Tetrahedron Letters No. 21, pp 1683-1686, 1975. Pergamon Press. Printed in Great Britain.

A NEW APPROACH TO THE DETERMINATION OF SULFOXIDE STEREOCHEMISTRY: CARBON-13 NUCLEAR MAGNETIC RESONANCE

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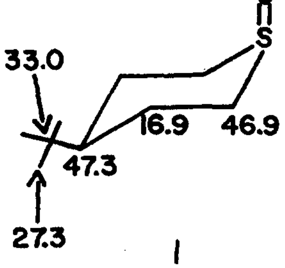
(Received in USA 11 February 1975; received in UK for publication 4 April 1975)

To date, a number of ^{1}H NMR methods have been developed for the assignment of configuration and conformation in cyclic sulfoxides. It has been found in 6-membered rings, that an axial oxygen bonded to sulfur deshields the β axial proton relative to its equatorial counterpart. Also, the methylene protons α to an equatorial oxygen show greater nonequivalence than when the oxygen is axial. More recently, aromatic solvent shifts and lanthanide shift reagents have been applied to the problem, and a review is available.(1)

These ^{1}H NMR methods, however, are plagued by the need for deuterated materials to facilitate spectral analysis, or a series of rather tedious dilution experiments. Furthermore, the differences in couplings or chemical shifts between isomers are relatively small.

We wish to report the marked sensitivity of carbon-13 NMR chemical shifts to the orientation of the exocyclic oxygen in six-membered cyclic sulfoxides, which should permit facile stereochemical assignments. Chemical shifts (δ downfield from TMS) for cis- and trans-4-t-butylthiane-1-oxide 1 and 2 are shown below.(2)



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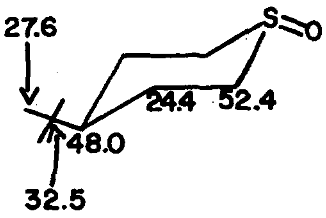

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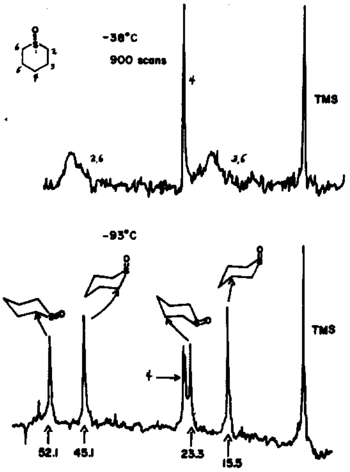
Assignments are unambiguous from off resonance and selective ^{1}H decoupling experiments. The largest effect is a 7.5 ppm shielding at C-3.5 of 1 relative to 2, which is reminiscent of ^{13}C shielding differences between epimeric trimethylene sulfites.(3) This can be interpreted in terms of the "gauche γ" steric shift (4) since C-3.5 of 1 are gauche to the exocyclic oxygen, whereas in 2 they are anti.

Interestingly, carbons 2.6 of 1 and 2 also show a marked chemical shift difference (5.5 ppm) and again the isomer with the axial exocyclic oxygen is more shielded.

As supporting evidence that the ^{13}C shielding differences are primarily due to stereochemical factors we have examined the low temperature behaviour of the conformationatly mobile thiane-1-oxide 3 in CD_2Cl_2 solution. It is known from ^{1}H NMR(5) that E_a for ring inversion of thiane-1-oxide is ca 14 kcal/mole in CH_2Cl_2 and a slight preference for axial oxygen (175 ± 30 cal/mole) was found. At room temperature in CD_2Cl_2 solution, compound 3 exhibits ^{13}C resonances at δ = 47.5, 18.9 and 24.7 ppm, corresponding to carbons 2.6, 3.5 and 4 respectively. Shieldings in $CDCl_3$ are within 0.1 ppm of these values.

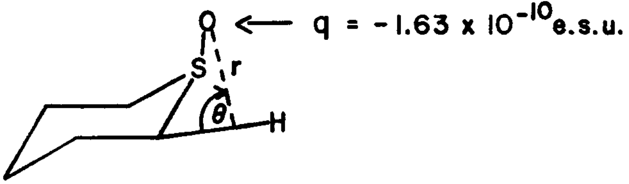
On lowering the temperature, the resonances at δ = 47.5 and 24.7 gradually broaden and show coalescence behaviour near -40° (spectrum shown below). When ring reversal is slow on the NMR timescale (spectrum at -93° shown) the resonances for both conformers of 3 are clearly evident.



From the relative peak areas (6) it is apparent that a preference for the chair form with the axial oxygen exists, in agreement with the ^{1}H results. The shielding differences between conformers of 3 are consistent with those observed in the model compounds 1 and 2, ie 7.0 ppm for C-2.6 and 7.8 ppm for C-3.5. Notably the spectrum at -93° shows only a small shift difference (0.1 ppm) between the C-4 positions of the two conformations of 3.

