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## QUANTITATIVE CONFORMATIONAL DATA IN 5-AMINO, AND 5-ACETYL-5-METHYL-1,3-DIOXANES.

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Recently we described(3) a method for the determination of the equilibrium state of a binary conformational mixture, using temperature-dependent nmr parameters (f.i. relative shifts of AB systems). Thus, observing H-2 and H-4(6) hydrogen signals below and above the coalescence temperature in the pmr spectrum of 1,3-dioxanes, and following the spectral changes with temperature, the total free energy difference  $\Delta\Delta G^\circ$  between the two conformers may be computed in function of the temperature. Using this method, excellent linear relationships between  $\Delta\Delta G^\circ$  and T were obtained (correlation coefficients  $> 0.998$ ), provided that the observed shift differences between the equatorial and axial hydrogens forming the AB spin systems are not too small ( $> 0.15$  ppm) and further that the slope  $\Delta\Delta G^\circ/T$  is not too steep(4).

Our method is now applied on 5-amino-, and 5-acetyl-5-methyl-m.dioxane, and the thermodynamic parameters are computed (TABLE I), enlarging the data obtained for a series of 5,5-gem.substituted dioxanic compounds(5).

The spectral parameters for both compounds are found in TABLE II.

TABLE I.

Equilibria data and thermodynamic parameters for 5-amino, and 5-acetyl-5-methyl-1,3-dioxane (conformational mixtures).

Compound	$\Delta\Delta G^\circ$ cal/mole	$\Delta\Delta H^\circ$ cal/mole	$\Delta\Delta S^\circ$ e.u.	$K_e$ 300°K	$T_c$ °C	correl. coëffic.
L = NH <sub>2</sub> (acetone)	156	339	0.61	0.77	-50	0.9998
L = Ac	-906 <sup>a</sup>	-517	1.3	0.20	~-55	0.9973
(in CS <sub>2</sub> )	-1327 <sup>b</sup>	-527	2.6	0.11		0.9993

<sup>a</sup>From the AB-pattern of H-2 hydrogens.

<sup>b</sup>From H-4(6) hydrogens.

TABLE II.

Spectral parameters for (A) 5-amino-5-methyl-1,3-dioxane in acetone- $d_6$  and (B) 5-acetyl-5-methyl-1,3-dioxane in  $CS_2$  at 100 Mc.

	$^2J$	(300°K) $\Delta\nu$ in cps.	$\Delta I^a$ (cps)	$\Delta II^a$ (cps)	Other parameters in $\delta$ (TMS intern)
A	H-2 6.1	7.0	45.9	57	Me-5 : 0.99
	H-4 10.3	8.3	b	b	$NH_2$ (rtmp) : 2.3
B	H-2 5.9	15.7	39.2	39.2	Me-5 : 0.93
	H-4 11.0	73.5	110.5	110.5	$CH_3$ -CO : 2.15

<sup>a</sup>Observed at  $T < T_c$ , one AB system for each conformation. Shift differences between essential eq. and ax. hydrogens

<sup>b</sup>Overlap with  $NH_2$ -signal.

<sup>c</sup>See figure 1

In the amine derivative, the amino group prefers the axial position (over Me), while the reversed situation is found with respect to the polar group in the acetyl derivative. The values of total free energy differ somewhat depending which AB system was analysed\*. Although the correlation coefficient is better from H-4 analysis (as is normal, due to the large shift differences) it is not sure this is the best value, because the AB system is only an approximation (at least an  $[AB]_2$  system as the result of long range coupling).

In the amino derivative, the two conformations are detected from H-2 inspection at  $T < T_c$ , but not from H-4(6). The shifts for the latter must be identical for both forms, and this situation is met for all hydrogens in the acetyl derivative. (see Figure 1).

The axial preference of  $NH_2$ -5 over Me is expected. It is f.i. known(6) that HO-5 in m.dioxane prefers the axial position as the result of intramolecular H-bridge bonding. The conformational preference has recently been evaluated to be 890 cal/mole(7). This may be compared with the (reversed) situa-

\*It was not possible to study the H-4(6) patterns for the amino derivative, because of the accidental overlap of the  $NH_2$ -signal in a certain temperature range.

tion in cyclohexane ( $\Delta G^\circ(\text{OH}) = -700$  cal/mole in THF(8)). From the value of  $\Delta\Delta G^\circ(\text{NH}_2, \text{Me})$  actually found and from the fact that the conformational energy for a Me-5 group is ca 800 cal/mole(9,10), an equatorial preference for  $\text{NH}_2$  in the mono 5-amino-m.dioxane of ca 650 cal/mole could be predicted. This is unexpected, but two factors must be kept in mind. The additivity principle may not be valid, especially when polar groups are involved. A large discrepancy for 5,5-gem. OH,Me against mono 5-OH-1,3-dioxane has also been found (7). Furthermore, intramolecular H-bonds of the axial amino group with the ring oxygen atoms may be overwhelmed by intermolecular bonding, especially in acetone, and this could preferentially stabilise an equatorial amino group. Unfortunately, we were unable to study the behaviour of the mono amino derivative, due to the low solubility, especially in solvents of low polarity.

