(neat) 3420, 3180, 2850, 1710, 1610, 1520 cm^{-1}.

Condensation of Dienone Acid 28 with Silylated Schiff Base To Give Aldehyde Derivative 31. Compound **31** was prepared similarly to compound **29**. The silylated Schiff base was prepared from propionaldehyde. The trans isomer was separated from the cis by chromatography. Trans isomer: λ_{max} (EtOH) 360 nm (ϵ 32000); NMR ($CDCl_3$) δ 0.8 (s, 3, 13-Me), 0.9 (s, 3, 10-Me), 2.1 (s, 3, 2′-Me), 5.9 (s, 1, 6-H), 6.2 (s, 1, 4-H), 10.1 (s, 1, 1′-H); IR ($CHCl_3$) 2860, 1710, 1630, 1580 cm^{-1}.

Condensation of 31 with Five-Carbon Nitrile Phosphonate To Give Nitrile 32. The five-carbon nitrile phosphonate (25 mg) derived from 3,3-dimethylacrylonitrile was added at room temperature to a slurry of 6 mg of 50% NaH in 4 mL of dry THF. The solution was stirred under argon for 30 min and then 40 mg of acid aldehyde **31** was added. The mixture was stirred for 20 min. The solution was acidified with oxalic acid and 50 mL of ether and 50 mL of water were added. The organic layer was washed with water and brine and dried, and the solvent was evaporated. The crude oil was chromatographed and eluted with ether to give 44 mg of a mixture of cis and trans **32**: λ_{max} (EtOH) 392 nm (ϵ 38000); NMR ($CDCl_3$) δ 0.8 (s, 3, 13-Me), 0.9 (s, 3, 10-Me), 2.1 (s, 3, 6′-Me), 2.2 (s, 3, 3′-Me of cis isomer), 2.25 (s, 3, 3′-Me of trans isomer), 5.20 and 5.25 (two s, 1, 2′-H of cis and trans isomers), 5.9 (s, 1, 6-H), 6.2 (s, 1, 4-H), 6.3, 6.4 (m, 2, 4′-H, 5′-H); IR ($CHCl_3$) 2850, 2200, 1710, 1580 cm^{-1}.

Reduction of Pentaene Nitrile 32 to Aldehyde 33. Nitrile **32** was reduced by diisobutylaluminum hydride, as in the case of nitrile **17**, and the product was chromatographed by using ether: λ_{max} (EtOH) 395 nm (ϵ 38000); NMR ($CDCl_3$) δ 0.8 (s, 3, 13-Me), 0.9 (s, 3, 10-Me), 2.1 (s, 3, 6′-Me), 2.25 (s, 3, 3′-Me of cis isomer), 2.35 (s, 3, 3′-Me of trans isomer), 6 (m, 3, 2′-H, 6′-H, 6-H), 6.3 (m, 3, 4′-H, 5′-H, 4-H), 10.15 (d, J = 9 Hz, 1′-H); IR ($CHCl_3$) 2850, 1710, 1640, 1580 cm^{-1}.

Condensation of 33 with Pyrrolidine Perchlorate and L(−)-Proline Perchlorate To Give 34 and 35, Respectively. The condensation was carried out in EtOH as described for **30**. Compound **34**: λ_{max} ($CHCl_3$) 541 nm (ϵ 44000), upon addition of triethylamine in chloroform the absorption maximum shifted to 545 nm, acidification with acetic acid caused the maximum to shift back to 542 nm; IR (neat) 3410, 3150, 2850, 1710, 1600, 1520 cm^{-1}. Compound **35**: λ_{max} ($CHCl_3$) 565 nm (ϵ 41000), addition of triethylamine shifted the absorption maximum to 542 nm; IR (neat) 3420, 3150, 2840, 1715, 1600, 1520 cm^{-1}.

Acknowledgment. We thank Professors B. Honig, A. Warshel, and T. Ebrey for discussions. The studies were supported by National Institutes of Health Grant EY 01253 and National Science Foundation Grant CHE-8110505.

Registry No. (*E*)-**1**, 85441-22-1; (*Z*)-**1**, 85441-24-3; (*E*)-**2**, 85405-80-7; (*Z*)-**2**, 85405-82-9; **3**, 85405-84-1; **4**, 72471-87-5; **5**, 85405-86-3; **6**, 85405-88-5; **7**, 85405-90-9; **8**, 85405-92-1; **9**, 85405-94-3; **10**, 85405-96-5; **11**, 85405-98-7; **12**, 85406-00-4; **13**, 85441-25-4; (*E*)-**14**, 85406-01-5; (*Z*)-**14**, 85441-26-5; (*E*)-**15**, 85406-02-6; (*Z*)-**15**, 85441-27-6; (*E*)-**16**, 85406-03-7; (*Z*)-**16**, 85441-28-7; (11*E*)-**17**, 85406-04-8; (11*Z*)-**17**, 85441-29-8; (11*E*)-**18**, 85406-05-9; (11*Z*)-**18**, 85441-30-1; **19a**, 638-10-8; **19b**, 107-86-8; (3*E*)-**20**, 85406-06-0; (3*Z*)-**20**, 85406-07-1; (3*E*)-**21**, 85441-31-2; (3*Z*)-**21**, 49831-80-3; (15*E*)-**22**, 85406-08-2; (15*Z*)-**22**, 85441-32-3; (15*E*)-**23**, 85406-09-3; (15*Z*)-**23**, 85441-33-4; (3*E*)-**24**, 85406-10-6; (3*Z*)-**24**, 85441-34-5; (3*E*)-**25**, 80172-51-6; (3*Z*)-**25**, 85441-35-6; **26**, 85406-11-7; 7α-**27**, 85406-12-8; 7β-**27**, 85406-13-9; **28**, 85406-14-0; (*Z*)-**29**, 85406-15-1; (*E*)-**29**, 85406-16-2; **30**, 85406-18-4; (*E*)-**31**, 85406-19-5; (*Z*)-**31**, 85421-51-8; (3′*E*)-**32**, 85406-20-8; (3′*Z*)-**32**, 85441-36-7; (3′*E*)-**33**, 85406-21-9; (3′*Z*)-**33**, 85441-37-8; **34**, 85406-23-1; **35**, 85406-25-3; $(EtO)_2POC(CH_3)CHCN$, 85406-26-4; $Me_3SiCH_2CH{=}NCMe_3$, 73198-78-4; $Me_3SiCH(CH_3)CH{=}NCMe_3$, 58707-01-1; pyrrolidine perchlorate, 22401-44-1; L-proline perchlorate, 67877-19-4; 2-(1-bromoethyl)-1,3-dioxolane, 5267-73-2.

Formation of α-Disulfoxides, Sulfinic Anhydrides, and Sulfines during the *m*-Chloroperoxybenzoic Acid Oxidation of Symmetrical *S*-Alkyl Alkanethiosulfinates[1,2]

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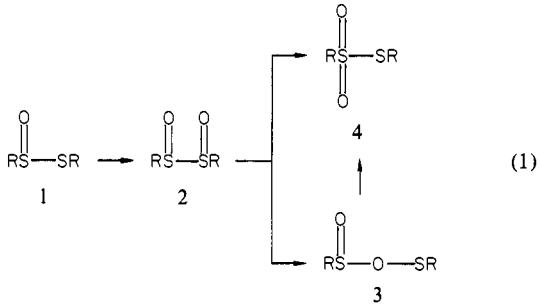
Contribution from the Department of Chemistry, University of California, Irvine, California 92717. *Received July 20, 1982*

Abstract: The *m*-chloroperoxybenzoic acid (MCPBA) oxidation of *S*-methyl methanethiosulfinate (**33**), *S*-propyl propanethiosulfinate (**34**), *S*-2-propyl 2-propanethiosulfinate (**35**), *S*-butyl butanethiosulfinate (**36**), and *S*-(phenylmethyl) phenylmethanethiosulfinate (**37**) has been studied at low temperatures and compared with the MCPBA oxidation of *S*-(2-methyl-2-propyl) 2-methyl-2-propanethiosulfinate (**26**) and *S*-(2,2-dimethylpropyl) 2,2-dimethylpropanethiosulfinate (**30**). Diastereomeric α-disulfoxides are observed with **33**–**36** at −40 °C, sulfinic anhydrides are observed with **33**, **35**, and **36** at −40 °C, and sulfines are observed on warming the product mixtures from **34**–**37** from −40 °C to −20 °C. The lachrymatory factor ((*Z*)-propanethial *S*-oxide, **47**) of the onion was observed during the oxidation of **35**. The absence of thiosulfonates at −40 °C and their presence at higher temperatures suggest that they are not formed in the initial oxidation process but from subsequent reactions of thiosulfinates and sulfinic acids. Various mechanisms for the formation of intermediates and products are discussed.

Peroxy acids oxidize thiosulfinates (**1**) to thiosulfonates (**4**).[3-14]



(1)

Although α-disulfoxides (**2**) and sulfenyl sulfinates (**3**) have been postulated as transient intermediates, it appears that the mechanism of oxidation varies with the structure of the thiosulfinate

(1) Abstracted from: Angeletakis, C. N. Ph.D. Thesis, University of California, Irvine, CA, 1982.
(2) Presented in part at the 8th Annual Meeting of the NOBCChE, Chicago, IL, April 24, 1981, and the 183rd National ACS Meeting, Las Vegas, NV, March 30, 1982.
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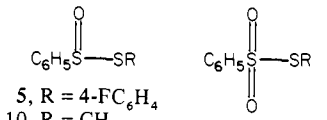
(1).

