α-Disulfoxide Formation during the *m*-Chloroperoxybenzoic Acid Oxidation of *S*-(2,2-Dimethylpropyl) 2,2-Dimethylpropanethiosulfinate[1,2]

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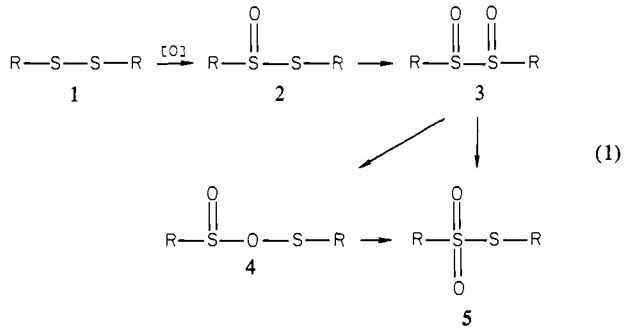
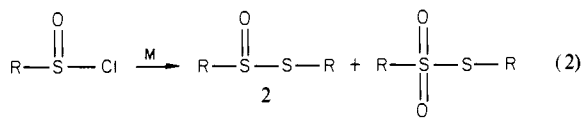
Abstract: Diastereomeric α-disulfoxides (**14**) have been detected as intermediates in the *m*-chloroperoxybenzoic acid (MCPBA) oxidation of neopentyl neopentanethiosulfinate (**6**) at −40 °C in $CDCl_3$ via ^1H NMR and ^{13}C NMR spectroscopy. The product mixture at −40 °C contained **6**, **14**, neopentyl neopentanethiosulfonate (**7**), and neopentanesulfinic acid (**11**). Oxidation of **6** at −20 °C, followed by warming to 0 °C and treatment with $NaHCO_3$, gave (*E*)- and (*Z*)-2,2-dimethylpropanethial *S*-oxides (**8** and **9**) in a ratio of 1.6:1, along with **6**, **7**, 2,2-dimethylpropanal (**10**), **11**, and neopentanesulfonic acid (**12**). α-Disulfoxides (**14**), sulfenyl sulfinate **15**, and sulfinic anhydride **19** are considered as possible precursors of the sulfines. The low yield of **7** suggests that direct oxidation of the sulfinyl sulfur atom of **6** is probably not a major pathway in the oxidation. The results of the oxidation of **6** are compared with the 2-equiv MCPBA oxidation of neopentyl disulfide (**13**).

Although the formation of α-disulfoxides (**3**) and sulfenyl sulfinates (**4**) as intermediates in the peroxy acid oxidation of disulfides (**1**) or thiosulfinates (**2**) to thiosulfonates (**5**) has been



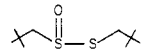
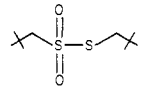
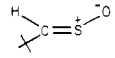
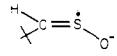
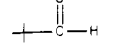
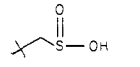
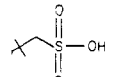
(1)

postulated for in vivo[3-5] and in vitro[5-21] reactions, there has been only one report[22] of the detection of **3** and two reports[11,23] for indirect observation of **4** during the oxidation of **2**. α-Disulfoxides (**3**) have also been implicated as intermediates in the reactions of sulfinyl chlorides with metals (Ag, Cu, Zn) to give **2** and/or **5**,[24-29] in the hydrolysis of methanesulfinyl chloride,[30-32] and in



(2)

Table I. Products from the MCPBA Oxidation of 6 and 13 at −20 °C, Followed by Treatment with $NaHCO_3$ Solution[a]

compd	compd no.	product distribution,[b] % from 6	product distribution,[b] % from 13
	6	48	46
	7	13	15
	8	8	7
	9	13	7
	10	2	1
	11	39	29
	12	4	4

[a] ^1H NMR yields are given. Analysis was done at 20-25 °C within 5 min after separation of layers. [b] Based on moles of 6 or 13.

(1) Abstracted from the Ph.D. Thesis of Christos N. Angeletakis, 1982, Department of Chemistry, University of California, Irvine, CA 92717.
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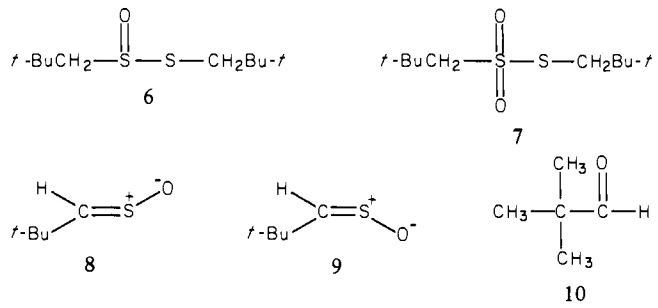
the reaction of methyl chloromethyl sulfide with dimethyl sulfoxide.[33] Moreover, it seems to be quite generally agreed that a head-to-tail combination of sulfinyl radicals gives sulfenyl sulfinates (**4**), which rearrange to thiosulfonates (**5**).[11,20-23,34-38]

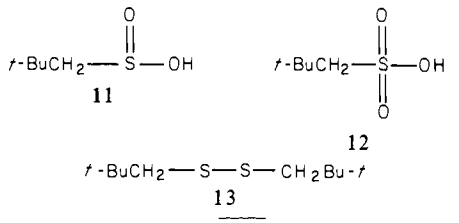
In order to obtain additional data concerning the intermediacy of α-disulfoxides (**3**) and sulfenyl sulfinates (**4**) and to obtain useful correlative ^1H NMR and ^{13}C NMR shifts for reaction intermediates,[39,40] we have investigated the low-temperature *m*-chloroperoxybenzoic acid (MCPBA) oxidation of *S*-(2,2-dimethylpropyl) 2,2-dimethylpropanethiosulfinate (neopentyl neopentanethiosulfinate, **6**) in $CDCl_3$. Owing to the presence of both sulfenyl and sulfinyl sulfur atoms in **6**, the question of nucleophilic oxygenation at sulfinyl sulfur and electrophilic oxygenation at sulfenyl sulfur by MCPBA must also be considered.[11,18,21-23,41]

Results

Thiosulfinate **6** was oxidized in a nitrogen atmosphere with 1 equiv of MPCBA at −20 °C in $CDCl_3$.[20] Most of the peracid was consumed after 1 h (iodometric assay). The reaction mixture was warmed to 0 °C and stirred with ice-cold 5% $NaHCO_3$ solution for 10 min, and the layers were separated. After being dried (Na_2SO_4), the organic phase was analyzed via ^1H NMR spectroscopy (Figure 1). Starting material (**6**), *S*-(2,2-dimethylpropyl)



2,2-dimethylpropanethiosulfonate (neopentyl neopentanethiosulfonate, **7**), (*E*)- and (*Z*)-2,2-dimethylpropanethial *S*-oxides (**8** and **9**), 2,2-dimethylpropanal (**10**), and *m*-chlorobenzoic acid (MCBA, 10%) were found. ^1H NMR analysis revealed that the aqueous layer contained MCBA and the respective sodium salts of 2,2-dimethylpropanesulfinic acid (**11**) and 2,2-dimethyl-



propanesulfonic acid (**12**). For comparison purposes, the 2-equiv MCPBA oxidation of 2,2-dimethylpropyl disulfide (neopentyl disulfide, **13**) was carried out under identical conditions at −20 °C. Table I summarizes the distribution of products.

