Formation of Elusive *vic*-Disulfoxides and *OS*-Sulfenyl Sulfinates during the *m*-Chloroperoxybenzoic Acid (MCPBA) Oxidation of Alkyl Aryl Disulfides and Their Regioisomeric Sulfinothioic Acid *S*-Esters[1,2]

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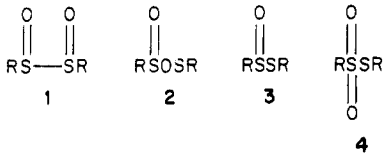
The initial step in the 1 equiv *m*-chloroperoxybenzoic acid (MCPBA) oxidation of 2,2-dimethylpropyl phenyl disulfide (**10**) and phenyl phenylmethyl disulfide (**14**) occurs predominantly at the sulfur atom bonded to the alkyl group to give *S*-phenyl 2,2-dimethylpropanesulfinothioate (**5**) and *S*-phenyl phenylmethanesulfinothioate (**6**), respectively. The 2 equiv MCPBA oxidation of disulfide **10** gives *S*-phenyl 2,2-dimethylpropanesulfonothioate (**23**) as the major product. The 1 equiv MCPBA oxidation of thiosulfinates **5** and **6** and *S*-2,2-dimethylpropyl benzenesulfinothioate (**9**) ultimately gives thiosulfonate **23**, *S*-phenyl phenylmethanesulfonothioate (**17**), and thiosulfonate **23**, respectively, as the major products. Thus, peroxidation of regioisomeric *S*-alkyl and *S*-aryl sulfinothioates **5** and **9** occurs predominantly at the sulfenyl sulfur atom to give diastereomeric *vic*-disulfoxides (*α*-disulfoxides) which may undergo cycloelimination to sulfines and sulfenic acids, dissociate to sulfinyl radicals, and rearrange intramolecularly to *OS*-sulfenyl sulfinates and/or to sulfonothioic acid *S*-esters. *OS*-Sulfenyl sulfinates may isomerize to sulfonothioic acid *S*-esters or dissociate to sulfinyl radicals and/or to thiyl and sulfonyl radicals. The sulfinyl radicals may combine to form *vic*-disulfoxides and/or *OS*-sulfenyl sulfinates while the thiyl and sulfonyl radicals may lead to sulfonothioic acid *S*-esters.

The question of the transitory existence of *vic*-disulfoxides (*α*-disulfoxides, **1**) and *OS*-sulfenyl sulfinates (**2**) during the peroxy acid oxidation of disulfides[3-5] or sulfinothioic acid *S*-esters (**3**, thiosulfinates)[6-23] to sulfonothioic acid *S*-esters (**4**, thiosulfonates) is of considerable mechanistic, synthetic, and biological interest. Low temperature ^{1}H NMR and ^{13}C NMR studies have confirmed the presence of diastereomeric *vic*-disulfoxides during the *m*-chloroperoxybenzoic acid (MCPBA) oxidation of symmetrical *S*-alkyl alkanesulfinothioates (**3**).[6,8,10] Although the long sought elusive *OS*-sulfenyl sulfinate intermediate (**2**) has been implicated in the MCPBA oxidation of thiosulfinates **3**,[6] *S*-phenyl 2,2-dimethylpropanesulfinothioate (**5**),[9] and *S*-phenyl phenylmethanesulfinothioate (**6**),[5,11] and thiosulfinates **7** and **8**,[4,15] no direct evidence for the presence of **2** in these peroxidations has been reported.[17-26]



5, R = *neo*-C_5H_{11}
6, R = $C_6H_5CH_2$
7, R = CH_3
8, R = CH_3
9, R = *neo*-C_5H_{11}

In order to determine regioselectivity, to compare the reactivity of regioisomeric sulfinothioate *S*-esters, to observe the influence of solvents, and to attempt to detect diastereomeric *vic*-disulfoxides **11** and *OS*-sulfenyl sulfinates **12** and **13**, we have examined the MCPBA oxidation of 2,2-dimethylpropyl phenyl disulfide (**10**) and its regioisomeric monoxide derivatives [**5** and *S*-2,2-dimethylpropyl benzenesulfinothioate (**9**)] in deuteriochloroform and in 50:50 (v/v) deuteriochloroform–methanol-d_4 from −40 to −20 °C. For comparison purposes and to better elucidate the mechanisms of peroxidation of unsymmetrical systems, thiosulfinate **6** and phenyl phenylmethyl disulfide (**14**) were also oxidized with MCPBA.[11]

Results

Oxidation of Disulfide 14. Disulfide **14** was treated with 2 equiv of MCPBA at −30 °C under nitrogen in deuteriochloroform for 1 h. The product mixture was

