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A LARGE CHEMICAL SHIFT DIFFERENCE FOR GEMINAL PROTONS

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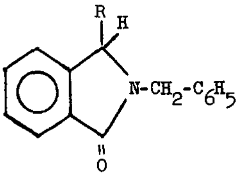
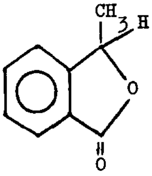
We wish to report that the nuclear magnetic resonance spectrum of 1-phenyl-2-benzylphthalimidine (I) (1) in carbon tetrachloride reveals the methylene protons as an AB system, approaching an AX system, with chemical shifts τ = 4.58 p.p.m. and 6.33 p.p.m.

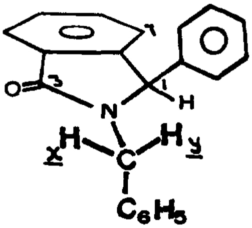




I R = C_6H_5 III

II R = CH_3

(J = 15 c.p.s.). The unusually large difference (1.75 p.p.m.) between the chemical shifts of these two protons can be readily explained on the basis of reasonable assumptions about the lowest energy conformation of I. It is assumed that in this conformation (IA) i) the N-C-C plane of the N-benzyl group is approximately perpendicular to the plane of the 5-membered ring (this minimizes non-bonded repulsions between the 1- and 3-positions of the 5-membered ring and the phenyl ring of the N-benzyl group), ii) the latter phenyl group is oriented anti to the phenyl group at C 1 and iii) the plane of the phenyl ring at C 1 is approximately perpendicular to the plane of the 5-membered ring (this practically eliminates steric compression between the ortho hydrogens of this phenyl ring and the two neighboring hydrogen atoms (the hydrogen atom labeled y and that at C 7).



IA

In this conformation (IA), the proton labeled x would probably lie in the deshielding region caused by the diamagnetic anisotropy of the carbonyl group while the proton labeled y would be located in the shielding region created by the ring current of the phenyl group at C 1.

In order to test this model, we have compared the chemical shift difference for the geminal protons of I with that of the corresponding protons of 1-methyl-2-benzylphthalimidine (II). The major effect of replacing the phenyl by a methyl group would be to decrease the shielding of proton y due to the removal of the ring current.* The magnitude of this effect can be calculated to be about 0.6 p.p.m., using the point dipole approximation (2) and taking the distance r between proton y and the center of the phenyl ring as 3.4 Å and the

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*It is assumed that the conformation would be unaffected by this replacement angle γ (by which a line extending from this hydrogen to the center of the benzene ring is displaced from the axis which is perpendicular to the plane of this ring) as 40°.[*] In addition, since proton *x* of I is slightly deshielded by the phenyl ring at C 1, the replacement of this ring by a methyl group should cause an upfield shift of the signal due to this proton. Using the same approximation (2), this effect can be estimated to involve a shift of about 0.1 p.p.m.[†] If it is assumed that the shielding values of the two methylene protons are affected to about the same extent by the difference (4) in inductive effects of the phenyl and methyl groups,[‡] then the substitution of the methyl for the phenyl group should result in an upfield shift of the signal of proton *x* (due to the inductive change and the removal of the deshielding effect of the phenyl ring) and a larger downfield shift of that of proton *y* (due primarily to the removal of the shielding effect of the ring current). Quantitatively, the shift difference between the geminal protons should be reduced by about 0.7 p.p.m. (0.6 + 0.1) upon replacement of a phenyl with a methyl group.

The methyl analogue II has been prepared by the method (1) used previously to prepare I. A mixture of benzylamine (25 mmoles)

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[*] These values were measured directly on a Barton Model (3) of IA, constructed to scale. This shielding value is rather insensitive to modest deviations from assumptions i) and iii) above.

[†] The measured distance r was taken as 4.6 Å and the angle γ as 65°. In this case, the value of the shielding is rather sensitive to errors in the angle. However, even the most extreme errors in this angle would change the value by less than a factor of 2.

[‡] This would only be rigorously true if the electrical effect were transmitted primarily by the inductive rather than by the field mechanism.

and benzylamine hydrochloride (0.8 mmole) was heated under nitrogen at 170° for 84 hr. with 3-methylphthalide (III) (9 mmoles), obtained (5) by zinc reduction of o-acetylbenzoic acid. A trace of yellow impurity could not be removed from the oily product either by bulb-to-bulb distillation or by chromatography on alumina. However, the infrared and n.m.r. spectra of this product clearly indicate that it is 1-methyl-2-benzylphthalimidine (II). The infrared spectrum of the neat liquid exhibits the characteristic carbonyl peak of a phthalimidine at 1658 cm^{-1} (I, in chloroform, absorbs at 1671 cm^{-1}). The n.m.r. spectrum in carbon tetrachloride exhibits a multiplet in the aromatic region (9 protons), a quartet centered at $\tau = 5.73$ p.p.m. (J = 6 c.p.s.) (1 proton, methine), a doublet at $\tau = 8.65$ p.p.m. (J = 6 c.p.s.) (3 protons, methyl) and two doublets (J = 15 c.p.s.) (1 proton each) for the benzylic protons.

In accord with the expectations outlined above, the lower field of these two doublets, which is centered at $\tau = 4.80$ p.p.m., is displaced upfield by 0.22 p.p.m. from the corresponding doublet of I, while the higher field doublet, which is centered at $\tau = 5.85$ p.p.m, is displaced downfield by 0.48 p.p.m. from the corresponding doublet of I. The difference between the separations of the gem. protons of I and II is thus 0.7 p.p.m., in good agreement with the value calculated on the basis of our model.

The chemical shift difference for the geminal protons of I and those reported in the accompanying communication for closely related systems by Southwick, Fitzgerald and Milliman (6) are apparently the largest known for noncyclic methylene groups (7). A considerably larger effect has recently been reported for a ring methylene group which is oriented in such a way that one proton is shielded and the other deshielded by the same ring current (8).

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