

The Proton and Carbon-13 NMR Spectra of Thioxanthone Sulfoxide, Thioxanthone Sulfone and Related Ylides - Chemical Shift Assignments

A. L. Ternay, Jr.,* J. A. Cushman, J. S. Harwood and C. P. Yu

Department of Chemistry, University of Texas at Arlington,

Arlington, Texas 76019

Received January 13, 1987

The proton and carbon-13 nmr spectra of thioxanthone sulfoxide, thioxanthone sulfone, thioxanthonium bis(carbomethoxy)methylide and thioxanthonium bis(carbomethoxy)methylide *S*-oxide are assigned using 2-D nmr techniques and compared to those of thioxanthone. The pseudo-equatorial methylide fragment shields C4a/5a by ~ 11 ppm relative to the corresponding sulfoxide and by ~ 4 ppm relative to thioxanthone. The pseudo-axial methylide fragment in the oxysulfonium ylide has the same effect upon C4a/5a as does the pseudo-axial oxygen of the corresponding sulfone. The sulfoxide and the sulfonium ylide have similar chemical shifts for C2/7 (~ 131 ppm) as do the sulfone and oxysulfonium ylide (~ 133 ppm).

J. Heterocyclic Chem., **24**, 1067 (1987).

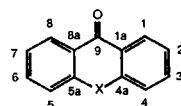
Introduction.

For a number of years we have conducted a detailed study of the stereochemistry and reactivity of many so-called "6,6,6" tricyclic heterocycles [1]. These systems included phenothiazine, thioxanthene, thioxanthone, phenoxathiin and so forth. Our interest in such structures has been stimulated, in part, by the extensive biological activity associated with heterocycles of this type. Included in such biologically active molecules are neuroleptic agents such as chlorpromazine, thioridazine, and thiothixene. These substances are well known pharmacological agents and have been the focus of structure-activity relationship studies [2].

In spite of continuing efforts, there remains an inadequate understanding of the role of electronic and conformational effects upon the pharmacological activity of such compounds. However, it is clear that the efficacy of these heterocycles as antipsychotic agents is strongly dependent upon (a) the nature of the atom(s) between the aryl rings (*i.e.*, at the meso positions) and (b) the presence and nature of a substituent *para* to the meso positions. When sulfur occupies a meso position, one very reasonable assumption is that a substituent *para* to it alters electron density in the ring to which it is bonded and, additionally, at sulfur. The ability of a substituent to influence bonding between this sulfur and atoms bonded to sulfur but not a part of the ring system (*e.g.*, the methylide carbon of a sulfonium ylide) has only recently been demonstrated [3]. Furthermore, we have recently shown that the C2 substituent exerts an effect upon the "unsubstituted" aryl ring and, in particular, influences the electron density at C6 and C7 of the thioxanthone ring system [4].

In the past we have examined the effect of the oxidation state of sulfur upon spectroscopic properties of sulfur-containing heterocycles. Recently, we have focused upon

the nature of sulfonium ylides and oxysulfonium ylides derived from sulfur-containing 6,6,6-tricyclic heterocycles. This has led us to investigate the similarities/dissimilarities of these ylides with the corresponding sulfoxides and sulfones. In this manuscript we report the complete proton and carbon chemical shift assignment for various oxidation states of thioxanthone. The compounds studied include the divalent sulfur species thioxanthone (**1**), the trivalent species thioxanthone sulfoxide (**2**) and thioxanthonium bis(carbomethoxy)methylide (**3**) and the tetravalent species thioxanthone sulfone (**4**), and thioxanthonium bis(carbomethoxy)methylide *S*-oxide (**5**).



Compound	X
1	S
2	S-O
3	S-C(CO ₂ CH ₃) ₂
4	S(O) ₂
5	S(O)(C(CO ₂ CH ₃) ₂)

Results and Discussion.

Chemical shift assignments were made *via* the use of two different variations of two-dimensional ¹³C-¹H chemical shift correlated spectra [5,1a]. These two-dimensional nmr techniques indicate which protons are coupled to a given ¹³C resonance, and can be optimized so as to correlate ¹³C signals with their attached proton(s) (CSCM spectrum), or to protons several (usually 3) bonds removed (LROCSCM, *i.e.*, Long-Range Optimized CSCM).

