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Semiempirical and *ab initio* Calculations *versus* Dynamic NMR on Conformational Analysis of Cyclohexyl-N,N-dimethylcarbamate

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As proporções dos confôrmeros axial-equatorial do *N,N*-dimetilcarbamato de cicloexila foram determinadas, pela primeira vez, pelo método de Eliel, pela ressonância magnética nuclear dinâmica(RMND) de ^1H e de ^{13}C e foram comparados com resultados obtidos através de cálculos teóricos. Pelo método de Eliel foram utilizados pelo menos cinco parâmetros experimentais independentes, em CCl_4, $CDCl_3$ e CD_3CN. Os experimentos de ^1H e de ^{13}C a baixas temperaturas foram realizados em CF_2Br_2/CD_2Cl_2. Os métodos semiempíricos MNDO, AM1 e PM3 e cálculos *ab initio* de orbital molecular nos níveis HF/STO-3G e HF/6-31G(d,p) também foram utilizados. Tanto os métodos que utilizaram a RMN como os cálculos teóricos corretamente indicaram a preferência do confôrmero equatorial em relação ao axial e os valores obtidos pelos diferentes métodos demonstraram boa concordância.

Axial–equatorial conformational proportions for cyclohexyl–*N,N*–dimethyl carbamate have been measured, for the first time, by the Eliel method, ^1H and ^{13}C dynamic nuclear magnetic resonance (DNMR). The results were compared against those determined by theoretical calculations. By the Eliel method at least five experimentally independent measureables were used in CCl_4, $CDCl_3$ and CD_3CN. The ^1H and ^{13}C low temperature experiments were performed in CF_2Br_2/CD_2Cl_2 . Semiempirical methods MNDO, AM1 and PM3 and *ab initio* molecular orbital calculations at the HF/STO-3G and HF/6-31G(d,p) levels have been performed on the axial and equatorial conformers populations. All applied methods correctly predict the equatorial conformer preference over the axial one. The resulting equatorial preferences determined by NMR data and theoretical calculations are in good agreement.

Keywords: conformational analysis; theoretical calculations; cyclohexane derivative; dynamic NMR

Introduction

The conformational analysis of six-membered rings has provided the foundation for modern stereochemistry investigation of the factors that determine conformational preferences of substituents on saturated six-membered rings (A values)[1,2] and have enriched our understanding of how atoms and functional groups interact with hidrocarbons fragments.

The conformational preference of a monosubstituted cyclohexane is determined largely by the interaction of the substituent with the syn-axial protons and the carbons to which the latter are attached.

There have been numerous studies aimed at determining the conformational preferences of monosubstituted cyclohexanes, and a wide range of different substituents were investigated[3,4]. As well known, when the time scale of observation is relatively long, the two forms equilibrate (eq. 1) and render measurements of distinct conformations impossible.


(1)
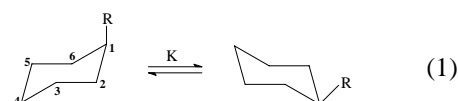
The most used methodology investigating this equilibrium have been NMR spectroscopy which involves low temperature experiments on which the equilibration is "slow" and the conformations may be observed individually. In that case on the assumption that signal intensity is directly proportional to the number of nuclei, equilibrium constants at the temperature of observation are obtained directly from ratios of signals areas[1,3,4,5].

Alternatively, we can use chemical shifts (δ) and / or coupling constants (J) since as these data for the simple system should be intermediate between those for the two conformational extremes of eq. 1, and the precise value is determined by the mole fractions N, as in eq. 2 where X is δ or J.

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$$X = N_{ax} X_{ax} + N_{eq} X_{eq} \qquad (2)$$

The extreme X_{ax} values can be obtained either from the low temperature spectra (valid just when $X = J$)[6] or through the use of model compounds, as 4-*t*-butyl derivatives (eq. 3)

$$(3)$$
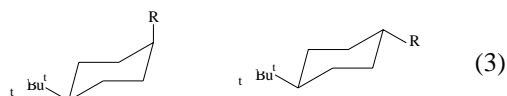
The X value is measured in the equilibrating system (eq. 1) and is the weighted average of the corresponding values in the individual conformers. The conformer populations N_{ax} and N_{eq} may be calculated from eq. 4 and the fact that $N_{ax} + N_{eq} = 1$.

$$N_{eq} = \frac{X - X_A}{X_{eq} - X_{ax}} \qquad (4)$$

This approach is attributed to Eliel[4,7] and has been applied widely[4,8] in spite of the probable adverse effects that a holding group such as 4-*t*-butyl may have[9].

