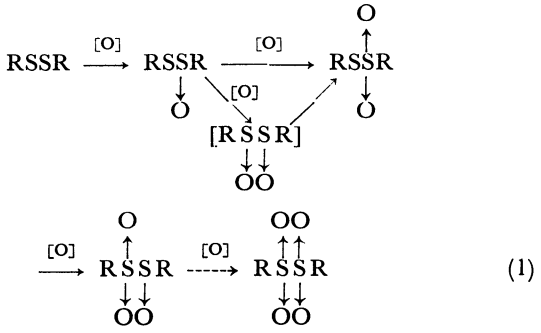
# Oxidation of Unsymmetrical Disulfide and Thiosulfinic S-Esters with Peroxy Acids. Search for Formation of α-Disulfoxide as An Intermediate in the Electrophilic Oxidation of Thiosulfinic S-Ester[1]

Shigeru OAE,* Toshikazu TAKATA, and Yong Hae KIM[2]
*Department of Chemistry, The University of Tsukuba, Sakura-mura, Ibaraki 305*
(Received January 7, 1982)

Oxidation of an unsymmetrical disulfide, methyl phenyl disulfide, with peroxy acids takes place mainly at more electron-rich sulfur atom to form thiosulfinic *S*-ester at the first stage, while oxidation of unsymmetrical thiosulfinic *S*-ester with peroxy acids gives usually four thiosulfonic *S*-esters, together with sulfinic and sulfonic acids, further oxidation products. Oxidation of *S*-methyl benzenethiosulfinate **6** affords, as one of the products, *S*-phenyl methanethiosulfonate **11**, in which the original sulfinyl oxygen is brought into methanesulfonyl group. A small amount of *S*-phenyl benzenethiosulfonate **9** (or benzenesulfonic acid **15**) is obtained in the oxidation of *S*-phenyl methanethiosulfinate **7**. $^{18}O$-Label of the starting thiosulfinic *S*-ester **6** was found to be incorporated to some extents into all four products, *i.e.* **8**—**11**, while a part of $^{18}O$-label of *S*-phenyl methanethiosulfinate **7** was also observed in *S*-phenyl benzenethiosulfonate **9** and benzenesulfonic acid **15**, although most of $^{18}O$-label of **7** was incorporated into *S*-phenyl methanethiosulfonate **11**. Thiosulfinic *S*-esters are stable and do not undergo disproportionation and $^{18}O$-exchange under the conditions. These observations suggest the formation of α-disulfoxide as an intermediate in the oxidation of thiosulfinic *S*-ester to thiosulfonic *S*-ester, especially in the oxidation of **6**, although no peak corresponding to α-disulfoxide was observed directly in the NMR spectra taken during the oxidations of a few thiosulfinic *S*-esters with peroxy acids. Mechanism of the oxidation is discussed.

Oxidation of disulfide is considered to proceed *via* various stable intermediates as shown in Eq. 1. When the disulfide is unsymmetrical, oxidation with peroxy acids usually affords two regioisomeric thiosulfinic *S*-esters (thiolsulfinates) as the initial oxidation products, of which the ratio depends on the electron density of the sulfur atom, *i.e.* the more electron-rich sulfur atom is known to be oxidized predominantly.[3a,b] However, when the electron-rich sulfur atom is substituted by a bulky group, the ratio is known to be controlled by the steric effect instead of the electronic effect.[3]



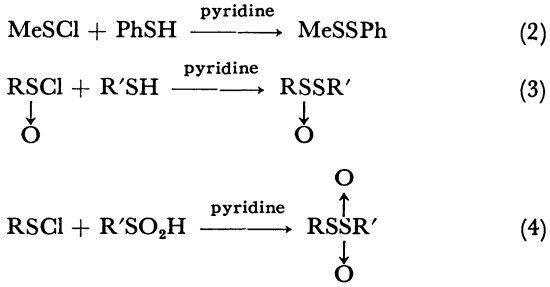
(1)

Mechanism of further oxidation of the thiolsulfinate has long been a matter of controversy, especially as to the question whether or not the oxidation of thiolsulfinate proceeds *via* forming "α-disulfoxide" as an intermediate. α-Disulfoxides have been long proposed as either stable products or intermediates in the oxidations of both disulfides[4,5] and thiolsulfinates.[5] Since the sulfenyl sulfur of thiolsulfinate is considered to be more prone to be oxidized than the sulfinyl sulfur, intermediary formation of α-disulfoxide has been believed in the oxidation of cystine.[5f-j] The fact that no one has succeeded in obtaining α-disulfoxide despite numerous attempts,[5k] by Barnard,[5b] Modena *et al.*,[5d,e] Kice and Chau,[5a] and others, is now explained in terms of the unusually small bond energy of "α-disulfoxide."[5a]

In order to understand the mechanism of oxidation of disulfide and thiolsulfinate with peroxy acids, the oxidations of unsymmetrical disulfide and thiolsulfinates have been investigated and evidence for formation of α-disulfoxide as an intermediate has now been obtained in the oxidation of thiolsulfinate. This paper describes our experimental observations and subsequent discussions.

## Results

Methyl phenyl disulfide **3**, an unsymmetrical disulfide, was prepared by the reaction of methanesulfenyl chloride with thiophenol in the presence of pyridine (Eq. 2).[6] Unsymmetrical thiolsulfinates **6** and **7** were prepared by treating sulfinyl chloride with thiol (Eq. 3) according to the usual method.[7] In the same manner, authentic samples of thiosulfonic *S*-esters (thiolsulfonates) **9**, **10**, and **11** were synthesized by treating sulfenyl chloride with sulfinic acid in the presence of pyridine (Eq. 4).[7]



(2)

(3)

(4)

The disulfide and the thiolsulfinate thus prepared were oxidized with either $H_2O_2$ in AcOH or *m*-chloroperbenzoic acid (MCPBA) in $CH_2Cl_2$.

Product analysis was performed by using NMR, GLC, and HPLC. As shown in Fig. 1, fortunately all these compounds were able to be separated by HPLC. $^1H$-

Table 1. NMR chemical shifts of compounds having methyl group ($\delta$ TMS, at *ca.* 27 °C)

| Compound | Solvent | | | |
|---|---|---|---|---|
| | $CDCl_3$ | $CCl_4$ | $CD_3COOD$ ($-D_2O$) | Others |
| MeSSMe **1** | 2.40 | 2.30[a] | | |
| MeSSMe **4** | [2.66<br>[2.98 | [2.67[a]<br>[3.00[a] | [2.36<br>[2.72 | |
| MeS(O)SMe **8** | [2.69<br>[3.30 | [2.69[b]<br>[3.28[b] | [2.36<br>[3.02 | |
| PhSSMe **3** | 2.37 | | 2.05 | |
| PhSSMe **6** | 2.53 | | 2.24 | |
| PhSSMe **7** | 2.90 | | 2.72 | |
| PhSSMe **10** | 2.48 | | 2.15 | |
| PhSSMe **11** | 3.15 | | 2.90 | |
| $MeSO_2H$ **12** | 2.70 | 2.93[b] | [2.39<br>[2.44<br>(+$D_2O$) | 2.48($D_2O$) |
| $MeSO_2Na$ | | | | [2.30($D_2O$)<br>[2.34($D_2O$)[b] |
| $MeSO_3H$ **14** | 3.18<br>(2.90)[a] | | 2.68 | [2.98($D_2O$)<br>[2.90(DMSO-$d_6$)[a] |
| $MeSO_3Na$ | | | | 2.80($D_2O$) |

a) E. Block, "Reactions of Organic Sulfur Compounds," Academic Press, New York (1978), p. 297. b) R. O. Norton, G. M. Beverly, and I. B. Douglass, *J. Org. Chem.*, **32**, 3645 (1967).

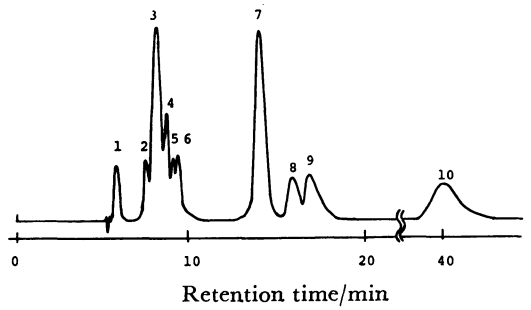
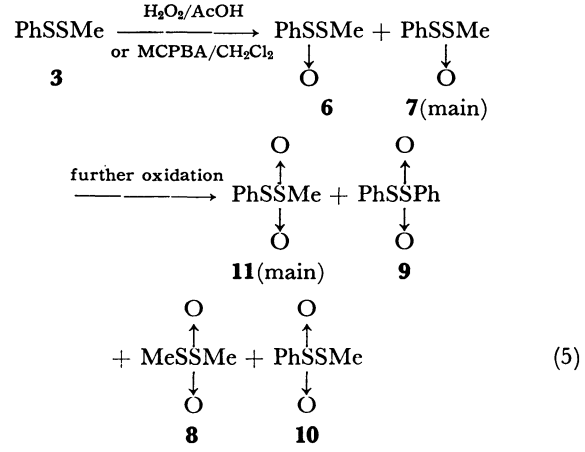



Fig. 1. High pressure liquid chromatography by Yanaco Model L-1030 at room temperature.
Column: Yanaco Gel 5510, carrier: MeOH, pressure: 125 kg/cm², flow rate: 16.1 ml/h.
Peak 1: $MeSS(O)_2Me$(**8**), 2: MeSSMe(**1**), 3: $PhSS(O)_2$-Me(**11**), 4: $PhS(O)_2SMe$(**10**), 5: PhSS(O)Me(**7**), 6: PhS(O)SMe(**6**), 7: $PhSS(O)_2Ph$(**9**), 8: PhSS(O)Ph-(**5**), 9: PhSSMe(**3**), 10: PhSSPh(**2**).
Peaks of $MeSO_2H$(**12**), $MeSO_3H$(**14**), $PhSO_2$(**13**), and $PhSO_3H$(**15**) appear earlier than that of peak of **8**, while peak of MeSS(O)Me(**4**) appears between peaks 1 and 2.