CSCM spectroscopy is useful for several reasons. First, it separates ¹³C or ¹H signals with similar chemical shifts into distinct responses. Thus, chemical shifts of individual resonances are determined more easily than by the use of conventional spectra, especially if overlapping coupled proton signals are present. Second, CSCM spectroscopy

facilitates proton chemical shift assignment if the assignments of the ^{13}C resonances are known, or vice-versa. In addition, the "multiplicity" of the response in the contour plot of the CSCM experiment often is the same as the gross multiplicity (*e.g.*, from *ortho* ^1H - ^1H couplings) of the proton signal that corresponds to that response. This can aid in distinguishing between otherwise permutable chemical shift assignments.

The analysis of the spectra of **5** is typical and is presented below.

The initial step in the assignment of proton and carbon chemical shifts involved the correlation of the carbonyl carbon (C9) to proton(s) on the aryl ring. This was done by employing an LROCSCM experiment that was optimized for three-bond C-H couplings. Therefore, only the proton at C1 (H1) would be expected to correlate with the C9 resonance.

The carbonyl carbon (177.02 ppm) shows only one three-bond correlation and that is to the proton resonance at 8.34 ppm, identifying the source of the 8.34 ppm signal as H1. The CSCM spectrum shows that a carbon resonance at 128.92 ppm correlates with H1 through a one-bond coupling, defining that carbon as C1. Two other carbons should correlate to H1 *via* a three-bond coupling, C3 and C4a. Indeed, two such correlations to H1 are observed in the LROCSCM spectrum - one at 134.37 ppm and the other at 140.06 ppm. One of these two carbons is a quaternary carbon and lacks a C-H one-bond coupling; consequently, it should not appear on the CSCM spectrum. Indeed, the resonance at 140.06 ppm is absent from this spectrum, identifying it as C4a. The other quaternary carbon, C1a, must give rise to the signal at 131.15 ppm. This leaves C3 to be assigned to the resonance at 134.37 ppm. In turn, the CSCM spectrum leads to the assignment of the resonance at 7.84 ppm to H3.

The remaining peaks at 133.92 ppm and 125.53 ppm in the CSCM spectrum show responses that are a "triplet" and "doublet", respectively. The peak at 125.53 ppm must therefore be C4, the attached proton (H4) being split into a doublet by H3. The remaining resonance, 133.92 ppm, is assigned to C2. The CSCM spectrum then gives assignments of H4 and H2. The responses of C1 and C3 are also a doublet and a triplet, respectively, supporting this interpretation.

The same type of analyses led to the carbon and proton chemical shift assignments of the remaining compounds. The results are summarized in Figure 1. The ^1H assignments for **1** agree with literature values [6]. The ^{13}C assignments resulting from our studies indicate that the previously reported assignments of **1** [7] are correct except that C2 and C4 assignments were transposed [8]. The spectrum of **1** used to reach this conclusion is shown in Figure 2.

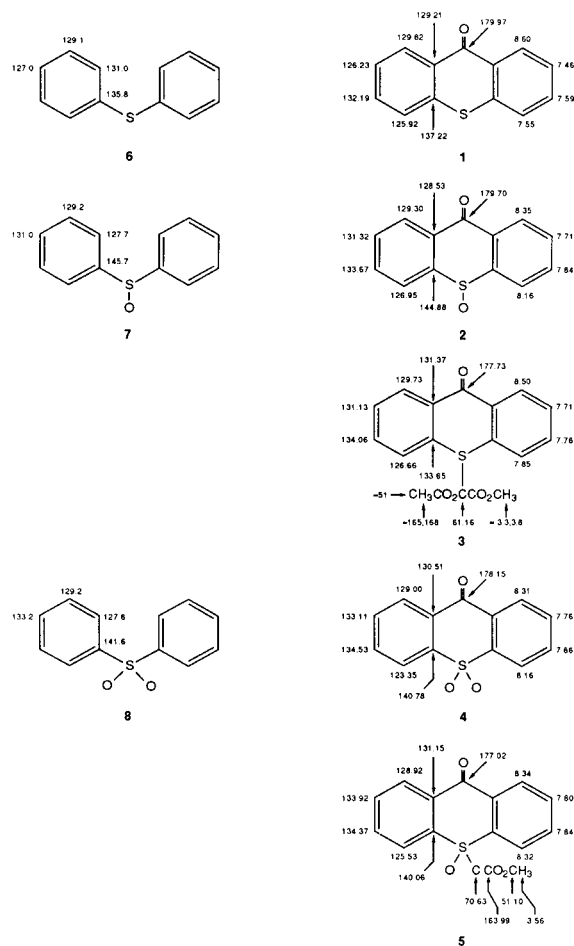


Figure 1. Proton and carbon chemical shifts.