(1) Abstracted from the Ph.D. Thesis of C. N. Angeletakis, 1982, University of California, Irvine, CA 92717.
(2) Presented in part at the 8th Annual Meeting of NOBCChE, Chicago, IL, April 25, 1981, p 65, and at the 1981 Pacific Conference on Chemistry and Spectroscopy, Anaheim, CA, Oct 21, 1981, p 102.
(3) (a) Marangelli, U.; Modena, G.; Todesco, P. E. *Gazz. Chim. Ital.* **1960**, *90*, 681; *Chem. Abstr.* **1961**, *55*, 16510i. (b) Modena, G.; Todesco, P. E. *Ric. Sci.* **1960**, *30*, 1788; *Chem. Abstr.* **1962**, *56*, 376g.
(4) Oae, S.; Takata, T.; Kim, Y. H. *Bull. Chem. Soc. Jpn.* **1982**, *55*, 2484.
(5) Bhattacharya, A. K.; Hortmann, A. G. *J. Org. Chem.* **1978**, *43*, 2728.
(6) Freeman, F.; Angeletakis, C. N. *J. Am. Chem. Soc.* **1983**, *105*, 4039.
(7) Freeman, F.; Angeletakis, C. N.; Pietro, W. J.; Hehre, W. J. *J. Am. Chem. Soc.* **1982**, *104*, 1161.
(8) Freeman, F.; Angeletakis, C. N. *J. Am. Chem. Soc.* **1982**, *104*, 5766.
(9) Freeman, F.; Angeletakis, C. N.; Maricich, T. J. *J.. Org. Chem.* **1982**, *47*, 3403.
(10) Freeman, F.; Angeletakis, C. N. *J. Am. Chem. Soc.* **1981**, *103*, 6232.
(11) Freeman, F.; Angeletakis, C. N. *J. Org. Chem.* **1981**, *46*, 3991.
(12) Freeman, F.; Angeletakis, C. N. *Tetrahedron Lett.* **1982**, *23*, 491.
(13) Freeman, F.; Angeletakis, C. N.; Maricich, T. J. *Tetrahedron Lett.* **1981**, *22*, 1867.
(14) Utzinger, F. E. *Experientia* **1961**, *17*, 374.
(15) Oae, S.; Kim, Y. H.; Takata, T.; Fukushima, D. *Tetrahedron Lett.* **1977**, 1195.
(16) Oae, S.; Takata, T. *Tetrahedron Lett.* **1980**, *21*, 3213.
(17) Chau, M. M.; Kice, J. L. *J. Am. Chem. Soc.* **1976**, *98*, 7711.
(18) Lee, S. H. Ph.D. Thesis, 1980, Washington University, St. Louis, MO.
(19) Gilbert, B. C.; Gill, B.; Ramsden, M. J. *Chem. Ind. (London)* **1979**, 283.
(20) Freeman, F. *Chem. Rev.* **1984**, *84*, 117.
(21) Freeman, F.; Keindl, M. C. *Sulfur Rep.*, in press.
(22) (a) Barnard, D. *J. Chem. Soc.* **1957**, 4673. (b) Barnard, D. *J. Chem. Soc.* **1957**, 4675. (c) Barnard, D., Percy, E. J. *Chem. Ind. (London)* **1960**, 1332.
(23) (a) Foss, O. *Acta Chem. Scand.* **1947**, *1*, 307. (b) Foss, O. In "Organic Sulfur Compounds"; Kharasch, N., Ed.; Pergamon Press: New York, 1961; Vol. I, pp 83–96.
(24) Howard, J. A.; Furimsky, E. *Can. J. Chem.* **1974**, *52*, 555.
(25) Freeman, F.; Angeletakis, C. N., unpublished data.
(26) Freeman, F.; Keindl, M. C., unpublished data.

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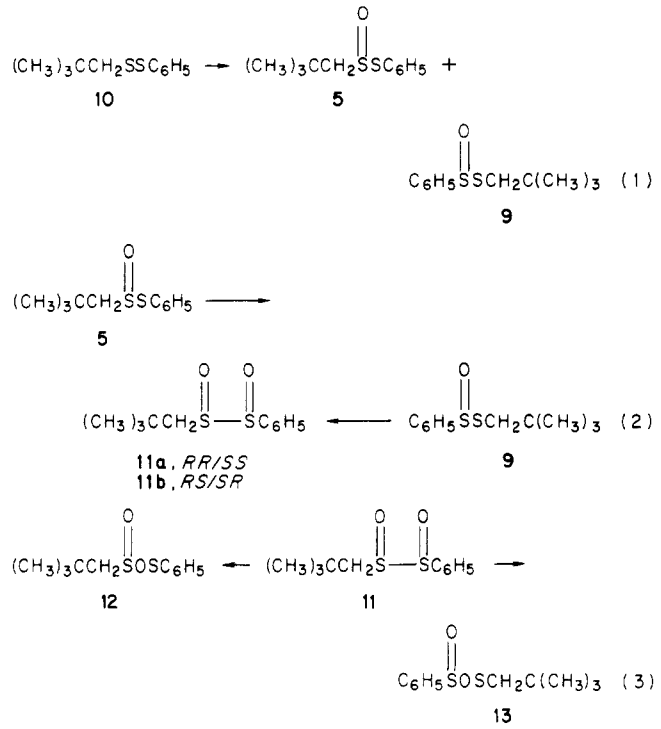


filtered in an inert atmosphere at −45 °C, warmed to 0 °C, and stirred with 10% sodium hydrogen carbonate solution for 10 min. Analysis of the product mixture via HPLC, ^{1}H NMR, ^{13}C NMR, and IR showed the presence of thiosulfinate **6**, thiosulfonate **15**, thiosulfinates **16** and **17**, thiosulfonate **18**, phenylmethanesulfinic acid (**19**), phenylmethanesulfonic acid (**20**), and (*Z*)-phenylmethanethial *S*-oxide (**21**, Table I).

Oxidation of Disulfide 10. Disulfide **10** was oxidized with 2 equiv of MCPBA as described above for the peroxidation of **14**, except the product mixture was warmed to 0 °C without filtering and stirred with 5% sodium hydrogen carbonate solution for 10 min. Analysis of the product mixture showed the presence of thiosulfinates **5** and **16**, thiosulfonates **15**, **22**, and **23**, 2,2-dimethylpropanesulfinic acid (**24**), 2,2-dimethylpropanesulfonic acid (**25**), thiosulfonate **26**, and (*E*)- and (*Z*)-2,2-dimethylpropanethial *S*-oxide (**27** and **28**, Table II).

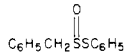
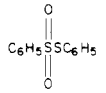
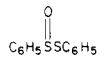
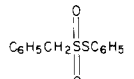
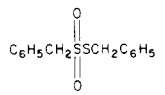
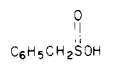
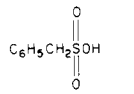
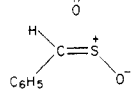
Oxidation of Thiosulfinates 5, 6, and 9. Thiosulfinates **5**, **6**, and **9** were separately oxidized with 1 equiv of MCPBA as described above for disulfides **14** (Tables I and II).[9,11]

Oxidation of Thiosulfinate 5 without Aqueous Workup. The 1 equiv MCPBA oxidation of thiosulfinate **5** was performed at −30 °C in deuteriochloroform under nitrogen for 1 h. The product mixture was filtered in an inert atmosphere at −45 °C and the ^{1}H NMR and ^{13}C NMR spectra of the filtrate were taken as soon as possible. Overnight storage of the reaction mixture at 22–24 °C led to the disappearance of the resonance of sulfinic acid **24** (δ_H 2.90) and an increase of the resonance of thiosulfonate **23** (δ_H 3.27).