NMR chemical shifts of methyl groups of these compounds are listed in Table 1 together with the NMR data of the related compounds.

*Oxidation of Disulfide* **3**. When methyl phenyl disulfide **3** was treated with $H_2O_2$ in AcOH, *S*-phenyl methanethiosulfinate **7** was formed predominantly over *S*-methyl benzenethiosulfinate **6**, as shown in Figs. 2 and 3, which are drawn following the changes of NMR signals of methyl groups of **3** and the other products during the oxidation of **3** with 30% $H_2O_2$ in deuterated acetic acid (Eq. 5). When the oxidation of **3** was followed




(5)

by HPLC, the products, which could not be detected in GLC, were detected in NMR. Comparison of Figs. 2 and 3 reveals that the rate of disappearance of **3** is very sensitive to the change of reaction temperature. Since the oxidant used was substantially in excess over the disulfide **3**, the oxidation proceeded further. In the oxidation of the following step, the major product isolated was *S*-phenyl methanethiosulfonate **11**, accompanied with quite a small amount of *S*-methyl benzenethiosulfonate **10**, as shown in Figs. 2 and 3. Besides the products having original S–S linkage (*i.e.* **10** and **11**), formations of symmetrical thiolsulfinates, both *S*-methyl

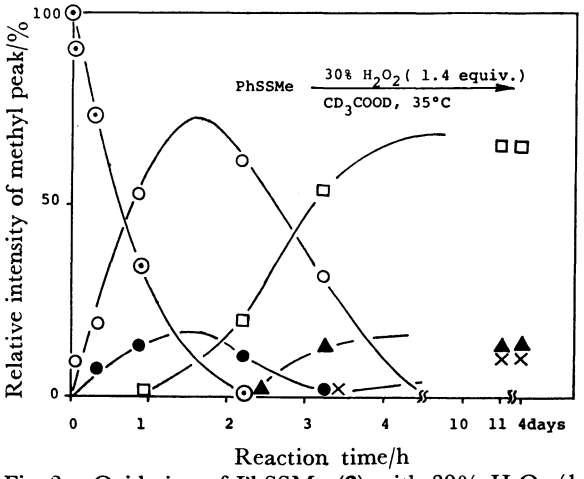



Fig. 2. Oxidation of PhSSMe (**3**) with 30% $H_2O_2$ (1.4 equiv.) in acetic acid at 35 °C.
Marks used in figures are common and as follows: ◑: MeSSMe (**1**), ⊙: PhSSMe (**3**), △: MeS(O)SMe (**4**), ●: PhS(O)SMe (**6**), ○: PhSS(O)Me (**7**), ▲: $MeSS(O)_2Me$ (**8**), ■: $PhS(O)_2SMe$ (**10**), □: $PhSS(O)_2Me$ (**11**), ◒: $MeSO_2H$ (**12**), ×: $MeSO_3H$(**14**).

TABLE 2. OXIDATION PRODUCTS OF PhSSMe (**3**)

| Entry | Oxidation system | Temp/°C | Time/h | Product (mol%)[a] | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | | **3** | **7** | **9** | **10** | **11** | **14** | **15** |
| 1 | 30% $H_2O_2$(1.4 equiv.) $CD_3COOD$ | 35 | 10 | 0 | 0 | 17 | 11 | 61 | 10 | ≈0 |
| 2 | 30% $H_2O_2$(1.5 equiv.) $CD_3COOD$ | 18 | 77 | 0 | 31 | 13 | 5 | 26 | ≈0 | ≈0 |
| 3 | 30% $H_2O_2$(2.4 equiv.) $CD_3COOD$ | 35 | 5 | 0 | 0 | 27 | 2 | 30 | 38 | — |
| 4 | MCPBA (1.0 equiv.) $CH_2Cl_2$ | 0 | 24 | 15 | 65 | ≈0 | ≈0 | 15 | — | —[b] |

a) Determined by NMR. b) Determined by HPLC.

TABLE 3. OXIDATION PRODUCTS OF PhSS(O)Me (**7**)

| Entry | Oxidation conditions | | | Product (mol%)[a] | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | System | Temp/°C | Time/h | **7** | **8** | **9** | **11** | **14** | **15** |
| 1 | 30% $H_2O_2$(1.2 equiv.) $CD_3COOD$ | 35 | 1 | ≈0 | 5 | 14 | 36 | 30 | 17 |
| 2 | 30% $H_2O_2$(1.2 equiv.) $CD_3COOD$ | 18 | 15 | ≈0 | 2 | 11 | 46 | 28 | 10 |
| 3 | 30% $H_2O_2$(1.0 equiv.) AcOH | 50 | 2/3 | —[c] | — | — | 55[b] | — | — |
| 4 | 30% $H_2O_2$(1.3 equiv.) AcOH | 19 | 11 | ≈0 | Trace | 12 | 46 | 31 | 5 |
| 5 | 30% $H_2O_2$(1.5 equiv.) AcOH | 25 | 13 | ≈0 | Trace | 20 | 27 | 45[d] | Trace |
| 6 | 30% $H_2O_2$(10 equiv.) AcOH | 70 | 5 | 0 | 0 | 0 | 0 | 50 | 50 |
| 7 | MCPBA(1.2 equiv.) $CH_2Cl_2$ | 0 | 7.5 | 17 | Trace | 8 | 48 | 23[e] | Trace |
| 8 | MCPBA(1.3 equiv.) $CH_2Cl_2$ | 0 | 3 | 21 | Trace | 15 | 49 | 15 | Trace |

a) Yield was determined by NMR, GLC, and HPLC. b) Yield after recrystallization from hexane. c) —: Not determined. d) Containing $MeSO_2H$ (16%). e) Containing $MeSO_2H$(9%).

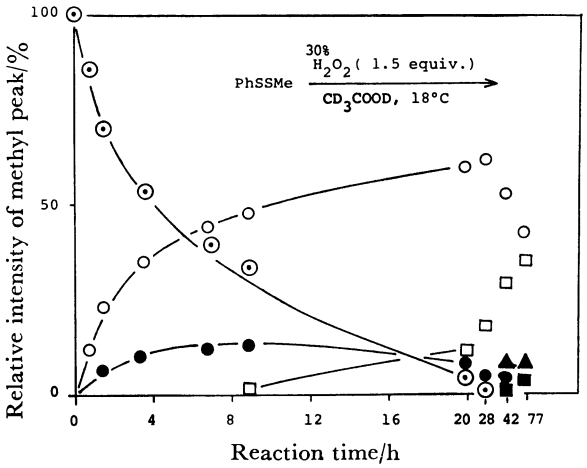



Fig. 3. Oxidation of PhSSMe with 30% $H_2O_2$ (1.5 equiv.) in acetic acid at 18 °C.
⊙: PhSSMe (**3**), ○: PhSS(O)Me (**7**), ●: PhS(O)SMe (**6**), □: $PhSS(O)_2Me$ (**11**), ■: $PhS(O)_2SMe$ (**10**).

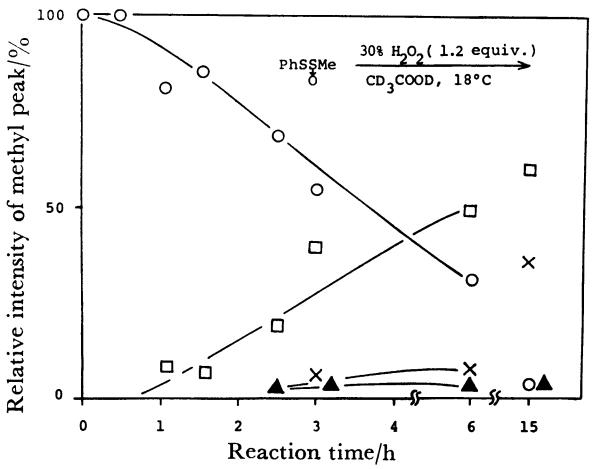



Fig. 4. Oxidation of PhSS(O)Me(**7**) with 30% $H_2O_2$ (1.2 equiv.) in acetic acid at 18 °C.
○: PhSS(O)Me (**7**), □: $PhSS(O)_2Me$ (**11**), ▲: $MeSS(O)_2Me$ (**8**), ×: $MeSO_3H$ (**14**).

methanethiosulfonate **8** and *S*-phenyl benzenethiosulfonate **9**, were also confirmed by GLC. Both methanesulfonic acid **14** and benzenesulfonic acid **15** were also detected by NMR and HPLC respectively, and found to be the end products upon oxidation with additional $H_2O_2$.