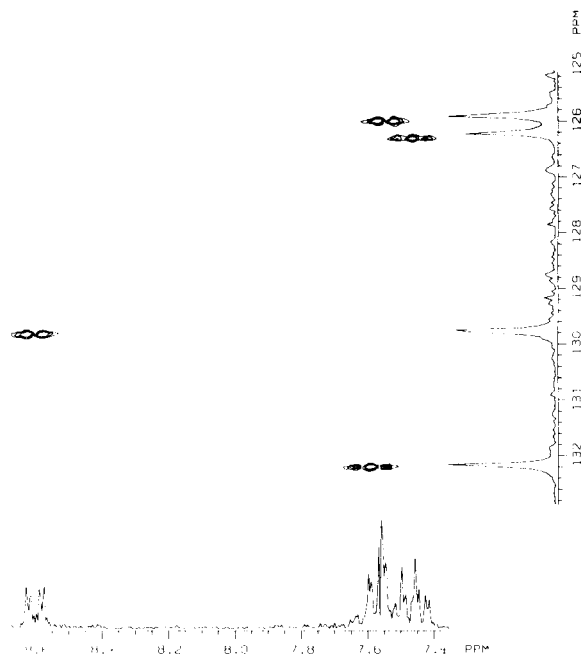
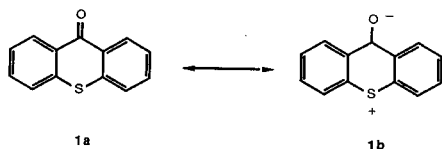


Figure 2. The CSCM spectrum of thioxanthone.

The discussion of these data begins with a comparison of **1**, its sulfoxide, **2**, and its sulfone, **4**.

Thioxanthenes are, as a group, essentially planar [9]. The carbonyl stretching frequency of thioxanthone is quite low, occurring at 1643 cm^{-1} [10,11]. These data indicate that resonance contributor **1b** plays a substantial role in describing the electron distribution within the ground state of **1** [12].



The extent that **1b** contributes to the electronic structure of **1** depends upon the electron donating ability of the sulfur atom. Oxidizing a sulfide to a sulfoxide will reduce the electron donating ability of the sulfur, resulting in an increased contribution of resonance forms analogous to **1a** for **2**. In a tetracoordinate sulfur species such as **4** there are no electron pairs to donate so that a contributor such as **1b** is impossible. This view is supported by the following data.

X-Ray crystallographic analysis shows the dihedral angle of **2** to be 155.7° [13]. This is consistent with some loss of aromaticity in the central ring of **2**, which removes the demand that this ring (and therefore the entire heterocycle) be planar. The carbonyl stretching frequencies of **2**, 1667 cm^{-1} , and **4**, 1679 cm^{-1} , indicate an increase in C - O double bond character in passing through the series **1**, **2**, **4**. This is completely consistent with a decrease in sulfur's electron-donating ability as lone-electron pairs on sulfur are replaced by atoms.

The C2,7 carbon chemical shift is a good probe of the electron donating/withdrawing ability of the sulfur functionality. These positions are as far removed from sulfur as is possible in this system, thus minimizing anisotropic effects arising from the substituent bonded to sulfur. However, its location *para* to the point of attachment of sulfur results in maximal sensitivity to electronic (resonance) changes in the aromatic rings induced by changes in the groups attached to sulfur. Since C2,7 is *meta* to the carbonyl group it will be relatively unaffected by changes in the nature of the carbonyl group.

For comparison purposes, Figure 1 also presents the ^{13}C chemical shifts for diphenyl sulfide (**6**), diphenyl sulfoxide (**7**), and diphenyl sulfone (**8**) [14]. In the thioxanthone series, the C2,7 chemical shift goes downfield from 126.23 ppm in **1** to 131.32 ppm in **2** and to 133.11 ppm in **4**. These changes are similar to those experienced by C4 in passing through the series **6**, **7**, and **8** (127.0 ppm, 131.0 ppm, and 133.2 ppm, respectively). The ^{13}C chemical shifts of C2,7 of **1** and C4 of **6** attest to the electron donating

ability of the sulfide group, these values being shifted upfield compared to benzene (128.5 ppm in deuteriochloroform). The ^{13}C shifts listed for compounds **2**, **4** and **7**, **8** indicate that (a) the sulfonyl is a more potent electron-withdrawing group than is the sulfoxide and (b) both are electron-withdrawing relative to sulfide. Therefore, it is reasonable to expect that resonance structures similar to **1b** contribute much less to the electronic structures of **2** than of **1**.

