Exchange Rates of Diastereotopic Protons in a Conformationally Frozen Sulphoxide

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THE benzylic protons of benzyl methyl sulphoxide have been reported to undergo base-catalysed exchange in heavy water at rates differing by a factor of 14.[1] The absolute stereochemistry of the monodeuteriosulphoxide was subsequently determined.[2] In addition MO calculations have been reported for the CH_2·SOH anion, a model for the transition state leading to exchange.[3] In view of both theoretical and experimental results it was suggested that the most stable carbanion conformation will have the electron pair bisecting the projected angle between the lone pair and oxygen of the adjacent sulphoxide. Two other examples of unequal rates of exchange of diastereotopic protons have appeared more recently.[4] It appeared to us that a second factor might contribute to the unequal rates of exchange. We recently reported evidence that the diastereotopic protons of benzyl phenyl and benzyl methyl sulphoxide are oriented differently with respect to the benzene ring.[5] This asymmetry in orientation could result in unequal rates of exchange.[6] We have therefore determined the relative rates of exchange of the two sets of diastereotopic protons in the conformationally fixed sulphoxide, 5,7-dihydro-1,11-dimethyldibenzo[*c*,*e*]thiepin 6-oxide (I). The exchange rates of two of the protons attached to the same carbon atom in (I) have been found to differ by a factor of 1250. The magnitude of this rate difference is unprecedented and strongly supports the predictions based on MO calculations.[3]

Sulphoxide (I) was obtained by periodate oxidation of the corresponding sulphide, which had been prepared previously.[7,†] Its n.m.r. spectrum [Figure 1(a)] shows separate doublets for each of the four benzylic protons.[‡]

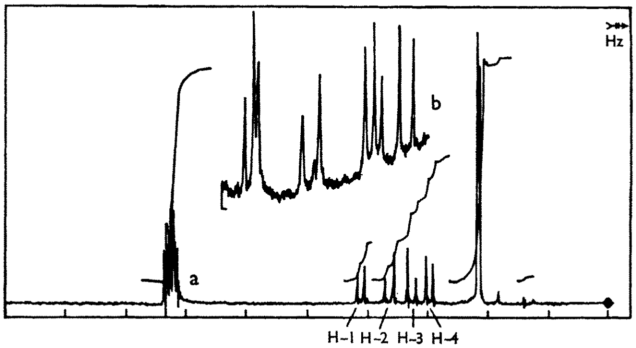

FIGURE 1. (a) *The* 100 *MHz n.m.r. spectrum of* (I) *in* $CDCl_3$; (b) *The* 100 *MHz spectrum of* (I) (5% w/v) *in* [O-^{2}H]-*t-butyl alcohol containing potassium t-butoxide* (0·005 M) *after* 135 *min.*

These will be referred to as H-1, H-2, H-3, and H-4 in order of their appearance from left to right. Solutions of (I) in [*O*-^{2}H]t-butyl alcohol containing potassium t-butoxide could be continuously monitored by n.m.r. and the rate of

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[†] A satisfactory analysis was obtained.

[‡] In addition to intensity loss, exchange is revealed by the appearance of a third peak for each hydrogen whose diastereotopi partner has been replaced by deuterium.

disappearance of the protons (H-1—H-4) determined by integration. Figure 1(b) shows a typical spectrum of partially exchanged sulphoxide. In this example signals for H-2 and H-4 have diminished to about 30% of their intensity, that for H-3 has diminished slightly, and H-1 has not yet undergone any detectable exchange.§ From the results of kinetic measurements at four different base concentrations the relative rates for H-1—H-4 were found to be 1:1100:310:1250,¶ the largest difference being between H-1 and H-4, which are attached to the same carbon atom. This large difference in the rate of one proton relative to the other three rules out any major influence of the benzene rings on the rates.

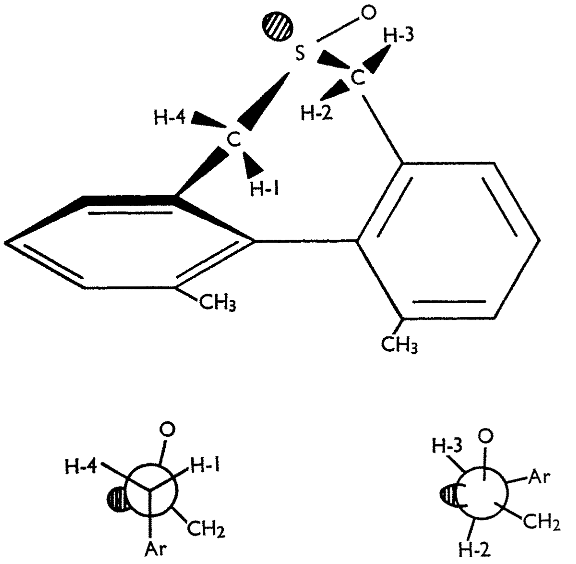

FIGURE 2. *A three-dimensional representation of sulphoxide* (I), *including Newman projection formulae of the two* C–S *bonds as estimated from a Dreiding model.*