Oxidation of Thiosulfinate 9 without Aqueous Workup. The MCPBA oxidation of thiosulfinate **9** in deuteriochloroform was carried out at −40 (1 h), −30, and −20 °C. The ^{1}H NMR spectrum (15 min after filtration at −45 °C) at 40 °C showed that the diastereotopic protons of thiosulfinate **9** accounted for 49% of the relative integral of the methylene region. Structures could not be assigned to the other resonances.[4,6,8,9,10,27-35] The ^{13}C NMR spectrum (17 min after filtration at −45 °C) showed nine peaks in the methylene region (δ_C 46–74) with a predominant peak for thiosulfinate **9** at δ_C 47.20. Six small peaks were observed between δ_C 69.38 and 72.85. Warming the product mixture to −20 °C did not lead to significant changes in the ^{13}C NMR spectrum. Warming this product mixture to 22–24 °C led to the gradual disappearance of all resonances except δ_C 47.27 (thiosulfinate **9**), δ_C 72.12 (thiosulfonate **23**), and δ_C 72.30 (sulfinic acid **24**).

The ^{1}H NMR spectrum (15 min after filtration) of the −30 °C product mixture from the oxidation of thiosulfinate **9** in deuteriochloroform showed a large number of nonresolvable (250 MHz) diastereotopic proton resonances in the methylene region with chemical shifts between those of thiosulfonate **23** (δ_H 3.39) and sulfinic acid **24** (δ_H 2.91). The ^{13}C NMR spectrum showed the presence of thiosulfinates **5** and **9**, thiosulfonate **23**, sulfinic acid **24**, and *possibly* 2,2-dimethylpropanesulfinic benzenesulfinic anhydride (**30**, eq 4). The addition of a small amount of sulfinic acid **24** led to an increase of the resonance at δ_H

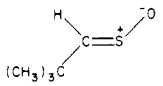
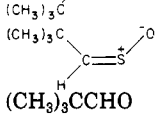
Table I. Products from the MCPBA Oxidation of *S*-Phenyl Phenylmethanesulfinothioate (6) and Phenyl Phenylmethyl Disulfide (14) in Deuteriochloroform Followed by Treatment with Sodium Hydrogen Carbonate Solution

		$C_6H_5CH_2SSC_6H_5$ (14), % yield		$C_6H_5CH_2\overset{O}{\overset{\|}{S}}SC_6H_5$ (6), % yield	
product	no.	^{1}H NMR[a]	HPLC	^{1}H NMR[a]	HPLC[b]
	6	24	32	24	28–30
	15	c	18	c	15–18
	16	c	5	c	0–5
	17	50[d]	58	52[d]	50–59
	18	3		3	
	19	8		11	
	20	11		9	
	21	3		trace	

[a] NMR yields (±3%) are given [b] Analyses from three experiments. [c] NMR yields of **15** and **16** could not be determined owing to their overlapping aromatic resonances. [d] Includes amount precipitated during filtration at −45 °C.

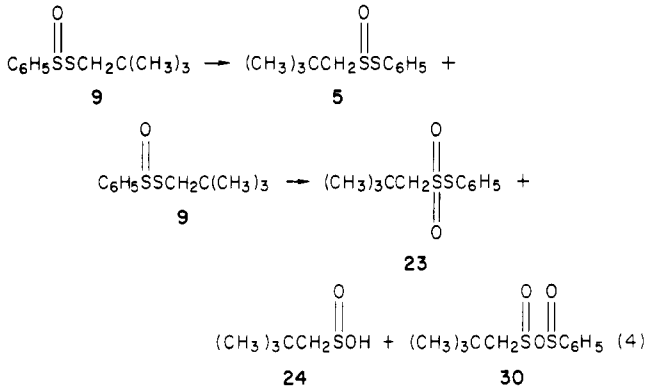
(27) Zwanenburg, B.; Strating, J. *Q. Rep. Sulfur Chem.* **1970**, *5*, 79.
(28) Block, E.; Revelle, L. K.; Bazzi, A. A. *Tetrahedron Lett.* **1980**, *21*, 1277.
(29) Zwanenburg, B. *Recl. Trav. Chim. Pays-Bas* **1982**, *101*, 1.
(30) Block, E. In "Organic Sulfur Chemistry", 9th International Symposium on Organic Sulfur Chemistry, Riga, USSR, June 9–14, 1980; Freidlina, R. Kh., Skorova, A. E., Ed.; Pergamon Press: Oxford, 1981.
(31) Freeman, F.; Angeletakis, C. N.; Maricich, T. J. *Org. Magn. Reson.* **1981**, *17*, 53.
(32) Freeman, F.; Angeletakis, C. N. *Org. Magn. Reson.* **1983**, *21*, 86.
(33) Freeman, F.; Angeletakis, C. N. *J. Org. Chem.* **1982**, *47*, 4194.
(34) Bass, S. W.; Evans, S. A., Jr. *J. Org. Chem.* **1980**, *45*, 710.
(35) Takata, T.; Kim, Y. H.; Oae, S.; Suzuki, K. T. *Tetrahedron Lett.* **1978**, 4303.

Table II. Products from the MCPBA Oxidation of *S*-Phenyl 2,2-Dimethylpropanesulfinothioate (5), 2,2-Dimethylpropyl Phenyl Disulfide (10), and *S*-2,2-Dimethylpropyl Benzenesulfinothioate (9) in Deuteriochloroform at −30 °C, Followed by Treatment with Sodium Hydrogen Carbonate Solution at 0 °C[a-c]

observed product	no.	$(CH_3)_3CCH_2S(O)SC_6H_5$ (5) yield, %		$(CH_3)_3CCH_2SSC_6H_5$ (10) yield, %		$C_6H_5S(O)SCH_2C(CH_3)_3$ (9) yield, %
		NMR	HPLC[d]	NMR	HPLC[d]	NMR
$(CH_3)_3CCH_2S(O)SC_6H_5$	**5**	22	21	16	17	10
$C_6H_5SO_2SC_6H_5$	**15**		12		15	
$C_6H_5S(O)SCH_2C(CH_3)_3$	**9**	0		0		14
$C_6H_5S(O)SC_6H_5$	**16**		2		3	
$(CH_3)_3CCH_2SO_2SCH_2C(CH_3)_3$	**22**	6		7		5
$(CH_3)_3CCH_2SO_2SC_6H_5$	**23**	43	65	48	52	35
$(CH_3)_3CCH_2SO_2H$	**24**	14 (14)[e]		6 (7)[e]		25 (26)[e]
$(CH_3)_3CCH_2SO_3H$	**25**	8		8		8
$C_6H_5SO_2SCH_2C(CH_3)_3$	**26**	2		5		3
	**27**	1		2		1
	**28**	2		2		2
$(CH_3)_3CCHO$	**29**	3		0		0

