The Chemistry of Alkyl Thiolsulfinate Esters. VI. Preparation and Spectral Studies

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Abstract: Full details are given of the synthesis, properties, and certain reactions of a variety of dialkyl thiolsulfinate esters. The S–S bond energy in MeS(O)SMe has been determined by appearance potential methods to be 46 kcal/mol, compared to a corresponding value of ~75 kcal/mol in MeSSMe. A reinvestigation of the peracid oxidation of 2-methyl-2-propyl ethyl disulfide has shown that the oxidation does not afford 2-methyl-2-propyl ethanethiolsulfinate (*t*-BuSS(O)Et) as the only product, as originally claimed, but rather gives a mixture of this product and ethyl 2-methyl-2-propanethiolsulfinate (*t*-BuS(O)SEt), with the latter compound predominating by a ratio of ~2:1. Synthetic approaches and spectral data are given for a variety of new, specifically deuterated mercaptans, disulfides, thiolsulfinates, and thiolsulfonates as well as nondeuterated thiolsulfinates and thiolsulfonates. The disproportionation of several unsymmetrically deuterated dialkyl thiolsulfinates has been studied using gc–ms techniques and it is concluded that unsymmetrical thiolsulfonate predominates over symmetrical thiolsulfonate. Electron impact induced processes of unsymmetrical dialkyl thiolsulfinates are described and contrasted with thermal processes. Contrary to the conclusions of a published study of the mass spectra of diaryl thiolsulfinates, it is concluded that disulfide formation is better explained in terms of a thermal rather than electron impact induced process. A unique feature of the fragmentation of EtS(O)SEt is the formation of H_2S_2O, corresponding to the unknown parent acid of thiolsulfinate esters. Other aspects of the fragmentation of dialkyl thiolsulfinates have been studied with deuterium labeling and metastable defocusing methods; these studies provide evidence for nonspecific hydrogen transfer processes.

Since the characterization of the antibacterial principle of the common garlic (*Allium sativuum*) as allyl 2-propene-1-thiolsulfinate (**1**; allicin),[1] consider-

$CH_2{=}CHCH_2S(O)SCH_2CH{=}CH_2$

1

able interest has focused on the structure, chemistry, and properties of thiolsulfinates, RS(O)SR, the organic esters of the hitherto hypothetical thiolsulfoxylic acid, **2**. Alkyl thiolsulfinates have been found to

$HS(O)SH \rightleftharpoons ? \rightleftharpoons HO{-}S{-}S{-}H$

2

possess tumor inhibiting,[2] antiviral,[3] and antifungal activity;[4] certain cyclic thiolsulfinates related to 1,2-dithiolane 1-oxide have been found to occur naturally and to possess biological activity.[5] A number of thiolsulfinates have been shown to inhibit the autoxidation of polyolefins and to have utility as stabilizers for synthetic rubber.[6]

A particularly significant characteristic of many molecules possessing the S(O)–S linkage is their unusual reactivity and low stability. In this regard, it would seem possible that *in vivo* conversion of key peptide disulfide linkages to the thiolsulfinate formed through the action of exogenous oxidants (*i.e.*, ozone, peroxyacetyl nitrate (PAN), singlet oxygen, etc.) could well have serious biochemical consequences.[7] Despite the remarkably broad spectrum of significant properties attributed to thiolsulfinates, the chemistry of dialkyl thiolsulfinates, the simplest members of this intriguing class of organosulfur compounds, has not been systematically explored.[8]

Anticipating that the dialkyl thiolsulfinate esters would be more suitable models for predicting the *in vivo* behavior of the cystinyl thiolsulfinate unit than the diaryl esters (a conclusion which now seems valid) as well as hoping to define the basis for the unusual instability of dialkyl thiolsulfinates, we have studied the thermal chemistry of these compounds in some detail. Serendipitously, we have also found that the readily available dialkyl thiolsulfinates are synthetically useful precursors of a variety of novel organosulfur structural types.[11] In this and the accompanying paper[11] we now report the full details of our investigation.[12]

Methyl methanethiolsulfinate, on standing by itself

* Visiting Professor, Harvard University, 1974.

(1) C. J. Cavallito, J. S. Buck, and C. M. Suter, *J. Amer. Chem. Soc.*, **66**, 1950 (1944).

(2) (a) A. S. Weisberger and J. Pensky, *Science*, **126**, 1112 (1957); (b) A. S. Weisberger and J. Pensky, *Cancer Res.*, **18**, 1801 (1958); (c) T. Kametani, K. Fukumoto, and O. Umezawa, *Jap. J. Pharm. Chem.*, **31**, 3, 60, 125, 132 (1959); (d) J. A. DePaolo and C. Carruthers, *Cancer Res.*, **20**, 431 (1960); (e) N. Isenberg, Ph.D. Thesis, Rensselaer Polytechnic Institute, 1963; (f) A. F. Hirsh, C. Piantadosi, and J. Logan Irvin, *J. Med. Chem.*, **8**, 10 (1965). (3) A. F. Frolov and E. L. Mishenkova, *Mikrobiol. Zh. (Kiev)*, **32**, 628 (1970); *Chem. Abstr.*, **74**, 74916 (1971).

(4) (a) L. D. Small, J. H. Bailey, and C. J. Cavallito, *J. Amer. Chem. Soc.*, **69**, 1710 (1947); (b) C. J. Cavallito and L. D. Small, U. S. Patent 2508745 (1950); (c) R. M. Dodson, V. Srinivasan, K. S. Sharma, and R. F. Sauers, *J. Org. Chem.*, **37**, 2367 (1972).

(5) A. Kato and M. Numata, *Tetrahedron Lett.*, 203 (1972); H. Yanagawa, T. Kato, and Y. Kitahara, *ibid.*, 1073 (1973).

(6) (a) D. Barnard, L. Bateman, M. E. Cain, T. Colclough, and J. I. Cunneen, *J. Chem. Soc.*, 5339 (1961); (b) L. Bateman, M. Cain, T. Colclough, and J. I. Cunneen, *ibid.*, 3570 (1962); (c) A. Rahman and A. Williams, *J. Chem. Soc. B*, 1391 (1970); (d) N. Neureiter and D. E. Bown, *Ind. Eng. Chem., Prod. Res. Develop.*, **1**, 236 (1962); (e) D. Barnard and J. I. Cunneen, British Patent 889112 (1962); (f) J. I. Cunneen and D. F. Lee, *J. Appl. Polym. Sci.*, **8**, 699 (1964).

(7) R. W. Murray, R. D. Smetana and E. Block, *Tetrahedron Lett.*, 299 (1971); R. W. Murray and S. L. Jindal, *Photochem. Photobiol.*, **16**, 147 (1972); *J. Org. Chem.*, **37**, 3516 (1972).

(8) In contrast, the chemistry of diaryl thiolsulfinates has been thoroughly explored, most notably by Kice[9] and by Fava.[10]

(9) J. L. Kice and J. P. Cleveland, *J. Amer. Chem. Soc.*, **95**, 109 (1973), and references therein.

(10) P. Koch, E. Ciuffarin, and A. Fava, *J. Amer. Chem. Soc.*, **92**, 5971 (1970), and references therein.

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

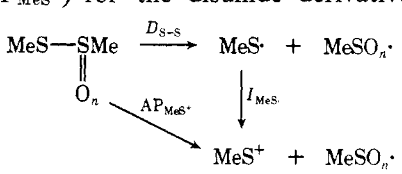
(12) For preliminary reports of this research, see (a) E. Block, *J. Amer. Chem. Soc.*, **94**, 642 (1972); (b) *ibid.*, **94**, 644 (1972); (c) E. Block and S. W. Weidman, *ibid.*, **95**, 5046 (1973); (d) E. Block and J. O'Connor, *ibid.*, **95**, 5048 (1973).

for several days at room temperature, spontaneously transforms into a mixture of dimethyl disulfide and methyl methanethiolsulfonate (eq 1).[13] At the onset

$$2MeS(O)SMe \longrightarrow MeSO_2SMe + MeSSMe \quad (1)$$

of our research no information was available on the mechanism of this facile disproportionation reaction of the dialkyl esters. A tantalizing communication by Barnard[14] suggested that the disproportionation of diaryl thiolsulfinate esters involved fission of the S–S bond rather than simple oxygen transfer, that something more complex than simple combination of the fragments ensued (considerable scrambling was observed with unsymmetrical esters), and that the reaction could be photochemically as well as thermally initiated. Recently, detailed support has been presented for a free radical mechanism for the uncatalyzed thermal disproportionation of diaryl esters;[10] Kice has also described a path for this same reaction involving concomitant acid and nucleophile catalysis.[9]

