Table VIII. Observed Pseudo-First-Order Rate Constants for the Reaction of Dicofol with Hydroxide Ion in the Presence of NaLS and LCC

10^3[NaLS], M	10^4k_ψ,[a] s^{-1}	10^3[NaLS], M	10^4k_ψ,[a] s^{-1}
	289	7.00	5.98
1.00	224	8.00	4.50
2.00	154	9.00	3.00
3.00	136	10.0	1.75
4.00	85.6	50.0	0.109
5.00	46.3	100	0.074
6.00	29.6		
10^3[LCC], M	10^4k_ψ,[b] s^{-1}	10^3[LCC], M	10^4k_ψ,[b] s^{-1}
	41.8	11.0	47.0
1.00	40.3	13.6	51.0
5.00	41.2	18.2	49.0
9.06	43.0		

[a] At pH 11.0, T = 30.0 °C. [b] At pH 10.34, T = 30.0 °C.

"wash out" hydroxide ion from the micellar surface.

As would be expected from consideration of Hartley's rules,[5] anionic and zwitterionic micelles do not catalyze the reaction of Dicofol with hydroxide ion. Table VIII shows experimental data obtained for various concentrations of NaLS and LCC. The inhibition produced by NaLS is relatively pronounced over the entire concentration range studied. LCC, which is in a zwitterionic form at the pH studied, does not affect the reaction rate to any significant extent. Indeed, the slight increase in the rate constant is in the range normally expected for a nonspecific salt effect.

Since micelles have often been used as elementary membrane models,[5,15,16] it would appear reasonable to suggest, in the light of the described results, that the decomposition of Dicofol leading to the formation of 4,4'-dichlorobenzophenone may proceed via a similar pathway in biological systems. Thus, in the presence of a positively charged biological interface, many of the steps outlined in Scheme I can be disregarded and the formation of DBP can be explained in terms of a process analogous to that reported for CTAB and CHEDAB.

Acknowledgment. The authors gratefully acknowledge financial assistance from the Conselho Nacional de Desenvolvimento Científico e Tecnológico-CNPq (Grants 2222.0070/78 and 1111.5805 to F.N. and Grant 1111.5713 to L.G.I.).

Registry No. Dicofol, 115-32-2; DBP, 90-98-2; chloroform, 67-66-3; CTAB, 57-09-0; CHEDAB, 20317-32-2; NaCl, 7647-14-5; NaBr, 7647-15-6; $NaNO_3$, 7631-99-4; Na_2SO_4, 15124-09-1; NaOTs, 657-84-1.

Carbon-13 Nuclear Magnetic Resonance Spectral Properties of Alkyl Disulfides, Thiolsulfinates, and Thiolsulfonates

S. Woody Bass and Slayton A. Evans, Jr.*

William Rand Kenan, Jr., Laboratories of Chemistry, The University of North Carolina at Chapel Hill, Chapel Hill, North Carolina 27514

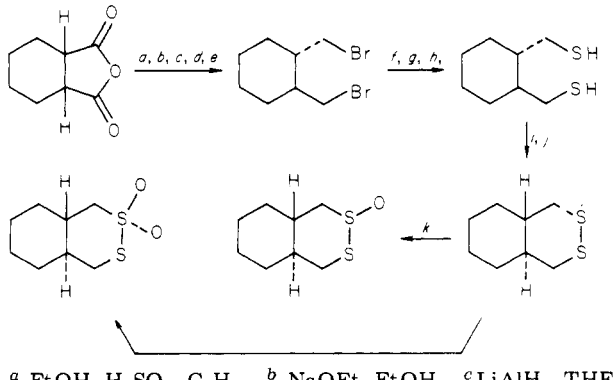
Received July 25, 1979

The ^{13}C nuclear magnetic resonance spectra, as well as substituent effects, of acyclic and some cyclic disulfides, thiolsulfinates, and thiolsulfonates are reported. β_{SO} effects are deshielding and range from 13.2 to 20.6 ppm. β_{SO_2} effects are also deshielding and slightly larger (+22.1 to +26.7 ppm) than the β_{SO} effects. The γ_{SO} values in the acyclic systems are shielding (-3.3 to -6.83) while the γ'_{SO} values reflect a gradual *decrease* in shielding (-8.30 to +2.3). Sulfur lone-pair electron back-donation into the C-S σ^* orbital and/or electron polarization has been proposed to account for this trend in the γ'_{SO} values. The γ'_{SO_2} values are about half the magnitude of the γ'_{SO} values and follow the same trend of decreasing shielding. Additional long-range substituent effects are in harmony with similar effects in other systems and these comparisons are mentioned briefly.

The disulfide bonds of various amino acid residues (e.g., L-cystine) play important roles in maintaining protein structure.[1] Detailed NMR studies designed to reveal conformational preferences about $RS(O)_nSR$ bonds in disulfides (n = 0), thiolsulfinates (n = 1), and thiolsulfonates (n = 2) are fundamentally important for understanding the factors which influence and ultimately control conformational mobility and stability of protein structure. Comparative ^1H and ^{13}C NMR chemical shift data would allow assignments of hydrogens and carbons proximal to the -SS-, -S(O)S-, and $-SO_2S-$ functional groups to be made with a high degree of certainty.[2]

Presently, there are few detailed ^{13}C NMR studies of simple acyclic disulfides and the corresponding oxide derivatives.[3,4] In this report, we have attempted to remedy this situation by describing some useful trends in ^{13}C NMR data obtained from a number of acyclic as well as cyclic

Scheme I



[a] EtOH, H_2SO_4, C_6H_6. [b] NaOEt, EtOH. [c] $LiAlH_4$, THF. [d] p-TsCl, Pyr. [e] LiBr, Me_2SO. [f] $(NH_2)_2C=S$, MeOH. [g] NaOH, reflux. [h] H_2SO_4. [i] $Pb(OAc)_2$, NaOAc. [j] S, C_6H_6. [k] MCPBA, $CHCl_3$. [l] KIO_4, Me_2CO-H_2O.

(1) (a) T. Takagi and N. Ito, *Biochim. Biophys. Acta*, **257**, 1 (1972); (b) Z. Takagi, R. Okano, and T. Miyazawa, *ibid.*, **310**, 11 (1973).