Regarding the chemical shift phenomena, one can interpret the shielding differences between isomers at C-3.5 to the "γ" steric shift.(4) The large shielding of C-2.6 ("β" effect) in all cases where the adjacent sulfur atom carries an axial oxygen, however, must have a different origin. Minor (2-3 ppm) shielding "β" effects are known in other molecules possessing "γ" shifts (7) but the large magnitude of the "β" shift in sulfoxides merits further comment. Recently (8) some success has been obtained in rationalizing ^{13}C shifts on the basis of electric field effects. A modified electric field calculation for the "β" position of epimeric sulfoxides is outlined below.

Employing a point charge of -1.63×10^{-10} e.s.u. at the oxygen end of the S-O dipole(9), one can calculate the induced dipole moment along each bond of the molecule, since the longitudinal bond polarizabilities (α_l) are known.(10) On the basis of X-ray data (11) chair-like geometries and S-O bond lengths of 1.48 Å were used for both isomers. (12) Models constructed to scale using the appropriate X-ray data (11) were used for measurement of r and θ values (r being the distance from the oxygen to the center of the bond under consideration).



Taking the dipole length as equal to the bond length, the net electron shifts to the termini of each bond of the molecule are found by simple division. Since 4.8×10^{-10} e.s.u. = 1 electron and 1 electron = 180 ppm for ^{13}C (7,13), conversion to ppm is accomplished.

Longitudinal bond polarizabilities ($\alpha_l \times 10^{-25}$ cm^3): CH, 7.9; CS, 17.5; and CC, 19.0.

$$|\underline{E}| = \frac{q}{r^2}, \quad \text{Induced dipole} = \alpha_l E$$

$$\text{Component} = \alpha_l \cos\theta \quad \text{Electron Shift} = \frac{\alpha_l \cos\theta}{\text{bond length}}$$

For the isomer of 3 with an axial oxygen, the net electron shift at C-2.6 is $.26 \times 10^{-10}$ e.s.u. toward carbon, whereas for the equatorial isomer the value is only $.02 \times 10^{-10}$ e.s.u. The difference of .24 e.s.u. $\simeq$ 9 ppm using the above conversion factors. Thus, the "β" shielding effect of *ca* 7 ppm is satisfactorily accounted for on the basis of electric field considerations.(14)

Application of ^{13}C NMR to stereochemical determination of cyclic sultines will be the subject of further reports.

Financial support from the National Research Council of Canada is gratefully acknowledged.

REFERENCES AND FOOTNOTES

1. R.R. Fraser, T. Durst, M.R. McClory, R. Viau and Y.Y. Wigfield, Int. J. Sulfur Chem. A. Vol. 1 133 (1971).
2. 0.2 M solutions in $CDCl_3$. ^{13}C spectra were obtained under conditions of complete ^1H noise decoupling in the Fourier Transform mode using a Varian XL-100-12 NMR spectrometer equipped with the Nicolet Technology Inc. data system.
3. G.W. Buchanan, J.B. Stothers and G. Wood, Can. J. Chem. 51, 3746 (1973).
4. N.K. Wilson and J.B. Stothers, Topics in Stereochemistry Vol. 8, 1 (1973).
5. J.B. Lambert and R.G. Keske. J. Org. Chem. 31, 3429 (1966).
6. Particular care must be exercised in the interpretation of ^{13}C peak areas in F.T. spectra obtained using ^1H noise decoupling conditions, since differences in ^{13}C T_1's and Overhauser enhancements can affect the observed areas. In this work, no change in the N.O.E.'s are noted

over a range of ± 50 Hz from the optimum ^{1}H decoupling frequency based on the low temperature ^{1}H shifts for 3 (5). Also, T_1's for C-3.5 and C-2.6 of 1 and 2 have been found to be nearly identical.

7. J.B. Stothers, Carbon-13 NMR Spectroscopy, Academic Press, New York, N.Y. 1972.
8. J.G. Batchelor, J.H. Prestegard, R.J. Cushley and S.R. Lipsky, J. Am. Chem. Soc., 95, 6358 (1973).
9. M.S. Goldenberg, P. Kruus and S.K.F. Luk, Can. J. Chem. 53, (in press) 1975.
10. J.O. Hirschfelder, C.F. Curtiss and R.B. Bird, Molecular Theory of Gases and Liquids - John Wiley and Sons, New York (1964).
11. H.M.M. Shearer, J. Chem. Soc. 1394 (1959).
12. Infrared evidence (K.W. Buck, Chem. Comm. 758, (1966), suggests the equatorial S-O bond may be shorter than the axial S-O. Shortening of the equatorial bond to 1.40 Å affects the calculated shift by less than 5%.
13. Conversion factors relating carbon shieldings to electron density have been reported which range from 160 to 200 ppm per electron. The value of 180 employed here represents an intermediate estimate.
14. Since part of the "β" shift probably arises from the "γ" interaction, the electric field effects need only account for 3-5 ppm of the shielding difference between epimers. Thus, the agreement between the calculated and observed is within a factor of two to three, which is in accord with the limits of expectation for electric field calculations.