Determination of the S–S Bond Energy in MeS(O)-SMe. In order to ascertain if there was a physical basis for the instability of dialkyl thiolsulfinates we sought to determine the S–S bond strength in methyl methanethiolsulfinate. The method chosen was that previously used to obtain the S–S bond strength in dimethyl disulfide, namely subtraction of the (known) ionization potential of MeS· ($I_{MeS\cdot}$) from the mass spectrometrically determined appearance potential of MeS^+ (AP_{MeS^+}) for the disulfide derivative (eq 2).[15]



(2)

$n = 0$ or 1

Two different determinations using two different appearance potential standards (see Experimental Section) gave values of 10.05–10.06 eV for AP_{MeS^+} from methyl methanethiolsulfinate. Subtracting the known value of $I_{MeS\cdot}$ = 8.06 eV[15] from AP_{MeS^+} gives a value of 46 kcal/mol as the S–S bond energy for MeS(O)SMe.[16] The S–S bond energy in dimethyl disulfide was similarly determined (see Experimental Section) to be 74.8 kcal/mol, in good agreement with literature values of 70.6–77.3.[17] Thus the S(O)–S linkage is ~29 kcal/mol weaker than the corresponding unoxidized S–S linkage.[19]

(13) (a) H. J. Backer and H. Kloosterziel, *Recl. Trav. Chim. Pays-Bas*, 73, 129 (1954). (b) In our hands this transformation even occurred, although slowly, in a freezer at −20°.

(14) D. Barnard, *J. Chem. Soc.*, 4675 (1957).

(15) (a) J. L. Franklin and H. E. Lumpkin, *J. Amer. Chem. Soc.*, **74**, 1023 (1952); (b) T. L. Allen, *J. Chem. Phys.*, **31**, 1039 (1959); (c) T. F. Palmer and F. P. Lossing, *J. Amer. Chem. Soc.*, **84**, 4661 (1962); (d) H. Mackle and R. G. Mayrick, *Trans. Faraday Soc.*, **58**, 33 (1962); (e) B. G. Gowenlock, J. Kay, and J. R. Majer, *ibid.*, **59**, 2463 (1963).

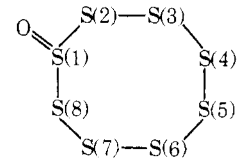
(16) Assumed to be accurate within ±0.2 eV or 4.6 kcal/mol.

(17) A recent study[18] suggests a value of $I_{MeS\cdot}$ = 7.60 eV. If this value is correct, it would increase the S–S bond energies in MeSSMe and MeS(O)SMe each by ~9 kcal/mol.

(18) W. R. Cullen, D. C. Frost, and M. T. Pun, *Inorg. Chem.*, **9**, 1976 (1970).

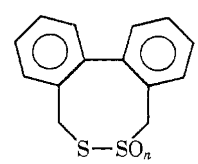
(19) Fava has determined, on kinetic grounds, a value of 34.5 kcal/mol for the S(O)–S bond energy in diaryl thiolsulfinates.[10] If it is assumed that the S–S linkage in diaryl disulfides is ~10 kcal/mol weaker than the corresponding bond in dialkyl disulfides, then our estimate of the weakening of the S–S bond on oxidation to S(O)–S in the alkyl system is in good agreement with the estimated bond weakening in the diaryl system. We thank Professor Fava for pointing out this agreement.

The weakness of the thiolsulfinate S–S bond should be reflected in a lengthening of this bond compared to disulfide S–S bonds. Recent X-ray crystallographic measurements provide support for this suggestion. Thus, studies of cyclooctasulfur oxide (**3a**)[20] reveal



3a

the unusually long value of 2.20 ± 0.004 Å for the S(O)–S bonds 1,2 and 1,8 of this thermally unstable sulfur oxide together with essentially normal values for the other S–S bonds ranging from 2.00 to 2.07 Å. Normal coordinate analysis of S_8O indicates force constants for the S(O)–S bonds 1,2 and 1,8 *ca.* half as large as the values for the other S–S bonds in this structure.[21] X-Ray crystallographic studies of 5*H*,8*H*-dibenzo[*d*,*f*][1,2]-dithiocin (**3b**),[22a] its 5-oxide (**3c**),[22b] and its *S*,*S*-dioxide



3b-d

b, $n = 0$
c, $n = 1$
d, $n = 2$

(**3d**)[23] indicate S–S bond lengths of 2.035, 2.098 and 2.048 ± 0.002 Å, respectively. A possible explanation[24] for the weakness of the thiolsulfinate S–S bond (compared, for example, to the thiolsulfonate S–S bond[25]) may lie in the considerable stability of the sulfinyl radical, R–S–O (a "saturated" radical in the Linnett sense, like the peroxy, ROO· and perthiyl, RSS·, radicals[26]) derived from homolysis of the thiolsulfinate S–S bond. In this context it should be noted that the S–S bond of MeSSSMe has been estimated from appearance potential data to have a dissociation energy of 46 kcal/mol.[27]

Synthetic Studies. In order to elucidate the mechanism of the disproportionation process we required quantitative information on products, detailed information on reaction kinetics, solvent effects (and effects of added reagents), and substituent effects as well as a knowledge of the path of the sulfinyl oxygen during the ensuing reactions. The last two requirements were best satisfied by a study of the thermolysis of *unsymmetrical* dialkyl thiolsulfinates. While sym-

(20) R. Steudel, P. Luger, H. Bradaczek, and M. Rebsch, *Angew. Chem., Int. Ed. Engl.*, 12, 423 (1973).

(21) R. Steudel, personal communication.

(22) (a) G. H. Wahl, Jr., J. Bordner, D. N. Harpp, and J. G. Gleason, *J. Chem. Soc., Chem. Commun.*, 985 (1972); (b) *Acta Crystallogr., Sect. B*, 28, 2272 (1973).

(23) G. H. Wahl, Jr., R. L. Greene, J. Bordner, D. N. Harpp and J. G. Gleason, personal communication.

(24) J. L. Kice in "Sulfur in Organic and Inorganic Chemistry," Vol. I, A. Senning, Ed., Marcel Dekker, New York, N. Y., 1971, Chapter 5.

(25) Preliminary appearance potential measurements suggest that the S–S bond in $MeSO_2SMe$ is considerably stronger than the thiosulfinate S–S bond.

(26) R. Firestone, *J. Org. Chem.*, **34**, 2621 (1969).

(27) T. L. Pickering, K. J. Saunders, and A. V. Tobolsky in "The Chemistry of Sulfides," A. V. Tobolsky, Ed., Interscience, N. Y., 1968.

metrical alkyl alkanethiolsulfinates are readily prepared through direct oxidation of disulfides, only one example of the preparation of an unsymmetrical dialkyl thiolsulfinate has appeared in the literature.[4]

Thus it is claimed[4] that peracids oxidize 2-methyl-2-propyl ethyl disulfide giving exclusively 2-methyl-2-propyl ethanethiolsulfinate (**4**), a structure assigned on

$$\text{EtSS-}t\text{-Bu} \xrightarrow{\text{RCO}_3\text{H}} \underset{\mathbf{4}}{\text{EtS(O)S-}t\text{-Bu}}$$

the basis of anticipated steric hindrance to oxidation at the sulfur next to the 2-methyl-2-propyl group. We have examined the oxidation of methyl and ethyl 2-methyl-2-propyl disulfides with peracids and find that *contrary to the reported results the oxidation is not regiospecific and furthermore the major thiolsulfinate in both cases has the oxygen on the sulfur adjacent to the 2-methyl-2-propyl group* (Scheme I; see Experimental Section for details).[28]

Scheme I. Oxidation of Unsymmetrical Dialkyl Disulfides

$$\text{EtSS-}t\text{-Bu} \xrightarrow{\text{RCO}_3\text{H}} \underset{1.74}{\text{EtSS(O)-}t\text{-Bu}} + \underset{1}{\text{EtS(O)—S-}t\text{-Bu}}$$

$$\text{MeSS-}t\text{-Bu} \xrightarrow{\text{RCO}_3\text{H}} \underset{2}{\text{MeSS(O)-}t\text{-Bu}} + \underset{1}{\text{MeS(O)—S-}t\text{-Bu}}$$

$$\text{MeSS-}t\text{-Bu (0.1 } M \text{ in MeOH)} \xrightarrow[\text{Methylene Blue}]{h\nu,\ \text{O}_2} \underset{1}{\text{MeSS(O)-}t\text{-Bu}} + \underset{5}{\text{MeS(O)—S-}t\text{-Bu}}$$

$$\text{MeSS-}t\text{-Bu (0.25 } M \text{ in MeOH)} \xrightarrow[\text{Methylene Blue}]{h\nu,\ \text{O}_2} \underset{1}{\text{MeSS(O)-}t\text{-Bu}} + \underset{2}{\text{MeS(O)—S-}t\text{-Bu}}$$

In an effort to improve the regioselectivity we briefly examined the distribution of thiolsulfinates obtained by photooxidation of 2-methyl-2-propyl methyl disulfide.[29] Surprisingly the regioselectivity observed under these conditions was the reverse of that obtained with peracids; the regioselectivity under these latter conditions also appears to be sensitive to disulfide concentration.

