Oxygen-17 N.M.R. Spectra of C(2)-Substituted Thioxanthones, Thioxanthone Sulphoxide, and Thioxanthone Sulphone

John S. Harwood and Andrew L. Ternay, Jr.*
Center for Medicinal Chemistry Research, Department of Chemistry, University of Texas at Arlington, Arlington, Texas 76019-0065, USA

The ^{17}O n.m.r. spectra of a series of ^{17}O-enriched 2-substituted thioxanthen-9-ones are reported. Analysis of the ^{17}O chemical shifts using the dual substituent parameter (DSP) method shows that the carbonyl oxygen chemical shift correlates precisely with σ_I and $\sigma_{R(+)}$ even though the carbonyl group is *meta* to the C(2)-substituent; interaction between them is apparently mediated by the heterocyclic sulphur. The carbonyl ^{13}C chemical shifts do not correlate well with the C(2)-substituent.

Enrichment with oxygen-17 was accomplished using ^{17}O-enriched water in hydrochloric acid–dioxane. Under these conditions, thioxanthenone *S*-oxide reacts to produce small amounts of enriched thioxanthenone and thioxanthenone *S,S*-dioxide in addition to enriched starting material.

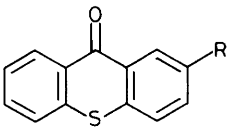
Recent research by our group has included the assignment and analysis of the ^{13}C n.m.r. spectra of thioxanthenone derivatives[1,2] with a view towards better understanding the electronic properties of these systems. For example, using approximate molecular-orbital calculations and the Taft dual substituent parameter method, it was found that the substituent in a series of 2-substituted thioxanthones controls the electron densities and ^{13}C chemical shifts at various locations in the thioxanthenone framework. It is noteworthy that some of these carbons are as many as seven or eight bonds removed from the substituent.[1b] Furthermore, the addition of substituents to the heterocyclic sulphur results in significant changes in the chemical shifts of some of the ring-carbon atoms.[2]

Oxygen-17 n.m.r. spectroscopy has been shown to be a useful method for studying substituent electronic effects.[3] For example, ^{17}O spectra have been reported and analysed for acetophenones,[3b,c] benzaldehydes,[3b] benzoic acids and related compounds,[3d] phthalic anhydrides and phthalides,[3e] pyridine 1-oxides,[3f] various unsaturated carbonyl compounds and their acyl derivatives,[3g] and substituted nitrobenzenes.[3h] The substituent effects upon the ^{17}O resonances in the series listed above were investigated in many different ways, including Hammett type single substituent parameter correlations,[3b,d] the Taft dual substituent parameter method,[3c,d,f,h] and comparisons with u.v.,[3b,c] i.r.,[3b] and ^{13}C spectra.[3g] In particular, the dual substituent parameter method showed correlations of high quality (f <0.10) between the ^{17}O chemical shift and σ_I and $\varphi_{R(+)}$ for *para*-substituted acetophenones,[3c] benzoic acids,[3d] and nitrobenzenes.[3h] It is well established, then, that ^{17}O n.m.r. spectroscopy is a useful method for the study of substituent electronic effects.

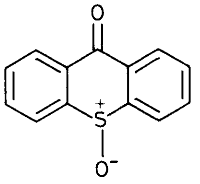
In the light of these findings, we became interested in the prospect of using oxygen-17 n.m.r. spectroscopy to investigate further the nature of electronic changes in the thioxanthenone ring brought about by various types of substitution. Our thrust in this work is twofold. First, we wanted to elucidate the changes, if any, in the sulphur-carbonyl resonance interaction which occurred as various substituents were changed. Second, we wanted to compare the sensitivities of ^{13}C and ^{17}O n.m.r. spectroscopy with changes occurring in the carbonyl group. In addition to investigating the effect of C(2)-substitution, changes due to oxidation of the sulphur atom will also be considered.

Results and Discussion

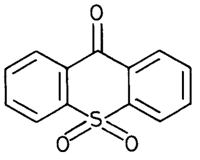
The structures of the compounds under investigation are shown below.