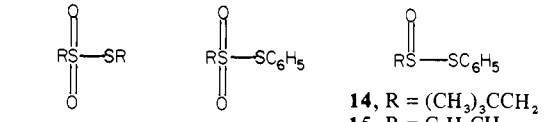
The peracetic oxidation of *S*-(4-fluorophenyl) benzenethiosulfinate (**5**)[8] gave thiosulfonates **6–8** and presumably **9**, and



5, R = 4-FC_6H_4
10, R = CH_3

6, R = 4-FC_6H_4
11, R = CH_3

oxidation of *S*-methyl benzenethiosulfinate (**10**) gave thiosulfonates **9**, **11**, **12**, and **13**.[9] Interestingly, low-temperature ^1H NMR and

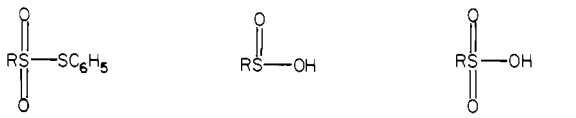


7, R = 4-FC_6H_4
12, R = CH_3

8, R = 4-FC_6H_4
9, R = C_6H_5
13, R = CH_3

14, R = $(CH_3)_3CCH_2$
15, R = $C_6H_5CH_2$

^{13}C NMR studies of the early stages of the low-temperature *m*-chloroperoxybenzoic acid (MCPBA) oxidation of *S*-phenyl 2,2-dimethylpropanethiosulfinate (**14**)[5] and *S*-phenyl phenylmethanethiosulfinate (**15**)[12] showed that **14**, *S*-phenyl 2,2-dimethylpropanethiosulfonate (**16**), 2,2-dimethylpropanesulfinic acid



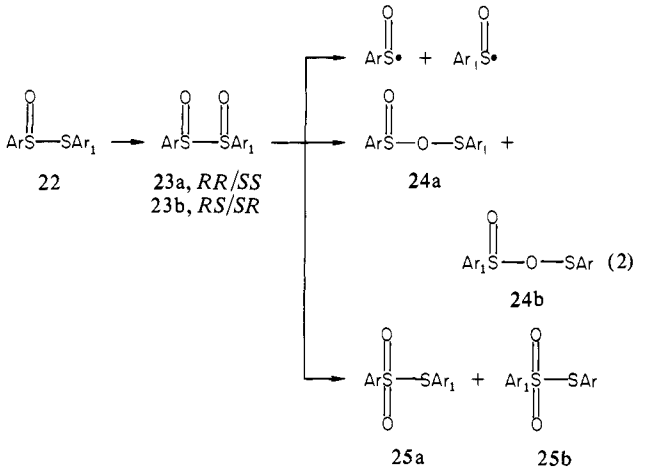
16, R = $(CH_3)_3CCH_2$
19, R = $C_6H_5CH_2$

17, R = $(CH_3)_3CCH_2$
20, R = $C_6H_5CH_2$

18, R = $(CH_3)_3CCH_2$
21, R = $C_6H_5CH_2$

(**17**), and 2,2-dimethylpropanesulfonic acid (**18**) were the major products from **14** while the major products from **15** were **15**, *S*-phenyl phenylmethanethiosulfonate (**19**), phenylmethanesulfinic acid (**20**), and phenylmethanesulfonic acid (**21**).

A variety of mechanisms has been proposed to account for the peroxidation of *S*-alkyl (e.g., **10**) and *S*-aryl arenethiosulfinates (**22**) to *S*-alkyl (e.g., **11**) and *S*-aryl arenethiosulfonates



22

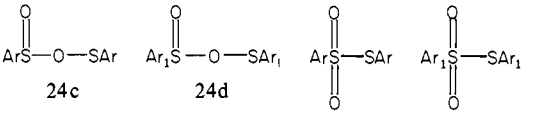
23a, *RR/SS*
23b, *RS/SR*

24a

24b (2)

25a 25b

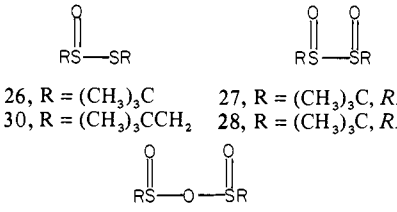
(**25**).[8-12,14-18] Homolysis of the weak S–S bond in α-disulfoxides **23** can lead to sulfinyl radicals (eq 2). Rearrangement of unsymmetrical **23** can lead to sulfenyl sulfinates **24a** and **24b** and/or thiosulfonates **25a** and **25b**. The sulfinyl radicals can combine to give **24a**, **24b**, and two symmetrical sulfenyl sulfinates (**24c** and **24d**).[15-19] These four sulfenyl sulfinates (**24a–d**) can rearrange to four aryl arenethiosulfonates (**25a–d**).



24c 24d 25c 25d

In order to eliminate the influence of the phenyl group, which can interact with the nonbonded electrons on the sulfenyl sulfur atoms in thiosulfinates, we have investigated the low-temperature MCPBA oxidation of symmetrical *S*-alkyl alkanethiosulfinates in order to determine the influence of structure on oxidation at the sulfenyl sulfur (to give α-disulfoxides, **2**) and at the sulfinyl sulfur (to give thiosulfonates, **4**). This study is also of interest because the only two symmetrical *S*-alkyl alkanethiosulfinates studied thus far[4,6,13] gave different oxidation products under similar experimental conditions.

The low-temperature MCPBA oxidation of *S*-(2-methyl-2-propyl) 2-methyl-2-propanethiosulfinate (**26**)[6] gave diastereomeric

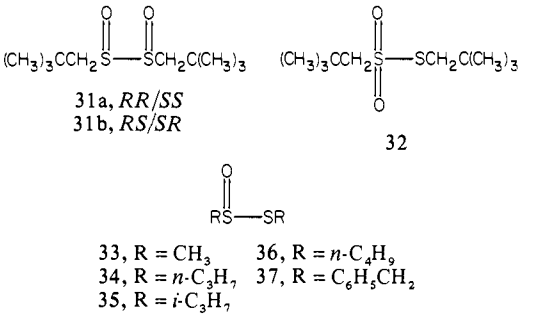


26, R = $(CH_3)_3C$
30, R = $(CH_3)_3CCH_2$

27, R = $(CH_3)_3C$, *RR/SS*
28, R = $(CH_3)_3C$, *RR/SS*

29a, R = $(CH_3)_3C$, *RR/SS*
29b, R = $(CH_3)_3C$, *RS/SR*

α-disulfoxides (**27** and **28**) and diastereomeric sulfinic anhydrides (**29**), while oxidation of *S*-(2,2-dimethylpropyl) 2,2-dimethylpropanethiosulfinate (**30**)[4,13] afforded 2,2-dimethylpropanesulfinic acid (**17**), 2,2-dimethylpropanesulfonic acid (**18**), diastereomeric α-disulfoxides (**31**), and *S*-(2,2-dimethylpropyl) 2,2-dimethylpropanethiosulfonate (**32**).



31a, *RR/SS*
31b, *RS/SR*

32

33, R = CH_3
34, R = n-C_3H_7
35, R = i-C_3H_7
36, R = n-C_4H_9
37, R = $C_6H_5CH_2$

Results

In order to determine the initial oxidation products, the following procedure was used for the low-temperature MCPBA oxidation of *S*-methyl methanethiosulfinate (**33**),[20] *S*-propyl propanethiosulfinate (**34**),[21] *S*-2-propyl 2-propanethiosulfinate (**35**),[21] *S*-butyl butanethiosulfinate (**36**),[21] and *S*-(phenylmethyl) phenylmethanethiosulfinate (**37**).[22] Table I summarizes the

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Table I. Yields of Products from the *m*-Chloroperoxybenzoic Acid (MCPBA) Oxidation of *S*-Alkyl Alkanethiosulfinates in Deuteriochloroform[a]

RSS(O)R		temp, °C	time,[b] min	products						
				RSS(O)R	RS(O)S-(O)R[c]	RS(O)S-(O)R[c]	RSO_2H	$(RSO_2)_2O$	RS-(O_2)SR	R'CH=S=O[d]
CH_3	33	−40	19 (69)	59 (56)[e]	20 (25)[e]	21 (19)[e]				
		−20	101	76		10	4	2	7	
n-C_3H_7	34	−40	17 (52)	47	19	32	3			
		−20	85	72		2	18		8	7 (*Z*)
i-C_3H_7	35	−40	15 (86)	52	9	25	10	<1		
		−20	122	78		1	14	2	4	10[f]
n-C_4H_9	36	−40	15 (71)	47	3	27	12	12		3 (*Z*)
		−20	97	64			25		10	8 (*Z*)
t-C_4H_9	26	−40	17[g]	47		28[h]		15, 10[i]		
		−20	130	61				23, 17[i]		
neo-C_5H_{11}	30	−40	15 (102)	43	34	14	7		1	4 (*Z*), 4 (*E*)
		−20	135	73			13		2	7 (*Z*), 9 (*E*)
$C_6H_5CH_2$	37	−40	15 (69)	67		22[h]	11			2 (*Z*)
		−20	88	81			13		7	6 (*Z*)

[a] Percent relative integrals of the sulfur-bonded carbon atoms are given (^{13}C NMR at 62.89 MHz). [b] Time measurement was started after filtration. Time at which ^{13}C NMR acquisition (200 scans in 15 min) was initiated is given. The time at which the temperature was raised to −20 °C is given in parentheses. [c] Assignments of diastereomers is uncertain. [d] The amounts of sulfines were estimated from the ^1H NMR spectra (250 MHz) obtained immediately before the ^{13}C NMR spectra. When R = n-C_3H_7, R' = C_2H_5; R = n-C_4H_9, R' = n-C_3H_7; R = neo-C_5H_{11}, R' = t-C_4H_9; R = $C_6H_5CH_2$, R' = C_6H_5. [e] Relative integral from the ^1H NMR spectrum at 15 min. [f] $(CH_3)_2C{=}S{=}O$. [g] Temperature was raised to −30 °C at 98 min and then to −20 °C at 114 min; see ref 6. [h] Only one signal that can be assigned to an α-disulfoxide was observed. [i] Yields of diastereomeric (*RR/SS*,*RS/SR*) sulfinic anhydrides are given. [j] Reference 4.

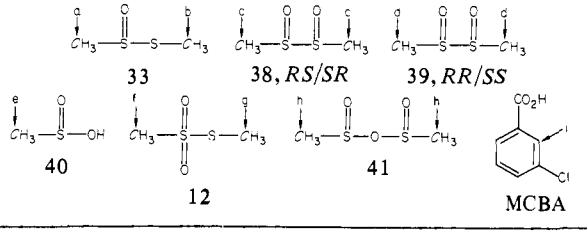
Table II. ^1H NMR and ^{13}C NMR Chemical Shifts of Products from the MCPBA Oxidation of *S*-Methyl Methanethiosulfinate (33) at −40 °C in $CDCl_3$[a-c]

compound	shift (−40 °C, 19 min[d])				shift (−20 °C, 101 min[e])	
	^1H NMR, δ	yield, %[f]	^{13}C NMR, δ	yield, %[g]	^{13}C NMR, δ	yield, %[g]
$CH_3S(O)SCH_3$ (33)	2.75	56	15.22	59	15.00	76
	3.08		42.02		42.18	
$CH_3S(O)S(O)CH_3$ (38), *RS/SR*	2.86	25	36.07	20		
$CH_3S(O)S(O)CH_3$ (39), *RR/SS*	3.04	19	36.17	21	36.23	10
CH_3SO_2H (40)					44.90	4
$CH_3SO_2SCH_3$ (12)					18.57	7
					48.63	
$(CH_3SO)_2O$ (41)					46.47	2

[a] Me_4Si was used as internal standard; the spectrometer frequency was 62.89 MHz for ^{13}C NMR and 250.13 MHz for ^1H NMR. [b] ^{13}C NMR spectra required 200 scans in 15 min with broad-band decoupling. [c] See Figure 1 for ^{13}C NMR resonance assignments. [d] Time measurement was started after filtration. [e] The temperature was raised to −20 °C at 69 min. [f] Percent relative integrals of ^1H NMR chemical shifts at 15 min after filtration. [g] Percent relative integrals of the carbon atoms bonded to sulfur.

