Allium Chemistry: Microwave Spectroscopic Identification, Mechanism of Formation, Synthesis, and Reactions of (*E*,*Z*)-Propanethial *S*-Oxide, the Lachrymatory Factor of the Onion (*Allium cepa*)

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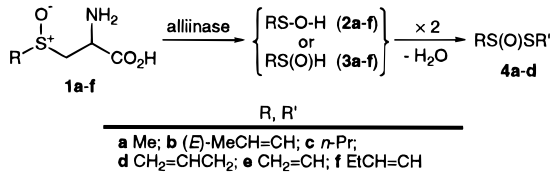
Abstract: Flow pyrolysis of 2-methyl-2-propyl 1′-propenyl sulfoxide (**9b**) affords a 98:2 mixture of (*Z*)- and (*E*)-propanethial *S*-oxide ((*Z*)- and (*E*)-**5b**), both characterized by Fourier transform microwave (FT-MW) spectroscopy. Sulfines (*Z*)- and (*E*)-**5b** are also identified by FT-MW in chopped onion volatiles and by NMR spectroscopy in onion extracts. Similarly, flow pyrolysis of 2-methyl-2-propyl vinyl sulfoxide (**9c**) affords (*Z*)- and (*E*)-isomers of ethanethial *S*-oxide (**5a**), identified by FT-MW methods. Pyrolysis in the presence of D_2O affords (*Z*)-**5a**-d_1 and (*Z*)-**5a**-d_2 from **9c** and (*Z*)-**5b**-d_1 from **9b**; (*Z*)-**5b**-d_1 is also produced when an onion is homogenized in D_2O. Pyrolysis of **9c** with ethyl propiolate gives ethyl (*E*)-3-(vinylsulfinyl)acrylate (**10**). Neat **5a** at 100 °C gives acetaldehyde. On standing, **5b** dimerizes to *trans*-3,4-diethyl-1,2-dithietane 1,1-dioxide (**12a**); $Me_3SiCH{=}S^{+}{-}O^{-}$ (**5f**) undergoes an analogous dimerization. Compound **5b** shows moderate potency as an anticarcinogen in inducing the enzyme quinone reductase.

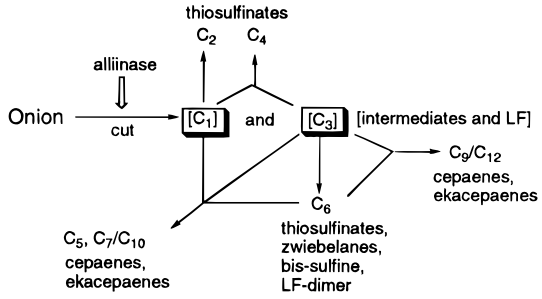
Introduction

The lachrymatory action and piquant flavor of freshly cut onion (*Allium cepa*) has been widely recognized and appreciated since the earliest cultivation of this venerable plant in central Asia more than 6000 years ago.[2,3] An extensive chemical literature, dating back to 1892, deals with attempts to determine the chemical composition of the odor and flavor of onion and, in particular, the nature of the tear-evoking principle (lachrymatory factor; LF).[4] We have investigated onion volatiles and extracts in an effort to characterize the various low molecular weight organosulfur constituents, to ascertain the mechanism of their formation from intact plant precursors **1a**−**c**[5] (Scheme 1), and to determine their subsequent reactions.[4,6,8] When an onion is cut, alliinase enzymes commingle with **1a**−**c** forming C_1 and C_3 intermediates from **1a** and **1b**,**c**, respectively (Scheme 2). These C_1 and C_3 intermediates form C_2, C_4, and C_6 thiosulfinates **4a**−**c**, C_6 zwiebelanes, bis-sulfine, C_5-C_9 cepaenes,

Scheme 1



Scheme 2



and related heavier compounds which are discussed elsewhere.[4,7] Methanesulfenic acid, the C_1 intermediate, when independently generated by flash vacuum pyrolysis (FVP) of synthetic precursors, was found by absorption microwave (MW) spectroscopy in earlier work to have structure $CH_3S{-}O{-}H$ (**2a**).[9] We have now employed the recently developed technique of flow pyrolysis pulsed-beam Fourier transform microwave (FT-MW) spectroscopy to characterize the C_3 intermediates and report (1) the structure of the LF, (*E*,*Z*)-propanethial *S*-oxide

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(2) E.g., the tear-producing effects of onion are mentioned in Shakespeare's plays (*Antony and Cleopatra*, I, ii, 173; *All's Well That Ends Well*, V, iii, 316; *The Taming of the Shrew*, Introduction, 122).

(3) Health benefits of onion associated with its lachrymatory action are noted in the Codex Ebers (a 15th century B.C. medical papyrus) and in the writings of the Roman naturalist Pliny the Elder (Gaius Plinius Secundus; AD 23−79).[4]

(4) For references, see: Block, E. *Angew. Chem., Int. Ed. Engl.* **1992**, *31*, 1135.

(5) *Chemical Abstracts* names of compounds not otherwise named in the abstract, text, or experimental: **1a**−**f**, L-cysteine *S*-oxides: *S*-methyl-, **1a**, *trans*-(+)-*S*-(1-propenyl)-, **1b**, *S*-*n*-propyl-, **1c**, *S*-(2-propenyl)-, **1d**, *S*-vinyl-, **1e**, *S*-(1-butenyl)-, **1f**; methanesulfinothioic acid *S*-methyl ester, **4a**; *n*-butanethial *S*-oxide (**5c**).

(6) For background and leading references, see footnotes 1 and 3 of ref 7a.

(7) (a) Block, E.; Thiruvazhi, M.; Toscano, P. J.; Bayer, T.; Grisoni, S.; Zhao, S.-H. *J. Am. Chem. Soc.* **1996**, *118*, 2790. (b) Block, E.; Bayer, T.; Naganathan, S.; Zhao, S.-H. *J. Am. Chem. Soc.* **1996**, *118*, 2799.

(8) Communications: (a) Block, E.; Penn, R. E.; Revelle, L. K. *J. Am. Chem. Soc.* **1979**, *101*, 2200. (b) Block, E.; Revelle, L. K.; Bazzi, A. A. *Tetrahedron Lett.* **1980**, *21*, 1277. (c) Block, E.; Bazzi, A. A.; Revelle, L. K., *J. Am. Chem. Soc.* **1980**, *102*, 2490. (d) Block, E.; Penn, R. E.; Bazzi, A. A.; Cremer, D. *Tetrahedron Lett.* **1981**, *22*, 29.

(9) Penn, R. E.; Block, E.; Revelle, L. K. *J. Am. Chem. Soc.* **1978**, *100*, 3622.

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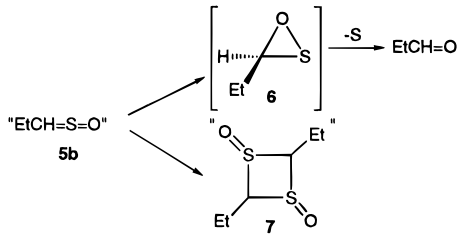
(EtCH═S^+−O^-; **5b**), from studies simulating enzymatic formation from **1b**, using both FT-MW and NMR spectroscopy; (2) FT-MW and NMR spectroscopic identification of the LF from cut onion; (3) FT-MW study of deuterium incorporation in LF produced pyrolytically and from an onion-D_2O homogenate; (4) dimerization of the LF; (5) parallel FT-MW and NMR studies of homologs of **5b**; and (6) anticarcinogen activity, measured by induction of quinone reductase. Points 1−5 elucidate the mechanism of formation and reactions of the LF.

Background

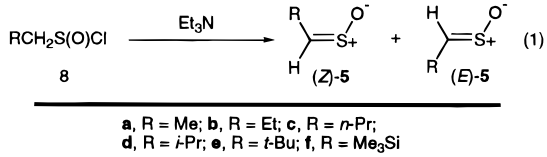
In 1961 Virtanen showed that **1b** (*ca.* 0.2% by weight in onion) is the precursor to the LF.[10a] Virtanen also found that the alliinase converts **1a** and **1c** (*ca.* 0.005−0.02% by weight in onion,[10b−d]) and **1d**, in garlic, to the respective thiosulfinates **4a**,**c**,**d** via the corresponding sulfenic acids (**2a**,**c**,**d** or **3a**,**c**,**d**; Scheme 1). Based on these results, Virtanen formulated the LF as MeCH═CHS(O)H (**3b**),[11] an assignment felt to be consistent with deuteration studies involving precursor **1b**. Thus, when the LF is generated enzymatically in D_2O, the molecular ion shifts from *m/z* 90 to 91, indicating one exchangeable proton. Fragmentation of the normal as well as LF-d_1 "shows that in both cases an OH-fragment is set free. The molecule contains therefore no OH-group (the hydrogen of which would be replaced by deuterium in D_2O)."[11b] Reaction of synthetic precursors **1e**,**f** with alliinase also produced lachrymators (Scheme 1), postulated as sulfenic acids CH_2═CHS(O)H (**3e**) and EtCH═CHS(O)H (**3f**), respectively, based on their mass spectra.[11]

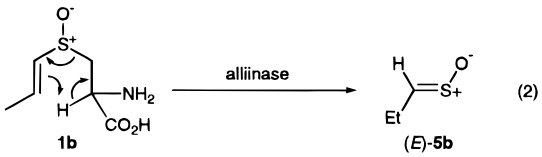
Simultaneous with the work of Virtanen, Wilkens[12] in 1961 used preparative GC to isolate the LF, depicted as "EtCH═S═O" (**5b**, Scheme 3). Evidence supporting structure **5b** included (1) the presence of strong IR absorption bands at 1113 and 1144 cm^{-1} (S═O region) together with the absence of bands attributable to S−H, O−H, or C═C and (2) ready decomposition of the LF to propanal (via 3-ethyloxathiirane (**6**)) and to a second compound with IR bands at 1140 and 1330 cm^{-1}, formulated as 2,4-diethyl-1,3-dithietane 1,3-dioxide (**7**).[12] Wilkins rationalized the inconsistency between the IR data for **7** which showed "absorption bands typical of the sulfone stretching modes", and the proposed disulfoxide structure **7** as due to "the proximity of the antipodal sulfinyl groups in this strained-ring structure ... postulated to induce a pseudo-sulfone infrared absorption, which would be of less intensity than that of a true sulfone".[12]