A satisfactory method of preparing unsymmetrical dialkyl thiolsulfinates uncontaminated by their isomers involves the coupling of sulfinyl chlorides with mercaptans in the presence of pyridine (eq 3).[13a] By this

$$\text{RS(O)Cl} + \text{R'SH} \xrightarrow[\text{ether, 0°}]{\text{pyridine}} \text{RS(O)SR'} \quad (3)$$

means a wide variety of unsymmetrical dialkyl thiolsulfinates (including a number of specifically deuterated compounds) could be prepared in good yields.[30] Studies with the unsymmetrical alkyl alkanethiolsulfinates indicate that they can be separated from their isomers by vpc (excepting, of course, compounds differing only in the extent and position of deuterium substitution), and that isomers display clearly different nmr spectra.[31] Major differences are also seen in the mass spectra of isomeric pairs (*vide infra*).

A number of unsymmetrical alkyl alkanethiolsulfonates have been previously synthesized; the new compounds required in this investigation were prepared by the previously reported methods (*cf.* Experimental Section).[30] The unsymmetrical dialkyl thiolsulfonates could generally be readily separated from isomeric structures and related thiolsulfinates by vpc. Infrared, nmr, and mass spectral methods were also of value in distinguishing between isomeric pairs.

Applications of Mass Spectrometry in Mechanistic Studies. The disproportionation of an unsymmetrical thiolsulfinates, RS(O)SR′, could take a variety of courses, *i.e.*, in Scheme II, A, B, C, D, or A + C with

Scheme II. Possible Product Distribution from Disproportionation of an Unsymmetrical Dialkyl Thiosulfonate RS(O)SR′

$$\text{RS(O)—SR'} \xrightarrow{\text{A}} \text{RSO}_2\text{SR} + \text{R'SSR'}$$

$$\xrightarrow{\text{B}} \text{RSO}_2\text{SR} + \text{RSO}_2\text{SR'} + \text{R'SSR'} + \text{RSSR'} + \text{RSSR}$$

$$\xrightarrow{\text{C}} \text{R'SO}_2\text{SR'} + \text{RSSR}$$

$$\xrightarrow{\text{D}} \text{R'SO}_2\text{SR} + \text{R'SO}_2\text{SR'} + \text{RSO}_2\text{SR} + \text{RSO}_2\text{SR'} + \text{RSSR} + \text{R'SSR'} + \text{R'SSR}$$

processes C and D involving some intermediate such as RS–O–SR′ capable of transferring oxygen from one sulfur to the other. A direct method of determining the course taken is to study the product distribution from the pyrolysis of unsymmetrically deuterated thiolsulfinates. This procedure has the advantage that it minimizes any substituent effects associated with the R groups. The analysis is conveniently carried out by subjecting the pyrolysate to gc–ms analysis and determining the isotopic composition of the well-separated disulfide and thiolsulfonate parent peaks under conditions minimizing fragmentation (*i.e.*, at 10 eV). Scheme III summarizes the data so obtained from pyrolysis of $\text{EtS(O)SCD}_2\text{Me}$. This particular experiment does not permit an assignment of the deuterium substitution pattern in the major thiolsulfonate but does make A and C, Scheme II, seem unlikely.

Considerably more mechanistic information can be obtained from a gc–ms study of the pyrolysis of MeS(O)-SCD_3. In preparation for this study, the mass spectra of MeSO_2SMe and $\text{MeSO}_2\text{SCD}_3$[33] were examined;[34] a major fragment was found in the spectrum of the former at m/e 81 (71% base peak; m/e 82 and 83 respectively 1 and 3% of the base peak; no significant peaks from m/e 84 to m/e 93) while in the spectrum of the d_3 compound this peak was displaced to m/e 83 (82% base; m/e 82 and 81 are 9 and 5% of base, respectively). The fragmentation has been formulated as in

(28) For somewhat similar results in the oxidative formation of thiolsulfonates from alkyl pyridyl disulfides, see W. Walter and P.-M. Hell, *Justus Liebigs Ann. Chem.*, 727, 35 (1969).

(29) For the photooxidation of symmetrical dialkyl disulfides, see ref 7.

(30) Data on these new compounds as well as new data on compounds previously synthesized will appear in Tables I and II following these pages in the microfilm edition of this volume. See paragraph at end of paper regarding supplementary material.

(31) The nmr spectra of many of the dialkyl thiolsulfinates are complicated by the presence of heterosteric protons or methyl groups. The analysis of certain of these nmr spectra through the use of chemical shift reagents has been reported.[32]

(32) L. E. Legler, S. L. Jindal, and R. W. Murray, *Tetrahedron Lett.*, 3907 (1972).

(33) We thank Professor Bentley for providing us with a sample of $\text{MeSO}_2\text{SCD}_3$.

(34) E. Block, M. D. Bentley, and F. A. Davis, manuscript in preparation.

Scheme III. Product Distribution from Disproportionation of Unsymmetrically Deuterated Dialkyl Thiosulfinates

$EtS(O)SCD_2Me$ (95.1%-d_2, 2.9%-d_1, 2.0%-d_0) $\xrightarrow[\text{neat, 100°}]{\Delta}$ thiolsulfonate: $C_4H_8D_2S_2O_2$ (71.0%) + $EtSO_2SEt$ (26.6%) + $MeCD_2SO_2SCD_2Me$ (<2.4%)

disulfide: $(EtS)_2$ (14%) + $EtSSCD_2Me$ (43%) + $(MeCD_2S)_2$ (43%)

$MeS(O)SCD_3$ (98.2%-d_3, 1.8%-d_2) $\xrightarrow[\text{neat, 200 sec}]{\Delta,\ 96°}$ thiolsulfinate: $MeS(O)SMe$ (10%) + $C_2H_3D_3S_2O$ (90%)

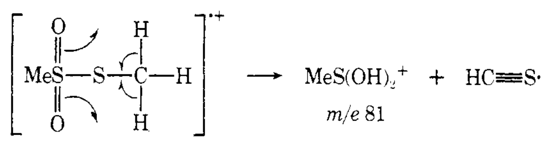
thiolsulfonate and disulfide not determined

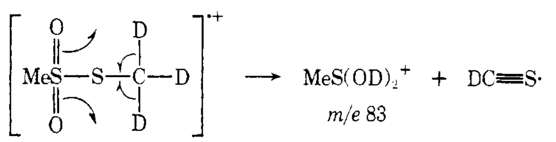
$\xrightarrow[\text{neat, 2000 sec}]{\Delta,\ 96°}$ thiolsulfonate: $MeSO_2SMe$ (29.7%) + $MeSO_2SCD_3$ (>68%)

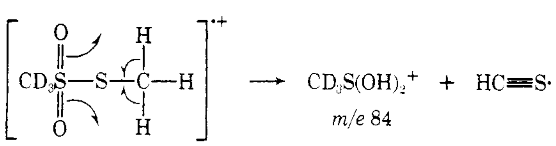
(+CD_3SO_2SMe (<2%) + $CD_3SO_2SCD_3$ (<0.2%))

disulfide not determined

eq 4a and b.[34] Since the isomer $CD_3SO_2SCH_3$ would


(4a)

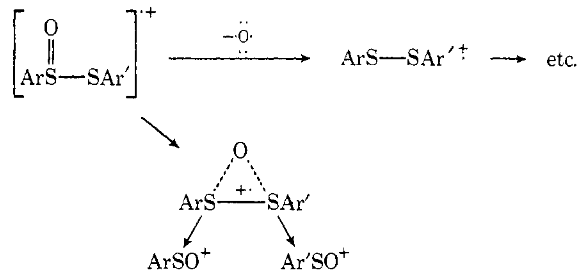

(4b)


(4c)

be expected to have a major fragment at *m/e* 84 (eq 4c), an analysis of the *m/e* 83/84 peaks together with the peaks in the parent region should give a reasonable picture of the isotopic distribution in the thiolsulfonates from pyrolysis of $MeS(O)SCD_3$. Scheme III summarizes the results of this study under conditions where the thiolsulfinate has been partially as well as completely consumed. Under conditions of incomplete consumption of $MeS(O)SCD_3$ a new peak appears at *m/e* 110 (not present in the mass spectrum of the starting material) corresponding to MeS(O)SMe. The origin of this symmetrical thiolsulfinate in the pyrolysis of unsymmetrical thiolsulfinate has important mechanistic implications and will be further substantiated and interpreted in the accompanying paper.[11] The results of the pyrolysis of $MeS(O)SCD_3$ to complete thiolsulfinate consumption provide convincing support for the occurrence of pathway B, Scheme II, as the major course of disproportionation of unsymmetrical thiolsulfinates and are of interest in indicating the predominance of unsymmetrical thiolsulfonate over symmetrical thiolsulfinate by a factor of *ca.* 2.3:1.[35] The concentrations of CD_3SO_2SMe and $CD_3SO_2SCD_3$ cited represent upper limits established by the method of analysis. A significantly lower limit can be placed on the concentration of thiolsulfonates derived from oxygen crossover in the disproportionation of unsymmetrical alkyl substituted thiolsulfinates (such as EtS(O)SMe) by quantitative vpc techniques, as will be discussed in the accompanying paper.[11]

(35) Through control experiments discussed in the accompanying paper[11] we have established that exchange processes involving the products are insignificant.

