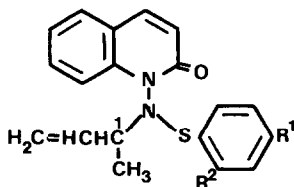


ROTATION BARRIERS IN N-HETEROARYLSULPHENAMIDES

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In the n.m.r. spectrum of the sulphenamide (1),¹ two doublets are observed for the methyl group at δ 0.93 and 1.48 (CFCl₃). Repeated crystallisation from light petroleum gave one diastereoisomer containing only the doublet at δ 0.93; the other diastereoisomer containing only the doublet at δ 1.48, was obtained by chromatography over Kieselgel.



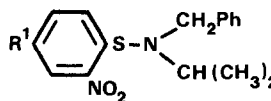
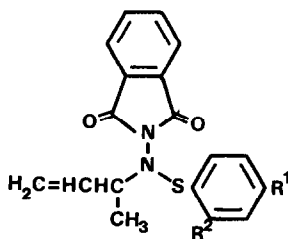
- (1) R¹ = Cl, R² = H
(7) R¹ = R² = NO₂

We present evidence which indicates that it is an abnormally high barrier to rotation around the N-N bond which is responsible for the additional chirality (a chiral axis) and hence the existence of diastereoisomers in (1).

In contrast to the sulphenamide (1), the phthalimido analogue (2) shows no evidence for the presence of diastereoisomers in its n.m.r. spectrum with only a single methyl doublet visible (δ 1.35 : CDCl₃). As a result of its symmetry, the phthalimido group cannot sustain a chiral axis, unlike the quinolone ring in (1).

Restricted rotation around S-N bonds has been studied by Raban and his co-workers,² who find that the barrier to rotation is significantly augmented by substitution of electron-withdrawing groups into a phenyl ring on sulphur. Thus sulphenamide (3) shows coalescence both of the diastereotopic protons of the benzyl group and the diastereotopic methyls of the isopropyl group in its n.m.r. spectrum at $\sim 64^{\circ}\text{C}$ as rotation around the S-N bond becomes fast on the n.m.r. time-scale. Whereas the barrier to rotation ΔG^{\ddagger} can be calculated to be 17.0 kcal/mole for (3),³ it falls to 15.0 kcal/mole for the mononitrophenyl analogue (4).

Restricted rotation around the S-N bond is also visible in (5) and (6) containing two and one nitro groups respectively in the phenyl ring on sulphur. Thus the methyl group in (5) appears as a pair of overlapping doublets (δ 1.36 and 1.42, J 7 Hz) at 220 MHz and 0°C. The presence of diastereoisomers on the n.m.r. time-scale is also apparent in the resonances of the dinitrophenyl ring and, in particular, the proton ortho to sulphur for which two doublets are also observed (δ 9.28 and 9.35, J 9.5 Hz, ratio 1:1.4 respectively). Coalescence of the latter pair of doublets and those of the methyl groups is observed at $\sim 39^\circ\text{C}$ indicating an associated barrier ΔG^\ddagger of 16.8 kcal/mole, in good agreement with the value for (3) above. In the corresponding mononitrophenyl analogue (6), the barrier falls to 14.6 kcal/mole which again suggests accelerated S-N rotation is responsible for the coalescence observed by comparison with (4) above.



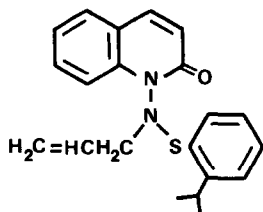
- (2) $R^1 = \text{Cl}, R^2 = \text{H}$
 (5) $R^1 = R^2 = \text{NO}_2$
 (6) $R^1 = \text{H}, R^2 = \text{NO}_2$
 (9) $R^1 = \text{H}, R^2 = \text{CH}(\text{CH}_3)_2$

- (3) $R^1 = \text{NO}_2$
 (4) $R^1 = \text{H}$

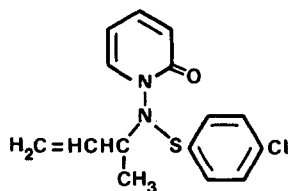
Of particular interest is the n.m.r. spectrum of (7), the dinitrophenyl analogue of (1); observation of four methyl doublets (δ 1.18, 1.32, 1.50 and 1.60 : ratio 7.3; 1; 2; 4.3 respectively) in its 220 MHz spectrum at -40°C is accounted for by the presence of two chiral axes (S-N and N-N) in addition to the chiral centre at C-1 giving four possible diastereoisomers. Significantly, coalescence of only two pairs of methyl doublets takes place at $\sim 0^\circ\text{C}$ as S-N bond rotation becomes fast on the n.m.r. time-scale.

Evidently the energy barrier which allows separation of diastereoisomers in (1) is grossly different in magnitude from that attributable to S-N bond rotation: the 1st-order conversion of one pure diastereoisomer of (1) into an equilibrium mixture of the two followed by n.m.r. enables a minimum⁴ activation energy of 27 kcal/mole to be calculated for what we presume to be rotation around the N-N bond.

The N-N chiral axis in these N-quinolone substituted sulphenamides can be recognised also by the diastereotopic methyls (δ 0.82 d, J 7.5 Hz and δ 1.02 d, J 7.5 Hz) in the isopropyl group of (8) in d_8 -toluene. No coalescence of the signals is observed up to 100°C above which temperature thermal decomposition takes place. Removal of the chiral axis as in the phthalimido analogue (9) results in the observation of only one doublet (δ 1.2, J 7.5 Hz) for the isopropyl methyl groups.



(8)



(10)

An alternative interpretation for the diastereoisomerism in (1) is that the sulphenamide nitrogen is pyramidal and not inverting. In this case, however, observation of diastereoisomers in (2) and (9) might also have been anticipated. Moreover, substitution of carbon by sulphur as a substituent on nitrogen lowers the barrier to inversion in aziridines⁵ and the inversion barrier at the sulphenamide nitrogen in (1), therefore, would be expected to be less than that in an acylated hydrazine.⁶ Evidence on this point comes from the n.m.r. spectrum of the sulphenamide (10). Two methyl doublets are again observed in the n.m.r. spectrum (δ 1.05 and 1.41; $CDCl_3$) but only at temperatures $< -20^\circ C$; coalescence takes place at $\sim 30^\circ C$. Evidently removal of the benzene ring in (1) eliminates the high barrier separating the two diastereoisomers. Since the quinolone ring in (1) is larger than the pyridone ring in (10), the effect upon a nitrogen inversion barrier would be expected to be the opposite to that actually observed.⁷

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References

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2. M. Raban, G.W.J. Kenney, and F.B. Jones, J. Amer. Chem. Soc., 1969, 91, 6677.
3. Raban et al (Ref.2) report a value of 16.5 kcal/mole in d_8 -toluene for (3); our values for (3) and (4) were measured in $CDCl_3$.
4. The actual process which interconverts the diastereoisomers in (1) is only formally rotation around the N-N bond: other processes, e.g. dissociation-recombination could lead to the same result.
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