The chemical shift of C3 in the series **6**, **7**, **8**, is essentially constant (129.2 ± 0.1 ppm). This is consistent with its location *meta* to the sulfur, since resonance interactions between *meta* groups are minimal. This suggests that the chemical shift of the analogous carbon in the thioxanthone series should be constant. However, the resonance of C3,6 in **1**, **2** and **4** shifts downfield from 132.19 ppm in **1** to 133.67 ppm in **2** to 134.53 ppm in **4**. Since C3,6 is *meta* to sulfur, and *para* to the carbonyl group, it is quite reasonable that instead of being affected directly by changes in the sulfur group, C3,6 is being affected by changes induced in the carbonyl group in the series **1**, **2**, and **4**.

The changes seen in the C3,6 resonance are consistent with the contention that the resonance form analogous to **1b** contributes less to the structure of **2** than of **1** and not at all to the structure of **4**. As the significance of resonance form **1b** decreases, the carbonyl group develops more double bond character. Concurrent with this change is an increased ability of the carbonyl group to withdraw electron density from the aryl ring (rather than from sulfur). This is because the now "normal" carbonyl group can participate in resonance interaction with the aryl rings and accept electron density, whereas the charge-separated carbonyl group present in **1b** cannot.

It can be seen that the C9 (carbonyl) ^{13}C chemical shift is not a good probe of *S*-substituent effects. It neither changes in any regular fashion as the sulfur group changes nor correlates, even approximately, with any other parameters that would be expected to be a reasonable probe of the *S*-substituent effects. For example, **2**, **3**, benzophenone (**9**) [15], and anthrone (**10**) have approximately the same carbonyl stretching frequency, $\sim 1665\text{ cm}^{-1}$. However, this same series exhibits a range of carbonyl ^{13}C chemical shifts from 177.7 to 196.1 ppm [16]. Furthermore, both **1** and **2** have similar carbonyl ^{13}C chemical shifts (179.8 ± 0.1 ppm) but vastly different carbonyl stretching frequencies (1643 cm^{-1} and 1667 cm^{-1} , respectively). Additionally, as the oxidation state of sulfur is changed, the C9 chemical shift does not change in a way which directly correlates with the change in the C2,7 chemical shift. We conclude that the C9 chemical shift is influenced by several factors, rendering it of questionable utility in assessing *S*-substituent effects in thioxanthenes.

A comparison of the spectra of thioxanthonium bis(carbomethoxy)methylide (**3**) and thioxanthonium bis(carbomethoxy)methylide *S*-oxide (**5**) also is instructive.

Comparing the C2,7 resonances indicates that the ylide fragment is essentially equivalent to an oxide fragment in terms of nmr effects upon conjugated, remote positions. This conclusion stems from the fact that the C2,7 resonances of **2** and **3** are very close to each other (131.32 and 131.13 ppm, respectively) as is the case for **5** and **4** (133.92 and 133.11 ppm, respectively). These shifts indicate that the sulfur groups in these two sets of compounds have similar electron-withdrawing abilities.

Other comparisons between the spectra of **3** and **5** and the spectra of **2** and **4** are more difficult because the ylide fragment in **3** is in the pseudo-equatorial position whereas the ylide fragment in **5** is pseudo-axial. This is evidenced by the differences in ylide carbon chemical shift, 61.2 ppm in **3** versus 70.6 ppm in **5**. These ylide carbon chemical shifts are consistent with values for structurally related ylides with the same geometries [17]. The resonances of the methylide fragment of **3** are broadened compared to that of **5**. This is also consistent with pseudo-equatorial location of the ylide fragment in **3** [18].