Scheme 3



In 1963−1964 the first syntheses of *S*-oxides of thials and thiones (termed *sulfines*) were reported, by dehydrochlorination of the corresponding sulfinyl chlorides (**8**; eq 1).[13a,b,14] Evidence was presented for a bent C−S−O group[13a,c,14] (e.g., the methyl groups in Me_2C═S^+−O^- are nonequivalent by NMR).[13a] In 1971 Brodnitz and Pascale[15] showed that sulfine **5b** (arbitrarily depicted by them as the (*E*)-isomer), synthesized by dehydrochlorination of *n*-PrS(O)Cl (**8b**) was identical by IR, ^{1}H-NMR, and MS to the natural onion LF. These authors proposed the mechanism for the formation of the LF from its known precursor **1b** shown in eq 2.[15] They also synthesized sulfines MeCH═S^+−O^- (**5a**) and *n*-PrCH═S^+−O^- (**5c**) from the corresponding sulfinyl chlorides **8a**,**c**. On the basis of the lachrymatory properties and mass spectra of **5a**,**e**, they suggested that Virtanen's sulfenic acids **3e** and **3f** were in fact **5a** and **5c**, respectively.[15] The stereochemistry of these sulfines was not considered. With few exceptions,[16] papers on the onion LF up to the time of our work[8a] ignored geometric isomerism in **5b**, despite extensive research on isomerism in thiocarbonyl *S*-oxides.[13,14] In some articles **5b** was depicted with a linear CSO grouping devoid of any stereochemistry,[12,17] while in other papers *(E)*-stereochemistry was arbitrarily indicated.[15,18]





By use of FVP-MW spectroscopic techniques it was found that pyrolysis of methyl 2-methyl-2-propyl sulfoxide (MeS(O)-*t*-Bu; **9a**)[5,19a] above 250 °C gave Me_2C═CH_2 and MeSOH.[9] The latter was shown to contain dicoordinate rather than tricoordinate sulfur (e.g., MeS−O−H (**2a**) not MeS(O)H (**3a**); Scheme 4),[9,20,21] contrary to the proposal of Virtanen. Ready exchange occurs between MeSOH and D_2O in the waveguide of the MW spectrometer affording MeSOD. When heated to

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(15) Brodnitz, M. H.; Pascale, J. V. *J. Agric. Food Chem.* **1971**, *19*, 269.

(16) Kurrn, R.; Nair, N. P.; Radhakrishnan, A. N.; Spande, T. F.; Yeh, H. J.; Witkop, B. *Biochemistry* **1974**, *13*, 4394.

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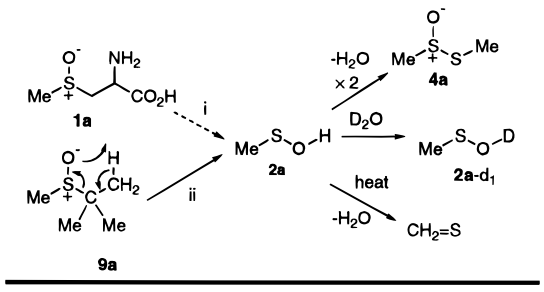
(18) Snyder, J. P. *J. Am. Chem. Soc.* **1974**, *96*, 5005.

(19) (a) Turecek, F.; Brabec, L.; Vondrak, T.; Hanus, V.; Hajicek, J.; Havlas, Z. *Coll. Czech. Chem. Commun.* **1988**, *53*, 2140. (b) Turecek, F.; McLafferty, F. W.; Smith, B. J.; Radom, L. *Int. J. Mass Spectrom. Ion Processes* **1990**, *101*, 283.

(20) Earlier work on sulfenic acids: (a) Shelton, J. R.; Davis, K. E. *Int. J. Sulfur Chem.* **1973**, *8*, 205. (b) Davis, F. A.; Billmers, R. L. *J. Org. Chem.* **1985**, *50*, 2593.

(21) Recent papers on isolable sulfenic acids: (a) Nakamura, N. *J. Am. Chem. Soc.* **1983**, *105*, 7172. (b) Yoshimura, T.; Tsukumichi, E.; Yamazaki, S.; Soga, S.; Shimasaki, C.; Hasegawa, K. *J. Chem. Soc., Chem. Commun.* **1992**, 1332. (c) Goto, K.; Tokitoh, N.; Okazaki, R. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 1124. (d) Saiki, T.; Goto, K.; Tokitoh, N.; Okazaki, R. *J. Org. Chem.* **1996**, *61*, 2924.

Scheme 4



[a] (i) = alliinase; - CH_2=CH(NH_2)CO_2H. (ii) FVP, - CH_2=CMe_2

800 °C under tandem pyrolysis conditions, MeSOH is dehydrated to CH_2S.[9] The structure of the parent sulfine, thioformaldehyde *S*-oxide (CH_2SO), was also determined using the same FVP-MW techniques.[22a]

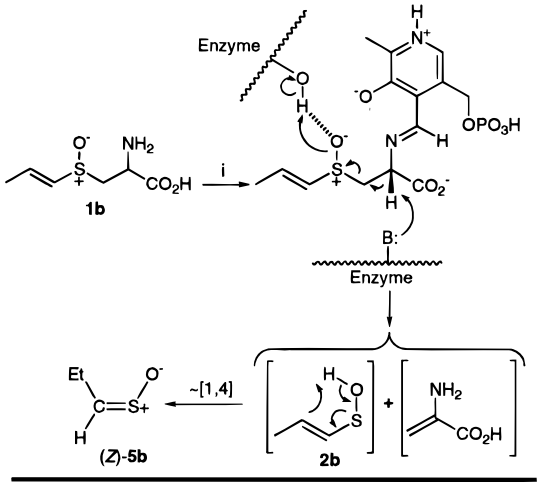
Results and Discussion

A. Structure, Origin, and Synthesis of the Onion LF. The work on the onion LF summarized above raises several questions. If we assume that the LF has structure **5b** as postulated by Wilkens[12] (Scheme 3) and later by Brodnitz/Pascale (eq 2),[15] how can the exchange of a single proton (Virtanen's deuteration studies[11]) be rationalized? Does **5b** indeed exist primarily with *E* (anti) stereochemistry? Can the same alliinase enzyme catalyze both a sulfoxide elimination reaction (Scheme 1) as well as a retro-ene type process (eq 2)? Evidence supporting an alternative mechanism (Scheme 5) that accommodates all of the facts is presented below.

1. Pulsed-Beam FT-MW Spectroscopic Studies of 5a,b. The above studies on MeSOH, CH_2SO, and preliminary FVP-MW work on **5a** were performed in the period 1976−1979 using Stark-modulation MW absorption techniques. Pulsed-beam FT-MW spectroscopy provides advantages over absorption MW methods for the study of transient chemical species. These include high resolution, and the extreme cooling of the gas bursts due to the supersonic expansion which gives a large reduction in the density of spectral lines and makes it possible to observe and assign the spectra of short-lived species. Pulsed solenoid valves are used to produce the molecular beam source in FT spectrometers. The valves are modified so that two gas flows, mixed on the high pressure side of the expansion orifice, exit through the normal gas input of the valve. A gas mixture is sampled and analyzed spectroscopically by actuating the solenoid to produce gas bursts in the Fabry-Perot cavity of the spectrometer. This dual flow valve has been used to study a number of van der Waals complexes composed of reactive monomeric species.[23] The method has been further developed in the present work to permit spectral characterization of transients produced from pyrolyses or from cutting onion in an inert gas flow upstream from the solenoid valve.[24]

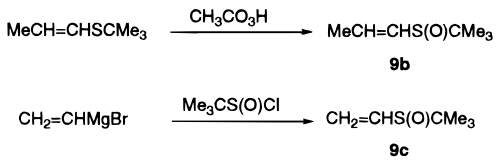
Pyrolyses of **9b**,**c**, prepared as shown in Scheme 6, were studied by FT-MW spectroscopy using Ar and He/Ne gas flows with a modified solenoid valve. As summarized in Schemes 7 and 8, under flow conditions of 5−20 psi above an atmosphere and 350 °C, **9b** is converted to isobutene and a 98:2 (*Z*)-**5b**/

Scheme 5



[a] (i) alliinase, pyridoxal phosphate

Scheme 6



(*E*)-**5b** mixture while **9c** gives isobutene and a 97:3 (*Z*)-**5a**/(*E*)-**5a** mixture. Complete MW investigations of **5a**,**b**, which discuss the pertinent spectral results, will appear elsewhere.[24] Spectral assignments of the ^{13}C and ^{34}S isotopomers provide definitive MW evidence for the stereochemistry of (*Z*)-**5a**,**b**. They also determine the gas phase geometries.[24] No MW assignments of isotopically-substituted species were possible for (*E*)-**5a**,**b** due to the low abundance of the (*E*) isomers in the gas bursts. The rotational constants of the normal isotopomers of (*E*)-**5a**,**b** calculated from the (*Z*)-**5a**,**b** structural parameters are in good agreement with the experimental spectral constants.[24] Also, the rotational transitions of (*E*)-**5a**,**b** require very little microwave power to attain full intensity, supporting the assignment of the spectral lines to very polar molecules. Bond moment calculations using the structural parameters of (*Z*)-**5a**,**b** predict that (*E*)-**5a**,**b** are polar with total electric dipole moments of 3.3 and 3.5 D, respectively ((*Z*)-**5a**,**b** have dipole moments of 3.29 and 3.35 D, respectively). These data, when combined with the NMR chemical shifts discussed below, offer strong support for the assignments of the observed MW spectra to (*E*)-**5a**,**b**.