We have gathered in Table 1 some previous determinations of conformational preferences of cyclohexanes substituted with groups that can be helpful to comparison with our data.

The objectives of this study were to apply Eliel and slow exchange methods to investigate the conformational equilibrium and to compare the results obtained from these methods against those obtained from semiempirical and *ab initio* calculations.

Table 1. Free Energies (ΔG^o) and Equatorial Percentages to Some Monosubstituted Cyclohexanes.

Substituent	Solvent	Temp. (°C)	ΔG^o/ kJ mol^{-1}	% equat.
- CH$_3$[a]	CBrF$_3$ – CD$_2$Cl$_2$	-116	7.53	99.7
- CH$_2$CH$_3$[a]	CBrF$_3$ – CD$_2$Cl$_2$	-116	7.32	99.6
- OCOCH$_3$[b]	CDCl$_3$ – CFCl$_3$	-90	3.64	91.6
- OCOPh[b]	CDCl$_3$ – CFCl$_3$	-85	2.05	78.9
- OCONHPh[b]	CDCl$_3$ – CFCl$_3$	-90	3.26	89.4

[a] Ref. 10; [b] Ref. 11.

Results and Discussion

Herein we report the conformational analysis of the cyclohexyl–*N,N*-dimethylcarbamate (**1**), comparing the investigation through experimental against the computational methods. We prepared the monosubstituted compound (**1**) and the 4-*tert*-butyl derivative in both *cis* (**2c**) and *trans* (**2t**) stereochemistries. The latter compounds were used as rigid models.

The compounds **1**, **2c** and **2t** were prepared by known procedures[12] and are described in the Experimental Section.

Assignments

Spectral assignments of the 1–H were unambiguous by the coupling constants inspection. The ^{13}C NMR signal were unambiguously assigned taking into account the substituent effects and the DEPT experiments.[13]

Table 2 contains the 1–H data used for the conformational calculations in CCl$_4$, CDCl$_3$ and CD$_3$CN.

1a   1e

2c   2t
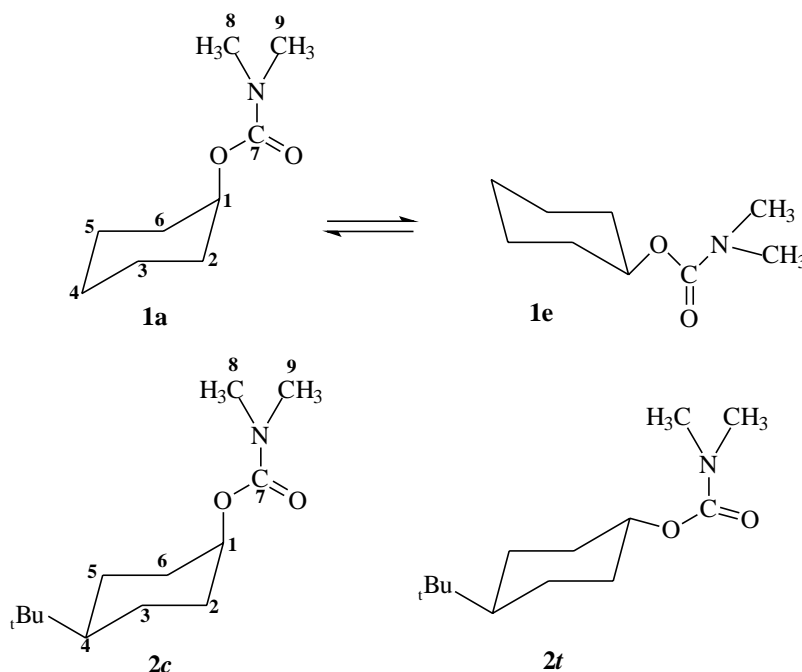
The J_T and W were measured as demonstrated in Figure 1. The difference between J_T and W is that the last correspond to the sum of the vicinal couplings (with 6-H and 2-H) plus any long range couplings.