Oxidation products of **3** are listed in Table 2, which shows that nearly the same result is obtained in MCPBA oxidation of **3** (entry 4). In direct NMR study as shown in Figs. 2 and 3, the rate of the oxidation of **3** was comparable to those of **6** and **7**.[5d]

The methyl signal, corresponds to α-disulfoxide (PhS(O)S(O)Me, [A]) which may be formed by the oxidation of more electron-rich sulfenyl sulfur atom of thiolsulfinate (*e.g.* **6** or **7**), was not observed in the NMR spectra obtained during the oxidation of **3**.

On the other hand, in NMR study on the oxidation of symmetrical disulfide (dimethyl disulfide, **1**) with $H_2O_2$ in deuterated acetic acid, the products observed through NMR spectra were at first only *S*-methyl methanethiosulfinate **2**, then **8** and eventually **14**, in the final stage with no other methyl peak. The same transformation was observed in the oxidation of **1** to **8** with MCPBA in $CDCl_3$.

*Oxidation of Thiosulfinic S-Esters* **6** *and* **7**: In the oxidation of **7** with $H_2O_2$ in AcOH or *m*-chloroperbenzoic acid (MCPBA) in $CH_2Cl_2$, **11** was obtained as the major product, along with other thiolsulfonates such as **8** and **9**, and acids (**12**—**15**) (Table 3, Fig. 4) (Eq. 6). The

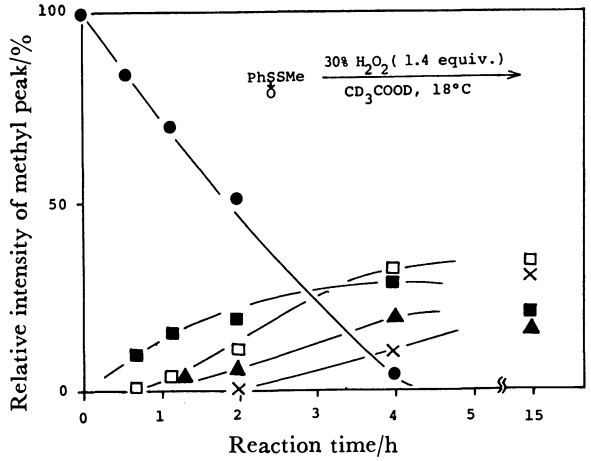



Fig. 5. Oxidation of PhS(O)SMe (**6**) with 30% $H_2O_2$ (1.4 equiv.) in acetic acid at 18 °C.
●: PhS(O)SMe (**6**), ■: $PhS(O)_2SMe$ (**10**), □: $PhSS(O)_2Me$ (**11**), ▲: $MeSS(O)_2Me$ (**8**), ×: $MeSO_3H$ (**14**).

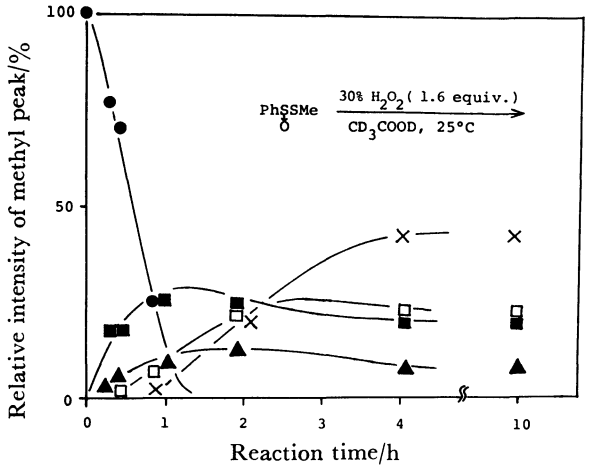


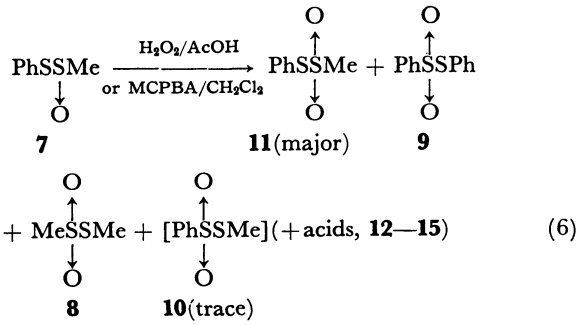

Fig. 6. Oxidation of PhS(O)SMe (**6**) with 30% $H_2O_2$ (1.6 equiv.) in acetic acid at 25 °C.
●: PhS(O)SMe (**6**), ■: $PhS(O)_2SMe$ (**10**), □: $PhSS(O)_2Me$ (**11**), ▲: $MeSS(O)_2Me$ (**8**), ×: $MeSO_3H$ (**14**).

Table 4. Oxidation products of PhS(O)SMe (**6**)

| Entry | Oxidation conditions: System | Temp/°C | Time/h | Product (mol%)[a]: **6** | **8** | **9** | **10** | **11** | **14** | **15** |
|---|---|---|---|---|---|---|---|---|---|---|
| 1 | 30% $H_2O_2$(1.2 equiv.) AcOH | 22 | 5 | — | 13[b] | 18[b] | — | 22[b] | — | — |
| 2 | 30% $H_2O_2$(1.4 equiv.) $CD_3COOD$ | 35 | <1 | 0 | 8 | 21 | 12 | 21 | 28 | 7 |
| 3 | 30% $H_2O_2$(1.4 equiv.) $CD_3COOD$ | 18 | <15 | 0 | 10 | 21 | 12 | 23 | 29 | 5 |
| 4 | MCPBA(1.1 equiv.) $CH_2Cl_2$ | 20 | 20 | ≈0 | 14 | 14 | 25 | 34 | 0 | —[c] |
| 5 | MCPBA(1.2 equiv.) $CH_2Cl_2$ | 0 | 4.5 | 6 | 7 | 7 | 27 | 32 | 10 | — |
| 6 | MCPBA(1.2 equiv.) $CH_2Cl_2$ | 0 | 9 | ≈0 | Trace | 15 | 13 | 30 | 30[d] | —[c] |

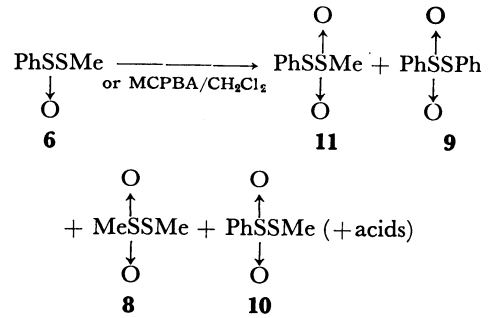
a) Yield was determined by NMR, GLC, and LLC. b) Isolated and purified yield. c) Unidentified methyl peak (14%) was observed. d) Containing $MeSO_2H$ (12%).

yield of **10** was only a trace or none in both oxidations. Although methyl signal of "α-disulfoxide" is expected to appear at 2.6—2.9 ppm (in $CD_3COOD$), no signal was observed in such a region during the oxidation of **7**. While the oxidation of **7** with 1.2 equiv. of 30% $H_2O_2$ was completed within 1 h at temperatures higher than 35 °C, the products obtained in the oxidation with ten equivalents of $H_2O_2$ in AcOH at 70 °C for 5 h, were only the sulfonic acids **14** and **15** as shown in Table 3 (entry 6).




(6)

Figures 5 and 6 show the changes of the NMR signals of the methyl groups of the starting thiolsulfinate and the products during the oxidation of **6** with $H_2O_2$ in $CD_3COOD$. One of the final products was also found to be **14**, though thiolsulfonates still remained. The oxidation of **6**, during which considerably complex methyl peaks were observed in NMR spectra, gave eventually two symmetrical and two unsymmetrical thiolsulfonates (**8**—**11**), along with further oxidation products (*i.e.* acids: **12**—**15**) (Eq. 7). This result is in contrast to that in the oxidation of **7**, and the oxidation of **6** gave nearly the same amounts of the four thiol-




(7)

sulfonates.† Yields of products in the oxidation of **6** are listed in Table 4. Inspection of the data in Table 4

† *S*-Methyl benzenethiosulfonate (**10**) was not confirmed at first[1] but then identified, since we found later that the $^1$H-NMR chemical shift of **10** was unusually *higher* than that of **6**. (T. Takata, Y. H. Kim, S. Oae, and K. T. Suzuki, *Tetrahedron Lett.*, **1978**, 4303).

