Stereoelectronic Interaction and Their Effects on Conformational Preference for 2-Substituted Methylenecyclohexane: An Experimental and Theoretical Investigation

Pedro R. Anizelli, Janaina D. Vilcachagua, Álvaro Cunha Neto, and Cláudio F. Tormena*

Department of Organic Chemistry, Chemistry Institute, University of Campinas-UNICAMP-CEP, P. O. Box 6154, 13084-971 Campinas, SP, Brazil

Received: June 2, 2008; Revised Manuscript Received: July 1, 2008

Conformational preferences for 2-substituted methylenecyclohexanes were determined using $^3J_{H_2H_3}$ spin−spin coupling constants, while stereoelectronic interactions were obtained by means of theoretical calculations and NBO analysis. The conformational equilibrium of compounds studied can be represented by their axial and equatorial conformers, the axial conformers being the most stable form in polar and nonpolar solvents. These conformational preferences were attributed to the hyperconjugative interactions between the $\pi_{C-C} \rightarrow \sigma^*_{C-Xax.}$ and $\sigma_{C-H} \rightarrow \sigma^*_{C-Xax.}$ orbitals, and the repulsive steric interaction observed between $\sigma_{C-H} \rightarrow n_{Xeq.}$.

Introduction

The investigation of conformational properties of six-membered rings has provided the foundation for modern stereochemistry.[1] Investigation of the factor that determines conformational preference has enriched our understanding of how atoms or functional groups interact to stabilize any conformation.

Several studies can be found in literature about the conformational preference of a six-membered ring system, such as 1,2-disubstituted cyclohexanes[2−9] and 2-substituted cyclohexanones;[10−15] however, the same attention was not dedicated to 2-substituted methylenecyclohexanes.[16,17]

This scarcity can be ascribed to the interconversion barrier observed for compounds containing a $C(sp^3)-C(sp^2)$ fragment, such as those observed in cyclohexanone[18] and methylenecyclohexane,[19,20] when compared to the barrier observed for cyclohexane[1] $C(sp^3)-C(sp^3)$.

The process that interconverts the *axial* and *equatorial* positions in equilibrium is faster for cyclohexanone and methylenecyclohexane than for cyclohexane. As a result, it is more difficult to obtain a slow-exchange NMR spectra for cyclohexanones and methylenecyclohexane, which provide distinct resonances for axial and equatorial groups. To overcome this difficulty, in the case of 2-substituted cyclohexanones, similar derivatives containing *tert*-butyl at C_4 were used as a model compounds in conformational analyses.[1] In this class of compounds, however, the same was not observed for 2-substituted methylenecyclohexanes.

In the case of 2-halocyclohexanone (Figure 1), the substituents tend to adopt the axial orientation when considering the isolated molecule (gas phase). The $\sigma_{C-X} \rightarrow \pi^*_{C-O}$ hyperconjugative interaction is responsible for the axial preference, due to the orbital overlap, which is more effective in the axial orientation of halogens (Figure 1) than for the conformer with the halogen in the equatorial position (Figure 1). The $\sigma_{C-X} \rightarrow \pi^*_{C-O}$ interaction increases in the following order F < Cl < Br < I, and the same trend is observed in the energy difference between conformers ($E_{equatorial} - E_{axial}$). Repulsive steric interactions between the lone pair from oxygen and the α-substituent; and repulsive dipole−dipole interactions, present in equatorial form,

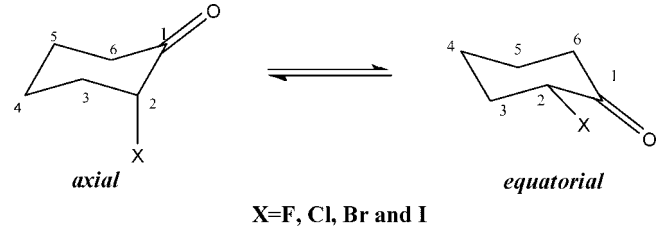

Figure 1. Conformational equilibrium for 2-X-cyclohexanone.

also contribute to the largest population of axial conformer.[11−13,21,22] In polar solvents (CD_3CN and dimethyl sulfoxide (DMSO)), except for the iodine derivative, the equatorial conformer is predominant (Figure 1).[11−13]

