the spatially more distant 2′-methyl is expected as a result of a small but significant methyl exchange rate at this temperature (23°).

Solvent effects were semiquantitatively examined by comparison of the line widths of the exchange broadened di-*o*-methyls of II-OH at several temperatures. At +10°, the half-height line widths in CD_2Cl_2 and DMSO-d_6 were 5.50 and 5.15 Hz, respectively, and at ambient temperature in CD_2Cl_2, $CDCl_3$, and DMSO, 2.90, 4.20, and 2.65 Hz at 100 MHz. These differences represent rate variations of less than a factor of about 3, and for this range of solvent polarities are considered insignificant.

The effect of the presence of carbonium ion on the exchange process of II-OH was examined by combining equimolar amounts of this carbinol (δ(av CH_3 at 30°) = 2.1) and its carbonium ion tetrafluoroborate (δ(30°) = 1.90). The line widths of the CH_3's of II-OH (9.5 and 17.5 Hz at 100 MHz in CD_2Cl_2 at +1.5 and −8°, respectively) are close to those expected for the carbinol alone. It was further noted that the addition of a fractional equivalent of CF_3COOH to II-OH near −10° generated an observable amount of the carbonium ion distinct from carbinol for which the line width was approximately that expected for II-OH alone in CD_2Cl_2.

Acknowledgment. We thank D. Dix for assistance in carrying out and interpreting the nuclear Overhauser experiment.

Nuclear Magnetic Resonance Studies on the Conformations of 2-Substituted 1,3-Oxathiolanes

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Murray Hill, New Jersey. *Received February 24, 1970*

Abstract: From analysis of coupling constants for a series of 2-substituted and 2,2-disubstituted 1,3-oxathiolanes, it has been possible to conclude that there is one highly preferred conformation but that rapid pseudorotation is occurring. The latter is confirmed by a low-temperature nmr study of 2-ethyl-1,3-oxathiolanes. The envelope conformations (**1** and **2**) most consistent with the observed coupling constants for monosubstituted oxathiolanes have the R group directed away from the center of the ring with either C-5 or O-1 as the flap atom. Postulated collision complexes based on these conformations explain the observed solvent shifts.

Low barriers to pseudorotation and the consequent profusion of nearly equi-energy conformers complicate the conformational analysis of five-membered rings,[2a] thus accounting for the dearth of information on such materials. Particularly lacking are data on five-membered sulfur-containing heterocycles.

On the basis of a derived barrier height of 2.8 kcal/mol for thiophane[2b] and assuming distorted cyclopentane geometries, conformational calculations indicated the C_2 form should be favored over the C_s conformer.[3] This low barrier for thiophane pseudorotation has been supported by recent studies,[4] and similar results were found for pyrrolidine and tetrahydrofuran.

Recent X-ray diffraction studies of ethylene sulfate indicate C_2 symmetry in the solid state with the C–C bond forming an angle of 20.6 ± 0.5° with the ring OSO plane.[5] The thiophane ring of the 1 : 1 thiophane–bromine complex appears planar on single crystal X-ray analysis, but this is attributed to the superposition of images from two static or dynamically interconverting C_s ring enantiomers.[6] By contrast in the crystal structure of cholestan-4-one-3-spiro(2,5-oxathiolane) the oxathiolane ring exists in a slightly distorted envelope conformation with the methylene carbon atom adjacent to oxygen lying 0.5 Å out of the plane defined by the other four atoms and with a torsional angle of 34.3° between the two carbon atoms.[7] The conclusion that 2-substituted 1,3-oxathiolanes exist in an envelope conformation not undergoing pseudorotation and with the oxygen atom out of the plane of the other atoms was reached by Pasto and coworkers upon interpretation of nmr spectra.[8]

Our conformational studies of the highly flexible 2-substituted 1,3-oxathiolane ring system were undertaken in order to understand some reactions of these compounds,[9,10] but we were also aware of the potential to obtain information about the pseudorotation of the ring afforded by the magnetically nonequivalent protons of the insulated ethylene group in the chiral molecule. Thus our studies were designed not only to define a dominant conformation of 1,3-oxathiolanes if any existed, but also to determine whether rapid pseudorotation were occurring on the nmr time scale.