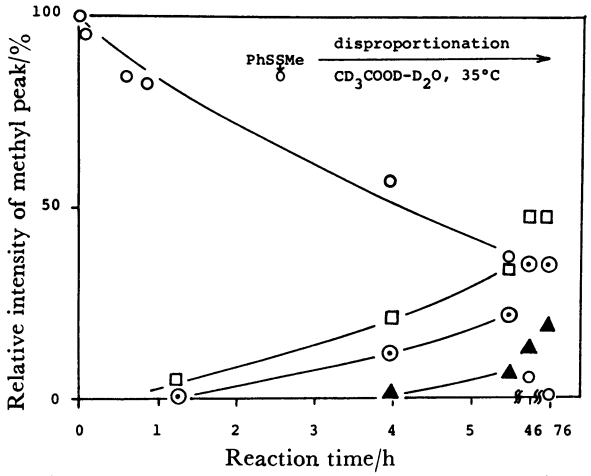



Fig. 7. Thermal Decomposition of PhSS(O)Me (**7**) in acetic acid–water at 35 °C.
○: PhSS(O)Me (**7**), □: PhSS(O)$_2$Me (**11**), ⊙: PhSSMe (**3**), ▲: MeSS(O)$_2$Me (**8**).

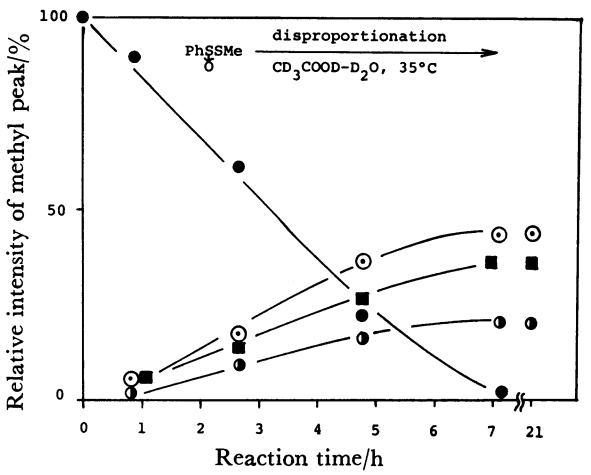



Fig. 8. Thermal Decomposition of PhS(O)SMe (**6**) in acetic acid–water at 35 °C.
●: PhS(O)SMe (**6**), ⊙: PhSSMe (**3**), ■: PhS(O)$_2$SMe (**10**), ◑: MeSSMe (**1**).

TABLE 5. $^{18}O$-TRACER EXPERIMENTS IN THE OXIDATION OF PhSS(O)Me (**7**)

| Entry | Excess $^{18}O$ content of **7** % | Oxidant | Reaction Temp/°C | Reaction Time/h | Product | Excess[a] $^{18}O$ content % | Incorporated $^{18}O$ % |
|---|---|---|---|---|---|---|---|
| 1a | PhSSMe ↓ O 0.615 | 1.3 equiv. $H_2O_2$ | 25 | 13 | **11** | 0.376 | 122 |
| | | | | | **9** | 0.076 | 24 |
| 1b | 0.549 | 10 equiv. $H_2O_2$ | 70 | 5 | $PhSO_2NH_2$ | 0.037 | 6.7[b] |
| 2a | 0.615 | 1.2 equiv. MCPBA | 0 | 7.5 | **11** | 0.342 | 112 |
| | | | | | **9** | 0.259 | 84 |
| 2b | 0.451 | 1.3 equiv. MCPBA | 0 | 3 | **11** | 0.211 | 94 |
| | | | | | **9** | 0.181 | 80 |

a) $^{18}O$ Content of $CO_2$. b) 20.1% for $PhSO_3H$ (Eq. 11).

reveals that the oxidation of **6** with MCPBA in $CH_2Cl_2$ gives nearly the same result as that with $H_2O_2$ in AcO H No methyl peak corresponding to α-disulfoxide (at 2.6—2.9 ppm) was also observed in NMR spectra during the oxidation.

Since thiolsulfinate has been known to disproportionate readily to afford mainly a mixture of disulfides and thiolsulfonates,[8] **7** was heated in NMR tube in $CD_3COOD$–$D_2O$ system at 35 °C for *ca.* 76 h and the disproportionation of **7** was found to proceed so slowly (Eq. 8, Fig. 7) that its contribution in product distribution can be neglected during the oxidation. Main products in the disproportionation of **7** were **11** and **3**, together with **8** and **2** as minor products. It is interesting to note that in the disproportionation of *S*-phenyl methanethiosulfinate **7** neither *S*-methyl not *S*-phenyl benzenethiosulfonates **9** and **10** was obtained.

$$\underset{\underset{\mathbf{7}}{\underset{\downarrow}{\overset{\uparrow}{O}}}}{PhSSMe} \xrightarrow[CD_3COOD\text{-}D_2O,\ 35\,^\circ C,\ 76\ h]{\text{disproportionation}} \underset{\underset{\mathbf{11}(42\%)}{\underset{\downarrow}{\overset{\uparrow}{O}}}}{PhSSMe} + \underset{\underset{\mathbf{8}(14\%)}{\underset{\downarrow}{\overset{\uparrow}{O}}}}{MeSSMe} + PhSSMe + PhSSPh + MeSSMe \quad (8)$$
$$\mathbf{3}(31\%) \quad \mathbf{2}(13\%) \quad \mathbf{1}(\approx 0\%)$$

In the disproportionation of **6** in $CD_3COOD$–$D_2O$ system at 35 °C, the same trend was observed as in the case of **7** (Eq, 9, Fig. 8). Namely, there was no product having methanesulfonyl group but only benzenesulfonyl derivatives **9** and **10** are the oxidation products. As shown in Fig. 6, Fig. 8 and Table 4, the disproportionation of **6** at 35 °C was much slower than the oxidation of **6** at the same temperature (≈1 h, Table 4, entry 2). Meanwhile, disproportionation was confirmed not to occur at 18—20 °C for 10—20 h.

$$\underset{\underset{\mathbf{6}}{\underset{\downarrow}{\overset{\uparrow}{O}}}}{PhSSMe} \xrightarrow[CD_3COO\text{-}D_2O,\ 35\,^\circ C]{\text{disproportionation}} \underset{\underset{\mathbf{10}(30\%)}{\underset{\downarrow}{\overset{\uparrow}{O}}}}{PhSSMe} + \underset{\underset{\mathbf{9}(10\%)}{\underset{\downarrow}{\overset{\uparrow}{O}}}}{PhSSPh} + PhSSMe + MeSSMe + PhSSPh \quad (9)$$
$$\mathbf{3}(36\%) \quad \mathbf{1}(17\%) \quad \mathbf{2}(7\%)$$

*$^{18}O$-Tracer Experiments.* In order to examine the oxygen transfer of **6** or **7** to the products, **11** or **10**, $^{18}O$-tracer experiments were carried out.

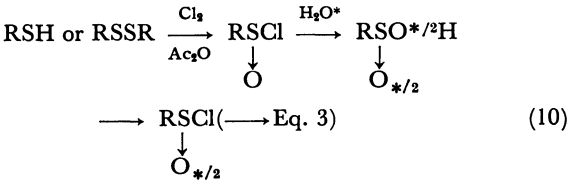
$^{18}O$-Labelled thiolsulfinate (**6** and **7**) were prepared (Eq. 3) by treating thiols with $^{18}O$-labelled sulfinyl chlorides which were prepared according to the following reactions (Eq. 10), as described in detail in experimental section.

$^{18}O$-Labelled **6** and **7** were treated with an equimolar

Table 6. $^{18}O$-Tracer experiments in the oxidation of PhS(O) SMe (**6**)

| Entry | Excess $^{18}O$ content of **6** % | Oxidant | Reaction Temp/°C | Reaction Time/h | Product | Excess $^{18}O$ content % | Incorporated $^{18}O$ % |
|---|---|---|---|---|---|---|---|
| 1a | PhSSMe (↓O) 0.636% | 1.4 equiv. $H_2O_2$ | 20 | 5 | **11** | 0.186 | 58 |
| | | | | | **9** | 0.378 | 118 |
| 1b | 0.578 | 1.2 equiv. $H_2O_2$ | 20 | 10 | **11** | 0.175 | 60 |
| | | | | | **9** | 0.354 | 122 |
| 1c | 0.515 | 1.2 equiv. $H_2O_2$ | 20 | 6 | **11** | 0.178 | 70 |
| | | | | | **9** | 0.319 | 124 |
| | | | | | **8** | 0.170 | 68 |
| 1d | 0.578 | 1.3 equiv. $H_2O_2$ | 20 | 9 | **11** | 0.188 | 66 |
| | | | | | **9** | 0.342 | 118 |
| 1e | 0.578 | 1.3 equiv. $H_2O_2$ | 20 | 5.5 | **11** | 0.169 | 58 |
| | | | | | **10** | 0.294 | 102 |
| 2a | 0.578 | 1.2 equiv. MCPBA | 0 | 9 | **11** | 0.316 | 109 |
| | | | | | **9** | 0.397 | 137 |
| 2b | 0.564 | 1.2 equiv. MCPBA | 0 | 3 | **11** | 0.286 | 102 |
| | | | | | **9** | 0.311 | 110 |

amount of 30% $H_2O_2$ in AcOH or with an equivalent of MCPBA in $CH_2Cl_2$. After the disappearance of most



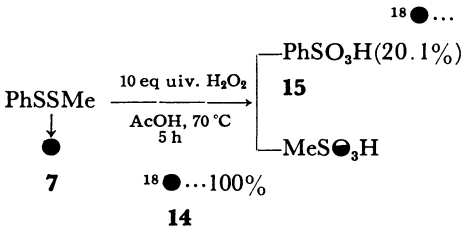
(10)

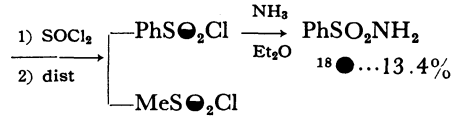
of **6** and **7** (monitored by TLC or HPLC), the reaction mixture was treated according to the usual work-up. The mixture of organic products was subjected directly to column chromatography (on silica gel, eluent : $CHCl_3$:EtOAc : hexane=1 : 1 : 4) to separate into each product component. The products thus obtained and the starting materials were then subjected to the routine $^{18}O$-analyses. The results are summarized in Tables 5 and 6.