Compound	R
(1)	H
(2)	F
(3)	Cl
(4)	CH_3
(5)	OCH_3
(6)	NH_2
(7)	NO_2



(8)



(9)

Table 1 presents the relevant spectroscopic data whilst Table 2 lists correlations of interest.

It can be seen immediately that for thioxanthen-9-one (**1**), 2-fluorothioxanthen-9-one (**2**), 2-chlorothioxanthen-9-one (**3**), 2-methylthioxanthen-9-one (**4**), 2-methoxythioxanthen-9-one (**5**), 2-aminothioxanthen-9-one (**6**), and 2-nitrothioxanthen-9-one (**7**), the ^{17}O chemical shifts do not correlate with the

Table 1. Chemical shifts.

Compound	$\delta^{17}O$[a]	$\delta^{13}C$[b]
(1)	462.7	179.87
(2)	465.4	179.06
(3)	466.2	178.82
(4)	461.4	179.89
(5)	460.4	179.55
(6)	457.5	179.82
(7)	469.3	178.55
(8)	507.7	179.70
(9)	528.2	178.15

[a] Measured at 60 °C. Chemical shifts in ppm from H_2O at 25 °C (0 ppm). See the Experimental section for details. [b] Measured at 25 °C. Chemical shifts in ppm from $SiMe_4$. See ref. 1(*b*) for details.

Table 2. Simple linear-regression ($y = mx + b$) analysis of ^{17}O chemical shifts and related data for compounds (**1**)–(**7**).

y	x	Slope	R
$\Delta\delta^{17}O$	σ_I, $\sigma_{R(+)}$[a]	See text	>0.99 ($f = 0.102$)
$\Delta\delta^{17}O$	$\Delta\delta^{13}C$[b]	−6.345	0.88
$\Delta\delta^{17}O$	Oπ-pop[c,d]		0.71
$\Delta\delta^{17}O$	Oσ-pop	−4 934	0.90
$\Delta\delta^{17}O$	*S* Mulliken charge	546.8	0.97
O π-pop	C(9) π-pop	−1.920	0.99
$\Delta\delta\ ^{13}C$	C(9) π-pop	−275.2	0.95

[a] Dual substituent parameter correlation; see ref. 1(*b*) and 4. [b] $\Delta\delta\ ^{13}C$ refers to the carbonyl carbon atom [C(9)]. [c] π- and σ-populations (pop) refer to calculated π- and σ-electron densities. [d] Calculated electronic parameters are from the PRDDO calculations presented in ref. 1(*b*). [e] Mulliken charge refers to the calculated[d] Mulliken charge for the heterocyclic sulphur atom.

carbonyl ^{13}C chemical shifts ($r = 0.88$). However, using the Taft dual-substituent parameter treatment,[1b,4] a correlation of high precision between the ^{17}O chemical shift and the substituent constants was found. The correlation follows equation (1) shown below:

$$\Delta\delta\ ^{17}O = 9.63\sigma_I + 4.09\sigma_{R(+)} \quad (f = 0.102,\ r = 0.995) \qquad (1)$$

The use of other σ_R parameters resulted in poorer r values ($r \leq 0.985$).

It is interesting to compare the correlation found in this work [equation (1)] with those in the literature obtained using the DSP relationship and ^{17}O n.m.r. spectroscopy. Most correlations were done using *para*-substituted systems. The following correlations were found for *para*-substituted acetophenones [equation (2)],[3c] *para*-substituted benzoates [carbonyl oxygen; equation (3)],[3d] and *para*-substituted nitropbenzenes [equation (4)]:[3h]

$$\Delta\delta^{17}O = 20.9\sigma_I + 21.9\sigma_{R(+)} \quad (f = 0.09); \qquad (2)$$

$$\Delta\delta^{17}O = 10.0\sigma_I + 9.01\sigma_{R(+)} \quad (f = 0.12); \qquad (3)$$

$$\Delta\delta^{17}O = 13.5\sigma_I + 15.6\sigma_{R(+)} \quad (f = 0.15). \qquad (4)$$