[a] Me_4Si was used as internal standard; the spectrometer frequencies were 62.89 MHz (^{13}C) and 250.13 MHz (^1H). [b] Based on moles of reactant. ^1H NMR yields (percent relative integrals, ±3%) are given. [c] The analysis was done within 5 min after separation of the layers. [d] Accurate HPLC analysis could not be done owing to the partial decomposition of **9** on silica gel in the product mixture. [e] Yield from potassium permanganate titration.

2.91 and the coalescence of the resonances at δ_C 71.01 (**24**) and δ_C 71.23 (thiosulfonate **23**) into a singlet (δ_C 71.30).



The ^{13}C NMR spectra obtained after warming the −30 °C reaction mixture *without* added sulfinic acid **24** to 0 °C for 1 h and then to 22–24 °C showed that the resonances due to thiosulfonate **23** and sulfinic acid **24** collapsed into one resonance at δ_C 71.30 while all others gradually disappeared. The ^1H NMR spectra obtained after warming this reaction mixture to 22–24 °C showed that the diastereotopic hydrogen resonances gradually disappeared and the methylene hydrogen resonance of thiosulfonate **23** at δ_H 3.27 were increasing. Resonances due to disulfide **10**, bis(2,2-dimethylpropyl) disulfide, and presumably diphenyl disulfide were also present.

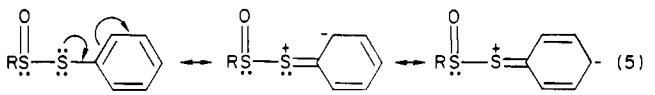
Oxidation of thiosulfinate **9** with MCPBA in deuteriochloroform at −20 °C gave an ^1H NMR spectrum at 22–24 °C (obtained within 5 min after completion of filtration at −45 °C) which was similar with those obtained when the reaction was run at −30 °C. Continuous scanning by ^1H NMR showed that the resonance of sulfinic acid **24** (δ_H 2.85) was decreasing at approximately the same rate as the one due to thiosulfonate **23** (δ_H 3.29) was increasing while the rest of the methylene region of the spectrum remained essentially unchanged (90 MHz). This process continued until (ca. 40 min) the ratio of the peaks at δ_H 2.82 (**24**) and δ_H 3.27 (**23**) was 1:2.

The −20 °C experiment described above was repeated, the ^1H NMR spectrum of the filtrate was obtained 10 min after filtration, and then a small amount of methanol-d_4 was added to the solution in the NMR tube. The singlet at δ_H 2.85 shifted to δ_H 2.68, and the decrease of the signal at δ_H 2.86 (**24**) and increase of the signal at δ_H 3.29 (thiosulfonate **23**) was much slower than without added methanol-d_4.

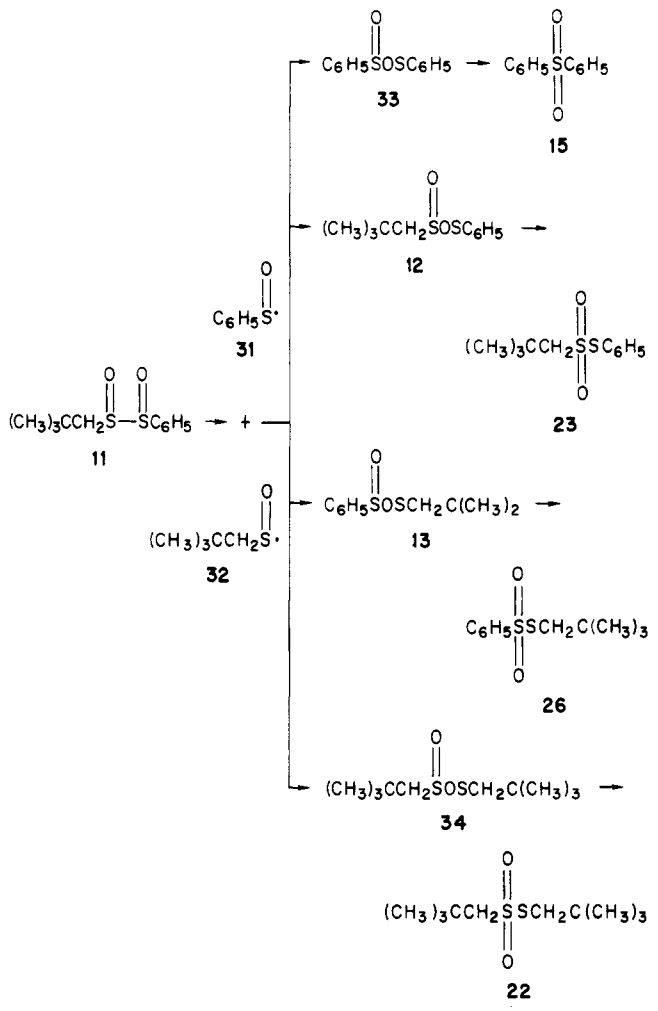
The IR spectrum ($CHCl_3$) of the −20 °C reaction mixture obtained within five min after warming to 25 °C without added methanol-d_4 showed three bands that can be attributed to thiosulfonates at 1330 cm^{-1} (**16** and **23**), 1147 cm^{-1} (**16**), and 1135 cm^{-1} (**23**). Also four overlapping bands were present in the S=O region, three of equal intensity at 1060, 1070, and 1079 cm^{-1}, and one of slightly less intensity at 1088 cm^{-1}. Continuous IR scanning (2 h) showed that the infrared bands in the S=O region were decreasing and the thiosulfonate bands at 1330, 1147, and 1135 cm^{-1} were increasing. HPLC analysis of the reaction mixture indicated that thiosulfonates **16** and **23** were the major components.

