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THE CONFORMATIONAL ANALYSIS OF SOME 3-SUBSTITUTED BICYCLO[3.3.1]NONANES BY MEANS OF Eu(DPM)$_3$ INDUCED N.M.R. SHIFTS

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Since the introduction of tris(dipivaloylmethanato)-europium (Eu(DPM)$_3$) as a shift reagent in n.m.r. spectroscopy[1], numerous reports have appeared on its applications. It has been shown that the reagent induces large downfield shifts of protons in compounds containing heteroatoms and that the magnitude of the downfield shift varies with the proton-heteroatom distance[1,2,3]. Further, it has been shown that a linear relationship exists between the extent of the shift ($\Delta\tau$) for a particular proton and the compound : Eu(DPM)$_3$ ratio. The discovery[4] of transannular shifts suggests that the shift influence is transmitted through space and not via the bond framework of a molecule.

In a conformationally mobile system containing a heteroatom, the distance of a particular proton from that heteroatom will differ in each conformation except, perhaps, in the case where the proton and the heteroatom are directly bound or geminal. Most conformational interconversions are fast compared with the n.m.r. timescale. It should, therefore, be possible to determine with reasonable accuracy the average distance of the protons in a suitable mobile system from the heteroatom in that system by n.m.r. measurements employing increasing amounts of Eu(DPM)$_3$. The method would, of course, be impracticable if addition of Eu(DPM)$_3$ to the system disturbed the equilibrium by imposing new non-bonded interactions. Such disturbance would alter the average proton-heteroatom distance and this would be reflected in the non-linearity of a plot of $\Delta\tau$ against the compound : Eu(DPM)$_3$ ratio.

The bicyclo[3.3.1]nonanes I-III were particularly attractive compounds on which to test these assumptions. Twist conformations in such a system are minimal and minor changes in conformational equilibrium would have a profound effect on the average distances between the heteroatom and the transannular C$_7$ protons. The symmetry of these compounds allowed ready analysis of their n.m.r. spectra in the presence of Eu(DPM)$_3$ and the heteroatom-proton distances for several protons were relatively insensitive to conformational changes within the molecule thus allowing estimation of other heteroatom-proton distances by comparison of the slopes of the plots of $\Delta\tau$ against compound : Eu(DPM)$_3$ ratio.

Bicyclo[3.3.1]nonan-3-one (I)

The 100 MHz n.m.r. spectrum of I (20 mg) in CCl_4 (0.5 ml) showed a broad singlet (6H) at δ 2.36 (2 x H_a, H_b, H_c) and a methylene envelope between δ 1.9-1.5. Successive additions of the shift reagent in 20 mg portions separated all protons in the n.m.r. spectrum as follows:- H_a (2H, doublet); H_b (2H, quartet), H_h (1H, multiplet); H_d (1H, doublet, J = 12Hz); H_c (2H, singlet); H_e (1H, doublet, J = 12Hz); H_f (2H, doublet); H_g + H_i (3H, triplet). All resonances were broad.

The relationship between the shifts of each proton and the amount of added Eu(DPM)$_3$ is shown in Fig. I. The plot of $\Delta\tau$ against the proportion of Eu(DPM)$_3$ is linear for each proton and suggests that the conformational equilibrium of I is unaffected by the shift reagent. These results indicate that the distances of each proton from the oxygen atom in I are in the order $H_{a\text{ or }b} < H_{b\text{ or }a} < H_h < H_d < H_c < H_g < H_e < H_f + H_i$.

A study of models shows that H_a and H_b can only vary in distance from the carbonyl oxygen by 60 pm and must fall between the limits 250-310 pm. Similarly H_c can only vary in distance from the oxygen atom between the limits 400-440 pm. Therefore the average distance of H_h and H_d from the oxygen atom must satisfy the requirement 250 pm < H_h distance < H_d distance < 440 pm. Further, because $\Delta\tau$ values for H_g and H_i are the same, the average conformational position in I demands that the O-H_g distance = O-H_i distance.

These requirements are satisfied if the cyclohexane ring containing the carbonyl group is flattened such that C_1,C_2 and C_3, C_4 and C_5 are planar. This gives the following average distances of protons from oxygen as:- H_a, 320 pm; H_b, 270 pm; H_c, 440 pm; H_d, 400 pm; H_h, 320 pm; H_g, 520 pm and H_i, 540 pm.

This suggests that I exists as a 1:1 mixture of conformers I_a and I_b at 30°, a result which explains only a moderate percentage of transannular reaction in derivatives of I[5].

exo Bicyclo[3.3.1]nonan-3-ol (II)

The n.m.r. spectra of II run with increasing amounts of Eu(DPM)$_3$ were similar to I. Each separate proton was visible and the linearity of all $\Delta\tau$: amount of Eu(DPM)$_3$ plots (Fig. II) indicated no upsetting of the conformational equilibrium by the shift reagent.

The slopes of the plots so obtained require that the average distance of protons from the oxygen atom must be in the order $H_a < H_{b\ or\ c} < H_{c\ or\ b} < H_e < H_d < H_i < H_f < H_g < H_h < H_j$.