It was of considerable interest to compare the thermal and electron impact induced processes of unsymmetrical dialkyl thiolsulfinates, particularly since Oae has claimed that fragmentation of diaryl thiolsulfinates involves direct (unimolecular) elimination of oxygen followed by cleavage of the S–S bond (eq 5) as well as oxygen crossover processes.[36]


(5)

To study the alleged deoxygenation process, we examined the mass spectra of rigorously purified samples of ethyl ethanethiolsulfinate (see Table III). While a peak

Table III. High-Resolution Mass Spectral Data for Ethyl Ethanethiolsulfinate

m/e	Formula	Assignment	% base
27	C_2H_3		55
29	C_2H_5		100
58.9983	C_2H_3S		10
60.0049	C_2H_4S	$CH_3CHS\cdot^+$	9
61.0118	C_2H_5S	EtS^+	61
61.9822	CH_2SO	$CH_2{=}S{=}O\cdot^+$	1
62.0183	C_2H_6S	$EtSH\cdot^+$	8
62.9891	CH_3SO	$CH_2{=}\overset{+}{S}{-}OH$	6
63.9421	S_2		18
65.9573	H_2S_2		5
75.0236	C_3H_7S		6
77.0029	C_2H_5SO	$EtSO^+$	5
78.0109	C_2H_6SO	$EtSOH\cdot^+$	8
81	HS_2O		17
81.9546	H_2S_2O	$HSSOH\cdot^+$	29
90.0502	$C_4H_{10}S$	$EtSEt\cdot^+$	2
108.9784	$C_2H_5S_2O$	$EtSSO^+$	4
109.9861	$C_2H_6S_2O$	$EtSSOH\cdot^+$	15
122.0227	$C_2H_6S_2$	$EtSSEt\cdot^+$	2
138.0172	$C_2H_6S_2O$	$EtS(O)SEt\cdot^+$ ($M\cdot^+$)	15

corresponding to diethyl disulfide was always observed (*m/e* 122.0227 (calcd for $C_4H_{10}S_2$, 122.0224)), the relative intensity of the peak was found to be markedly sensi-

(36) S. Kozuka, H. Takahashi, and S. Oae, *Bull. Chem. Soc. Jap.*, **43**, 129 (1970). This is the only published study of the mass spectra of thiolsulfinate esters.

Table IV. Comparison of Selected Fragmentation Patterns in Deuterated and Undeuterated Ethyl Ethanethiolsulfinate

m/e	Formula		% parent[a]		
		EtS(O)SEt	EtS(O)SCD$_2$Me	EtS(O)SCH$_2$CD$_3$	MeCD$_2$S(O)SCD$_2$Me
78	C_2H_6SO	53	34	77	9
79	C_2H_5DSO		32	21	52[b]
82	H_2S_2O, DS_2O	193	50	66	100
83	HDS_2O		27	74	43
84	D_2S_2O				13
109	$C_2H_5S_2O$	27		3	
110	$C_2H_6S_2O$, $C_2H_4DS_2O$	100	11	5	
111	$C_2H_5DS_2O$, $C_2H_3D_2S_2O$		18	7	17
112	$C_2H_4D_2S_2O$, $C_2H_2D_3S_2O$		64	23	43
113	$C_2H_3D_3S_2O$, $C_2HD_4S_2O$		5	49	9
122	$C_4H_{10}S_2$	16	5	8	
124	$C_4H_8D_2S_2$		5		
125	$C_4H_7D_3S_2$			28	
126	$C_4H_6D_4S_2$		25		43
128	$C_4H_4D_6S_2$			13	
138	$C_4H_{10}S_2O$	100	2	5.5	
139	$C_4H_9DS_2O$		2		
140	$C_4H_8D_2S_2O$		100	10.5	
141	$C_4H_7D_3S_2O$			100	4.7
142	$C_4H_6D_4S_2O$				100

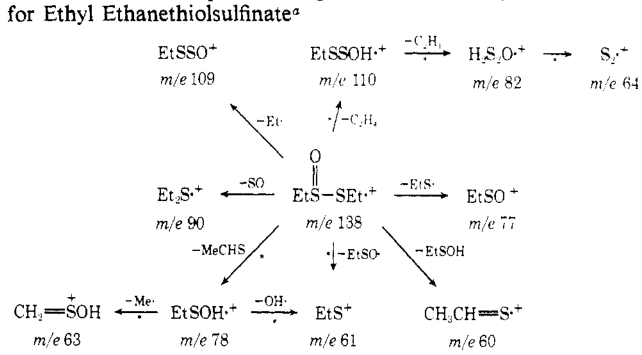
[a] Peaks due primarily to ^{34}S contributions are not shown. [b] $C_2H_3D_2SO$.

tive to the method of sample introduction and to the length of time spent in the mass spectrometer. Under the mildest conditions used (sample adsorbed on powdered graphite and introduced *via* a probe directly into the source)[37] the *m/e* 122 peak was only 16% of the intensity of the parent (*m/e* 138; a peak at *m/e* 154 assumed to be thiolsulfonate was only 1.5% of the intensity of the parent); under more vigorous conditions (gc–ms; 1-l. glass expansion bulb) the *m/e* 122 peak was more substantial. Furthermore, neither defocused metastable studies[38] of the *m/e* 122 peak nor direct analysis of daughter ions ("DADI") studies[39] of the *m/e* 138 parent revealed a daughter/parent relationship between these two respective peaks. Finally the mass spectrum of $C_2H_5S(O)SCD_2CH_3$, obtained under mild conditions, shows fragments corresponding to the *three* disulfides, $(C_2H_5S\text{–})_2$, $C_2H_5SSCD_2CH_3$, and $(CH_3CD_2S\text{–})_2$, in the ratio 2:2:11 (Table IV).[40] These results are clearly incompatible with unimolecular deoxygenation following electron impact as the exclusive origin of disulfide. We suggest that in our own work and in the studies by Oae,[36] disulfide is produced principally in a bimolecular process occurring in the sample introduction system of the mass spectrometer, perhaps promoted by association of thiolsulfinate and by the high vacuum, rather than by electron impact.[41,42]

If the oxygen crossover process proposed by Oae[36] occurs during fragmentation of dialkyl thiolsulfinates, then it might be expected that the mass spectra of two isomeric thiolsulfinate esters, such as MeS(O)SEt and EtS(O)SMe, would be identical. That this is not the case is shown by a comparison of the mass spectra (obtained under gc–ms conditions) of these two compounds (Figures 1 and 2). Furthermore, the occurrence of the crossover processes of eq 5 in the fragmentation of MeS(O)SEt would be expected to lead to the formation of both $EtSO^+$ (*m/e* 77) and $MeSO^+$ (*m/e* 63); in fact there is a significant ion at *m/e* 63 (34% of base) while only a minute ion at *m/e* 77 (1% of base).

Further chemically interesting aspects of the fragmentation of dialkyl thiolsulfinates are shown for ethyl ethanethiolsulfinate in Scheme IV, incorporating data

Scheme IV. Mass Spectral Fragmentation Pathways for Ethyl Ethanethiolsulfinate[a]



[a] Processes indicated by * confirmed by metastable analysis on EtS(O)SEt or, in a few cases, on other dialkyl thiolsulfinates.

(37) This technique was developed by the staff of the mass spectroscopy laboratory of the University of Illinois—Urbana.

