which afforded a single epoxy ketone **18** (Y = O, 80%, mp 84.5-85.5 °C (α), mp 122-123 °C (β)). Olefination of this ketone in ethanol gave the *E*- and *Z*-unsaturated esters **18** (Y = $CHCO_2Et$) in a ratio of 3:1, respectively, whereas in benzene the *Z* isomer was obtained with >95% stereoselectivity, a result which, if similar approach control occurs in both solvents, would be consistent with a more facile collapse of *erythro*- and *threo*-alkoxyphosphonates to starting materials relative to products in going from a polar protic to nonpolar aprotic solvent.[18] On exposure to acid, this *Z* isomer (**18**, Y = $CHCO_2Et$) gave a mixture of hydroxylactones[19] which when treated with base provided triene lactone **6** (mp 111-113 °C). Hydrogenation[15] of this lactone (**6**) afforded lactone **4** (mp 100-102 °C; 57% overall from **18**, Y = O) with >80% stereoselectivity (i.e., 95% stereoselectivity per center). This stereochemical assignment was subsequently confirmed by conversion[16] of lactone **4** into (±)-confertin (**2**, mp 112-113.8 °C).[20]

In summary, the above strategy allows for the stereoselective synthesis of (±)-damsinic acid (**1**) and (±)-confertin (**2**) in ~20% (11 steps) and 5-10% (12 steps) overall yield, respectively, via a readily available and potentially general pseudoguaiane precursor, dienone **7**. Moreover, the methodology used in this approach should be readily adaptable to other objectives in the previously noted families. Further studies are in progress.

Acknowledgment. This work was supported by a Public Health Service Research Grant (Ca 21136) from the National Cancer Institute. We thank Professor Raymond Doskotch for a sample of natural damsinic acid and Professor Martin Semmelhack for a sample of synthetic confertin.

References and Notes

(1) A preliminary account of this work was presented at the 176th National Meeting of the American Chemical Society, Miami Beach, Fla., Sept. 1978; American Chemical Society: Washington, D.C., 1978; ORGN 055.

(2) For representative examples, see Devon, T. K.; Scott A. I. "Handbook of Naturally Occurring Compounds", Academic Press: New York, 1972; Vol. II.

(3) Pertinent recent publications include the following. Pettit, G. R.; Herald, C. L.; Judd, G. F.; Vanell, L. D.; Lehto, E.; Pase, C. P. *Lloydia* **1978**, *41*, 29. Lee, K. H.; Mar, E. C.; Okamoto, M.; Hall, I. H. *J. Med. Chem.* **1978**, *21*, 819. Lee, K. H.; Ibuka, T.; Wu, R. Y.; Geissman, T. A. *Phytochemistry* **1977**, *16*, 1177. Rodriguez, E.; Towers, G. H. N.; Mitchell, J. C. *ibid.* **1976**, *15*, 1573, and references cited therein.

(4) Evans, F. J.; Soper, C. J. *Lloydia* **1978**, *41*, 193.

(5) Previous pseudoguaiane syntheses include damsin (Kretchmer, R.; Thompson, W. J. *J. Am. Chem. Soc.* **1976**, *98*, 3379, and DeClercq, P.; Vanderwalle, M. *J. Org. Chem.* **1977**, *42*, 3447), confertin (Marshall, J. A.; Ellison, R. H. *J. Am. Chem. Soc.* **1976**, *98*, 4312, and Semmelhack, M. F.; Yamashita, A.; Tomesch, J. C.; Hirotsu, J. *ibid.* **1978**, *100*, 5565), damsin, ambrosin, helenalin, and psilostachyin C (Grieco, P. A.; Ohfune, Y.; Majetich, G. *ibid.* **1977**, *99*, 7393, and Ohfune, Y.; Grieco, P. A.; Wang, C.-L. J.; Majetich, G. *ibid.* **1978**, *100*, 5946), and damsinic acid (Lansbury, P. T.; Serelio, A. K. *Tetrahedron Lett.* **1978**, 1909).

(6) This prediction was supported, in part, by pseudoguaiane degradation studies (e.g., Herz, W.; Watanabe, H.; Miyazaki, M.; Kishida, Y. *J. Am. Chem. Soc.* **1962**, *82*, 2601; Joseph-Nathan, P.; Romo, J. *Tetrahedron* **1966**, *22*, 1723; and Herz, W.; Romo de Vivar, A.; Romo, J.; Viswanathan, N. *ibid.* **1963**, *19*, 1359) and our model work (Filosa, M. P. unpublished results) and has been corroborated by recent syntheses.[5]

(7) Wender, P. A.; Filosa, M. P. *J. Org. Chem.* **1976**, *41*, 3490. Cf. ref 8 for an independent study on this and an alternative approach for the preparation of divinylcyclopropanes and related synthetic studies.