The difference in location of the ylide fragment cannot be discounted when comparing these spectra. In particular, C4a,5a is close enough to the ylide group that the difference in ylide geometry may influence these resonances. The unusual upfield shift of C4a,5a in **3** indicates that the equatorial ylide group shields C4a,5a relative to **1**, whereas, these carbons are deshielded in **2**. When the methylide fragment is removed to the a' position this effect is diminished (compare **4** and **5**). Consequently, this effect is considered by us to be due to anisotropic effects rather than inductive effects. As an example of this, the C4a,5a resonance in **5** is only shifted upfield ~0.7 ppm compared to **4**, which indicates that the ylide group is not any less electron-withdrawing than a sulfoxide group.

Further work is underway to investigate the effect of the ylide group on the spectra of the aryl carbons. At this point, however, we must conclude that the sulfonium ylide fragments under investigation are analogous to the sulfinyl group with regard to electron withdrawing/inductive effects. However, the anisotropic effects of these groups clearly are different [19].

The above discussions exemplify one of the important advantages that 2-D nmr spectroscopy has compared to conventional techniques. This is that at no time during the chemical shift assignment process were any chemical shift arguments used; all assignments were made using information from the 2-D spectra alone. This is significant because it provided chemical shift assignments that were not biased by any expectations regarding electron

donating/withdrawing properties of the sulfur-containing moieties. Furthermore, assignments were not biased by extrapolations of data from related heterocycles. Therefore, such properties could be assessed accurately. This, coupled with the fact that some of the compounds studied had resonances too close to each other to be assigned by simple means, explains the need for using 2-D spectroscopy even for such apparently simple compounds.

EXPERIMENTAL [20]

Compounds **1-4** were prepared according to previously reported methods [21]. All compounds had purities of >97% as determined by hplc [22].

Thioxanthonium Bis(carbomethoxy)methylide *S*-Oxide (**5**).

A dry 250 ml 3-necked round bottom flask was fitted with a thermometer, nitrogen inlet, magnetic stirring bar, and condenser connected to a mineral oil bubbler. After purging with nitrogen for 10 minutes, the flask was charged with 10.25 g (44.96 mmoles) of thioxanthone sulfoxide, 7.9 g (50 mmoles) of dimethyl diazomalonate [23], 1.0 g (6.3 mmoles) of anhydrous copper(II) sulfate, and 100 ml of dry toluene. The reaction was initiated by heating the stirred mixture to 100° for a few minutes [24]. The mixture then was stirred for one hour, at each of the following temperatures (sequentially): 60, 70, 75, and 85°. The reaction mixture then was cooled to 50°, diluted with 10 ml of chloroform, and immediately filtered while hot through a bed of Celite. Upon cooling, the filtrate yielded a precipitate which was removed by filtration [25]. The resulting filtrate was concentrated *in vacuo* to half its volume to afford 6.71 g (41%) of a yellow solid, mp 183-185.5°. Recrystallization from benzene-ethanol (50/50, v/v) removed some yellow crystals (impurities) as a precipitate [26]. The resulting filtrate was left to partially evaporate overnight and the crystals which formed recrystallized from benzene-ethanol (50/50, v/v) to afford 3.0 g (19%) of yellow crystals, mp = 184-185°; ir (Nujol): 1675, 1575, 1183, and 1100 cm⁻¹; ¹H nmr (deuteriochloroform): δ 8.50-8.25 (m, 4 H), 7.90-7.65 (m, 4H), 3.56 (s, 6 H); ms: m/z 358 (M⁺), 228 (Base).

Anal. Calcd. for C₁₈H₁₄O₆S: C, 60.32; H, 3.94. Found: C, 60.57; H, 3.90.

One-Dimensional Spectra.

All spectra were obtained using saturated deuteriochloroform solutions, prepared at 20°, of each compound in 12 mm tubes. Typical parameters for ¹H spectra were: 30° tip angle, 8K data points, 2400 Hz sweep width, quadrature detection, 16 transients, a 2-3 second recycle delay, and a digital resolution of 0.6 Hz. Typical ¹³C parameters were: 30° tip angle, 16K data points, 12,048 Hz spectral width, quadrature detection, broad-band, bi-level ¹H decoupling, a 3-5 second recycle delay, 1 Hz line broadening, and a digital resolution of 1.5 Hz.

2-D Spectra.