These correlations [equations (2)–(4)] are all consistent with one another and show significant inductive and resonance effects upon the ^{17}O chemical shifts for *para*-substituents. Only one of these papers reported DSP results for *meta*-substituted compounds; the correlation obtained for *meta*-substituted nitrobenzenes was found to be [equation (5)]:[3h]

$$\Delta\delta^{17}O = 6.5\sigma_I + 0.6\sigma_{R(-)} \quad (f = 0.12) \qquad (5)$$

This correlation is consistent with common conceptions of substituent effects; *i.e.* that substituent effects are substantially reduced at *meta* positions and that inductive effects predominate at *meta* positions. Both of these ideas are confirmed by comparing correlations (4) and (5).

Comparing correlations (4) and (5) with the correlation found in this work [equation (1)] is instructive. Both the sensitivity of, and the resonance contribution to, the substituent effect found in correlation (1) (this work) is between those found in correlations (4) and (5). In fact, the resonance contribution is significantly larger in correlation (1) than in correlation (5). To a first approximation, this suggests that the carbonyl ^{17}O chemical shifts in thioxanthen-9-ones behave as if the carbonyl group was neither *meta* nor *para* relative to the C(2)-substituent, but somehow in between those two locations. It is believed that sulphur-carbonyl resonance interaction (mentioned earlier) is responsible for the behaviour of this correlation.

The changes in the ^{17}O chemical shift are probably due in large part to the substituent effect upon the electron-donating ability of the sulphur atom, which is *para* to the substituent and *ortho* to the carbonyl. This location ensures substantial resonance interactions between the C(2)-substituent and the sulphur, and between the sulphur and the carbonyl. Therefore, the C(2)-substituent affects the sulphur, which in turn affects the carbonyl ^{17}O chemical shift. This can account for the significant resonance term in the DSP correlation of the carbonyl ^{17}O shift. Consequently, one can picture the sulphur as 'relaying' some electronic effects of the C(2)-substituent to the carbonyl oxygen, in addition to direct inductive effects between the C(2)-substituent and the carbonyl. This contention is supported by the good correlation between the sulphur Mulliken charge and the carbonyl ^{17}O chemical shift (discussed below).

The high precision of the correlation found between ^{17}O chemical shift and C(2)-substituent constants establishes that the C(2)-substituent interacts with the carbonyl group in these thioxanthenones. This conclusion is the opposite of that which could have been reached if ^{13}C n.m.r. data had been used alone, since the carbonyl carbon chemical shifts did not correlate with the C(2)-substituent constants.[1b] This observation suggests that as many different probes as possible need to be utilized when investigating substituent electronic effects; sometimes correlations may be masked by coincidental combinations of factors so that certain probes may not detect such correlations.

We have carried out approximate molecular-orbital calculations, using the PRDDO[5] approximation, on several of the thioxanthenones reported in this work.[1b] The calculations provided information about electron densities and atomic charges, and these data were found to correlate quite well with the ^{13}C chemical shifts of interest.[1b] Such correlations were consistent with the idea that substituent-induced ^{13}C chemical shift changes in a series of closely related molecules follows the changes in electron density at that carbon atom since, in this case, the changes in electron density dominate the paramagnetic shielding term,[6] S_{para}:

$$S_{para} = -k(\Delta E^{-1})(r^{-3})_{2p}\Sigma Q_{AB}$$

The relationship of S_{para} to electron density is in the 'r^{-3}' term which has been shown to depend on the electron density; the result is that the change in total shielding will follow the substituent-induced electron-density changes.[6,1b]

There has been some discussion as to whether substituent-induced ^{17}O chemical shift changes are dominated by electron-density changes or by changes in the ΔE term (ΔE is the mean value of the electronic excitation energy).[3b,c] Correlations between ^{17}O chemical shifts and calculated electron densities have been reported.[3c,h] Fiat, *et al.*,[3b] reported correlations between ^{17}O data and lowest-energy u.v. transition frequencies (n–π^*) for *para*-substituted acetophenones, although these results were later called into question.[3c] Therefore, it was of interest to see whether the ^{17}O chemical shifts in the thioxanthenone series correlated with the calculated electron densities of the carbonyl oxygen.