(8) (a) Piers, E.; Nagakura, I. *Tetrahedron Lett.* **1976**, 3237. (b) Marino, J. P.; Browne, L. J. *ibid.* **1976**, 3245.

(9) Compounds **9b** and **10b** were prepared using the procedure given in ref 7 from the corresponding cyclopropyl bromides which were synthesized by an adaptation of a method reported by Kitatani, K.; Hiyama, T.; Nozaki, H. *J. Am. Chem. Soc.* **1975**, *97*, 949. These methods consistently gave a mixture containing predominantly the **9b** isomer.

(10) All new compounds reported were homogeneous (TLC and/or VPC) and gave satisfactory IR and NMR spectra and exact mass or combustion analyses.

(11) For related reports on this problem, see ref 8b and Piers, E.; Nagakura, I.; Morton, H. E. *J. Org. Chem.* **1978**, *43*, 3630.

(12) Corey, E. J.; Suggs, J. W. *Tetrahedron Lett.* **1975**, 2547. Suggs, J. W. Ph.D. Thesis, Harvard University, 1976.

(13) The generality of this PCC-based oxidation has not been studied although a recent report suggests that it would also apply to the oxidation of cyclohexa-1,4-dienes (Marshall, J. A.; Wuts, P. G. M. *J. Org. Chem.* **1977**, *42*, 1794).

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(15) The stereochemical outcome of these hydrogenations is sensitive to solvent, catalyst, and temperature variations. For example, hydrogenation of dienone **7** in ethanol gave **17** with ~67% stereoselectivity, while with benzene as solvent **17** was formed with 93% stereoselectivity. Full details will be discussed in a future report.

(16) The methylenation procedure followed that reported by Danishefsky, S.; Kitahara, T.; McKee, R.; Schuda, P. F. *J. Am. Chem. Soc.* **1976**, *98*, 6715. The overall yield for this sequence was typically 50-75%.

(17) The IR, NMR, exact mass, and chromatographic properties of this material were identical in all respects with those of a sample of natural damsinic acid kindly provided by Professor R. W. Doskotch. For studies on the structure of damsinic acid, see Doskotch, R. W.; Hufford, C. D. *J. Org. Chem.* **1970**, *35*, 486.

(18) Wadsworth, W. S.; Emmons, W. D. *J. Am. Chem. Soc.* **1961**, *83*, 1733. Wadsworth, W. S. *Org. React.* **1977**, 25. Asato, A. E.; Liu, R. S. H. *J. Am. Chem. Soc.* **1975**, *97*, 4128.

(19) Bensel, N.; Marschall, H.; Weyerstahl, P. *Tetrahedron Lett.* **1976**, 2293.

(20) The IR, NMR, exact mass, chromatographic properties, and melting point of this material were identical in all respects with those of a sample of synthetic confertin kindly provided by Professor Semmelhack. The mixture melting point was not depressed. A preprint of Professor Semmelhack's synthesis[5] which included X-ray structure determination and references to previous structural work is gratefully acknowledged.

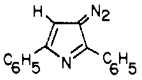
Paul A. Wender,* Michael A. Eissenstat,
Michael P. Filosa
Department of Chemistry, Harvard University
Cambridge, Massachusetts 02138

Received November 27, 1978

Unusual Substituent and Multiplicity Effects in Carbenic Ring Expansion and Substitution Reactions of Benzenes with 3-Diazo-2,5-diphenylpyrrole

Sir:

Reactions of carbenes with benzenoid derivatives have had limited study.[1] We now report that (1) thermolysis and photolysis of 3-diazo-2,5-diphenylpyrrole (**1**) result in ring expansion of benzene (**2a**) and benzenes **2b,c** containing electron-withdrawing substituents to give 1,3-diphenyl-2*H*-cycloocta[*c*]pyrroles **3a–c″**, a new heterocyclic system, whereas benzenes **2d,e** containing electron-donor groups undergo directed substitution to yield 2,3,5-triarylpyrroles **4a–c′** and (2) photosensitization of **1** in **2a** and **2b** leads to aromatic substitution (**4a,d**) rather than ring expansion. The unusual substituent and multiplicity effects in ring expansion and substitution of **2** by **1** contribute to the theory and the synthetic applicability of reactions of carbenes with aromatic substrates.[1]