In cyclohexane derivatives the 1-H_e is more deshielded than the 1-H_a.[14] The 1–H_a resonance in the *trans–tert–*butyl isomer (**2t**) should show 16 lines, but as the coupling constants $J_{1-Ha/2-Ha}$ and $J_{1-Ha/6-Ha}$ and also the $J_{1-Ha/2-He}$ and $J_{1-Ha/6-He}$ have the same values, the observed number of lines is 9 (see Figure 1). In the 1–H_e resonance (**2c**) only five lines were observed because all the coupling constants are small and the signal was poorly resolved.

Table 3 presents the ^{13}C chemical shifts for the cyclohexyl-*N,N*-dimethylcarbamate (**1**) and the 4-*tert*-butyl derivatives (**2c** and **2t**).

The carbons C-8 and C-9 were assigned considering the analog effects observed in amides, where the anti N-methyl group resonances occurs at lower field than the syn N-methyl groups.[15] The chemical shifts of these carbons can not be used for the conformational calculations because they show the same values in compounds **2c** and **2t**. Even in the low temperature experiments, (in CF_2Br_2 / CD_2Cl_2 were not observed any variation in the chemical shifts of C-8 and C-9.

Carbons C-7 and C-4 chemical shifts for the compound **1** are not between the extreme values, obtained from the *t*-butyl derivatives, and were also not used for the conformational calculations. The C-7 shows only one signal for the two conformers at –100[0]C.

Conformational equilibrium by NMR

Conformational preferences were determined in CCl_4, $CDCl_3$, CD_3CN and CF_2Br_2/CD_2Cl_2 by the Eliel method, eq. 4, using ^1H and ^{13}C NMR data from Tables 2 and 3, respectively.

Table 2. ^1H NMR data for Conformational Calculations.

Solvent	Compd.	δ	J	J_T[a]	W[b]
	1	4.54	1-H / 2-H_a or 6-H_a = 8.3	24.9	25.8
			1-H / 2-H_e or 6-H_e = 4.2		
CCl_4	**2c**	4.82	1-H_e / 2-H_a or 6-H_a = 2.7	10.8	11.8
			1-H_e / 2-H_e or 6-H_e = 2.7		
	2t	4.38	1-H_a / 2-H_a or 6-H_a = 10.7	29.4	32.0
			1-H_a / 2-H_e or 6-H_e = 4.3		
	1	4.66	1-H / 2-H_a or 6-H_a = 8.4	24.3	26.9
			1-H / 2-H_e or 6-H_e = 4.1		
$CDCl_3$	**2c**	4.88	1-H_e / 2-H_a or 6-H_a = 2.8	11.1	12.1
			1-H_e / 2-H_e or 6-H_e = 2.8		
	2t	4.47	1-H_a / 2-H_a or 6-H_a = 11.1	31.2	33.0
			1-H_a / 2-H_e or 6-H_e = 4.5		
	1	4.54	1-H / 2-H_a or 6-H_a = 8.4	24.3	26.1
			1-H / 2-H_e or 6-H_e = 4.1		
CD_3CN	**2c**	4.80	1-H_e / 2-H_a or 6-H_a = 2.8	11.1	12.4
			1-H_e / 2-H_e or 6-H_e = 2.8		
	2t	4.41	1-H_a / 2-H_a or 6-H_a = 11.1	30.9	32.5
			1-H_a / 2-H_e or 6-H_e = 4.5		

[a] Sum of all 1-H Couplings, determined by the separation between the external lines. [b] Line width at half–height (see Figure 1).

Table 3. ^{13}C NMR Chemical Shifts[a].