We have found many reasonable correlations between ^{13}C chemical shifts and PRDDO-calculated electron densities for many of the thioxanthenone ring carbon atoms,[1b] including C(9) (Table 2). This suggests that the PRDDO method accurately predicts the electron distributions in these heterocycles. However, as can be seen from the data in Table 2, the ^{17}O shifts correlate only very approximately with the calculated σ-electron densities and do not correlate at all with the calculated π-electron densities. It is possible that changes in the ΔE term might occur in these compounds and that the ^{17}O chemical shift may be sensitive to these changes, but at this point no firm conclusion can be made.

The ^{17}O n.m.r. data do give some additional insight into the sulphur-carbonyl resonance interaction that is possible in these compounds. For example, Table 2 shows that the ^{17}O chemical shift in the series (**1**)–(**7**) correlates ($r = 0.97$) with the calculated Mulliken charges for the sulphur atom.[1b] This correlation has a slope of $+546.8$ ppm e. This indicates that as the sulphur atom becomes more positive, such as when the 2-substituent is electron withdrawing, it is less able to donate electrons to the carbonyl group. In turn, the oxygen nucleus becomes less shielded and the ^{17}O signal moves downfield. The opposite occurs when the substituent is electron donating.

The types of changes seen in the ^{17}O chemical shifts of (**1**)–(**7**) are consistent with those seen in the series thioxanthenone (**1**), thioxanthenone *S*-oxide (**8**) and thioxanthone *S,S*-dioxide (**9**). Here, as oxygen atoms are added to it, the sulphur changes successively from an electron donor to an electron withdrawing group. The result is that the ^{17}O resonance moves downfield from 462.7 in (**1**) to 507.7 in (**8**) and to 528.2 ppm in (**9**). This 'sulphur-induced' change in the ^{17}O shift is consistent with the changes induced by the C(2)-substituent, and serves to support the idea that sulphur can 'relay' substituent effects from the C(2)-substituent to the carbonyl.

In conclusion, we find that ^{17}O n.m.r. spectroscopy is a useful method for investigating substituent electronic effects in these heterocyclic systems. The ^{17}O chemical shift is quite sensitive to substitution at sulphur and to changes in ring substitution. In the latter case, the ^{17}O chemical shifts correlated well with the substituent parameters σ_I and $\sigma_{R(+)}$, whereas the corresponding ^{13}C n.m.r. data did not show any such correlations.

A number of workers have examined the reaction of sulphoxides with hydrochloric acid–dioxane mixtures[7] or hydrogen chloride in organic solvents,[8,*] largely because of the ability of these reagents to cause sulphoxide stereomutation.[9] Some of these reports have indicated that thioxanthenone sulphoxide is reduced (deoxygenated) to thioxanthenone under these or similar conditions;[7a,8a] however, these workers failed to note the formation of any oxidized organic material. During the current study we have observed that the thioxanthenone *S*-oxide (**8**) reacts in the presence of hydrochloride acid–dioxane–$H_2{}^{17}O$ to form both thioxanthenone sulphone (**9**) and thioxanthenone (**1**). Their identities were established by both ^{13}C and ^{1}H n.m.r. spectroscopy, and were consistent with the ^{17}O spectrum of the mixture. Further, (**9**) was found to be labelled at both the carbonyl and sulphonyl groups.

The ratio of compounds (**1**), (**8**), and (**9**) obtained from the exchange reaction of (**8**) was determined by ^{13}C n.m.r. to be approximately 3:17:1. The unequal amounts of (**8**) and (**9**) produced, and the dilution used in our labelling experiments, argue against a simple acid-catalysed oxygen transfer (disproportionation) between two molecules of (**8**). Moreover, in a separate experiment, it was found that the sulphonyl oxygens of (**9**) did not exchange under the same conditions used for the exchange reaction of (**8**). Therefore, we conclude that the ^{17}O-enriched sulphonyl oxygens present in the by-product of the exchange reaction of (**8**) must have been incorporated directly from enriched water rather than from ^{17}O exchange of any unenriched (**9**). Additional work is necessary in order to establish the mechanism of formation of (**9**).