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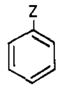

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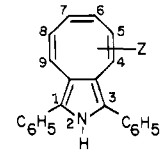

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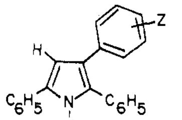

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2a, Z = H
2b, Z = CN
2c, Z = NO_2
2d, Z = OCH_3
2e, Z = CH_3

3a, Z = H
3b-b″, Z = 4,5 and 6-CN
3c-c″, Z = 4,5 and 6-NO_2

4a, Z = H
4b, Z = *p*-OCH_3
4c-c′, Z = *o* and *p*-CH_3
4d, Z = *o*-CN

Thermolysis (175 °C) or photolysis[2] of **1** in benzene (**2a**, 560 equiv) yields 1,3-diphenyl-2*H*-cycloocta[*c*]pyrrole (**3a**, 69%, mp 196.5-197.5 °C, yellow). Similarly, **1** ring expands benzonitrile (**2b**) to 4-, 5-, and 6-cyano-1,3-diphenyl-2*H*-cycloocta[*c*]pyrroles **3b–b″** (47 and 36%).[3] Aromatic substitution of **2b** is not detectable. Further, **1** converts nitrobenzene (**2c**) at 170 °C to 4-, 5-, and 6-nitro-1,3-diphenyl-2*H*-cycloocta[*c*]pyrroles **3c–c″** (32%).[3,4] Pyrroles **3a**, **3b–b″**, and **3c–c″** are assigned from elemental analyses, mass and IR spectra,

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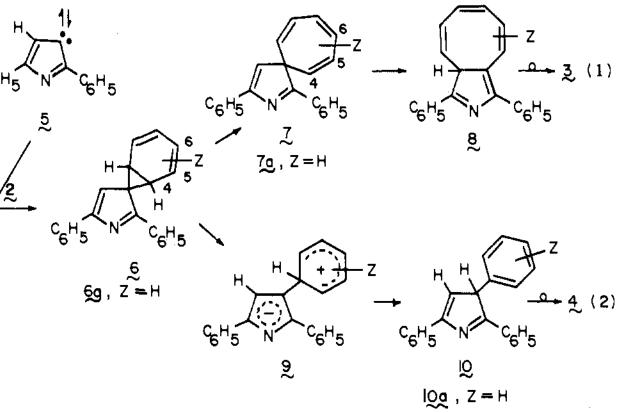
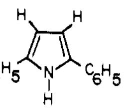
^{1}H NMR olefinic multiplets and olefinic to aromatic proton ratios, the absence of ^{1}H NMR for hydrogen on their pyrrole rings, and ^{13}C NMR.

Conversions of **2a–c** by **1** to **3a–c″** parallel (1) photolysis of 5-*tert*-butyl-3-diazopyrazole in **2a** to yield 2-*tert*-butylpyrazolo[3,2-*a*]azocine (5–10%)[1i] and (2) photolysis of diazocyclopentadiene in **2a** to form spiro[2,4-cyclopentadiene-1,7′-norcaradiene (2′,4′)] which isomerizes to bicyclo[6.3.0]undeca[1^8.2.4.6.9]pentaene.[1d,f] In the present systems, ring expansion to **3** presumably involves decomposition of **1** to singlet 2,5-diphenyl-3*H*-pyrrolylidene (**5**), addition of **5** to **2** to form spironorcaradiene **6**, electrocyclic isomerization to spirocycloheptatriene **7**, (1,5 sigmatropic) rearrangement to **8**, and then hydrogen migration.



Conversions of **2b** and **2c** to their respective three isomeric cycloocta[*c*]pyrroles (**3b–b″** and **3c–c″**) imply that the various isomeric spiropyrrolonorcaradienes (**6**, Z at C-4, C-5, and C-6 are CN and NO_2, respectively) are formed (as syn and/or anti isomers) in each case. Production of **3c″** as the major cycloocta[*c*]pyrrole (60%) from **2c** may be rationalized on the basis that **5**, an electrophile, attacks **2c** selectively at a meta position with preferential ring closure at C-4 to give the spiropyrrolonorcaradiene **6** (Z = NO_2 at C-5) of maximal conjugation.