Table III. Conditions and Compounds for Figure 1

time, min	temp, °C	operation
0	−45	filtration completed
15	−40	^1H NMR spectrum obtained
19	−40	^{13}C NMR spectrum obtained
69-70	−20	temperature raised to −20 °C
85	−20	^{13}C NMR spectrum obtained
101	−20	^{13}C NMR spectrum obtained
128	−20	^1H NMR spectrum obtained
132-133	0	temperature raised to 0 °C
150	0	^{13}C NMR spectrum obtained
193	0	^{13}C NMR spectrum obtained



products from the MCPBA oxidation of **26**, **30**, **33–36**, and **37**.

Thiosulfinates **33–37** were oxidized with 1 equiv of MCPBA at −40 to −35 °C for 45 min in $CDCl_3$ under dry nitrogen.[4,6] After the product mixture was filtered as quickly as possible under nitrogen at −50 °C in order to remove *m*-chlorobenzoic acid (MCBA), the filtrate was thermostated immediately in the NMR spectrometer at −40 °C and the ^1H NMR and ^{13}C NMR spectra were recorded. Selected examples of the changes occurring in

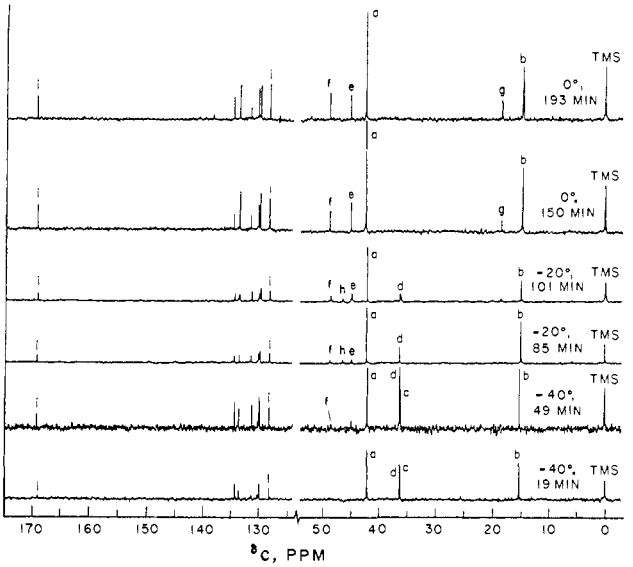


Figure 1. Temperature and time dependent ^1H NMR and ^{13}C NMR spectra of the products from the MCPBA oxidation of *S*-methyl methanethiosulfinate (**33**) in $CDCl_3$.

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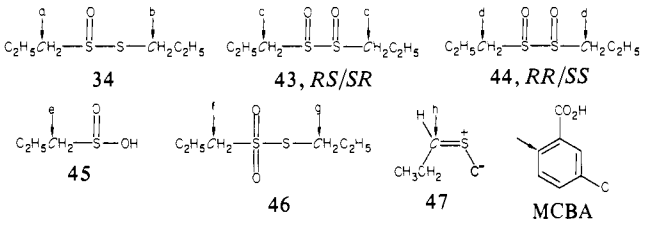
Table IV. ^1H NMR and ^{13}C NMR Chemical Shifts of Products from the MCPBA Oxidation of *S*-Propyl Propanethiosulfinate (34) at −40 °C in $CDCl_3$[a-c]

compound	^{13}C NMR, δ_C (−40 °C, 17 min[d])	yield, %[e]	^{13}C NMR, δ_C (−20 °C, 85 min[f])	yield, %[e]
$C_2H_5CH_2S(O)SCH_2C_2H_5$ (34)	34.91	47	35.01	72
	57.02		57.30	
$C_2H_5CH_2S(O)S(O)CH_2C_2H_5$ (43), *RS/SR*	51.13	19		
$C_2H_5CH_2S(O)S(O)CH_2C_2H_5$ (44), *RR/SS*	51.45	32	51.63	2
$C_2H_5CH_2SO_2H$ (45)	60.53	3	59.40	18
$C_2H_5CH_2SO_2SCH_2C_2H_5$ (46)			38.14	
			64.00	8
$C_2H_5CH{=}S^+{-}O^-$ (47)			180.48 (8.28)[g]	(7)[h]

[a] Me_4Si was used as internal standard; the spectrometer frequency was 62.89 MHz for ^{13}C NMR and 250.13 MHz for ^1H NMR. [b] ^{13}C NMR spectra required 200 scans in 15 min with broad-band decoupling. [c] See Figure 3 and Table V for ^{13}C NMR resonance assignments. [d] Time measurement was started after filtration. [e] Percent relative integrals of the sulfur-bonded carbon atoms. [f] The temperature was raised to −20 °C after 52 min. [g] ^1H NMR chemical shift of vinyl proton (t, J = 8.1 Hz, see ref 27 and 28). [h] Relative amount estimated from ^1H NMR spectrum.

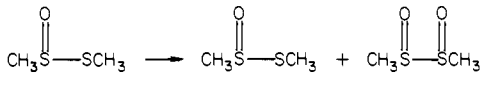
Table V. Conditions and Compounds for Figure 3

time, min	temp, °C	operation
0	−45	filtration completed
15	−40	^1H NMR spectrum obtained
17	−40	^{13}C NMR spectrum obtained
52-53	−20	temperature raised to −20 °C
82	−20	^1H NMR spectrum obtained
85	−20	^{13}C NMR spectrum obtained
100-101	0	temperature raised to 0 °C
115	0	^{13}C NMR spectrum obtained
147	0	^{13}C NMR spectrum obtained



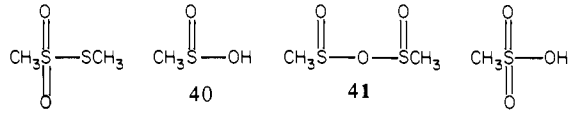
the NMR spectra are described below. Additional NMR data from **35–37** are included in the supplementary material.

Oxidation of *S*-Methyl Methanethiosulfinate (33). Tables II and III and Figures 1 and 2 show the ^1H NMR and ^{13}C NMR spectra of the products from the MCPBA oxidation of **33** at various times and temperatures. These data show that the product mixture at −40 °C contained **33** and diastereomeric methyl di-



(3)

sulfoxides (**38** and **39**). The resonance assigned to α-disulfoxide **38** disappeared on warming the product mixture to −20 °C while the resonance ascribed to α-disulfoxide **39** decreased and the resonances for **33** increased. At −20 °C ^{13}C NMR resonances were observed for *S*-methyl methanethiosulfonate (**12**),[20,23]



methanesulfinic acid (**40**),[24] and methanesulfinic anhydride (**41**).[6,25,26] No resonance was observed for methanesulfonic acid (**42**).[24]

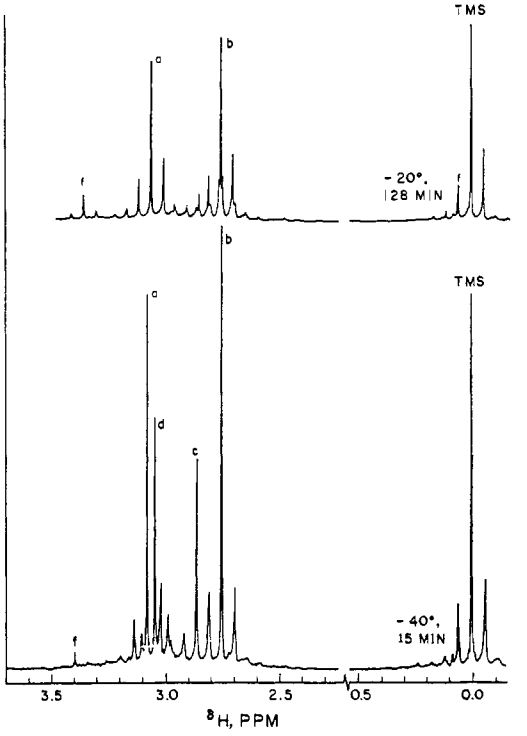


Figure 2. ^1H NMR spectrum of the product mixture from the MCPBA oxidation of *S*-methyl methanethiosulfinate (**33**) in $CDCl_3$. The legend is the same as in Figure 1.

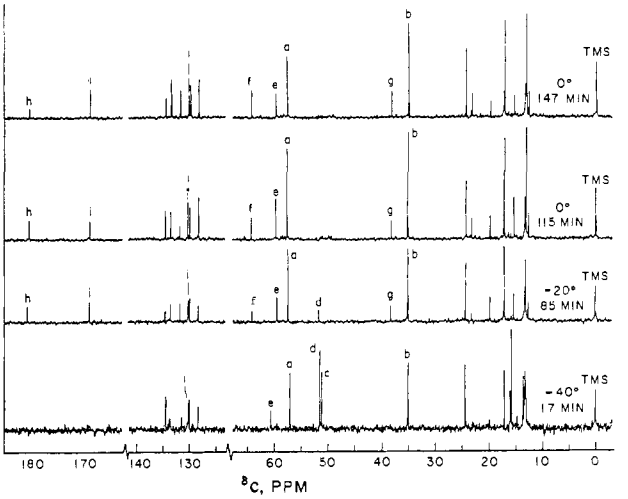
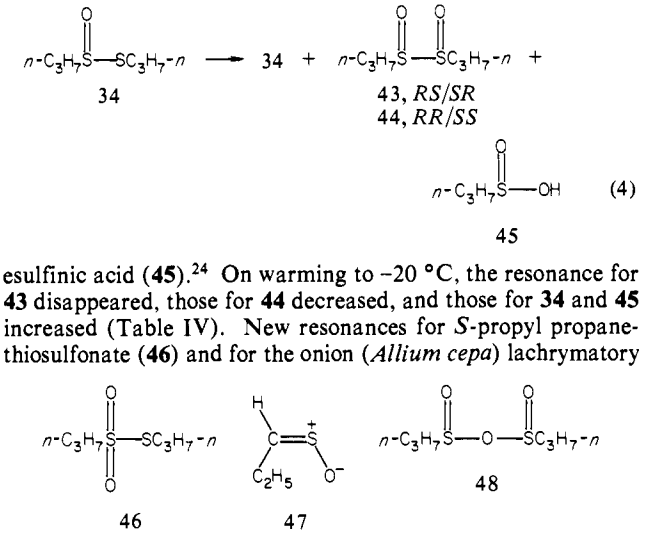


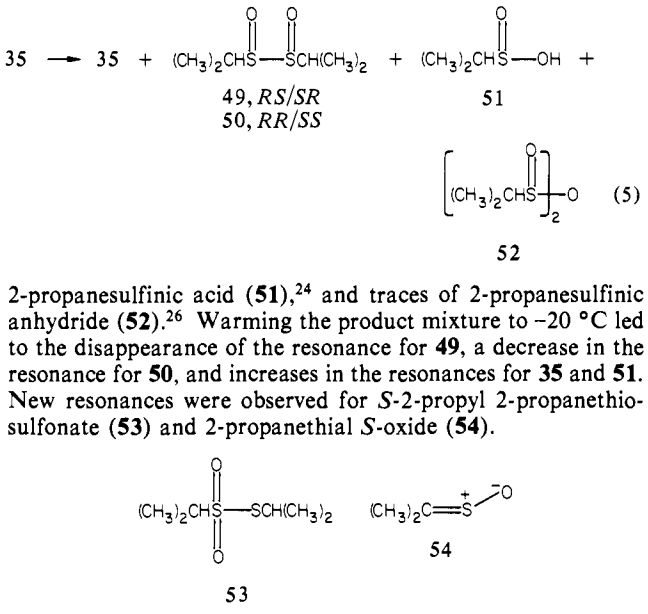
Figure 3. Temperature and time dependent ^1H NMR and ^{13}C NMR spectra of the products from the MCPBA oxidation of *S*-propyl propanethiosulfinate (**34**) in $CDCl_3$.