Previous studies[23,24] demonstrated that alkylidenecyclohexane adopts an axial conformation when the alkyl group (CH_3) is bonded at carbon-2 (Figure 2). The preference for axial conformations is caused by the strong repulsive interaction between alkyl groups in equatorial form; therefore, this interaction is known as the allylic strain. Molecular mechanics calculations indicated that the axial conformer with $R = CH_3$ (Figure 2) is 2.6 kcal mol^{-1} more stable than the equatorial conformation (Figure 2) with exocyclic isopropylidene group ($R' = R'' = CH_3$).[24]

The conformational preference for 2-methoxymethylenecyclohexane was determined by experimental[16,17] and theoretical analyses.[25,26] On the basis of the experimental data, the axial conformer (Figure 2) was found to be the most stable form, and this result was supported by theoretical calculations. The axial conformer stability was assigned due to $\pi_{C=C} \rightarrow \sigma^*_{C-O}$ orbital interaction (hyperconjugative interaction). This interaction only occurs when the σ^*_{C-O} antibonding orbital of the OMe group at carbon 2 is in the axial position because of the symmetry with the $\pi_{C=C}$ orbital.

In the present work, 2-fluoromethylenecyclohexane (**1**), 2-chloromethylenecyclohexane (**2**), 2-bromomethylenecyclohexane (**3**), 2-(*N,N*-dimethylamino)methylenecyclohexane (**4**), and 2-methoxymethylenecyclohexane (**5**) (Figure 3) were chosen as probes to perform the conformational analysis and to describe the interaction involved in the most stable forms of these compounds. To do this, the experimental and theoretical $^3J_{HH}$, spin−spin nuclear coupling constant were used in the analysis

* To whom correspondence should be addressed. E-mail: tormena@iqm.unicamp.br.

10.1021/jp8048636 CCC: $40.75
Published on Web 08/20/2008

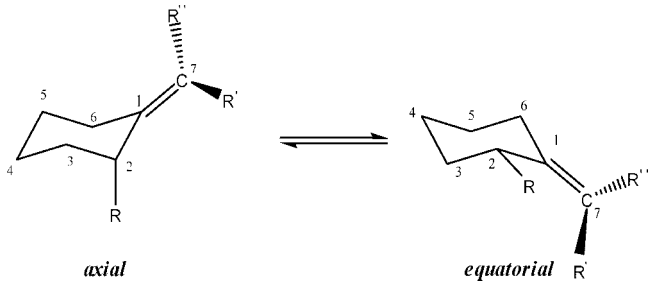

Figure 2. Conformational equilibrium in the alkylidenecyclohexane.

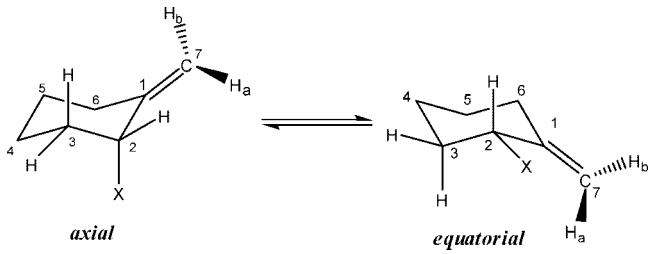

Figure 3. Conformational equilibrium in the 2-X-methylenecyclohexane (X = F, Cl, Br, $N(CH_3)_2$, and OMe).

of their conformational equilibrium. The experimental data was supported by density functional theory (DFT) calculations, together with the natural bond orbital (NBO)[27] analysis.

Computational Details

All structures were fully optimized at the B3LYP functional[28−30] and aug-cc-pVDZ basis set[31] level using the Gaussian03[32] program. The aug-cc-pVDZ basis set was chosen for the correct description of fluorine, chlorine, bromine, oxygen, and nitrogen atoms. This basis set includes additional diffuse functions (prefix aug-), which were used to take into account the relatively diffuse nature of the lone pairs. Electronic structures from compounds **1**−**5** were studied using NBO analysis[27] at the B3LYP/cc-pVDZ level using the geometries optimized.

The $^3J_{HH}$ couplings in compounds **1**−**5** were also calculated using the CP-DFT methodology[33] as implemented in the Gaussian03 package[32] of programs. All four terms of $^3J_{HH}$ spin−spin coupling constant (Fermi contact, FC; spin dipolar, SD; paramagnetic spin orbit, PSO, and diamagnetic spin orbit, DSO) were carried out using the EPR-III basis set,[34] which is a triple-ζ type and includes diffuse and polarization functions. The *s* part of this basis set is enhanced to better reproduce the electronic density in the nuclear regions, since this point is particularly important when calculating the FC term.[35] The EPR-III basis set was used for the carbon and hydrogen atoms and the cc-pVDZ basis set for other atoms present in the molecules studied.