(38) For a recent discussion, see D. H. Smith, A. M. Duffield, and C. Djerassi, *Org. Mass Spectrom.*, 7, 367 (1973).

(39) Also referred to as mass-analyzed ion kinetic energy spectra (MIKES). For a recent review of the technique, see J. H. Beynon, R. G. Cooks, J. W. Amy, W. E. Baitinger, and T. Y. Ridley, *Anal. Chem.*, **45**, 1023 (1973).

(40) The mass spectra reported by Oae[36] for unsymmetrical aryl benzenethiolsulfinates show significant peaks corresponding to diphenyl disulfide as well as aryl phenyl disulfides, a point not discussed by Oae.

(41) Disproportionation of diaryl thiolsulfinates is reported to be significantly accelerated by high vacuum,[14] with particular sensitivity in this respect shown by *p*-tolyl benzenethiolsulfinate, one of the aryl thiolsulfinates studied by Oae.[36] Thus, *p*-tolyl benzenethiolsulfinate which was "stable for several months under normal atmospheric conditions.... decomposed after five minutes at 10^{-5} mm."[14] Oae's results are also suspect in view of the high temperature (200°) used in the sample introduction system. Furthermore, in contrast to the spectra reported in this paper, negligible parent peaks were observed by Oae from the diaryl thiolsulfinates. Using the same mild sample introduction and source conditions employed for the dialkyl thiolsulfinates, we have been able to obtain a significant parent peak for phenyl benzenethiolsulfinate, although disulfide formation still seems to dominate.

(42) There were only very minor peaks in the mass spectra of dialkyl thiolsulfinates corresponding to thiolsulfonates. Contrary to the conclusion of Oae,[36] this observation is not necessarily incompatible with the proposed origin of mixed disulfide from a bimolecular process. We have shown that thiolsulfinate disproportionation is a multistep process.[11,12c] It is unlikely under the conditions existing in the mass spectrometer that all of these steps are followed with any frequency. It is more reasonable to expect that the earliest steps (*i.e.*, those leading to disulfide formation) would occur, with the intermediates or radical or ionic fragments produced along with the disulfide undergoing electron-impact induced processes instead of chemical reactions.

Scheme V. Deuterium Distribution in Fragments from Deuterated Thiolsulfinates[43]

$EtS(O)SCH_2CD_3 \longrightarrow CD_3CH_2SSOH\cdot^+ (>87\%), CH_3CH_2S(O)SD\cdot^+ (<10\%), CH_3CH_2S(O)SH\cdot^+ (<3\%)$

$\longrightarrow EtSOH\cdot^+ (>80\%), EtSOD\cdot^+ (<20\%)$

$EtS(O)SCD_2CH_3 \longrightarrow \begin{cases} CH_3CD_2SSOH\cdot^+ (>80\%), \\ CH_3CH_2S(O)SH\cdot^+ (<15\%) \\ CH_3CD_2SSO^+ \text{ (no } EtS(O)S^+) \end{cases} \longrightarrow \begin{cases} H_2S_2O\cdot^+ \\ DHS_2O\cdot^+ \end{cases}$

$CH_3CD_2S(O)SCD_2CH_3 \longrightarrow \begin{cases} CH_3CD_2SSOH\ (91\%) \\ CH_3CD_2SSOD\ (9\%) \end{cases} \longrightarrow \begin{cases} H_2S_2O\cdot^+ \\ DHS_2O\cdot^+ \end{cases}$

$CH_3S(O)SCD_3 \longrightarrow CD_3SSO^+ (91\%), CH_3S(O)S^+ (9\%)$

$\longrightarrow CH_3SOH\cdot^+ \longrightarrow \begin{cases} CH_3S^+ (31\%) \\ CD_3S^+ (69\%) \end{cases}$

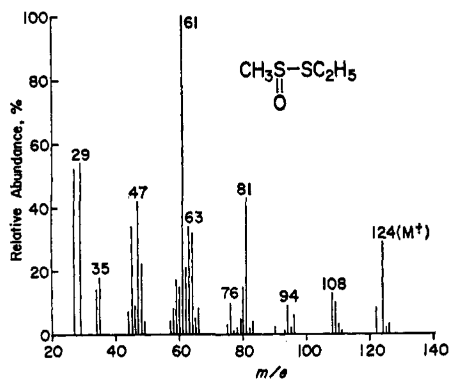


Figure 1. Mass spectrum of ethyl methanethiolsulfinate at 70 eV.

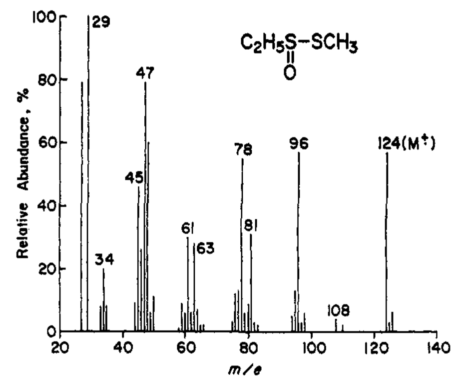
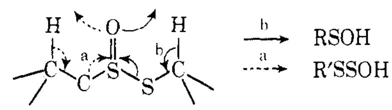


Figure 2. Mass spectrum of methyl ethanethiolsulfinate at 70 eV.

obtained from exact mass measurements (Table III) and from mass spectral studies on specifically deuterated forms of ethyl ethanethiolsulfinate (Table IV and Scheme V[43]) and other deuterated or nondeuterated dialkyl thiolsulfinates. A unique aspect is the formation of the fragment H_2S_2O, corresponding to the unknown parent acid of thiolsulfinate esters, thiosulfoxylic acid (or if it exists with a S=O group, dihydridooxodisulfur). The studies with specifically deuterated ethyl ethanethiolsulfinate (Scheme V) indicate that although there is a preference for abstraction of the β and β' hydrogens in forming H_2S_2O, significant nonspecific hydrogen transfer does occur (as has been previously observed in rearrangement reactions of sulfoxides and sulfides).[44] Another significant observation is the formation from EtS(O)SEt of fragments corresponding to EtSOH and EtSSOH. Novel features of these processes include: (1) incomplete site specificity for hydrogen transfer, in contrast to pyrolytic studies (see accompanying paper[11]), (2) persistence of the peaks corresponding to EtSOH, $CH_3CH{=}S$, and EtSSOH in the mass spectrum of EtS(O)SEt at low electron voltage (8.6 eV), suggesting thermal as well as electron impact derived origins for these products (the presence of metastable transitions supports a direct electron impact route to RSOH and RSSOH), (3) variation in the RSSOH/R′SOH ratio with thiolsulfinate structure. In the latter instance, the relative ease of thermal and electron impact induced processes a and b (eq 6) show considerable variation on



(6)

replacement of the α-sulfenyl protons with deuterium or on alkyl substitution. Thus for the thiolsulfinates *i*-PrS(O)SMe, EtS(O)SMe, $EtS(O)SCD_3$, EtS(O)SEt, $EtS(O)SCD_2Me$, and $EtS(O)SCH_2CD_3$, the respective intensity ratios for R′SSOH:RSOH are 25:1, 1:1, 3:1, 2:1, 5:1, and 0.7:1; these trends are in qualitative agreement with expectations based on primary and secondary deuterium isotope effects. A more detailed consideration of the processes of eq 6 is the subject of the accompanying paper.[11]

Experimental Section

The melting points are corrected. The ir spectra, unless otherwise noted, were determined as a thin film on either a Perkin-Elmer 137 or 337 infrared spectrophotometer. The uv spectra were de-

(43) The relative amounts of deuterated forms of key fragments are given for each fragment type. These approximate values have been corrected for contributions from heavy isotopes (C, S, O) and incomplete deuteration. Several other factors warrant consideration. (1) Because of the incomplete deuteration of the several thiolsulfinates, isotope effects could pose a problem. To circumvent these effects, evidence for incomplete site specificity is based on the detection of fragments richer in deuterium than expected if the process in question was site specific (isotope effects would normally be expected to discriminate *against* transfer of deuterium when equivalent hydrogen is available[44,45a]). (2) Possible label scrambling *prior* to fragmentation may pose a problem.[45a] However extensive hydrogen randomization prior to initial hydrogen transfer in several labeled dialkyl sulfoxides has been excluded;[43] such randomization of label is made less likely in our studies by the occurrence of high site selectivity observed in the formation of certain fragments (*i.e.*, the formation of $CH_3CD_2SSO^+$ but not $C_2H_5(O)S^+$ from $EtS(O)SCD_2CH_3$). (3) It was not possible to resolve (even with a resolution of ~70,000) nominally isobaric fragments differing only by having two hydrogen atoms instead of one deuterium atom. In most cases where two formulas are possible for a given fragment one formula is generally much less likely than the other, either because it contains more deuterium atoms than the molecular ion itself or because it corresponds to a fragment of lower relative abundance than the alternative formula of the same nominal mass in the spectrum of the undeuterated material. In an instance of irresolvable ambiguity, *i.e.*, DS_2O and H_2S_2O in *m/e* 82, the relative amounts of each type of fragment cannot be estimated; the presence of a substantial peak corresponding to HDS_2O (from $EtS(O)SCD_2Me$ and $MeCD_2S(O)SCD_2Me$) suggests, however, that hydrogen transfer is nonspecific.