HPLC analysis of the organic phase from the oxidation of **6** showed peaks for **6** and **7** and two UV-active peaks besides **6**, probably the sulfines **8** and **9**. Flash chromatography of the organic phase showed that eluted **8** and **9** decomposed when the

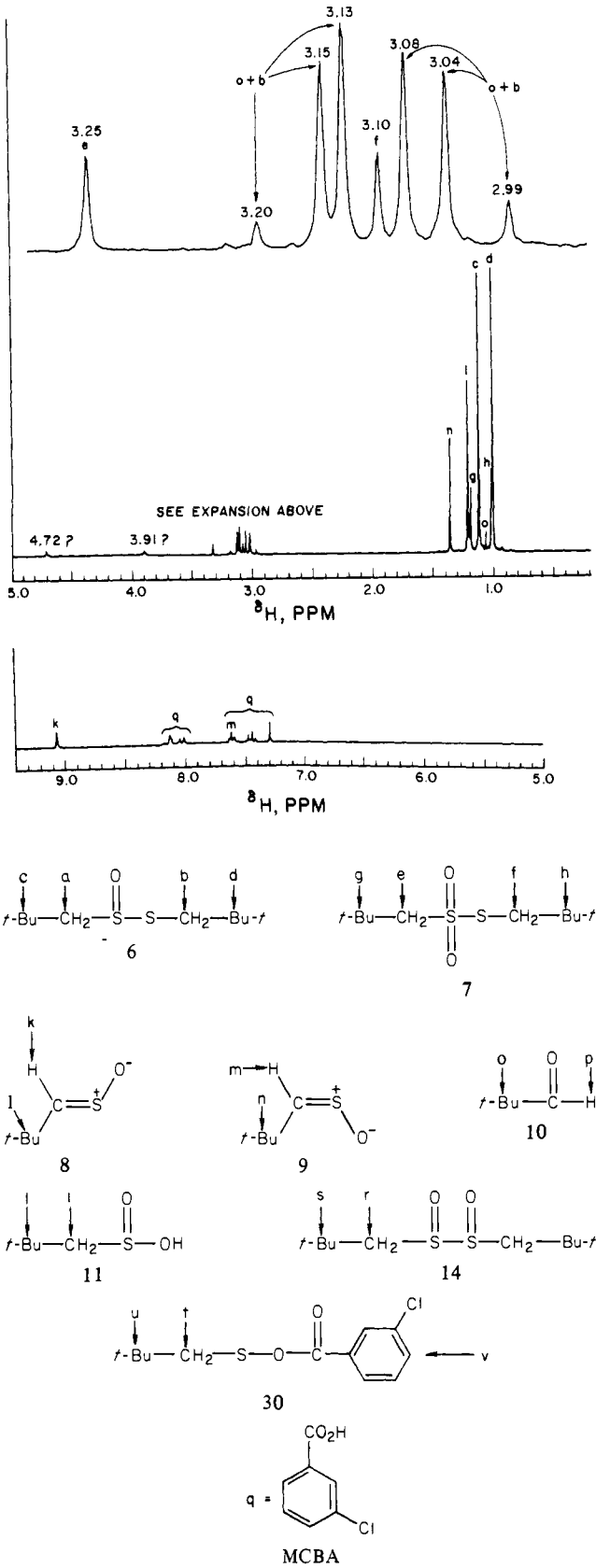


Figure 1. ^1H NMR spectrum, at ~25 °C, of the organic phase from the −20 °C MCPBA oxidation of **6** after treatment with 5% $NaHCO_3$ at 0 °C.

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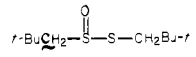
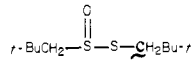
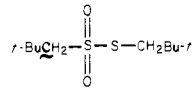
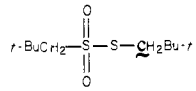
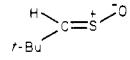
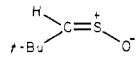
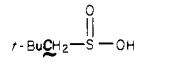
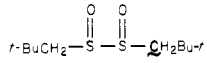
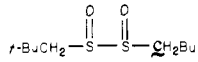
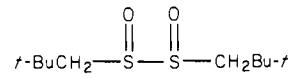
Table II. ^{13}C NMR Chemical Shifts (δ) of Products from the MCPBA Oxidation of 6 at −40 °C in $CDCl_3$[a,b]

compd	compd no.	−40 °C, 15 min[c]	% [b]	−40 °C, 68 min	% [b]	−20 °C, 135 min[c,d]	% [b]
	6	70.44	22	70.44	24	70.73	36
	6	46.85	21	46.85	27	46.94	37
	7	74.15	1	74.17	1	74.4	2
	7	49.76	<1	49.76	2	49.82	3
	8	(1.26, 9.18)[e] 184.03	(4)[f]			(1.25, 9.16)[g] 183.91	(9)[f]
	9	(1.40, 7.61)[e] 195.73	(4)[f]			(1.39, 7.69)[g] 195.5	(7)[f]
	11	71.59	7	71.59	13	71.85	21
	14a	64.00	34	64.03	24		
	14b	64.35	14	64.38	9		

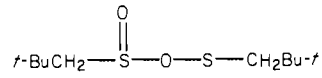
[a] Chemical shifts of samples in deuteriochloroform ($CDCl_3$) solutions with Me_4Si as internal standard. Spectrometer frequency is 62.89 MHz. [b] Relative integrals of the methylene carbon atoms are tabulated. [c] Time acquisition was started after filtration at −50 °C. [d] At 100 min the temperature was raised to −20 °C. [e] ^1H NMR chemical shifts of sulfines 8 and 9 from ^1H NMR spectrum (250 MHz) obtained at 13 min (−40 °C). [f] Relative amounts of 8 and 9 estimated from ^1H NMR spectrum. [g] ^1H NMR chemical shifts of sulfines 8 and 9 from ^1H NMR spectrum (250 MHz) obtained at 133 min (−20 °C).

fractions were concentrated. After standing overnight in the dark at 25 °C, the organic phase was analyzed via HPLC and ^1H NMR, and IR spectroscopy. The results of these analyses showed that sulfines **8** and **9** had disappeared, and the concentration of aldehyde **10** had increased. Aldehydes are known decomposition products of thial *S*-oxides.[20,44,45]

In order to determine whether 2,2-dimethylpropyl disulfoxides (neopentyl α-disulfoxides, **14**) and/or 2,2-dimethylpropyl per-



14a, *RR/SS*
14b, *RS/SR*



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oxy-2,2-dimethylpropanethiosulfinate (**15**) are stable at lower temperatures and to seek the precursor of sulfinic acid **11**, we repeated the −20 °C experiment at −40 °C to −35 °C for 45 min. After filtration of the product mixture under nitrogen as quickly as possible at −50 °C in order to remove MCBA, it was thermostated immediately in the NMR spectrometer at −40 °C (Figure 2). The ^{13}C NMR chemical shifts for the methylene carbon atoms are shown in Table II.[39,40,42,43]

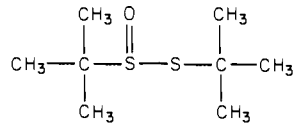
The ^{13}C NMR spectrum (Figure 2) shows two intermediates at δ 64.00 and 64.35, which disappeared in warming to −20 °C. These resonances are tentatively assigned to the *RR,SS* and *RS,SR* diastereomers of α-disulfoxide **14**.

The ^1H NMR spectrum (Figure 3) at −40 °C was complex owing to the presence of diastereotopic α protons in the reactant (**6**) and in **14**. The ^1H NMR spectrum showed a singlet at δ 1.21 in the *tert*-butyl region and a prominent AB quartet (δ_A 2.81, δ_B 2.96, J = 13.6 Hz). The coupling constant of this AB quartet is identical with that of the protons α to the sulfinyl group in **6** and several other neopentyl- and benzyl-substituted thiosulfinates.[39]

As in the ^{13}C NMR spectrum, the singlet at δ 1.21 and the AB quartet in the ^1H NMR spectrum disappeared on warming to −20 °C (Figure 4). These ^1H NMR resonances are also ascribed to the diastereomeric α-disulfoxides **14**.