(2) (a) G. Jung, E. Breitmaier, W. Voelter, T. Keller, and C. Tanzer, *Angew. Chem.*, **82**, 882 (1970); *Angew. Chem., Int. Ed. Engl.*, **9**, 894 (1970); (b) E. Breitmaier, G. Jung, and W. Voelter, *Angew. Chem.*, **83**, 659 (1971); *Angew. Chem., Int. Ed. Engl.*, **10**, 673 (1971).

(3) See S. W. Bass and S. A. Evans, Jr., 175th National Meeting of the American Chemical Society, Anaheim, CA, Mar 13-17, 1978, No. ORGN 148.

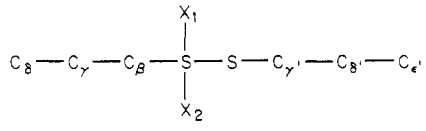
(4) T. Takata, Y. H. Kim, and S. Oae, *Tetrahedron Lett.*, 4303 (1978).

0022-3263/80/1945-0710$01.00/0

disulfides, thiolsulfinates, and thiolsulfonates. Our goal is to provide useful correlative ^{13}C NMR data which can be used in assessing the degree of oxidation of the -SS- component of a disulfide by observing the magnitudes of the ^{13}C NMR shift differences.[5]

Syntheses. All of the dialkyl disulfides are commercially available or can be prepared by a number of conventional synthetic routes.[6] Commercial bis(2-methyl-2-propyl) disulfide (**4**) contains 12% bis(2-methyl-2-propyl) trisulfide (**22**), and homogeneous samples of both substances can be obtained by preparative GLC techniques.[7] Procedures for preparing the corresponding dialkyl thiolsulfinates and thiolsulfonates as well as 1,2-dithiane (**6**) and its oxide derivatives (**13** and **20**) are described in the Experimental Section. The preparations of *trans*-2,3-dithiadecalin (**7**) and its 2-oxide, **14**, and 2,2-dioxide, **21**, are summarized in Scheme I.

NMR Spectra. The ^{13}C NMR chemical shift assignments were made by off-resonance decoupling techniques and by observation of the expected downfield shifts due to changes in the electronegativity of divalent sulfur upon oxidation to the sulfinyl and sulfonyl functions.[8] The carbons of interest are labeled as β, γ, γ', δ, δ', and ϵ' with respect to the lone-pair electrons or the oxygen substituent(s) on sulfur as described below.



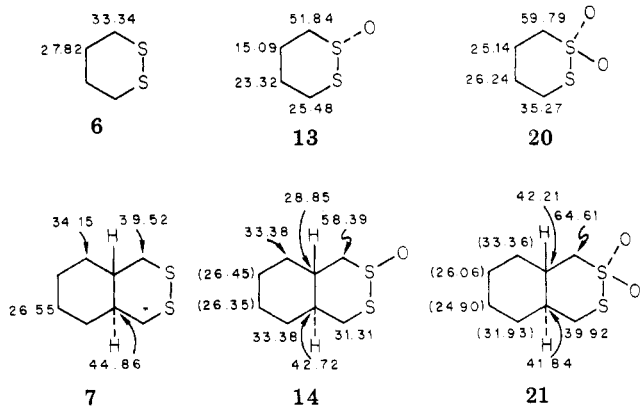
X_1 = X_2 = lone pair electrons (disulfide)

X_1 = X_2 = oxygen atom (thiolsulfonate)

X_1 = oxygen atom; X_2 = lone pair electrons (thiolsulfinate)

β_{SO} and β_{SO_2} Effects. Oxidation of the disulfide linkage to the thiolsulfinate group results in the expected deshielding of the C_β carbon, affording β_{SO} values ranging from 13.2 to 20.6 ppm (Table II). This β_{SO} effect, where $\beta_{SO} = \delta_{C_\beta}$(thiolsulfinate) - δ_{C_β}(disulfide), arises from an inductive effect caused by the partial positive charge on the sulfinyl sulfur[8] combined with the β effect from the sulfinyl oxygen atom.[9] This trend of *less deshielding* or diminishing β_{SO} values with increased alkyl substitution (second column, Table II) is entirely consistent with previous observations involving ^{13}C NMR shifts in branched alkyl-substituted hydrocarbons[10a] and alkylthioacetaldehyde dimethyl acetals and the *S*-oxide derivatives.[10b] In the latter study, the suggestion is made that increased steric congestion involving C_β will diminish significantly the deshielding contribution of a β-substituent effect. This phenomenon is clearly evident in substituted cyclohexanes where the sterically congested axial substituents *deshield* C_β *less* than in the equatorial epimers.[11] Although we were unsuccessful in our preparation of *both* thiolsulfinates of

Chart I[a]



[a] ^{13}C NMR absorptions which exhibit similar chemical shifts and could not be accurately assigned are parenthesized. All chemical shifts are given in δ units.

14, we were able to assign the stereochemistry of the sulfinyl oxygen of the crystalline material (mp 64.5–66 °C) obtained by oxidation of **7** as axial, **14β**. This assignment is reasonable and consistent with the magnitudes of ^{13}C chemical shift differences at both C_β and C_γ of conformationally homogeneous sulfoxides and the parent sulfides[12] (see Chart I).

The β_{SO} effect (18.5 ppm) resulting from oxidation of 1,2-dithiane, **6** → **13**, is virtually identical with the β_{SO} effect (18.87 ppm) obtained in the comparison of C_β from **7** to **14**. Dithiadecalin **7** and the axial 2-oxide, **14β**, are conformationally homogeneous, and the nearly identical β_{SO} values imply that the conformationally mobile dithiane oxide **13** must exist exclusively with the sulfinyl oxygen in the axial conformation at ambient temperature. This conclusion corroborates an earlier ^1H NMR experiment by Harpp et al.[13] where it is estimated that the axial sulfinyl oxygen atom stability in **13** is >2 kcal/mol over that of the equatorial sulfinyl oxygen atom. This result is not particularly surprising since increased thermodynamic stability favoring the axial sulfinyl oxygen in both **13** and **14** is predicted on the basis of the tenets of the gauche effect.[14]

Oxidation of the disulfide to the thiolsulfonate (-SS- → -SO_2S-) results in substantial deshielding of C_β: β_{SO_2} [=δ_{C_β}(thiolsulfonate) - δ_{C_β}(disulfide)] ranges from 21.9 to 26.7 ppm (column eight, Table II). The magnitudes of the β_{SO_2} values observed for these systems are generally 2–3 ppm larger than those in some acyclic organosulfur compounds.[9,10b] The increased inductive effect of the sulfonyl group and the double β effect of the two oxygen atoms on C_β are clearly evident from the magnitude of β_{SO_2} as compared to β_{SO}: β_{SO_2} - β_{SO} ranges from 5.2 to 8.0 ppm. In acyclic sulfoxides and sulfones, β_{SO_2} - β_{SO} is normally quite

(5) G. G. Freeman and F. McBreen, *Biochem. Soc. Trans.*, 1, 1150 (1973).