(23) Freeman, F.; Angeletakis, C. N.; Maricich, T. J. *Org. Magn. Reson.* **1981**, *17*, 51.
(24) Freeman, F.; Angeletakis, C. N. *Org. Magn. Reson.* **1983**, *21*, 86.
(25) Kice, J. L.; Ikura, K. *J. Am. Chem. Soc.* **1968**, *90*, 7378.
(26) In principle, diastereomeric sulfinic anhydrides are possible.

Oxidation of *S*-Propyl Propanethiosulfinate (34). Tables IV and V and Figure 3 show the ^1H and ^{13}C NMR spectra of the products from the MCPBA oxidation of **34**. It is seen from the ^{13}C NMR spectrum that the product mixture at −40 °C contained **34**, diastereomeric propyl disulfoxides (**43** and **44**), and propanesulfinic acid (**45**).[24] On warming to −20 °C, the resonance for **43** disappeared, those for **44** decreased, and those for **34** and **45** increased (Table IV). New resonances for *S*-propyl propanethiosulfonate (**46**) and for the onion (*Allium cepa*) lachrymatory factor (LF) (*Z*)-propanethial *S*-oxide (**47**) appeared.[27-29] No resonance was observed for propanesulfinic anhydride (**48**).[26]

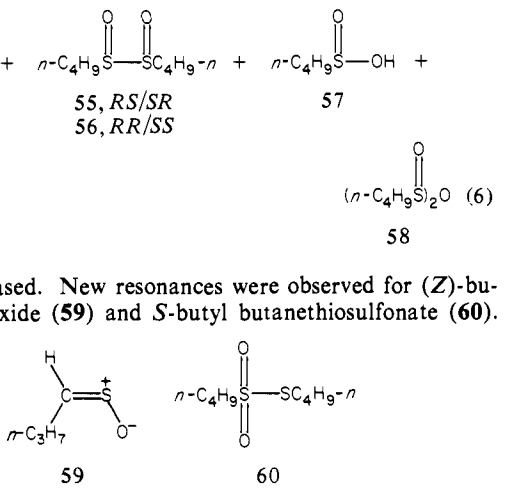


Oxidation of *S*-2-Propyl 2-Propanethiosulfinate (35). The product mixture from the MCPBA oxidation of **35** at −40 °C contained **35**, diastereomeric 2-propyl disulfoxides (**49** and **50**), 2-propanesulfinic acid (**51**),[24] and traces of 2-propanesulfinic anhydride (**52**).[26] Warming the product mixture to −20 °C led to the disappearance of the resonance for **49**, a decrease in the resonance for **50**, and increases in the resonances for **35** and **51**. New resonances were observed for *S*-2-propyl 2-propanethiosulfonate (**53**) and 2-propanethial *S*-oxide (**54**).

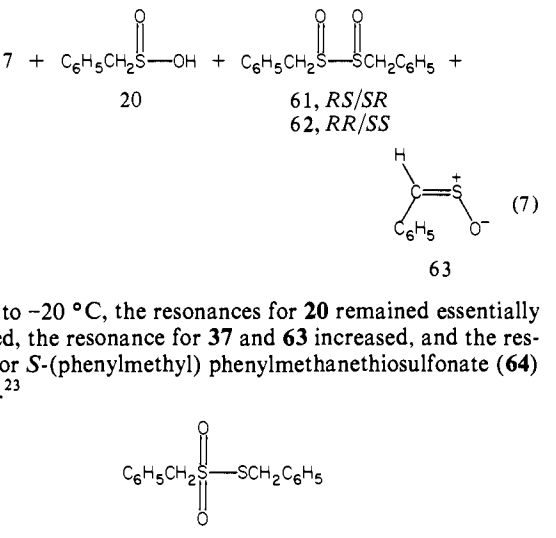


When the oxidation of **35** was carried out at −30 °C, instead of −40 °C, for 60 min, the ^{13}C NMR spectrum of the reaction mixture, which was obtained 15 min after filtration, showed that the peak for sulfinic anhydride **52** is larger than the peak for α-disulfoxide **50** (*RR/SS*). Both **50** and **52** are minor components in the product mixture.

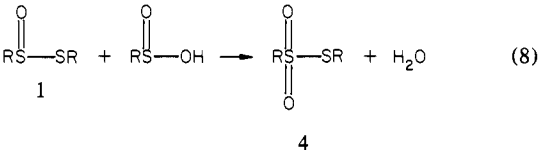
Oxidation of *S*-Butyl Butanethiosulfinate (36). The MCPBA oxidation of **36** at −40 °C led to **36**, butyl disulfoxides (**55** and **56**), butanesulfinic acid (**57**), and butanesulfinic anhydride (**58**).[26] On warming to −20 °C, the resonances for α-disulfoxides **55** and **56** and sulfinic anhydride **59** disappeared and resonances for **36** and **57** increased. New resonances were observed for (*Z*)-butanethial *S*-oxide (**59**) and *S*-butyl butanethiosulfonate (**60**).



Oxidation of *S*-(Phenylmethyl) Phenylmethanethiosulfinate (37). The MCPBA oxidation of **37** at −40 °C afforded phenylmethanesulfinic acid (**20**), **37**, phenylmethyl disulfoxides (**61** and/or **62**), and (*Z*)-phenylmethanethial *S*-oxide (**63**). On warming to −20 °C, the resonances for **20** remained essentially unchanged, the resonance for **37** and **63** increased, and the resonances for *S*-(phenylmethyl) phenylmethanethiosulfonate (**64**) appeared.[23]



Warming Product Mixtures to 0 °C. When the product mixtures obtained by oxidation of alkanethiosulfinates **33**–**37** at −40 °C were warmed to 0 °C, the respective sulfinic acids present in the reaction mixture reacted with the corresponding thiosulfinates to afford the corresponding thiosulfonates (eq 8).[21,30] All of the reactions appeared to be complete within 60 min.



In order to determine whether the reaction shown in eq 8 is catalyzed by a component of the reaction mixture, equivalent amounts of *S*-butyl butanethiosulfinate (**36**) and butanesulfinic acid (**57**) were mixed at 0 °C in $CDCl_3$ at the same dilution used in the −40 °C MCPBA oxidation experiment. The rate of reaction, which was followed via ^{13}C NMR, was similar to that observed in the −40 °C oxidation experiment. This nonquantitative kinetic experiment suggests that no external catalyst is necessary for the reaction in eq 8 to take place between **36** and **57**.

At 0 °C ^1H NMR and ^{13}C NMR analyses showed that sulfines **47**, **54**, **59**, and **63** had decomposed to give the corresponding

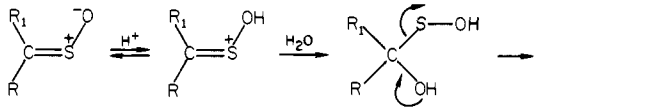
(27) Block, E.; Penn, R. E.; Revelle, L. K. *J. Am. Chem. Soc.* **1979**, *101*, 2200.
(28) Block, E.; Revelle, L. K.; Bazzi, A. A. *Tetrahedron Lett.* **1980**, *21*, 1277.
(29) Block, E., private communication.
(30) Kice, J. L.; Large, G. B. *J. Org. Chem.* **1968**, *33*, 1940.

Table VI. Comparison of ^{13}C NMR Chemical Shifts of Alkyl α-Disulfoxides with Those of the Corresponding Alkyl Thiosulfinates

alkyl α-disulfoxide	compd	obsd δ_C of α-carbon atom of α-disulfoxide	obsd δ_C of α-carbon atom of corresponding thiosulfinate	α'_{SO}[a]	calcd δ_C[b]	obsd δ_C − calcd δ_C
$CH_3S(O)S(O)CH_3$	38, 39	36.07, 36.17	42.02	−7.60	34.42	1.74, 1.65
$C_2H_5CH_2S(O)S(O)CH_2C_2H_5$	43, 44	51.13, 51.45	57.02	−6.35	50.67	0.77, 0.46
$(CH_3)_2CHS(O)S(O)CH(CH_3)_2$	49, 50	49.56, 50.00	55.12	−2.87[c]	52.25	−2.25, −2.69
$C_3H_7CH_2S(O)S(O)CH_2C_3H_7$	55, 56	49.20, 49.53	55.09	−6.06	49.03	0.50, 0.17
$(CH_3)_3CS(O)S(O)C(CH_3)_3$	27, 28	57.20	59.44	2.30[c]	61.74	−4.54
$(CH_3)_3CCH_2S(O)S(O)CH_2C(CH_3)_3$	31	64.00, 64.35	70.44	−9.03	61.41	2.60, 2.94
$C_6H_5CH_2S(O)S(O)CH_2C_6H_5$	61, 62	55.38	60.71	−7.23	53.48	1.91

[a] The α'_{SO} substituent effect was calculated from $\delta_C(S(O)SC)-\delta_C(CSSC)$; see ref 23, 24, and 41. [b] Calculated $\delta_C = \delta_C$ of the α-carbon atom of the thiosulfinate at −40 °C + α'_{SO}. [c] Reference 20.

carbonyl compounds. The decomposition of sulfines on warming the product mixtures from −40 to 0 °C may occur via interaction with the sulfinic acids (eq 9 and 10).[27-29,31-33]



