

# The conformational behaviour of methylenecyclohexanes revisited

Heidi M. Muchall, Petrina R.N. Kamyra, and Jean Lessard

**Abstract:** Conformational analyses on 2-substituted (methoxy, vinyloxy, and acetoxy) methylenecyclohexanes have been performed computationally with HF, B3LYP, PBE0, and MP2 and the 6-31G(d) basis set. The global minimum for the methoxy substituent is an axial conformer. For the vinyloxy substituent, except with PBE0, an axial conformer is determined as the global minimum. The acetoxy substituent prefers the equatorial orientation. This sequence is in keeping with the operation of an “unsaturation effect” in addition to an anomeric effect. For a full conformational analysis, torsional potentials for the substituents have been generated, which show further low-energy minima, which affect the equilibrium composition. In general, axial conformers dominate the equilibria. To reproduce the experimentally observed predominance of equatorial conformers for vinyloxy and acetoxy substituents, PBE0 has to be employed. CSGT isotropic shielding tensors at the B3LYP/6-311+G(d,p)//B3LYP/6-31G(d) level have been employed for comparison with experimentally observed  $^{13}\text{C}$  chemical shifts.

*Key words:* conformational analysis, methylenecyclohexanes, anomeric effect, unsaturation effect.

**Résumé :** On a réalisé une analyse conformationnelle de méthylèncyclohexanes portant des substituants (méthoxy, vinyloxy et acétoxy) en position 2 en faisant appel à des méthodes de calcul théorique à l'aide de HF, B3LYP, PBE0, MP2 et l'ensembles de bases 6-31G(d). Le minimum global pour le substituant méthoxy est le conformère axial. Pour le substituant vinyloxy, tous les ensembles à l'exception du PBE0 attribuent le minimum global au conformère axial alors que le substituant acétoxy occupe préférentiellement l'orientation équatoriale. Cette séquence est en accord avec l'opération de l'effet d'insaturation en plus de l'effet anomère. Pour une analyse conformationnelle complète, on a généré les potentiels de torsion des substituants qui mettent en évidence d'autres minima de basse énergie qui affectent la composition de l'équilibre. En général, les conformères axiaux prédominent à l'équilibre. Afin de reproduire la prédominance des conformères équatoriaux observée expérimentalement pour les substituants vinyloxy et acétoxy, il faut utiliser l'ensemble PBE0. Pour pouvoir faire une comparaison avec les valeurs observées expérimentalement pour les déplacements chimiques  $^{13}\text{C}$ , on a utilisé des tenseurs de blindage isotrope CSGT au niveau B3LYP/6-311+G(d,p)//B3LYP/6-31G(d).

*Mots clés :* analyse conformationnelle, méthylèncyclohexanes, effet anomère, effet d'insaturation.

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## Introduction

2-Substituted oxanes exhibit an anomeric effect, i.e., a substituent  $-\text{OR}$  prefers the axial (*gauche*) rather than the equatorial (*anti*) position. The commonly accepted reason for this is a stabilizing  $n_{\text{O}}-\sigma^*_{\text{C-O}}$  interaction in the axial orientation, but electrostatic (dipole–dipole) interactions destabilizing the equatorial orientation are most probably involved as well (1, 2). If the heteroatom of the oxane ring is replaced by a double bond, such as in 3-methoxycyclohexene and 2-methoxymethylenecyclohexane (**1**), the methoxy group also prefers the pseudoaxial or axial orientation, and this preference has been explained by a stabilizing  $\pi-\sigma^*_{\text{C-O}}$  interaction, electrostatic (dipole–quadrupole) interactions being considered less impor-

tant than the orbital interaction (3). The axial preference is larger for an acetoxy group than for a methoxy group in 2-substituted oxanes (4–6) and in 3-substituted cyclohexenes (5, 6), as expected from larger  $n_{\text{O}}-\sigma^*_{\text{C-O}}$  or  $\pi-\sigma^*_{\text{C-O}}$  interactions of the axial conformer in the case of the acetoxy group, which is more electron withdrawing and thus a better electron acceptor (i.e.,  $\sigma^*_{\text{C-O}}$  is lower in energy) than the methoxy group (1, 7).