In addition, it should be mentioned that the reaction described by Castrillon and Szmant[7a] was repeated during the course of this work. This reaction involves treating the thioxanthenone *S*-oxide (**8**) with a mixture of concentrated hydrochloric acid in dioxane (1:2 v/v). These workers obtained a precipitate after the mixture was left to stand (although they do not state for how long) that was identified as thioxanthenone (**1**) by m.p. determination and t.l.c. Unfortunately, the contents of the dioxane solution were not reported, nor was a material balance given.

After this procedure had been repeated using thioxanthen-9-one *S*-oxide (**8**) (0.5 g) and a 4-day reaction time, thioxanthen-9-one (**1**) precipitated (0.11 g). This was found to be *ca.* 95% pure by ^{1}H and ^{13}C n.m.r. spectroscopy, with (**8**) and thioxanthen-9-one *S,S*-dioxide (**9**) as impurities. At this point the resulting dioxane filtrate was neutralized with sodium hydroxide (pH 9) and a precipitate was obtained. This latter solid (0.30 g) was found by ^{1}H and ^{13}C n.m.r. spectroscopy to be (**1**) (*ca.* 38%) and the thioxanthenone *S,S*-dioxide (**9**). Therefore, out of the 80% recovery from this reaction, *ca.* 45% of the material is (**9**) and *ca.* 55% is (**1**). This finding shows unequivocally that oxidation of (**8**) can occur in the presence of hydrochloric acid–dioxane mixtures and is consistent with the results obtained in the ^{17}O-exchange reaction of (**8**) described above.

Experimental

N.M.R. Spectra.—Oxygen-17 n.m.r. spectra were acquired at 27.13 MHz using a Nicolet NT-200 spectrometer. Typically, n.m.r. samples consisted of 40–60 mg of ^{17}O enriched (see below) thioxanthenone in spectroscopic grade acetonitrile (9 cm^3). Spectra were acquired at 60 ± 1 °C using 20 mm sample tubes containing a concentric 5 mm tube filled with D_2O. The D_2O was used as the lock and the internal reference; δ_O D_2O at 60 °C = -3.8 ppm relative to H_2O at 25 ± 1 °C. The samples were not spun. The low concentrations were used to ensure that no concentration effects would compromise the chemical-shift data; the high temperatures were used to reduce to a minimum the linewidth of the ^{17}O peaks.[3c]

Typical spectroscopic parameters were: pulse length 25 μs (*ca.* 90°), pre-acquisition delay 100 μs, acquisition time 42 ms using 2k data points, interpulse delay 50 ms, 30 000 to 200 000 scans acquired. The FIDs were conditioned using exponential multiplication (line-broadening 10 Hz) and zero-filled to 8k prior to plotting. If necessary, the first few points of the FID were zeroed out to remove probe ringdown effects which would result in severely rolling baselines. Chemical shifts were determined by computer line-fitting of the peaks. The fitting was done at least twice for each spectrum; the data were processed and phased independently before each fitting. The results in Table 1 are the averages of all the fits carried out for each compound. The ^{17}O shifts are estimated to be accurate to ± 1 ppm.

^{1}H (200 MHz) and ^{13}C (50 MHz) N.m.r. spectra were obtained as reported previously.[1a,2]

Mass Spectra.—Mass spectra were obtained using a Finnegan MAT TSQ-70 spectrometer at 70 eV ionization energy.