Results

2-Ethyl-1,3-oxathiolane. The nmr spectrum of 2-ethyl-1,3-oxathiolane at 60 MHz in carbon tetrachloride

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[1] (a) Polytechnic Institute of Brooklyn; (b) Bell Telephone Laboratories.

[2] (a) See, for example, E. L. Eliel, N. L. Allinger, S. J. Angyal, and G. A. Morrison, "Conformational Analysis," Wiley, New York, N. Y., 1965, Chapter 2; C. Romers, C. Altona, H. R. Buys, and E. Havinga, "Topics in Stereochemistry," E. L. Eliel and N. L. Allinger, Ed., Vol. 4, Interscience, New York, N. Y., 1969, Chapter 2; (b) W. N. Hubbard, H. C. Finta, D. W. Scott, J. P. McCullough, C. Katz, M. E. Gross, J. F. Messerly, R. E. Pennington, and G. Waddington, *J. Amer. Chem. Soc.*, **74**, 6025 (1952).

[3] K. S. Pitzer and W. E. Donath, *ibid.*, **81**, 3213 (1959).

[4] G. A. Crowder and D. W. Scott, *J. Mol. Spectrosc.*, **16**, 122 (1965).

[5] F. P. Boer, J. J. Flynn, E. T. Kaiser, O. R. Zaborsky, D. A. Thomalia, A. E. Young, and Y. C. Tong, *J. Amer. Chem. Soc.*, **90**, 2970 (1968).

[6] G. Allegra, G. E. Wilson, Jr., E. Benedetti, C. Pedone, and R. Albert, *ibid.*, **92**, 4002 (1970).

[7] A. Cooper and D. A. Norton, *J. Org. Chem.*, **33**, 3535 (1968).

[8] D. J. Pasto, F. M. Klein, and T. W. Doyle, *J. Amer. Chem. Soc.*, **89**, 4368 (1967).

[9] G. E. Wilson, Jr., *ibid.*, **87**, 3785 (1965).

[10] G. E. Wilson, Jr., and M. G. Huang, unpublished data.

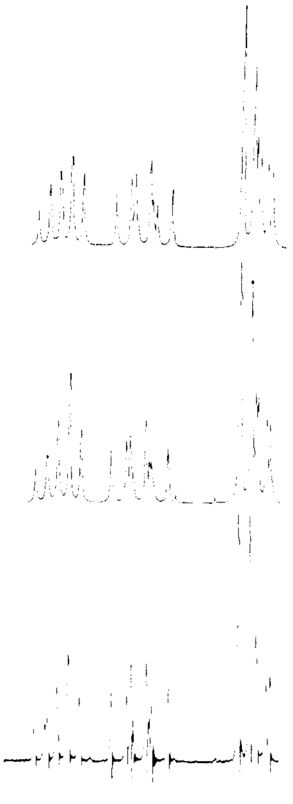

Figure 1. AMXY portion of 60-MHz spectrum of 2-ethyl-1,3-oxathiolane in CCl_4: top, calculated using Pasto's parameters; center, calculated, this work; bottom, observed.

shows a complex pattern for the ethylene grouping typical of an AMXY system. The positions of the centers of the resonances and the multiplet shapes are changed by the addition of benzene, but simplification does not occur. Spin decoupling of a 100-MHz spectrum in deuteriochloroform by irradiation in the region of the methylene next to sulfur caused the AM portions to collapse to a simple quartet with $J_{gem} \simeq 9.2$ Hz. Irradiation of the A and M portions resulted in simplification of the upfield resonances, but without the formation of an easily deciphered pattern. The 60-MHz spectrum of 2-ethyl-1,3-oxathiolane-5,5-d_2 showed a single envelope for the methylene next to sulfur with a half-width of 2.47 Hz. Allowing for the H–D coupling, this result is still clearly incompatible with the values 177.76 and 173.75 Hz calculated by Pasto, Klein, and Doyle for these protons.[8] Furthermore, even a 220-MHz spectrum was too complex to solve by first-order techniques. The chemical shifts and coupling constants were derived by computer from the spectral data for 2-ethyl-1,3-oxathiolane (Figure 1) and are tabulated in Table I together with those of Pasto and coworkers.[8] Figure 1 shows the fit of the 60-MHz spectrum calculations compared to those of Pasto.[11] Particularly significant in verifying the derived values for 2-ethyl-1,3-oxathiolane are the two weak combination peaks which appear downfield of the main CH_2S multiplet in both the calculated and observed spectra (see Figure 1). These peaks, which are expected in such a tightly coupled system, became apparent only when a good fit had been obtained.