Discussion

Site of Oxidation. Sulfenyl vs. Sulfinyl Sulfur. The similarity of the product distributions from the MCPBA oxidation of thiosulfinates **5**, **6**, and **9** suggests that oxidation occurs not only at the sulfinyl sulfur atom, but also at the sulfenyl sulfur atom to give *vic*-disulfoxides (eq 2). The large yield of thiosulfonate **23** from the MCPBA oxidation of thiosulfinate **9** lends further support for the intermediacy of *vic*-disulfoxides **11** and/or *OS*-sulfenyl sulfinates **12** and **13** (eq 3).[4-6,8-11,15,18] In an analogous manner, the 2 equiv MCPBA oxidation of disulfide **10** also proceeds primarily via thiosulfinate **5** and *vic*-disulfoxides **11** and/or *OS*-sulfenyl sulfinates **12** and **13**. The regioselectivity observed in the oxidation of **5**, **6**, and **9** can be partially explained in terms of the mesomeric effect exerted by the benzene ring which decreases the electron density distribution around the sulfenyl sulfur (eq 5).[32] In addition, the electron-releasing character of the alkyl group should increase the electron density around the sulfenyl sulfur atom in thiosulfinate **9**.



Scheme I

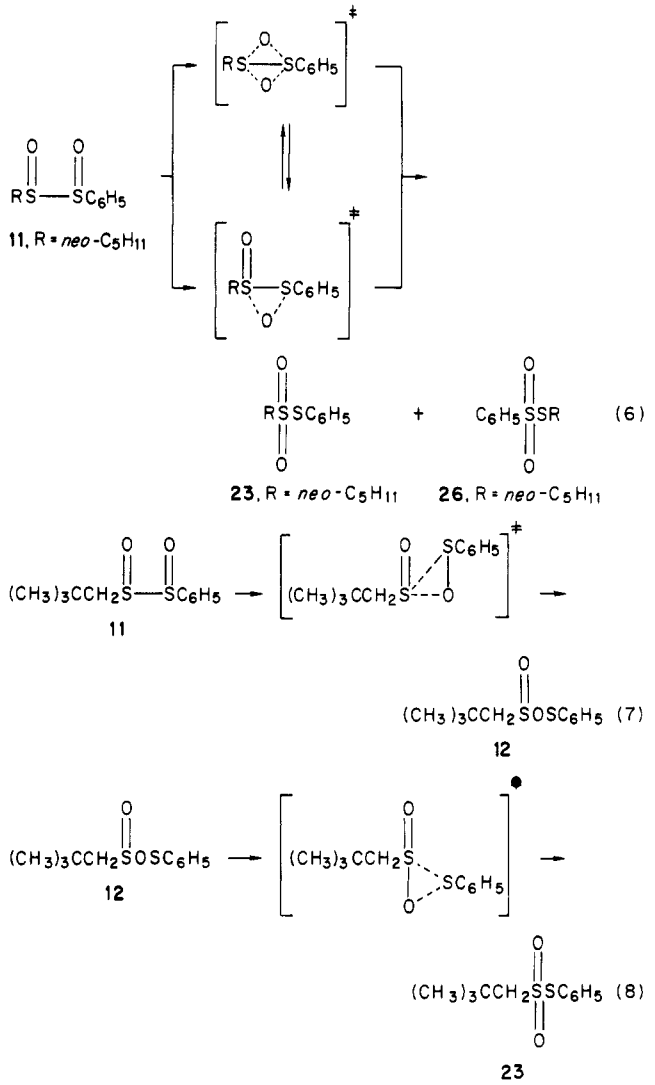


The yield of thiosulfonate **23** from the oxidation of thiosulfinate **5** at −30 °C in deuteriochloroform is 28% (Tables II, III) while the yield of thiosulfonate **23** from the oxidation of thiosulfinate **9** under identical conditions is 17% (Table II). These results suggest that oxidation at the sulfinyl sulfur atom in thiosulfinate **5** is only a minor pathway which may represent at most 11% of the total reaction. Peroxidation of thiosulfinate **5** with less than 1 equiv of MCPBA at −20 °C revealed that the initial oxidation products were thiosulfonate **23** and sulfinic acid **24** in a ratio of 1.9:1. This ratio may be considered as the *maximum* reasonable ratio for oxidation of the sulfinyl vs. sulfenyl sulfur atom in thiosulfinate **5** under these conditions.

These data suggest that most of the oxidation products from the oxidation of thiosulfinates **5** and **9** and disulfide **10** probably arise from the diastereomeric *vic*-disulfoxides **11**, the *OS*-sulfenyl sulfinates **12** and **13**, and their rearrangement and reaction products (eq 2 and 3). Moreover since only trace amounts (2–3%) of thiosulfonate **26** were observed from the oxidation of thiosulfinate **9**, *direct* oxidation of sulfinyl sulfur by MCPBA can be ruled out as a major pathway.[4,9,15,18]

Rearrangement of *vic*-Disulfoxides to *OS*-Sulfenyl Sulfinates and/or Thiosulfonates. In contrast to the oxidation of symmetrical *S*-alkyl alkanesulfinothioates (**3**),[6,8,10,13] the oxidation of *S*-phenyl alkanesulfinothioates **5** and **6**[5,11] does not proceed readily at −40 °C. Since dialkyl *vic*-disulfoxides (**1**) rearrange at temperatures above −40 °C, alkyl aryl *vic*-disulfoxides, might be expected to rearrange and/or decompose at the same temperature or lower. The S–S bond in an alkyl aryl *vic*-disulfoxide is expected to be weaker than the S–S bond in a dialkyl *vic*-disulfoxide since the S–S bond in dialkyl sulfinothioates is 10 kcal mol^{-1} stronger than in aryl arenesulfinothioates.[36,37]

Intramolecular isomerization of *vic*-disulfoxides **11** without S–S bond cleavage can afford thiosulfonates **23** and **26** directly (eq 6). Alternatively, *vic*-disulfoxide **11** can undergo intramolecular rearrangement to *OS*-sulfenyl sulfinates **12** and **13** which can isomerize to thiosulfonates **23** and **26**, respectively (eq 7 and 8, cf. eq 3).[4,6,8,10]