Solvent	Compd.	C-1	C-2/C-6	C-3/C-5	C-4	C-7	C-8	C-9	C-10[d]	C-11[e]
	1	72.35	32.10	23.80	25.76	155.15	36.18	35.75	——	——
CCl_4	**2c**	68.81	30.58	21.56	47.31	154.73	35.93	35.49	32.42	27.37
	2t	73.45	32.47	25.41	47.20	154.92	35.93	35.49	32.23	27.61
	1	72.97	31.93	23.56	25.45	156.31	35.92	35.92	——	——
$CDCl_3$	**2c**	69.72	30.66	21.53	47.27	156.12	35.85	35.85	32.34	27.25
	2t	74.22	32.50	25.36	47.09	156.30	35.85	35.85	32.14	27.45
	1	73.65	32.71	24.37	26.27	157.01	36.40	36.18	——	——
CD_3CN	**2c**	70.45	31.45	22.45	48.22	156.82	36.91	36.35	33.07	27.94
	2t	74.99	33.43	26.29	48.06	156.98	36.91	36.35	32.84	27.72
	1[b]	73.88	33.17	24.82	26.67	156.93	37.06	36.54	——	——
CF_2Br_2 /CD_2Cl_2	**1a**[c]	70.55	30.71	21.42	26.28	——	36.55	36.05	——	——
	1e[c]	74.43	33.11	25.20	25.79	156.40	36.55	36.05	——	——

[a]In ppm from TMS; [b]Spectrum obtained at -10[o]C; [c]Spectrum obtained at -100[o]C; [d]Quaternary carbon of tert-butyl; [e]Methyls of tert-butyl.

Table 4. Equatorial Conformer Populations of Cyclohexyl-*N,N*-dimethylcarbamate (**1**), Calculated from ^{1}H NMR Data.

Solvent				Parâmetros		
	δ_{H1}	J (1-H/2-H$_a$ or 6-H$_a$)[a]	J (1-H/2-H$_e$ or 6-H$_e$)[b]	J_T[c]	W[c]	Av[d]
CCl$_4$	64	70	94	76	69	75±9
CDCl$_3$	54	67	76	66	71	67±6
CD$_3$CN	66	67	76	67	68	69±5

[a]The coupling constants $J_{1-H/2-Ha}$ and $J_{1-H/6-Ha}$ have the same value. [b]The coupling constants $J_{1-H/2-He}$ and $J_{1-H/6-He}$ have the same value. [c]See footnotes a-b in Table 2. [d]Mean of all values for the solvent.
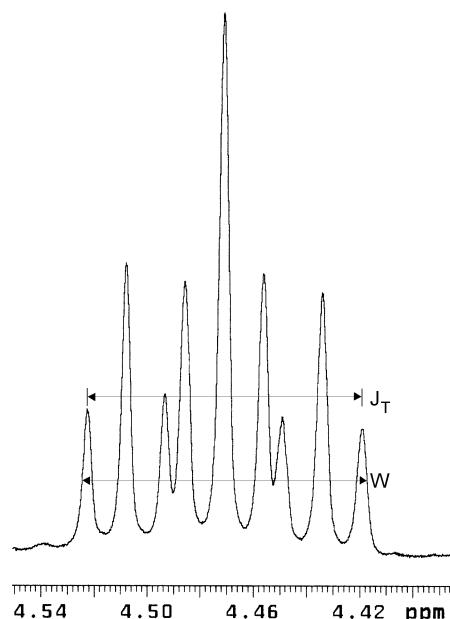
Figure 1. Measurements illustration of the total coupling constant (J_T) and line width at half – height (W) for the 1-H signal compound **2t**.

At least five different parameters were used to estimate the conformational preferences through the eq. 4 in which the observable X was (1) the chemical shift of the 1-H (δ_{H1}); (2) the coupling constants of the 1-H ($J_{1-H/2-Ha\ or\ 6-Ha}$ and $J_{1-H/2-He\ or\ 6-He}$); (3) the coupling constant of the 1-H measured between the extreme lines of the signal (J_T); (4) the line width at half-height of the 1-H resonance (W) and (5) the ^{13}C chemical shifts.

Application of eq. 4 to the data from Tables 2 and 3 readily gave conformer populations, which we express in Table 4 and 5, respectively, as equatorial percentages.

Table 5. Equatorial Conformer Populations of Cyclohexyl-*N,N*-dimethylcarbamate (**1**) Calculated from ^{13}C NMR Data.

Solvent	C-1	C-2/C-6	C-3/C-5	Av [a]
CF$_2$Br$_2$/CD$_2$Cl$_2$[b]	86	....	90	88 ± 2
CCl$_4$	76	80	58	72 ± 8
CDCl$_3$	72	69	53	65 ± 8
CD$_3$CN	71	64	50	61 ± 8

[a]Mean of all values for the solvent; [b]Values estimated by signal integration in spectrum obtained at -100°C (see Fig. 2).