Experimental Section

NMR Experiments. The solvents were commercially available and used without further purification. ^{1}H NMR spectra were recorded on spectrometers operating at 250 and 300 MHz for ^{1}H. Measurements were carried out at a probe temperature of 25 °C, using solutions of ca. 10 mg cm^3 in different solvents. The ^{1}H spectra were based on the tetramethylsilane (TMS) refrence. Typical conditions for ^{1}H spectra were as follows: 16 transients; spectral width, 24 kHz; with 64k data points, giving an acquisition time of 10.02 s and zero filled to 128k to give a digital resolution of 0.01 Hz/point.

TABLE 1: Experimental $^3J_{HH}$ Coupling Constant (Hz) in Different Solvents for Compounds 1−5

		$^3J_{H2H3}$				
solvent	ε	**1**	**2**	**3**	**4**	**5**
$CDCl_3$	4.8	7.33	4.42	3.04	3.84	4.50
CD_2Cl_2	9.1	7.39	4.43	3.04	3.76	5.34
acetona-d_6	20.7	7.61	4.36	3.05	3.50	4.93
CD_3CN	37.5	7.38	4.41	3.31	3.68	5.56
DMSO-d_6	46.7	7.45	4.35	3.40	3.68	5.48

Syntheses. ***(a) 2-Fluoromethylenecyclohexane..***[36−38] Reaction of cyclohexene oxide (10.0 mL; 198 mmol) with KHF_2 (20.0 g; 260.0 mmol) resulted in *trans*-2-fluorocyclohexan-1-ol which was distilled at 55 °C/(0.1 mmHg) (8.45 g; 46%). The compound *trans*-2-fluorocyclohexan-1-ol, which suffered oxidation by Jones reagent, provided the 2-fluorocyclohexanone, and which was distilled at 44 °C/(2.0 mmHg) (5.25 g; 67%). Olefination of 2-fluorocyclohexanone (1.2 g; 10.3 mmol), using the Wittig reaction, provided the 2-fluoromethylenecyclohexane at 13% yield, after purification by chromatography column (pentane).

(b) 2-Chloromethylenecyclohexane..[38] Olefination of 2-chlorocyclohexanone (1.7 g, 13.4 mmol), using the Wittig reaction, provided a 2-chloromethylenecyclohexane at 15% yield after purification by chromatography column (85:15 hexane/acetate).

(c) 2-Bromomethylenecyclohexane:.[38,39] Reaction of cyclohexanone (10.0 mL; 95.2 mmol) with bromine provided the 2-bromocyclohexanone which was distilled at 62 °C/(3.0 mmHg) (8.15 g; 49.0%). Olefination of 2-bromocyclohexanone (2.37 g; 13.4 mmol), using Wittig reaction, provided the 2-bromomethylenecyclohexane at 13% yield after purification by chromatography column (85:15 hexane/acetate).

(d) 2-(N,N-Dimethylamino)methylenecyclohexane:.[39,40] Reaction of cyclohexanone (10.0 mL; 95.2 mmol) with bromine provided the 2-bromocyclohexanone, which was distilled at 62 °C/(3.0 mmHg) (8.15 g; 49.0%). After distillation, the pure 2-bromocyclohexanone was placed in a reactor with *N,N*-dimethylamine solution (40%), providing the 2-(*N,N*-dimethylamino)cycloexanone, which was distilled at 56 °C/(4.0 mmHg). Olefination of 2-(*N,N*-dimethylamino)cycloexanone (1.60 g; 11.4 mmol), using Wittig reaction, provided the 2-(*N,N*-dimethylamino)methylenecyclohexane at 16% yield afer purification by chromatography column (85:15 hexane/acetate).

(e) 2-Methoxymethylenecyclohexane:.[39] Olefination of 2-methoxycyclohexanone (0.686 g; 5.36 mmol), using the Wittig reaction, provided 2-methoxymethylenecyclohexane at 16% yield after purification by chromatography column (85:15 hexane/acetate).