When the reaction mixture was warmed to −20 °C, the disappearance of the ^1H NMR and ^{13}C NMR resonances ascribed to **14** was accompanied by an increase of the resonances of **6**, **7**, **11**, and sulfines **8** and **9** to give a product distribution similar to that obtained from the sodium bicarbonate extraction experiment (Table I). However, sulfines **8** and **9** decomposed in the reaction mixture at −20 °C to give aldehyde **10**. The decomposition of sulfines **8** and **9** at such a low temperature may be due to the presence of sulfinic acid **11** in the reaction mixture.[46]

The peroxidation of *S*-(2-methyl-2-propyl) 2-methyl-2-propanethiosulfinate (**16**) leads to 2-methyl-2-propyl disulfoxide



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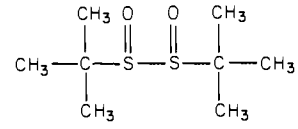

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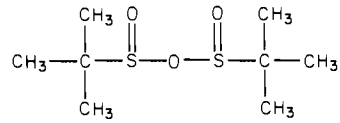

18

(**17**), which appears to decompose to give mainly 2-methyl-2-propanesulfinic anhydride (**18**).[22] It is possible that α-disulfoxides **14** can decompose in an analogous manner to give 2,2-dimethylpropanesulfinic anhydrides (**19**). Attempted preparation of **19** by the coupling of the silver salt (**20**) of sulfinic acid **11** with 2,2-dimethylpropanesulfinyl chloride (**21**) was unsuccessful[47] and

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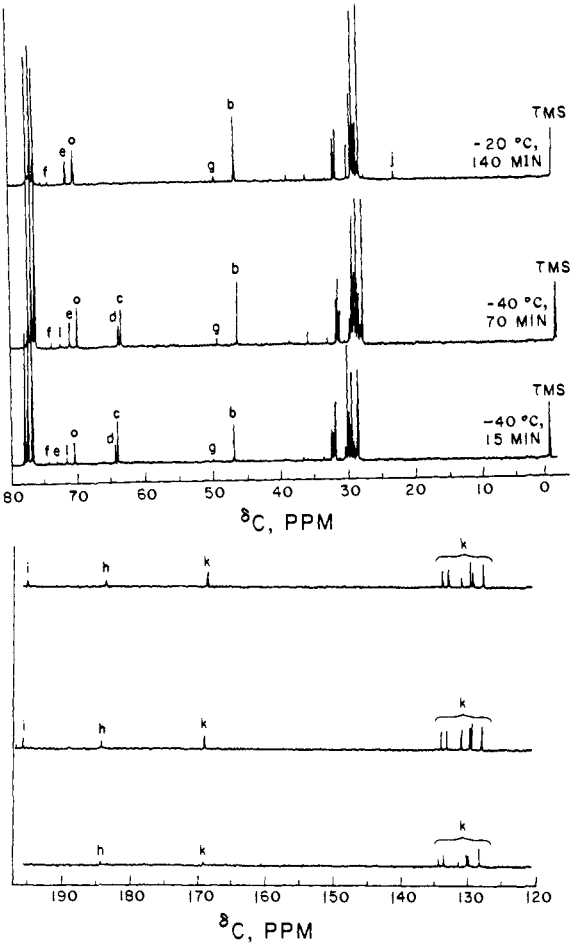
(47) Kice, J. L.; Ikura, K. *J. Am. Chem. Soc.* **1968**, *90*, 7378.



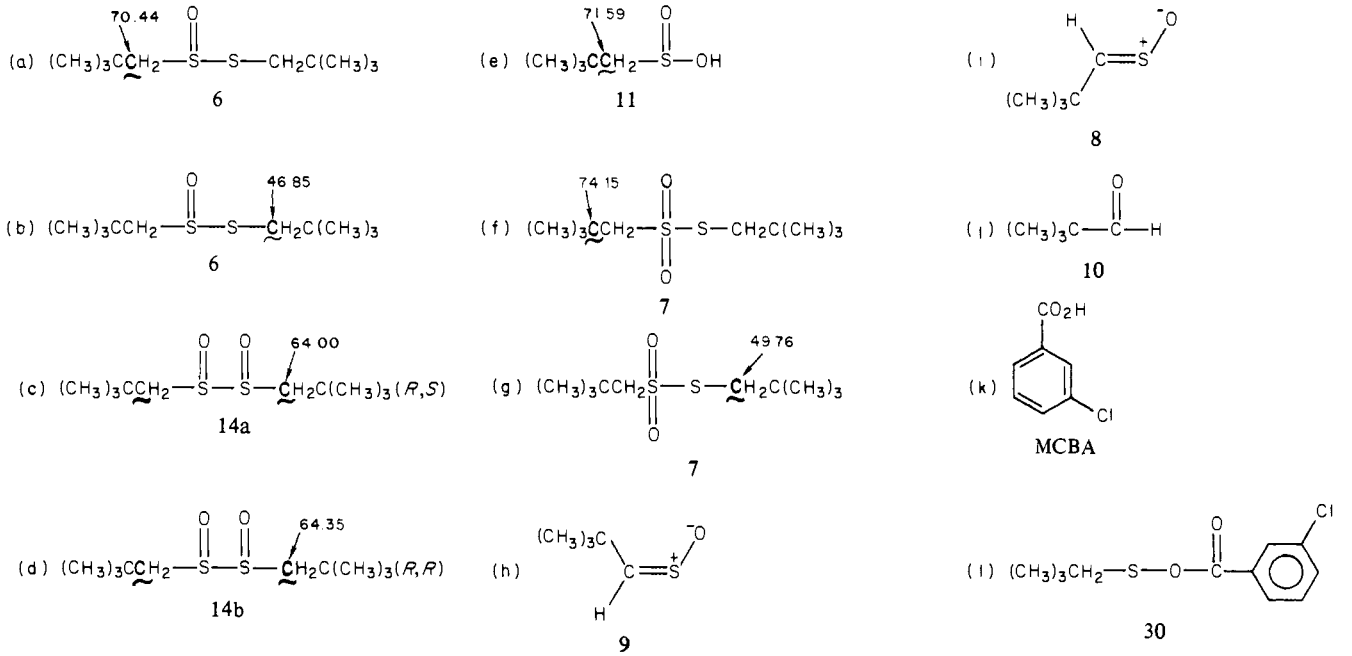


Figure 2. Low-temperature ^{13}C NMR spectra of the reaction of *S*-(2,2-dimethylpropyl) 2,2-dimethylpropanethiosulfinate (**6**) with MCPBA in $CDCl_3$. 0 min, −45 °C, filtration completed; 13 min, −40 °C, ^1H NMR spectrum obtained; 15 min, −40 °C, ^{13}C NMR spectrum obtained; 70 min, −40 °C, ^{13}C NMR spectrum obtained; 102 min, −20 °C, temperature raised to −20 °C; 133 min, −20 °C, ^1H NMR obtained; 140 min, −20 °C, ^{13}C NMR spectrum obtained.

gave 2,2-dimethylpropyl 2,2-dimethylpropanesulfinyl sulfone (**22**) as the only isolated product (eq 3).

Although no evidence of diastereotopic methylene protons for **19** was obtained, the large amount of sulfinic acid (**11**) ultimately isolated indicates that there is almost certainly some species having a −S(O)O− group present in the product mixture. Easily hydrolyzable sulfinyl groups are present in **14**, **15**, and **19**.