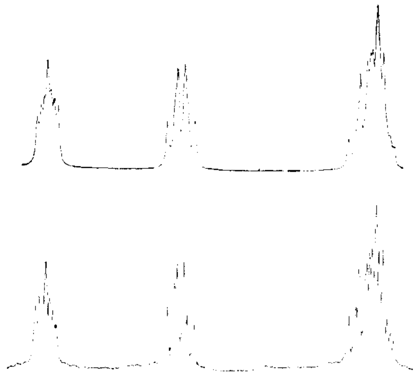

Figure 2. Calculated (top) and observed (bottom) 220-MHz spectrum of ethylene protons of 2-ethyl-1,3-oxathiolane in C_6D_6.

Table I. Chemical Shifts (Hertz) and Coupling Constants for 2-Ethyl-1,3-oxathiolane

		60 MHz	
	220 MHz[a]	This work[b]	Ref 8[b]
δ_{H_1}	933.35	255.69	254.98
δ_{H_2}	815.08	222.97	221.71
δ_{H_3}	645.74	176.187	177.76
δ_{H_4}	644.96	176.184	173.75
J_{12}	−9.29 ± 0.4	−9.28 ± 0.1	−8.99
J_{13}	3.71 ± 0.3	4.01 ± 0.1	4.40
J_{14}	5.47 ± 0.3	5.44 ± 0.1	4.96
J_{23}	3.79 ± 0.3	4.37 ± 0.1	6.13
J_{24}	10.63 ± 0.3	10.36 ± 0.1	8.05
J_{34}	−9.28 ± 0.4	−10.06 ± 0.1	−9.95

[a] Run in $CDCl_3$. [b] Run in CCl_4.

The 220-MHz spectrum of 2-ethyl-1,3-oxathiolane (Figure 2) was solved in parts. Successive approximations to the downfield portions were made using LAOCN3.[12] However, when LAOCN3 was used in the final minimizations, and all parameters were free to be adjusted, divergence occurred. Thus, the approximate values obtained from LAOCN3 were used with NMRIT[13] to obtain the best fit. A similar procedure was used in other cases as necessary when initial trials with either LAOCN3 or NMRIT led to false minima. Final minimizations for 2-phenyl- and 2-ethyl-1,3-oxathiolane in benzene were obtained using LAOCN3. For the others NMRIT was used. In the assignment of resonances in different solvents (Table II) a constancy in spatial relationship between numbered protons is implied except for 2-methyl-2-phenyl-1,3-oxathiolane where we feel no clear choice can be made for assigning δ_3 and δ_4. By successive additions of benzene to a carbon tetrachloride solution of the oxathiolane we established for 2-ethyl-1,3-oxathiolane that the order of the downfield resonances (δ_1 and δ_2) is independent of solvent.

The spectrum of 2-ethyl-1,3-oxathiolane in carbon disulfide was investigated as a function of temperature. The results are presented in Table III. Figures 3 and 4 present experimental and calculated spectra for 2-*n*-propyl-1,3-oxathiolane and 2-methyl-2-phenyl-1,3-oxathiolane, respectively.

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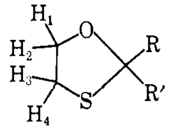
(11) Spectra were drawn with a Calcomp 27 using a program (LORE) which sums Lorentzian curves substituted for each calculated spectral line.

(12) S. Castellano and A. A. Bothner-By, *J. Chem. Phys.*, 41, 3853 (1964). We wish to thank Professor Bothner-By for making the latest version of his program available to us.