The reactions of **1** with benzenes containing electron-releasing groups are different from those of **2a–c**. Thermal decomposition or irradiation[2] of **1** in anisole (**2d**) yields 3-(*p*-methoxyphenyl)-2,5-diphenylpyrrole (**4b**, 50 and 43%) and 2,5-diphenylpyrrole (**11**, 16 and 9%).[3] Thermolysis or photolysis[2] of **1** in toluene (**2e**) gives 2,5-diphenyl-3- (*o*- and *p*-tolyl-) pyrrole (**4c–c′**) in 40 and 34% total yields in 1:1:1 ratio with **11** (14 and 6%) and 1,2-diphenylethane (2 and 4%). Synthesis establishes **4b** (mp 116–117 °C), **4c′** (mp 144–145 °C), and **12** (mp 83 °C), **11** is identical with authentic material,[5] and **4c** is assigned from its spectra and by mechanistic principles. There is no evidence for cycloocta[*c*]pyrroles **3** in the reactions of **1** with **2d** or **2e**.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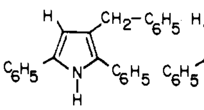
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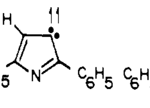
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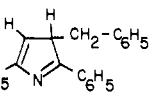
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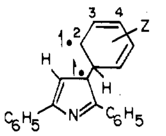
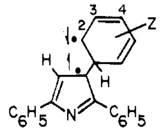
Ortho and/or para substitution rather than ring expansion of **2d** and **2e** is interpretable by selective electrophilic attack of **5** to give spiropyrrolonorcaradienes **6** which collapse to dipolar σ complexes **9** in which generation of the benzenium moieties is controlled by the electron-donor (ortho,para directing) substituents; 1,5-sigmatropic rearrangement(s) of hydrogen possibly via **10** will yield **4**. An alternate to **4** is direct substitution of **2d,e** by **1**. Whatever the timing to **4**, an important mechanistic feature is that spiropyrrolocycloheptatrienes **7** are avoided. That **2d** does not ortho substitute implies that **1** is sensitive to steric and/or field effects.

Pyrrole **11** as obtained from **2d** or **2e** is indicative of triplet 2,5-diphenyl-3*H*-pyrrolylidene (**13**) which abstracts hydrogen from the methyl groups to give the 2,5-diphenyl-1-pyrrolyl radical which in turn abstracts hydrogen.[6] Formation of **12** may result from hydrogen abstraction from **2e**, spin pairing and recombination to yield **14**, and then hydrogen rearrangement. Production of 1,2-diphenylethane, presumably by dimerization of benzyl radicals, indicates further the earlier involvement of **13**. Significant triplet reactions thus accompany the presumed singlet aromatic substitution (and ring expansion) processes.

The behavior of **1** upon photosensitization in **2a** is different from that upon thermolysis or photolysis. Thus photosensitization of **1** with thioxanthen-9-one in **2a** gives **4a** (45%). Irradiation of Michler's ketone in **1** and **2a** yields **4a** along with **11** as major products. Ring expansion to **3a** or products therefrom is not detectable in these experiments.

Photosensitized substitution of **2a** may be rationalized as involving **13** and/or its triplet diazo precursor. A route to **4a** involves addition of **13** to **2a** to give triplet diradical **15**, intersystem crossing to singlet diradical **16**, hydrogen migration to yield **10a**, and then further hydrogen rearrangement (1,5 sigmatropic). An important feature of this sequence is conversion of **15** to **16** and rearrangement rather than ring closure to spironorcaradiene **6a**. To be sure, alternate related mechanisms to **4a** may be envisaged involving addition of the diazo triplet of **1** to **2a** and then loss of nitrogen at various stages. Photolytic conversion of **1** in the presence of Michler's ketone to **11** is also consistent with involvement of **13** which abstracts hydrogen from (the methyl groups of) the photosensitizer to give the 2,5-diphenyl-1-pyrrolyl radical which itself abstracts hydrogen.


15, Z = H
17, Z = 2-CN


16, Z = H
18, Z = 2-CN

The behavior of **2b** with **1** also differs upon photosensitization as compared to photolysis and thermolysis. Thus photosensitization of **1** with thioxanthen-9-one in **2b** results in aromatic substitution to give 3-(*o*-cyanophenyl)-2,5-diphenylpyrrole (**4d**). Neither 3- (*p*- and *m*-cyanophenyl-) 2,5-diphenylpyrroles nor **3b–b″** are detectable. Interestingly, formation of **4d** is rationalizable on the basis of generation of **17** (the triplet diradical of greatest extended conjugation), spin inversion to singlet **18**, and hydrogen migration.

Study of the singlet and triplet reactions of simple carbenes with substituted benzenes is to be initiated.