Assignment of stereochemistry to protons H-1—H-4 can be made as follows. It is well known that in thian 1-oxides the chemical shift difference between methylene protons adjacent to an axial sulphoxide oxygen is smaller and their geminal coupling constant larger in magnitude than when the sulphoxide oxygen is equatorial.[8] In sulphoxide (I), the arrangement of the two methylene groups relative to the sulphoxide closely resembles the two α-methylenes of axial and equatorial thian 1-oxides as shown in Figure 2. Thus H-1 and H-4 are assigned to the methylene group with a C–H bond *trans* to the lone pair of the sulphoxide, since they have the larger non-equivalence and smaller coupling constant (11·4 compared to 13·7 c./sec. for the close-spaced AB quartet).

The specific assignments for H-1 and H-4 in Figure 2 account well for the fact that H-1 exchanges at a vastly different rate from H-2 or H-3. Were H-1 and H-4 reversed, it would not be possible to explain the relative inertness of H-1, since one of H-2 or H-3 would be in an almost identical environment with respect to the sulphoxide group. The similarity in line-widths of signals for H-1 and H-2 is probably due to long-range coupling with the aromatic protons, greatest when the benzylic C–H is co-linear with the benzene π-orbitals.[9] For this reason, H-2 is assigned to the position in which this coupling should be larger. Interchange of H-2 and H-3 remains a possibility but this would not alter our main conclusion.

The observed slow exchange rate for H-1, which is *trans* to the lone pair on sulphur, confirms the earlier MO predictions.[3] The carbanion in this conformation was calculated to be 12·8 kcal. less stable than in the orientation possessed by H-4. The observed difference in exchange rates for H-1 and H-4 implies a 4·3 kcal. difference in transition states, a result quite compatible with theory. The relative rates of exchange of H-2 and H-3 do not agree with theory, in that H-3 should exchange more rapidly. It is possible that the effect of orientation with respect to the benzene ring could be responsible for this minor deviation.

The large energetic preference for a carbanion *gauche* to both the lone pair and oxygen should have a dominant effect on the stereochemical outcome of any of its subsequent reactions. Observations of this nature have been reported.[10]

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§ All spectra were measured on a Varian HA-100 n.m.r. spectrometer.

¶ The specific pseudo-first order rate constant for exchange of H-4 in [O-^{2}H]t-butyl alcohol (0·025M in t-butoxide) was 9·6 × 10^{-4} sec.$^{-1}$. All rate constants are accurate to ± 10%. The large solvent peak nearby reduced the accuracy of measurement of the integrals and the alternative method of tracing and weighing gave first-order plots of the same accuracy.

[1] A. Rauk, E. Buncel, R. Y. Moir, and S. Wolfe, *J. Amer. Chem. Soc.*, 1965, **87**, 5498.
[2] S. Wolfe and A. Rauk, *Chem. Comm.*, 1966, 778.
[3] S. Wolfe, A. Rauk, and I. G. Csizmadia, *J. Amer. Chem. Soc.*, 1967, **89**, 5712; *Canad. J. Chem.*, 1969, **47**, 113.
[4] E. E. Bullock, J. M. W. Scott, and P. D. Goldin, *Chem. Comm.*, 1967, 168; M. Nishio, *Chem. Comm.*, 1968, 562.
[5] R. R. Fraser, Gurudata, C. Reyes-Zamora, and R. B. Swingle, *Canad. J. Chem.*, 1968, **46**, 1595.
[6] P. T. Lansbury, J. F. Bieron and A. J. Lacher, *J. Amer. Chem. Soc.*, 1966, **88**, 1482.
[7] K. Mislow, M. A. W. Glass, H. B. Hopps, E. Simon and G. H. Wahl, jun., *J. Amer. Chem. Soc.*, 1964, **86**, 1710.
[8] A. B. Foster, T. D. Inch, M. H. Qadir, and J. M. Webber, *Chem. Comm.*, 1968, 1086; R. C. Cookson and T. A. Crabb, *Tetrahedron*, 1968, **24**, 2385, and references in these papers.
[9] H. Rottendorf and S. Sternhell, *Austral. J. Chem.*, 1964, **17**, 1315; M. Karplus, *J. Chem. Phys.*, 1960, **33**, 1842.
[10] T. Durst, *J. Amer. Chem. Soc.*, in the press.