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The Unusual Hydrogen Bond of Dihydrotazettine Methine Alcohol

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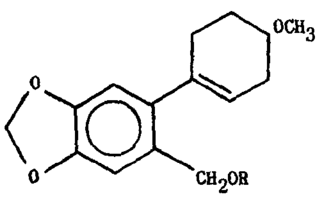
Recently, examination of the n.m.r. spectrum of dihydrotazettine methine has shown that the structure must be 1, a revision of the previous structure (1) requiring only the shift of the double bond from the unconjugated position (2). Basic hydrolysis of this ester provides the alcohol 2, m.p. 63-64°, the infrared spectrum of which shows hydroxyl stretching absorption at 3620 and $3500\ cm.^{-1}$, the latter with a width at half height of $80\ cm.^{-1}$ (CCl_4, unchanged on dilution to 0.004 M). The low frequency and broad character of the second



1, R = $\overset{\overset{O}{\|}}{C}CH_2NMe_2$

2, R = H

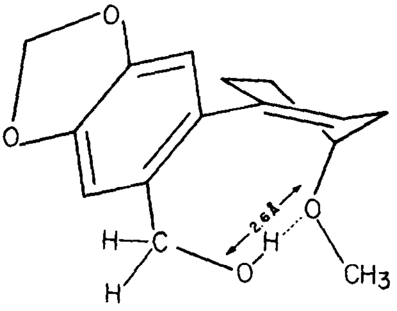


Figure 1

band demonstrate a strong hydrogen bond, which the dilution studies show must be intramolecular (3).

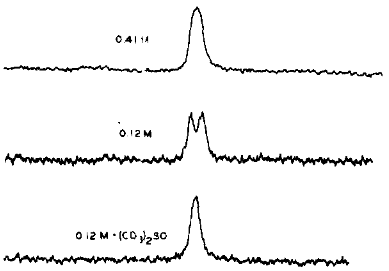


Figure 2, n.m.r. spectrum of benzylic protons of 2 in CCl_4 at δ = 4.7 p.p.m.

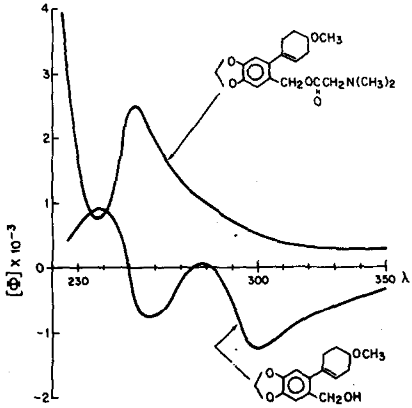


Figure 3, O.R.D. curves of 1 and 2 in hexane solution.

That absorption at 3500 $cm.^{-1}$ reveals interaction of the hydroxyl with the double bond is unlikely, for hydroxyl groups so bonded seldom absorb below 3550 $cm.^{-1}$ (4). Construction of Dreiding models of this molecule reveals the probable nature of this bond, for the hydroxyl can approach within 1.6 Å of the methoxyl, with a linear conformation and an O···O distance of 2.6 Å (see Figure 1).

This unusual hydrogen bond adds rigidity to the molecular conformation, which is revealed in the n.m.r. spectrum of the benzylic methylene group. This appears as an AB quartet, which coalesces to a singlet at approximately 68°. Other compounds of this series (e.g., 1) have not shown this phenomenon. It is clear that the non-equivalence of the methylene group is dependent upon the hydrogen bond, for concentrated solutions in CCl_4 do not show this effect, which appears on dilution (see Figure 2). Addition of a drop of polar material, here $(CD_3)_2SO$, to a dilute solution similarly destroys the non-equivalence by disrupting the hydrogen bond (3,5).

The rigidity thus demonstrated results in the alcohol existing in dilute non-polar solution as a skewed styrene, an assymetric chromophore that should be revealed by the optical rotatory dispersion. It can be seen from Figure 3 that this is indeed the case, for a hexane solution of the alcohol reveals a negative Cotton effect superimposed upon the positive plain curve of the ester 1. A methanolic solution of the dihydrotazettine methine alcohol 2 reveals only the plain curve from 350 to 250 mμ.

The configuration represented by Figure 1 apparently conforms to these observations. The approach of the hydroxyl group to the methoxyl is close enough to permit the strong hydrogen bond observed. The chirality of the styrene system is that of the skewed styrenes of known configuration which produce similar Cotton effects (6). The benzylic methylene group is seen to lie near the saturated carbon atoms of the cyclohexenyl system; in an alternative configuration, this group lies with one atom much nearer the double bond, a relation which should produce a much greater disparity in chemical shift than that observed for these two atoms. The double bond is nearly normal to the aromatic system, a state consistent with the failure of the ultraviolet absorption to show any conjugation (7). It is seen that the methoxyl group must occupy the energetically less favored axial position, but the energy difference of the axial and equatorial conformations is evidently comparable to that of the hydrogen bond.

REFERENCES

1. R. J. Highet and W. C. Wildman, Chemistry and Industry, 1159 (1955).
2. J. C. N. Ma, P. F. Highet and R. J. Highet, to be published.

3. G. C. Pimentel and A. L. McClellan, *The Hydrogen Bond*, p. 87. W. H. Freeman and Company, San Francisco (1960).
4. cf. (a) H. M. Fales and W. C. Wildman, *J. Am. Chem. Soc.*, **85**, 784 (1963); (b) P. von R. Schleyer, D. S. Trifan and R. Backsai, *ibid*, **80**, 6691 (1958); (c) P. von R. Schleyer, C. Wintner, D. S. Trifan and R. Backsai, *Tetrahedron Letters*, No. 14, 1 (1959); (d) it is further unlikely that the olefin is involved in the hydrogen bond because 2-hydroxymethylbiphenyls fail to show bonding of the hydroxyl to the adjacent aromatic ring. cf. W. F. Baitinger, P. von R. Schleyer and K. Mislow, *J. Am. Chem. Soc.*, **87**. 3168 (1965).
5. Because the outer limbs of the quartet are lost in the instrumental noise, the signal appears as a doublet, which might result from coupling of the methylene protons with the hydroxyl proton. However, the hydroxyl signal appears as a singlet, and exchanging the proton for a deuterium atom does not alter the absorption of the benzylic methylene group.
6. P. Crabbé, *Optical Rotatory Dispersion and Circular Dichroism in Organic Chemistry*, p.253. Holden-Day, San Francisco (1965).
7. This property is common to this series, and to 1-(2-tolyl)-cyclohexene.