

Is the intramolecular hydrogen bonding responsible for the conformational preference of *trans*-2-fluorocyclohexanol?

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Abstract

The occurrence of intramolecular hydrogen bond involving fluorine and hydroxyl group (F---H-O) for the *trans*-2-fluorocyclohexanol has been reinvestigated through NMR and Infrared spectroscopy supported by theoretical calculations. The energies and geometries for the most stable conformers for *trans*-2-fluorocyclohexanol were determined theoretically applying DFT and MP2 approaches. In addition, the wave functions of the most stable conformers were analysed through NBO, QTAIM and NCI methodologies to evaluate theoretically the occurrence of intramolecular hydrogen bond F---H-O and its influence on the conformational preference.

Conformational analysis, Nuclear Magnetic Resonance, theoretical calculation

Introduction

It has been suggested¹ that the *diequatorial* conformer stability of 2-halocyclohexanol (halo=F, Cl, Br and I) is due to the formation of an intramolecular hydrogen bond. However, recent results of our group² have shown that the intramolecular hydrogen bond is not the origin of the stability observed for the *cis* arrangement (O-H---F) of 2-fluorophenol in the gas phase or in non-polar solvents, for example. In the present work, the conformational stability of *trans*-2-fluorocyclohexanol was reinvestigated to evaluate the occurrence of intramolecular hydrogen bond in conformational preference applying IR spectroscopy and NBO analysis, QTAIM and NCI topological methodologies.

Results and Discussion

The *trans*-2-fluorocyclohexanol was synthesized according procedure described in the literature.¹ The infrared analysis for the O-H vibrational frequency (from 3300 to 3700 cm⁻¹) was performed for solutions with increasing concentration (0.04 to 0.3 mM). It was observed two vibration frequencies, the first one centred in 3620 cm⁻¹ due to the free O-H vibration, while the second one is a broad band due to intermolecular hydrogen bond. It can be concluded that the intramolecular hydrogen bond is absent because the spectrum does not show the characteristic band for this interaction.³

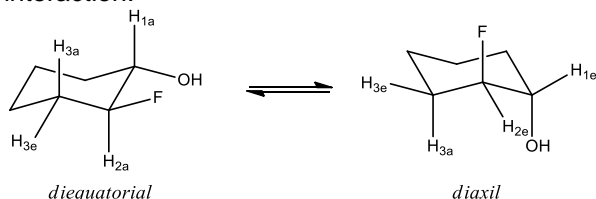


Figure 1. Numbered structure for the *trans*-2-fluorocyclohexanol.

The experimental values for $^3J_{H_2aH_1a}$ and $^3J_{H_2aH_3a}$ coupling constants (Fig. 1) obtained from 1H NMR spectra, suggested that *diequatorial* conformation (Fig. 1) is present in solution. To investigate the origin of *diequatorial* stability over *diaxial*, the topological QTAIM analysis was applied and it was found no BCP involving fluorine atom and hydrogen from OH group, suggesting the absence of intramolecular hydrogen bond. This result is in agreement with Infrared spectroscopy. In addition, the NBO analysis did not show a hyperconjugative interaction between the non-bonding electron pairs of fluorine atom and the antibonding orbital of OH group ($LP_3F \rightarrow \sigma^*_{O-H}$), which suggests that the stabilization of the equatorial conformation is not due to the presence of a hydrogen bond. The NCI methodology suggest that the stability observed for *diequatorial* is due to nonbonding interaction between OH and fluorine.

Conclusions

The stability acquired for the *diequatorial* form was assigned to be due to nonbonding interaction, based on the NCI topological analysis. The intramolecular hydrogen bond does not appear to have a significant influence on the conformational preference for this molecule.

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1 M.P. Freitas, et al. *J. Mol. Struct.*, **570**, 175 (2001).

2 R.A. Cormanich, et al. *Magn. Reson. Chem.* **49**, 763 (2011)

3 R.T. Conley, *Infrared Spectroscopy*, 2th edition, pg 129-131, (1972).¹