So that additional reference spectra might be obtained, the ^1H

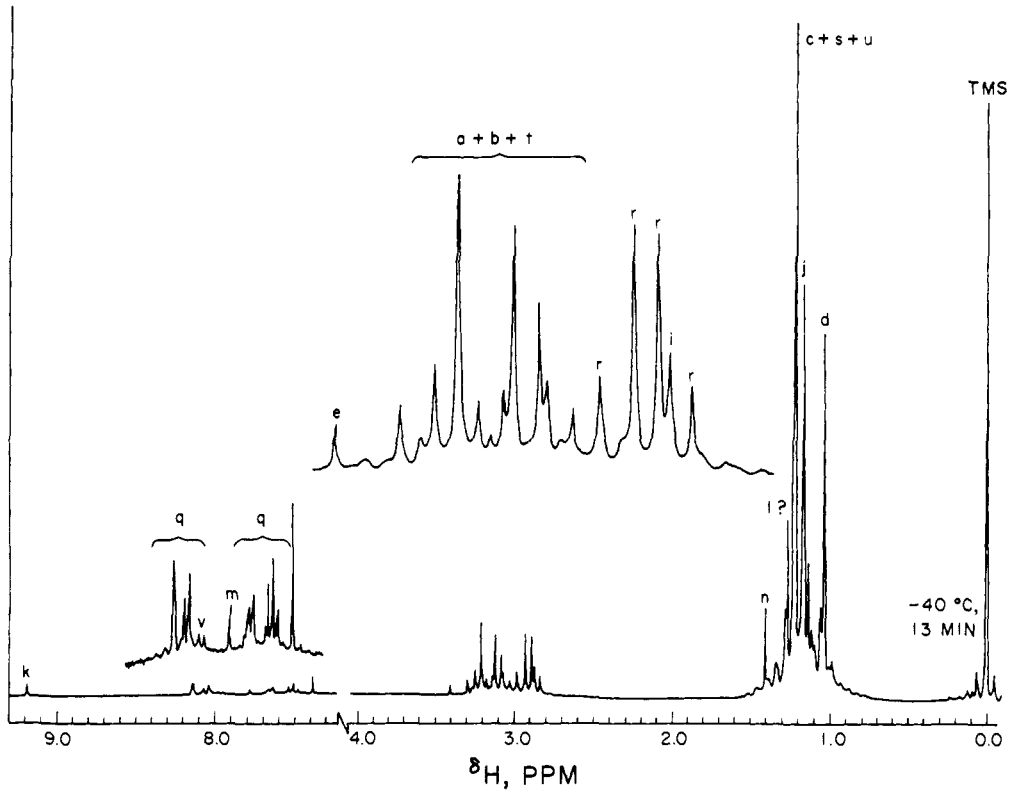
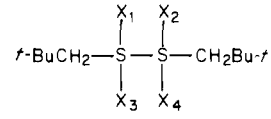


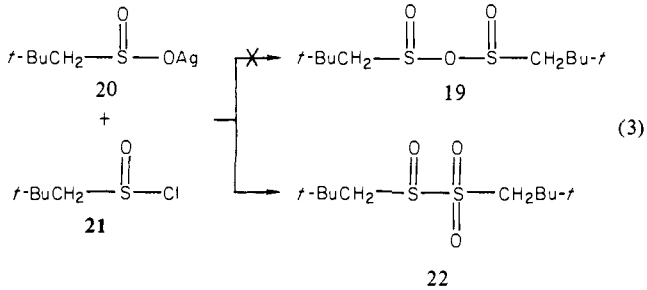
Figure 3. ^{1}H NMR spectrum at −40 °C of the MCPBA oxidation products from **6**. The legend is the same as in Figure 1.

Table III. ^{1}H NMR and ^{13}C NMR Spectra of Neopentyl Disulfide (13) and Its Oxide Derivatives[a,b]

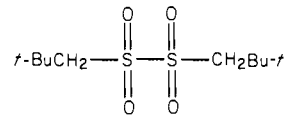


compd	position	δ_H		δ_C		
		$C(CH_3)_3$	CH_2	$C(CH_3)_3$	$C(CH_3)_3$	CH_2
6	α	1.14	3.06, 3.11 (J = 13.2 Hz)	29.56	32.26	71.55
6	α'	1.03	3.01, 3.16 (J = 4.2 Hz)	28.72	32.07	46.93
7	α	1.21	3.10	29.76	33.47	74.95
7	α'	1.04	3.35	28.86	32.12	49.92
13	α	1.02	2.76	28.83	30.31	55.96
14[c]	α	1.21	2.81, 2.96 (J = 13.6 Hz)	*d*	*d*	64.35
22[e]	α	1.27	3.19, 3.52 (J = 13.8 Hz)	29.96	32.93	62.48
22[e]	α'	1.20	2.79, 3.16 (J = 13.6 Hz)	29.76	32.61	62.19
23	α	1.28	3.35	29.82	33.00	59.35

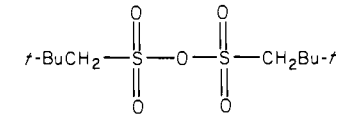
[a] Chemical shifts of samples in deuteriochloroform ($CDCl_3$) solutions with Me_4Si as internal standard. ^{1}H NMR at 250 MHz; ^{13}C NMR at 62.89 MHz. All spectra at room temperature except where noted. [b] 6, $X_1 = 0$, $X_2 \rightarrow X_4$ = lone pair electrons; 7, $X_1 = X_3 = 0$, $X_2 = X_4$ = lone pair electrons; 13, $X_1 \rightarrow X_4$ = lone pair electrons; 14, $X_1 = X_2 = 0$, $X_3 = X_4$ = lone pair electrons; 22, $X_1 \rightarrow X_3 = 0$, X_4 = lone pair electrons; 23, $X_1 \rightarrow X_4 = 0$. [c] From Table II. [d] Not determined. [e] Assignments of ^{13}C NMR shifts uncertain.



NMR and ^{13}C NMR spectra of **22**, 2,2-dimethylpropyl 2,2-dimethylpropyl disulfone (**23**) (Table III) and 2,2-dimethylpropanesulfonic anhydride (**24**)[48] were recorded.



23



24

Attempts to prepare sulfenyl sulfinate **15** from **20** and 2,2-dimethylpropanesulfenyl bromide (neopentanesulfenyl bromide, **25**) gave **7**.

$$\mathbf{20} + t\text{-}BuCH_2\text{-}S\text{-}Br \rightarrow \mathbf{7} \qquad (4)$$
$$\mathbf{25}$$

(48) King, J. F.; Aslam, M. *Can. J. Chem.* **1979**, *57*, 3278.

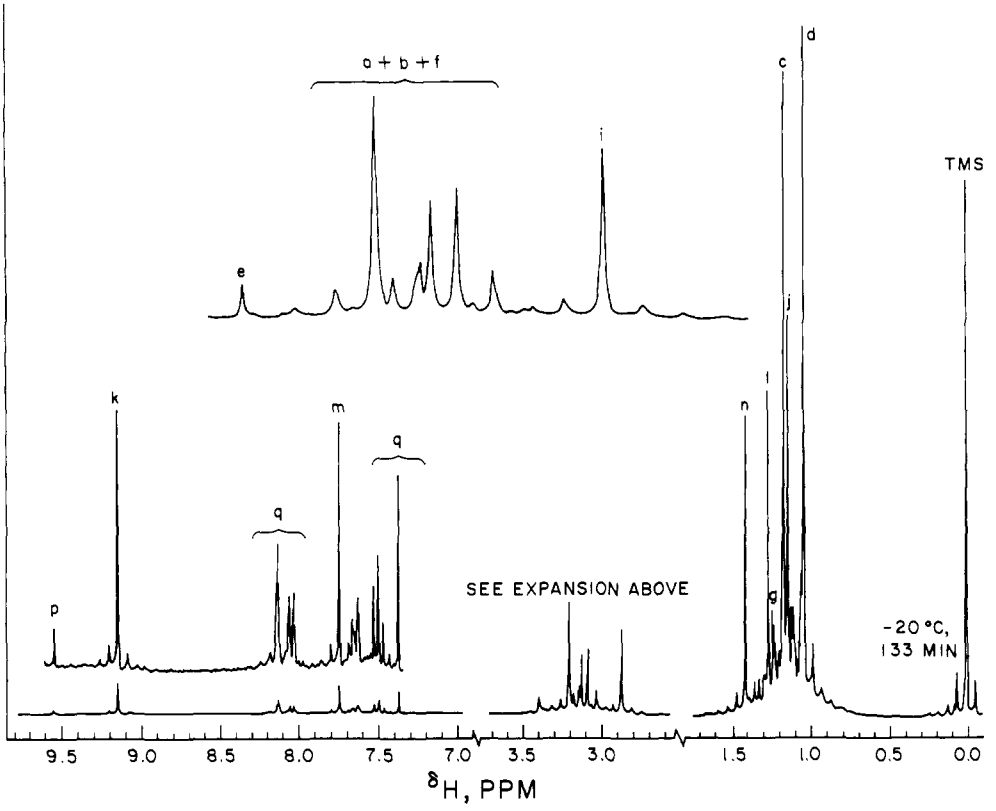
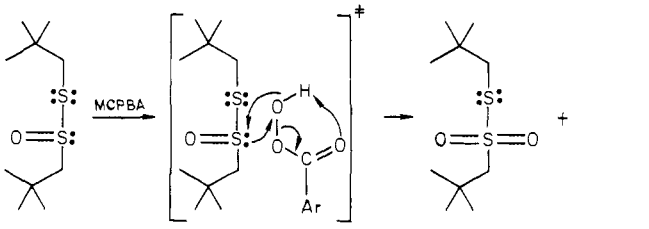