Oxygen-17 Exchange Reactions.—For all compounds except (**6**), ^{17}O enrichment was carried out using dioxane–HCl–$H_2{}^{17}O$ solution in a method similar to those used by St. Amour, *et al.*[3b] and by Chandrasekaran *et al.*[10] The composition of the exchanged compounds was checked using ^{1}H n.m.r. (200 MHz; $CDCl_3$). No changes in composition were found for any of the compounds except the thioxanthenone *S*-oxide (**8**). In this instance, the recovered material contained approximately 81% thioxanthen-9-one *S*-oxide (**8**), 14% thioxanthen-9-one (**1**), and 5% thioxanthen-9-one *S,S*-dioxide (**9**), as determined by both

---

[*] Unless extreme care is taken, it would seem impossible to work in an absolutely anhydrous environment. Thus, many studies employing hydrogen chloride may also have inadvertently involved traces of hydrochloric acid.

^1H and ^{13}C n.m.r. The ^{17}O spectrum of (**8**) was acquired using this mixture. In addition to the expected peak at 507.7 ppm due to the carbonyl of (**8**), there were also peaks in the ^{17}O spectrum at approximately 463 [(**1**), C=*O*], 163 [(**9**), S-O_2], and 1 ppm [(**8**), S-*O*] and a shoulder upfield of the main peak [(**9**), C=*O*]. These extra peaks in the ^{17}O spectrum are consistent with the composition of the mixture as determined by ^1H and ^{13}C n.m.r. spectroscopy.

The general exchange procedure was as follows. To a mixture of the thioxanthenone (0.10 g) in dioxane (4.0 cm^3) under nitrogen was added 160 mm^3 of a dioxane–HCl* solution followed by 1.25–2.0 equiv. of $H_2{}^{17}O$ (20% ^{17}O, Cambridge Isotope Labs). After being stirred for 2–3 days at 60–70 °C, the mixture was cooled and the solvents removed. After being dried (approximately 12 h) *in vacuo* the product was weighed and the n.m.r. spectra obtained. The recovery was usually *ca.* 90%. The increase of the $M + 1$ peak during mass spectroscopy, indicated that generally the enrichment was approximately 5%.

For 2-aminothioxanthen-9-one (**6**) a different procedure was used. To a solution of (**6**) (0.10 g, 0.44 mmol) in dioxane (5 cm^3) there was added (0.02 g, 0.50 mmol) of NaOH. This solution was sealed under nitrogen. Then, 100 $H_2{}^{17}O$ (20% ^{17}O, Cambridge Isotope Labs; 100 mm^3) was added to the dioxane solution and the mixture stirred at 60–70 °C for 3 days. After being cooled to room temperature, the dioxane solution was poured into deionized water (100 cm^3). The yellow precipitate that formed was removed by filtration, washed with deionized water (2 × 3 cm^3) and dried *in vacuo* (2 h) to afford 0.09 g (90% recovery) of enriched 2-aminothioxanthen-9-one.

Repeat of Castrillon and Szmant's Procedure.[7a]—Thioxanthen-9-one *S*-oxide (0.52 g, 0.0023 mol) and dioxane–hydrochloric acid (40 cm^3; 2:1 v/v) were placed in a 50 cm^3 round bottom flask and stirred at room temperature for 4 days. A yellow precipitate formed that was removed by vacuum filtration, washed with a few cm^3 of water, then dried in an Abderhalden drying pistol (acetone under reflux, phosphorus pentaoxide desiccant) for 4 h. This material (product A) was then weighed (0.11 g).

The filtrate was diluted with water (20 cm^3) adjusted to pH *ca.* 9 (Hydrion paper) with sodium hydroxide (solid). Another precipitate formed (product B), which was removed by filtration, washed with a few cm^3 of water, then dried in an Abderhalden drying pistol (acetone under reflux, phosphorus pentaoxide desiccant) for 4 h. The product B was then weighed: 0.30 g.

The ^1H and ^{13}C n.m.r. spectra (200/50 MHz; $CDCl_3$) of products A and B were obtained. The identities of the products were discerned by comparison of these with the published spectra of thioxanthen-9-one, thioxanthen-9-one *S*-oxide, and thioxanthen-9-one *S*,*S*-dioxide.[1a,2] The ratios of the components cited in the discussion were then determined by integrating the ^1H spectra.