(13) J. D. Swalen and C. A. Reilly, *J. Chem. Phys.*, 37, 21 (1962). This program was obtained from the Quantum Chemical Program Exchange, Bloomington, Ind.

Table II. Chemical Shifts and Coupling Constants (Hz) for Some 1,3-Oxathiolanes



R	R'	Solvent	ν_0, MHz	δ_1	δ_2	δ_3	δ_4	J_{12}	J_{13}	J_{14}	J_{23}	J_{24}	J_{34}	Error
Et	H	$CDCl_3$	220	4.24	3.70	2.935	2.932	−9.29	3.71	5.47	3.79	10.63	−9.28	±0.4
		CCl_4	60	4.26	3.71	2.936	2.936	−9.28	4.01	5.44	4.37	10.36	−10.06	±0.1
		PhH	220	3.90	3.36	2.556	2.625	−8.89	2.96	6.41	5.93	9.19	−9.56	±0.07
n-Pr	H	CCl_4	60	4.27	3.72	2.973	2.974	−9.04	3.92	5.28	4.36	10.02	−9.52	±0.06
t-Bu	Me	CCl_4	60	4.28	3.95	2.914	2.829	−9.15	2.27	6.36	4.65	10.31	−10.25	±0.05
		PhH	60	3.98	3.70	2.563	2.564	−9.25	2.43	5.87	5.09	10.10	−10.31	±0.07
Ph	CH_3	CCl_4	60	4.08	3.73	2.953	2.77	−9.22	6.59	4.41	7.79	6.18	−10.02	±0.06
		PhH	60	3.93	3.67	2.76	2.59	−9.23	6.55	4.62	7.71	6.15	−10.22	±0.04
Ph	H	PhH	220	3.96	3.39	2.56	2.73	−8.59	2.79	6.72	6.51	8.39	−9.31	±0.1

Table III. Temperature Dependence of the Spectrum of 2-Ethyl-1,3-oxathiolane in CS_2 at 60 MHz

T, °C	δ_1, Hz	δ_2, Hz	δ_3, Hz	δ_4, Hz	J_{12}	J_{13}	J_{14}	J_{23}	J_{24}	J_{34}
Ambient	250.76	218.91	174.68	174.16	−8.72	3.02	5.11	4.79	9.47	−9.25
−50	254.13	215.50	174.98	174.01	−8.78	2.97	5.26	4.49	10.44	−9.30
−90	259.24	215.86	176.56	175.10	−9.17	2.5	5.46	4.49	10.98	−9.3

Discussion

Pseudorotation of the 1,3-oxathiolane ring system may be considered as the process by which the dihedral angle ψ_1, between the C_5–O and C_4–S bonds (see Figure 5), varies between extreme values about −40 and +40°[14] with the dihedral angle ψ_2 between the C_2–S and C_4–C_5 bonds remaining positive for the larger part of one traverse for ψ_1 and negative for the larger part of the return. For convenience of analysis, several points, defined by the values of ψ_1 and ψ_2, representing envelope conformations **1**–**4** and **1a**–**4a** along this pathway, may be singled out for detailed consideration. These envelopes, any of which might represent a good model for a local minimum in the energy surface for pseudorotation, are passed in the order **2** → **1** → **5a** → **4a** → **3a** → **2a**, for one-half of a complete cycle. Ring conformers *i* and *j* with $\psi_{1i} = -\psi_{1j}$ and $\psi_{2i} = -\psi_{2j}$ bear an enantiomeric relationship to each other, and thus we may divide all the ring conformers into two enantiomeric sets (**1**–**4** and **1a**–**4a**) based on the sign of ψ_1.

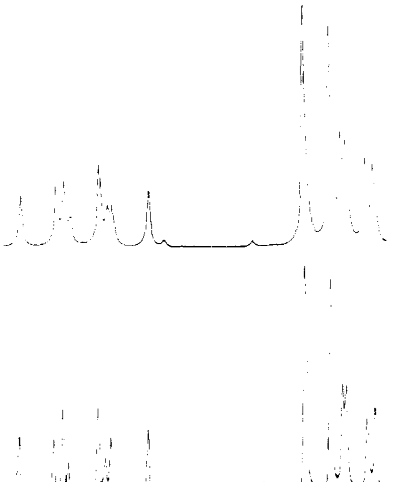


Figure 3. Calculated (top) and observed (bottom) 60-MHz spectrum of ethylene protons of 2-*n*-propyl-1,3-oxathiolane in CCl_4.