The pulse sequence employed for CSCM and LROCSCM spectra is described by Bax [5]. Phase cycling was employed to achieve quadrature detection in both dimensions and the coherence transfer echo was detected. The data were displayed as contour plots in the absolute value mode. Typical parameters are as follows: ¹³C spectral widths were between 500-900 Hz for CSCM and 3200 Hz for LROCSCM; proton spectral widths used were 400-500 Hz. Between 70-128 blocks of 1K or 2K data points were acquired. Processing was done using exponential and/or double exponential multiplication for the t₂ dimension. Processing of the t₁ dimension included zero-filling to 256 data points followed by appropriate signal conditioning (see above). Mixing delays Δ₁ and Δ₂ for CSCM spectra were 3.3 mseconds and 2.0 mseconds (J = 150 Hz). Corresponding delays of 50 mseconds and 30 mseconds (J = 10 Hz) were used for LROCSCM spectra [27].

Acknowledgements.

We wish to thank Dr. Jim Hudson (Alcon Laboratories, Fort Worth, Texas) for mass spectral analyses. This research was supported by Grant V-484 from the Robert A. Welch Foundation.

REFERENCES AND NOTES

- [1] See, for example, [a] A. L. Ternay, Jr. and J. S. Harwood, *J. Heterocyclic Chem.*, **23**, 1879 (1986); [b] M. Kluba, J. Harwood, P. K. Casey, and A. L. Ternay, Jr., *J. Heterocyclic Chem.*, **22**, 1261 (1985); [c] E. W. Tsai, L. Throckmorton, R. McKellar, M. Baar, M. Kluba, D. S. Marynick, K. Rajeshwar and A. L. Ternay, Jr., *J. Electroanal. Chem.*, **210**, 45 (1986); [d] G. E. Martin, R. T. Gampe, Jr., M. Robert Willcott, M. Morgan and A. L. Ternay, Jr., *J. Heterocyclic Chem.*, **20**, 1063 (1983); [e] I. Vickovic, W. H. Watson and A. L. Ternay, Jr., *Acta Cryst.*, **C40**, 842 (1984); [f] M. R. Cairn, W. H. Watson, A. L. Ternay, Jr., and R. McKellar, *Acta Cryst.*, **C40**, 1710 (1984), and references cited therein.
- [2] See, for example, [a] A. S. Horn and S. H. Snyder, *Proc. Nat. Acad. Sci. U. S.*, **68**, 2325 (1971); [b] J. J. Kaufman and E. Karman, *Int. J. Quantum Chem.*, **10**, 559 (1976); [c] J. F. Muren and B. M. Bloom, *J. Med. Chem.*, **13**, 17 (1970).
- [3] A. L. Ternay, Jr. and R. McKellar, submitted for publication.
- [4] A. L. Ternay, Jr. and J. S. Harwood, manuscript in preparation.
- [5a] A. Bax, "Two-Dimensional Nuclear Magnetic Resonance in Liquids", Delft University Press, D. Reidel Publishing Co., Boston, 1984, pp 50-64; [b] A. Bax and G. A. Morris, *J. Magn. Reson.*, **42**, 501 (1981).
- [6] N. E. Sharpless, R. B. Bradley and J. A. Ferretti, *Org. Magn. Reson.*, **6**, 115 (1974).
- [7] I. W. Still, N. Plavac, D. M. McKinnon and M. S. Chauhan, *Can. J. Chem.*, **54**, 280 (1976).
- [8] The assignments of ^{13}C shifts for **1** reported here are identical to those reported by us previously [1a]. However, we had earlier [1a] indicated complete agreement with the literature.
- [9] For the single crystal X-ray structure of 2-chlorothioxanthone see S. S. C. Chu and H. T. Yang, *Acta Cryst.*, **B32**, 2248 (1976).
- [10] E. R. H. Jones and F. G. Mann, *J. Chem. Soc.*, 294 (1958) report a value of 1645 cm^{-1} for thioxanthone and 1632 cm^{-1} for *N*-phenyl-acridone.
- [11] The value for anthrone, where resonance interaction between the two meso carbonyl groups is impossible, is 1665 cm^{-1} (CS_2): M.-L. Josien and N. Fuson, *Bull. Soc. Chim. France*, 389 (1952). For a summary of carbonyl stretching frequencies see, for example, D. Dolphin and A. Wick, "Tabulation of Infrared Spectral Data", J. Wiley and Sons, New York, 1977, pp 175-240.
- [12] A. R. Katritzky and A. P. Ambler, in their review, noted that in such systems "...interaction occurs between [the heteroatom] and the C=O group", A. R. Katritzky and A. P. Ambler in "Physical Methods in Heterocyclic Chemistry", A. R. Katritzky, ed, Academic Press, New York, 1963, Vol II, Ch 10.