The conformational equilibrium of compound **1** was also investigated by NMR low temperature experiments.

Figure 2 shows both, ^{1}H and ^{13}C spectra as a function of temperature in CF$_2$Br$_2$ containing 10% CD$_2$Cl$_2$. In the ^{1}H spectra we were able to integrate just the 1-H resonance from each conformer. In the ^{13}C spectrum all signals from the cyclohexanic ring were well separated and the ratio of the intensities can be determined by signal integration. As the integrated signals are from nuclei in the two conformers, the nuclear overhauser effects and relaxation times do not affect the measure[4,5,10].
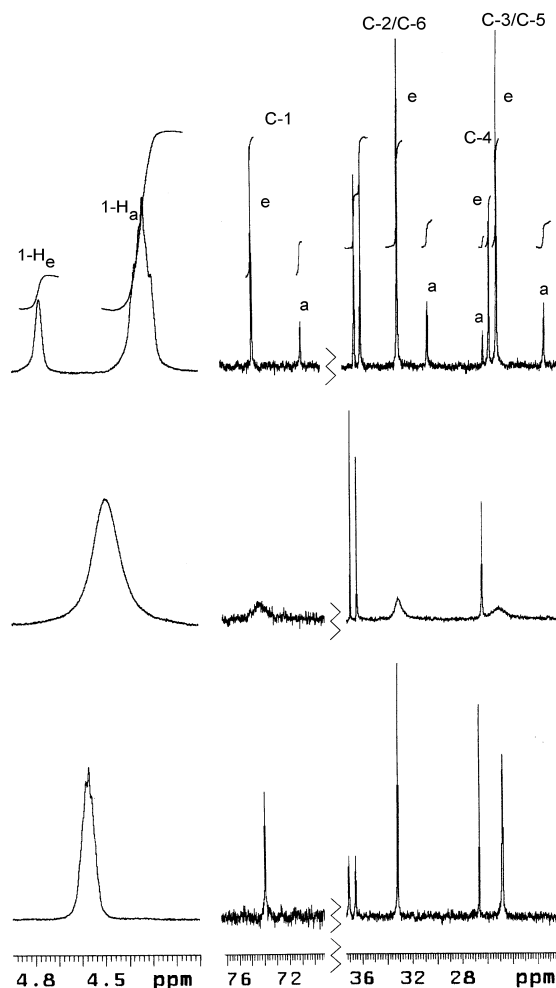
Figure 2. The ^{1}H and ^{13}C spectra of cyclohexyl-*N,N*-dimethyl-carbamate (**1**) in CF$_2$Br$_2$ containing 10% CD$_2$Cl$_2$ as a function of temperature: (top) -100°C, (middle) -50°C, (bottom) -10°C. Integrals: 1-H$_a$ (85%), C–1$_e$ (81%), C–2$_e$ / C–6$_e$ (81%), C–3$_e$ / C–5$_e$ (82%).

From such spectra we determine that the percentage of equatorial dimethylcarbamate is about 85% by the ^{1}H spectra and, in the average, 82% (± 1) by the ^{13}C spectra.

The differences between the results obtained from chemical shifts and coupling constants (Tables 4 and 5) indicated the inherent difficulties of the method. Errors in conformational proportions could arise either statistically because the Eliel method relies on small differences between numbers or systematically because the *tert*-butyl system has structural differences from the mono-substituted cyclohexane.

From all methods used in this study, the signal integration of spectra obtained at low temperatures, undoubtedly, gave us the most precise results. The percentage of equatorial conformer determined by this method was around 83%. All the results obtained from ^{1}H and ^{13}C NMR data applied to Eliel method (Table 4 and 5), also predict the preference of the equatorial conformer and in the average, the results estimated through this method were only a little lower than those determined from low temperature experiments. The C-1 and C-3/C-5 chemical shifts obtained from spectra at low temperature in CF_2Br_2 / CD_2Cl_2 (Table 3) applied to eq. 4 led us to an equatorial proportion around 88% (Table 5) that is in good agreement with the results determined by the signal integration at –100ºC. The C-4 and C-2/C-6 chemical shifts, as expected, show a nonlinear behavior over the temperature range used, and the values obtained at –10ºC do not correspond to the weight average between **1a** and **1e** conformers obtained at –100ºC.