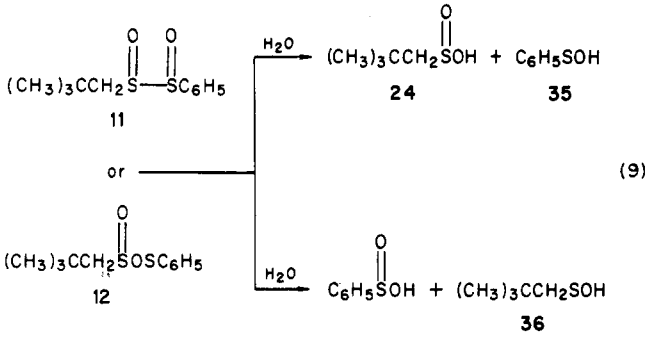
Dissociation of *vic*-Disulfoxides to Sulfinyl Radicals. Homolytic dissociation of *vic*-disulfoxide **11** can lead to benzenesulfinyl radical (**31**) and 2,2-dimethylpropanesulfinyl radical (**32**) which can recombine in random fashion to give the four possible *OS*-sulfenyl sulfinates (**12**, **13**, **33**, and **34**).[3,4,6,8,10,17,19–21,38,39] *OS*-Sulfenyl sulfinates **12**, **13**, **33**, and **34** may isomerize to their respective thiosulfinates **23**, **26**, **15**, and **22** via a concerted mechanism (cf. eq 6–8), by reaction with thiosulfinate (possibly via an ionic mechanism),[9,11] or via cleavage of the weaker O–SR bond to give sulfonyl and thiyl radicals followed by recombination to form the S–S bond (Scheme I).

(36) Kice, J. L.; Liao, S. *J. Org. Chem.* **1981**, *46*, 2691.
(37) Kice, J. L. *Adv. Phys. Org. Chem.* **1980**, *17*, 65.
(38) Barnard, D. *J. Chem. Soc.* **1957**, 4675.
(39) Chatgilialoglu, C.; Gilbert, B. C.; Gill, B.; Sexton, M. D. *J. Chem. Soc., Perkin Trans. 2* **1980**, 1141.

The absence of thiosulfonates **15** and **26** and the low yields of thiosulfonates **22** and **23** in the *initial* product mixture from the −30 °C oxidation of thiosulfinate **5** in deuteriochloroform may argue against major involvement of radical mechanisms in the oxidation of *S*-phenyl alkanesulfinothioates.[11] However, only thiosulfonate **23** was identifiable in the complex ^{13}C NMR spectrum of the product mixture from the oxidation of disulfide **10** at −30 °C in deuteriochloroform.

Formation and Reactions of Sulfenic Acids. An unsuccesful attempt was made to trap sulfenic acids with excess (*Z*)-2-butene during the MCPBA oxidation of thiosulfinate **5** at −20 °C in deuteriochloroform.[40,41]

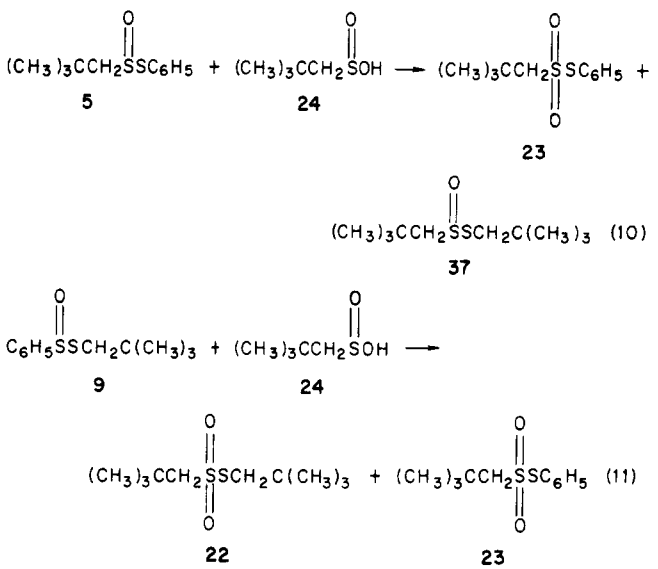
Hydrolysis of *vic*-disulfoxide **11** or *OS*-sulfenyl sulfinate **12** can lead to sulfinic acid **24**, benzenesulfenic acid (**35**), benzenesulfinic acid, and 2,2-dimethylpropanesulfenic acid (**36**, eq 9). The absence of benzenesulfinic acid and benzenesulfonic acid in the product mixtures from the oxidation of thiosulfinates **5**, **6**, and **9**, and disulfide **10** in deuteriochloroform at −30 °C suggests that aralkyl *vic*-disulfoxide **11** may react preferentially with water to give alkanesulfinic acid **24** and/or preferentially rearranges to *OS*-sulfenyl sulfinate **12**. Dehydration of sulfenic acids **35** and **36** would lead to the symmetrical and unsymmetrical thiosulfinates observed in the product mixtures.



Formation and Reactions of Sulfinic Acids. One of the major products obtained from the MCPBA oxidation of disulfide **10** and its regioisomeric thiosulfinates (**5** and **9**) is sulfinic acid **24** (eq 9). In addition, the respective NMR spectra of the product mixtures from the MCPBA oxidation of thiosulfinates **5** and **9**, without sodium hydrogen carbonate treatment, showed that storage of these mixtures at 22–24 °C led to the disappearance of sulfinic acid **24** and formation of thiosulfonate **23**.

In order to determine the rate at which thiosulfinates **5** and **9** react with sulfinic acid (**24**), each thiosulfinate was treated with an equimolar amount of sulfinic acid **24** in deuteriochloroform at 22–24 °C and the reaction followed by ^1H NMR. The reaction of thiosulfinate **5** with sulfinic acid **24** was complete in 111 min. The products were thiosulfinate **37** and thiosulfonate **23** (eq 10). Thiosulfinate **37** probably arises from cyclodehydration of sulfenic acid **36**. The reaction of thiosulfinate **9** and sulfinic acid **24** was only 48% complete after 15.5 h (eq 11), which suggests that it is probably not involved in the MCPBA oxidation of thiosulfinate **9**.