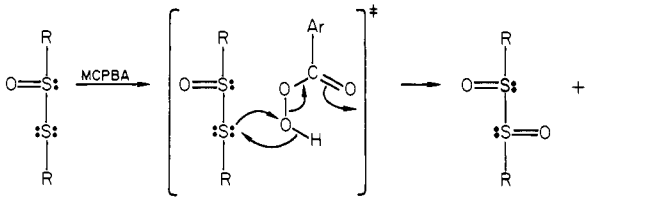
(9)

$$HSOH \rightarrow H_2O + S + H_2S + SO_2 + H_2SO_4 \quad (10)$$

Low-Temperature Infrared Spectra. The low-temperature IR spectrum of the product mixture obtained from the MCPBA oxidation of **35** at −40 °C was obtained as quickly as possible after filtration at −50 °C (within 15 min). The IR spectrum showed a band at 1100 cm^{-1} that decreased in intensity as the reaction mixture was warmed to −20 °C. Conclusive assignment of this band to the S=O stretch of the α-disulfoxides **49** and **50** could not be made owing to its proximity to the S=O band of **35** at 1050 cm^{-1} and the appearance at −20 °C of the IR band at 1080 cm^{-1} (S=O) for **54**.[34]

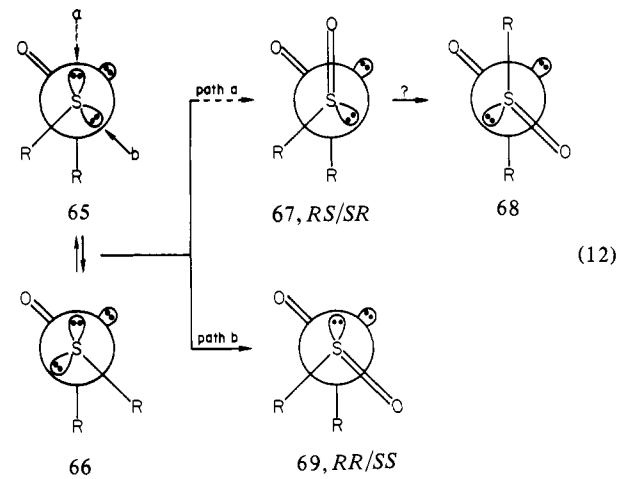
Discussion

The low yield of thiosulfonates in the initial product mixtures obtained from the MCPBA oxidation of thiosulfinates **26**,[6] **30**,[4,13] **33–36**, and **37** and the inertness of the corresponding thiosulfonates under the experimental conditions[35,36] are consistent with the formation of α-disulfoxides (**2**), probably via eq 11. Since kinetic



(11)

studies have shown that sulfenyl sulfur is more reactive toward peroxybenzoic acid,[37] the proposed electrophilic attack by MCPBA at the sulfenyl sulfur atom of **1** is reasonable. Thus, oxidation of thiosulfinate **1** can occur via attack of peroxy acid at two sites (**65**, eq 12).



(12)

α-Disulfoxides (**2**) contain two chiral sulfur atoms and can exist as diastereomers **67** (*RS/SR*, meso) and **69** (*RR/SS*, *d,l*). Although the chemical shift data on α-disulfoxides (**2**) are not sufficient to definitively assign the resonances of the respective diastereomers, several observations concerning their stereochemistry and structures can be made from a study of molecular models and physical properties.

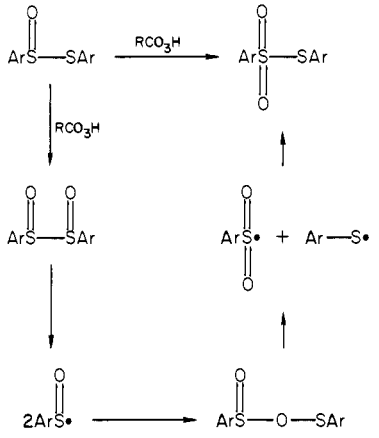
The chemical shifts of the α-carbon atoms of α-disulfoxides are consistent with the ^{13}C NMR trends of oxidized derivatives of disulfides.[24,41] The difference between the chemical shifts of the α-carbon atoms of α-disulfoxides and the α-carbon atoms in the corresponding thiosulfinates may be due mostly to the α'_{SO} effect [$\alpha'_{SO} = \Delta\delta = \delta_C(C-S(O)-S-C) - \delta_C(C-S-S-C)$]. The calculated value of the chemical shift of the α-carbon atom of an α-disulfoxide is $\delta_C(C-S(O)-S-C) + \alpha'_{SO}$. The deviations of the observed chemical shifts of the α-carbon atoms of straight-chain alkyl α-disulfoxides from the expected values are less than 2 ppm, and they reach a maximum of −4.54 ppm for the *tert*-butyl-substituted α-disulfoxides **27** and **28** (Table VI).

On the basis of dipole moment measurements[38-40] and ^1H NMR and ^{13}C NMR shielding trends,[3,23,24,41] it appears that disulfides and their known oxidized derivatives exist predominantly in the gauche conformation in solution. It is reasonable to assume that the gauche conformations are also favored with α-disulfoxides **67** and **69**. However, in the case of the meso (*RS/SR*) diastereomer, conformation **68** contains the maximum number of gauche interactions between lone pairs and S=O and C–S bonds and has to be seriously considered.[38,41]

The α-carbon atoms in the *RS/SR* diastereomer (meso, **67**) experience significant steric compression since in the gauche

(31) A characteristic behavior of sulfines is the loss of elemental sulfur to give carbonyl compounds under thermal and particularly photolytic conditions.[32] No search for the oxathiirane intermediate was made in this study.
(32) (a) Zwanenburg, B. *Recl. Trav. Chim. Pays-Bas* **1982**, *101*, 1 and references cited therein. (b) Snyder, J. P. *J. Am. Chem. Soc.* **1974**, *96*, 5005. (c) Walter, W.; Vosz, J. *Liebigs Ann. Chem.* **1966**, *87*, 695.
(33) Strating, J.; Thijs, L.; Zwanenberg, B. *Recl. Trav. Chim. Pays-Bas* **1967**, *86*, 641.
(34) Brodnitz, M. H.; Pascale, J. V. *J. Agric. Food Chem.* **1971**, *19*, 269.
(35) Farng, L. O.; Kice, J. L. *J. Am. Chem. Soc.* **1981**, *103*, 1137.
(36) (a) Allen, P., Jr.; Brook, J. W. *J. Org. Chem.* **1962**, *27*, 1019. (b) Das Neves, J. J. C.; Godhinko, L. S. *Tetrahedron* **1979**, *35*, 2053.
(37) Curci, R.; Giovine, A.; Modena, G. *Tetrahedron* **1966**, *22*, 1235 and references cited therein.
(38) Dembech, P.; Vivarelli, P.; Jehlicka, V.; Exner, O. *J. Chem. Soc., Perkin Trans. 2* **1973**, 488.
(39) Exner, O.; Harpp, D. N.; Gleason, J. G. *Can. J. Chem.* **1972**, *50*, 548.
(40) McClellan, A. L. "Tables of Experimental Dipole Moments"; Freeman: San Francisco, 1963.
(41) Freeman, F.; Angeletakis, C. N. *J. Org. Chem.* **1982**, *47*, 4194.

Scheme I



conformation **67** the sulfinyl oxygens are γ-gauche to each other. In contrast, in the *RR/SS* diastereomers (**69**) the sulfinyl oxygen atoms are in an anti arrangement, which minimizes steric interactions between the α-carbon atoms. Therefore, it is reasonable to assume that the α-carbon atoms in the *RS/SR* diastereomer (**67**, meso) experience higher shielding (farther upfield) than their counterparts in the *RR/SS* diastereomer (**69**).[38,41,42]

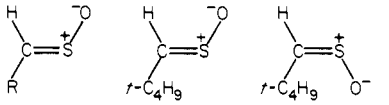
Continuous ^{13}C NMR scanning at −40 °C of the product mixtures from the MCPBA oxidation of **26**,[6] **30**,[4,13] **33–35**, and **36** showed that in each case the *upfield* resonance of the α-carbon atoms in the *RS/SR* diastereomer (**67**) decreased much faster than the corresponding *downfield* resonance due to the α-carbon atoms in the *RR/SS* diastereomers (**69**). This implies that the *RS/SR* diastereomer **67** stereomutates to the *RR/SS* diastereomers (**69**) and/or decomposes or rearranges to other products owing to the presence of inordinate oxygen–oxygen repulsion.

Although the relative ^{1}H NMR integrals of the diastereomers of methyl disulfoxide (**38** and **39**, Table II) do not agree very well with those obtained by ^{13}C NMR, it is interesting to note that the ^{13}C NMR relative integral ratios of the α-carbon atoms in **38**, **39**, **43**, **44**, **49**, **50**, **55**, and **56** are in favor of the *RR/SS* diastereomers (**69**). Although no evaluation can be made of α-disulfoxides **61** and **62**, α-disulfoxides **31a** and **31b** are exceptions with an initial *RR/SS:RS/SR* ratio of 1:2.5.[4] Possibly in the oxidation of **30** path a is favored (eq 12) owing to steric hindrance from the 1,1-dimethylethyl group.

Thiosulfonates are the major products in the peroxidation of alkyl and aryl arenethiosulfinates (**22**) at −20 and −30 °C.[5,8–12,14,16–18] A radical decomposition pathway has been proposed for aralkyl and aryl α-disulfoxides (eq 12, Scheme I).[15–19,43] The "bond weakening effect" of S=O when it is a partner of an S—S bond has been noted and has been ascribed to the relative stability of sulfinyl radicals.[44] Recent studies of sulfinyl radicals have shown that they are relatively stable and are relatively delocalized π-type radicals that can combine to give sulfenyl sulfinates, which can rearrange to thiosulfonates.[45–47]

The low-temperature spectral data of the product mixtures obtained from the oxidation of alkanethiosulfinates **26**,[6] **30**,[4,13] and **33–37** show that the initial products of the decomposition and/or rearrangement of alkyl α-disulfoxides (**2**) are sulfines, sulfinic acids, and thiosulfinates. Therefore, it is reasonable to assume that sulfinyl radicals do not play a major role in the decomposition and/or rearrangement of alkyl α-disulfoxides (**2**).[3,4,6] The greater tendency of aryl α-disulfoxides to form sulfinyl radicals may be due to the mesomeric effect of the aryl groups. Thus, with alkyl α-disulfoxides, ionic mechanisms are expected to compete effectively with radical mechanisms initiated by homolytic scission of the S–S bond in **2**. Moreover, dialkyl thiosulfinates have stronger S–S bonds than diaryl and, presumably, aralkyl thiosulfinates.[48] If this is also true for α-disulfoxides, the dialkyl disulfoxides would be less likely than diaryl disulfoxides to undergo homolysis of the S–S bond.