When the pyrolyses are repeated with inert gas flows containing D_2O vapor, an 88:12 (*Z*)-**5b**/(*Z*)-**5b**-d_1 mixture is obtained from **9b** and a 66:32:3 (*Z*)-**5a**/(*Z*)-**5a**-d_1/(*Z*)-**5a**-d_2 isotopic mixture is formed from **9c**, respectively. Due to the high resolution and molecular isotopic specificity of MW spectroscopy, there is no ambiguity associated with the sites of deuterium isotopic substitution in (*Z*)-**5a**,**b**. Two (*Z*)-**5b**-d_1 isotopomers are possible with distinct MW spectra which are readily distinguishable from one another. Only one isotopomer is observed, corresponding to the deuterium located *syn* to the oxygen, as shown in Scheme 7. Since the molecular structure is determined from the rest of the MW isotopomer data, the frequencies of the rotational transitions can be calculated to within ca. 10 to 20 MHz. Extensive spectral searches over much larger ranges ruled out the presence of the second isotopomer ((*Z*)-**5b′**-d_1) at concentrations greater than 0.01−0.02 times the levels of (*Z*)-**5b**-d_1. The absence of (*Z*)-**5b′**-d_1 is consistent with the fact that small isotopic differences in zero point vibrational

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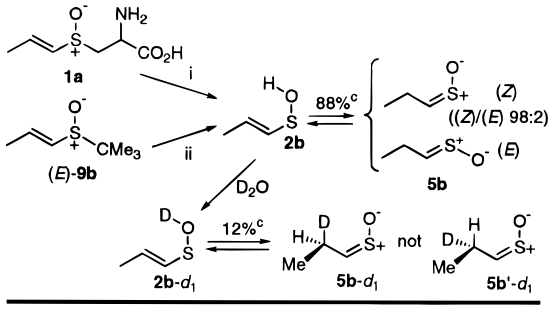
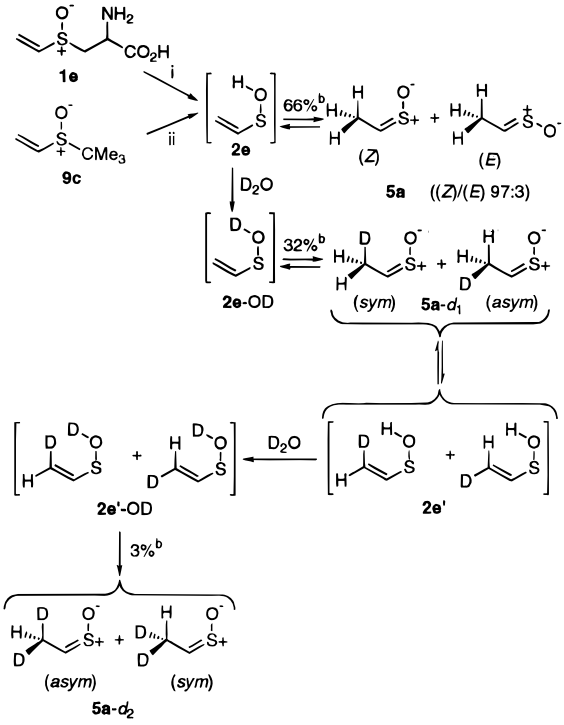
Scheme 7



[a](i) alliinase; - CH_2=CH(NH_2)CO_2H. (ii) flow pyrolysis, - CH_2=CMe_2. [b]For clarity, only the (*E*)-isomer of **9b** is shown. [c]Variable: see text.

Scheme 8



[a] (i) alliinase; - CH_2=CH(NH_2)CO_2H. (ii) flow pyrolysis, - CH_2=CMe_2. [b]Variable: see text.

energies can lead to significant population of solely the lowest energy isotopomer in the cold gas bursts. Although the small deuterium enrichment for (*Z*)-**5b**-d_1 suggests that **2b** rearranges to **5b** at a faster rate than it undergoes deuterium exchange, surface adsorbed H_2O exchange with D_2O vapor in the gas lines makes it difficult to determine the deuterium enrichment in the water vapor. The (*Z*)-**5b**/(*Z*)-**5b**-d_1 ratio was found to vary from experiment to experiment, reflecting variations in the water vapor deuterium content.

The deuterium exchange for the pyrolysis of **9c** to **5a** is complicated by the presence of two distinct rotamers of both (*Z*)-**5a**-d_1 and (*Z*)-**5a**-d_2. Scheme 8 illustrates the structural differences of the **5a**-d_1 and the **5a**-d_2 pairs of rotamers. The *sym* designation corresponds to deuterium substitution which maintains the plane of symmetry in both **5a**-d_1 and **5a**-d_2, while the *asym* labels identify asymmetric deuteration. Details of the complete MW spectral assignments of these four deuterated isotopomers of **5a** are presented elsewhere.[24b] The observation of the **5a**-d_2 pair indicates that the rearrangement of **2e** to **5a** is reversible as shown in Scheme 8, if the reasonable assumption is made that the methyl hydrogens of **5a** do not directly exchange with D_2O. The least intense rotamer, *sym*-**5a**-d_2, has an estimated isotopic abundance less than the ^{13}C isotopomers observed in natural abundance.[24b] The MW spectrum of **5a**-d_3 was not observed, which is not unexpected considering the factor of ten decrease in the abundance of **5a**-d_2 compared to **5a**-d_1.

The MW-D_2O exchange data provide strong evidence for thermal rearrangements of **2b** to **5b** and of **2a** to **5a**, as shown in Schemes 7 and 8. The MW spectra of CH_3CDSO or CH_3-CH_2CDSO were not observed, which further demonstrates that the exchange is site specific as expected for the mechanisms shown in Schemes 7 and 8. Recently a combination of FVP of **9c** with neutralization−reionization MS was used to identify **2e** and its thermal rearrangement to **5a**.[19b] Extensive MW searches were carried out in the spectral regions where **2e** is predicted to have intense rotational transitions. No unassigned lines were found in these regions, which suggest that **2e** is too short-lived to be detected under the conditions of flow-pyrolyses.

2. In Situ Detection of 5b in Cut Onion by Pulsed-Beam FT-MW Spectroscopy. The pulsed-beam FT-MW technique utilizing the modified solenoid valve for continuous gas flow is easily adapted to studies of stable and transient species in volatiles above biological samples. Freshly prepared onion macerate was placed in a tube and the volatiles carried in He/Ne to the solenoid valve which sampled the gas mixture for analysis in the FT-MW spectrometer. Rotational transitions of (*Z*)- and (*E*)-**5b** were observed, and spectral intensity measurements indicate approximately the same relative abundance as found for the pyrolysis of **9c**. Figure 1 shows the $J = 4_{04}$-3_{03} rotational transition of the normal isotopomer of (*Z*)-**5b** recorded at 8K resolution taking the Fourier transform of the average of the free induction decay (FID) for 1024 pulses. Continuous flow through the pulse solenoid valve was essential in order to observe the spectrum of (*Z*)-**5b**. The $J = 4_{04}$-3_{03} rotational transition of (*Z*)-**5b**-d_1 was observed when the above experiment was repeated using an onion macerate prepared with D_2O. It was necessary to average the FID from 10 000 gas pulses in order to obtain a signal-to-noise ratio of 3/1. Typically the $J = 4_{04}$-3_{03} rotational transition of (*Z*)-**5b** was seen for a period of 15 min from one batch of onion macerate. Due to the long data aquisition times needed to record the $J = 4_{04}$-3_{03} rotational transition of (*Z*)-**5b**-d_1, it was not possible to obtain even a qualitative estimate of the amount of (*Z*)-**5b**-d_1 relative to (*Z*)-**5b**. Only onion macerate which caused significant tearing gave a spectral signal at the known frequency of the $J = 4_{04}$-3_{03} rotational transition of (*Z*)-**5b**.[24a] Onion-to-onion variation in pungency (LF production) is well known. These studies with fresh onion provide strong evidence that the onion LF is predominantly (*Z*)-**5b**. The formation of (*Z*)-**5b**-d_1 from onion macerate prepared with D_2O is consistent with our proposal for 1,4-rearrangement of **2b** to **5b** (Scheme 4). It is also consistent with Virtanen's findings (discussed above in background section), if it is assumed that 1,4-rearrangement of the deuterated sulfenic acid, formulated as MeCH═CHSOD (**2b**) rather than MeCH═CHS(O)D (**3b**), giving **5b**-d_1 precedes electron-impact-induced fragmentation. Sulfine **5b**-d_1 should undergo electron-impact induced loss of OH rather than OD, if the hydrogen atoms on C-2 are indeed involved, due to the deuterium isotope effect. Our mechanism also has the advantage of allowing a common mode of enzymatic decomposition for LF precursor **1b** and cysteine sulfoxides **1a**,**c**,**d**. The preference for the (*Z*)-isomer in the case of both aliphatic and aromatic thioaldehyde *S*-oxides (see section 4 below) has been interpreted by a "syn effect" which stabilizes the Z configuration through σ and π bonding interactions between the hydrogens of the alkyl group and the oxygen atom.[8d,25a]

