

## Solvent Effects and Hydrogen Bonding on the Conformational Equilibrium of *Cis*-3-*N,N*-Dimethyl Aminocyclohexanol through $^1\text{H}$ NMR Spectroscopy

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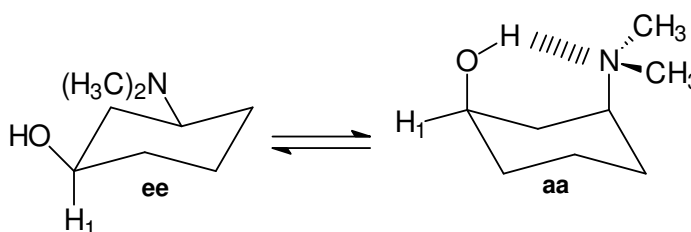
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**Abstract:**  $^1\text{H}$  NMR Spectroscopy has been a very effective tool for the study of conformational equilibria, mostly when an intramolecular hydrogen bonding (IHB) is involved. Although some papers on 1,3-disubstituted cyclohexanes have been published, none has focused on the title compound, which may present an IHB. Here, the occurrence of an IHB, through the measurements of  $H-1$  coupling constant in different solvents, is reported. The increase of  $^3J$  with the increase of solute concentration and also on going from non-polar to polar solvents indicate that, in the vapor phase (Gaussian-98; B3LYP/6-311+g\*\*) and at low concentration in non-polar solvents, the *aa* conformer predominates due to an IHB. However, in more polar solvents the equilibrium is shifted to the *ee* conformer that presents two equatorial substituents, consequently more easily solvated and preventing the formation of an IHB.

$^1\text{H}$  NMR Spectroscopy has been very effective to identify the variation in the proportions of conformers in a conformation equilibrium, mainly in the presence of an intramolecular hydrogen bonding (IHB).<sup>1,2</sup>

Although some papers on 1,3-disubstituted cyclohexanes have been published, none has focused on the title compound, which may present an IHB (Figure 1).



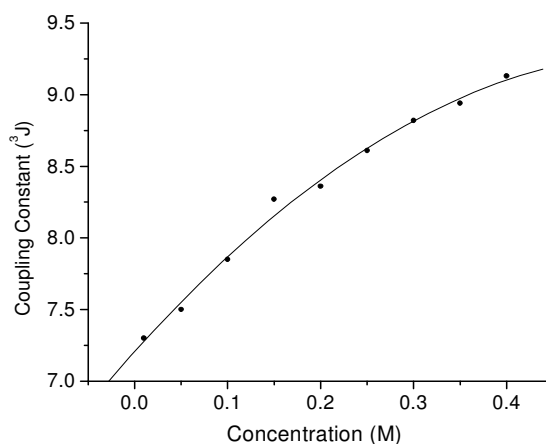
**Figure 1.** Conformational equilibrium of *cis*-3-*N,N*-dimethylaminocyclohexanol.

The NMR spectra were recorded on a 500 INOVA Varian spectrometer in the following conditions: sweep width of 3500 Hz with 64k data points and zero filling to 128k, giving a digital resolution of 0.05 Hz/point. The concentration of the samples was 0.05 M, and the results are shown in Table 1. Figure 2 shows the changes in the  $^3J_{H_1/H_{2a}}$  or  $H_{6a}$  coupling constant with solute concentration, at

22°C, in  $\text{CCl}_4$ , which is an apolar solvent and should not prevent the formation of an IHB. The observed changes (Figure 2) indicate that the conformational equilibrium is strongly affected by an IHB, since the increase in concentration leads to intermolecular interactions (intermolecular hydrogen bonding), which favours the *ee* conformer characterized by a larger  $^3J$ . In the experiments performed for

different solvents (Table 1), it was found that for apolar or less polar solvents the **aa** conformer predominates, while in more polar

solvents the equilibrium is shifted to the **ee** conformer.



**Figure 2.**  $^3J_{H_1/H_{2a}}$  or  $H_{6a}$  coupling constant (Hz) compared with concentration in  $CCl_4$  with 10% of  $C_6D_6$ , for the *cis*-3-N,N-dimethylaminocyclohexanol.

This **ee** conformer is more effectively solvated by polar solvents, as it presents two substituents in the equatorial position, which are far from each other.

The solvent effect on the conformation equilibrium here described is remarkable since

the theoretical calculations (Gaussian-98; B3LYP/6-311+g\*\*) showed that **aa** predominates in the vapor phase (75.3%), whereas the spectra in the polar solvents indicated that **ee** is the prevailing conformer.

**Table 1.** Coupling constants ( $^3J$ )<sup>a</sup> of hydrogen H-1 of *cis*-3-N,N-dimethylamino cyclohexanol in different solvents<sup>b</sup>

Solvent	$\epsilon^c$	$^3J_{H_1/H_{2a}}$ or $H_{6a}$	$^3J_{H_1/H_{2e}}$ or $H_{6e}$
$C_6D_{12}$	2.06	6.82	2.99
$CCl_4$	2.24	7.50	3.68
$CDCl_3$	4.81	7.67	3.82
$CD_2Cl_2$	9.08	7.96	3.84
Pyridine- $d_5$	12.40	10.50	4.02
Acetone- $d_6$	20.70	10.09	4.01
$CD_3CN$	37.50	9.89	3.83
DMSO- $d_6$	46.70	10.43	3.48

<sup>a</sup> In Hz. <sup>b</sup> Concentration in 0.05 M. <sup>c</sup> Dielectric constants.

Therefore, it can be concluded that in the vapor phase and at low concentration in less polar solvents, the **aa** conformer is favored by the formation of internal hydrogen bonding. In addition, in more polar solvents the **ee** conformer predominates in the equilibrium due to solvation effects.

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#### **References**

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