In 1979, dynamic  $^{13}\text{C}$  NMR studies of 2-substituted methylenecyclohexanes, such as and including **1–3**, revealed an unexpected conformational behaviour (5). From low-temperature experiments (3% solutions in  $\text{CHFCl}_2-\text{CD}_2\text{Cl}_2$  (4:1 v/v) at  $-110^\circ\text{C}$ ), the chemical shifts of  $\text{C}^4$  of the axial (ax) and equatorial (eq) species were determined. The assignment of the observed chemical shifts as belonging to the

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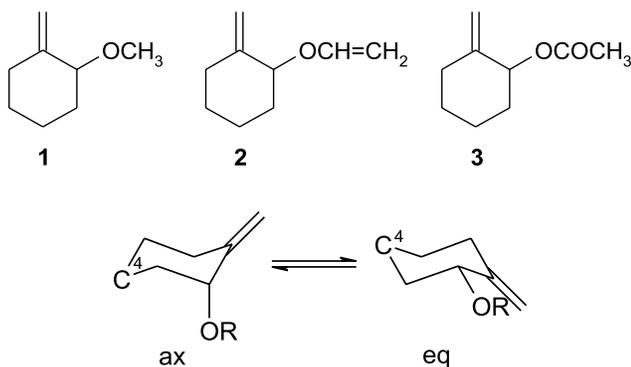
*Dedicated to Professor Don Arnold for his contributions to chemistry.*

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axial or equatorial conformer was based on the  $\gamma$ -effect, in that a  $^{13}\text{C}$  nucleus in the  $\gamma$ -position from the substituent is shielded by 4.5 ppm in the axial relative to the equatorial conformer. From the individual chemical shifts and the observed averaged  $\text{C}^4$  chemical shift  $\delta_m$  at  $0^\circ\text{C}$ , the proportion  $x$  of the equatorial conformer was calculated as  $\delta_m = x\delta_{\text{eq}} + (1-x)\delta_{\text{ax}}$ . With a  $\delta_m$  of 22.6 ppm for **1**, 23.3 ppm for **2**, and 23.9 ppm for **3**, it was concluded that the equatorial orientation is preferred for unsaturated substituents: **1** 41% eq, **2** 61% eq, and **3** 80% eq. At  $-110^\circ\text{C}$ , by integration of the signals, the proportion of the equatorial conformer was determined to be 33% for **1** and more than 95% for **3** (6). This unexpected substituent behaviour was termed the “unsaturation effect” (5, 6).

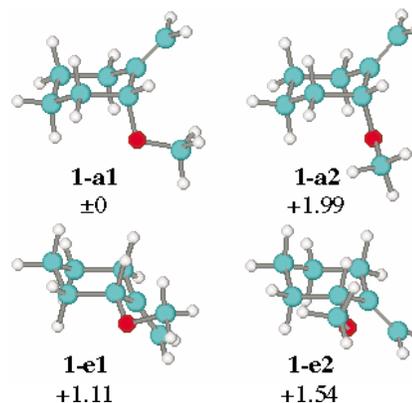


As was pointed out in a contribution by Forsyth and Sebag (8), even though chemists are nowadays able to accurately calculate  $^{13}\text{C}$  chemical shifts of organic compounds by ab initio methods, this is still not being done routinely. Accurate geometries are needed for calculated chemical shifts to be useful, and for a conformationally flexible system this means establishing the important conformers and evaluating their contribution to an equilibrium. To our knowledge, there are no computational studies as to the conformational behaviour of 2-substituted methylenecyclohexanes. Here we present a computational study of the conformational behaviour of the three representative species, **1**, **2**, and **3**, that illustrates the importance of a full conformational analysis that takes the rotamers of the substituent into account.