Results and Discussion

Table 1 shows that there are no changes in $^3J_{H2H3}$ coupling constants for **1**−**4** in solvents with different polarities, indicating that there is no change in the conformer populations. This is supported by a slight variation on the dipole moments (Table 2) obtained from theoretical calculations between axial and equatorial conformers.

The conformer population in equilibrium shown in Figure 3 can be estimate approximately by eq 1:[41]

$$J_{obs} = J_{ax.}n_{ax.} + J_{eq.}n_{eq.} \quad (1)$$

where $n_{ax.} + n_{eq.} = 1$, J_{obs} is the experimental $^3J_{H2H3}$ coupling constant (Table 1), $J_{ax.}$is the calculated $^3J_{H2eq.H3eq.}$ coupling constant for the axial conformer; $J_{eq.}$ is the calculated $^3J_{H2ax.H3ax.}$

TABLE 2: Theoretical Data for $^3J_{HH}$ Coupling Constant (Hz), Dipole Moment (D), and Relative Energy (kcal mol^{-1}) at the B3LYP/aug-cc-pVDZ Level

	1		2		3		4		5	
parameters	ax.	eq.	ax.	eq.	ax.	eq.	ax.	eq.	ax.	eq.
$^3J_{HH}$	3.78	11.88	3.16	12.82	3.41	13.3	3.29	12.37	3.28	11.82
μ	2.0	2.4	2.3	2.7	2.5	2.8	0.5	1.0	0.6	1.4
$E_{rel.}$	0.0	0.3	0.0	1.2	0.0	1.9	0.0	1.5	0.0	1.0

TABLE 3: Population of Axial Conformer in Different Solvents for Compounds 1−5

		$n_{ax.}$				
solvent	ε	1	2	3	4	5
$CDCl_3$	4.8	0.56	0.87	1.0	1.0	0.85
CD_2Cl_2	9.1	0.55	0.87	1.0	1.0	0.76
acetona-d_6	20.7	0.53	0.88	1.0	1.0	0.81
CD_3CN	37.5	0.55	0.87	1.0	0.95	0.73
DMSO-d_6	46.7	0.54	0.88	1.0	0.95	0.74

coupling constant for the equatorial conformer, $n_{ax.}$ is the molar fraction for the axial conformer and $n_{eq.}$ is the molar fraction for the equatorial conformer.

Table 2 lists the theoretical calculations of $^3J_{H2H3}$ coupling constant for both conformers. Tables 1 and 2 data allow us to estimate approximately the population (Table 3) for each conformer in solution.

According to data from Table 3, the axial conformer is the unique stable form found in all solvents used for compounds **3** and **4**. The equatorial form is present in equilibrium with an appreciable amount for the other compounds **1**, **2**, and **5**.

These trends can be supported by analyzing the experimental $^3J_{H2H3}$ couplings (Table 1). While the $^3J_{H2H3}$ for **1** showed intermediate values (around 7.5 Hz) between calculated $^3J_{H2eq.H3eq.} = 3.78$ Hz for the axial conformer and $^3J_{H2ax.H3ax.} = 11.88$ Hz for the equatorial form (Table 2). The $^3J_{H2H_3}$ experimental values for compounds **3** and **4** are almost equal (Table 1) to that calculated for the axial conformer (Table 2).

It can be observed that the axial form is present in equilibrium with 85% in $CDCl_3$ (Table 3), decreasing to 74% in DMSO-d_6, for the compound **5**. With the increase of solvent polarity, there is an increment in the population of the equatorial conformer caused by the higher dipole moment for the equatorial form (Table 2), which should be stabilized in polar media. The calculated dipole moment for **5** is $\mu = 1.4$ D for equatorial and $\mu = 0.6$ D for axial conformers, supporting the tendency that compound **5** is more sensitive to change in solvent polarity, leading to the stabilization of equatorial form.

In polar solvents (CD_3CN and DMSO), except for the iodine derivative, the equatorial conformer is predominant, for the 2-halocyclohexanones (Figure 1).[12,13] In the case of 2-X-methylenecyclohexane derivatives (**1**−**5**), the axial form is majority, in the same solvents. Therefore, the change of carbonyl group (C═O) by the methylene group (C═C) leads to inversion in conformational behavior for the studied methylenecyclohexanes, in comparison to cyclohexanones in polar solventes (CD_3CN and DMSO).