The data in Tables 4 and 5 indicate the effect on conformational equilibrium of the cyclohexyl-*N,N*-dimethylcarbamate (**1**), when the solvent was changed from CCl_4 to CD_3CN. In CD_3CN the equatorial conformational preference was minor than in CCl_4, that is consistent with a solvation of the carbamate group which reduces 1,3 diaxial interactions[11], leading to an increase on the axial conformer population.

In the present study we endeavored to improve accuracy by developing a whole family of observables that could independently provide data X for eq. 4.

Theoretical calculations

Semiempirical and *ab initio* calculations were also applied to investigate the conformational equilibrium of cyclohexyl-*N,N*-dimethylcarbamate. The potential energy surfaces (PES) were obtained using semi-empirical methods, AM1, PM3 and MNDO, for conformers **1a** and **1e**. The PES were obtained varying the dihedral angles ϕ_1, ϕ_2 and ϕ_3 (eq. 5) for both conformers with an increment of 10º, ranging from 0º to 360º. Analyzing these PES we found global minimum for conformer **1a** and another one for **1e**, which were fully optimized using semi-empirical (AM1, PM3, MNDO) and *ab initio* methods at HF/STO-3G

and HF/6-31G(d,p) levels. The geometrical parameters using HF/6-31G(d,p) level are shown in Table 6.
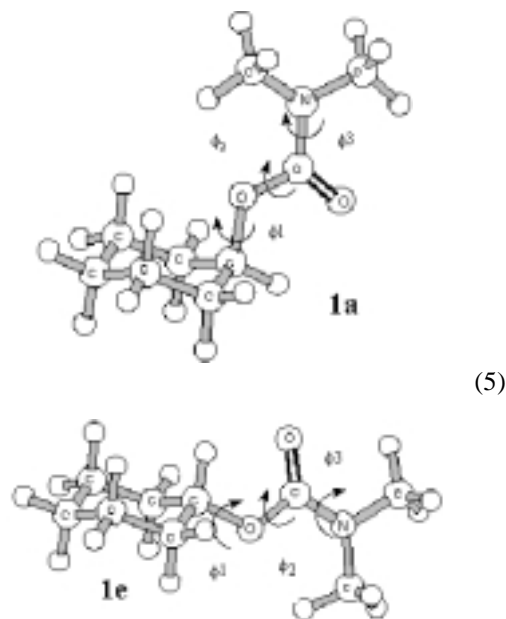

(5)

Table 6. Calculated geometries through HF/6-31g(d,p) method for conformers **1a** and **1e**.

Parameters	1a	1e
r(C=O)	1.200	1.200
r(C-N)	1.353	1.354
r(C-O)	1.436	1.430
r(O-C)	1.328	1.328
r(N-C$_{11}$)	1.447	1.448
r(C$_1$-C$_2$)	1.525	1.522
r(C$_2$-C$_3$)	1.531	1.532
r(C$_3$-C$_4$)	1.531	1.531
r(C$_4$-C$_5$)	1.531	1.531
r(C$_5$-C$_6$)	1.532	1.532
r(C$_6$-C$_1$)	1.525	1.524
ZC$_1$-O$_7$-C$_8$	118.2	118.3
ZO-C=O	123.2	123.4
ZO=C-N	124.2	124.3
ZC$_8$-N-C$_{11}$	119.3	118.7
ZC$_1$-C$_2$-C$_3$	112.4	110.8
ZC$_2$-C$_3$-C$_4$	111.5	111.5
ZC$_3$-C$_4$-C$_5$	111.3	111.2
ZC$_4$-C$_5$-C$_6$	111.4	111.6
ZC$_5$-C$_6$-C$_1$	112.7	110.8
ZC$_6$-C$_1$-C$_2$	111.9	111.7
ZC$_{11}$-N-C$_{12}$	116.1	116.5
ϕ H-C-O-C	36.6	-36.7
ϕ O-C-N-C$_{12}$	0.1	-8.2
ϕ O=C-N-C$_{11}$	0.6	7.2
ϕ C-O-C=O	-0.1	56.2
ϕ C$_6$-C$_1$-O-C	155.1	83.3
ϕ C$_5$-C$_6$-C$_1$-O	68.4	174.7
ϕ C$_4$-C$_5$-C$_6$-C$_1$	53.5	-55.2
ϕ C$_3$-C$_4$-C$_5$-C$_6$	-54.8	54.6
ϕ C$_2$-C$_3$-C$_4$-C$_5$	55.2	-54.6
ϕ C$_1$-C$_2$-C$_3$-C$_4$	-54.1	55.2
ϕ C$_6$-C$_1$-C$_2$-C$_3$	52.2	-56.2
ϕ C$_5$-C$_6$-C$_1$-C$_2$	-52.0	56.2