(44) R. Smakman and Th. J. de Boer, *Org. Mass Spectrom.*, **3**, 1561 (1970); S. Sample and C. Djerassi, *J. Amer. Chem. Soc.*, **88**, 1937 (1966).

(45) (a) For an excellent discussion of the pitfalls of mass spectrometric labeling studies, see J. T. Bursey, M. M. Bursey, and D. G. I. Kingston, *Chem. Rev.*, **73**, 191 (1973). (b) J. F. Franklin, J. G. Dillard, H. M. Rosenstock, J. T. Herron, K. Draxl, and F. H. Field, National Bureau of Standards Publication No. 26, 1969.

termined in 95% ethanol on a Perkin-Elmer 202 or 450 UV spectrophotometer. Analyses were carried out by Chemalytics, Tempe, Ariz. Nmr spectra were obtained with a Varian T-60 instrument using tetramethylsilane as an internal standard. Mass spectra and appearance potentials were determined on an A.E.I. MS-12 mass spectrometer. Exact mass measurements were made on a Varian MAT 731 high-resolution double focusing mass spectrometer by the staff of the mass spectrometry laboratory at the University of Illinois—Urbana. Defocusing and DADI studies were performed on a Varian/MAT CH5 double focusing mass spectrometer also at the University of Illinois—Urbana. Vapor phase chromatography (vpc) was accomplished on a Hewlett Packard Model 5750 gas chromatograph (flame ionization detector) equipped with a Hewlett Packard Model 3370A digital integrator. A $^1/_8$ in. × 6 ft column of 10% silicone rubber UCW98 on 80–100 mesh Chromosorb W was used for analytical purposes. Coupled gas chromatography–mass spectrometry (gc–ms) was accomplished using the latter column in the above described gas chromatograph coupled, *via* an all-glass Watson-Biemann separator, to the source of the MS-12 mass spectrometer. A number of mass spectra were also obtained under gc–ms conditions using an LKB Model 9000 integrated gc–ms system (analyses performed by Professor William Sherman at the Washington University School of Medicine). Under the mild gc–ms operating conditions even the most thermally labile thiolsulfinates studied gave excellent reproducible mass spectra. Preparative layer chromatography (plc) was performed on Merck PF_{254} silica gel plates 1.5 mm thick.

Determination of the Appearance Potential of MeS^+ from MeS(O)SMe. A mixture of carefully purified MeS(O)SMe and argon was introduced into a 1-l. glass expansion chamber (maintained at room temperature) connected to the mass spectrometer. The concentrations of the two components were adjusted so that the relative intensities of the *m/e* 47 peak from MeS(O)SMe (MeS^+; the base peak) and the argon *m/e* 40 peak (MeS(O)SMe has no peak in its mass spectrum at *m/e* 40) were within 10% of each other. Ionization efficiencies (relative to the ionization efficiencies at 50 eV) were determined manually (using an ion collector meter) for the two peaks from 20 eV down to the voltage where the peak intensity could no longer be measured. Semilog plots were made of the data on the two peaks.[15] It was determined graphically that the ionization efficiency curves were approximately parallel between 0.1 and 0.01% of the intensity at 50 eV;[15] in this region the average separation of the curves was 5.70 ± 0.05 eV. Since the ionization potential of argon is 15.76 ± 0.01 eV,[45b] the appearance potential of MeS^+ is 10.06 ± 0.06 eV.

In a separate run, ionization efficiencies at varying potentials were determined for the *m/e* 47 peak of MeS(O)SMe and the *m/e* 72 and 43 peaks of methyl ethyl ketone ($C_4H_8O\cdot^+$ and $C_2H_3O^+$, respectively) under conditions identical with those described above. The differences in potential of the *m/e* 47 ionization efficiency curve from the *m/e* 72 and 43 curves were measured at the point where the difference between the potentials of the *m/e* 72 and 43 curves corresponded to the known difference between the ionization potential of the *m/e* 72 species (IP = 11.40 eV)[45b] and the appearance potential of the *m/e* 43 ion (AP = 9.58 eV).[45b] In this manner a value of 10.05 eV was obtained for the appearance potential of MeS^+.

Using methyl ethyl ketone and the *m/e* 47 peak of dimethyl disulfide, an appearance potential of 11.31 eV was determined for MeS^+ from the disulfide (literature values: 11.38,[15a] 11.12,[15c] 11.23[18]).

Synthesis of Unsymmetrical Thiolsulfinates: Methyl 2-Methyl-2-propanethiolsulfinate. 2-Methyl-2-propanesulfinyl chloride was most conveniently prepared in good yield in a two-step process from di(2-methyl-2-propyl) disulfide[46] by oxidation with an equivalent of 30% H_2O_2 at 0° followed by dilution with water and extraction into chloroform, chlorinolysis at 10° of the dried solution until an equivalent of chlorine had been absorbed, and *in vacuo* fractionation. In a slightly modified version of the general method of Backer and Kloosterziel,[13a] a solution of 86 g of so-prepared 2-methyl-2-propanesulfinyl chloride (0.62 mol) in 700 ml of anhydrous ether was added during the course of 2 hr to a vigorously stirred solution of 35 ml of methanethiol (0.62 mol), 60 ml of anhydrous pyridine, and 1200 ml of anhydrous ether maintained at 3.° A heavy white precipitate formed during addition. After completion of the addition, the solution was stirred for an additional 15 min at 3°, treated with vigorous stirring with 25 ml of chilled 1 *M* H_2SO_4, and extracted with three 250-ml portions of ice-cold 1 *M* H_2SO_4 and eight 250-ml portions of ice–water. The aqueous layer was saturated with ammonium sulfate and extracted with a total of 2300 ml of methylene chloride. The ether and methylene chloride layers were separately dried over magnesium sulfate and concentrated *in vacuo*. Analysis of each concentrate by ir indicated primarily thiolsulfinate with little thiolsulfonate (bands at ~7.7 and ~8.7 μ) so the concentrates were combined and distilled giving 77.5 g of *t*-BuS(O)SMe (82% yield) as a practically colorless liquid.[30]

The other unsymmetrical dialkyl thiolsulfinates were prepared by this same procedure[30] except that in the preparation of less sterically hindered thiolsulfinates (*e.g.*, ethyl methanethiolsulfinate), the ether layer, after extraction with acid and water, contained substantial quantities of disulfide and thiolsulfonate and only minimal amounts of thiolsulfinate and was therefore discarded. If high purity was desired, the lower alkyl thiolsulfinates were twice distilled at a vacuum of at least 0.05 mm. Vpc analysis, with injection port and column temperatures kept below *ca.* 100°, indicated, for each new compound described, a single sharp peak easily separated in retention time from the peak for the isomeric unsymmetrical thiolsulfinate. In all cases studied, the unsymmetrical thiolsulfinate with the sulfinyl group attached to the smaller of a pair of alkyl groups had a shorter retention time than its isomer (*i.e.*, MeS(O)-SBu-*t* precedes *t*-BuS(O)SMe).

The alkyl thiolsulfinates are quite unstable thermally and should be stored in the dark at temperatures of −20° or lower; in the case of the lowest molecular weight thiolsulfinates (dimethyl and ethyl/methyl) storage at Dry Ice temperatures is recommended if the compounds are not to be used immediately. *Caution should be exercised in the handling of alkyl thiolsulfinates as contact with skin can cause severe dermatitis.*

Oxidation of 2-Methyl-2-propyl Methyl Disulfide. (1) With Peracetic Acid. To a solution of 13.57 g (0.1 mol) of 2-methyl-2-propyl methyl disulfide[47] in 300 ml of chloroform at 5° was added 19.01 g (0.1 mol) of 40% peracetic acid during 30 min. After an additional 30 min at 5° the reaction mixture was analyzed by quantitative vpc (previously calibrated under identical conditions of analysis with authentic samples of methyl 2-methyl-2-propanethiolsulfinate and 2-methyl-2-propyl methanethiolsulfinate) which indicated a 2:1 ratio of methyl 2-methyl-2-propanethiolsulfinate to 2-methyl-2-propyl methanethiolsulfinate, in addition to *ca.* 9% unreacted disulfide. The same thiolsulfinate ratio could be obtained by nmr: singlets were observed (in $CDCl_3$) at δ 1.38 (area 6), 1.56 (area 3), 2.62 (area 2), and 2.96 (area 1) (the first and third peaks correspond exactly to methyl 2-methyl-2-propanethiolsulfinate while the second and fourth peaks correspond to 2-methyl-2-propyl methanethiolsulfinate).