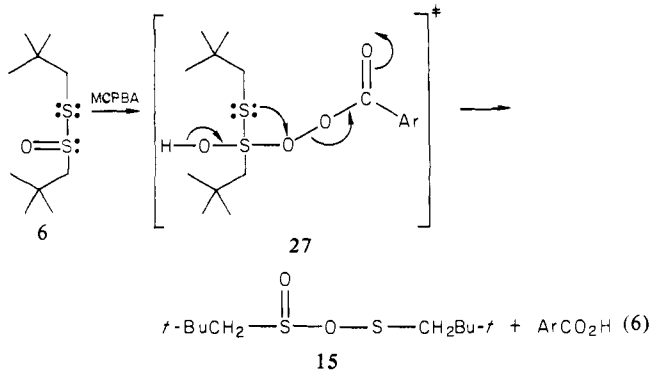
Figure 4. ^1H NMR spectrum of the MPCBA oxidation products from **6** after warming to −20 °C. The legend is the same as in Figure 1.

Discussion

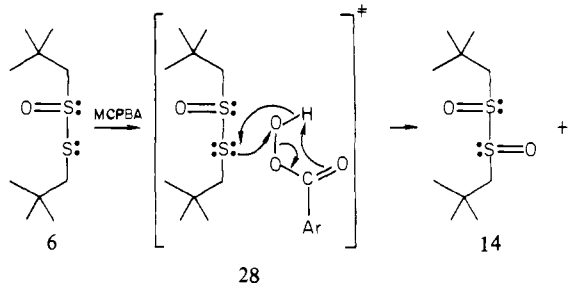
The low yield of **7** from the oxidation of **6** by MPCBA and the inertness of **7** under the experimental conditions[49,50] suggest that attack by oxidant at the sulfinyl sulfur atom (eq 5) is not a major



reaction pathway in this system.[11-13,18,20-23] However, MCPBA might add across the sulfinyl group to give intermediate **27** (eq 6), which could rearrange to sulfenyl sulfinate **15**. This latter



mechanism is considered unlikely owing to the absence or small dissociation of MCPBA in $CDCl_3$.[11,22] Electrophilic attack by MCPBA at the sulfenyl sulfur atom would lead to the α-disulfoxides **14**,[11-13,17,18,20-23,41] which can rearrange to thiosulfonate **7** or to sulfenyl sulfinate **15** (eq 7).

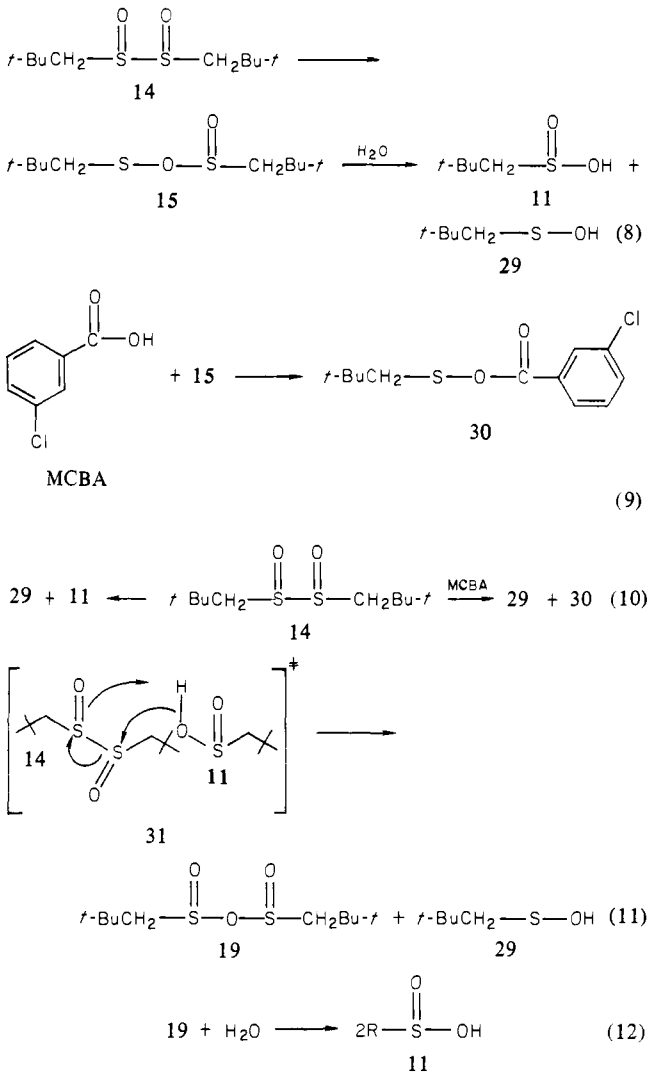


The ^1H NMR and ^{13}C NMR data in Tables I–III and Figures 1–4 are consistent with the formation of diastereomeric α-disulfoxides **14**, probably via eq 7. Although no detectable amounts of sulfenyl sulfinate **15** were present, it is still a possible intermediate. The yields of thiosulfinate **6** and sulfinic acid **11** seem to require the intermediacy of **15**. Sulfenyl sulfinate **15**, which is expected to be easily hydrolyzed by water (eq 8) or traces of MCBA (eq 10), can give **11** and 2,2-dimethylpropanesulfenic acid (neopentanesulfenic acid, **29**) or 3-chlorobenzoyl 2,2-dimethylpropanesulfenate (**30**).[51]

Alternate pathways for the formation of **6**, **11**, **29**, **30**, and possibly **19**, which involve α-disulfoxides **14**, are shown in eq 12–14.[22]

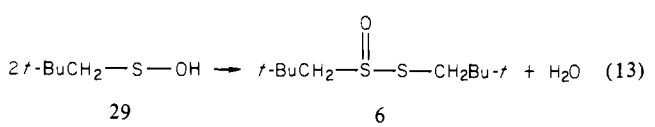
(49) Das Neves, J. J. C.; Godhinho, L. S. *Tetrahedron* **1979**, *35*, 2053.
(50) Allen, P., Jr.; Brook, J. W. *J. Org. Chem.* **1962**, *27*, 1019.

(51) In the −40 °C ^{13}C NMR spectrum, a small peak at δ 72.852 (1.7%) was observed. The aromatic region in the ^1H NMR spectrum contained small peaks (the ortho hydrogens were deshielded 0.1 ppm relative to MCBA). The resonances in both spectra, which may be due to the presence of **30**, disappeared on warming to −20 °C.

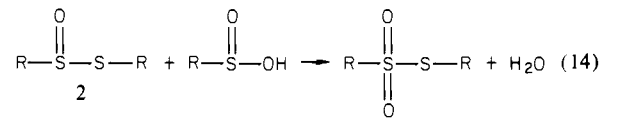


It can also be speculated[54] that sulfenic acid **29** can lead to thiosulfonate **7**, presumably via t-$BuCH_2\dot{S}O$.[37,55] Since the disproportionation of a sulfinic acid (**11**) can lead to the formation of a thiosulfonate (**7**), it is also possible that **29** is oxidized to **11**, which then yields **7**.[56-62] Thus, the amount of **7** formed by direct oxidation of **6** (eq 5) or via α-disulfoxides **14** cannot be determined from the experimental results.