r = bond lengh given in Aº, Z = angle and ϕ = dihedral angle given in degrees

The lowest energy calculated denotes which one is the most stable conformer and their energy difference allow us to determine the ΔH value.

Assuming that the ΔS values are not significant[16,17], ΔG will be equal to ΔH and the conformers population can be calculated using equation 6,

$$\Delta G = - RT \, ln \, K \qquad (6)$$

where $K = N_{1e} / N_{1a}$ is the equilibrium constant (N_{1e} and N_{1a} are the molar fractions of conformers **1e** and **1a**, respectively), R the gas constant (8.33×10^{-3} kJ mol^{-1}K^{-1}) and T the temperature (298.5 K).

The results obtained from the theoretical calculations are sumarized in Table 7.

Table 7. Calculated Minimum Conformational Energy (E)[a], Free Energy (ΔG^o)[b] and Percentage of Equatorial Conformer for Cyclohexyl-*N,N*-dimethylcarbamate.

Método	E_{1e}	E_{1a}	$-\Delta G^o$	% eq
AM1	-106.13	-104.84	5.41	89.8
PM3	-108.20	-107.11	4.57	86.3
MNDO	-98.89	-98.56	1.38	63.6
STO-3G	-343739.90	-343739.57	1.40	63.7
6-31G(d)	-348078.29	-348077.70	2.46	72.9

[a]In kcal/mol (1 cal = 4.184 J); [b]DG^o = E_{1e} – E_{1a} in kJ/mol.

The conformers population of cyclohexyl-*N,N*-dimethylcarbamate obtained through theoretical calculations (Table 7) correctly predict that the equatorial conformation is prefered over the axial conformation.

Between the semiempiricals methods, the AM1 and PM3 shown an excelent agreement with the experimental results. However, the MNDO method did not show the same tendency, what could be expected since it is the predecessor of the AM1 and PM3 methods, which represent a major advance, including a larger number of experimental parameters and an individual treatment for the nuclei.

We also carried out *ab initio* calculations at HF/STO-3G and HF/6-31G(d,p) levels with zero point correction (ZPE), expecting them to be more reliable in predicting conformational preferences than the semiempirical methods. The results were closely each other and denote that at higher levels we should have better results.

In general, the theoretical calculations, semi-empirical and *ab initio*, are in agreement with the experimental results, because both theories demonstrated the major *equatorial* preference, although the *ab initio* results are considered in the vapor phase, while the experimental values were performed in solution. However, semi-empirical methods take into account experimental parameters which are obtained in the condensed phase. Consequently, it is not strictly legitimate to make a quantitative comparison of the experimental results with our calculations (which refer to enthalpies of isolated molecules in the gas phase).

We also measure the torsional angles (ω) on the compounds **1e** and **1a**, previously optimized through the semiempirical and *ab initio* calculations(Table 8). These torsional angles were used on Karplus[18,19] equation (eq. 7) to calculate the coupling constants of the 1-H.

$$^3J_{HH} = A + B \cos \omega + C \cos 2\omega \qquad (7)$$
$$A = 7, \ B = -1 \ \text{and} \ C = 5$$

The calculated coupling constants were compared against the 1-H coupling constants measured in the isomers **2c** and **2t** ^{1}H spectra.

