** with O_2^- are considered to proceed via one electron transfer processes.

EXPERIMENTAL

General. Melting points were taken on a Yanako instrument and are uncorrected. NMR spectra were recorded on a Hitachi Perkin Elmer R-20 Spectrometer. Infrared spectra were obtained on a Hitachi 215 IR Spectrometer and were uncorrected. Mass spectra were recorded on a Hitachi RMU-6MG Mass Spectrometer. Gas and liquid chromatograms were obtained by Shimazu GC-6A and Yanako L-1030 instruments respectively. Chemicals, except some solvents, were of commercial quality. KO_2 was obtained from Ventron Alfa Products. 18-Crown-6-ether was a gift from Nippon Soda Co. and used after drying *in vacuo* at 60–70°. Extra pure commercial grade pyridine (Wako Pure Chemical Ind.) was distilled on KOH and dried over KOH under Ar. Extra pure commercial grade CH_3CN was distilled from P_2O_5 and dried over molecular sieves under Ar. Dry $CHCl_3$ and CCl_4 were obtained by distillation of first grade commercial products and then dried with $CaCl_2$ before use. Benzene and ether were purified by distillation similarly and dried over metal Na wire under Ar.

Preparation of disulfide **1**. Disulfides which are not commercially available were synthesised by known method.[14] To a benzene solution (150 ml) of thiol (0.05 mole) and pyridine (0.055 mole) was added dropwise I_2 (0.025 mole) dissolved in benzene (*ca* 50 ml). When the color of the solution changed to brown by excess I_2, the addition was stopped. The reaction mixture was washed with water, 5%-HCl soln, $Na_2S_2O_3$ soln., then water again, and the organic layer was dried over Na_2SO_4. After evaporation of benzene, the residual disulfide was purified by recrystallization, usually from hexane. Yields were nearly quantitative. 1,2-Dithiane was prepared according to the method of Isenberg *et al.*[26]

Di-p-tolydisulfide **1f**; mp 45–7° (lit.[27] 46°), MS; *m/e* 246 ($M^{\cdot+}$, 100%).

Di-p-chlorophenyldisulfide **1g**; mp 72° (lit.[28] 73°), MS; *m/e* 302 ($M^{\cdot+}$ + 4, 15%), 300 ($M^{\cdot+}$ + 2, 72%), 298 ($M^{\cdot+}$, 100%).

Preparation of thiolsulfinate **2**.[15,16] A desired sulfinyl chloride was prepared by treating the corresponding thiol or disulfide with gaseous Cl_2 in the presence of one or two molar amounts of Ac_2O or AcOH at lower than *ca* −10°.[15] After removal of excess gaseous Cl_2 and AcCl by sucker, the pale yellow sulfinyl chloride was purified by distillation *in vacuo*. Sulfinyl chlorides are highly water-sensitive. To a CCl_4 soln. (200 ml) of the distilled sulfinyl chloride (0.03 mole) in a two necked flask which was well dried and flushed with argon, dry pyridine (0.033 mole) was added with cooling at *ca* −20°. Soln. of a thiol (0.03 mole) in CCl_4 (150 ml) was added dropwise at −20 to −10° to the resulting mixture containing pyridinium salt of sulfinyl chloride. White precipitates of pyridinium salt of HCl instead of that of the sulfinyl chlorides were gradually produced. After the addition of the thiol was completed, the reaction mixture was stirred for a short time until the temperature reached *ca* 0°. A heterogeneous reaction mixture containing the white precipitate was transferred to a separatory funnel and washed four times with cold water. The organic layer was dried with $CaCl_2$ and solvent was removed by evaporation carefully because the product thiolsulfinate is thermally unstable. The yield of the crystallized thiolsulfinate ranged from 80 to 95% and the slightly yellow crystals should be recrystallized quickly from a hexane-chloroform mixed solvent. The product must be stored in a refrigerator. Note that an excess thiol did not give improved yields since the side reaction of product with excess thiol takes place.[29]

Phenyl benzenethiolsulfinate **2c**; mp 69–70° (lit.[30] 69–70°), IR ($CHCl_3$, cm^{-1}) 3055, 1577, 1475, 1093 (S=O), 1060 (S=O).

p-*Tolyl* p-*toluenethiolsufinate* **2d**; mp 87° (lit.[31] 87.5°). IR ($CHCl_3$, cm^{-1}) 3050, 1590, 1490, 1090 (S=O), 1060 (S=O).