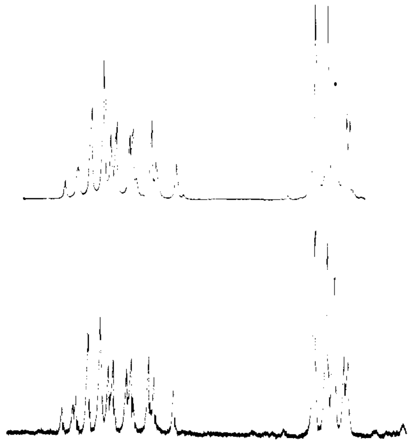


Figure 4. Calculated (top) and observed (bottom) 60-MHz spectrum of ethylene protons of 2-*t*-butyl-2-methyl-1,3-oxathiolane in C_6H_6.

For mixtures of rapidly interconverting enantiomeric conformer sets of 2,2-disubstituted oxathiolanes in which both enantiomeric states are equally populated two conformationally averaged vicinal coupling constants define the spectrum.

When a chiral center is generated at C_2, the degeneracy of the magnetic environment above and below the average plane defined by four of the ring atoms for the enantiomeric conformer sets (see Figure 6) is removed with the consequence that the protons at C_4 and at C_5 become diastereotopic.

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(14) ψ_1 = 0° for the eclipsed butane conformation. The nearer C–X bond in a Newman projection is used as the reference in defining the sign of rotation.

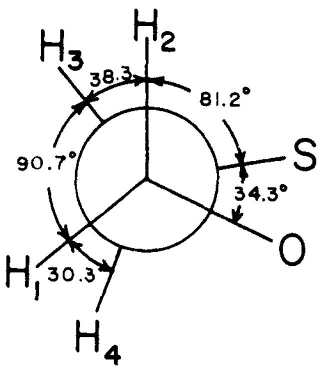

Figure 5. Assignments of rotational angles and stereochemical relationships between coupled hydrogen atoms in the 1,3-oxathiolane ring system.

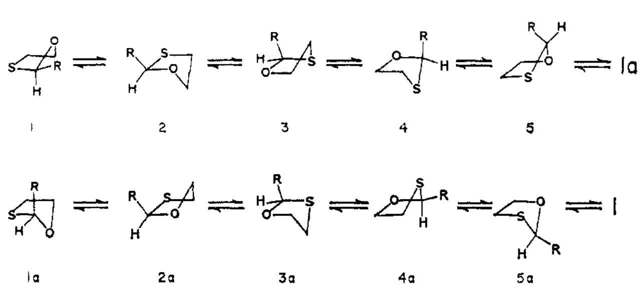

Figure 6. Pseudorotation in the 1,3-oxathiolane ring system.

The large magnitude of J_{24} calculated for the monosubstituted oxathiolanes is consistent only with large populations of conformations **1**, **2**, and **3**, or **2a** and **3a**, with low populations of any or all of the other pseudorotamers. From the observations that only δ_2 undergoes a large shift and that the value of J_{24} does not vary greatly in changing from 2-ethyl- to 2-*t*-butyl-2-methyl-1,3-oxathiolane, we conclude steric effects are most important in determining the dominant conformer. Thus the larger substitutent in each case must occupy the position shown as the R group in Figure 6, and H_2 must be both axial and *anti* to R.[15] On the basis of this analysis, **1**, **2**, or **3** are expected to provide the best approximation of the dominant conformer in solution. Of the available conformations we tend to favor **1** or **2** over **3** because the positioning of the *t*-butyl group in **3** should lead to substantial interactions with the axial proton at C_4. These repulsions should be virtually absent in either **1** or **2**. In this respect it is perhaps significant that a conformation similar to **2** is the one found by Cooper and Norton.[7]