Conformational Preferences and Orbital Interactions. The stereoelectronic interactions can be used to explain the conformational stability for axial in equatorial conformers. The NBO analyses provided some important stereoelectronic interactions, which support the stabilization of the axial conformer.

The interactions between $\pi_{C1-C7} \rightarrow \sigma^*_{C2-Xax}$, $\sigma_{C2-Xax} \rightarrow \pi^*_{C1-C7}$, and $\sigma_{C3-Hax} \rightarrow \sigma^*_{C2-Xax}$, for compounds **1**−**3**, present higher energy for the axial than for the equatorial conformer. The delocalization energy for these interactions increases in the following order F < Cl < Br (Table 4). The interaction $LPX_{ax} \rightarrow \pi^*_{C1-C7}$ which is observed only for the axial form for compounds **1**−**3** also contributes to stabilize this conformer. The axial conformer stabilization for compounds **4** and **5** is also due to hyperconjugative interactions. For these compounds the delocalization interactions are also more effective for the axial than for the equatorial conformer. In these compounds there are two extra interactions involving $\sigma_{C2-Heq} \rightarrow \sigma^*_{C1-C6}$ and $\sigma_{C2-Heq} \rightarrow \sigma^*_{C3-C4}$ orbitals in comparison to compounds **1**−**3** (Table 4).

Data from Table 4 leads to better understanding of the conformational equilibrium for compound **1** (Table 3). The sum of delocalization interaction energy is almost equal ($\Delta\sum = 4.2$ kcal mol^{-1}) for axial and equatorial conformers (Table 4) when compared to compounds **2**−**5**. This is probably the reason why, for **1,** the axial and equatorial conformers are present in the equilibrium with the same amount.

The $\sigma_{C-X} \rightarrow \pi^*_{C-O}$ delocalization interaction observed for 2-X-cyclohexanones is more effective than $\sigma_{C-X} \rightarrow \pi^*_{C-C}$ in-

TABLE 4: Energies (kcal mol^{-1}) for Hyperconjugatives Interactions in 1−5, Calculated at the B3LYP/cc-pVDZ Level

	axial						equatorial				
interaction	1	2	3	4	5	interaction	1	2	3	4	5
$\pi_{C1-C7} \rightarrow \sigma^*_{C2-Xax}$	8.1	8.9	9.8	4.7	6.2	$\pi_{C1-C7} \rightarrow \sigma^*_{C2-Hax}$	3.1	2.9	2.9	2.4	2.7
$\sigma_{C2-Xax} \rightarrow \pi^*_{C1-C7}$	1.9	3.7	4.8	1.5	1.6	$\sigma_{C2-Hax} \rightarrow \pi^*_{C1-C7}$	4.7	4.2	4.1	3.6	4.1
$\sigma_{C3-Hax} \rightarrow \sigma^*_{C2-Xax}$	5.5	6.6	7.1	4.9	4.7	$\sigma_{C3-Hax} \rightarrow \sigma^*_{C2-Hax}$	3.3	3.4	3.4	3.0	3.3
$\sigma_{C2-Xax} \rightarrow \sigma^*_{C3-Hax}$	1.6	2.5	2.8	1.2	1.5	$\sigma_{C2-Hax} \rightarrow \sigma^*_{C3-Hax}$	3.3	3.2	3.2	3.4	3.3
$LPX_{ax} \rightarrow \pi^*_{C1-C7}$	1.5	1.4	1.2	–	1,3	$LPX_{ax} \rightarrow \pi^*_{C1-C7}$					
$\sigma_{C2-Heq} \rightarrow \sigma^*_{C1-C6}$	–	–	–	4.3	4.4	$\sigma_{C2-Xeq} \rightarrow \sigma^*_{C1-C6}$				2.0	1.8
$\sigma_{C2-Heq} \rightarrow \sigma^*_{C3-C4}$	–	–	–	3.6	3.5	$\sigma_{C2-Xeq} \rightarrow \sigma^*_{C3-C4}$				1.3	1.7
$\sum$	18.6	23.1	25.7	21.5	21.9	$\sum$	14.4	13.7	13.6	15.7	16.9