### Computational details

The Gaussian 98 program package was employed in all calculations (9). All minimum-energy conformations were initially optimized at HF/6-31G(d) and followed with optimizations at B3LYP/6-31G(d) (10, 11). Optimizations were also performed with the “parameter free” density functional PBE0 (12, 13) (Gaussian keyword PBE1PBE) and for **3** also with MP2(full). If not stated otherwise, representative geometry parameters in the text are given for B3LYP/6-31G(d), but the optimized species from all levels are virtually superposable. Frequency calculations were performed at HF/6-31G(d) and PBE0/6-31G(d) for zero-point vibrational (ZPV) energies, which are reported unscaled. Torsional analyses (relaxed scans) were performed at HF/6-31G(d) and in one case (for  $\phi_1$  in **3**, see below) also at B3LYP/6-31G(d) (partial optimizations in the gas phase) and PBE0/6-31G(d) (partial optimizations in dichloromethane). In our torsional analyses, minima with a relative energy of more than

**Fig. 1.** Low-energy conformers (**a** axial, **e** equatorial) of 2-methoxymethylenecyclohexane (**1**). Relative energies (B3LYP/6-31G(d)) are given in kcal/mol.



2.5 kcal/mol were not studied further, as the corresponding conformers do not contribute significantly to an overall equilibrium.

For an evaluation of a solvent influence, HF/6-31G(d)//HF/6-31G(d) and PBE0/6-31G(d)//PBE0/6-31G(d) calculations were carried out with dichloromethane (dielectric constant 9.08) and the self-consistent isodensity polarized continuum model (SCI-PCM) at an isodensity value of 0.0004. Isotropic shielding tensors were calculated with B3LYP/6-311+G(d,p)//B3LYP/6-31G(d) using the CSGT (continuous set of gauge transformations) method (14). To obtain chemical shifts, the values were corrected for the calculated absolute shielding for carbon in tetramethylsilane (181.98; the experimental value is 188.1 (15)) at this level of theory.

## Results

### Conformations

#### 2-Methoxymethylenecyclohexane (**1**)

To locate all relevant minima on the potential energy surface, the H-C-O-C torsion angle  $\phi$  was twisted through  $360^\circ$  in both the axial and equatorial forms in  $30^\circ$  steps. Four low-energy conformations of **1** were identified. These were fully optimized at HF/6-31G(d), B3LYP/6-31G(d), and PBE0/6-31G(d). The B3LYP-optimized conformers are given in Fig. 1; all energies are listed in Table 1.

As expected from a possible, stabilizing  $\pi\text{-}\sigma_{\text{C-O}}^*$  interaction and in analogy to the anomeric effect, the global minimum is an axial species, **1-a1** ( $\phi -50^\circ$ ). A low-energy barrier ( $\phi 0^\circ$ ) connects rotamers **1-a1** and **1-a2** ( $\phi +43^\circ$ ). Similarly, a low-energy barrier connects **1-e1** ( $\phi -34^\circ$ ) and **1-e2** ( $\phi +37^\circ$ ). All model chemistries agree on one order of stability for the four conformers, and the relative energies indicate that all four are populated significantly at  $0^\circ\text{C}$ . We have calculated the equilibrium populations at 273 K at all levels of theory employed (Table 1). As can be seen from Table 1, the relative energies and the resulting equilibrium composition are virtually identical for the gas-phase calculations. The population of the axial conformers is about 80%; that of the equatorial conformers is about 20%. As expected, the use of free energies does not show a significant change from these values (data not given). In contrast, the inclusion of solvent