While $^{18}O$-labelled oxygen of **7** was found to be retained nearly completely in the major product **11**, the minor product **9** was also incorporated with a small amount of $^{18}O$-label during the oxidation of **7** with 30% $H_2O_2$ in AcOH (Table 5, entry 1a). A similar trend was also seen in the $^{18}O$ distributions among the products formed in the oxidation of **7** with MCPBA (Table 5, entry 2). However, the $^{18}O$ incorporation of the minor product **9** was considerably larger in the oxidation with MCPBA than that with $H_2O_2$.

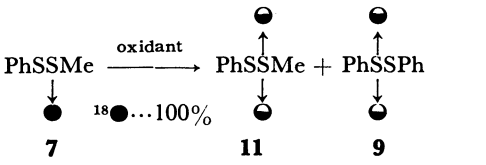
In another way to examine the possible oxygen transfer from methanesulfinyl group of **7** to the phenylthio moiety in the oxidation of **7** with $H_2O_2$, both acids **14** and **15** obtained under vigorous oxidation conditions (10 equiv. $H_2O_2$, 70 °C, 5 h: Table 5, entry 1b), were converted to the corresponding sulfonyl chlorides with $SOCl_2$ (eq. 11). Benzenesulfonyl chloride was purified by distillation and then treated with gaseous ammonia in dry ether to afford the sulfonamide. $^{18}O$-Analysis of the sulfonamide showed that benzenesulfonic acid contained 20% of the original $^{18}O$-label of **7**.

The $^{18}O$-tracer experimental results in the oxidations



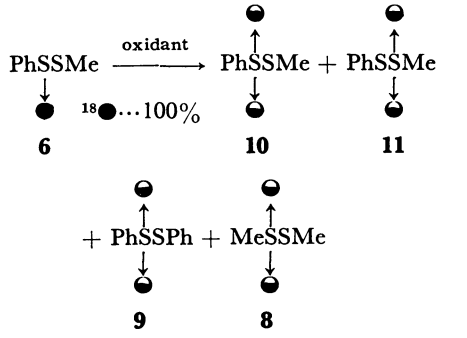
(11)



(12)

$^{18}O$-Incorporation

| Oxidant | **11** | **9** |
|---|---|---|
| $H_2O_2$/AcOH | 122% | 24% |
| MCPBA/$CH_2Cl_2$ | 94—112% | 80—84% |



(13)

$^{18}O$-Incoroporation

| Oxidant | **10** | **11** | **9** | **8** |
|---|---|---|---|---|
| $H_2O_2$/AcOH | 102% | 58—70% | 108—124% | 68% |
| MCPBA/$CH_2Cl_2$ | — | 102—109% | 110—137% | — |

TABLE 7. $^{18}O$ INCORPORATION % OF RECOVERED THIOLSULFINATE **6** IN THE OXIDATION OF **6** WITH $H_2O_2$ IN AcOH

| Entry | Excess $^{18}O$ content of **6** / % | Oxidation system | Reaction Temp/°C | Reaction Time/h | Excess $^{18}O$ content of **6** recovered/% (Incorporated %) |
|---|---|---|---|---|---|
| 1 | 0.53 | No $H_2O_2$/AcOH–$H_2O$ | 19 | 3 | 0.56 (106) |
| 2 | 0.53 | 1.2 equiv. 30% $H_2O_2$/AcOH | 20 | 0.5 | 0.52 ( 98) |
| 3 | 0.53 | 1.2 equiv. 30% $H_2O_2$/AcOH | 20 | 2.5 | 0.50 ( 94) |

of **7** are summarized in Eq. 12. Meanwhile, as summarized in Table 6 and Eq. 13, all four thiolsulfonates obtained in the oxidation of **6** were incorporated with considerable amounts of the original $^{18}O$-label of the $^{8}O$-labelled **6**. A significant product **11**, obviously oxygen-transfered oxidation product formed from **6**, contained 58—70% of the original $^{18}O$-label in the oxidation of **6** with $H_2O_2$/AcOH, while, 100% of the original $^{18}O$-label was incoroporated into **11** in the oxidation with MCPBA/$CH_2Cl_2$. More than 100% of the original $^{18}O$-label of **6** was incorporated into **9** and the incorporation was a little greater in the oxidation with MCPBA/$CH_2Cl_2$ than in that with $H_2O_2$/AcOH.

In both oxidations of $^{18}O$-labelled **6** and **7**, the following observations may be noteworthy. i) The thiolsulfonate which was formed by apparent simple oxidation of sulfinyl sulfur, keeping the original S–S bond of the thiolsulfinate, *i.e.* **10**, in the case of **6** or **11** in the case of **7**, retained completely the original $^{18}O$-label in the starting materials, regardless of the oxidation conditions. ii) In the thiolsulfonates in which their sulfonyl groups are originally the sulfenyl groups of the starting thiolsulfinates, *i.e.* **9** (or **15**) from **7** and **8** and **11** from **6**, $^{18}O$-incorporations of **9** from **7** and **11** from **6** in the oxidation with $H_2O_2$/AcOH dramatically increased in the oxidation with MCPBA/$CH_2Cl_2$.

Control experiments show that **6** is sufficiently stable in AcOH–$H_2O$ system in the absence of oxidant for 20 h at 20 °C and no $^{18}O$-label was lost under the conditions (Table 7). The thiolsulfinate **6** recovered after partial oxidation of $^{18}O$-labelled **6** with $H_2O_2$ in AcOH retained almost completely the original $^{18}O$-label of **6** (Table 7).

## Discussion

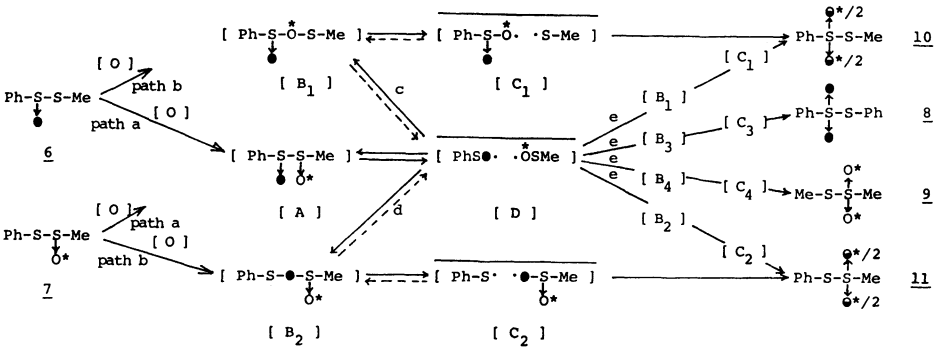
The orientation in the oxidation of unsymmetrical disulfide **3** with peroxy acid or hydrogen peroxide was in complete accordance with the reported results in which the more electron-rich sulfur atom of disulfide is mainly oxidized,[3] since the oxidation of **3** with such an electrophilic oxidant as MCPBA or $H_2O_2$/AcOH is expected to take place on the sulfur atom attached to methyl group of **3**. In direct NMR study no detectable intermediate was observed and therefore the oxidation must proceed *via* usual electrophilic attack of the oxidant at sulfur atom attached to methyl group. Further continuous oxidation gave a mixture of thiolsulfonates which are well-known products in the oxidation of unsymmetrical thiolsulfinate.[5c] The formation of sulfinic and sulfonic acids was confirmed to be derived by further oxidation of thiolsulfonate ($RSO_2SR$) in the control experiments.[9] The fact that there was no observable peak corresponding either to α-disulfoxide ([A]) or other possible intermediates in the NMR spectra during the oxidation, may not rule out the formation of [A] as an intermediate because of the expected instability of [A].[5a]

Since the total amount of **11** is comparable to that of **7** in the oxidation of **3**, **11** seems to be formed *via* direct oxidation of sulfinyl sulfur of **7** without breaking the S–S bond. However, only a trace amount of **10** was detected (*e.g.* Fig. 3) in further oxidation of **3**, during which a substantial amount of **6** was formed. This observation suggests that the oxidation of **6** does not always give **10**. Then a question remains if there is any direct oxidation of the electron-*poor* sulfinyl sulfur of thiolsulfinate to corresponding thiolsulfonate. This question may now be answered by scrutinizing the various data accumulated on the product analyses, NMR studies, and $^{18}O$-tracer experiments in the oxidations of thiolsulfinates, **6** and **7**.