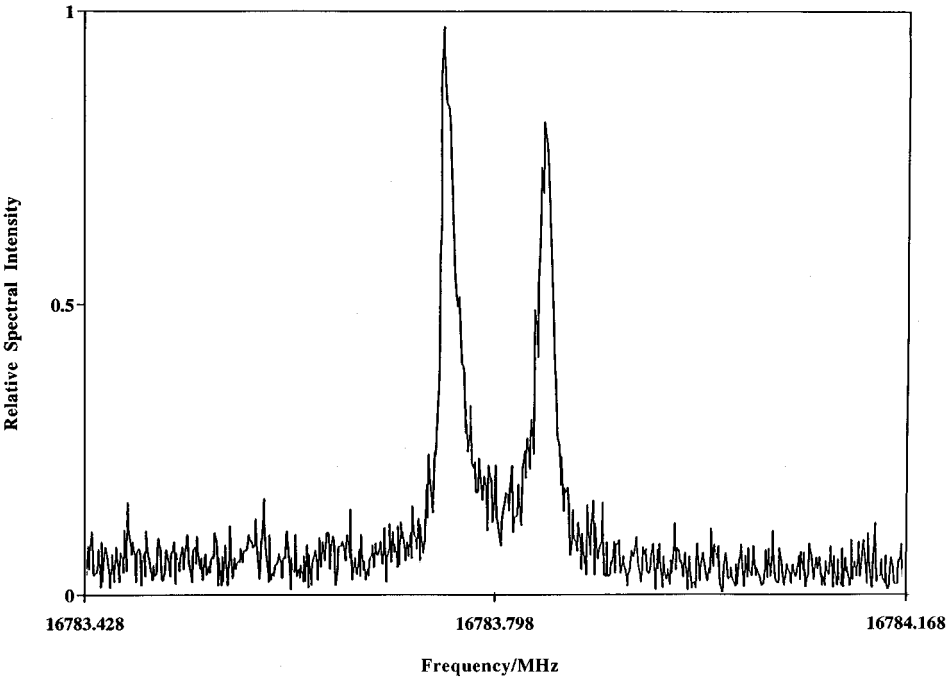
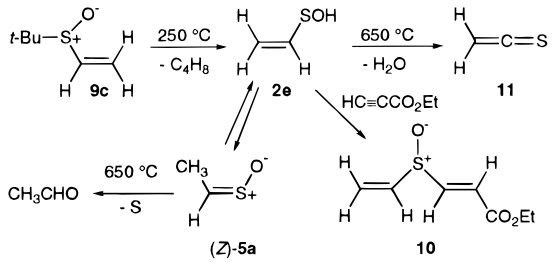


Figure 1. The $J = 4_{04} - 3_{03}$ rotational transition of (*Z*)-**5b** generated from macerated onion.

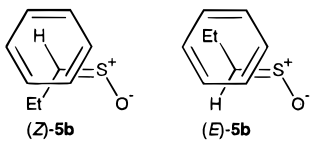
Scheme 9



3. Trapping and Other Pyrolysis Experiments. Heating a solution of **9c** in excess ethyl propiolate (a sulfenic acid trap[21,25b,c]) at 100 °C affords sulfenic acid adduct **10** (29%). Neat **9c** decomposes within 4 h at 100 °C to give, among other products, acetaldehyde, which we have separately found to be a major decomposition product of sulfine **5a**. It was previously found by MW spectroscopic analysis[8a] that sulfine **5a** decomposes under high temperature FVP conditions (650−750 °C) to both acetaldehyde and thioketene (**11**)[26] (Scheme 9).

4. NMR Spectroscopic Studies of the LF and Other Sulfines. The onion LF **5b** was prepared by pulverizing a white globe onion frozen with dry ice, extracting ($CFCl_3$), drying ($MgSO_4$), concentrating *in vacuo* (−78 °C), and distilling (trap-to-trap, −35 to −196 °C, 0.001 mm). The ^{1}H NMR spectrum of the LF was in good agreement with the spectrum of synthetic **5b** from *n*-PrS(O)Cl or from pyrolysis of **9b** (eq 1; Scheme 8; Table 1) and with the published spectrum of the previously isolated LF and synthetic counterpart.[15] Each sample of **5b** showed, in addition to a low field triplet at δ 8.17 ppm, a second, smaller low field triplet at δ 8.86 ppm with 2−5% of the area of the δ 8.17 ppm triplet. This minor triplet, which is not reported in earlier NMR studies of the onion LF, was shown to be neither a spinning side band nor a satellite band nor was it due to propanal (a known LF decomposition product showing a triplet at 9.79 ppm). After 4.5 h at 30 °C the LF ^{1}H NMR signal at 8.17 ppm was reduced to *ca.* half of its original intensity, the 8.86 ppm signal was now about 10% of the area of the 8.17 triplet, and the propanal signal at 9.79 had increased to *ca.* the same intensity as the 8.17 ppm signal.

In C_6D_6 the major and minor low field triplets of **5b** appear at δ 7.61 and 8.37 ppm, respectively (see Table 1). Sulfine **5b** also showed major and minor low field sp^2 carbon ^{13}C NMR peaks in $CDCl_3$ at δ 179.6 and 184.5 ppm, respectively. The aromatic solvent induced shift (ASIS) data is consistent with (*Z*)- and (*E*)-configurations for the major and minor isomers of **5b** in benzene, respectively. The *anti*-proton in the (*Z*)-isomer should experience greater shielding (e.g., $\Delta\delta$ 0.56 ppm) than the *syn*-proton in the (*E*)-isomer (e.g., $\Delta\delta$ 0.49 ppm; see drawings below), analogous to the ASIS effects in RCH═NX, where X = OH, OMe, N(Me)Ph, NHMe, NHPh, etc.[27] In the case of the sp^2 protons in both the nitrogen compounds and **5b**, resonance occurs at lower field when *syn* than when *anti* to X (or O).



To augment our NMR analysis we have synthesized the related sulfines $CH_3CH{=}S^+{-}O^-$ (**5a**), $(CH_3)_2CHCH{=}S^+{-}O^-$ (**5d**), and $(CH_3)_3CCH{=}S^+{-}O^-$ (**5e**) from sulfinyl chlorides **8** (eq 1) and, in the case of **5a**, from sulfoxide **9c** (Scheme 8) and determined their ^{1}H, ^{17}O, and ^{13}C NMR spectra.[28] We have also prepared and characterized $(CH_3)_3SiCH{=}S^+{-}O^-$ (**5f**), a new type of functionalized sulfine, from $(CH_3)_3SiCH_2S(O)Cl$ (**8f**).[5,29] Compound **5f** is a colorless, mildly lachrymatory liquid purified by trap-to-trap distillation at −20 °C. The ^{1}H NMR shift and ASIS data for **5a**,**d**,**e** (Table 1), showing the (*Z*)-isomer

(25) (a) Cremer, D. *J. Am. Chem. Soc.* **1979**, *101*, 199. (b) Block, E.; O'Connor, J. *J. Am. Chem. Soc.* **1974**, *96*, 3929. (c) Shelton, J. R.; Davis, K. E. *J. Am. Chem. Soc.* **1967**, *89*, 718.

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(27) Karabatsos, G. J.; Osborne, C. E. *Tetrahedron* **1968**, *24*, 3361 and earlier papers in series.

(28) (a) Following our initial reports[8b,14a] others have prepared **5e** and reported its NMR spectra,[28b] which agree well with our values. (b) Barbaro, G.; Battaglia, A.; Giorgianni, P.; Bonini, B. F.; Maccagnani, G.; Zani, P. *J. Org. Chem.* **1990**, *55*, 3744.

Table 1. NMR Data for **5a**,**b**,**d**−**f** and Related Sulfines and for Sulfine Dimers **13a**,**b**

		NMR Chemical Shifts[a] (coupling constants, Hz)		
Compound	% isomer	^{1}H	^{13}C	^{17}O
CH_2=SO[d]		7.84 (5.5), 7.73 (5.5)[b]	158.8[c]	
MeCH=SO (Z)	97%	8.31 (7.33), 2.24 (7.33)	173.4, 11.0	196.7
5a		*7.43 (7.32), 1.69 (7.32)*		
(*E*)	3%	8.88 (8.79), 2.06 (8.79)	177.6, 14.2	
		8.12 , 1.54		
EtCH=SO (Z)	98%	8.17 (7.9), 2.76 (7.8), 1.15 (7.8)	179.6, 19.7, 12.5	198.8
5b		*7.61 (7.82), 2.42 (7.82), 0.75 (7.4)*		
(*E*)	2%	8.86 (8.5); *8.37 (8.89)*	184.5, 14.4	
i-PrCH=SO (Z)	92%	8.09 (9.28), 3.93-3.57, 1.16 (6.8)	184.7, 26.4, 21.4	199.6
5d		*7.45 (9.28), 0.74 (6.8)*		
(*E*)	8%	8.78 (9.76), 1.06 (6.83)	189.1, 27.8, 22.5	
		8.37 (9.76)		
t-BuCH=SO (Z)	75%	7.61, 1.38; *6.86, 1.10*	183.6, 45.8, 29.4	187.2
5e (*E*)	25%	9.00, 1.24; *8.50, 0.72*	194.8	226
Me_3SiCH=SO (Z)[e]	66%	8.23, 0.05; *7.59, 0.10*	178.6, -1.5; *177.6, -1.2*	277.8
5f (*E*)[e]	33%	8.56, 0.05; *8.27, -0.18*	175.1, -1.5; *173.9, 1.29*	
[OS=CHCHMe-]$_2$[7b]		8.09 (9.6), 3.73, 1.24 (6.5)	179.6, 36.1, 17.3	
		7.06 (9.6), 3.3, 0.60 (6.3)		
 **12a**		*4.35 (6.10, 7.82), 2.73 (6.10, 7.82), 1.91 (m), 1.36 (m), 0.71 (7.3), 0.51 (7.3)*	*97.9, 39.2, 29.5, 24.3, 12.7, 11.3*	243, 210
 **12b**		5.06 (8.8), 2.91 (8.8), 0.25, 0.19	88.4, 14.8, -2.6, -3.1	

[a] Unless otherwise indicated solvent is $CDCl_3$ or C_6D_6 (italics). [b] In CF_3Cl. [c] In CF_3Cl + CD_2Cl_2. [d] Vallée, Y.; Ripoll. J.-L.; Lafon, C.; Pfister-Guillouzo, G. *Can. J. Chem.* **1987**, *65*, 290−291. [e] Structural assignment by analogy to structure of **5b**,**d**,**e**.

as the major component in each case but with an increasing (*E*)-/(*Z*)-ratio with increasing bulk of R in RCH=S^+−O^-, is fully consistent with the above analysis of the NMR data for the LF, and with NMR data on related RCH=N-X systems.[27] The (*Z*)-isomer is also favored in the case of aromatic thioaldehyde *S*-oxides.[28b,30] While the (*E*,*Z*)-assignment for **5f** is based on the same type of ^{1}H ASIS analysis used for **5a**,**d**,**e**, the low-field ^{13}C signal of the major isomer is found at *lower field* than the corresponding signal of the minor isomer, in contrast to the cases of **5a**,**d**,**e** (Table 1). In the absence of additional NMR studies to explain this anomaly, the stereochemical assignment for **5f** must be viewed as tentative.