The difference in reactivity between thiosulfinates **5** and **9** toward sulfinic acid **24** may be ascribed to the difference in the basicity of the sulfinyl sulfur oxygen atoms in **5** and **9**. The mesomeric effect of the phenyl group is expected to reduce the basicity in thiosulfinate **9** (cf. eq 5). Steric



effects exert some influence since sulfinic acid **24** does not react readily with thiosulfinate **37**.[8]

The ^1H NMR spectra of the product mixture obtained from the oxidation of thiosulfinate **9** at −20 °C showed that the resonance for sulfinic acid **24** was disappearing quickly while the resonance for thiosulfonate **23** was increasing as the reaction mixture was warmed to 24 °C. The relatively rapid disappearance of sulfinic acid **24** and appearance of thiosulfonate **23** suggests that reactions other than the one shown in eq 11 are involved. Sulfenic acids **35** and **36** may be involved in the reactions of thiosulfinate **5** or **9** with sulfinic acid **24**.[42,43]

The product mixture obtained from the oxidation of thiosulfinate **9** with MCPBA at −40 °C contains significant amounts of species that are apparently products of secondary reactions since 49% of **9** is still present. Three of the six ^{13}C NMR resonances between δ_C 69.38 and 72.85 can be ascribed to thiosulfinate **5**, thiosulfonate **23**, and sulfinic acid **24**. Two other resonances can be *tentatively* assigned to diastereomers of sulfinic anhydride **30**.

When the oxidation of thiosulfinate **9** was performed at −30 °C, the −30 °C ^{13}C NMR spectrum showed one peak that can be assigned to sulfinic anhydride **30** and resonances that can be assigned to thiosulfinate **5**, thiosulfinate **9**, thiosulfonate **23**, and sulfinic acid **24**.

Oxidation of sulfinic acid **24** leads to 2,2-dimethylpropanesulfonic acid (**25**). The formation of greater amounts of 2,2-dimethylpropanesulfonic acid (**25**) in deuteriochloroform–CD_3OD (cf. Table II) may be due to increased competition of sulfinic acid **24** for oxidant in the more polar solvent. Sulfinic acids are thermally unstable and are known to decompose to sulfonic acids and thiosulfonates.

Summary

Several reasonable conclusions concerning the intermediacy of *vic*-disulfoxides and *OS*-sulfenyl sulfinates during the peroxidation of alkyl aryl disulfides and thiosulfinates are available from this investigation. (1) The initial step in the 1 equiv MCPBA peroxidation of 2,2-dimethylpropyl phenyl disulfide (**10**) and phenyl phenylmethyl disulfide (**14**) occurs predominantly at the relatively more electron rich sulfur atom bonded to the alkyl group (electronic effect). Thus it appears that inductive effects are of primary importance in determining

(40) Davis, F. A.; Rizvi, S. Q. A.; Ardecky, R.; Gosciniak, D. J.; Friedman, A. K.; Yocklovich, S. G. *J. Org. Chem.* **1980**, *45*, 1650.
(41) Davis, F. A.; Jenkin, R. H., Jr. *J. Am. Chem. Soc.* **1980**, *102*, 7967 and references therein.
(42) Kice, J. L.; Cleveland, J. P. *J. Am. Chem. Soc.* **1973**, *95*, 104.
(43) Kice, J. L.; Cleveland, J. P. *J. Am. Chem. Soc.* **1973**, *95*, 109.

the regioselectivity of the initial oxidation step.[4,5,9,11,15,18] (2) The 2 equiv MCPBA oxidation of disulfide **10** gives *S*-phenyl 2,2-dimethylpropanesulfonothioate (**23**) as the major product via thiosulfinate **5**. Similarly, the 2 equiv MCPBA oxidation of disulfide **14** gives *S*-phenyl phenylmethanesulfonothioate (**17**) as the major product via thiosulfinate **6**. (3) The 1 equiv MCPBA oxidation of thiosulfinates **5**, **6**, and *S*-2,2-dimethylpropyl benzenesulfinothioate (**9**) gives the respective *S*-phenyl alkanesulfonothioates **23**, **17**, and **23** as the major products. The predominant formation of *S*-phenyl alkanesulfonothioates **17** and **23** is explicable in terms of *vic*-disulfoxides and/or *OS*-sulfenyl sulfinates. (4) The intermediate *vic*-disulfoxides and *OS*-sulfenyl sulfinates may rearrange via radical and nonradical pathways. (5) One major pathway to sulfonothioate *S*-esters during peroxidation of some thiosulfinates is probably via the reaction of sulfinic acids and sulfinothioic acid *S*-esters.

Experimental Section

Melting points were obtained on a Thomas Hoover melting point apparatus and are uncorrected. Elemental analyses were performed by Robertson Laboratory, Florham Park, NJ.

Mass spectra were obtained on a Finnigan GC/EI-CI mass spectrometer with a Nova 3 data system. NMR spectra were obtained on Bruker WH-90 and WM-250 Fourier Transform NMR spectrometers which were controlled by B-NC-12 and Bruker Aspect 2000 computers, respectively, and on a Varian EM-360 NMR spectrometer. IR spectra were obtained on a Perkin Elmer 283 spectrometer.

HPLC was accomplished on an EM "Hibar" silica gel analytical column using 3% (v/v) ethyl acetate–2,2,4-trimethylpentane as eluant. Flash column chromatography was modified as previously described.[8]

Commercial (Aldrich) $CDCl_3$ was used. Other reagents and solvents were purified by standard procedures.