(6) (a) L. Field and Y. H. Kim, *J. Org. Chem.*, **37**, 2710 (1972); (b) I. D. Rae and P. M. Pojer, *Tetrahedron Lett.*, 3077 (1971); (c) C. N. Yiannios and J. V. Karabinos, *J. Org. Chem.*, **28**, 3246 (1963).

(7) See Experimental Section for details.

(8) J. B. Lambert, D. A. Netzel, H. Sun, and K. K. Lilianstrom, *J. Am. Chem. Soc.*, **98**, 3778 (1976).

(9) The comparison of β effects derived from an oxygen atom bonded to sulfur and an oxygen atom bonded to carbon has been previously mentioned: see G. Barbarella, P. Dembech, A. Garbesi, and A. Fava, *Org. Magn. Reson.*, **8**, 108 (1976).

(10) (a) For a theoretical assessment of the effects of alkyl substitution of ^{13}C shifts, see J. Mason, *J. Chem. Soc. A*, 1038 (1971); (b) S. S. McCrachren and S. A. Evans, Jr., *J. Org. Chem.*, **44**, 3551 (1979).

(11) (a) J. B. Stothers, C. T. Tan, and K. C. Teo, *Can. J. Chem.*, **54**, 1211 (1976); (b) D. G. Gorenstein, *J. Am. Chem. Soc.*, **99**, 2254 (1977).

(12) (a) The differences in γ_{SO} effects between axial and equatorial sulfoxides are considerably larger than the differences in β_{SO} effects and can be more effectively employed as probes for sulfoxide stereochemistry. For example, in the bicyclic system *trans*-1-thiadecalin 1-oxide with an axial sulfinyl oxygen the γ carbons are shielded by 12.9 and 12.5 ppm while the γ carbons for the equatorial isomer are shielded by 5.5 and 6.5 ppm relative to the sulfide. Thus, the γ_{SO} value of -16.0 ppm resulting from the comparison between C_γ in **7** and **14** is entirely consistent with an axial sulfinyl oxygen atom.[17b] (b) R. P. Rooney and S. A. Evans, Jr., *J. Org. Chem.*, in press. (c) See also, G. W. Buchanan and T. Durst, *Tetrahedron Lett.*, 1683 (1975).

(13) D. N. Harpp and J. G. Gleason, *J. Org. Chem.*, **36**, 1314 (1971).

(14) (a) S. Wolfe, *Acc. Chem. Res.*, **5**, 102 (1972). (b) S. Wolfe, L. M. Tel, J. H. Liang, and I. G. Csizmadia, *J. Am. Chem. Soc.*, **94**, 1361 (1972). (c) The relative high stability of **14β** is also in keeping with our unsuccessful attempts to equilibrate the axial isomer with the equatorial one (**14α**) by using procedures which are known to catalyze the equilibration of sulfoxides. See K. Mislow, T. Simmons, J. T. Melillo, and A. L. Ternay, Jr., *J. Am. Chem. Soc.*, **86**, 1452 (1964).

small, ranging from −2 to +2 ppm.[9,10b] As with the thiolsulfinates, it seems clear that as the steric congestion about C_β increases, β_{SO_2} tends to diminish. This point has been previously made by Fawcett et al.[15] in their ^{13}C NMR study of acyclic sulfones.

γ Effects. The effects of the sulfinyl and sulfonyl groups on C_γ shifts are shielding, with γ_{SO} values of −2.2 to −6.3 ppm. The chemical shift differences for γ carbons in the disulfide–thiolsulfinate comparisons where R = Et, *i*-Pr, and *t*-Bu are nearly constant (−6.4 ppm average), but the difference diminishes for R = *i*-Bu (−3.3 ppm). This deviation from the average γ_{SO} value for the compound where R = *i*-Bu is surprising since the dialkyl disulfides show dihedral angles not much different from 90°,[16] and the corresponding thiolsulfinates are predicted to exhibit dihedral angles near 60°.[17] From the existing data it is not clear to us at the present time why the γ_{SO} effect resulting from the **5** → **12** conversion is not similar to the case where R = Et. γ_{SO} doubles when a six-membered-ring disulfide is oxidized to a thiolsulfinate, **6** → **13** (−12.72 ppm), and increases by more than 2.5 times for the conversion **7** → **14** (−16.01 ppm). To our knowledge, this latter γ_{SO} value is the *largest reported upfield shift of a carbon γ gauche to a sulfinyl oxygen atom.* Even though thiolsulfinate **14** is conformationally homogeneous and **13** is nearly so (vide supra), it is evident that the sulfinyl oxygen has a more pronounced effect on a tertiary, rigid carbon atom than on a flexible secondary carbon.

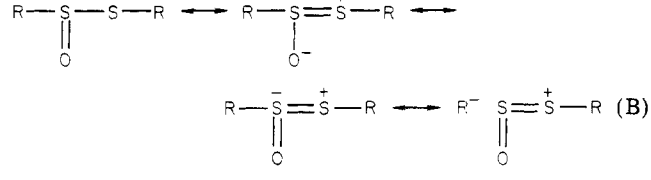
In 2-propyl 2-propanethiolsulfinate (**10**), the diastereotopic isopropyl C_γ methyls are evidence of the chiral sulfinyl sulfur[18] and exhibit a chemical shift difference of 0.93 ppm. On the other hand, the $C_{\delta'}$ isopropyl methyls are farthest from the chiral center, and the degree of anisochronism is, as expected, small ($\Delta\delta$ = 0.11 ppm).[19]

The nature of the shielding contributions to both gauche and antiperiplanar γ effects is not well understood, although several proposals of general applicability, including (a) steric shift effects,[20] (b) electric field effects,[12c,21] and (c) hyperconjugative interactions,[22] have been advanced.