Phenyl p-*toluenethiolsulfinate* **2a**; mp 82° (lit.[30] 83–84°), IR ($CHCl_3$, cm^{-1}) 3050, 1590, 1470, 1095 (S=O), 1065 (S=O).

p-*Tolyl benzenethiolsulfinate* **2b** mp 70–71° (lit.[30] 68°), IR ($CHCl_3$), cm^{-1}) 3050, 1590, 1470, 1095 (S=O), 1055 (S=O).

Preparation of thiolsulfonate **3**.[17,18] Sulfenyl chloride was prepared by treating thiol or disulfide with gaseous Cl_2 in CCl_4 at *ca* 0°. Free sulfinic acids other than those which were obtained by acidification of commercial sodium sulfinate with conc. HCl, were synthesized by hydrolysis of the corresponding sulfinyl chlorides which were prepared by the method described in the preparation of thiolsulfinate. To a dry CCl_4 soln. (150 ml) of sulfenyl chloride (0.03 mole) which was freshly prepared and was freed from Cl_2 under reduced pressure, was added dropwise dry pyridine (0.033 mole) at lower than 0° and a precipitate of pyridinium salt of sulfenyl chloride formed. A soln. containing free sulfinic acid (0.03 mole) in dry CCl_4 or ether (*ca* 50 ml) was added to that soln. at lower than 0°. A new precipitate formed gradually as the addition proceeded. After stirring the reaction mixture for *ca* 30 min and subsequent warming to room temp., the reaction mixture was washed with 5%-HCl soln and then water. The organic layer was dried over $CaCl_2$ and solvent was evaporated. From the residue the thiolsulfonate was obtained in 80–95% yield and recrystallized from EtOH.

Phenyl benzenethiolsulfonate **3a**; mp 44–45° (lit.[19c] 44–45°), IR (KBr, cm^{-1}) 3050, 1578, 1471, 1440, 1325 (SO_2), 1310 (SO_2), 1147 (S=O), MS; *m/e* 250 ($M^{\cdot+}$, 39%), 125 ($M^{\cdot+}$-PhSO, 100%).

p-*Tolyl* p-*toluenethiolsulfonate* **3b**; mp 72–74° (lit.[32] 76°), IR (KBr, cm^{-1}) 3050, 1590, 1490, 1380, 1325 (SO_2), 1295 (SO_2), 1138 (S=O), MS; *m/e* 278 ($M^{\cdot+}$, 63%), 139 ($M^{\cdot+}$-p-tolSO, 100%).

Phenyl p-*toluenethiolsulfonate* **3d**; mp 78–80° (lit.[19c] 78°), IR ($CHCl_3$, cm^{-1}) 3025, 1597, 1443, 1335 (SO_2), 1145 (S=O), MS; *m/e* 264 ($M^{\cdot+}$, 68%), 155 ($M^{\cdot+}$-PhS, 100%).

p-*Tolyl benzenethiolsulfonate* **3c**; mp 52° (lit.[19c] 54°), IR ($CHCl_3$, cm^{-1}) 3030, 1598, 1498, 1450, 1330 (SO_2), 1145 (S=O), MS; *m/e* 264 ($M^{\cdot+}$, 39%), 139 ($M^{\cdot+}$-PhSO, 100%).

p-*Tolyl* p-*chlorobenzenethiolsulfonate* **3e**: mp 129–131°, IR (KBr, cm^{-1}) 3080, 1590, 1570, 1490, 1470, 1320 (SO_2), 1300 (SO_2), 1140 (S=O), MS; *m/e* 300 ($M^{\cdot +}$ + 2, 7%), 298 ($M^{\cdot +}$, 18%), 139 ($M^{\cdot +}$-*p*-ClC_6H_4SO, 100%). Found: C, 52.25; H, 3.74. Calc. for $C_{13}H_{11}O_2S_2Cl$; C, 52.25; H, 3.71%.

p-*Clorophenyl* p-*toluenethiolsulfonate* **3f**; mp 87–88, IR (KBr, cm^{-1}) 3080, 1590, 1567, 1472, 1447, 1390, 1320 (SO_2), 1293 (SO_2), 1140 (S=O), MS; *m/e* 300 ($M^{\cdot +}$ + 2, 17%), 298 ($M^{\cdot +}$, 40%), 155 ($M^{\cdot +}$ − *p*-ClC_6H_4S, 100%). Found: C, 52.13; H, 3.49. Calc. for $C_{13}H_{11}O_2S_2Cl$; C, 52.25; H, 3.71%.