Acknowledgment. We acknowledge support of this research by the National Cancer Institute (5-R01-CA11185).

References and Notes

(1) (a) M. J. S. Dewar and K. Narayanaswami, *J. Am. Chem. Soc.*, **86**, 2422 (1964); (b) D. Schonleber, *Chem. Ber.*, **102**, 2026 (1969); (c) H. Dürr and L. Schrader, *ibid.*, **102**, 2026 (1969); (d) H. Dürr and G. Scheppers, *ibid.*, **103**, 380 (1970); (e) H. Dürr and G. Scheppers, *Justus Liebigs Ann. Chem.*, **734**, 141 (1970); (f) W. Kirmse, "Carbene Chemistry", Academic Press, New York, 1971, pp 381–395 and references therein; (g) H. Dürr and H. H. Köber, *Tetrahedron Lett.*, 1255, 1259 (1972); (h) H. Dürr, H. Köber, I. Halberstadt, U. Neu, T. T. Coburn, T. Mitsuhashi, and W. M. Jones, *J. Am. Chem. Soc.*, **95**, 3818 (1973); (i) W. L. Magee and H. Shechter, *ibid.*, **99**, 633 (1977).

(2) Effected with a Hanovia 450-W, medium-pressure lamp in Immersion equipment.

(3) Amorphous polar products are also formed from **1** apparently by reaction with **5** and/or the aromatic substrate (**2**).

(4) (a) 3-(*m*-Nitrophenyl)-2,5-diphenylpyrrole (8%) is also produced apparently by acid-catalyzed decomposition of **1** in the presence of **2c** at 170 °C and subsequent cationic substitution of **2c**. (b) Diazonium salts prepared from **1** effect meta substitution of **2c**.

(5) S. Kapf and C. Paal, *Chem. Ber.*, **21**, 3061 (1888).
(6) The 2,5-diphenyl-1-pyrrolyl radical might be converted to **11** by hydrogen transfer to nitrogen and/or by hydrogen abstraction to give 2,5-diphenyl-3*H*-pyrrole and then hydrogen migration.

M. Nagarajan, H. Shechter*
Department of Chemistry, The Ohio State University
Columbus, Ohio 43210
Received July 11, 1978

Structure and Origin of the Onion Lachrymatory Factor. A Microwave Study[1-3]

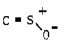
Sir:

A variety of structures have been proposed for the lachrymatory factor (LF) of the onion (*Allium cepa*) since the molecular formula C_3H_6SO was first determined in 1956[4] and the cellular precursor *trans*-(+)-*S*-(1-propenyl)-L-cysteine sulfoxide (**1a**) identified in 1961.[5] Among the possibilities

$RS(O)CH_2CH(NH_2)COOH$
1a R = E-$CH_3CH{=}CH$
b R = $CH_2{=}CH$
c R = $CH_3CH_2CH_2$

$HOCH_2CH_2CHS$
2

(E)-$CH_3CH{=}CHS(O)H$
3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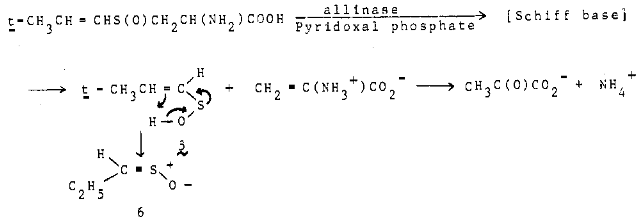
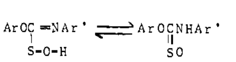
suggested for the LF have been β-hydroxypropanethial (**2**),[4] (*E*)-1-propenesulfenic acid S–H tautomer (**3**),[6] (*E*)-propanethial *S*-oxide (**4**),[7] and an interconverting mixture of the latter two structures.[10] Recently we reported the application of flash vacuum pyrolysis (FVP) spectroscopic approaches to the study of structures related to **2–4**, namely thioformaldehyde, CH_2S,[13] methanesulfenic acid, CH_3SOH,[14] and sulfine, CH_2SO.[2] We now report the application of microwave (MW) and FVP-MW techniques to the characterization of the onion LF, for which we report a revised structure together with a unifying proposal for its genesis. We also report a new synthesis of sulfines discovered during the course of these studies.