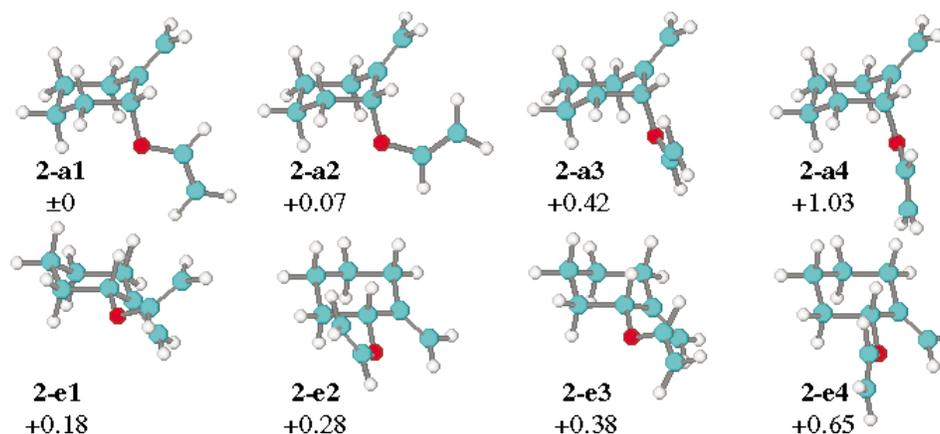
**Table 1.** Total energies (hartrees (1 hartree =  $4.359 \times 10^{-18}$  J)) for axial (a) and equatorial (e) conformers of **1**.

	1-a1	1-a2	1-e1	1-e2
HF/6-31G(d)	-385.933163 (0) 84.0%	-385.930019 (1.97) 2.5%	-385.931364 (1.13) 10.1%	-385.930367 (1.75) 3.4%
+ZPVE	-385.709792 (0) 82.0%	-385.706806 (1.87) 2.5%	-385.708085 (1.07) 11.5%	-385.707265 (1.59) 4.1%
SCI-PCM	-385.935232 <sup>a</sup> (0) 69.9%	-385.932664 (1.61) 3.5%	-385.934164 <sup>b</sup> (0.67) 20.3%	-385.933124 (1.32) 6.3%
B3LYP/6-31G(d)	-388.480611 (0) 82.0%	-388.477433 (1.99) 2.5%	-388.478850 (1.11) 10.7%	-388.478163 (1.54) 4.9%
PBE0/6-31G(d)	-388.017400 (0) 79.4%	-388.014048 (2.10) 1.6%	-388.015907 (0.94) 14.3%	-388.014994 (1.51) 4.8%
+ZPVE	-387.807388 (0) 76.9%	-387.804235 (1.98) 2.3%	-387.805965 (0.89) 14.6%	-387.805213 (1.36) 6.2%
SCI-PCM	-388.019239 (0) 64.9%	-388.016446 (1.75) 2.6%	-388.018368 (0.55) 23.4%	-388.017552 (1.06) 9.1%

**Note:** Relative energies (kcal/mol) in parentheses, equilibrium populations at 273 K.

<sup>a</sup>Total energy from an optimization that includes solvent at this level is -385.935274 hartrees.

<sup>b</sup>Total energy from an optimization that includes solvent at this level is -385.934210 hartrees.

**Fig. 2.** Low-energy conformers (a axial, e equatorial) of 2-vinyloxymethylencyclohexane (**2**). Relative energies (B3LYP/6-31G(d)) are given in kcal/mol.

does not change the order of stability of the four conformers but decreases all energy differences. This causes an almost doubling of the equatorial population in the equilibrium, and the sum of the axial conformers decreases to about 70%. In the dynamic  $^{13}\text{C}$  NMR experiments of **1**, the equilibrium composition at  $0^\circ\text{C}$  was estimated to be 59% axial in  $\text{CHFCl}_2\text{-CD}_2\text{Cl}_2$  (**5**, **6**) and 65% axial in the less polar  $\text{CF}_2\text{Br}_2\text{-CD}_2\text{Cl}_2$  (**6**), which is in reasonable agreement with our calculated data.

### 2-Vinyloxymethylencyclohexane (**2**)

Energy profiles were obtained for two torsion angles, H-C-O-C ( $\phi_1$ ) and C-O-C-C ( $\phi_2$ ). From the information in these profiles, eight low-energy conformations were identi-

fied and optimized at HF/6-31G(d), B3LYP/6-31G(d), and PBE0/6-31G(d). The B3LYP-optimized conformers are given in Fig. 2, energies are listed in Table 2.