(2) With *m*-Chloroperbenzoic Acid. Identical results were obtained as with peracetic acid.

(3) Photooxidation. A solution of 200 ml of methanol, 0.1 *M* in 2-methyl-2-propyl methyl disulfide, containing 0.05 g of Methylene Blue, was irradiated with a 650-W General Electric DWY lamp with vigorous circulation of oxygen through the solution. Quantitative vpc analysis after 2.5 hr indicated a 1:5 ratio of methyl 2-methyl-2-propanethiolsulfinate to 2-methyl-2-propyl methanethiolsulfinate in addition to *ca.* 20% 2-methyl-2-propyl methyl disulfide.

In a second run, a solution of 100 ml of methanol, 0.25 *M* in 2-methyl-2-propyl methyl disulfide, containing 0.05 g of Methylene Blue, was photooxidized as above until vpc analysis indicated the absence of disulfide. Both quantitative vpc and nmr analysis of the concentrated (treated with pentane to remove the Methylene Blue) indicated a 1:2 ratio of methyl 2-methyl-2-propanethiolsulfinate to 2-methyl-2-propyl methanethiolsulfinate (50% crude yield of thiolsulfinates).

Oxidation of 2-Methyl-2-propyl Ethyl Disulfide. To a chilled solution of 0.308 g (2.05 mmol) of 2-methyl-2-propyl ethyl disulfide[46] in 6 ml of chloroform at 0° was added dropwise with stirring 0.421 g (2.2 mmol) of *m*-chloroperbenzoic acid in 3 ml of chloroform. The mixture was stirred at 0° for 15 min and then allowed to warm to room temperature. The heavy white precipitate was removed by filtration and the residue concentrated *in vacuo* and subjected to preparative tlc (since vpc analysis indicated minor amounts of disulfide and thiolsulfonate) using methylene chloride as eluent.

The main tlc band (lowest R_f value) was shown to be homogeneous by vpc and had ir (neat) 9.28 μ (S=O); the mass spectrum had a peak at *m/e* 166 ($C_6H_{14}S_2O$) although considerable decom-

(46) H. Asakawa, K. Kamiya, and S. Takai, *Takeda Kenkyusho Nempo*, **29**, 610 (1970); *Chem. Abstr.*, **74**, 125, 603 (1971).

(47) D. T. McAllan, T. V. Cullum, R. A. Dean, and F. A. Fidler, *J. Amer. Chem. Soc.*, 73, 3627 (1951).

position occurred in the source as indicated by the presence of peaks corresponding to diethyl, di(2-methyl-2-propyl), and 2-methyl-2-propyl ethyl disulfides. The nmr ($CDCl_3$) spectrum showed bands at δ 1.37 (superimposed t and s), 1.55 (s, total area of high field peaks *ca.* 10 H), and 3.7 (q, 2 H). Correcting the δ 1.37 peak for the superimposed triplets from the ethyl groups gave a ratio of areas under the δ 1.37 and 1.55 singlets of 1.74:1 corresponding to a ratio of 1.74:1 of *t*-BuS(O)SEt/*t*-BuSS(O)Et.

Methyl-d_3 Mercaptan. (The following procedure is a slightly modified version of a synthesis developed by Professor I. B. Douglass; we thank Professor Douglass for making this useful procedure available to us.) To a solution of 2.8 g (0.037 mol) of thiourea in 75 ml of acetone was added 5 g (0.034 mol) of methyl-d_3 iodide.[48] After refluxing the solution briefly, the acetone was removed *in vacuo* to give 7.6 g (97.5% yield) of thiuronium salt. This salt was mixed with 7.5 g (0.081 mol) of aniline in a 25-ml flask equipped with a stirring bar and connected to a calibrated Dean-Stark trap topped by a Dry Ice condenser. The thiuronium salt was heated to 125–155° (bath temperature) and 1.1 ml (0.95 g, assuming the same density as for methyl mercaptan) of methyl-d_3 mercaptan was collected. Based on mass spectral analysis of derivatives (see below), an estimate of 98% CD_3SH and 2% CD_2HSH can be made for this sample of methyl-d_3 mercaptan. The mercaptan was diluted to exactly 50.0 ml with ether and aliquots were withdrawn to prepare methyl-d_3 alkanethiolsulfinates.[30]

Ethyl-*2,2,2*-d_3 Mercaptan. In a 25-ml flask equipped with a small sintered glass continuous extraction device was placed 6.68 g of ethyl-*2,2,2*-d_3 alcohol (0.136 mol; prepared from perdeuterioacetic acid[47] by the method of Friedman[49]) and 1.6 g of red phosphorus (0.0516 mol); 18 g of iodine (0.142 mol) was placed in the extraction device and the ethanol was brought to vigorous reflux (percolating through the iodine in the extractor). After completion of the reaction, the product was distilled, the distillate washed with water, concentrated hydrochloric acid, saturated aqueous sodium bisulfite, and again with water, and dried yielding 16.43 g (76%) of ethyl-*2,2,2*-d_3 iodide. Following the procedure used in the preparation of methyl-d_3 mercaptan, 5 g (0.031 mol) of ethyl-*2,2,2*-d_3 iodide was converted into 2.0 ml (1.68 g, assuming the same density as for ethyl mercaptan; 82% yield) of ethyl-*2,2,2*-d_3 mercaptan. Based on mass spectral analysis of derivatives (see below), the isotopic composition could be estimated as 86.2% d_3, 9.0% d_2, and 4.8% d_0 ethyl mercaptan.

Ethyl-*1,1*-d_2 Mercaptan. Following the above procedure, ethyl-*1,1*-d_2 iodide (prepared *via* lithium aluminum deuteride[48] reduction of acetic anhydride using a 1.35:1 molar ratio of these reagents, followed by treatment of the resulting ethyl-*1,1*-d_2 alcohol with phosphorus and iodine, as described above) was converted into ethyl-*2,2,2*-d_3 mercaptan in 55% yield. Based on mass spectral analysis of derivatives (see below), the isotopic composition could be estimated as 95.1% d_2, 2.9% d_1, and 2% d_0 ethyl mercaptan.

Bis(ethyl-*1,1*-d_2) Disulfide. A solution of 1.0 ml (~0.013 mol) of ethyl-*1,1*-d_2 mercaptan in 5 ml of methanol was added to a solution of 6 g of $FeCl_3 \cdot 6H_2O$ (0.022 mol) and 0.1 g of KI in 15 ml of 1:1 methanol–water in a small separatory funnel. After vigorously shaking the mixture, extracting the solution with a total of 30 ml of pentane, washing the pentane solution with dilute aqueous $NaHSO_3$ followed by several portions of water, drying over $MgSO_4$ and concentrating and distilling at atmospheric pressure, there was obtained 0.59 g (72% yield) of diethyl-*1,1*-d_2 disulfide of good purity as indicated by vpc analysis. Mass spectral analysis indicated 96.4% d_4 and 3.6% d_3 disulfide; the nmr spectrum (CCl_4) had a broad singlet at δ 1.39.

Bis(ethyl-*2,2,2*-d_3) Disulfide. Prepared as described above for bis(ethyl-*1,1*-d_2) disulfide; nmr (CCl_4) δ 2.63 (broad singlet), ir (film) 4.50 μ (C-D). Mass spectral analysis indicated 87% ethyl-d_6 disulfide and 13% ethyl-d_5 disulfide.

Synthesis of Symmetrical Thiolsulfinates: Ethyl-*1,1*-d_2 Ethane-*1,1*-d_2-thiolsulfinate. A chloroform solution containing 3.06 mmol of bis(ethyl-*1,1*-d_2) disulfide was oxidized with an equimolar amount of 40% peracetic acid, affording, after work-up, a product which analyzed by quantitative vpc for approximately 91% thiolsulfinate[30] in addition to disulfide and thiolsulfonate.

Because of the small scale used in the preparation of the symmetrical or unsymmetrical deuterated thiolsulfinates, no effort was made to remove the minor amounts of disulfide and thiolsulfonate impurities by distillation. Mass spectra of "pure" deuterated thiolsulfinate were most conveniently obtained by gc–ms methods utilizing the original, dried methylene chloride solution of the thiolsulfinate and the mildest possible gc and separator conditions. For pyrolysis studies on the neat deuterated thiolsulfinates, the methylene chloride concentrate was exposed to oil pump vacuum at room temperature to remove traces of solvent.