TABLE 5: Energies (kcal mol^{-1}) for the Most Important Repulsive Steric Interactions for Compounds 1−5 Calculated at the B3LYP/cc-pVDZ Level

	axial						equatorial				
interaction	1	2	3	4	5	interaction	1	2	3	4	5
$\sigma_{C2-Heq} \rightarrow \sigma_{C1-C6}$	3.8	4.4	4.5	4.0	3.7	$\sigma_{C2-Xeq} \rightarrow \sigma_{C1-C6}$	4.1	5.2	5.8	3.8	3.8
$\sigma_{C3-C4} \rightarrow \sigma_{C2-Heq}$	4.2	4.7	4.7	4.3	4.3	$\sigma_{C3-C4} \rightarrow \sigma_{C2-Xeq}$	4.3	5.6	6.3	3.9	4.4
$\sigma_{C7-Ha} \rightarrow \sigma_{C2-Heq}$	1.7	1.9	1.8	1.8	1.8	$\sigma_{C7-Ha} \rightarrow \sigma_{C2-Xeq}$	0.7	1.0	1.2	0.6	0.5
$\sigma_{C2-Xax} \rightarrow \pi_{C1-C7}$	5.2	7.3	8.3	4.4	4.6	$\sigma_{C2-Hax} \rightarrow \pi_{C1-C7}$	6.2	6.0	6.0	4.3	5.3
						$\sigma_{C7-Ha} \rightarrow LPX_{eq}$	1.4	2.8	3.0	2.3	1.4

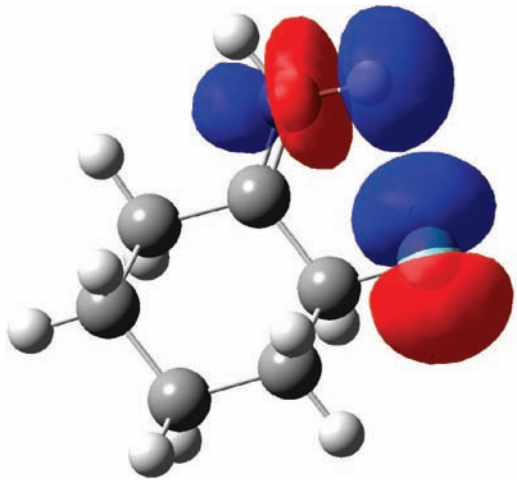

Figure 4. Repulsive steric interactions between X and σ_{C7-Ha} orbital for the equatorial conformation for 2-X-methylenecyclohexane [X = F, Cl, Br, $N(CH_3)_2$, and OMe].

teraction for 2-X-methylenecyclohexanes in axial form. It was expected then that the equatorial form should be more stabilized for 2-X-methylenecyclohexanes in comparison to 2-X-cyclohexanones. However, the back-donation $\pi_{C-C} \rightarrow \sigma^*_{C-X}$ is more effective for 2-X-methylenecyclohexane than for 2-X-cyclohexanones ($\pi_{C-O} \rightarrow \sigma^*_{C-X}$), stabilizing the axial form.

Besides the delocalization interaction (Table 4), the repulsive steric interaction (Table 5) can be used to elucidate the conformational preference for studied compounds. The energy of these repulsive interactions are almost similar for both conformers in all compounds, excluding the interaction involving $\sigma_{C7-Ha} \rightarrow n_{Xeq}$, which is observed only for the equatorial form (Table 5). This repulsive interaction ($\sigma_{C7-Ha} \rightarrow n_{Xeq}$) is caused by the proximity of the lone pair from F, Cl, Br, N, and O with the C7−Ha bond (Figure 4). The repulsive interaction $\sigma_{C7-Ha} \rightarrow LPX_{eq}$ increases in the following order 1 < 5 < 4 < 2 < 3.

It can be seen that the great attractive delocalization interaction observed in the axial conformer and the higher repulsive steric interaction present in the equatorial conformer help to stabilize the axial conformation.

Conclusions

The conformational analysis for the 2-X-methylenecyclohexane (X = F, Cl, Br, $N(CH_3)_2$, and OMe), revealed that conformational equilibrium for 2-fluoromethylenecyclohexane (**1**) occurs in almost equal populations for axial and equatorial conformers. For the 2-chloromethylenecyclohexane (**2**), 2-bromomethylenecyclohexane (**3**), and 2-(*N,N*-dimethylamino)methylenecyclohexane (**4**), the axial form predominates over equatorial with 90, 100, and 95−100%, respectively.