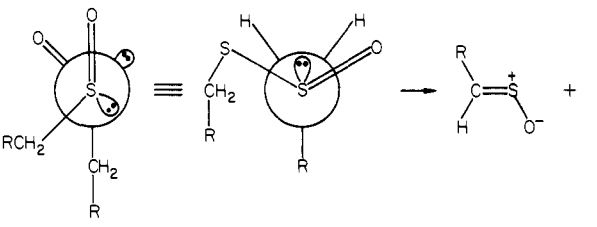
The thermodynamically favored *Z* isomer of sulfines **47**, **59**, and presumably **63** is obtained in the MCPBA oxidation of **34**,



47, R = C_2H_5
59, R = n-C_3H_7
63, R = C_6H_5

70 71

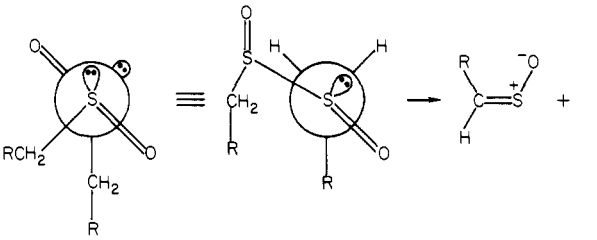
36, and **37**, respectively. However, in the peroxidation of **30**, the *E*:*Z* ratio of sulfines **70**:**71** is 1.6:1. These results and the ^{13}C NMR relative integral ratios of the diastereomers of the corresponding α-disulfoxides (vide supra) suggest the mechanisms in eq 13 and 14 for the formation of sulfines. The formation of



67, *RS/SR*

$RCH_2S—OH$ (13)

72

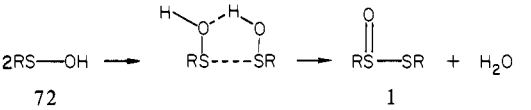


69, *RR/SS*

$RCH_2S—OH$ (14)

72

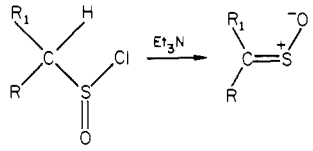
sulfines in the decomposition of alkyl α-disulfoxides (**2**) may be due to an unfavorable interaction of the two adjacent partially negatively charged sulfinyl oxygen atoms, which enhances the tendency toward a cycloelimination reaction (eq 13 and 14). The sulfenic acid (**72**) formed is expected to dimerize to give thiosulfinate (**1**, eq 15).[48,49]



72 1

The 1,2-dehydrochlorination of sulfinyl chlorides (**73**) bearing an α-hydrogen atom is one of the first methods used to prepare stable aliphatic sulfines.[31,50–52] An interesting feature of this

(42) Wolfe, S. *Acc. Chem. Res.* **1972**, *5*, 102.
(43) Sulfinyl radicals have been invoked for the peroxidation of *S*-(2-methyl-2-propyl) 2-methyl-2-propanethiosulfinate (**26**).[15]
(44) Kice, J. L. "Free Radicals"; Kochi, J. K., Ed.; Wiley: New York, 1973; Vol. II, Chapter 24.
(45) Chatgilialoglu, C.; Gilbert, B. C.; Gill, B.; Sexton, M. D. *J. Chem. Soc., Perkin Trans. 2* **1980**, 1141.
(46) Gilbert, B. C.; Kirk, C. M.; Norman, R. O. C.; Lave, H. A. H. *J. Chem. Soc., Perkin Trans. 2* **1977**, 497.
(47) Gilbert, B. C.; Gill, B.; Sexton, M. D. *J. Chem. Soc., Chem. Commun.* **1978**, 78.
(48) Block, E.; O'Connor, J. *J. Am. Chem. Soc.* **1974**, *96*, 3921.
(49) Davis, F. A.; Jenkin, R. H., Jr. *J. Am. Chem. Soc.* **1980**, *102*, 7967.
(50) Block, E. in "Organic Sulfur Chemistry", 9th International Symposium on Organic Sulfur Chemistry, Riga, USSR, June 9–14, 1980; Friedlina, R. Kh., Skosova, E., Eds.; Pergamon Press: Oxford, 1981.



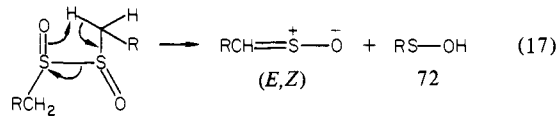
(16)

73

elimination to thioaldehyde S-oxides is that the more thermodynamically favored Z isomer is preferentially formed.[27-29,32a,50] This stereochemical preference for the Z configuration in RCH=S=O has been explained by invoking attracting electrostatic interactions as well as stabilizing through-space orbital (π and σ) interactions between the methylene group and the sulfine oxygen atom.[28,53] It is also of interest to note that the parent sulfine (CH_2=S=O) cannot be obtained from methanesulfinyl chloride upon treatment with triethylamine[51,54,55] or from the MCPBA oxidation of **33**.

Although (*Z*)-**71** is expected to be thermodynamically more stable than (*E*)-**70**, the greater formation of **70** over **71** can be kinetically favored in the peroxidation of **30** owing to predominant formation of the *RS*/*SR* diastereomer of **31a** by path a (eq 12–14).[4,13] The greatest yield of sulfines is obtained in the peroxidation of **30** while no sulfine is observed in the peroxidation of **33**. This may be interpreted as being due to the increased acidity of the α-hydrogen atoms, which aids cycloelimination on increased methyl substitution at the β-carbon atom of an α-disulfoxide.

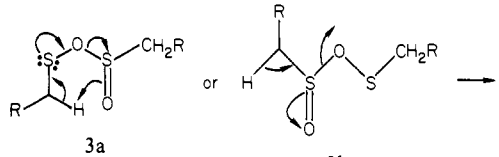
Although α-disulfoxides (**2**) can undergo cycloelimination to afford sulfines and sulfenic acids, which dimerize to thiosulfinates (eq 15 and 17), the formation of sulfines from sulfinyl radicals,



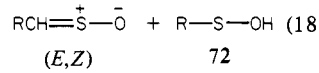
(17)

2

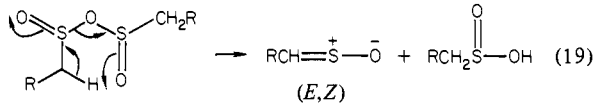
sulfenyl sulfinates (eq 18), or sulfinic anhydrides (**74**, eq 19) must



3a 3b



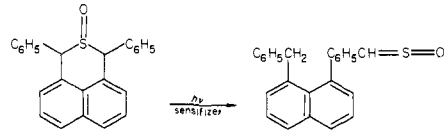
(18)



74

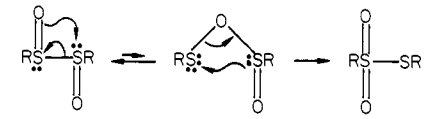
(19)

(51) Sheppard, W. A.; Diekmann, J. *J. Am. Chem. Soc.* **1964**, *86*, 1891.
(52) Strating, J.; Thijs, L.; Zwanenburg, B. *Recl. Trav. Chim. Pays-Bas* **1964**, *83*, 631.
(53) Block, E.; Penn, R. E.; Bazzi, A. A.; Cremer, D. *Tetrahedron Lett.* **1981**, *22*, 29.
(54) (a) Optiz, G. *Angew. Chem.* **1967**, *79*, 161; *Angew. Chem., Int. Ed. Engl.* **1967**, *6*, 107. (b) Truce, W. E.; Norell, J. R. *J. Am. Chem. Soc.* **1963**, *85*, 3231.
(55) (a) Sulfinyl radicals may also be involved in the photoreaction of the cyclic sulfoxide i to the *E* and *Z* sulfines ii.[55b,c] (b) Schultz, A. G.; Schlessinger, R. H. *J. Chem. Soc., Chem. Commun.* **1969**, 1483. (c) Schultz, A. G.; DeBoer, C. D.; Schlessinger, R. H. *J. Am. Chem. Soc.* **1968**, *90*, 5314.



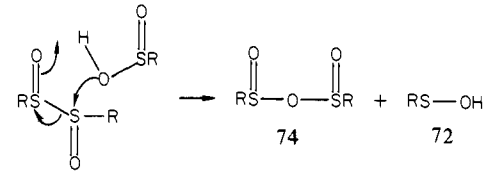
i ii

also be considered since these species can be formed from the corresponding α-disulfoxides (eq 20 and 21).[55] Although peaks



(20)

2 3 4

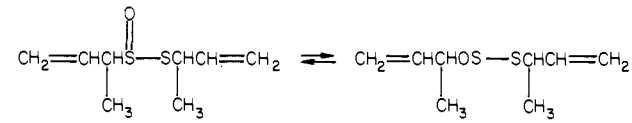


(21)

2 74 72

that can be assigned to sulfenyl sulfinates (**3**) are absent from the low-temperature ^{1}H NMR and ^{13}C NMR spectra, they are still possible intermediates.

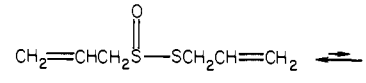
The low concentration of sulfenyl sulfinate **3** may be due to an unfavorable equilibrium between it and α-disulfoxide **2**. The possibility that the equilibrium between **2** and **3** lies far to the left (eq 20) is supported by comparison with similar sulfur compounds. For example, although the free energy difference is small, the sulfoxide (>S=O) structure is generally thermodynamically more stable than the sulfenate (—S—O—) structure.[56] It has been reported that *S*-(1-methylpropenyl) 1-methylpropenthiosulfinate (**75**) isomerizes readily to the thiosulfoxylate **76**.[57]



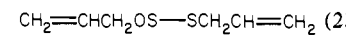
75 76

(22)

However, in a system lacking the methyl groups, *S*-propenyl propenethiosulfinate (**77**), the equilibrium with thiosulfoxylate **78** lies so far to the left that **78** cannot be observed.



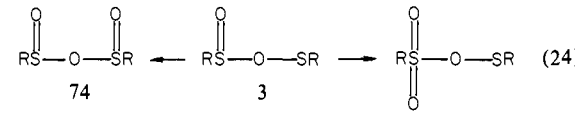
77



(23)

78

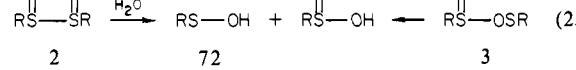
Sulfenyl sulfinate **3**, once formed, can compete with thiosulfinate (**1**) for oxidant to give sulfinic anhydrides (**74**) or, less likely, sulfenyl sulfonate (**79**). α-Disulfoxides (**2**) or sulfenyl sulfinates



(24)

74 3 79

(**3**) are expected to be easily hydrolyzed to sulfenic (**72**) and sulfinic acids (eq 25), while sulfinic anhydrides (**74**) may be

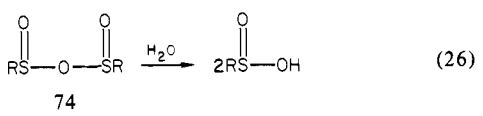


(25)

2 72 3

hydrolyzed to sulfinic acids (eq 26; cf. eq 21). The reactions shown in eq 20, 24, and 25 are important since nucleophilic

(56) Kice, J. L. *Adv. Phys. Org. Chem.* **1980**, *17*, 100.
(57) Baldwin, J. E.; Höfle, G.; Choi, S. C. *J. Am. Chem. Soc.* **1971**, *93*, 2810.



