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ON THE LACK OF AN INTRAMOLECULAR HYDROGEN BOND IN 5-HYDROXYMETHYL-1,3-DIOXANE AND RELATED COMPOUNDS.

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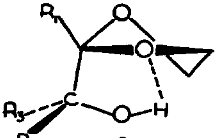
Introduction of an alcohol function in the 1,3-dioxane system may lead to intramolecular hydrogen-bonding of the OH...O type between the hydroxyl group and one or both of the heterocyclic oxygens.A strong hydrogen bond is indeed observed in 5-hydroxymethyl-1,3-dioxane (1)[1,2] :its geometry is not particularly appealing - eclipsing of a lone pair on oxygen with the C(5)-H bond plus marked deviation from O-H...O colinearity.[3] Likewise,2-hydroxyalkyl-1,3-dioxolanes (2) display strong OH...O bonds.[2] We have examined closely another structural variation,exemplified by 5-hydroxymethyl-1,3-dioxane (3 R_1=R_2=R_3=H).

1a 1e



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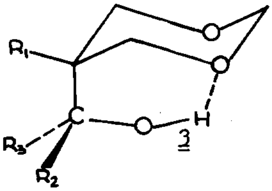


3

Such molecules exist in the chair conformation, as indicated by the magnitude of the interproton coupling constants : the geminal protons at C(2) and at C(4) are coupled by 6.5 and 12.0 Hz respectively [4] in 3 (R_1=CH_3,R_2=R_3=H).

We have ascertained by two independent methods the absence of intramolecular hydrogen-bonding in molecules of type 3.[5] Figure 1 shows dilution curves in which the OH chemical shift is plotted as a function of the concentration of the alcohol in carbon tetrachloride, at 39 ± 2°C. The apparent equilibrium constants for self-association [6] extracted from these curves are K=4.0 l/mole for 3 ($R_1=CH_3, R_2=R_3=H$) versus K=1.0 l/mole for neopentyl alcohol taken as a model.

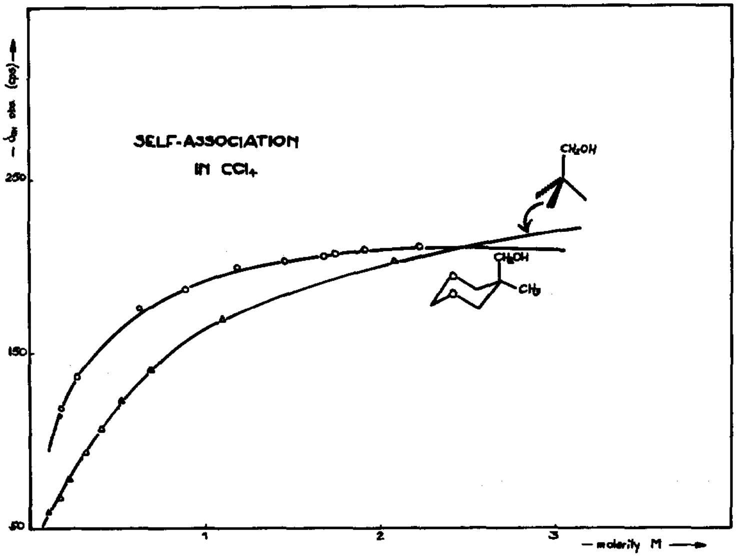
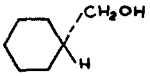
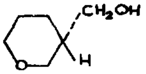
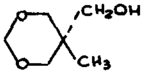
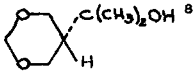


Figure 1

The former alcohol is more liable to intermolecular hydrogen-bonding than the latter ! Furthermore the 60 MHz methyl chemical shift is constant at 47-48.5 Hz in pure carbon tetrachloride when the concentration is varied between 0 and 2.2 M, and in CCl_4-DMSO mixtures (0-60 % DMSO).

This would indicate that the position of the conformational equilibrium remains unchanged in the presence or in the absence of DMSO, a strong hydrogen-bond acceptor. The equatorial methyl conformer appears to predominate, if ones relies upon model values from 2-t-butyl-5,5-dimethyl-1,3-dioxane : 40.7 Hz (equatorial CH_3) and 66.9 Hz (axial CH_3).[7] These nmr studies point to the absence of the looked-for OH...O internal hydrogen bond. This conclusion is supported by the infrared data (Table 1);

TABLE 1. Infrared absorption in the OH stretching region, CCl_4.

Compound (0.03 M)	ν_{max}	$\nu_{1/2}$	(cm^{-1})
	3629	26	
	3626	30	
	3641	12	
 [8]	3615	20	

All these OH absorption bands have comparable asymmetry parameters *ca.* 0.6 and their position are characteristic of *free* OH groups. The variations in the values of ν_{max} conform to the rules stated by Joris, Schleyer, and Osawa.[9] The absence of intramolecular hydrogen-bonding in 5-hydroxymethyl-1,3-dioxanes has also been reported by Eliel and Kaloustian.[10]

What is the cause for such an unexpected result ?

(i) repulsion between the OH and the CH_2-O-CH_2 ring dipoles; we have calculated the magnitude of such interactions for various geometries.[11] For molecule 1, these favor the hydrogen-bonded conformation by an additional 0.6 kcal/mole. For the heterocyclic molecules in Table 1, hydrogen-bonded conformations would indeed be disfavored by 0.1-0.3 kcal/mole. However, such small energies should be totally offset by the much greater - typically 5 kcal/mole - heat of formation of an OH...O hydrogen bond.

(ii) entropy loss in the hydrogen-bonded form would be greater for molecules 3 than for 1. Again, this factor seems unable to account quantitatively for the observations.

(iii) "non-bonded" repulsions. However, it would seem that the O-H group could easily minimize such interactions with the heterocyclic oxygens by relatively small angle-twisting and bending.

(iv) solvation effects, always invoked when other explanations have failed !

The phenomenon we have described appears strongly reminiscent of the anomeric effect.[12]

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