Preparation of sodium thiolate **4**. The distilled thiol (11 mmole) in dry ether was added with syringe to metallic sodium (11 mmole) suspended in dry ether (15 ml) in a well dried and Argon substituted two necked flask equipped with a reflux condenser and the whole mixture was stirred at room temp. until metal Na disappeared with heating to reflux if necessary. The residual white solid after removal of ether and any excess thiol *in vacuo* was washed with dry hexane to remove the remaining thiol, and dried again *in vacuo*. White powder sodium thiolate was obtained nearly quantitatively. This salt must be stored in a refrigerator and in the dark to avoid decomposition. It must be washed again with dry hexane before use.

Preparation of sodium sulfinate **5**. A dry ether soln (*ca* 5 ml) of free sulfinic acid (1.0 mmole) was added with syringe onto chipped metal Na (1.0 mmole) under dry Argon at room temp. The heterogeneous mixture was stirred to dissolve meal Na. Sometimes it is necessary to reflux the mixture. Anhydrated sodium sulfinate, resulted by removal of ether under reduced pressure, was used directly for the reaction with O_2^-.

Reaction with O_2^-. The reaction with O_2^- was carried out in a well dried and Argon substituted two necked flask. A mixture containing substrate (1.0 mmole) and dry 18-crown-6-ether (0.5 mmole for **1** 3, 1.0 mmole for **4**, **5** and **8**) in 7 ml of dry solvent was added slowly onto finely powdered potassium superoxide (1.0–6.0 mmole, see Tables) under Argon at a set temp. for each substrate (see Equations). After the addition the heterogeneous reaction mixture was stirred for a certain prescribed period (see Tables) for each substrate to allow the reaction to complete, by monitoring the reaction by gas or liquid chromatography. When the starting material disappeared, the reaction mixture was poured into cold water containing crushed ice to quench the reaction and the mixture was extracted three times with $CHCl_3$. The combined organic layer was washed with water and dried over $CaCl_2$. After much of solvent was removed under reduced pressure, the $CHCl_3$ soluble organic mixture which contained mainly disulfide and crown ether, was subjected to GC assay.

The aqueous layers were combined and then concentratedto *ca* 10 ml by evaporation. Then excess MeI (*ca* 20 mmole) was added to the aqueous soln, to which MeOH (5 10 ml) was added to make the mixture homogeneous. After stirring the mixture overnight at room temp, it was extracted three times with $CHCl_3$ after evaporation of much of MeOH and subsequent addition of water (30 ml). The combined organic layer was washed with water, dried over $CaCl_2$ and subjected to quantitative GC analysis of the sulfone formed, using a calibration curve.

The combined aqueous layer was concentrated to *ca* 10 ml. After acidification with excess conc. HCl (total volume of solution: less than *ca* 20 ml) *S*-benzylisothiuronium chloride (2.0 mmole), which was prepared by benzyl chloride and thiourea in refluxing 95% EtOH for an hour and was recrystallized from EtOH (mp 139°, lit.[11] 146–8°),§ was added to the aqueous solution and the mixture was heated to dissolve the salt. After standing colorless needles of the *S*-benzylisothiuronium salt of sulfonic acid appeared. This salt was purified by recrystallization from water or CH_3CN.

Authentic samples of sulfones were obtained by the oxidation of the corresponding sulfide with H_2O_2 in AcOH. S-*Benzylisothiuronium methanesulfonate* **14a**: Colorless crystals from water. mp 149° (lit.[11] 149°), IR (KBr, cm^{-1}) 3600–2800, 1640, 1240, 1225, 1210, 1190, 1055, 700, NMR (CD_3OD, δ, external TMS), 2.28 (s, 3H, $CH_3SO_3^-$), 4.00 (s, 2H, -CH_2Ph), 4.34 (s, 4H, -$SC(NH)NH_3^+$), 6.95–7.07 (m, 5H, arom.).