(26)

74

substitutions at sulfinyl sulfur are very rapid and much faster than analogous reactions at carbonyl groups.[58]

It is of interest to compare the products from the MCPBA oxidation of **33–37** with those obtained from *S*-(2-methyl-2-propyl) 2-methyl-2-propanethiosulfinate (**26**)[6] and *S*-(2,2-dimethylpropyl) 2,2-dimethylpropanesulfinate (**30**).[4] The rearrangement pathways

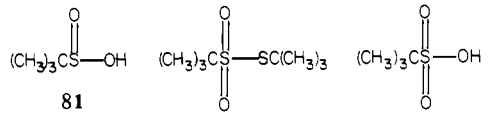
26, R = *t*-C_4H_9 27, R = *t*-C_4H_9, *RR/SS*; 28, R = *t*-C_4H_9, *RS/SR*

(27)

29a, R = *t*-C_4H_9, *RR/SS*
29b, R = *t*-C_4H_9, *RS/SR*

80

of 2-(methyl-2-propyl) disulfoxides **27** and **28**, which are observed on warming the product mixture from −40 to −20 °C, are different than the paths of the α-disulfoxides from **30**, **33–36**, and **37**. It appears that α-disulfoxides **27** and **28** are converted to **26** and 2-methyl-2-propanesulfinic anhydride (**29**). The conversion of **27** and **28** to **29** is relatively slow at −30 °C. The ^{13}C NMR spectrum of the product mixture showed a small amount of another unstable intermediate (δ_C 28.45, 50.99), which disappeared on warming to −20 °C. These resonances are tentatively assigned to 2-methyl-2-propanesulfenic acid (**80**).[49,59–61] Rearrangement of **27** and **28** to **29** and **80** can occur via the reactions shown in eq 21, 25, and 26. Resonances for 2-methyl-2-propanesulfinic acid (**81**) and possibly small amounts of *S*-(2-methyl-2-propyl)



81 82 83

2-methyl-2-propanethiosulfonate (**82**) were also observed on warming the spectrum from the oxidation of **26** to 25 °C.[6] No resonances were observed for 2-methyl-2-propanesulfonic acid (**83**).[6]

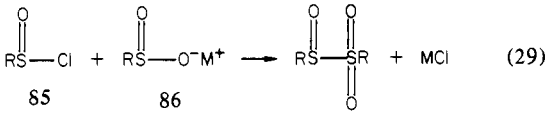
When the reaction mixture obtained from the oxidation of **30** at −40 °C was warmed to 0 °C, the only change observed by ^1H NMR and ^{13}C NMR was the decomposition of sulfines **70** and **71** to 2,2-dimethylpropanal. In contrast to **36** and **57**, 2,2-di-

$$(CH_3)_3CCH{=}S{=}O \rightarrow (CH_3)_3CCHO + S \qquad (28)$$
70 or **71**

methylpropanesulfinic acid (**17**) reacts slowly with thiosulfinate **30** even at 25 °C.

The resonances ascribed to sulfinic anhydride **41** appear only in the −40 °C spectrum and those to anhydrides **29**, **52**, and **58** appear in both the −40 and −20 °C spectra. 2-Methyl-2-propanesulfinic anhydride (**29**) is stable in the product mixture at 24 °C for approximately 30 min, 2-propanesulfinic anhydride (**52**) decomposes or rearranges at 0 °C, and *n*-butanesulfinic anhydride (**58**) decomposes or rearranges at −20 °C.

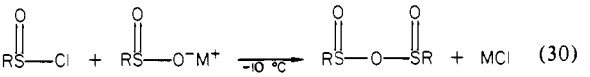
The anhydrides of sulfinic acids normally have the sulfinyl sulfone structure **84** rather than the isomeric structure of the sulfinic anhydride (**74**). Thus, sulfinic acids, like sulfenic acids (**72**), prefer to form an anhydride with a S–S bond (eq 15).[62] The products isolated from the reaction of sulfinyl chlorides (**85**) with



(29)

85 86 84

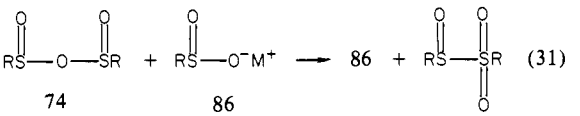
silver or sodium sulfinate salts (**86**) at −10 °C are the sulfinyl sulfones (**84**),[63] except for the *tert*-butyl-substituted compound.[25]



(30)

85 86 74

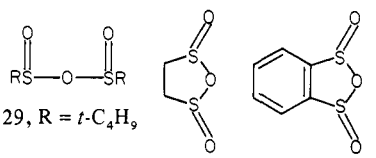
However, whether **84** results because *S*-sulfinylation is kinetically preferred or comes about because the sulfinic anhydride resulting from O-sulfinylation is readily converted by some of the remaining sulfinate ion (**86**) to the thermodynamically more stable sulfinyl sulfone (**84**) (eq 31) has not been definitely established.[64,65]



(31)

74 86 84

Although the sulfinyl sulfone structure **84** is thermodynamically more favorable, there are three reports where the sulfinic anhydride structure is favored (**29**,[25] ethane-1,2-disulfinic anhydride (**87**),[66] and benzene-*O*-disulfinic anhydride (**88**)[67]). The sulfinic anhy-

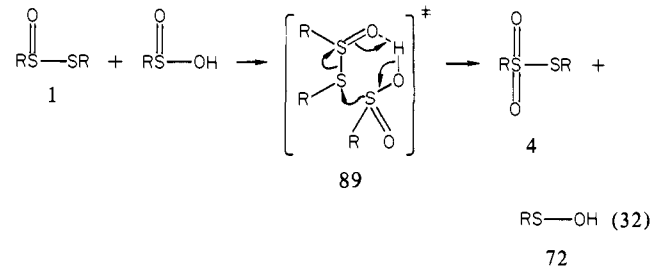


29, R = *t*-C_4H_9 87 88

drides obtained in the oxidation of dialkyl thiosulfinates in this study are produced at lower temperatures than the temperatures used for the reaction shown in eq 30. The possible isomerization of these sulfinic anhydrides (**74**) to sulfinyl sulfones (**84**) via the reaction shown in eq 31 is expected to be a minor pathway owing to the low concentration of sulfinic acids and the facile reactions of **74** with water (eq 26).

On warming the product mixtures from −40 to 0 °C, the sulfinic acids react readily with thiosulfinates (**1**) to give thiosulfonates (**4**, eq 8), except for sterically hindered **30**. This is probably the major pathway by which thiosulfonates (**4**) form in the peroxidation of alkanethiosulfinates. A concerted mechanism with an activated complex (**89**) involving a front-side nucleophilic displacement at the sulfenyl sulfur atom of **1**, which is assisted by a "push–pull" weakening of the S–S bond, has been proposed to describe the reaction of alkanethiosulfinates (**1**) with alkanesulfinic acids (eq 32).[21] In contrast, the reaction of arenesulfinic acids with arenethiosulfinates (**22**) is much slower without added catalysts.[67,68] Presumably, the aryl compounds cannot attain

(58) Reference 56, p 119.
(59) Davis, F. A., private communication. The ^{13}C NMR spectrum of 2-methyl-2-propanesulfenic acid (**80**) shows resonances at δ 27.69 [$(CH_3)_3C$-SOH] and 47.00 [$(CH_3)_3CSOH$] in C_6D_6.
(60) Davis, F. A.; Freedman, A. J.; Nadir, U. K. *J. Am. Chem. Soc.* **1978**, *100*, 1044.
(61) Davis, F. A.; Billmers, R. L. *J. Am. Chem. Soc.* **1981**, *103*, 7016.
(62) Kice, J. L.; Margollis, H. C. *J. Org. Chem.* **1975**, *40*, 3623.
(63) Brodereck, H.; Wagner, A.; Beck, H.; Klein, R. J. *Chem. Ber.* **1960**, *93*, 2736.
(64) Kice, J. L.; Wu, S. M. *J. Org. Chem.* **1981**, *46*, 3191.
(65) Campbell, J. Ph.D. Thesis, Oregon State University, Corvalis, OR, 1973.
(66) Mueller, W. H.; Dines, M. B. *Chem. Commun.* **1969**, 1205.
(67) Kice, J. L.; Liao, S. *J. Org. Chem.* **1981**, *46*, 2691.
(68) Kice, J. L.; Venier, C. G.; Heasley, L. *J. Am. Chem. Soc.* **1967**, *89*, 3557.



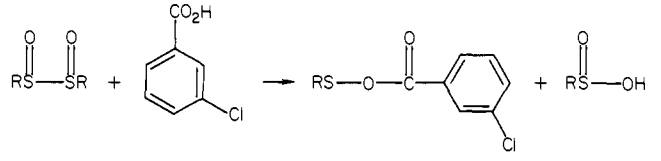
RS—OH (32)

72

activated complex **89** easily because the basicity of the sulfinyl oxygen atom in an arenethiosulfinate (**22**) is less than that in an alkanethiosulfinate (**1**) owing to the mesomeric effect of the aryl group.

Inspection of Tables I, II, and IV shows that disappearance of the signals assigned to α-disulfoxides on warming leads to regeneration of sizable amounts of the starting thiosulfinates. Two pathways have been suggested, as shown above, to account for this. Namely, an α-disulfoxide can give one molecule of sulfenic acid and one molecule of sulfine (eq 17) or sulfinic acid (eq 25), and two molecules of sulfenic acid can eliminate water to give one molecule of thiosulfinate (eq 15). However, the amount of thiosulfinate produced upon warming of the reaction mixtures relative to the amount of sulfine and sulfinic acid produced is much larger than what is predicted from the stoichiometry outlined above. For example, in the oxidation of *S*-propyl propanethiosulfinate (**34**) the amount of **34** at −20 °C that cannot be accounted for by the reactions shown in eq 15, 17, and 25 is 14%.