Torsion angles  $\phi_1$  in all eight conformers are in the range of either  $+50^\circ$  or  $-50^\circ$ , which are similar values to those found in **1**. While the conformer with  $\phi_1$  near  $180^\circ$  is a high-energy minimum, **2** does not exhibit a significant preference ( $0^\circ$  over  $180^\circ$ ) for  $\phi_2$ . All model chemistries, except for the uncorrected (ZPV energies not included) PBE0/6-31G(d) and the solvent calculations at this level, agree on an axial species, **2-a1**, as the global minimum. This is in contrast to the interpretation from the NMR experiments and in line with a stabilizing  $\pi^*\text{-}\sigma_{\text{C-O}}$  interaction. For the two PBE0 calculations, **2-e1** is the global minimum. The other seven con-

**Table 2.** Total energies (hartrees) for axial (a) and equatorial (e) conformers of **2**.

	<b>2-a1</b>	<b>2-a2</b>	<b>2-a3</b>	<b>2-a4</b>
HF/6-31G(d)	-423.781976 (0) 37.3%	-423.781181 (0.50) 14.9%	-423.780530 (0.91) 7.1%	-423.780096 (1.18) 4.1%
+ZPVE	-423.553742 (0) 45.5%	-423.552335 (0.88) 9.1%	-423.551635 (1.32) 4.1%	-423.551861 (1.18) 5.0%
SCI-PCM	-423.784806 (0) 34.2%	-423.783538 (0.80) 7.9%	-423.783100 (1.07) 4.8%	-423.783368 (0.90) 6.5%
B3LYP/6-31G(d)	-426.566617 (0) 21.7%	-426.566507 (0.07) 19.1%	-426.565948 (0.42) 10.0%	-426.564977 (1.03) 3.3%
PBE0/6-31G(d)	-426.057756 (0.31) 13.3%	-426.058144 (0.07) 20.9%	-426.057470 (0.49) 9.5%	-426.055928 (1.46) 1.7%
+ZPVE	-425.843308 (0) 21.6%	-425.842983 (0.20) 14.9%	-425.842322 (0.62) 6.9%	-425.841385 (1.21) 2.4%
SCI-PCM	-426.060355 (0.30) 12.6%	-426.060401 (0.27) 14.0%	-426.059870 (0.60) 7.6%	-426.058919 (1.20) 2.5%
	<b>2-e1</b>	<b>2-e2</b>	<b>2-e3</b>	<b>2-e4</b>
HF/6-31G(d)	-423.780962 (0.64) 11.6%	-423.780455 (0.95) 6.3%	-423.781090 (0.56) 13.4%	-423.780247 (1.08) 5.2%
+ZPVE	-423.552241 (0.94) 8.2%	-423.551650 (1.31) 4.1%	-423.552893 (0.53) 16.8%	-423.552163 (0.99) 7.3%
SCI-PCM	-423.783722 (0.68) 9.6%	-423.783172 (1.03) 5.1%	-423.784482 (0.20) 23.6%	-423.783576 (0.77) 8.2%
B3LYP/6-31G(d)	-426.566326 (0.18) 15.6%	-426.566172 (0.28) 13.0%	-426.566017 (0.38) 10.9%	-426.565581 (0.65) 6.5%
PBE0/6-31G(d)	-426.058253 (0) 23.7%	-426.058007 (0.15) 17.8%	-426.057416 (0.53) 9.0%	-426.056760 (0.94) 4.3%
+ZPVE	-425.843259 (0.03) 20.3%	-425.842876 (0.27) 13.2%	-425.842902 (0.25) 13.4%	-425.842414 (0.56) 7.6%
SCI-PCM	-426.060832 (0) 22.9%	-426.060563 (0.17) 16.7%	-426.060514 (0.20) 15.8%	-426.059926 (0.57) 8.0%

Note: Relative energies (kcal/mol) in parentheses, equilibrium populations at 273 K.