Acknowledgements

The authors thank J. A. Cushman and Professor D. W. Boykin for helpful discussions, and C. P. Yu and J. Wang for obtaining the mass spectra. Thanks are also due to Dr. J. Hudson and Mr. R. Canez of Alcon Labs, Fort Worth, for preliminary mass spectroscopic analyses. This work was supported by grant Y-484 from the Robert A. Welch foundation.

References

1 (*a*) A. L. Ternay, Jr. and J. S. Harwood, *J. Heterocycl. Chem.*, 1986, **23**, 1879; (*b*) J. S. Harwood, D. S. Marynick, and A. L. Ternay, Jr., *J. Chem. Soc., Perkin Trans. 2*, 1989, 325.

2 A. L. Ternay, Jr., J. A. Cushman, J. S. Harwood, and C. P. Yu, *J. Heterocycl. Chem.*, 1987, **24**, 1067.

3 (*a*) T. St. Amour and D. Fiat, *Bull. Magn. Reson.*, 1980, **1**, 118; (*b*) T. E. St. Amour, M. I. Burgar, B. Valentine, and D. Fiat, *J. Am. Chem. Soc.*, 1981, **103**, 1128; (*c*) R. T. C. Brownlee, M. Sadek, and D. J. Craik, *Org. Magn. Reson.*, 1983, **21**, 616; (*d*) P. Balakrishnan, A. L. Baumstark, and D. W. Boykin, *ibid.*, 1984, **22**, 753; (*e*) D. W. Boykin, A. L. Baumstark, M. M. Kayser, and C. M. Soucy, *Can. J. Chem.*, 1987, **65**, 1214; (*f*) M. Sawada, Y. Takai, S. Kimura, S. Misumi, and Y. Tsuno, *Tetrahedron Lett.*, 1986, **27**, 3013; (*g*) C. Delseth, T. T.-T. Nguyen, and P. Kintzinger, *Helv. Chim. Acta*, 1980, **63**, 498; (*h*) D. J. Craik, G. C. Levy, and R. T. C. Brownlee, *J. Org. Chem.*, 1983, **48**, 1601.

4 (*a*) S. Ehrenson, R. T. C. Brownlee, and R. W. Taft, *Prog. Phys. Org. Chem.*, 1973, **10**, 1; (*b*) D. J. Craik and R. T. C. Brownlee, *ibid.*, 1983, **14**, 1.

5 (*a*) T. A. Halgren and W. N. Lipscomb, *J. Chem. Phys.*, 1973, **58**, 1569; (*b*) D. S. Marynick and W. N. Lipscomb, *Proc. Natl. Acad. Sci. USA*, 1982, **79**, 1341.

6 M. Karplus and J. A. Pople, *J. Chem. Phys.*, 1963, **38**, 2803.

7 (*a*) J. P. A. Castrillon and H. H. Szmant, *J. Org. Chem.*, 1967, **32**, 976; (*b*) I. Ookuni and A. Fry, *ibid.*, 1971, **36**, 4097.

8 (*a*) D. W. Chasar, T. M. Pratt, and J. P. Shockor, *Phosphorus Sulfur*, 1908, **8**, 183; (*b*) R. H. Rynbrandt, *Tetrahedron Lett.*, 1971, 3555.

9 K. Mislow, T. Simmons, J. T. Melillo, and A. L. Ternay, Jr., *J. Am. Chem. Soc.*, 1964, **86**, 1452.

10 S. Chandrasekaran, W. D. Wilson, and D. W. Boykin, *Org. Magn. Reson.*, 1984, **22**, 757.

Received 13*th June* 1988; *Paper* 8/02351D

---

* This was prepared by saturating dioxane at room temperature with HCl gas, then stirring the dioxane–HCl solution for 2 h at 75 °C. Then (after it was cooled) the dioxane–HCl mixture was titrated with NaOH and found to be 1.3 N in HCl. This mixture was stored in the dark under N_2.