The similarity of solvent shifts for 2-ethyl- and 2-*t*-butyl-2-methyl-1,3-oxathiolane provide supporting evidence for a quite similar dominant conformation. The somewhat larger shifts for H_1 and H_3 coupled with the insensitivity of the shift of the 2-substituent to solvent change leads us to attribute the solvent effects to a dipole–induced dipole interaction in which the benzene adopts a position in the collision complex such that the sixfold axis is approximately perpendicular to the midpoint of the C_4–C_5 bond and lies nearly in the plane of the oxathiolane ring. This collision complex structure is only slightly different from that suggested by Anderson for the 1,3-dioxolanes.[16] By contrast, the solvent complex for the 2-phenyl-2-methyl derivative must be considerably different.

It is interesting to speculate on the pseudorotamers with $\psi_1 < 0$ which make important contributions to the time-averaged structure. In our opinion steric effects should also be important in determining the most favorable higher energy form. Thus, when two equally spatially demanding R groups are present, there appears to be little choice among the four enantiomeric pairs **1–1a** to **4–4a**. This would be our expectation for 2-methyl-2-phenyl-1,3-oxathiolane. On the other hand, when one of the substituents is significantly more sterically demanding than the other, we expect that pseudorotameric states **3a** and **4a** should be more highly populated than **1a** or **2a** because of the minimization of steric repulsions between the substituent and the transannular hydrogen atoms. This leads us to the conclusion that ΔG values calculated by Pasto and coworkers may not be an accurate index of the energy difference between "axial" and "equatorial" substitution of any one enantiomeric pair, but may represent instead the difference in energy between **1** or **2** and **3a**, **4a**, or some intermediate conformation.

Temperature effects on the spectra of monosubstituted 1,3-oxathiolanes within the available extremes are not expected to arise from freezing out the pseudorotation process since the barriers are expected to be relatively low (<5 kcal/mol).[17] Instead they are expected to arise from changes in the distribution between populated pseudorotameric states. The low-temperature nmr spectra of 2-ethyl-1,3-oxathiolane down to −110° show a continuing increase in the magnitude of J_{24} with an accompanying decrease in that of J_{13}. A larger shift (9 Hz) of δ_1 to lower field is accompanied by a somewhat smaller shift (3 Hz) of δ_2 to a higher field. All these facts are consistent with expectations, and we conclude that a conformation similar to **1** or **2** becomes relatively more stable than all others. The erratic course of δ_4 as the temperature decreases could be taken as evidence that more than one conformer other than the highly preferred one is a contributor to the time-averaged spectra. For δ_4 the ambient and −50° runs, however, are just about within the limit of error, so no firm conclusion can be drawn. Our results do require the conclusion that rapid pseudorotation[18] about $\psi_1 = 0°$ is occurring in all the 1,3-oxathiolane systems we have studied. If

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[15] (a) Making the drastic assumption that the anisotropy of the new carbon–carbon bond is the main contributor to the shift of δ_2 and ignoring the carbon–hydrogen bonds lead by use of the McConnell equation[15b] to a predicted upfield shift. The discrepancy between prediction and observation could reflect the shielding by the C–H bonds which lie in close proximity to H_2; (b) H. M. McConnell, *J. Chem. Phys.*, **27**, 226 (1957).

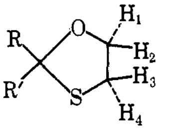
[16] J. E. Anderson, *Tetrahedron Lett.*, 4713 (1965).

[17] Should two or more pseudorotamers be frozen out the spectra would be extremely complex and assignment of lines to the two AMXY patterns would be virtually impossible.

[18] It is necessary to differentiate pseudorotation from the processes of pseudolibration and conformational inversion. Pseudolibration [C. Altona, H. R. Buys, and E. Havinga, *Recl. Trav. Chim. Pays-Bas.*, **85**, 973 (1966)] refers to coupled changes of rotational and bond angles which take place within the bounds of a conformational energy minimum. The use of pseudolibration to explain our results would require the existence of an energy minimum close to conformations **5** or **5a**, a highly unlikely event. Conformational inversion refers to the process of interconverting enantiomeric ring conformers (*e.g.*, **1** and **1a**) directly through the planar form. We consider (*vide supra*) that conformer **1a** represents a poor model for a second energy minimum, and thus we consider unsound interpretation based on conformational inversion without pseudorotation. Finally, pseudorotation refers to the process by which coupled changes of rotational and bond angles occur leading from one energy minimum to another.

there were slow pseudorotation, the spectra would not be time averaged and cooling would lead to no change in coupling constants.