The natural abundance ^{17}O NMR data for sulfines **5** collected in Table 1 represents the first[14a] such data obtained for sulfines and is notable for the strong deshielding of the sulfine oxygen compared to simple acyclic or cyclic sulfoxides.[31] This deshielding may be a consequence of the enhanced electronegativity of carbon-sp^2 orbitals atttached to the sulfine sulfur compared to carbon-sp^3 orbitals utilized in simple sulfoxides since other sulfinyl compounds containing electronegative substituents on sulfur are also deshielded relative to simple sulfoxides.[31]

5. Mechanistic Considerations and GC Quantitation of LF in Onion. Scheme 4 postulates a reversible [1,4]-sigmatropic rearrangement of **2b**, a reaction resulting in (*Z*)-stereochemistry for sulfine **5b**. This reaction, which constitutes a new synthesis of sulfines, finds precedence in the known tautomerism of thioamide *S*-oxides[33] as well as related sulfine-1-alkenesulfenic acid interconversions.[34] *Ab initio* (HF/6-31G*) calculations of the **2e** to **5a** interconversion (e.g., Scheme 7) view these compounds as sulfur-extended analogs of vinyl alcohol and acetaldehyde, respectively, and conclude that (*Z*)-**5a** is more stable than **2e** by 12 kJ mol^{-1} with a 137 kJ mol^{-1} barrier separating them.[19b] The intermediacy of the Schiff base shown in Scheme 4 is consistent with the requirement for pyridoxal phosphate as a cofactor for the enzymatic reaction[35] and the demonstration that sulfenic acids can be eliminated from related structures in vitro at neutral pH and ambient temperatures.[36] At high temperatures **2e** undergoes dehydration to thioketene (**11**; Scheme 9), presumably by a unimolecular process analogous to the high temperature dehydration of CH_3SOH (Scheme 4).

As described elsewhere,[7,37] onion extracts contain thiosulfinates of type MeCH=CHS(O)SR and MeCH=CHSS(O)R (R = Me, *n*-Pr). Evidence has also been presented for the intermediacy of thiosulfinates MeCH=CHS(O)SCH=CHMe, which rapidly rearrange to isomeric zwiebelanes.[7] Under GC conditions optimized for analysis of thiosulfinates and zwiebelanes, fresh onion juice contains 0.9 μmol of LF and 0.4 μmol of combined thiosulfinates and zwiebelanes per gram of juice (1 g of onion ≅ 0.53 g juice).[37] Under GC conditions optimized for LF analysis,[38] LF concentrations ranged from 2 to 10 μmol LF/g juice with peak values of 22 μmol LF/g juice. These values correspond well with reported levels of ca. 20 μmol **1a**/g onion.[39] We have observed that the LF levels, the combined (thiosulfinates + zwiebelanes) levels, and the (thiosulfinates + zwiebelanes)/LF ratio all increase with increasing levels of sulfur fertilization.[40] These observations suggest that, competitive with the unimolecular process in Scheme 5, **2b** condenses with other sulfenic acids and that these bimolecular condensation reactions become more favorable relative to unimolecular rearrangement as local concentrations of **2a**−**c** increase. These studies provide additional support for the formation of **2b** as the immediate precursor of the LF.

B. Bimolecular Self-Reactions of the LF 5b and Precursor 2b. In 1961 Wilkens reported that the onion LF **5b** spontaneously dimerized affording 2,4-diethyl-1,3-dithietane 1,3-dioxide (**7**; Scheme 3).[12] The proposed structure **7** seemed to us to be at odds with the IR spectrum of the dimer which indicated the presence of a sulfonyl group. Examination of the IR spectra of authentic *cis*- and *trans*-1,3-dithietane 1,3-dioxides[22b] failed to show the type of unusual "pseudo-sulfone infrared absorption"

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(31) Compare sulfinyl oxygen shifts in $SOCl_2$, $(MeO)_2S$=O, and Me_2S=O of 292, 176, and 13 ppm, respectively,[32a] and in Ar_2C=S^+−O^- of 210−230 ppm.[32b]

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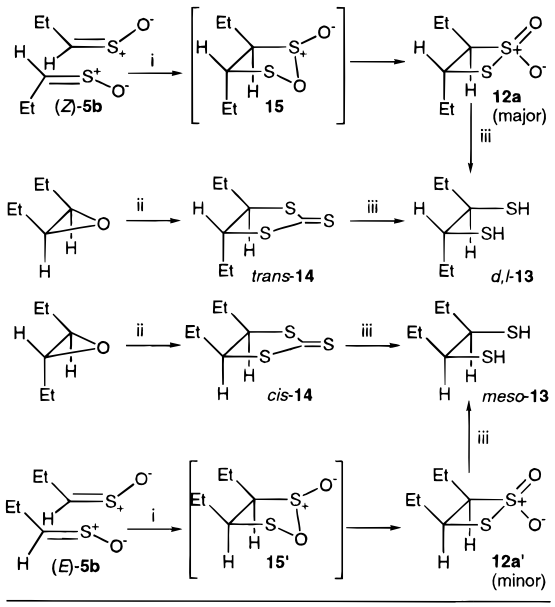
(37) Block, E.; Putman, D.; Zhao, S.-H. *J. Agric. Food Chem.* **1992**, *40*, 2431.

(38) (a) Extraction of onion juice (1:1 v:v CH_2Cl_2) 2 min after juice is expressed and GC analysis (5 m × 0.54 mm OV-1; initial oven/injector 60/63 °C; He 8.5 mL/min). (b) Schmidt, N. E. et al. *J. Agric. Food Chem.*, in press.

(39) Randle, W. M.; Lancaster, J. E. *Proc. Natl. Onion Res. Conf.* **1993**, 91.

(40) Randle, W. M.; Block, E.; Littlejohn, M. H.; Putman, D.; Bussard, M. L. *J. Agric. Food Chem.* **1994**, *42*, 2085.

Scheme 10



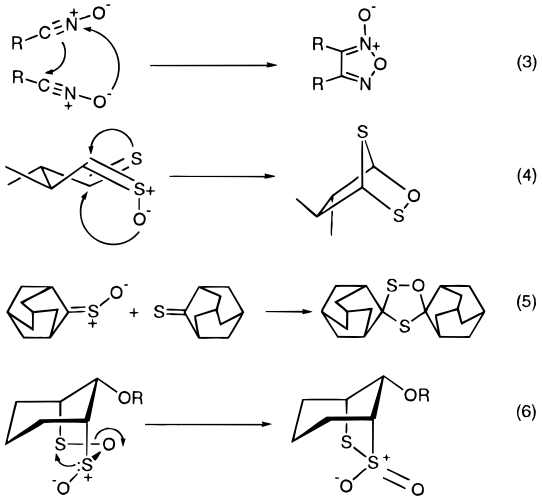
[a] (i) C_6H_6, 3 °C, 7 d. (ii) KSC(S)OMe. (iii) $LiAlH_4$.

proposed by Wilkens to explain the spectrum of the LF dimer. Furthermore, the stability of the 1,3-dithietane 1,3-dioxides contrasts with the instability of the LF dimer. Finally, it is mechanistically difficult to reconcile the formation of 2,4-diethyl-1,3-dithietane 1,3-dioxide from propanethial *S*-oxide with the reported formation of *trans*-4,5-diphenyl-1,2,3-trithiolane 1,1-dioxide from thiobenzaldehyde *S*-oxide.[41] In view of the uncertainty of the structure of the LF-dimer we reexamined the self-condensation of the LF.[8c]

A sample of LF **5b** from natural or synthetic sources was purified by trap-to-trap distillation at −30 °C, dissolved in about twice its volume of freshly dried benzene and kept in the dark at 5 °C for 7 days. The slightly yellow, nonlachrymatory solution was concentrated *in vacuo*, and the residue subjected to molecular distillation (50 °C, 10^{-3} mm) affording a practically colorless, clear liquid with a strong onion-like odor. Analysis by GC-MS indicated a single major product, *trans*-3,4-diethyl-1,2-dithietane 1,1-dioxide (**12a**), with retention time slightly longer than that of *n*-$PrSO_2SPr$-*n*, along with ca. 10% of an isomeric minor product, presumably the *cis*-isomer, **12a′** (Scheme 10). Table 1 summarizes the ^1H, ^{13}C, and ^{17}O NMR spectroscopic data for **12a**. The formula $C_6H_{12}O_2S_2$ was confirmed by HRMS. The IR spectrum showed bands at 1139 and 1333 cm^{-1} ($-SO_2-$) similar to that published by Wilkens.[12]

The ^1H and ^{13}C NMR data clearly indicate the presence of two substantially different, coupled "CHEt" groups, e.g., $-SO_2$-CHEt and −SCHEt. The striking difference in δ_c of the two methine carbons can be interpreted in terms of an unusual deshielding effect characteristic of four-membered-ring sulfones,[42] a further deshielding effect seen for the α-sulfonyl carbons of thiosulfonates compared with that for sulfones[43] and a vicinal deshielding effect due to the *trans* ethyl groups[44] giving the α-sulfonyl δ_c of 97.9 which contrasts with the α-sulfenyl δ_c of 39.2. The ^{17}O NMR spectrum is the first to show diastereotopic sulfone oxygens.[42] The stereochemistry of major LF dimer **12a** was established by chemical means as *trans* by $LiAlH_4$ reduction to *d*,*l*-hexane-3,4-dithiol (*d*,*l*-**13**), shown by NMR to be identical with an authentic sample (prepared stereospecifically from *trans*-4,5-diethyl-1,3-dithiolane-2-thione (*trans*-**14**) from *cis*-3,4-epoxyhexane[45]) and different from *meso*-**13** (prepared from *cis*-4,5-diethyl-1,3-dithiolane-2-thione (*cis*-**14**) from *trans*-3,4-epoxyhexane) as shown in Scheme 10.