The control experiments on the disproportionation of both **6** and **7** reveal that the oxidations of **6** and **7** are not complicated by the disproportionation. Neither the oxygen migration nor S–O bond fission, was found to occur, although cleavage of S–S bond usually takes place. Even when the cleavage of S–S bond takes place in the disproportionations of both **6** and **7**, there is no thiolsulfonate in which the sulfenyl sulfur of original thiolsulfinate is oxidized among the products (Eqs. 8 and 9). No $^{18}O$-exchange was observed with $^{18}O$-labelled thiolsulfinate under the conditions (Table 7). Thus, no side reaction was observed in the oxidations.

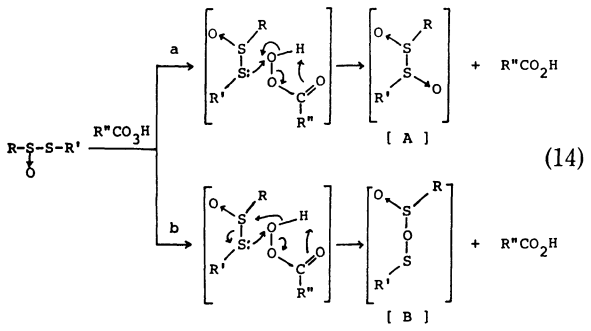
Formation of a trace or none of **10** in the oxidation of **7** is in keeping with the result of the oxidation of **3** with excess $H_2O_2$. Formation of **11** as the main product and little or no formation of **10** in the oxidation of **7** indicate that the oxidation appears to take place mainly at sulfinyl sulfur atom of **7**, although the electron-rich sulfenyl sulfur atom is usually oxidized more readily than the electron-poor sulfinyl sulfur. However, the formation of small amounts of **9** (Eq. 6) from **7** may indicate the possible formation of α-disulfoxide as an intermediate. Especially, formation of a considerable amount of **11** from **6** strongly suggests the intermediary formation of α-disulfoxide. The $^{18}O$-tracer results also support the formation of α-disulfoxide (Tables 5—7).

However, the difference in the product distributions between the two oxidations of **6** and **7** with both $H_2O_2$/AcOH and MCPBA/$CH_2Cl_2$, clearly indicates that the mechanism of the oxidation of **6** is somewhat different from that of **7**. Namely, the *S*-substituent, *i.e.* phenyl *vs.* methyl, may affects substantially the distribution of products. Therefore, the oxidations of **6** and **7** cannot be explained simply by assuming the formation of a common intermediate (*i.e.* α-disulfoxide, [A]). In



1. ●, O* ------ $^{18}O$ or $^{16}O$( one of which is $^{18}O$ )
2. path e: diffusion path
3. [ $B_3$ ]( R= Ph ), [ $B_4$ ]( R= Me ) in [ R-S(=O)-O· ·S-R ]
4. [ $C_3$ ]( R= Ph ), [ $C_4$ ]( R= Me ) in [ R-S(=O)-O-S-R ]

Chart



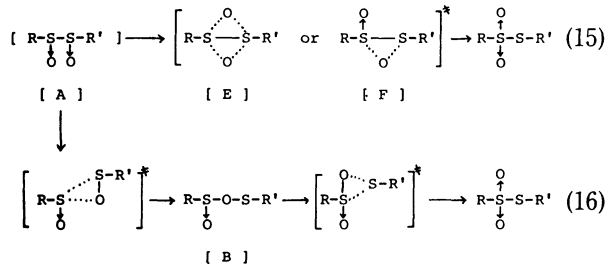
(14)

fact, the yields of the products formed by the cleavage of S–S bond (*i.e.* **8** and **9**) are greater in the oxidation of **6** than that of **7**. This may suggest that the oxidation of **6** proceeds *via* forming an intermediate of which S–S bond cleavage takes place more readily than that which would be formed in the oxidation of **7**.

Based on all these data on the product analyses and $^{18}O$-tracer experiments, a few conceivable mechanistic pathways for the oxidation of unsymmetrical thiolsulfinates are illustrated in Chart. According to this chart, the initial oxidation step may involve the following two paths (Eq. 14). Path a involves the formation of *α*-disulfoxide *via* direct electrophilic attack of oxygen of oxidant, while path b involves the nucleophilic attack of oxygen on the sulfinyl sulfur to result in the oxygen insertion into S–S linkage to form *S*-sulfenyl sulfinate [B] which is considered to be more stable than *α*-disulfoxide. The oxidation of **6** may takes place mainly *via* path *a* to form *α*-disulfoxide, since sulfenyl sulfur of **6** is expected to be rather reactive to the electrophilic oxygen of peroxy acid. Actually, the rate of the oxidation of **6** seems to be slightly faster than that of **7**. This process is in good accordance with Kice's process on the product balance[5a] and explain the substituent effect in this oxidation.

In the mechanistic pathways, the $^{18}O$-exchange process is neglected, since the homolytic cleavage of S–S bond of [A] thus formed would proceed very readily even at a low temperature to give a caged sulfinyl radical pair,[5a] which then recombines immediately to give *O*-sulfenyl sulfinate, [$B_1$] and [$B_2$]. The intermediate [B] must be also unstable and collapse to a caged radical pair [C] which recombines between both sulfur atoms to give thiolsulfonates. Since there is no energy barrier in the recombination of [C] to form stable S–S bond, the recombination of radical pair must be even faster than the diffusion of two radicals out of cage. In fact, no symmetrical disulfide was observed in our direct NMR studies, as reported earlier.[5a,e] On the other hand, since the recombination of two sulfinyl radicals [D] makes energy-rich S–O bond to form [B] (path c and d), some activation energy may be required for this process. Therefore, the diffusion of the radical pair may be faster than the recombination process. Sulfinyl radicals thus diffused may give finally two unsymmetrical thiolsulfonates (**10** and **11**) and two symmetrical thiolsulfonates (**8** and **9**), *via* [B] and [C].

The following concerted isomerization pathway cannot be completely excluded (Eqs. 15 and 16),



(15)

(16)

however, it is quite unlikely in view of a somewhat similar oxygen migration in the oxygen scrambling of aroyl alkyl carbonate.[10]

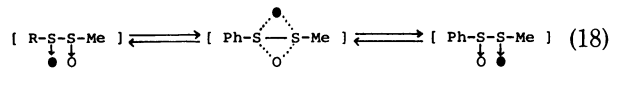
On the other hand, phenylthio group in **7** is a good leaving group and, the oxidation of **7** may proceed mainly *via* path b to form directly [$B_2$] which changes eventually to the thiolsulfonate **11** *via* [$C_2$]. This hypothesis may be supported by the following two observations: i) the formation of **11** predominates over those of other thiolsulfonates, *i.e.* **8**, **9**, and **10**, in the oxidation of **7**, ii) the $^{18}O$-label of **11** retained nearly completely the original $^{18}O$-label of **7** (Table 5).

There are following mechanistic pathways conceivable for the formation of $^{18}O$-labelled **8** in the oxidation of $^{18}O$-labelled **6** and that of $^{18}O$-labelled **9** from $^{18}O$-labelled **7**. i) If the homolytic fission-recombination

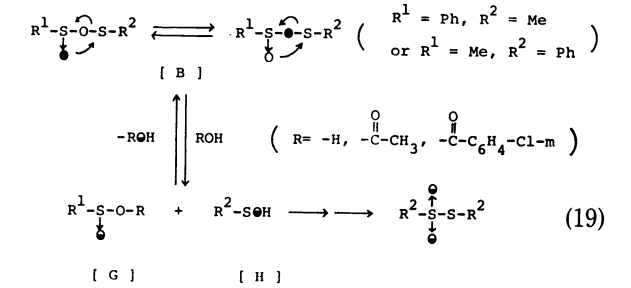
processes are all reversible as shown in Eq. 17, $^{18}O$-scrambling should take place within the sulfinyl radical pair [D] and hence both **8** and **9** should be incorporated

$$[C_1] \rightleftharpoons [B_1] \rightleftharpoons [D] \rightleftharpoons [B_2] \rightleftharpoons [C_2] \quad (17)$$

with $^{18}O$-label. ii) The following concerted oxygen scrambling in [A] as shown in Eq. 18 may be also




(18)




(19)

conceivable. iii) The ionic path shown above is also conceivable in [B] (Eq. 19). According to this mechanistic path (iii), [B] may lose $^{18}O$-label by the following reversible process, *i.e.* [B]⇄[G]+[H]. This $^{18}O$-loss in [B] by this process must be greater in the oxidation system with $H_2O_2$/AcOH than in that with MCPBA/$CH_2Cl_2$. This hypothetical $^{18}O$-exchange reaction between [B] and the medium can explain the fact that $^{18}O$-incorporations in **11** obtained from **7** and both **9** and **11** from **6** (Eqs. 12 and 13) are greater in the oxidation with MCPBA/$CH_2Cl_2$ than those in the oxidation with $H_2O_2$/AcOH (Tables 5 and 6). Another explanation may be that the ionic $^{18}O$-exchange process (Eqs. 18 and 19) is facilitated in less polar aprotic solvents while solvation of [B] and [C] does not promote the $^{18}O$-exchange in a polar protic solvent.