Di(1-adamantyl) Disulfide. A solution of 4 g of 1-adamantanethiol[50] (24 mmol) in 120 ml of a 1:1 mixture of ethanol and 1,2-dimethoxyethane containing 1.3 g of sodium methoxide was treated with a solution of 3 g (12 mmol) of iodine in 60 ml of ethanol, the mixture was concentrated *in vacuo*, and the residue was added to water to give, after filtration and drying, 3.6 g of di(1-adamantyl) disulfide (90% yield) as a colorless fine powder, mp 221–225°, λ_{max} (cyclohexane) 235 nm (sh, ϵ 690). A sublimed sample had mp 225.6–227.6° and gave a satisfactory elemental analysis.

1-Adamantyl 1-Adamantanethiolsulfinate. A 1-g sample of disulfide (3 mmol) in 175 ml of a 1:1 mixture of methanol–benzene was photooxidized in the presence of 0.012 g of Methylene Blue at 6° for 2 hr. The Methylene Blue could be conveniently removed by addition of ether or pentane to the concentrate (in which solvents Methylene Blue is insoluble) followed by filtration, concentration, and recrystallization of the residue from absolute ethanol. In this manner there was obtained 0.62 g (59% yield) of the title compound as colorless crystals: mp 240–241° dec; ir (KBr pellet) 9.25 μ (S=O, vs); λ_{max} (cyclohexane) 258 nm (ϵ 2300); nmr (CCl_4) δ 1.6–2.3 (three peaks; in the presence of the Eu(fod)-d_{27} shift reagent six distinct peaks appeared in the ratio of 2:2:2:2:1:1); mass spectrum *m/e* 350 ($C_{20}H_{30}S_2O$, parent) and 135 ($C_{10}H_{15}$, base). An analytical sample, prepared by preparative tlc followed by recrystallization and drying at 80° and 0.04 mm for 6 hr had mp 244.5–246.5° and gave a satisfactory elemental analysis.

Unsymmetrical Thiolsulfonates: Methyl 2-Methyl-2-propanethiolsulfonate. Following the procedure of Douglass[51] equimolar quantities (15 mmol each) of 2-methyl-2-propanesulfinyl chloride,[46] freshly prepared methanesulfenyl chloride[51] and water were mixed at −10° and allowed to warm to room temperature during 1 hr. After 2 days at room temperature the mixture was treated with sodium bicarbonate until gas evolution ceased and dried ($MgSO_4$) and the filtrate distilled to give 1.69 g (67% yield) of the title compound.[30]

Ethyl-*1,1*-d_2 Ethane-*1,1*-d_2-thiolsulfonate. Ethyl-*1,1*-d_2 ethane-*1,1*-d_2-thiolsulfinate (1.33 mmol) was heated on a steam bath for 45 min. The yellow product, consisting mainly of disulfide and thiolsulfonate, was subjected to preparative layer chromatography (CH_2Cl_2 eluent) and the band of R_f 0.55 was isolated giving 0.049 g (40% yield) of the title compound as a slightly yellow oil.[30]

Disproportionation of Ethyl-*1,1*-d_2 Ethanethiolsulfinate. Neat ethyl-*1,1*-d_2 ethanethiolsulfinate[30] was kept at 100° for 40 min. The resulting yellow oil was subjected to gc–ms analysis. An analysis of the parent region (at 10 eV) of the mass spectrum of the thiolsulfonate peak indicated the composition (corrected for contributions from isotopes of carbon, oxygen, and sulfur: 26.6% $C_4H_{10}S_2O_2$ (*m/e* 154), 71.0% $C_4H_8D_2S_2O_2$ (*m/e* 156), and a maximum of 2.4% $C_4H_6D_4S_2O_2$ (*m/e* 158). This latter concentration might be considerably less; errors associated with small peak size and corrections for isotopic contributions limit the accuracy of this number. From an analysis of the mass spectrum of the disulfide peak, the approximate isotopic composition could be estimated as $C_4H_{10}S_2$ (*m/e* 122), 14%, $C_4H_8D_2S_2$ (*m/e* 124), 43%, $C_4H_6D_4S_2$ (*m/e* 126), 43%.

Disproportionation of Methyl-d_3 Methanethiolsulfinate. Neat $CH_3S(O)SCD_3$[30] was pyrolyzed at 96° in a sealed capillary tube for 3.5 min (~50% disproportionation) and for 30 min (~100% disproportionation) giving yellow products which were subjected to gc–ms analysis. The results of analysis of the mass spectra of the gc peaks corresponding to methyl methanethiolsulfonate-d_n and recovered methyl methanethiolsulfinate-d_n are summarized in Scheme III.

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Supplementary Material Available. Full spectral, chromatographic and analytical data for all new alkyl alkanethiolsulfinates and alkanethiolsulfonates prepared in this study (as well as some new data on previously prepared compounds) will appear as Tables I and II following these pages in the microfilm edition of this volume of the journal. Photocopies of the supplementary material from this paper only or microfiche (105 × 148 mm, 24× reduction, negatives) containing all of the supplementary material for the papers in this issue may be obtained from the Journals Department, American Chemical Society, 1155 16th St., N.W., Washington, D. C. 20036. Remit check or money order for $3.00 for photocopy or $2.00 for microfiche, referring to code number JACS-74-3921.

The Chemistry of Alkyl Thiolsulfinate Esters. VII. Mechanistic Studies and Synthetic Applications

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Abstract: The pyrolysis of alkyl thiolsulfinates is shown to afford alkanesulfenic or alkanethiosulfoxylic acids which may be trapped in good yields with acetylenes giving α,β-unsaturated sulfoxides or thiolsulfinates, respectively. In the absence of trapping agents the sulfenic acids can undergo a variety of reactions including dehydration to thiolsulfinate and exchange (*via* nucleophilic displacement) with thiolsulfinate leading to a scrambling process if two different thiolsulfinates are involved. The sulfenic acids can initiate more complicated sequences leading to formation of thiolsulfonate and disulfide (disproportionation) or to α-alkanesulfinyl and α-alkanesulfonyl disulfides (Pummerer rearrangement). Mechanisms are proposed for the various thermal reactions of thiolsulfinates based on detailed product studies and study of substituent, solvent, and catalyst effects. The mechanisms advanced bear on the mode of antioxidant action of thiolsulfinates and provide a possible explanation for the unusually low optical stability of optically active thiolsulfinates. Photochemical reactions of dialkyl thiolsulfinates are also discussed. A number of typical reactions for the α-alkanesulfinyl disulfide, 2,3,5-trithiahexane 5-oxide, are presented including selective deoxygenation without S–S scission, Pummerer rearrangement with acetic anhydride, and selective sulfinyl sulfur–carbon bond cleavage. Evidence is presented for the facile formation of the first known example of a discrete α-disulfide carbanion.

Dialkyl thiolsulfinates, RS(O)SR, are a readily available class of organic sulfur compounds whose fundamental chemistry has not been systematically explored, this despite possible advantages which may be realized from similarities in chemical behavior between alkyl thiolsulfinates and alkyl sulfoxides, compounds of great and varied synthetic utility.[1] Presumably the reputation of the lower dialkyl thiolsulfinates as malodorous, unstable substances is responsible for the neglect of this class of compounds. In the accompanying paper[2] we have discussed aspects of the synthesis and properties of dialkyl thiolsulfinates. In this paper we present details of several synthetically useful reactions of alkyl thiolsulfinates and provide evidence concerning the mechanisms of these reactions.[3] Some novel aspects of the chemistry of several new classes of organic sulfur compounds, discovered during the course of this research, will also be discussed. Finally, since we have found alkyl thiolsulfinates to be useful precursors of alkanesulfenic (and related) acids, some new features of the chemistry of these latter elusive sulfur acids will be described.

Preparation and Reactions of Alkanesulfenic Acids; a Convenient Synthesis of α,β-Unsaturated Sulfoxides. A limited number of reports in the literature provide evidence for the similarity in chemical behavior of thiolsulfinates and sulfoxides. For example the reaction in eq 1[4] is analogous to the allyl sulfoxide–allyl sulfenate interconversion,[5] that in eq 2[6] to the Pummerer reaction of sulfoxides,[1] and that in eq 3[7] to the reduction of sulfoxides to sulfides under analogous conditions.[8]

Examples are known from sulfoxide chemistry of both C–S homolysis[9] and cycloelimination[10] reactions

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