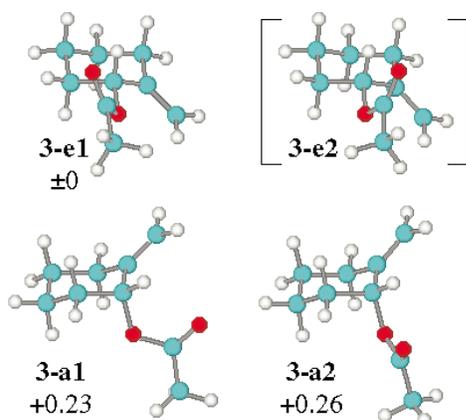
formers lie within 1.5 kcal/mol for all methods, but the model chemistries do not agree on the order of stability. In particular, gas-phase HF/6-31G(d) calculations give a relatively large energy difference between **2-a1** and **2-e3**, the most stable of the equatorial conformers (Table 2), which results in an equilibrium concentration of the axial conformers of over 60%. Relative energies from B3LYP and from HF solvent calculations lead to a sum of the axial conformers that is significantly smaller at about 50%. The sum of axial conformers only drops below 50% with PBE0, in accord with experiment. All model chemistries reproduce the experimentally observed increase in equatorial conformer concen-

tration from **1** and therefore the "unsaturation effect". At the PBE0 level this trend is reproduced particularly well, with the experimental equilibrium composition of **2** at 0°C of 39% axial and 61% equatorial (5).

### 2-Acetoxyethylenecyclohexane (3)

Energy profiles were obtained for two torsion angles, H-C-O-C ( $\phi_1$ ) and C-O-C-O ( $\phi_2$ ). From the information in these profiles, four low-energy conformations were identified and optimized with HF/6-31G(d) and MP2(full)/6-31G(d). With B3LYP/6-31G(d) and PBE0/6-31G(d), only three conformers, **3-e1**, **3-a1**, and **3-a2** were identified. The

**Fig. 3.** Low-energy conformers (**a** axial, **e** equatorial) of 2-acetoxymethylenecyclohexane (**3**). Relative energies (B3LYP/6-31G(d)) are given in kcal/mol. Compound **3-e2** was obtained with PBE0/6-31G(d) (geometry optimization in CH<sub>2</sub>Cl<sub>2</sub>, SCI-PCM).



B3LYP-optimized conformers are given in Fig. 3, energies are listed in Table 3.

For **3**, the model chemistries agree on neither the order nor the number of the conformers. In agreement with the interpretation of the NMR studies (5, 6), in the gas phase, HF, B3LYP, and PBE0 give an equatorial species, **3-e1**, as the global minimum. With MP2, **3-a1** is most stable. Yet while there are four low-energy conformers at the HF and MP2 levels, there are only three with B3LYP and PBE0. With HF and MP2, in addition to the three conformers shown in Fig. 3, the fourth conformer **3-e2** has a torsion angle  $\phi_1$  of  $-18^\circ$  (with  $\phi_2$  at  $0^\circ$ ), in analogy to **1-e1**, **2-e1**, and **2-e3**; for B3LYP and PBE0 (gas-phase geometries), the potential energy surface does not possess a stationary point in that region. This is evident from the torsional analysis of  $\phi_1$  using B3LYP/6-31G(d) and starting with the optimized **3-e1** (diamonds in Fig. 4). The equilibrium composition varies widely with the model chemistry chosen. At MP2 and furthest from experiment, the composition shows about 80% axial conformers. With HF and B3LYP this value drops to just above 50%. The experimentally observed equatorial predominance (5, 6) is only reproduced with PBE0. But even there, the equatorial conformer (gas-phase geometry) is only present with just over 50%, instead of the estimated 80% at  $0^\circ\text{C}$  from experimental data.