Thus, all these hypotheses seem to be in accordance with all above experimental results in this study.

Our new selective oxidation of unsymmetrical thiolsulfinate with $NaIO_4$ gives quantitatively the corresponding unsymmetrical thiolsulfonate[11,12] by the selective oxidation of sulfinyl sulfur with $IO_4^-$ ion without any cleavage of S–S linkage, in contrast to the oxidation with $H_2O_2$/AcOH or MCPBA/$CH_2Cl_2$ as mentioned in this paper.

## Experimental

*General.* Melting points were taken on a Yanaco instrument and were uncorrected. NMR spectra were recorded on a Hitachi Perkin-Elmer R-20 spectrometer. Infrared spectra were obtained on a Hitachi 215 spectrometer and are uncorrected. Mass spectra were recorded on a Hitachi RMU-6MG mass spectrometer. Gas and liquid chromatographs were obtained by Shimadzu GC-6A and Yanaco L-1030 instruments, respectively.

Both oxidizing agents, 30% $H_2O_2$ and MCPBA were obtained from Kanto Chemicals and Wako Pure Chemicals, respectively. Deuterated acetic acid and water were of Merck.

*Disulfide.* Both diphenyl and dimethyl disulfides are commercially available (Tokyo Kasei Kogyo Co.). Methyl phenyl disulfide was prepared by the following procedure, according to the reported method.[7]

Methanesulfenyl chloride (0.03 mol) which was prepared by the reaction of dimethyl disulfide with gaseous chlorine in $CCl_4$,[13] according to the known method and purified by distillation, was dissolved in dry $CCl_4$ (100 ml) which was cooled to *ca.* −10 °C. To the $CCl_4$ solution of MeSCl, dry pyridine (0.033 mol) was added and then thiophenol (0.03 mol) in dry $CCl_4$ (*ca.* 50 ml) was added dropwise under cooling below 0 °C. After the addition of thiophenol, cooling bath was removed and the heterogeneous reaction mixture was stirred until the solution reached room temperature. The resulting reaction mixture was transfered into a separatory funnel, and washed with water, 5% $NaHCO_3$ aq solution, and again water. Organic layer was dried over $CaCl_2$ and $CCl_4$ was evaporated. The residual crude oil was purified by distillation under reduced pressure (71—72 °C/2.5—3.0 Torr, lit,[6] 79—81 °C/1.0 Torr, 1 Torr=133.322 Pa). Complete purification of unsymmetrical disulfide is very difficult. Methyl phenyl disulfide purified by the distillation also contained a small amount of diphenyl disulfide (≈5%) which was detected by GLC. Yield was *ca.* 85%. NMR ($CDCl_3$, $\delta$, TMS) 2.40 (s, 3H, $CH_3$).

*Thiolsulfinate.* S-*Methyl methanethiosulfinate* (***4***)[14] used as an authentic sample, was prepared by direct oxidation of dimethyl disulfide **1** with $H_2O_2$ in AcOH and purified by distillation (46—47 °C/1.5 Torr). *S*-Phenyl benzenethiosulfinate (**5**), *S*-methyl benzenethiosulfinate (**6**), and *S*-phenyl methanethiosulfinate (**7**) were also prepared by the condensation of the corresponding sulfniyl chlorides and thiols in the presence of pyridine at low temperature (<0 °C), according to the usual method.[7] Yields were 80—95%. Purification of **5** was carried out by recrystallization from hexane–chloroform while **6** and **7** were purified carefully by column chromatography (silica gel, eluent: hexane: $CHCl_3$: EtOAc= 4 : 1 : 1).

S-*Phenyl Benzenethiosulfinate* ***5***: Mp 69—70 °C (lit,[15] 69—70 °C).

S-*Methyl Benzenethiosulfinate* ***6***: Mp 26—28 °C; NMR ($CDCl_3$, $\delta$, TMS) 2.53 (s, 3H, $CH_3$), 7.30 (m, 5H, Ar); IR (neat, $cm^{-1}$) 3050, 2975, 2900, 1570, 1470, 1095, and 1060 (S=O), (lit,[16] 1088 ($CHCl_3$)).

S-*Phenyl Methanethiosulfinate* ***7***: Mp 15—20 °C; IR (neat, $cm^{-1}$) 3050, 2980, 2900, 1570, 1470, 1090 (S=O), (lit,[16] 1079 ($CHCl_3$)).

*Thiolsulfonate.* S-*Methyl Methanethiosulfonate* ***8*** was prepared by the oxidation of dimethyl disulfide with $H_2O_2$ in AcOH and purified by distillation (59—61 °C/2.5 Torr, (lit,[17] 56.5 °C/1.0 Torr)); NMR (Table 1); IR (neat, $cm^{-1}$) 2925, 1430, 1410, 1335, and 1305 ($SO_2$), 1140 (S=O), 960, 755.

Other thiolsulfonates, **9**, **10**, and **11**, were synthesized by condensation of sulfenyl chlorides with free sulfinic acids in the presence of pyridine, as reported.[7] Products were purified by column chromatography, in a yield of 80—95%. Purification of **11** was performed also by recrystallization from hexane.

S-*Phenyl Benzenethiosulfonate* ***9***: Colorless crystals from EtOH; mp 44—45 °C (lit,[18] 44—45 °C).

S-*Methyl Benzenethiosulfonate* ***10***: Colorless oil, IR (neat, $cm^{-1}$) 3050, 3000, 2920, 1580, 1475, 1445, 1330, and 1302 ($SO_2$), 1042 (S=O); NMR (Table 1). Found: C, 44.92; H, 4.18%. Calcd for $C_7H_8O_2S_2$: C, 44.66; H, 4.28%.

S-*Phenyl Methanethiosulfonate* ***11***: Colorless crystals from hexane having mp 85—86.5 °C; IR (KBr, $cm^{-1}$) 3050, 3000, 2905, 1565, 1465, 1310 ($SO_2$), 1130 (S=O); NMR (Table 1). Found: C, 44.78; H, 4.25%. Calcd for $C_7H_8O_2S_2$: C, 44.66; H, 4.28%.

*Sulfinic and Sulfonic Acids.* Methanesulfinic acid **12** was prepared by hydrolysis of methanesulfinyl chloride.[19] Free benzenesulfinic acid **13** was obtained by acidification of commercial sodium benzenesulfinate (Tokyo Kasei Kogyo Co.) with concd HCl and purified by recrystallization from water. Both methanesulfonic (**14**) and benzenesulfonic acids (**15**) were obtained commercially.

*$^{18}O$-Labelled Thiolsulfinates, 6 and 7.* $^{18}O$-Labelled **6** and **7** were prepared using both $^{18}O$-labelled benzenesulfinyl and methanesulfinyl chlorides, respectively, as starting materials. $^{18}O$-Labelled sulfinyl chlorides were derived from non-labelled sulfinyl chlorides and $^{18}O$-enriched water (*ca.* 1.5%) (eqs. 10 and 3).

To a dry ether solution (30 ml) of benzenesulfinyl chloride (0.03 mol) which was purified by distillation (72 °C/2.0 Torr), was added dropwise $^{18}O$-enriched water (0.05 mol) under ccoling with ice–water bath. The reaction was considerably exothermic, with evolution of HCl gas. Benzenesulfinic acid obtained after evaporation of ether and excess water under reduced pressure, was dissolved again in ether (*ca.* 20 ml). To the stirring ether solution of the free sulfinic acid, excess distilled thionyl chloride (0.067 mol) was added then a vigorous endothermic reaction took place evolving gaseous $SO_2$ and HCl. The residual oil after evaporation of ether and excess thionyl chloride was purified by distillation.

$^{18}O$-Labelled thiolsulfinate (**6**) was prepared by treating $^{18}O$-labelled benzenesulfinyl chloride with methanethiol in the presence of pyridine,[7] as mentioned above. $^{18}O$-Labelled methanesulfinyl chloride was also prepared by the same method. Since the crude thiolsulfinate decomposes readily, the crude thiolsulfinate thus obtained were immediately subjected to purification by careful column chromatography (on silica gel, eluent: hexane: $CHCl_3$: EtOAc=4 : 1 : 1), in order to avoid the fast catalytic decomposition by impurities. Purified $^{18}O$-labelled thiolsulfinates (**6** and **7**) were fairly stable for several days under cooling below 0 °C and contained *ca.* 0.7—0.8 atom% of $^{18}O$.