Examination by microwave spectroscopy of the LF isolated from onions[15] provided unambiguous evidence that the principal component corresponds to (*Z*)-propanethial *S*-oxide, **6.**

Scheme I



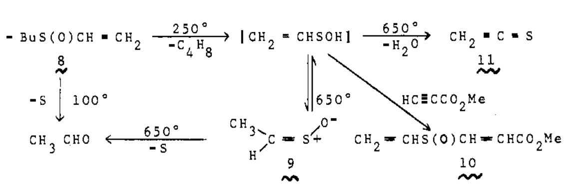
The formation of the LF **6** from precursor **1a** seems best explained by the sequence indicated in Scheme I.[16] It should be noted that the step linking **5** (structure preferred over **3** on the basis of the known structure of CH_3SOH[14]) and **6** requires *Z* stereochemistry in **6**, and that the conversion of **5** to **6** is analogous to the known tautomerism of thioamide *S*-oxides (eq 1).[17]



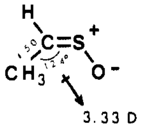
$$\underset{\text{S-O-H}}{\text{ArOC}}{=}\text{NAr}' \rightleftharpoons \text{ArO}\underset{\text{SO}}{\overset{}{\text{C}}}\text{NHAr}' \qquad (1)$$

To test the possibility that 1-alkenesulfenic acids could rearrange to sulfines, we have examined the pyrolysis of (*E,Z*)-2-methyl-2-propyl 1′-propenyl sulfoxide (**7**) and 2-methyl-2-propyl vinyl sulfoxide (**8**).[18,19] We find that both **7** and **8** are efficiently converted by FVP at 250 °C to the respective sulfines **6** and (*Z*)-ethanethial *S*-oxide (**9**), as characterized by both microwave and NMR spectroscopy (see Scheme II).[15] Sulfine **9**, while not of natural origin, is likely formed by the action of onion alliinase on sulfoxide **1b**.[11] Neat **8** decomposes within 4 h at 100 °C to give, among other products, acetaldehyde which we have found to be a major decomposition product of sulfine **9.**[12] At 100 °C a solution of **8** in excess methyl propiolate affords sulfenic acid adduct **10**[19,20] (Scheme II). Finally, under FVP conditions (650–750 °C) microwave analysis indicates that sulfine **9** decomposes to both acetaldehyde and thioketene **11** (Scheme II).[21] We postulate that at these high temperatures **9** is in equilibrium with ethenesulfenic acid which undergoes dehydration to thioketene.[22]

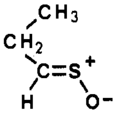
Scheme II



The structures of (*Z*)-ethanethial *S*-oxide (**9**) and (*Z*)-propanethial *S*-oxide (**6**) were determined through analysis of the microwave spectra of the respective normal isotopic species. Since rotational constants are available only for a single isotopic species for each, structural conclusions are based upon the assumption that the -CHSO framework is the same as that of sulfine[2] and that the methyl group are tetrahedral with C–H = 1.093 Å. For **9** a structure fit to the observed rotational constants (with the above constraints) gives C–C = 1.50 Å, ∠CCS = 124°, a *Z* (syn) CCSO arrangement, a dipole moment of 3.33 (2) D, and a CH_3 internal rotation barrier of 0.8 kcal mol^{-1}. There is no microwave evidence for the presence of the *E* (anti) isomer of **9.**



9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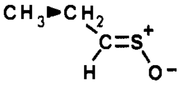
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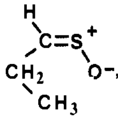
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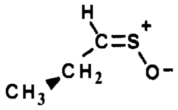
6b

For propanethial *S*-oxide **4** or **6**, without multiple isotopic substitution, only the overall molecular conformation can be determined with certainty. Internal rotation about the CH–CH_2 bond gives this sulfine an additional conformational degree of freedom with the four most likely conformations being *Z* cis (**6a**), *Z* skew (**6b**), *E* cis (**4a**), and *E* skew (**4b**). Assuming the ethanethial *S*-oxide framework determined above, and C–CH_3 = 1.525 Å and ∠CCC = 109.5°, the rotational constants for the four likely conformers **4a**, **4b**, **6a**, and **6b** have been calculated and compared with the observed constants. Only **6b** and **4a** have rotational constants similar to the observed values and of these two only the *Z*-skew rotamer **6b** fulfills the heavy-atom nonplanarity implied by the observed constants. The torsional angle about the CH–CH_2 bond which best reproduces the observed *Z*-skew **6b** rotamer's rotational constants is ~125° (displaced from methyl, S=O cis as in **6b′**), but is uncertain by an estimated ±10° owing to the many structural assumptions involved. The intense torsional satellite