With exception of R = *t*-Bu, the γ'_{SO} effects are largely shielding in both the cyclic and acyclic disulfide–thiolsulfinate comparisons (γ'_{SO} ranges from −2.9 to −10.0 ppm). In the acyclic systems, γ'_{SO} is largest for R = Me in the **1** → **8** conversion (−8.30 ppm) and then diminishes to the extent that γ_{SO} (−6.83 ppm) and γ'_{SO} (−6.0 ppm) for R = Et are coincidentally similar. Actually, close inspection of column five of Table I reveals that the γ'_{SO} effects gradually decrease or become *less shielding* throughout the series as the steric bulk of the substituent, R, increases. The shielding and deshielding contributions to both γ_{SO} and γ'_{SO} are complex and involve variations in the γ gauche relationships between alkyl fragments (from RSSR to RS(O)SR) as well as carbon–sulfinyl oxygen interactions. However, in an attempt to explain the gradual increase in the deshielding component of γ'_{SO} in the Me → *t*-Bu series, the results of a number of theoretical calculations on the conformational preferences of dialkyl disulfides have been useful. The suggestion is made that hyperconjugation, which affords a mechanism for π bonding between sulfurs, is believed to be enhanced when the p orbital of the unshared electron pair on one sulfur is coplanar with the S–R bond of the other sulfur.[23] Essentially equivalent to this model is one based on a stabilizing back-donation of the lone-pair electrons on sulfur into the antibonding S–R σ* orbital at the other end of the molecule[23] as shown in A. With this background, we suggest that as the torsional

$$R{-}S{-}S{-}R \leftrightarrow R^- S{=}S^+{-}R \qquad (A)$$

angle increases from 60° in the thiolsulfinates[17] as a result of increased steric requirements of the larger alkyl groups, contributions from hyperconjugation or stabilizing back-donation also increase and become maximized as the torsional angle approaches 90°. The net effect would be to gradually reduce the magnitude of the γ'_{SO} shielding effect due to the increased inductive effect at $C_{\gamma'}$ through structures like B.[24] The influence of structures depicted in B has been invoked to explain trends in solvent-depedent UV studies of alkyl and aryl thiolsulfinates.[24]



In the cyclic thiolsulfinates where there is considerably less tendency of the C–S(O)–S–C fragment to assume a torsional angle greater than 60°, the shielding contribution of γ'_{SO} predominates apparently resulting from inefficient sulfur–sulfur orbital interactions: γ'_{SO} = −7.86 ppm for the **6** → **13** conversion and −8.21 ppm for **7** → **14**.

Table I. ^{13}C NMR Spectra of Alkyl Disulfides,[a] Thiolsulfinates and Thiolsulfonates (RXSR)

	X	R	C_β	C_γ	C_δ	$C_{\gamma'}$	$C_{\delta'}$	$C_{\epsilon'}$
1	S	Me	22.04					
2		Et	32.82	14.50				
3		*i*-Pr	41.14	22.60				
4		*t*-Bu	45.63	30.51				
5		*i*-Bu	48.60	28.21	21.78			
8	SO	Me	42.66			13.74		
9		Et	49.88	7.67		26.81	16.26	
10		*i*-Pr	55.26	15.70		38.27	24.57	
				16.63			24.68	
11		*t*-Bu	58.81	24.01		47.93	32.20	
12		*i*-Bu	65.18	24.92	21.58	41.54	26.69	21.66
					22.52			
15	SO_2	Me	48.74			18.23		
16		Et	56.94	8.31		30.54	15.12	
17		*i*-Pr	63.25	16.26		42.70	24.22	
18[b]		*t*-Bu	68.02	23.74		56.29	31.52	
19		*i*-Bu	70.48	25.21	22.48	44.57	28.90	21.68

[a] In the disulfide series, C_β, C_γ, and C_δ are referenced to the lone pair of electrons on sulfur. [b] Private communication from Professor John Kice.

(15) A. H. Fawcett, K. J. Ivin, and C. D. Stewart, *Org. Magn. Reson.*, 11, 360 (1978).
(16) (a) N. A. Rosenthal and G. Oster, *J. Am. Chem. Soc.*, **83**, 4445 (1961); (b) H. Bock and G. Wagner, *Angew. Chem., Int. Ed. Engl.*, 11, 150 (1972).
(17) P. Dembech, P. Vivarelli, V. Jehlicka, and O. Exner, *J. Chem. Soc., Perkin Trans. 2*, 488 (1973).
(18) J. L. Kice and G. B. Large, *J. Am. Chem. Soc.*, **90**, 4069 (1968).
(19) The ^1H NMR spectrum of **10** in the presence of a shift reagent has been examined previously: see L. E. Legler, S. L. Jindal, and R. W. Murray, *Tetrahedron Lett.*, 3907 (1972).
(20) B. V. Cheney and D. M. Grant, *J. Am. Chem. Soc.*, **89**, 5319 (1967).
(21) J. G. Batchelor, *J. Am. Chem. Soc.*, **97**, 3410 (1975).
(22) E. L. Eliel, W. F. Bailey, L. D. Kopp, R. L. Willer, D. M. Grant, R. Bertrand, K. A. Christensen, D. K. Dalling, M. W. Duch, E. Wenkert, F. M. Schell, and D. W. Cochran, *J. Am. Chem. Soc.*, **97**, 322 (1975).
(23) (a) D. B. Boyd, *J. Am. Chem. Soc.*, **94**, 8799 (1972); (b) D. B. Boyd, *Theor. Chim. Acta*, **30**, 137 (1973); (c) G. Winnewisser, M. Winnewisser, and W. Gordy, *J. Chem. Phys.*, **49**, 3465 (1968).
(24) (a) H. J. Backer and H. Bloosterziel, *Recl. Trav. Chim. Pays-Bas*, 73, 129 (1954). (b) Chemical evidence which might be considered supportive of structures represented as B comes from the reaction of 1-methyl-1,2-dithianyl 2,4,6-trinitrobenzenesulfonate ($TNBS^-$) with 2,3-dimethyl-1,3-butadiene to give *cis*-1,3,4-trimethyl-6-thia-1-thiona-3-cyclodecene ($TNBS^-$). See N. E. Hester, G. K. Helmkamp, and G. L. Alford, *Int. J. Sulfur Chem., Part A*, 1, 65 (1971).