Sulfenic acids are known to dimerize to thiosulfinates (eq 13).[52,53] It is also known[61,62] that sulfinic acids react with

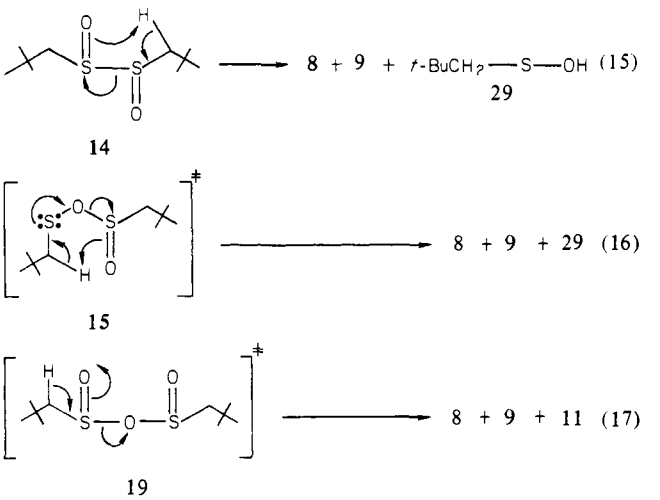


thiosulfinates (**2**) to give thiosulfonates (**5**, eq 14). Although arenesulfinic acids react quickly with arenethiosulfinates only with



acid or nucleophilic catalysis,[62-65] the alkane analogues generally react much faster without catalysis.[61,66] However, the *tert*-butyl and neopentyl analogues do not react,[22] probably due to steric hindrance.

The ratio (**8**:**9** = 1.6:1) of sulfines obtained from the MCPBA oxidation of **6** is different than the ratio (**8**:**9** = 1:3) obtained from the treatment of **21** with triethylamine.[44] Sulfines **8** and **9** could arise from α-disulfoxides (**14**, eq 15), sulfenyl sulfinate **15** (eq 16), and/or sulfinic anhydride **19** (eq 17).[20] However, formation



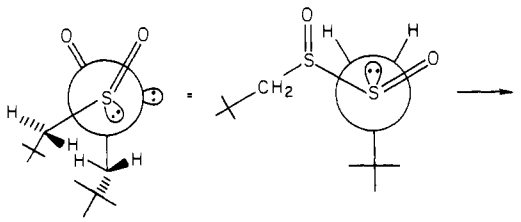
of sulfines from either **15** or **19** may be considered unlikely for the following reasons. The functional groups present in **15** and **19** are not expected to aid in a cycloelimination reaction under the mild conditions used in this study. The acidity of hydrogens next to a sulfonyl group is far greater than those next to a sulfinyl group. For example, the pK_a of dimethyl sulfone is 4 pK units larger than that of dimethyl sulfoxide.[67] Thus, solely on the basis of the inductive effect of the sulfur involved, α-disulfone **23** should be much more likely to undergo a cycloelimination reaction to give a sulfene than either **15** or **19** to give a sulfine, but it does not. Also, direct substitution by nucleophiles at a sulfinyl sulfur is normally 10^4–10^6 faster than the rate of the same substitution at sulfonyl sulfur.[68] Therefore, **15** and **19**, if formed, would be expected to undergo nucleophilic reactions much faster than a cycloelimination mechanism.

The formation of sulfines from the oxidation of a thiosulfinate (**2**) has been recently reported.[20,44,45] Dialkyl thiosulfinates have stronger S–S bonds than diaryl and, presumably, aralkyl thiosulfinates.[52] If this is also true for α-disulfoxides, compounds **14** would not be expected to decompose solely via homolytic scission, as has been postulated for aryl α-disulfoxides.[11,17,32] Thus, α-disulfoxides **14** can afford sulfines **8** and **9** and/or lead to other possible sulfine precursors such as **15** and **19** via a polar or ionic mechanism as a result of strong dipole–dipole interactions of the two sulfinyl groups.

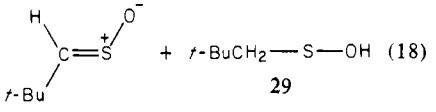
The possible activated complexes for formation of sulfines are shown for the two diastereomers of **14** in eq 18 and 19.[23]

Although **9** is expected to be thermodynamically more stable than **8**,[44,69] formation of **8** over **9** can be kinetically favored in the

(52) Block, E.; O'Connor, J. *J. Am. Chem. Soc.* **1974**, *96*, 3921.
(53) Davis, F. A.; Jenkin, R. H., Jr. *J. Am. Chem. Soc.* **1980**, *102*, 7967.
(54) Kice, J. L.; Lee, T. W. S.; Pan, S.-T. *J. Am. Chem. Soc.* **1980**, *102*, 4448.
(55) Keolewijn, P.; Berger, H. *Recl. Trav. Chim. Pays-Bas* **1972**, *91*, 1725.
(56) Kice, J. L.; Guaraldi, G.; Venier, C. G. *J. Org. Chem.* **1966**, *31*, 3561.
(57) Kice, J. L.; Bowers, K. W. *J. Am. Chem. Soc.* **1962**, *84*, 605.
(58) Bredereck, H.; Wagner, A.; Beck, E. H.; Berlinger, H.; Kottenhahn, K. G. *Angew. Chem.* **1958**, *70*, 268.
(59) von Braun, J.; Weissback, K. *Chem. Ber.* **1930**, *63*, 2837.
(60) Pauly, C.; Otto, R. *Chem. Ber.* **1877**, *10*, 2182.
(61) Block, E.; O'Connor, J. *J. Am. Chem. Soc.* **1974**, *96*, 3929.
(62) Kice, J. L.; Venier, C. G.; Heasley, L. *J. Am. Chem. Soc.* **1967**, *89*, 3557.
(63) Kice, J. L.; Large, G. B. *J. Am. Chem. Soc.* **1968**, *90*, 4069.
(64) Kice, J. L.; Pawlowski, N. E. *J. Am. Chem. Soc.* **1964**, *86*, 4898.
(65) Kice, J. L.; Venier, G. B.; Heasley, L. *J. Am. Chem. Soc.* **1969**, *91*, 2028.
(66) Freeman, F.; Angeletakis, C. N., unpublished data.
(67) Mathews, V. S.; Bares, J. E.; Bordwell, F. G.; Cornforth, F. J.; Drucker, G. E.; Margolin, Z.; McCallum, R. I.; McCollum, G. J.; Vanier, N. R. *J. Am. Chem. Soc.* **1975**, *97*, 7006.
(68) Kice, J. L. *Adv. Phys. Org. Chem.* **1980**, 65.