- [13] S. S. C. Chu, *Acta Cryst.*, **B32**, 1583 (1976).
- [14] M. S. Chauhan and I. W. J. Still, *Can. J. Chem.*, **53**, 2880 (1975).
- [15] H. W. Thompson and D. A. Jameson, *Spectrochim. Acta*, **13**, 236 (1958).
- [16] The values for **2** and **3** are found in Figure 1. For **9** see: M. J. Shapiro, *Tetrahedron*, **33**, 1091 (1977). For **10** see: J. F. Castelao, O. R. Gottlieb, R. A. DeLima, A. A. L. Mesquita, H. E. Gottlieb and W. Wenkert, *Phytochemistry*, **16**, 735 (1977).
- [17a] J. Galloy, W. H. Watson, D. Craig, C. Guidry, M. Morgan, R. McKellar, A. L. Ternay, Jr. and G. Martin, *J. Heterocyclic Chem.*, **20**, 399 (1983), and references cited therein; [b] A series of C2-substituted analogs of **5** have been prepared and all exhibit a methylene resonance at about 70 ppm. These all are assigned to an a' methylene carbon, A. L. Ternay, Jr. and C. P. Yu, manuscript in preparation. See, also, ref [1e].
- [18] The broadening in **3** has been ascribed to a restricted rotation in the pseudo-equatorial geometry [1b]. The pseudo-axial geometry, which is less hindered, is believed to allow relatively free rotation of the S-C bond. On the other hand, it does not follow that the differences in the band-widths of these signals *must* mean different geometries; the two ylide fragments might exist in the same conformation but have different rotational barriers because of the replacement of a nonbonding electron pair of sulfur in **3** with an oxygen in **5**. It is our belief that this effect is minor compared to that resulting from a change in conformation (*i.e.*, a' vs e').
- [19] Only in a simplified model can one suggest that the anisotropic effects of the carbanionic fragment of a sulfonium ylide and an oxysulfonium ylide will be the same.
- [20] Melting points were determined on a Mel-Temp capillary melting point apparatus and are uncorrected. The mass spectrum of **5** was determined using a Finnigan MAT TSQ 46 GC-MS/MS mass spectrometer. Elemental analyses was performed by Micro-Analysis, Inc., Wilmington, DE. Infrared (ir) spectra were determined in Nujol on a Perkin-Elmer Model 599B spectrophotometer and in chloroform on a Bio-Rad Model 3240 SPC FTIR. ^1H and ^{13}C nmr spectra were obtained in deuteriochloroform on a Nicolet NT-200 spectrometer equipped with a Nicolet 1280 data processor and model 293A' programmable pulser. Probe temperature was maintained at 25° throughout the acquisition of all spectra. Proton (200 MHz) chemical shifts are reported in parts per million relative to residual protiochloroform (7.26 ppm). Chemical shifts for ^{13}C (50.3 MHz) are referenced to the center peak of the deuteriochloroform triplet (77.00 ppm). All chemical shifts reported are those obtained at 25° and are accurate to ± 0.05 ppm.
- [21] Compounds: **1**, Eric Gordon Davis and Samuel Smiles, *J. Chem. Soc.*, **97**, 1290 (1910); **2**, Tse-Lok Ho and C. M. Wong, *Synthesis*, 561 (1972); **3**, M. A. Abbady, D. Craig, and A. L. Ternay, Jr., *J. Org. Chem.*, **46**, 1793 (1981); **4**, F. Ullmann and O. Van Glenck, *Ber.*, **49**, 2509 (1916).
- [22] Varian Model 5000 hplc was employed using a 150×4 mm Alltech C8-reverse phase column, acetonitrile/water ($\sim 50/50$, v/v) as the mobile phase, and equipped with a uv detector set at 254 nm.
- [23] W. Ando, S. Kondo, and T. Migita, *Bull. Chem. Soc. Japan*, **44**, 571 (1971).
- [24] Evidence that the reaction had begun was evolution of gas in the reaction mixture and bubbling at the mineral oil bubbler.
- [25] This solid, 0.6 g (mp $155-159^\circ$), was discarded.
- [26] This solid, with a weight of 0.5 g and mp $210-211^\circ$, was discarded.
- [27] See reference [5a], pages 55-59, especially Figure 2.9.