Formation of **12a** from **5b** is suggested to involve a [3 + 2] cycloaddition sequence, in which **5b** functions as both a 1,3-dipole and a dipolarophile, followed by rearrangement of the unstable cyclic sulfenyl sulfinate ester **15** to cyclic thiosulfonate **12a**. The first step is analogous to the well-known dimerization of nitrile oxides to furoxans (eq 3).[46a] Formation of the cyclic sulfenyl sulfinate **15** via a two-step process cannot be excluded. In contrast to the formation of a carbon−carbon bond in the dimerization of **5b**, intra-[7b] or intermolecular[46b] 1,3-dipolar addition of sulfines to thiones or thials leads to cycloadducts having only carbon−hetero bonds, e.g., eqs 4 and 5, respectively.[46c] Folkin and Harpp have described rearrangement of cyclic sulfenyl sulfinates to cyclic thiosulfonates (eq 6) and suggest that it occurs in a concerted manner.[46e]



We find that $Me_3SiCH{=}S^+{-}O^-$ (**5f**) also dimerizes on storage at room temperature for several days to afford 1,2-dithietane **12b** in 42% yield as a colorless, crystalline solid. The structure follows from the MS molecular weight (corresponding to $C_8H_{20}O_2S_2Si_2$), the IR spectrum (1325 (s), 1125 (s) cm^{-1}), and the ^1H and ^{13}C NMR spectra (given in Table 1). Compound **12b** affords *d*,*l*-1,2-bis(trimethylsilyl)-1,2-ethanedithiol on reduction and *trans*-2,3-bis(trimethylsilyl)thiirane and *trans*-1,2-bis(trimethylsilyl)ethene on photolysis.[29] Other sulfines have recently been reported to dimerize to 1,2-dithietane 1,1-

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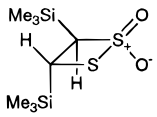
dioxides.[47] Compounds **12** are the first examples of isolable 1,2-dithietane derivatives.[48]



12b

We have shown that when an onion is cut, two highly reactive, chemically distinct organosulfur functionalities are formed in rapid succession, one from the other, namely sulfenic acid **2b** and sulfine **5b**. Both **2b** and **5b** can each undergo various reactions including self-reaction and reaction with each other. The self-reaction of **5b** (giving **12a**) has already been discussed. Evidence for the self-reaction of **2b** via bimolecular dehydration is indirect, but nonetheless compelling, as described elsewhere.[7] The third possibility, reaction of **2b** with **5b**, is thought to be the initial step in formation of cepaenes (MeCH═CHS(O)CHEtSSCH═CHMe).[4]

C. Phase II Enzyme Induction Activity of LF. Green onions, along with broccoli, are capable of inducing enzymes that detoxify carcinogens (phase II enzymes), as assayed by quinone reductase (QR) or glutathione *S*-transferase (GST) activity in murine hepatoma cells.[49a] Inducers are typically Michael reaction acceptors, characterized by olefinic bonds rendered electrophilic by conjugation with electron-withdrawing substituents.[49b,c] Since both onion LF **5b** and thiosulfinates **4** can be considered as Michael acceptors, it was of interest to determine if these compounds are responsible for the anticarcinogenic activity of onions as assayed by QR. The potency, expressed as the concentration (μM) required to double the QR specific activity, is listed after the individual broccoli or onion compounds: benzyl isothiocyanate (broccoli), 1-2; sulforaphane, MeS(O)$(CH_2)_4$N═C═S (broccoli), 0.18; **5b**, 17-19; (*E*)-MeCH═CHS(O)SPr-*n*, 10.4; (*E*,*Z*)-MeCH═CHSS(O)Pr-*n*, 10.4; (*E*,*Z*)-MeCH═CHSS(O)Me, 14.0. While the onion components are nontoxic toward cells at 20 μM and are moderately potent and almost equipotent inducers, comparable or superior to many common olefinic Michael acceptors,[49b] they are less active than the broccoli components.

Experimental Section[50]

1-Propanesulfinyl Chloride (8b).[51a] A stirred mixture of dipropyl disulfide (10 g, 66 mmol) and Ac_2O (13.6 g, 0.132 mol) in CH_2Cl_2 (100 mL) at −10 °C was treated dropwise with SO_2Cl_2 (29.7 g, 0.218 mol), maintaining the temperature at 0−5 °C. The solution at once turned yellow and the color persisted until the addition of sulfuryl chloride was complete. Acetyl chloride and CH_2Cl_2 were removed at room temperature by vacuum distillation (water aspirator; dry ice trap collection of distillate). The residual product was distilled in vacuo giving **8b** as a very pale yellow oil (13.1 g, 79% yield): bp 55 °C/12 mmHg (lit.[51a]: 66 °C/12 mmHg), IR (ν_{max}, neat) 1135 cm^{-1} (S═O), ^{1}H NMR ($CDCl_3$) δ 3.38 (dt, J = 8.5, 1.1 Hz, 2 H), 1.97 (sextet, J = 7.5 Hz, 2 H), 1.13 (t, J = 7.4 Hz, 3 H); ^{13}C NMR δ 66.22, 16.15, 12.97.

(*Z*,*E*)-Propanethial *S*-Oxide (5b). *Caution should be exercised in handling concentrated or neat samples of **5b** and related low molecular weight alkanethial S-oxides as these compounds are intensely (and painfully) lachrymatory!* Propanesulfinyl chloride (13.1 g, 0.10 mol) was added all at once to a stirred solution of Et_3N (10.5 g, 0.10 mol) in diethyl ether (500 mL) at −78 °C. The solution turned white immediately, indicating the presence of Et_3N·HCl, and the mixture began to thicken. The flask was capped and placed in a freezer (−20 °C) overnight. The resultant slurry was then vacuum filtered through a pad of $MgSO_4$ covered with a layer of decolorizing carbon. Extra diethyl ether was used as needed to facilitate removal of the slurry from the flask and filtering. The intensely lachrymatory, pale yellow filtrate was concentrated *in vacuo* (water aspirator) in a water bath (∼20 °C) until one quarter of the volume remained. The water bath was then removed, and the remainder of the mixture was allowed to concentrate *in vacuo* at room temperature (air). Careful inspection of volume and flask temperature was needed as an indication of complete removal of diethyl ether without removal of **5b**. Finally, **5b** was gently bubbled with Ar until all traces of diethyl ether were removed, giving 7.77 g (83%) of the title compound as a light colored oil. When concentrated, **5b** undergoes rapid self-condensation, so neat **5b** should be generated and used as needed. In diethyl ether at −20 °C, **5b** appears to be indefinitely stable. If desired **5b** can be purified by trap-to-trap distillation from −35 °C/0.001 mmHg to −196 °C through wide-bore stopcocks. Compound **5b** shows: MS EI *m/z* (rel intensity) 92 (M + 2, 2), 90 (M+, 32), 41 (100). See Table 1 for ^{1}H, ^{13}C, and ^{17}O NMR data.

Determination of 5b in Onion Sample. A Hamilton Beach Model 395W Juice extractor was employed, affording 87 g of juice from 165 g of sliced, peeled, and trimmed white onion. The juice was saturated with NaCl, allowed to sit for 5 min, vacuum filtered through a bed of Celite, and then extracted twice with equal volumes of freshly distilled diethyl ether. The ether extracts were combined and concentrated at 20 mmHg at room temperature to a volume of 1 mL. Analysis by GC-MS using benzyl alcohol as internal standard indicated 0.4 μmol total thiosulfinate-zwiebelanes and 0.94 μmol total **5b** per g of juice (0.21 μmol total thiosulfinate-zwiebelanes and 0.50 μmol total **5b** per g of fresh weight of onion). Control experiments using synthetic **5b** dissolved in distilled water (5.6 μmol/mL) as well as work done by others[38b] indicate that our **5b** extraction process is rather inefficient. The actual levels of **5b**, which tend to be rather variable, are in the range of 1−20 μmol of total **5b** per g fresh weight of onion.

2-Methyl-2-propyl (*E*,*Z*)-1′-Propenyl Sulfoxide (9b). To a mixture of 2-methyl-2-propyl 1′-propenyl sulfide[52] (13.0 g, 0.1 mol), acetic acid (60 mL), and CH_2Cl_2 (10 mL) at 0 °C was added peracetic acid (35%, 21 mL, 0.11 mol) dropwise with stirring, maintaining the temperature at 0−5 °C during the course of the addition. After completion of the addition, the mixture was warmed to room temperature, stirred for 1 h, then diluted with water (250 mL), and extracted with CH_2Cl_2 (3 × 50 mL). Solid $NaHCO_3$ was added to the organic layer until no more gas evolution occurred, and then the solution was washed with water, dried ($MgSO_4$), and concentrated affording a yellow oil which was distilled to give the title compound (10.5 g, 72% yield) as a colorless oil: bp 85−87 °C/1 mmHg, IR (ν_{max}, neat) 1640 (C═C) and 1036 (s) cm^{-1} (S═O). Chromatographic separation using a Chromatotron (silica gel; ethyl acetate) gave a 3:1 mixture of two isomers, (*E*)-**9b** and (*Z*)-**9b**, with GC retention times of 10.27 and 10.74 min, respectively (30 m × 0.32 mm HP-5 column; 5 min at 50 °C, then 15 °C/min to 200 °C).