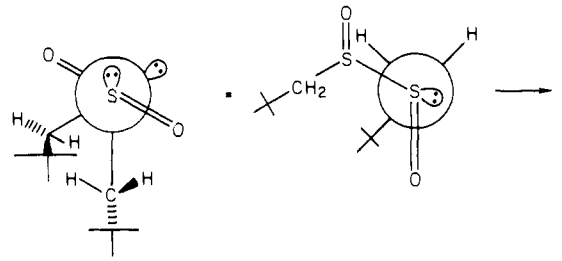


14a, *RS,SR*

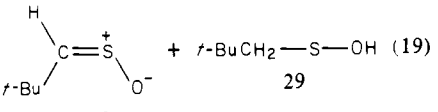


(18)

(*E*)-8



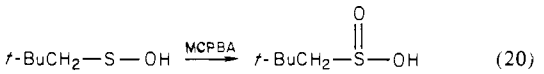
14b, *RR,SS*



(19)

(*Z*)-9

peroxidation of **6** due to increased reactivity of **14b** toward cycloelimination arising from greater dipole–dipole interaction between the sulfinyl oxygens. In the peroxidation of **13**, the yields of **8** and **9** are lower and the yield of sulfinic acid **11** is higher compared to the corresponding yields in the peroxidation of **6**. Although the needed kinetic studies on the peroxidation of alkyl disulfides and thiosulfinates are not available, a possible reason is as follows. It is possible that **6** competes effectively with **13** for oxidant, the resultant α-disulfoxide decomposes by eq 8 and 9, and the sulfenic acid (**29**) formed is oxidized to sulfinic acid **11** (eq 20). Compound **11** then can react with **14b** preferentially

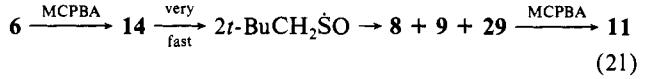


(20)

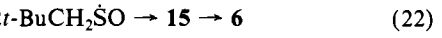
(which is less sterically hindered than **14a**) to give sulfinic anhydride **19** (eq 11), which can hydrolyze to give more **11** (eq 12).

Although no evidence of diastereotopic methylene protons for **19** was obtained, the large amount of sulfinic acid (**11**) ultimately isolated indicates that there is almost certainly some species having a –S(O)O– group present (**14**, **15**, **19**) in the product mixture.

Other logical routes to thiosulfonate **7**, sulfines **8** and **9**, and sulfinic acid **11** are shown in eq 21 and 22.[20] Formation of **6**



(21)



(22)

could result from combinative termination of two *t*-$BuCH_2\dot{S}O$ radicals, followed by rearrangement of sulfenyl sulfinate **15**. Very rapid homolytic dissociation of α-disulfoxides has been suggested before for aryl α-disulfoxides.[11-13,17,18,20-23] Termination of two *t*-$BuCH_2\dot{S}O$ radicals by disproportionation seems very reasonable, given the tendency for this type of radical termination to occur frequently in other radical reactions.[37,55]

The results described above clearly show that α-disulfoxides **14** are intermediates in the oxidation of **6** and **13**. In contrast to what is generally accepted, thiosulfonate **7** is *not* the major oxidation product in the early stages of the reaction, which suggests thiosulfonates (**5**) may arise other than by direct MCPBA oxidation of thiosulfinates (**2**) and that thiosulfinates (**2**) may be formed from some of the oxidation products. The above results are consistent with the MCPBA oxidation of **16**, which does not give the corresponding thiosulfonate but diastereomeric α-disulfoxides (**17**) and diastereomeric anhydrides (**18**).[22]

Several interesting aspects of NMR were observed during this investigation. For example, it is of interest to note that both methylene groups in **22** show magnetic nonequivalence and about equally large J_{AB} values (Table III). Moreover, the ^{13}C NMR chemical shifts of the α-carbons of the α-disulfoxides **14** are consistent with those of the other oxidized derivatives of neopentyl disulfide (**13**).[39] Dipole moment measurements[70-72] suggest that thiosulfinates, thiosulfonates, and α-disulfones exist mainly in the gauche conformation in the solution.[73] The shift difference between the methylene carbon of **13** and the methylene carbon bonded to the sulfenyl sulfur of **6** is –9.03 ppm. This difference can be attributed to the γ-gauche shielding effect exerted by the sulfinyl oxygen. Moreover, the deshielding effect of an SO_2 group on the α-carbon is almost identical with that of an SO group in simple acyclic sulfones and sulfoxides.[74] Therefore, the predicted chemical shift of the α-carbon atoms of **14**, **22**, and **23** is 71.55 – 9.03 = 62.52 ppm (Table I). Inspection of Table III shows that the α-carbon atoms of **14**, **22**, and **23** are shielded relative to the predicted value by about 3, 0, and –3 ppm, respectively.[75,76]

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–Cl mass spectrometer with a Nova 3 data system. 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, 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 column with 3% ethyl acetate–2,2,4-trimethylpentane 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*-(2,2-Dimethylpropyl) 2,2-Dimethylpropanethiosulfinate (6).** Oxidation of neopentyl disulfide (**13**)[77] with 1 equiv of MCPBA in $CHCl_3$ at 0 °C gave **6**, which was purified by flash chromatography on silica gel. Recrystallization from hexane gave **6** (66%): mp 68–69 °C; IR ($CDCl_3$) 1060 cm^{-1} (S=O); CI mass spectrum (*i*-C_4H_{10}) *m/z* 223 (MH^+).[78]

***S*-(2,2-Dimethylpropyl) 2,2-Dimethylpropanethiosulfonate (7).** Thermal decomposition of neopentanesulfinic acid (**11**) afforded crude **7**. Chromatography on silica gel followed by recrystallization from petroleum ether (30–60 °C) gave white crystals: mp 59–60 °C; IR ($CHCl_3$) 1320, 1130 cm^{-1} (SO_2); CI mass spectrum (*i*-C_4H_{10}) *m/z* 239 (MH^+).[78] Anal. ($C_{10}H_{22}O_2S_2$) C, H.

Compound **7** was also prepared by the reaction of silver neopentanesulfinate (**16**) with neopentanesulfenyl bromide (**25**). To a solution of bromine (0.08 g, 1 mmol) in 2 mL of $CHCl_3$, which was cooled to –10

(69) Block, E.; Penn, R. E.; Buzzi, A. A.; Cremer, D. *Tetrahedron Lett.* **1981**, 29.
(70) Dembech, P.; Vivarelli, P.; Jehicka, V.; Exner, O. *J. Chem. Soc., Perkin Trans. 2* **1973**, 489.
(71) Exner, O.; Harpp, D. N.; Gleason, J. G. *Can. J. Chem.* **1972**, *50*, 548.
(72) McClellan, A. L. "Tables of Experimental Dipole Moments"; W. H. Freeman: San Francisco, 1963.
(73) Wolfe, S. *Acc. Chem. Res.* **1972**, *5*, 102.
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(75) The ^{13}C NMR chemical shifts of the α and α′ carbon atoms of **7** do not conform with these shielding trends. This may be due to conformational effects that violate the Edward–Lemieux principle.[76]
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°C, was added dropwise with stirring a solution of neopentyl disulfide (**13**, 0.10 g, 0.05 mmol) in 3 mL of $CHCl_3$. To this solution was added a mixture of 0.24 g (1 mmol) of **16** in 5 mL of $CHCl_3$. The stirring was continued for 2 h at −10 °C and the AgBr removed via filtration. The IR and NMR spectra of the resultant mixture were essentially identical with the ones for compound **7**.

2,2-Dimethylpropanesulfinic acid (11) was prepared in quantitative yield by the reaction of NaOEt with phthalimidomethyl neopentyl sulfone in EtOH.[79,80] (Other compounds involved in the synthesis were phthalimidomethyl neopentyl sulfide (mp 84–86 °C, 92% yield) and phthalimidomethyl neopentyl sulfone (mp 165–166 °C, 54% yield; ^1H NMR of **11** ($CDCl_3$, 60 MHz) δ 1.12 (s, 9 H), 2.85 (s, 2 H); ^1H NMR of the sodium salt of **11** (D_2O, 90 MHz, 3-(trimethylsilyl)propanesulfonic acid sodium salt (DSS) internal standard) δ 1.07 (s, 9 H), 2.42 (s, 2 H); IR ($CHCl_3$) 1060 cm^{-1} (S=O).) The silver salt (**20**) of **11** was prepared by the reaction of the sodium salt of **11** with 1 equiv of $AgNO_3$ solution.