Table II. ^{13}C NMR Substituent Effects from Oxidation of Disulfides to Thiolsulfinates and Thiolsulfonates[a]

R	β_{SO}	γ_{SO}	δ_{SO}	γ'_{SO}	δ'_{SO}	ϵ'_{SO}	β_{SO_2}	γ_{SO_2}	δ_{SO_2}	γ'_{SO_2}	δ'_{SO_2}	ϵ'_{SO_2}
Me	20.62			−8.30			26.70			−3.81		
Et	17.06	−6.83		−6.01	1.76		24.12	−6.19		−2.28	0.62	
i-Pr	14.12	−6.43[b]		−2.87	2.03[b]		22.11	−6.34		1.56	1.62	
t-Bu	13.18	−6.50		2.30	1.69		22.39	−6.77		10.66	1.01	
i-Bu	16.58	−3.29	0.27[b]	−7.06	−1.52	−0.12[c]	21.88	−3.00	0.70	−4.03	0.69	−0.10

[a] The substituent effects (e.g., β_{SO}, γ_{SO}, β_{SO_2}, γ_{SO_2}, etc.) are calculated as $\Delta\delta = \delta_C(\text{-SS(O)}_n\text{-}) - \delta_C(\text{-SS-})$, where $n = 1$ or 2. See text for explanation of C_β, C_α, etc. [b] The substituent effect is based on an average value for the diastereotopic methyl resonances. [c] The $C_{\epsilon'}$ methyls in **12** are equivalent.

The γ_{SO_2} effect (Table II, column 9) is largely shielding, and for the four entries the values mirror the γ_{SO} values for R = Et, *i*-Pr, *t*-Bu, and *i*-Bu. This trend is expected, since in other acyclic organosulfur systems, the γ_{SO_2} effects are only marginally different from the γ_{SO} effects.[9,10b] However, in the comparisons of the NMR shift of C_γ, going from the cyclic disulfides to the cyclic thiolsulfonates, γ_{SO_2} = −2.68 ppm for **6** → **20** and −2.65 ppm for **7** → **21**. These values are considerably smaller than the γ_{SO} values for these systems but the diminished γ_{SO_2} effects are in agreement with what is observed in *trans*-1-thiadecalin, *trans*-1,4-dithiadecalin, *trans*-1,4-oxathiadecalin, and the corresponding sulfones.[12b] The γ_{SO_2} value is also smaller than the γ_{SO} value in the conformationally homogeneous 9-thiabicyclo[3.3.1]nonane and the *S,S*-dioxide derivative.[25]

The γ'_{SO_2} effects (Table II, column 11) are only slightly shielding for R = Me and Et, reflecting less than half of the magnitude of the γ'_{SO} values. The γ'_{SO_2} effects show a progressive decrease in shielding as the steric bulk of the substituent increases, and this is maximized when R = *t*-Bu (γ'_{SO} = +10.66 ppm). Since the trend in γ'_{SO_2} values is similar to that of the γ'_{SO} values, it seems likely that the hyperconjugation and/or polarization of the sulfur lone-pair electrons toward the sulfonyl group would develop electropositive character at $C_{\gamma'}$ in a manner analogous to that described previously for the trend in γ'_{SO} values.[23,24]

In both the 1,2-dithiane and the *trans*-1,2-dithiadecalin systems, γ'_{SO_2} effects are slightly *deshielding* and imply that possible inductive withdrawal of electrons at $C_{\gamma'}$ is perhaps more important than contributions from γ gauche shielding schemes between sulfonyl oxygen and carbon. Qualitatively, Drieding molecular models show that the distance between the sulfonyl oxygen and C_γ is about 3.3 Å, while the sulfonyl oxygen–$C_{\gamma'}$ distance is 3.8 Å, assuming chair conformations for **20** and **21**. The greater distance between S–O and $C_{\gamma'}$ is undoubtedly related to the absence of a sizeable γ gauche shielding effect.

δ Effects. Only in the case where R = *i*-Bu is there a δ_{SO} effect. The average chemical shift of the diastereotopic $C_{\delta'}$ methyls is δ 22.05, and this represents only a marginal downfield shift of 0.27 ppm for comparisons of **5** to **12**. The magnitude and sign of the δ_{SO} effect here are in keeping with what is known about the influence of substituents on ^{13}C shifts separated by four bonds. A syn axial array of substituents tends to deshield the terminal carbon, and this phenomenon has been well documented for methyl hydroxyl interactions in conformationally rigid systems.[26] We anticipate that a similar effect will ensue when similar substituents assume 1,3-syn axial arrays in conformationally mobile systems.

In general, the δ'_{SO} values for the acyclics reflect deshielding and average less than 2 ppm. The diastereotopic $C_{\delta'}$ methyls of **10** have an average absorption of δ 24.63, and they are shielded by 2.03 ppm when compared to disulfide **3**. The δ'-carbon chemical shift for the comparison of **5** to **12** indicates a net shielding effect. In the cyclic systems, δ'_{SO} values are largely negative. In 1,2-dithiane 1-oxide, $C_\delta \equiv C_{\delta'}$, and therefore, $\delta_{SO} \equiv \delta'_{SO}$ = −4.50. Similarly, in 2,3-dithiadecalin 2-oxide, C_δ and $C_{\delta'}$ are also identical and γ gauche to the electropositive sulfinyl sulfur, giving $\delta_{SO} = \delta'_{SO}$ = −2.14. The remaining δ carbon (C_8) in this bicyclic system is γ anti to the sulfinyl sulfur in **14β** and is shielded to a lesser extent: δ_{SO}(anti) = −0.77.[27] Lambert et al.[8] have demonstrated that the δ-carbon chemical shift of a series of pentamethylene heterocycles vs. electronegativity gives basically a straight line of negative slope (approximately −8 ppm/electronegativity unit). This indicates that an increase in the electronegativity of the α heteroatom results in an upfield shift at C_δ.

The substituent effects at C_δ and $C_{\delta'}$ upon oxidation of –SS– to –SO_2S– in the acyclic series are deshielding, with values varying from 0.7 to 1.6 ppm. In the cyclic systems, the reverse is true. For example, in the comparison of C_δ in **6** and **20**, $\delta'_{SO_2} = \delta_{SO_2}$ = 26.24 − 27.82 = −1.58 ppm, while for **7** and **21**, $\delta'_{SO_2} = \delta_{SO_2}$ = −3.02 ppm at C_{10}, and the δ_{SO_2} effect at C_8 is −0.79 or −2.22 ppm.

ϵ Effects. Only one ϵ'_{SO} (−0.12 ppm) and one ϵ'_{SO_2} (−0.10 ppm) effect are reported, and these two values are shielding for R = *i*-Bu. The effects are small and imply, as expected, that oxidation at sulfur to either the sulfinyl or sulfonyl derivative hardly affects the chemical shift of $C_{\epsilon'}$.