This requirement is not met by any of the three conformations IV_a-VI_a and can only be obtained on models if the average conformational situation in II is that of an extremely "flattened" chair-chair form of II such that C_1, C_2, C_3, C_4 and C_5 are almost planar and also C_5, C_6, C_7, C_8 and C_1 are similarly almost planar. Thus the conformational equilibrium in II requires that the average H_a-H_i distance is about 280 pm and the C_3-C_7 distance about 330 pm.

A similar study on endo-bicyclo[3.3.1]nonan-3-ol (III) failed to give a linear plot of $Eu(DPM)_3$ concentration against $\Delta\tau$ for any proton inferring that addition of shift reagent upsets the conformational equilibrium. However at low concentrations of shift reagent $\Delta\tau$ values for protons infer that proton-oxygen distances **are** in the order $H_{b\ or\ c} < H_{c\ or\ b} < H_i < H_e < H_d$. This suggests that the major conformation of III is V_b.

Variable temperature studies of the n.m.r. of these systems in the presence of $Eu(DPM)_3$ are now underway.

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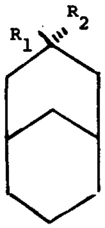
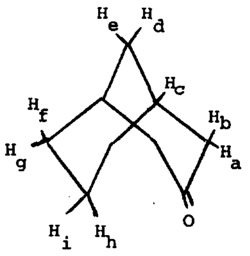
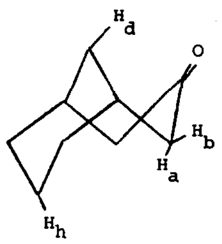


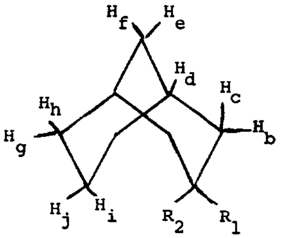


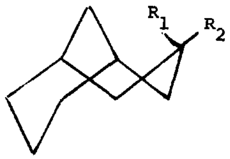


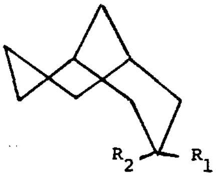
I R_1,R_2 = O; II R_1 = OH, R_2 = H, III R_1 = H, R_2 = OH

I_a

I_b







IV_a R_1 = OH, R_2 = H_a; IV_b R_1 = H_a, R_2=OH

V_a R_1 =OH, R_2 = H_a
V_b R_1 =H_a, R_2 = OH

VI_a R_1 = OH, R_2 = H_a
VI_b R_1 = H_a, R_2 = OH

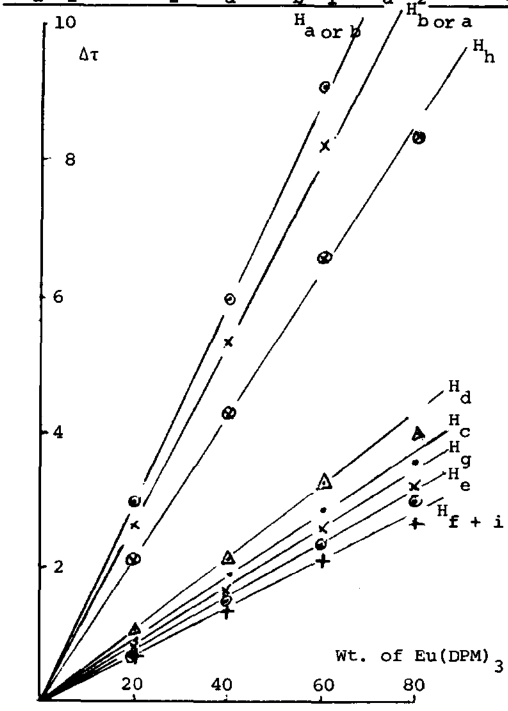


Fig. I. Change in chemical shift of the protons of I (20 mg/0.5 ml CCl_4) with increasing amounts (in mg) of $Eu(DPM)_3$.

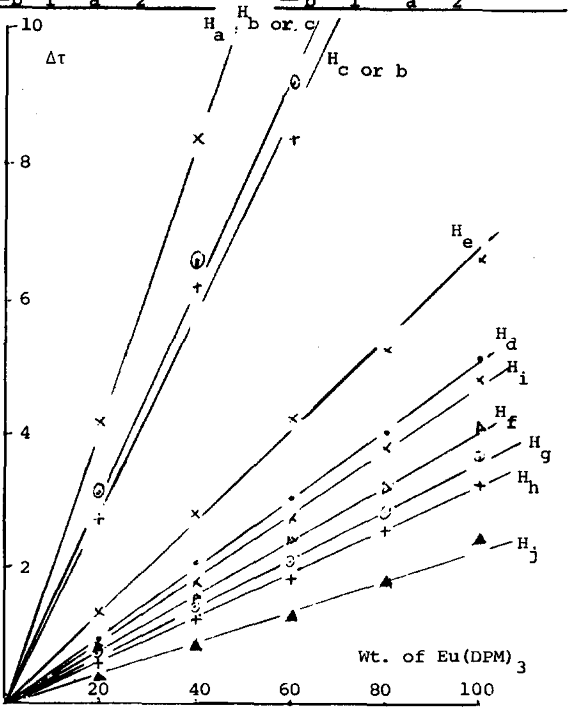


Fig. II. Change in chemical shift of the protons of II_a (20 mg/0.5 ml CCl_4) with increasing amounts (in mg) of $Eu(DPM)_3$.