For the 2-methoxymethylenecyclohexane (**5**), it was observed that increasing solvent polarities increases the population of the equatorial conformer. These results corroborate with the theoretical evidence (Table 2) that the equatorial form is more polar than the axial and should be stabilized in polar solvents. However due to the higher delocalization interactions present in the axial conformer, there is no inversion in the conformational equilibrium; thus, only a slight amount (25%) of the equatorial form is observed in polar solvents.

The conformational stability acquired for the axial conformers for all compounds studied can be justified to the great attractive delocalization interaction observed in the axial and also because of the higher repulsive steric interaction present in the equatorial conformer, leading to stabilization of the axial conformation.

Acknowledgment. The authors gratefully acknowledge financial support from FAPESP (Grant 05/59649-0 and 06/03980-2), a fellowship (to A.C.N.), and CNPQ to a scholarship (to J.D.V.) for fellowships (to C.F.T.) and CAPES to scholarship (to P.R.A.).

References and Notes

(1) Eliel, E. L.; Samuel, H. W.; Doyle, M. P. *Basic Organic Stereochemistry*; Wiley-Interscience: New York, 2001.
(2) Freitas, M. P.; Tormena, C. F.; Rittner, R. *J. Mol. Struct.* **2001**, *570*, 175.
(3) Freitas, M. P.; Tormena, C. F.; Oliveira, P. R.; Rittner, R. *J. Mol. Struct. (THEOCHEM)* **2002**, *589*−*590*, 147.
(4) Freitas, M. P.; Tormena, C. F.; Luizar, C.; Ferreira, M. M. C.; Rittner, R. *J. Mol. Struct. (THEOCHEM)* **2002**, *618*, 219.
(5) Freitas, M. P.; Tormena, C. F.; Rittner, R.; Abraham, R. J. *J. Phys. Org. Chem.* **2003**, *16*, 27.
(6) Freitas, M. P.; Tormena, C. F.; Rittner, R.; Abraham, R. J. *J. Mol. Struct.* **2005**, *734*, 211.
(7) Freitas, M. P.; Rittner, R.; Tormena, C. F.; Abraham, R. J. *Spectrochim. Acta A* **2005**, *61*, 1771.
(8) Bocca, C. C.; Basso, E. A.; Fiorin, B. C.; Tormena, C. F.; dos.Santos, F. P. *J. Phys. Chem. A* **2006**, *110*, 9438.
(9) Cedran, J. C.; dos Santos, F. P.; Basso, E. A.; Tormena, C. F. *J. Phys. Chem. A* **2007**, *111*, 11701.
(10) Garbisch, E. W. *J. Am. Chem. Soc.* **1964**, *86*, 1780.
(11) Basso, E. A.; Kaiser, C.; Rittner, R.; Lambert, J. B. *J. Org. Chem.* **1993**, *58*, 7865.
(12) Freitas, M. P.; Rittner, R.; Tormena, C. F.; Abraham, R. J. *J. Phys. Org. Chem.* **2001**, *14*, 317.
(13) Yoshinaga, F.; Tormena, C. F.; Freitas, M. P.; Rittner, R.; Abraham, R. J. *J. Chem. Soc., Perkin Trans. 2* **2002**, 1494.
(14) Freitas, M. P.; Tormena, C. F.; Garcia, J. C.; Rittner, R.; Abraham, R. J.; Basso, E. A.; Santos, F. P.; Cedran, J. C. *J. Phys. Org. Chem.* **2003**, *16*, 833.
(15) Freitas, M. P.; Tormena, C. F.; Rittner, R. *Spectrochim. Acta A* **2003**, *59*, 1177.
(16) Lessard, J.; Tan, P. V. M.; Martino, R.; Saunders, J. K. *Can. J. Chem.* **1977**, *55*, 1015.
(17) Lessard, J.; Saunders, J. K.; Viet, M. T. P. *Tetrahedron Lett.* **1982**, *23*, 2059.