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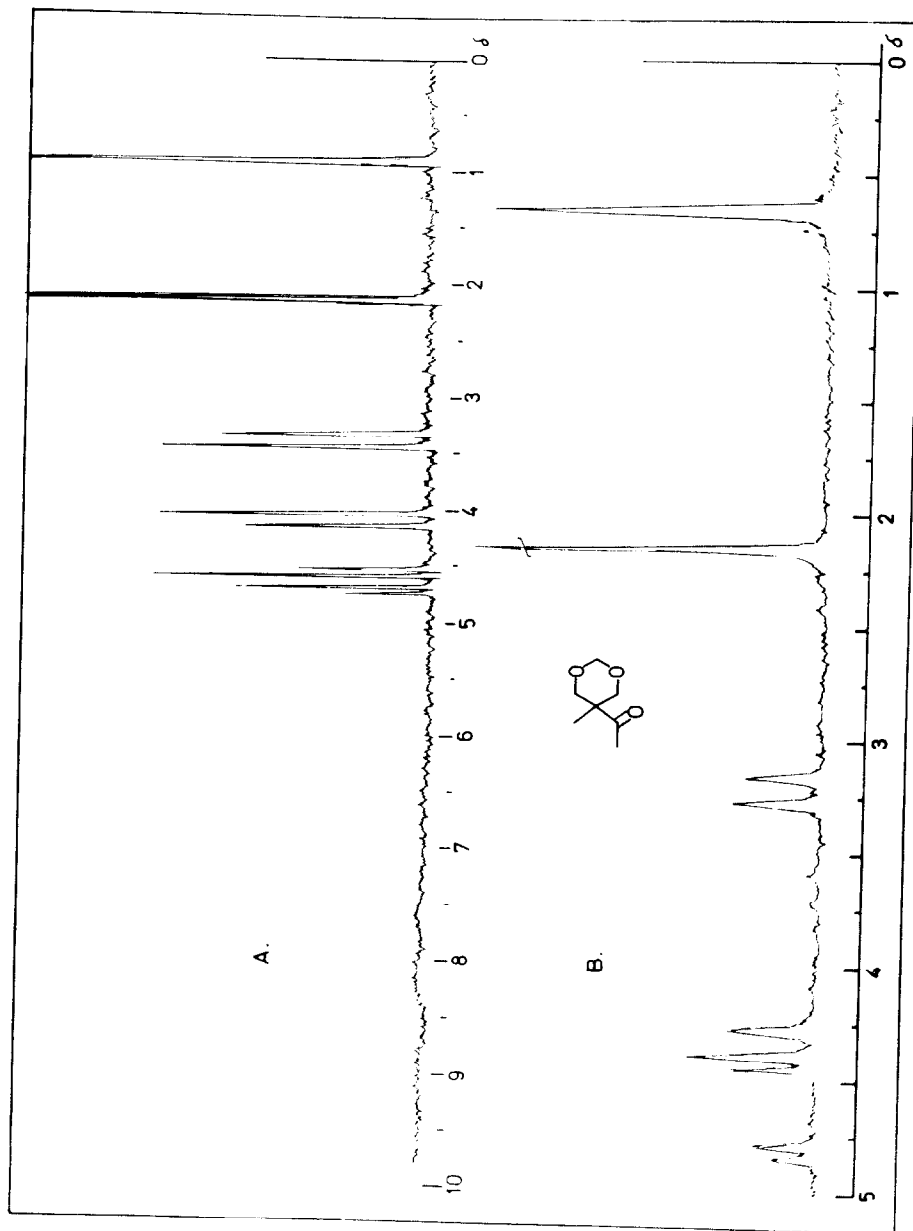


Figure 1 : PMR spectrum at 100 Mc in  $\text{CS}_2$  (TMS internal) - A. at room temperature.  
B. at  $-90^\circ\text{C}$ .