The following compounds were prepared as previously reported: *S*-2,2-dimethylpropyl 2,2-dimethylpropanesulfinothioate (**37**),[8,9] *S*-phenyl 2,2-dimethylpropanesulfinothioate (**5**),[9] *S*-phenyl benzenesulfonothioate (**15**),[44] *S*-2,2-dimethylpropyl benzenesulfinothioate (**9**),[9] phenyl phenylmethyl disulfide (**14**),[5] *S*-phenyl benzenesulfinothioate (**16**),[45] *S*-phenyl 2,2-dimethylpropanesulfonothioate (**23**),[9] 2,2-dimethylpropanesulfinic acid (**24**),[8,9] 2,2-dimethylpropanesulfonic acid (**25**),[8,9] and *S*-2,2-dimethylpropyl benzenesulfonothioate (**26**).[9]

2,2-Dimethylpropyl Phenyl Disulfide (10). A solution of pyridine (0.80 mL, 0.99 mmol) in 40 mL of anhydrous diethyl ether was added dropwise during 10 min to a stirred solution of *S*-2,2-dimethylpropyl benzenesulfonothioate (**26**) (2.42 g, 9.9 mmol) and thiophenol (1.01 mL, 9.9 mmol) in 60 mL of anhydrous diethyl ether at 24 °C under nitrogen. The mixture was stirred for 2.5 h, transferred to a separatory funnel, and washed with 20 mL of water and then with 20 mL of 5% $NaHCO_3$ solution. The ether layer was dried ($MgSO_4$) and the solvent evaporated in vacuo at 25 °C. Evaporative distillation of the crude residue at 60 °C (0.2 mm) afforded pure disulfide **10** as a pale yellow oil. Anal. C, H.

Oxidation of *S*-Phenyl 2,2-Dimethylpropanesulfinothioate (5), 2,2-Dimethylpropyl Phenyl Disulfide (10), and *S*-2,2-Dimethylpropyl Benzenesulfinothioate (9) and Phenyl Phenylmethyl Disulfide (14) in $CDCl_3$. The previously reported procedure was used at −30 °C, except 2 equiv of MCPBA were used for disulfides **10** and **14** (Tables II and III).[6,8,9,11]

Oxidation of 5, 9, and 10 with MCPBA in $CDCl_3$ Followed by Treatment with $NaHCO_3$ Solution. The previously reported procedure[6,8,9,11] was used at −30 °C, except 2 equiv of MCPBA were used for disulfides **10** and **14**. The HPLC analyses were performed within 5 min after separation of the layers.

Oxidation of *S*-2,2-Dimethylpropyl Benzenesulfinothioate (9) with MCPBA in $CHCl_3$ at −20 °C. The chloroform used in this reaction was dried over activated basic alumina immediately before use. A solution of thiosulfinate **9** (0.194 g, 0.85 mmol) in 0.7 mL of $CHCl_3$ was cooled to −20 °C in a 10-mL flask equipped with a sidearm that was fitted with a medium size glass frit. A solution of 85% MCPBA (0.164 g, 0.85 mmol) in 1.3 mL of $CHCl_3$ was added to the solution of thiosulfinate **9** with stirring. The mixture was stirred at −20 °C for 1 h and filtered. The filtrate was warmed to 24 °C, part of it was placed in an IR solution cell, and the remainder was placed in an NMR tube. After the NMR spectrum was taken (ca. 10 min after filtration), 0.10 mL of CD_3OD was added to the mixture in the NMR tube and the sequential spectra were obtained.

Oxidation of Thiosulfinates 5 and 9 in 52% (v/v) $CDCl_3/CD_3OD$ Followed by Treatment with $NaHCO_3$ Solution. The solvent mixture was prepared by mixing 1.45 mL of $CDCl_3$ and 1.33 mL of CD_3OD. In a nitrogen atmosphere, thiosulfinate **5** or **9** (1.6 mmol) was dissolved in 1 mL of the solvent mixture at −30 °C. MCPBA (82.4% pure, 0.329 g, 1.6 mmol) which was dissolved in the remainder of the solvent mixture (1.78 mL) was added dropwise to the solution of thiosulfinate **5** or **9** with stirring. The mixture was stirred at −30 °C for 1 h. The temperature was raised to 0 °C, 7 mL of a saturated aqueous solution of $NaHCO_3$ was added, and the mixture was stirred 10 min, transferred to a separatory funnel, and shaken. The layers were separated and the organic phase was dried ($MgSO_4$). Water was removed from the aqueous phase under vacuum. A part of the aqueous residue was dissolved in D_2O and analyzed via ^1H NMR. After the ^1H NMR analysis, the D_2O solution was added to the remainder of the residue from the aqueous phase. This residue was diluted with water and titrated with standard $KMnO_4$ solution. The organic layer was analyzed via ^1H NMR and HPLC.

Reaction of *S*-Phenyl 2,2-Dimethylpropanesulfinothioate (5) or *S*-2,2-Dimethylpropyl Benzenesulfinothoate (9) with 2,2-Dimethylpropanesulfinic Acid (24).[9] A solution of thiosulfinate **5** or **9** (0.42 g, 1.77 mmol) in 0.3 mL of $CDCl_3$ was mixed with an equimolar amount of sulfinic acid **24** in a 5-mm NMR tube. The reaction was followed by ^1H NMR (250 MHz), starting 7 min after mixing. The formation of *S*-2,2-dimethylpropyl 2,2-dimethylpropanesulfinothioate (**37**) and *S*-phenyl 2,2-dimethylpropanesulfonothioate (**23**) in the reaction of thiosulfinate **5** and sulfinic acid **24** and the formation of *S*-2,2-dimethylpropyl 2,2-dimethylpropanesulfonothioate (**22**) and thiosulfonate **23** in the reaction of thiosulfinate **9** and sulfinic acid **24** was confirmed by comparison of ^1H NMR chemical shifts and TLC analyses 24 h after mixing.

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Registry No. **5**, 80318-99-6; **6**, 78609-87-7; **9**, 80319-00-2; **10**, 80318-98-5; **14**, 16601-17-5; **15**, 1212-08-4; **16**, 1208-20-4; **17**, 37945-60-1; **18**, 16601-40-4; **19**, 4403-73-0; **20**, 100-87-8; **21**, 94944-59-9; **22**, 75142-07-3; **23**, 80319-01-3; **24**, 78607-81-5; **25**, 44820-66-8; **26**, 80319-02-4; **27**, 74635-31-7; **28**, 74635-32-8; **29**, 630-19-3; **30**, 94944-60-2; **37**, 78607-80-4; bis(2,2-dimethylpropyl) disulfide, 37552-63-9; MCPBA, 937-14-4.

(44) Kice, J. L.; Rogers, T. E. *J. Am. Chem. Soc.* **1974**, *96*, 8015.
(45) Kice, J. L.; Venier, C. G.; Heasley, L. *J. Am. Chem. Soc.* **1967**, *89*, 3557.