Experimental Section

Melting points were obtained in a Mel-Temp melting point apparatus with an open capillary tube and are uncorrected.

Microanalyses were performed by Galbraith Laboratories, Inc., and Integral Microanalytical Laboratories, Inc.

Infrared spectra were obtained as thin films or solutions and were recorded on Perkin-Elmer Model 257 and 421 IR spectrophotometers with polystyrene (1601.4 cm^{-1}) as external reference.

Gas–liquid partition chromatography (GLC) analyses were performed on a Hewlett-Packard Model 5754B research gas chromatograph. Technical grade bis(2-methyl-2-propyl) disulfide (**4**) was purchased from Aldrich Chemical Co. Homogeneous samples of disulfide **4** and trisulfide **22** were obtained by preparative GLC separation of technical grade **4** on a Varian Aerograph Series 2700 gas chromatograph (20% UC-W98 on Chromosorb W, 200 °C column temperature).

Thin-layer chromatography (TLC) was performed on neutral alumina (Woelm, ICN Pharmaceuticals) or silica gel (Silicar TLC-7GF) plates (20 × 10 cm). Visualization of the separated components was accomplished in iodine vapor chambers.

^1H NMR spectra were recorded on Varian Model XL-100-12 and Perkin-Elmer Model R24B NMR spectrometers. ^{13}C NMR

(25) J. R. Wiseman, H. O. Krabbenhoft, and B. R. Anderson, *J. Org. Chem.*, **41**, 1518 (1976).

(26) (a) S. H. Grover, J. P. Guthrie, J. B. Stothers, and C. T. Tan, *J. Magn. Reson.*, **10**, 227 (1973); (b) J. B. Stothers and C. T. Tan, *Can. J. Chem.*, **54**, 917 (1976).

(27) P. K. Claus, W. Rieder, and F. W. Vierhapper, *Monatsh. Chem.*, **109**, 631 (1978). These authors note that δ carbons in thiane and thiadecalin-1-imides are shielded when compred to the starting sulfide, and the magnitudes of the shielding appear to be independent of the stereochemistry of the *N*-aryl imide group. This is also the case for C_δ in the axial and equatorial conformers of thiane 1-oxide compared to thiane.[12c]

Table III. ^1H and ^{13}C NMR Spectra of 22 and 23 (δ)

	^{13}C				^1H[a]	
compd	C-S	C-SO_2	$(CH_3)_3CSO_2$	$(CH_3)_3CS$	$(CH_3)_3CS$	$(CH_3)_3CSO_2$
22	48.45			29.81	1.36	
23	49.97	70.12	24.29	29.92	1.38	1.43

[a] In ref 33, the ^1H NMR spectrum of 23 is reported as δ 1.42 for $(CH_3)_3CS$ and 1.47 for $(CH_3)_3CSO_2$ in carbon tetrachloride. The differences observed here are probably the result of a solvent effect.

Fourier transform spectra were recorded on the Varian Model XL-100-12 NMR spectrometer controlled by a 620/f computer. All Fourier transform spectra were based on 8K data points with noise decoupling. All ^1H and ^{13}C chemical shifts of samples as 5–15% (w/w) deuteriochloroform ($CDCl_3$) solutions are presented in parts per million (δ) downfield from internal tetramethylsilane (Me_4Si). ^1H NMR absorptions are designated as follows: s = singlet, d = doublet, q = quartet, t = triplet, m = multiplet, and dd = doublet of doublets.

General Preparative Procedure for Acyclic Thiolsulfinates and Thiolsulfonates. The following procedure was used to prepare methyl methanethiolsulfinate, ethyl ethanethiolsulfinate, 2-propyl 2-propanethiolsulfinate, and 2-methyl-1-propyl 2-methyl-1-propanethiolsulfinate (**8**, **9**, **10**, and **12**) and methyl methanethiolsulfonate, ethyl ethanethiolsulfonate, and 2-methyl-1-propyl 2-methyl-1-propanethiolsulfonate (**15**, **16**, and **19**).

General Procedure. A solution of *m*-chloroperoxybenzoic acid (MCPBA) (1 equiv for formation of the thiolsulfinate and 2 equiv for the thiolsulfonate) in chloroform (100 mL) was added dropwise (1 h) to a solution of the disulfide (1 equiv) in chloroform (200 mL) at 0 °C (ice bath). The solution was stirred for 1–3 h and washed with a saturated solution of sodium bicarbonate (100 mL) and water (100 mL), and the resulting chloroform solution was dried (Na_2SO_4). Removal of the solvent (rotary evaporator) afforded the thiolsulfinate or thiolsulfonate as an oil. Purification by distillation at reduced pressure afforded the product (60–80% yield).[28]

2-Propyl 2-propanethiolsulfonate (**17**) was prepared by using the procedures published by Buckman et al.,[28e] while a number of reports have successfully detailed the preparation of 2-methyl-2-propyl 2-methyl-2-propanethiolsulfinate (**11**).[28b,c,f] *trans*-2,3-Dithiadecalin (**7**) was prepared in acceptable yield by procedures previously described by Casey and Martin[29] and a modification of the procedures presented by Cragg and Weston.[30] A useful synthesis of 1,2-dithiane has been reported by Claeson et al.[31a] and more recently by Field and Barbee[31b] while Harpp and Gleason[32] have reported the preparation of 1,2-dithiane 1-oxide.

Isolation of Bis(2-methyl-2-propyl) Trisulfide *S,S*-Dioxide (23) from the Oxidation of Commercial Bis(2-methyl-2-propyl) Disulfide (4). A commercial sample of **4** (17.8 g) was dissolved in acetic acid (150 mL), dioxane (150 mL), and 12 M HCl (50 mL). Anhydrous tungsten(VI) oxide (93 mg, 4.0 mmol) (heated previously at 110 °C for ca. 15 h) was added and the mixture heated to 50 °C. Hydrogen peroxide (35 mL of 30% H_2O_2 solution, 300 mmol) was added and the mixture stirred for 24 h. The acid was slowly neutralized with a saturated solution of sodium bicarbonate and the mixture extracted with chloroform (2 × 200 mL). The organic layer was dried (Na_2SO_4) and the solvent removed under reduced pressure (rotary evaporator). TLC analysis (silica gel, hexane as eluent) showed at least three components; the two with the highest R_f values were easily identified as disulfide **4** and trisulfide **22** by comparison with authentic material while the third component was attributed to product. The reaction mixture was separated into its components by using column chromatography [silica gel, hexane–benzene–ethyl acetate (3:1:1 by volume) as eluent]. One of the colorless solid components isolated from the column was identified as **23**: mp 61–62 °C;[33] IR ($CHCl_3$) 2963, 2928, 2900, 2860, 1362, 1319 (SO_2), 1261, 1160, 1116 (SO_2), 1024 cm^{-1}. Anal. Calcd for $C_8H_{18}O_2S_3$: C, 39.64; H, 7.48; S, 39.68. Found: C, 39.58; H, 7.61; S, 39.55.