Table IV. Solvent Shifts, $\Delta\delta_{\mathrm{PhH}}^{\mathrm{CCl_4}}$, for Some 1,3-Oxathiolanes



R	R′	$\Delta\delta_{\mathrm{PhH}}^{\mathrm{CCl_4}}$ H₁	H₂	H₃	H₄	R′
Et	H	+0.34	+0.35	+0.38	+0.30	+0.07
t-Bu	CH_3	+0.30	+0.25	+0.35	+0.26	0.0
Ph	CH_3	+0.15	+0.06	+0.17	+0.18	+0.03

Finally, using the Cooper model to obtain dihedral angles we have calculated[19] the expected coupling contants for conformation **2** (Figure 6). The results are presented in Table V. Although the calculated values are high on the basis of the simple Karplus relationship[19,20] the internal consistencies within the calculated and observed sets support our conclusion that conformation **2** can in fact be the major one in solution.

Table V. Calculated and Observed Coupling Constants for 2-Ethyl-1,3-oxathiolane (See Figure 5)

ij	ϕ_{ij}	J_{ij} Calcd[a]	Obsd[b]	Obsd[c]
13	90.7	−0.28	4.01	2.5
23	38.3	3.93	4.37	4.49
24	159.3	8.07	10.36	10.98
14	30.3	4.01	5.44	5.46

[a] Cooper and Norton model. [b] CCl_4, ambient temperature. [c] CS_2, −90°.

Experimental Section

The 60-MHz nmr spectra were run as 20% v/v solutions on a Varian Associates spectrometer, Model A-60, equipped with a variable-temperature accessory, Model V-4341/V-6057, on charts calibrated immediately prior to use by the side-band method. Alternatively, calibration was effected directly using a Hewlett-Packard Model 200CD wide-range oscillator and a Monsanto Model 100A frequency counter. The 100- and 220-MHz spectra were obtained on 5% v/v solutions using Varian Associates spectrometers, Models HA-100 and HR-220, respectively.

The oxathiolanes were prepared from freshly distilled 2-mercaptoethanol and ketones.[21]

2-Mercaptoethanol-1,1-*d*₂. To a slurry of 2.0 g (0.5 mol) of lithium aluminum deuteride in 250 ml of boiling ether was added 10.37 g (0.07 mol) of *n*-butyl thioglycolate dropwise during a 2-hr period. The addition was controlled to maintain gentle reflux. The reaction was then heated under reflux for 5 hr, after which the resulting suspension was cooled with an ice–water bath. Slow addition of 4 ml of water was followed by acidification with concentrated sulfuric acid. The mixture was digested under reflux for 1 hr and cooled, and the clear organic layer was separated by decantation. The digestion and decantation were repeated using 250 ml of ether and a trace of concentrated sulfuric acid. The combined ethereal extracts were dried over anhydrous potassium carbonate and filtered, the solvent was removed using a rotary evaporator, and the resulting residue was distilled to give 2.80 g (50%) of 2-mercaptoethanol-1,1-*d*₂, bp 75–80° (35 mm).

Acknowledgment. The authors wish to thank Mr. J. J. Ryan for obtaining the 100- and 220-MHz spectra, Mr. H. Talts for the low-temperature spectra, and the P.I.B. computer center for the use of their facilities.

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(19) M. Karplus, *J. Amer. Chem. Soc.*, **85**, 2870 (1963).

(20) The average coupling constant of vicinal protons in systems which allow free rotation is known to be directly related to the sum of the electronegativities of the atoms about the vicinal carbons: R. J. Abraham and K. G. R. Pachler, *Mol. Phys.*, 165 (1963).

(21) G. E. Wilson, Jr., and M. G. Huang, *J. Org. Chem.*, **33**, 2133 (1968).