*Oxidation of Disulfide and Thiolsulfinate. Oxidation with $H_2O_2$ in AcOH*: Acetic acid (*ca.* 15 ml) dissolving *ca.* 1.0 g of the substrate (disulfide or thiolsulfinate) was cooled down to nearly freezing, by an ice–water bath. Thirty percent $H_2O_2$ (amount shown in Tables 2—7) was added slowly dropwise to the cooled and stirred solution of the substrate and the temperature of the solution rose up by the addition. After the whole addition of $H_2O_2$ the mixture was warmed up to a set temperature and stirred further at the same temperature until the starting material disappeared upon monitoring by TLC or HPLC. After the reaction, the reaction mixture was diluted with 50 ml of water, transfered into a separatory funnel and extracted three times with $CHCl_3$ ($\approx$100 ml). The combined organic layer was washed with water, sat. $NaHCO_3$ aq solution, and then water again to remove AcOH and other acid species. $CHCl_3$ was evaporated and NMR spectrum of the residue was taken. The residue was, then, subjected to separation by column chromatography (silica gel, eluent: hexane: $CHCl_3$: EtOAc=4 : 1 : 1). First fraction gave *S*-phenyl benzenethiosulfonate, **9**, second one gave *S*-methyl benzenethiosulfonate **10**, then *S*-phenyl methanethiosulfonate **11** was eluted and the last fraction contained *S*-methyl methanethiosulfonate **8**. Thiolsulfinates, **5**, **6**, and **7** were eluted between **11** and **8**, while **4** appeared after **8**. **10** and **11** were separated completely by repeated column chromatography in which first fraction gave colorless solid **11** and the following fraction afforded colorless oil **10**. They were identified by comparing their NMR, IR, GLC, HPLC, and melting points with those of authentic samples prepared independently.

Meanwhile, the combined aqueous layer which was neutralized by sat. $NaHCO_3$ solution was concentrated by complete evaporation of water. Sulfinic and sulfonic acids (salts) were determined by NMR spectra in $D_2O$ in which methyl signals of both sodium salts of **12** and **14** appeared in the range of 2.15—2.30 and 2.75—2.82 ppm, respectively, depending on the pH of the solution.

*Oxidation with MCPBA in $CH_2Cl_2$*: To a cooled (*ca.* 0 °C) solution of *ca.* 1.0 g of the substrate in $CH_2Cl_2$ (*ca.* 20 ml) was added powdered MCPBA (1.0—2.0 equiv., amount are shown in Tables 2—7) slowly. The reaction mixture was warmed and stirred at a set temperature until the starting material disappeared upon monitoring by TLC or HPLC. The reaction mixture was washed with 5% $NaHCO_3$ aq. solution and water after the reaction. Both the organic and aqueous layers were treated with the same procedures as described above.

Yields of the products which were determined in connection with the data of NMR, GLC, and HPLC, are shown in Tables 2—7.

*Oxidation in NMR Sample Tube*: An NMR spectrum of the substrate (0.4—0.5 mmol) was measured in $CD_3COOD$ or $CDCl_3$ (430 $\mu$l). To the solution in NMR sample tube 30% $H_2O_2$ or powdered MCPBA (amount listed in Tables 2—7) was added at a set temperature and immediately MNR spectra of the resulting mixture were taken at a few time intervals. After the reaction completed, GC and HPLC of the reaction mixture were measured to determine the yields of the products.

*$^{18}O$-Tracer Experiments*: Products thus obtained and purified were well dried *in vacuo* with slightly heating. $^{18}O$-Labelled *S*-methyl benzenethiosulfinate **6** recovered during the oxidation was purified by column chromatography (silica gel, eluent: hexane: $CHCl_3$: EtOAc=4 : 1 : 1). It was eluted as a colorless oil after **9**, **10**, and **11**.

$^{18}O$-Tracer analysis was carried out by the method developed by Rittenberg and Ponticorvo,[20] with a slight modification, using $Pb(OAc)_2$ to remove $H_2S$ gas formed by the thermolysis of the sample.

Twenty mg of sample was pyrolyzed with 300 mg of purified $HgCl_2$ and $Hg(CN)_2$, respectively, in an evacuated, sealed Pyrex tube at *ca.* 500 °C for 12 h. Then the tube was broken in a vacuum line and $CO_2$ gas formed was purified by distillation and the mass peaks of *m/e* 44 and 46 which correspond to $C^{16}O_2$ and $C^{16}O^{18}O$, respectively, were recorded on a mass spectrometer.

*Derivation of Benzenesulfonamide from Benzenesulfonic Acid in the Oxidation of $^{18}O$-Labelled Thiolsulfinate 7 with $H_2O_2$/AcOH*: The reaction mixture resulted by the complete oxidation of $^{18}O$-labelled *S*-phenyl methanethiosulfinate **7** (437 mg) with ten equivalents of 30% $H_2O_2$ (2.65 g) in AcOH (9 ml) at 70 °C for 5 h, contained only both methane- and benzenesulfonic acids. To the reaction mixture a small amount of $MnO_2$ was added to decompose excess $H_2O_2$. After filtration, acetic acid and water were evaporated by heating. Into the residue containing two sulfonic acids, was added excess thionyl chloride (10 mmol). The resulting mixture, after evaporation under reduced pressure to remove excess thionyl chloride, was distilled to separate two fractions (bp 62 °C/21 Torr and 70 °C/1 Torr) which were methane- and benzenesulfonyl chlorides, respectively. Distilled benzenesulfonyl chloride was dissolved in dry ether and gaseous ammonia was introduced into the solution. The white solid of $NH_4Cl$ was filtered. The solid residure after evaporation of ether was benzenesulfonamide (43 mg) which was purified by recrystallization from ether–ethyl acetate mixed solvent (30 : 1) and then subjected to the routine $^{18}O$-analysis.

**References**

1) S. Oae, Y. H. Kim, T. Takata, and D. Fukushima, *Tetrahedron Lett.*, **1977**, 1195.

2) Address correspondence to Department of Chemistry, The Korea Advanced Institute of Science, P. O. Box 150, Chongyangni, Seoul, Korea.

3) a) G. Leandri, and A. Tundo, *Ann. Chim. (Rome)*, **44**, 74 (1964); b) W. Walter and P.-M. Hell, *Justus Liebigs Ann. Chem.*, **727**, 35 (1969); c) E. Block and J. O'Connor, *J. Am. Chem. Soc.*, **96**, 3291 (1974).

4) a) H. Kawasaki and H. Yonemoto, *Yakugaku Zasshi*, **77**, 640 (1957); b) I. Utsumi, T. Watanabe, K. Harada, and G. Tsukamoto, *Chem. Pharm. Bull.*, **15**, 1485 (1967).

5) a) M. M. Chau and J. L. Kice, *J. Am. Chem. Soc.*, **98**, 7711 (1976); b) D. Barnard, *J. Chem. Soc.*, **1957**, 4637; c) D. Barnard and E. J. Percy, *Chem. Ind.*, **1960**, 1332; d) U. Marangelli, G. Modena, and P. E. Todesco, *Gazz. Chim. Ital.*, **90**, 681 (1960); e) G. Modena and P. E. Todesco, *Ric. Sci.*, **30**, 1788 (1960); f) T. F. Lavine, G. Toennies, and E. C. Wagner, *J. Am. Chem. Soc.*, **56**, 242 (1934); g) W. E. Savige, J. Eager, J. A. Maclaren, and C. M. Ruxburgh, *Tetrahedron Lett.*, **1964**, 3289; h) G. Toennies and T. F. Lavine, *J. Biol. Chem.*, **113**, 57 (1936); i) T. F. Lavine, *ibid.* **113**, 583 (1936); j) G.E. Utzinger, *Experientia*, **16**, 136 (1960); **17**, 374 (1961); k) After completion of this work, Freeman *et al.* reported the detection of α-disulfoxide in direct NMR study at low temperature: F. Freeman and C. N. Angeletakis, *J. Am. Chem. Soc.*, **103**, 6232 (1981).

6) S. Oae, Y. H. Kim, D. Fukushima, and K. Shinhama, *J. Chem. Soc., Perkin Trans. 1*, **1978**, 913.

7) S. Oae, T. Takata, and Y. H. Kim, *Tetrahedron*, **37**, 37 (1981).

8) P. Koch, E. Ciuffarin, and A. Fava, *J. Am. Chem. Soc.*, **92**, 5971 (1970).

9) S. Oae and T. Takata, *Chem. Lett.*, **1981**, 845.

10) S. Oae, Y. Uchida, K. Fujimori, and S. Kozuka, *Bull. Chem. Soc. Jpn.*, **46**, 1741 (1973).

11) Y. H. Kim, T. Takata, and S. Oae, *Tetrahedron Lett.*, **1978**, 2305.

12) S. Oae and T. Takata, *Tetrahedron Lett.*, **21**, 3213 (1980).

13) C. J. M. Stirling, *J. Chem. Soc.*, **1957**, 3597.

14) L. D. Small, J. H. Baily, and C. J. Cavallito, *J. Am. Chem. Soc.*, **69**, 1710 (1947).

15) S. Oae, Y. Yoshikawa, and W. Tagaki, *Bull. Chem. Soc. Jpn.*, **42**, 2899 (1969).

16) G. Ghersetti and G. Modena, *Spectrochim. Acta*, **19**, 1809 (1963).

17) E. Block and J. O'Connor, *J. Am. Chem. Soc.*, **96**, 3929 (1974).

18) S. Oae, R. Nomura, Y. Yoshikawa, and W. Tagaki, *Bull. Chem. Soc. Jpn.*, **42**, 2903 (1969).

19) F. Wudl, D. A. Lightner, and D. J. Cram, *J. Am. Chem. Soc.*, **89**, 4099 (1967).

20) D. Rittenberg and L. Ponticorvo, *J. Appl. Rad. Isotopes*, **1**, 208 (1956).