(*E*)-9b: Major component; GC retention time 16.2 min (50 °C for 5 min, 5 °C/min to 150 °C); ^{1}H NMR ($CDCl_3$) δ 6.38 (dq, J = 15.2, 6.8 Hz, 1 H), 6.08 (dq, J = 15.2, 1.6 Hz, 1 H), 1.88 (dd, J = 6.8, 1.6 Hz, 3 H), 1.15 (s, 9 H); ^{13}C NMR ($CDCl_3$) δ 138.10, 129.20, 54.22, 22.79, 17.99; EI-MS *m/z* (rel intensity) 146 (M^+, 2%), 90 (P − C_4H_8, 100%), 57 (100%); HRMS molecular weight *m/z* 146.0766 (Calcd for $C_7H_{14}OS$; 146.0765).

(*Z*)-9b: Minor component; GC retention time 17.3 min; ^{1}H NMR ($CDCl_3$) δ 6.31 (dq, J = 10.2, 7 Hz, 1 H), 5.98 (dq, J = 10.2, 1.6 Hz,

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1 H), 1.90 (dd, $J = 7.0$, 1.6 Hz, 3 H), 1.18 (s, 9 H); ^{13}C NMR ($CDCl_3$) δ 139.21, 131.79, 54.80, 22.56, 15.76; EI-MS same as (*E*)-**9b**. Anal. Calcd (found) for $C_7H_{14}OS$: C, 57.49 (57.28); H, 9.65 (9.90).

2-Methyl-2-propyl Vinyl Sulfoxide (9c). To a THF solution of CH_2═CHMgBr (prepared from 0.5 mol each of CH_2═CHBr and Mg turnings using 350 mL of dry THF and decanting the clear supernatant liquid away from accumulated white salts) at −10 °C internal temperature under argon in a 1 L three-necked flask was added dropwise a solution of 2-methyl-2-propanesulfinyl chloride[53] (51 g, 0.37 mol) in THF (125 mL). The brown solution was concentrated *in vacuo*, and the thick brown residue was treated with saturated aqueous NH_4Cl (50 mL) and 1 N HCl (10 mL) and then extracted with $CHCl_3$ (2 × 100 mL). The extract was dried ($MgSO_4$), filtered, and concentrated *in vacuo* and the residue was distilled to afford **9c** (16 g, 35% yield) as a colorless liquid: bp 65−70 °C/2 mmHg, IR (ν_{max}, neat) 1600 (C═C) and 1050 cm^{-1} (S═O), ^{1}H NMR ($CDCl_3$) δ 6.59 (dd, $J = 9.9$, 16.6 Hz, 1 H), 6.09 (d, $J = 16.5$ Hz, 1 H), 6.04 (d, $J = 10.0$ Hz, 1 H), 1.24 (s, 9 H); ^{13}C NMR ($CDCl_3$) δ 136.46, 123.46, 54.46, 22.61; MS *m/z* (rel intensity) 132 (M^+, 6), 76 ($P - C_4H_8$, 25), 57(100). Anal. Calcd (found) for $C_6H_{12}OS$: C, 54.50 (54.48); H, 9.15 (9.29).

FT-MW Spectroscopic Methods. Pyrolysis precursors **9b** or **9c** were placed in a stainless-steel trap pressurized to 20 psi with 4:1 Ne/He. The output mixture from the trap was flowed by way of a 1 mm id quartz capillary tube through a 30.5 cm furnace region maintained at 350 °C. A continuous flow of products was maintained by passing the furnace effluent through one port of a dual flow pulsed valve (described previously[23]) and a bubbler before being exhausted into a hood. A precision double-ended micrometer needle valve located between the pulsed-solenoid valve and the exhaust hood allowed the pressure in the gas line to be adjusted between 1 and 30 psi while maintaining the gas flow at 2−5 mL/min. Spectra were most intense when the precursors of **5a**,**b** were heated to 50 and 60 °C, respectively. Spectral searches were initiated when transitions of the coproduct isobutene were observed. With this flow system, it normally took 4−8 h of conditioning of the gas lines leading from the furnace to the pulse valve in order to see spectral transitions of **5a**,**b**. The deuteration experiments using the precursors were done by putting D_2O (99.9% D; ca. 20 mL) into a 6 L steel cylinder, pressurizing it with Ar or the Ne/He mixture, and flowing this gas through the precursor trap and into the furnace as described above.

The procedure for observing the LF directly from the onion also utilized the flow nozzle. A 4:1 Ne/He stream was used to purge a standard drying tube, which had an outlet coupled to a 30.5 cm tube leading into the pulse nozzle. While purging, a yellow onion was macerated in a kitchen food processor. Then, a toggle valve was closed to isolate the nozzle and the onion mash was placed in the drying tube while maintaining a slow Ne/He flow through the tube. The spectrometer was tuned to rotational transitions of (*Z*)-**5b** and (*E*)-**5b**,[24a] and the spectrum appeared as soon as the toggle valve leading to the nozzle was opened. The intensity of the transition varied considerable from one onion to the next, as well as over time. Figure 1 illustrates the best signal to noise obtained for the $J = 4_{04}$-3_{03} transition of (*Z*)-**5b** at 16783.7989 MHz.[24a] The deuteration of the LF was done in the same manner except that D_2O (ca. 20 mL) was added to the food processor and blended with the onion. The $J = 4_{04}$-3_{03} transition of (*Z*)-**5b**-d_1 at 16674.3963 MHz was monitored.[24a]

FVP-Mass Spectroscopic Study of 9c. At 200−250 °C new species *m/z* 76 (C_2H_4SO) and 56 (C_4H_8) were produced as the parent molecule ion *m/z* 132 disappeared. The decomposition appeared to be clean in this temperature range.

Trapping of Ethenesulfenic Acid (2e) in Solution as Ethyl (*E*)-3-(Vinylsulfinyl)acrylate (10). A solution of **9c** (1 g; 7.5 mmol) in ethyl propiolate (38 mmol) was refluxed under Ar for 20 h. The reaction mixture was concentrated in vacuo and subjected to column chromatography (silica gel; CH_2Cl_2 followed by 1:19 EtOAc/CH_2Cl_2) giving **10** (0.384 g, 29% yield), a yellow liquid; IR (ν_{max}, neat) 1724 (C═O), 1620 (C═C), 1293 (C-O) and 1074 cm^{-1} (S═O), ^{1}H NMR ($CDCl_3$) δ 7.48 (d, $J = 14.9$ Hz, 1 H), 6.60 (dd, $J = 16.5$, 9.6 Hz, 1 H), 6.55 (d, $J = 15.0$ Hz, 1 H), 6.09 (d, $J = 16.6$ Hz, 1 H), 5.93 (d, $J = 9.9$ Hz, 1H), 4.20 (q, $J = 7.1$ Hz, 2 H), 1.26 (t, $J = 7.1$ Hz, 3 H); ^{13}C NMR ($CDCl_3$) δ 163.67, 148.41, 138.74, 124.96, 122.42, 61.32, 14.01; EI-MS, *m/z* (rel intensity) 174 (M^+, 14), 59 (100). Anal. Calcd (found) for $C_7H_{10}O_3S$: C, 48.26 (48.58); H, 5.79 (6.07).

Gas-Phase Pyrolysis of 9c. The pyrolysis apparatus consisted of a 25 cm quartz tube fitted with 14/20 joints containing a thermocouple held against the outside of the tube by a strip of asbestos. The asbestos was covered with coiled nichrome wire wrapped the length of the tube, and this in turn was covered with layers of glass wool and asbestos. A sample of 2 g of **9c** maintained at 30 °C was evaporated during 13 h through the tube, heated to 400 °C, at a pressure of 0.01 mmHg. In a trap cooled by liquid N_2 a colorless, lachrymatory pyrolysate collected. ^{1}H NMR analysis showed this product to consist of isobutene and 95:5 (*Z*)/(*E*) ethanethial *S*-oxide (**5a**).

Gas-Phase Pyrolysis of 9b. Using the procedure described above, pyrolysis of **9b** afforded a mixture of isobutene and 97:3 (*Z*)-/(*E*)-propanethial *S*-oxide (**5b**; by NMR analysis).

Liquid-Phase Pyrolysis of 9b. In a 5 mL flask fitted with a short path distillation head cooled with circulating ice water was placed 0.5 g of **9b**. The flask was heated at 110 °C for 3 h whereupon ca. 0.1 mL of colorless liquid was collected in the receiving flask. Analysis by ^{1}H NMR spectroscopy identified the distillate as principally acetaldehyde.

(*E*,*Z*)-Ethanethial *S*-Oxide (5a). Following the procedure detailed for the preparation of **5b**, ethanesulfinyl chloride[51] (prepared in 94% yield from ethyl thioacetate[51b]) was treated with Et_3N in $CFCl_3$ at −78 °C (4 h) to −20 °C (overnight). Isolation of **5a** was achieved in a manner similar to that for **6** except that the final trap-to-trap distillation was conducted at −40 °C/0.001 mmHg. See Table 1 for ^{1}H, ^{13}C, and ^{17}O NMR data.

(*E*,*Z*)-2-Methylpropanethial *S*-Oxide (5d). Following the procedure described for the preparation of **5b**, 2-methyl-1-propanesulfinyl chloride[51] (prepared in 95% yield from (*Z*)-2-methyl-1-propyl thioacetate[51b]) was treated with Et_3N in $CFCl_3$ at −40 °C (6 h) to −20 °C (overnight). Isolation of **5d** was achieved as described for **5b** except that the final trap-to-trap distillation was conducted at −25 to −30 °C/0.001 mmHg. See Table 1 for ^{1}H, ^{13}C, and ^{17}O NMR data.