S-*Benzylisothiuronium benzenesulfonate* **14b**; Colorless needles from CH_3CN. mp 152.5–153.5° (lit.[11] 144°), IR (KBr, cm^{-1}) 3500–2750, 1685, 1670, 1445, 1225, 1170, 1125, 1035, 1015. NMR (CD_3OD, δ, external TMS), 3.92 (s, 2H, CH_2Ph), 4.32 (s, 4H, -$SC(NH)NH_3^+$), 6.57–7.44 (m, 10H, arom.).

S-*Benzylisothiuronium* p-*toluenesulfonate* **14c**; Colorless needles from CH_3CN, mp 184–6° (lit.[11] 178°). IR (KBr, cm^{-1}) 3400–2700, 1690, 1665, 1595, 1495, 1450, 1218, 1170, 1125, 1100, 1035, 810, 720. NMR (CD_3OD, δ, external TMS), 1.89 (s, 3H, Ar–CH_3), 3.94 (s, 2H, –CH_2Ph), 4.31 (s, 4H, -$SC(NH)NH_3^+$), 6.72 (d, 2H, arom., J = 8.1 Hz), 6.88 (s, 5H, Ph), 7.22 (d, 2H, arom., J = 8.1 Hz).

S-*Benzylisothiuronium* p-*chlorobenzenesulfonate* **14d**: Colorless needles from CH_3CN. mp 176°, IR (KBr, cm^{-1}) 3600–2800, 1680, 1660, 1470, 1220, 1170, 1030, 1002, 815, 755, 710, 690. NMR (CD_3OD, δ, external TMS), 3.93 (s, 2H, –CH_2Ph), 4.32 (s, 4H, –$SC(NH)NH_3^+$), 6.80–7.13 (m, 7H, Ph and p-ClC_6H_4, J = 7.8 Hz). Found: C, 47.05; H, 4.12; N, 7.81. Calc. for $C_{14}H_{15}N_2O_3S_2Cl$: C, 46.85; H, 4.21; N, 7.80%.

Isolation of bis(*arythio*)*acetonitrile* **15**; A side product **15** friom the reaction of disulfide with O_2^- in CH_3CN was isolated and purified by column chromatography (eluent; hexane:chloroform:ethyl acetate = 4:1:1, on silica gel, R_f = *ca* 0.7) of the residue of organic extract of the reaction mixture, and was obtained as pale yellow viscous oil.

Bis(*phenylthio*)*acetonitrile* **15a**; IR (neat, cm^{-1}) 3060, 2920, 2230 (C≡N), 1580, 1475, 1439, 1022, 760 NMR ($CDCl_3$, δ, TMS), 4.97 (s, 1H, $-\mathrm{CH}\langle$), 7.30–7.75 (m, 10H, arom.). MS; *m/e* 257 ($M^{\cdot +}$, 18%), 148 ($M^{\cdot +}$-PhS, 100%). Found: C, 65.46; H, 4.31; N, 5.44. Calc. for $C_{14}H_{11}NS_2$: C, 65.33; H, 4.30; N, 5.44%.

Bis(p-*tolylthio*)*acetonitrile* **15b**; IR (neat, cm^{-1}) 3020, 2915, 2860, 2225 (C≡N), 1595, 1490, 1442, 1400, 808. NMR ($CDCl_3$, δ, TMS), 2.31 (s, 6H, –CH_3), 4.61 (s, 1H, $-\mathrm{CH}\langle$), 7.03 (d, 4H, arom. J = 7.6 Hz), 7.37 (d, 4H, arom. J = 7.6 Hz). MS; *m/e* 285 ($M^{\cdot +}$, 28%), 162 ($M^{\cdot +}$-*p*-tolS, 100%). Found: C, 67.33; H, 5.23; N, 4.92. Calc. for $C_{16}H_{15}NS_2$: C, 67.33; H, 5.29; N, 4.90%.

Alkaline autoxidation of diphenyldisulfide. A mixture of diphenyldisulfide (2.4 mmole), 85% KOH (12 mmole) and 18-crown-6-ether (2.4 mmole) in pyridine-water (6 ml, 2:1) was stirred for 20 h at room temp. under O_2. The resulting reaction mixture was subjected to the same quantitative analysis as used in "Reaction with O_2^-". Yields of methyl phenyl sulfone and *S*-benzylisothiuronium benzenesulfonate were 50% and 41%, respectively.

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