***trans*-2,3-Dithiadecalin (7).** *trans*-1,2-Bis(mercaptomethyl)cyclohexane (24.4 g, 0.138 mol) was dissolved in 50 mL of benzene and added to a vigorously stirred solution of lead(II) acetate (55.0 g, 0.145 mol) in 150 mL of water. The bright yellow precipitate was filtered and dried at 80 °C (2 torr) to afford 50.7 g (96.1%) of dithiolate. The dithiolate (50.0 g, 0.132 mol) was suspended in 300 mL of benzene and added to a solution of sulfur (4.30 g, 0.133 mol) in 40 mL of carbon disulfide. The mixture was stirred for 1.5 h, and finally the lead sulfide was filtered. The organic phase was concentrated (rotary evaporator) to approximately 100 mL and dried (Na_2SO_4), and the solvent was removed (rotary evaporator) to afford an oil which subsequently crystallized at −20 °C. Purification by recrystallization from a solution of 3:1 hexane–methanol provided homogeneous **7**: mp 56.5–57.5 °C;[34] ^1H NMR ($CDCl_3$) δ 2.46 (m, 4 H, CH_2S), 1.0–2.0 (br m, 10 H, CH_2's); IR ($CHCl_3$) 2920, 2890, 2850, 1402, 1228 cm^{-1}.

***trans*-2,3-Dithiadecalin 2β-Oxide (14).** A solution of MCPBA (406 mg of 85% reagent, 2.00 mmol) in 30 mL of chloroform was added dropwise (1 h) to a solution of *trans*-2,3-dithiadecalin (349 mg, 2.00 mmol) in 30 mL of chloroform at 0–5 °C (ice bath). The mixture was stirred for 1 h, washed with a saturated solution of sodium bicarbonate (50 mL) and water (50 mL), and then dried (Na_2SO_4), and the solvent was removed (rotary evaporator) to afford a residue. Partial purification by recrystallization from hexane gave 204 mg (53.6%) of **14**. However, sublimation (55 °C, 2 torr) of crude **14** gave homogeneous **14**: mp 64.5–66.0 °C; ^1H NMR ($CDCl_3$) δ 2.5–4.1 (br band, 4 H, $CH_2S(O)SCH_2$), 2.0–2.5 (br band, 2 H, $CHCH_2S(O)SCH_2CH$), 0.7–2.0 (br band, 8 H, CH_2's); IR ($CHCl_3$) 2945, 2858, 1445, 1418, 1400, 1312, 1298, 1262, 1235, 1175, 1133 (S=O), 1056, 1010, 833 cm^{-1}. Anal. Calcd for $C_8H_{14}SO_2$: C, 50.49; H, 7.41; S, 33.69. Found: C, 50.11; H, 7.31; S, 33.40.

***trans*-2,3-Dithiadecalin 2,2-Dioxide (21).** *trans*-2,3-Dithiadecalin (470 mg, 2.66 mmol) was dissolved in dioxane (40 mL) and added to a stirred aqueous solution (30 mL) of potassium metaperiodate (2.52 g, 11.0 mmol). The mixture was stirred at ambient temperature for 4 days and then extracted with chloroform (2 × 50 mL). The organic layer was washed with water (50 mL), dried (Na_2SO_4), and concentrated to give 680 mg of a yellowish solid. Sublimation (50 °C, 1 torr) afforded 398 mg of a colorless solid: mp 78.5–79.0 °C; mass spectrum (70 eV) molecular ion at *m/e* 206; ^1H NMR ($CDCl_3$) δ 2.9–3.4 (br band, 4 H, $CH_2SO_2SCH_2$), 2.1–2.3 (br band, 2 H, $CHCH_2SO_2SCH_2CH$), 0.9–2.0 (br band, 8 H, CH_2); IR ($CHCl_3$) 2938, 2860, 1452, 1348, 1337, 1314 (SO_2), 1136 (SO_2), 1178, 1062, and 828 cm^{-1}.

Acknowledgment is made to the University of North Carolina's Research Council, North Carolina Science and Technology Committee, for support of this work. We are grateful to Professor John Kice for communicating his experimental procedures for the preparation of sulfonate

(28) (a) L. D. Small, J. H. Bailey, and C. J. Cavallito, *J. Am. Chem. Soc.*, **69**, 1710 (1947); (b) R. W. Murray and S. L. Jindal, *J. Org. Chem.*, **37**, 3516 (1972); (c) T. L. Moore and D. E. O'Connor, *ibid.*, **31**, 3587 (1966); (d) D. Barnard, *J. Chem. Soc.*, 4673 (1957); (e) J. D. Buckman, M. Bellas, H. K. Kim, and L. Field, *J. Org. Chem.*, **32**, 1626 (1967); (f) I. B. Douglass and R. V. Norton, *ibid.*, **33**, 2104 (1968); (g) H. S. Schultz, H. B. Freyermuth, and S. R. Buc, *ibid.*, **28**, 1140 (1963); (h) L. Field and T. F. Parsons, *ibid.*, **30**, 657 (1965).

(29) J. P. Casey and R. B Martin, *J. Am. Chem. Soc.*, **94**, 6141 (1972).

(30) R. H. Cragg and A. F. Weston, *Tetrahedron Lett.*, 655 (1973).

(31) (a) G. Claeson, G. Androes, and M. Calvin, *J. Am. Chem. Soc.*, **83**, 4357 (1961); (b) L. Field and R. B. Barbee, *J. Org. Chem.*, **34**, 36 (1969).

(32) D. N. Harpp and J. G. Gleason, *J. Org. Chem.*, **36**, 1314 (1971).

(33) Block has previously demonstrated that **23** also results from the thermal degradation of **11**. See E. Block and J. O'Connor, *J. Am. Chem. Soc.*, **96**, 3929 (1974).