(*E*,*Z*)-2,2-Dimethylpropanethial *S*-Oxide (5e). 2,2-Dimethyl-1-propanesulfinyl chloride (5.1 g, 33 mmol; prepared in 83% yield by chlorination of bis(2,2-dimethyl-1-propyl) disulfide[54] in Ac_2O; the sulfinyl chloride had bp 35−45 °C/0.2 mmHg; IR (ν_{max}) 1140 cm^{-1} and ^{1}H NMR ($CDCl_3$) 3.53 (s, 2 H), and 1.18 (s, 9 H)) was treated at −10 °C with Et_3N (3.3 g, 33 mmol) in $CFCl_3$ (125 mL) and kept at −15 °C for 2 days. The nonlachrymatory, rather unstable product was isolated as above with purification by distillation at 10−15 °C/0.01 mmHg. See Table 1 for ^{1}H, ^{13}C, and ^{17}O NMR data.

***trans*-3,4-Diethyl-1,2-dithietane 1,1-Dioxide (12a).** A sample of freshly distilled **5b** was dissolved in twice its volume of freshly dried benzene. The mixture was transferred to a 5 mL vial, flushed with dry argon, stoppered tightly with a rubber septum, and kept in the dark at 5 °C. Several samples were prepared in the same manner, and the progress of the reaction was followed daily by NMR analysis. The samples turned deep yellow after 7 days and NMR analysis showed complete decomposition of **5b**. The yellow solution, now devoid of lachrymatory properties, was concentrated *in vacuo* leaving a yellow oil. The oil was subjected to molecular distillation (50 °C, 10^{-3} mmHg) yielding a practically colorless, clear liquid with a strong onion-like odor. GC analysis showed a single major product with a retention time of 9.45 min at 140 °C (3 mm × 1.2 m, 10% Apiezon L/Chromosorb W column): HRMS molecular weight *m/z* 180.0278 (Calcd for $C_6H_{12}O_2S_2$: 180.0279); UV λ_{max} (C_2H_5OH or hexane) at *ca.* 280 (ϵ 100, sh); IR (ν_{max}, neat) 1139, 1133 cm^{-1} (SO_2). See Table 1 for ^{1}H, ^{13}C, and ^{17}O NMR data.

***trans*-4,5-Diethyl-1,3-dithiolane-2-thione (*trans*-14).** *cis*-3,4-Epoxyhexane (8 g, 80 mmol; bp 78−79 °C), prepared in 80% yield by peracetic acid oxidation at 0 °C of *cis*-3-hexene in CH_2Cl_2,[55] was slowly added to a stirred solution of potassium methyl xanthate (11.2 g, 0.2 mol KOH; 18.24 g, 0.24 mol CS_2; 75 mL of CH_3OH) and the mixture was stored at 25 °C for 6 days. Treatment of the mixture with water

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followed by distillation of the dried and concentrated ether extract afforded the title compound (7.5 g; 49% yield), a yellow liquid, bp 102−104 °C/0.01 mmHg; IR (ν_{max}, neat) 1087 cm^{-1} (C═S); ^{1}H NMR ($CDCl_3$) δ 3.94 (quintet, J = 5.73 Hz, 2 H), 1.98 (m, 4 H), 1.08 (t, J = 7.30 Hz, 6 H); ^{13}C NMR ($CDCl_3$) δ 226.70, 66.72, 27.52, 12.35; EI-MS, *m/z* (rel intensity) 192 (M^+, 100). Small scale purification of *trans*-**14** was achieved with a Chromatotron (silica gel, 7:3 hexane−CH_2Cl_2). HRMS molecular weight *m/z* 192.0103 (Calcd for $C_7H_{12}S_3$; 192.0101).

***d,l*-Hexane-3,4-dithiol (*d,l*-13).** A solution of *trans*-**14** (5 g, 25 mmol) in anhydrous ether (10 mL) was added dropwise with stirring to a slurry of $LiAlH_4$ (1.98 g, 52 mmol) in anhydrous ether (40 mL) contained in a 100 mL three-necked flask at room temperature. The mixture was then cooled to 0 °C, slowly treated with water (*ca.* 5 mL), then acidified with ice-cold 6 N HCl (5 mL), and immediately extracted with ether. The ether layer was washed with saturated aqueous $NaHCO_3$, dried ($MgSO_4$), filtered, and concentrated at atmospheric pressure. The residue was distilled (34 °C, 0.01 mmHg) to afford *d,l*-**13** (2.4 g, 61% yield), a colorless oil with moderate "thiol" odor. GC analysis (100 °C) showed a single component: FT-IR (ν_{max}, neat) 2550 cm^{-1} (SH); ^{1}H NMR (CS_2) δ 2.75 (m, 2 H), 1.62 (m, 4 H), 1.30 (d, 2 H), 1.00 (t, 6 H); ^{13}C NMR (CS_2) δ 56.31, 38.21, 20.08; EI-MS, *m/z* (rel intensity), 150 (M^+, 19), 75 (100). HRMS molecular weight *m/z* 150.0537 (Calcd for $C_6H_{14}S_2$, 150.0537).

***cis*-4,5-Diethyl-1,3-dithiolane-2-thione (*cis*-14).** *trans*-3,4-Epoxyhexane (18 g, 180 mmol, bp 76−77 °C), prepared as above in 90% yield from *trans*-3-hexene, was converted by the above described procedure (25.3 g, 0.45 mol KOH; 41.0 g, 0.54 mol CS_2; 120 mL MeOH) to *cis*-**14** (6.5 g, 20% yield), a yellow liquid, bp 106−108 °C/0.01 mmHg; IR (ν_{max}, $CDCl_3$) 1082, 1058 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 4.20 (m, 2 H), 1.83 (m, 4 H), 1.00 (t, J = 7.35 Hz, 6 H); ^{13}C NMR ($CDCl_3$) δ 227.39, 65.51, 21.81, 12.57; EI-MS, *m/z* (rel intensity) 192 (M^+, 100). Small scale purification of *cis*-**14** was achieved using a Chromatotron (silica gel, 7:3 hexane−CH_2Cl_2). The EI-MS fragmentation pattern was very similar to that for *trans*-**14**. GC retention times for *trans*- and *cis*-**14** are 14.89 and 15.18 min (30 m × 0.32 mm HP-5 column; 5 min at 50 °C, then 15 °C/min to 200 °C), respectively, determined using an isomer mixture. HRMS molecular weight *m/z* 192.0103 (Calcd for $C_7H_{12}S_3$; 192.0101).

***meso*-Hexane-3,4-dithiol (*meso*-13).** A solution of *cis*-**14** (6 g, 21 mmol) in anhydrous ether (15 mL) was added dropwise to a slurry of $LiAlH_4$ (2.28 g, 61 mmol) in ether at 25 °C. Workup as above gave 2.52 g (54% yield) of *meso*-**13** as a colorless liquid, bp 38 °C/0.01 mmHg. GC analysis (100 °C) showed a single peak with retention time of 7.13 min (under these conditions *d,l*-**13** had a retention time of 6.86 min by spiking experiments); FT-IR (ν_{max}, neat) 2550 cm^{-1} (SH); ^{1}H NMR (CS_2) δ 2.74 (m, 2 H), 1.63 (m, 4 H), 1.48 (d, 2 H), 1.03 (t, 6 H); ^{13}C NMR (CS_2) δ 57.80, 35.68, and 19.88; EI-MS, *m/z* (rel intensity), 150 (M^+, 7), 41 (100). HRMS molecular weight *m/z* 150.0537 (Calcd for $C_6H_{14}S_2$, 150.0537).

***d,l*-3,4-Hexanedithiol (*d,l*-13) from *trans*-3,4-Diethyl-1,2-dithietane 1,1-Dioxide (12a).** A solution of **12a** (150 mg; 0.177 mmol) in of anhydrous ether (5 mL) was added dropwise to a slurry of $LiAlH_4$ (42 mg, 1.1 mmol) in ether (15 mL). The reaction generated enough heat to cause a spontaneous gentle reflux. After the addition was complete, the mixture was refluxed for an additional 3 h and cooled to 0 °C. Water was then cautiously added followed by cold 6 N HCl (5 mL), and the mixture was extracted with ether. The ethereal extracts were washed with a saturated solution of $NaHCO_3$ and dried ($MgSO_4$). Concentration gave 22 mg (53%) of hexane-3,4-dithiol which by GC analyzed for 90% of *d,l*-**13**, retention time 6.86 min, and 10% of *meso*-**13**, retention time 7.13 min. The FT-IR, ^{1}H and ^{13}C NMR, and EI-MS data were identical to those for *d,l*-**13**.

***(E,Z)*-(Trimethylsilyl)methanethial *S*-Oxide (5f).** Freshly distilled (trimethylsilyl)methanesulfinyl chloride **8f**[29] (8.0 g, 0.047 mol) was dissolved in dry $CFCl_3$ (100 mL) in a three-necked flask and was cooled to −78 °C under Ar. Dry Et_3N (0.047 mol, 4.75 g) was added dropwise via syringe. A colorless precipitate formed immediately. The reaction mixture was stirred at −78 °C for 4 h and was stored overnight at −20 °C. The mixture was filtered under Ar through a Celite/$MgSO_4$ mixture, and the $CFCl_3$ was removed at 0.01 mmHg at −60 to −30 °C. Compound **3** distilled between −20 and 5 °C as a yellow oil (2.4 g, 38% yield): IR (ν_{max}, CCl_4) 1255, 1200, 1175, and 1040 cm^{-1}. See Table 1 for ^{1}H, ^{13}C, and ^{17}O NMR data.

***trans*-3,4-Bis(trimethylsilyl)-1,2-dithietane 1,2-Dioxide (12b).** A solution of **5f** (1.9 g, 0.014 mol) in $CDCl_3$ (2 mL) was kept at room temperature in a sealed vial for 48 h. Concentration gave a solid which was recrystallized from hexane giving colorless crystals (0.8 g, 42% yield), mp 100−101 °C: IR (ν_{max}, KBr) 1325 (s), 1125 (s) cm^{-1}; MS (field desorption) *m/z* 268 (M^+). See Table 1 for ^{1}H and ^{13}C NMR data.

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