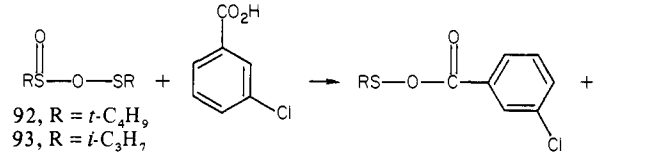
Small peaks were observed in the aromatic region of the −40 °C ^{1}H NMR spectra of the product mixtures from the MCPBA oxidation of **26** and **35**. These peaks in which the ortho hydrogens were deshielded 0.1 ppm relative to those of MCBA disappeared on warming to −20 °C. These peaks can be attributed to the presence of 3-chlorobenzoyl 2,2-dimethylpropanesulfenate (**90**) and 3-chlorobenzoyl 2-propanesulfenate (**91**). Sulfenates **90** and



90, R = t-C_4H_9
91, R = i-C_3H_7

(33)

91 could result from the reactions of MCBA with α-disulfoxides **27** and **28** or **49** and **50** (eq 33) or sulfenyl sulfinates **92** or **93** (eq 34).[12]



92, R = t-C_4H_9
93, R = i-C_3H_7

90, R = t-C_4H_9
91, R = i-C_3H_7

(34)

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.[69] NMR spectra were obtained on Bruker WH-90 and WM-250 Fourier transform NMR spectrometers that were controlled by B-NC-12 and Bruker Aspect 2000 computers,

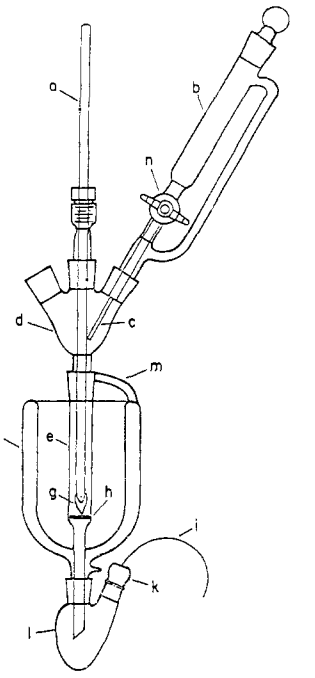


Figure 4. (a) Glass stirring rod; (b) addition funnel; (c) $^1/_8$-in. Teflon tube; (d) modified three-neck 25-mL flask; (e) 10-mL cylinder; (f) glass Dewar; (g) paddle; (h) medium glass frit; (i) $^1/_{16}$-in. Teflon tube; (k) septum; (l) two-neck 10-mL pear-shaped flask; (m) support rod; (n) Teflon stopper.

respectively, and on a Varian EM-360 spectrometer. IR spectra were obtained on a Perkin-Elmer 283 spectrometer.

HPLC was accomplished on an EM "Hibar" silica gel analytical column with 3% ethyl acetate–isooctane as eluant. Flash column chromatography was modified as follows: the material to be separated was placed on top of the column (400-mesh EM silica gel) without preadsorption. The elution rate was 0.5 in. of column length per min regardless of the diameter of the column. Analytical TLC was performed on Analtech silica gel coated (25 μm) prescored slides. Preparative TLC was done on commercial 250 μm silica gel plates.

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

***S*-Methyl methanethiosulfinate (33)[20] and *S*-(phenylmethyl) phenylmethanethiosulfinate (37)[70]** were prepared as previously described.

***S*-Propyl Propanethiosulfinate (34).[21]** To a stirred solution of propyl disulfide (3.0 g, 20 mmol) in 10 mL of CH_2Cl_2 at 0 °C was added dropwise (one drop/s) a solution of 4.24 g (20 mmol) of 81% MCPBA in 50 mL of CH_2Cl_2. The reaction mixture was stirred for 15 min at 0 °C and filtered. The filtrate was washed with 20 mL of 5% $NaHCO_3$ solution and 20 mL of water, and the organic layer was dried (Na_2SO_4). Pure **34** (2.55 g, 77%) was obtained, after solvent removal, via flash chromatography on silica gel. *The purification step must be performed as quickly as possible.*

***S*-2-Propyl 2-propanethiosulfinate (35) and *S*-butyl butanethiosulfinate (36)** were prepared in 83% and 74% yields, respectively, via the procedure described above for the preparation of **34**.[21]

***S*-Methyl methanesulfonate (12), *S*-propyl propanethiosulfonate (46), *S*-2-propyl propanethiosulfonate (53), and *S*-butyl butanethiosulfonate (60)** were prepared by the thermal decomposition of the corresponding sulfinic acids.[35,71,72] The decomposition mixtures were dissolved in ether and the ether solutions were extracted with water. The ether layers were dried (Na_2SO_4) and evaporated at 24 °C. Flash column chromatography of the residues from the ether layers (20% ether–hexanes) gave pure thiosulfonates as colorless oils.[35,71,72] The water extracts, which contained the sulfonic acids, were evaporated in vacuo at less than 60 °C. The sulfonic acids were dried by azeotroping off the remaining water with benzene.[71]

***S*-(Phenylmethyl) phenylmethanethiosulfonate (64)** was prepared as previously described.[22]

(69) Freeman, F.; Angeletakis, C. N. *Org. Mass Spectrom.* **1982**, *17*, 114.

(70) Legler, L. E.; Jundal, S. L.; Murray, R. W. *Tetrahedron Lett.* **1972**, 3907.

(71) von Braun, J.; Weissbach, K. *Chem. Ber.* **1930**, *63*, 2836.

(72) Filby, W. G.; Günther, K.; Penzhorn, R. D. *Z. Naturforsch., B* **1976**, *31B*, 463.

Sulfinic acids 17,[4] **20**,[73] **40**,[35] **45**,[74] **51**,[75] **57**,[74] and **81**[76,77] were prepared as previously described. The sodium or magnesium salts of the sulfinic acids were carefully acidified with 60% sulfuric acid in water at 0 °C, extracted three times with ether, and dried ($MgSO_4$). The combined ether extracts were concentrated to give the sulfinic acids.

Reaction of S-Butyl Butanethiosulfinate (36) and Butanesulfinic Acid (57). A solution of **57** (0.126 g, 1.03 mmol) in 1.5 mL of $CDCl_3$ was added to an equimolar amount of **36** (0.200 g, 1.03 mmol) in 1.5 mL of $CDCl_3$ in a 10-mm NMR tube at 0 °C. After 7 min, the reaction was followed by ^{13}C NMR at 0 °C. The reaction was essentially complete after 40 min at 0 °C. The disappearance of the resonances of the sulfur-bonded carbon atoms of **36** and **57** was used to monitor the reaction.

Oxidation of Alkanethiosulfinates with MCPBA. The oxidation was carried out using the previously described techniques.[4,6,12,41] The general procedure for the low-temperature ^1H NMR and ^{13}C NMR experiments is given below.

The apparatus used for these experiments is shown in Figure 4. It consists of a 10-mL cylinder surrounded by a vacuum jacketed Dewar flask with a medium glass frit at the bottom. A 25-mL three-neck flask with a ground-glass joint at the bottom of it was placed on top of the 10-mL cylinder. A nitrogen inlet, an overhead stirrer, and a 10-mL addition funnel were placed on the three-neck flask. The bottom delivery tube of the addition funnel was fitted with a small piece of $^1/_8$-in.-diameter Teflon tubing, which ended directly above the 10-mL cylinder. Below the glass frit, the tube ended in a male ground-glass joint (Figure 4), which was connected to one neck of a two-neck 10-mL pear-shaped flask. A septum with a $^1/_{16}$-in. Teflon tube through it was placed on the other neck of the pear-shaped flask. The Teflon tube was inserted about 1 cm through the septum and the outside of the Teflon tube was clamped.

In a typical experiment, after the apparatus was thoroughly dried in an oven and cooled while nitrogen was bled into the 10-mL cylinder, 1.7 mmol of thiosulfinate dissolved in 0.5 mL of $CDCl_3$ was placed inside the 10-mL cylinder. The Dewar was charged with 2-propanol and cooled to the desired temperature with dry ice while a positive pressure of nitrogen was applied from the top, and the stirrer was started. Three minutes after the desired temperature in the Dewar was achieved, a solution of 1.7 mmol of 81% MCPBA dissolved in 4.5 mL of $CDCl_3$ was added dropwise within a 5-min period. The addition funnel was then removed and replaced with a ground-glass stopper. After 45–60 min, the stirrer was stopped and the temperature of the bath brought to −45 °C. Another dry ice/2-propanol bath at −40 °C was placed around the 10-mL pear-shaped flask.

A nitrogen pressure of 5 lb was applied to the apparatus while the stopper and the stirrer fitting on the other two necks of the three-neck flask were kept in place by hand. After filtration of the solution into the pear-shaped flask (5–10 min), a 10-mm NMR tube in which the air was replaced with nitrogen was placed in a dry ice/2-propanol bath at −40 °C. The outside end of the Teflon tube was unclamped and placed inside the NMR tube, and the end of the Teflon tube inside the septum was pushed to the bottom of the pear-shaped flask. Nitrogen pressure through a needle that pierced the septum forced the solution into the NMR tube within 10–15 s. The NMR tube was immediately capped and a narrow strip of parafilm was placed along the lower edge of the cap. The NMR tube, which was still immersed in the dry ice/2-propanol bath, was taken immediately to the NMR spectrometer.

The WM-250 NMR spectrometer was fitted with the multinuclear probe and the synthesizer was tuned to the frequency of the ^{13}C nucleus. In addition to ^{13}C NMR spectra, ^1H NMR spectra were obtained with this probe by using the broad-band decoupler as the receiving coil and the ^1H NMR preamplifier instead of the multinuclear synthesizer. Nucleus changeover, including change of acquisition parameters in the computer, required 2–3 min. Owing to the presence of sidebands, the ^1H NMR spectra obtained in this manner were not as well resolved as those obtained with the ^1H probe.

Preliminary experiments showed that when 5-mm instead of 10-mm NMR tubes were used to contain the cold solutions, the temperatures of the solutions rose during the 30–60-s interval required for the transfer of the NMR tube from the dry ice/2-propanol bath to the probe of the spectrometer. Since the available ^1H NMR probe only accepted 5-mm NMR tubes, it was not used for these experiments.

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Supplementary Material Available: Tables and figures of product distributions from MCPBA oxidation and NMR chemical shifts of products (11 pages). Ordering information is given on any current masthead page.

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Enantioselective Synthesis of the Carbocyclic Nucleosides (−)-Aristeromycin and (−)-Neplanocin A by a Chemicoenzymatic Approach

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Abstract: An efficient synthesis of the carbocyclic nucleosides (−)-aristeromycin and (−)-neplanocin A has been developed in an enantioselective and stereocontrolled manner starting from the Diels–Alder adduct of cyclopentadiene and dimethyl acetylenedicarboxylate. The symmetric unsaturated dimethyl ester, dimethyl (3aα,4β,7β,7aα)-3a,4,7,7a-tetrahydro-2,2-dimethyl-4,7-methano-1,3-benzodioxole-5,6-dicarboxylate, was quantitatively hydrolyzed with pig liver esterase to yield a half-ester with reasonably high optical yield. Decarboxylative ozonolysis followed by chemical transformation afforded versatile chiral intermediates of cyclopentylamine and cyclopentenylamine that were converted to (−)-aristeromycin and (−)-neplanocin A, respectively.

Since the pioneering synthesis of the racemic carbocyclic analogue of adenosine[1] by Shealy and Clayton and subsequent isolation of aristeromycin (**1**) as the (−) enantiomer from *S. citricolor* n.sp.,[2] the interest in this class of compounds has grown

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