(34) G. M. Whitesides and F. D. Gutowski, *J. Org. Chem.*, **41**, 2882 (1976).

18 as well as its ^{13}C NMR chemical shifts. We also thank Dr. David L. Harris, Mrs. Susan Morris-Natschke, and Mr. John C. Dyer for recording numerous ^{1}H and ^{13}C spectra related to this work. Purchase of the NMR instrument was made possible by NSF Instrument Grant No. GU-2059,2059-Amendment I and GP-37602 and by NIH Grant No. 5S05RR07072.

Registry No. 1, 624-92-0; 2, 110-81-6; 3, 4253-89-8; 4, 110-06-5; 5, 1518-72-5; 6, 505-20-4; 7, 20268-02-4; 8, 13882-12-7; 9, 18542-39-7; 10, 38739-06-9; 11, 31562-40-0; 12, 72360-72-6; 13, 7153-76-6; 14, 72360-73-7; 15, 2949-92-0; 16, 682-91-7; 17, 10027-69-7; 18, 31562-41-1; 19, 59917-29-2; 20, 18321-15-8; 21, 72360-74-8; 22, 4253-90-1; 23, 52754-01-5; *trans*-1,2-bis(mercaptomethyl)cyclohexane, 72401-49-1; *trans*-1,2-bis(mercaptomethyl)cyclohexane diacetate, 72360-75-9; *trans*-2,3-dithiadecalin, 20268-02-4.

Asymmetric Induction in Liquid Crystals: Optically Active *trans*-Cyclooctene from Hofmann Elimination in New Cholesteric Mesophases

Patrick Seuron and Guy Solladie*

Laboratoire de Chimie Organique de l'Ecole Nationale Supérieure de Chimie, ERA du CNRS No. 687, Université Louis Pasteur, BP 296/R8-67008 Strasbourg, France

Received June 7, 1979

Optically active *trans*-cyclooctene was obtained by Hofmann elimination of trimethylcyclooctyl ammonium hydroxide in new cholesteric liquid crystals. The extent of asymmetric induction rose 7%. Enantiomeric equilibration of racemic *trans*-cyclooctene in cholesteric medium, at 180 °C, leads to a 2% enantiomeric excess. These asymmetric induction results are interpreted in terms of solute–solvent interactions enhanced by the local ordering of the mesophase.

Recently several papers pointed out a large controversy on the possibility of controlling the stereochemistry of reactions by a chiral organized medium such as cholesteric liquid crystals.

On one hand, several research groups reported moderate extents of asymmetric induction during high-temperature reactions conducted in cholesteric mesophases such as the Claisen rearrangement of *O*-allyl aryl ethers,[1] enantiotopic decarboxylation,[2] or enantiomeric equilibration of sulfoxides.[3]

On the other hand, Kagan and co-workers[4] did not succeed in reproducing these literature results and reported no detectable asymmetric induction during several photochemical processes. On the basis of these results these authors concluded by stating that they doubted that a cholesteric mesophase could afford appreciable asymmetric induction and that the effect of mesomorphic anisotropy ordering on asymmetric induction remains to be clearly established.

In this paper, we report our own results, dealing with Hofmann pyrolysis of quaternary ammonium salts in cholesteric medium and enantiomeric equilibration of *trans*-cyclooctene. We also offer evidence that the stereochemical outcome of the reactions conducted in liquid crystals is dependent on the nature of the mesophase. All these results suggest that the asymmetric induction is governed by the "local" asymmetry of the mesophase.

Results

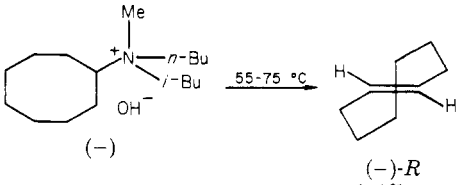
Our first work using cholesteric liquid crystals as solvent was actually a pyrolysis study of *N*-amine oxides. By heating *N*,*N*-dimethyl-4-methyl and *N*,*N*-dimethyl-4-*tert*-butylcyclohexylamine *N*-oxide in cholesteryl benzoate and propionate, we did not detect any significant optical activity in the produced substituted cyclohexene. Table I reports some of our results.

This absence of asymmetric induction is consistent with the results obtained by Dewar,[7] during a study of Claisen rearrangements in nematic liquid crystals, who claimed that the orientation effect of the mesophase should have a very small effect on intramolecular rearrangements.

For this reason we turned our attention to the Hofmann degradation of quaternary ammonium salts which proceeds by polar transition states and so could be more sensitive to a liquid crystal environment.

Since the pionneering work of Cope,[8] *trans*-cyclooctene can be produced by Hofmann elimination of a cyclooctyl quaternary ammonium salt.

(−)-*trans*-Cyclooctene (1.4% ee) was also obtained by Cope[9] by pyrolysis of a chiral cyclooctylammonium hydroxide as the result of a chirality transfer from the asymmetric nitrogen atom to the dissymetric cyclooctene.



(−) (−)-*R*
1.4% ee
34/66 cis/trans

(1) F. D. Saeva, P. E. Sharpe, and G. R. Olin, *J. Am. Chem. Soc.*, **97**, 204 (1975).
(2) L. Verbit, T. R. Halbert, and R. B. Patterson, *J. Org. Chem.*, **40**, 1649 (1975).
(3) W. H. Pirkle and P. L. Rinaldi, *J. Am. Chem. Soc.*, **99**, 3510 (1977).
(4) C. Eskenazi, J. F. Nicoud, and H. B. Kagan, *J. Org. Chem.*, **44**, 995 (1979).
(5) G. Belluci, G. Ingroso, A. Marsili, E. Mastrorilli, and J. Morelli, *J. Org. Chem.*, **42**, 1079 (1977).
(6) G. Berti and G. Belluci, *Tetrahedron Lett.*, 3853 (1964).
(7) M. J. S. Dewar and B. D. Nahlovsky, *J. Am. Chem. Soc.*, **96**, 460 (1974).
(8) A. C. Cope, K. Banholzer, F. N. Jones, and H. Keller, *J. Am. Chem. Soc.*, **88**, 4700 (1966).
(9) A. C. Cope, W. R. Funke, and F. B. Jones, *J. Am. Chem. Soc.*, **88**, 4693 (1966).
(10) A. C. Cope and B. A. Pawson, *J. Am. Chem. Soc.*, **87**, 3649 (1965).

0022-3263/80/1945-0715$01.00/0