(18) Buncort, R. *Top. Stereochem.* **1974**, *8*, 159.
(19) Gerig, J. T. *J. Am. Chem. Soc.* **1968**, *90*, 1066.
(20) Jensen, F. R.; Beck, B. H. *J. Am. Chem. Soc.* **1968**, *90*, 1065.
(21) Neyer, A. Y.; Allinger, N. L.; Yuh, Y. *Isr. J. Chem* **1980**, *20*, 57.
(22) Abraham, R. J.; Griffiths, L. *Tetrahedron* **1981**, *37*, 575.
(23) Johson, F. *Chem. Rev.* **1968**, *68*, 375.
(24) Allinger, N. L.; Hirsch, J. A.; Miller, M. A.; Tyminski, I. J. *J. Am. Chem. Soc.* **1968**, *90*, 5773.
(25) Muchall, H. M.; Kamya, P. R. N.; Lessard, J. *Can. J. Chem.* **2003**, *81*, 689.
(26) Mawhinney, R. C.; Muchall, H. M.; Lessard, J. *Can. J. Chem.* **2003**, *81*, 1101.
(27) Reed, A. L.; Curtiss, L. A.; Weinhold, F. *Chem. Rev.* **1988**, *88*, 899.
(28) Becke, A. D. *Phys. Rev. A* **1988**, *38*, 3098.
(29) Becke, A. D. *J. Chem. Phys.* **1993**, *98*, 5648.
(30) Lee, C. T.; Yang, W. T.; Parr, R. G. *Phys. Rev. B* **1988**, *37*, 785.
(31) Dunning, T. H.; Peterson, K. A.; Wonn, D. E. *Encyclopedia of Computational Chemistry*; Wiley: New York, 1998; Vol. 1, p 88.
(32) Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Montgomery, J. A., Jr.; Vreven, T.; Kudin, K. N.; Burant, J. C.; Millam, J. M.; Iyengar, S. S.; Tomasi, J.; Barone, V.; Mennucci, B.; Cossi, M.; Scalmani, G.; Rega, N.; Petersson, G. A.; Nakatsuji, H.; Hada, M.; Ehara, M.; Toyota, K.; Fukuda, R.; Hasegawa, J.; Ishida, M.; Nakajima, T.; Honda, Y.; Kitao, O.; Nakai, H.; Klene, M.; Li, X.; Knox, J. E.; Hratchian, H. P.; Cross, J. B.; Bakken, V.; Adamo, C.; Jaramillo, J.; Gomperts, R.; Stratmann, R. E.; Yazyev, O.; Austin, A. J.; Cammi, R. ; Pomelli, C.; Ochterski, J. W.; Ayala, P. Y.; Morokuma, K.; Voth, G. A.; Salvador, P.; Dannenberg, J. J.; Zakrzewski, V. G.; Dapprich, S.; Daniels, A. D.; Strain, M. C.; Farkas, O.; Malick, D. K.; Rabuck, A. D.; Raghavachari, K.; Foresman, J. B.; Ortiz, J. V. ; Cui, Q. ; Baboul, A. G.; Clifford, S.; Cioslowski, J.; Stefanov, B. B.; Liu, G. ; Liashenko, A.; Piskorz, P.; Komaromi, I.; Martin, R. L.; Fox, D. J.; Keith, T.; Al-Laham, M. A.; Peng, C. Y.; Nanayakkara, A.; Challacombe, M.; Gill, P. M. W.; Johnson, B.; Chen, W.; Wong, M. W.; Gonzalez, C.; Pople, J. A. *Gaussian 03*, Revision D.02; Gaussian: Wallingford, CT, 2004.

(33) Sychrovshý, V.; Gräfenstein, J.; Cremer, D. *J. Chem. Phys.* **2000**, *113*, 3530.
(34) Barone, V. *J. Chem. Phys.* **1994**, *101*, 6834.
(35) Peralta, J. E.; Scuseria, G. E.; Cheeseman, J. R.; Frisch, M. J. *Chem. Phys. Lett.* **2003**, *375*, 452.
(36) Guss, C. O.; Rosenthal, R. *J. Am. Chem. Soc.* **1955**, *77*, 2549.
(37) Eisenbraun, E. J. *Org. Synth.* **1973**, *5*, 310.
(38) Gaoni, Y.; Tomazic, A.; Potigieter, E. *J. Org. Chem.* **1985**, *50*, 2943.
(39) Allinger, J.; Allinger, N. L. *Tetrahedron* **1958**, *2*, 64.
(40) Mouseron, M.; Julian, J.; Tolchini, Y. *Bull. Soc. Chim. Fr.* **1952**, *19*, 757.
(41) Abraham, R. J.; Bretschneider, E. Internal Rotation. In *Molecules*; Orville-Thomas, E., Ed.; Wiley: New York. 1974; Chapter 13.

JP8048636