2,2-Dimethylpropanesulfonic acid (12) was prepared by oxidation of neopentanethiol (**31**) with HNO_3.[81] Decomposition of the Pb salt of **12** with H_2S followed by drying overnight in vacuo at 24 °C over P_2O_5 led to a solid that slowly liquefied: ^1H NMR ($CDCl_3$, 250 MHz) δ 1.12 (s, 9 H), 2.98 (s, 2 H); ^1H NMR of the sodium salt of **12** (D_2O, 250 MHz, DSS as internal standard) δ 1.12 (s, 9 H), 2.94 (s, 2 H); IR ($CHCl_3$) 1060 cm^{-1} (S=O). Compound **12** was converted to the *S*-benzylthiuronium sulfonate, mp 184–185 °C, which was analyzed.

Anal. Calcd for $C_{13}H_{22}N_2O_3S_2$: C, 49.02; H, 6.96; S, 20.13. Found: C, 48.81; H, 7.17; S, 19.37.

2,2-Dimethylpropyl Disulfide (13), mp 40–41 °C (lit.[77] mp 40–41 °C), was prepared by the iodine oxidation of 2,2-dimethylpropanethiol (**31**).[77,79]

2,2-Dimethylpropanesulfinyl chloride (21) was prepared by the procedure of Douglass and Norton,[82] except CH_2Cl_2 was used as the solvent. Compound **21**, which was obtained in 83% yield, had bp 60–61 °C (5 mm).

2,2-Dimethylpropyl 2,2-Dimethylpropanesulfinyl Sulfone (22). Silver neopentanesulfinate (**20**) (0.78 g, 3.2 mmol, dried overnight over P_2O_5 in vacuo at 24 °C) was suspended in 5 mL of ether, and the mixture was cooled to −10 °C. Neopentanesulfinyl chloride (**21**) (0.5 g, 3.2 mmol) in 10 mL of ether was added dropwise to the cooled suspension. The mixture was stirred at −10 °C for 3 h and filtered, and the ether was distilled at 0 °C. The distillate gave a negative 2,4-dinitrophenylhydrazine test (no aldehyde). The semicrystalline residue was recrystallized 3 times below 24 °C from ether and then washed with ether to give 0.08 g (10% yield) of **22**: mp 94–95 °C; ^1H NMR ($CDCl_3$, 250 MHz) δ 1.20 (s, 9 H), 1.27 (s, 9 H), 3.19, 3.52 (AB q, J = 13.8 Hz, 2 H), 2.79, 3.16 (AB q, J = 13.6 Hz, 2 H); ^{13}C NMR ($CDCl_3$, 250 MHz) δ 29.76, 29.96 ($C(CH_3)_3$), 31.61, 32.93 ($C(CH_3)_3$), 62.19, 62.48 (CH_2); UV ($CHCl_3$ br shoulder 220–250 nm, $\epsilon \sim 6000$; IR ($CHCl_3$) 1320, 1200, 1165, 1125, 1072 cm^{-1} (S=O); CI mass spectrum (i-C_4H_{10}), m/z 255 (MH^+).[78] Anal. ($C_{10}H_{22}O_3S_2$) C, H.

2,2-Dimethylpropyl Disulfone (23). *S*-(2,2-Dimethylpropyl) 2,2-dimethylpropanethiosulfonate (**7**, 0.21 g, 0.90 mmol) and 0.45 g (2.16 mmol) of 82% MCPBA were dissolved in 7 mL of methylene chloride, and the solution was allowed to stand at room temperature for 5 days. The precipitate of *m*-chlorobenzoic acid was filtered off, and the filtrate was washed with 5% sodium bicarbonate and then dried ($MgSO_4$). After removal of the solvent, the residue was recrystallized from ethanol, giving 0.04 g of 2,2-dimethylpropyl disulfone (**23**): mp 148–150 °C; IR ($CDCl_3$) 1341 and 1116 cm^{-1} (s, $>SO_2$). Anal. Calcd for $C_{10}H_{22}S_2O_4$: C, 44.41; H, 8.20; S, 23.71. Found: C, 44.31; H, 8.30; S, 24.40.

2,2-Dimethylpropanesulfonic anhydride (24) was prepared in 31% yield by the reaction of **12** with *p*-tolylcarbodiimide in benzene:[48] mp 79–80 °C (lit.[48] mp 79–80 °C); ^{13}C NMR ($CDCl_3$, 62.89 MHz) δ 66.93 (CH_2). Anal. ($C_{10}H_{22}O_5S_2$) C, H, S.

2,2-Dimethylpropanethiol (31). In a 250-mL, three-neck, round-bottom flask equipped with a mechanical stirrer and dry ice condenser was added 60 mL of methoxyethanol, followed by 3.6 g (0.15 mol) of sodium. The solution was saturated with H_2S until H_2S began to reflux on the dry-ice condenser. The dry-ice condenser was replaced with a take-off distilling head, neopentyl tosylate (**32**,[83] 18 g, 8.9 mmol) was added, and the mixture was heated. The distillate boiling at 100–110 °C was collected, washed with water, and dried ($MgSO_4$).[84] This material was found to be over 97% pure by NMR (250 MHz) (lit.[85] bp 95–100 °C (688 mm)): IR ($CDCl_3$) 1355, 1380, 2855, 2905, 2920, and 2950 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.07 (s, q, *t*-Bu), 1.12 (t, 1, J = 9 Hz, S-H), and 2.37 (d, 2, J = 9 Hz, S-CH_2); ^{13}C NMR ($CDCl_3$) δ 28.06 ($C(C-H_3)_3$), 31.79 ($C(CH_3)_3$), and 38.79 (CH_2).

Oxidation of *S*-(2,2-Dimethylpropyl) 2,2-Dimethylpropanethiosulfinate (6) with MCPBA. Method A. Treatment with $NaHCO_3$ Solution. In a nitrogen atmosphere, **6** (0.30 g, 1.35 mmol) was dissolved in 3 mL of $CDCl_3$ and cooled to −20 °C in a dry ice/2-propanol bath. A solution of 81% MCPBA (0.29 g, 1.35 mmol) in 5.3 mL of $CDCl_3$ was added dropwise with stirring. The reaction mixture was stirred for 1 h at −20 °C and warmed to 0 °C, and 6.8 mL of ice-cold 5% aqueous $NaHCO_3$ solution was added. Stirring was for 10 min, the layers were separated, and the organic phase was dried (Na_2SO_4). Toluene was used as the NMR standard for the organic layer and NaOAC for the aqueous layer. An unidentified peak at δ 1.04, which accounted for ~5% of the *tert*-butyl groups, was present. This compound was not present when the reaction was carried out at half the concentration. The ^1H NMR of the organic phase showed, in addition to resonances for **6**, **7**, and MCBA, peaks at δ 1.23, 1.38, 7.58, and 9.00, which support the presence of **8** and **9**. Concentration of the solvent led to the disappearance of **8** and **9** and the formation of **10** (δ_H 1.08, 9.48; δ_C 23.47 [$C(CH_3)_3$], 42.2 [$C(CH_3)_3$], 203.3 (C=O). The ^{13}C NMR spectrum of the organic layer showed peaks for MCBA, **6**, **7**, and additional resonances at δ 27.81 (?), 29.20, 29.39 ($C(CH_3)_3$), 36.24, 39.24 ($C(CH_3)_3$), and 183.40, 195.96 (O=S-(C-$C(CH_3)_3$). The IR spectrum showed absorptions for MCBA, **6**, and **7**, and at 1130, 1080, and 1050 cm^{-1} (**8** and **9**), which disappeared after this sample was allowed to stand overnight in the dark at 20 °C. The AB quartet for the methylene hydrogens nearest the sulfenyl sulfur atom of **6** (J = 4.15 Hz) collapsed to a doublet in the presence of **8** and **9**. After 12 h in the dark at 24 °C, the outer satellites of this AB quartet reappeared, the resonances for **8** and **9** disappeared, and peaks for **10** appeared. Compound **10** was distilled from the product mixture in vacuo at 24 °C and derivatized as its 2,4-dinitrophenylhydrazone (mp 208–209 °C).

Method B. Low-Temperature NMR Experiment. This was the same as method A except the reaction temperature was −40 °C, reaction time was 45 min, and the filtration was carried out at −50 °C.

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