The calculated coupling constants (J_C) are in an acceptable range considering the typical values for a ciclohexane derivative.[4] The coupling constants J_C and J_E for the 1-H$_a$ are in good agreement. Since the experimental results were determined on the *t*-butyl derivatives and the theoretical calculations were performed on compounds **1e** and **1a**, this agreement indicate that the use of the rigid models provide a good qualitative account of the conformational analysis of the compound **1**. Unfortunately the 1-H$_e$ signal was poorly resolved and the coupling constants can not be precisely determined.

Table 8. Torsional Angles (ω) Calculated by Semiempirical and *ab initio* Methods and Coupling Constants for the 1-H in the Compounds **1a** and **1e**.

Compd.	Atoms	AM1	PM3	MNDO	STO-3G	6-31G(d,p)	ω_M[a]	J_C[b]	J_E[c]
1e	H_{1a}-C_1-C_2-H_{2e}	55	58	54	58	57	56.3	4.5	4.5
	H_{1a}-C_1-C_2-H_{2a}	172	175	171	175	174	173.4	12.9	11.0
	H_{1a}-C_1-C_6-H_{6e}	54	58	55	57	55	55.9	4.6	4.5
	H_{1a}-C_1-C_6-H_{6a}	172	175	171	175	173	173.2	12.9	11.0
1a	H_{1e}-C_1-C_2-H_{2e}	63	65	73	63	59	64.5	3.4	2.8
	H_{1e}-C_1-C_2-H_{2a}	54	50	41	54	59	51.6	5.2	2.8
	H_{1e}-C_1-C_6-H_{6e}	63	65	74	62	57	64.1	3.5	2.8
	H_{1e}-C_1-C_6-H_{6a}	55	50	41	54	61	52.0	5.2	2.8

[a]Mean of all values for each torsional angle; [b]Coupling constant calculated applying eq. 7 to ω_M values; [c]Coupling constant experimental measured in the compounds **2c** and **2t**.

Experimental

NMR measurements

The ^1H and ^{13}C NMR spectra, including those at low-temperature, were recorded on Varian Gemini-2000 / 300 spectrometer. The samples were prepared as 0.5M solutions in $CDCl_3$, CCl_4 and CD_3CN in a 5mm tube. When the solvent was CCl_4, $CDCl_3$ was used into an insert tube as an external reference. The espectra were obtained using 32k of points and sweep widths of 12 – 18 kHz, a pulse width of 6.7 µs ($\cong 45^o$ tip angle), acquisition time of 0.6s and relaxation delay of 1.0s. Low-temperature experiments were recorded with samples prepared as 1.0M solution in CF_2Br_2 / CD_2Cl_2 (10 : 1 by volume). The same parameters as noted above were employed except that the pulse width was 4.5 µs ($\cong 30^o$ flip angle) and 32 k of poits were used.

Materials

Cyclohexanol and 4-*t*-butylcyclohexanol were commercially available from Aldrich.

Cyclohexyl–*N,N*-dimethylcarbamate (**1**). Cyclohexanol was treated with Na^0 by 4 h under reflux in THF. Dimethylcarbamyl chloride it was added and the reaction was mantained in reflux over night.

4-*tert*-butyl-1-*N,N*-dimethylcarbamatecyclohexane (**2**) was obtained as a mixture of *cis* and *trans* isomers by the same procedure described above for compound **1**.

The trans (**2t**) isomer was isolated from the mixture by elution in a silica column (flash chromatography).

Calculations

The semiempirical (MNDO, AM1 and PM3) and *ab initio* calculations were carried out using Gaussian 94,[20] running on a Pc – Pentium Pro 200 with 128 Mbyte memory and on a IBM Risc 6000 only for the 6-31G(d,p) level. All structures were fully optimized using procedures standard to the Gaussian 94 system of computer programs. The Hartree – Fock (HF) theory was employed for the *ab initio* calculations using the STO-3G and 6-31G(d,p) basis sets.

Conclusions

The results of this study demonstrate that we can use a large number of measurables to investigate the conformational equilibrium of a particular system. The values obtained through Eliel method, dynamic nuclear magnetic ressonance and theoretical calculations are in good agreement, indicating that the calculations are also appropriated to investigate conformational equilibrium. The conformer population of the cyclohexyl-*N,N*-dimethylcarbamate show to be solvent dependent. The equatorial preferences in non polar solvent is around 80% that agrees with the values determined by the NMR signal integration at -100ºC.

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