In an attempt to identify the source of this discrepancy between experiment and theory for **3**, which is absent for both **1** and **2**, we obtained the torsional profile for **3** with an equatorial substituent using PBE0/6-31G(d), performing geometry optimizations in the solvent, and covering the region of  $\phi_1$  in which the “missing” conformer **3-e2** should be. The result is given in Fig. 4 (squares). Obviously, while the relative energy is increasing monotonously from the optimized **3-e1** at  $30^\circ$  for the gas phase species (diamonds), there is an additional minimum with the inclusion of solvent. A subsequent

geometry optimization at PBE0/6-31G(d) in this region confirmed that the fourth conformer **3-e2** is recovered when the solvent is considered in the geometry optimization (Table 3). This conformer is given in Fig. 3 in brackets.

Unfortunately, we were not able to optimize **3-a1** or **3-a2** with the inclusion of solvent (at any level), which would be needed to determine the equilibrium composition.<sup>2</sup> At this point, an assumption seems feasible. Checks on selected species (**1-a1**, **1-e1**, and **3-e1**) at the HF level have revealed that it matters little in which manner the solvent is considered in the calculations. Regardless of whether the geometry is optimized in the solvent cavity (the total energies for the three species are given in Tables 1 and 3) or whether the energy is just evaluated for the gas-phase geometry in the solvent cavity, the magnitude of the stabilization due to the solvent is about the same. If we thus assume that the solvent-optimized conformers **3-a1** and **3-a2** are also both 0.45 kcal/mol less stable than **3-e1** (Table 3), then the equilibrium exhibits 67% equatorial species, which finally is in much better agreement with the experimental value.

## Chemical shifts

### $\gamma$ -Effect

We tested our choice level of theory for NMR calculations by checking for the reproducibility of the  $\gamma$ -effect (16) in methylcyclohexane (**4**). With B3LYP/6-31G(d), **4-a** is 2.15 kcal/mol higher in energy than **4-e**, in good agreement with the experimental A value of 1.74 kcal/mol (17). The calculated relative energy leads to an equilibrium composition at 273 K of 98% **4-e** : 2% **4-a** or 97% **4-e** : 3% **4-a** at room temperature. The experimental and calculated chemical shifts for the ring carbon atoms of **4-e**, **4-a**, and cyclohexane are given in Fig. 5.

As expected, with our choice of model chemistry, the experimental chemical shifts are reproduced well. For cyclohexane, there is a difference between calculated and experimental chemical shifts  $\Delta\delta$  of 5.5 ppm. A difference of this magnitude is also found for **4**. The averaged calculated values for the equilibria at 0 and  $25^\circ\text{C}$  are C<sup>1</sup> 40.5 ( $\Delta\delta = 7.5$  ppm), C<sup>2</sup> 39.9 ( $\Delta\delta = 4.3$  ppm), C<sup>3</sup> 32.0 ( $\Delta\delta = 5.4$  ppm), and C<sup>4</sup> 31.6 ppm ( $\Delta\delta = 5.0$  ppm).

As can be seen from Fig. 5, the  $\gamma$ -effect is reproduced qualitatively: C<sup>3</sup> in **4-a** is shielded by 6.0 ppm in comparison to **4-e**.

### Methylenecyclohexanes

The calculated chemical shifts for C<sup>4</sup> of all conformers of **1–3** are given in Table 4. The chemical shift for **3-e2** was estimated as follows: chemical shifts were determined for **3-e1** and **3-e2** at B3LYP/6-311+G(d,p)//HF/6-31G(d); for **3-e1**, the difference from the B3LYP/6-311+G(d,p)//B3LYP/6-31G(d) value was determined and the chemical shift for **3-e2** was adjusted accordingly. Within an axial or equatorial series, the C<sup>4</sup> chemical shift varies little with the choice of substituent at C<sup>2</sup>, while it is systematically larger for those

<sup>2</sup>We have since been able to optimize the geometries of all conformers of **1–3** and of several 7-substituted **1** in dichloromethane using PBE0 and COSMO, and the equilibrium composition based on zero-point corrected total energies agrees exceedingly well with experiment for all three compounds. The compositions based on free energy differences again do not differ significantly from these. A manuscript is in preparation.

**Table 3.** Total energies (hartrees) for axial (a) and equatorial (e) conformers of **3**.

	<b>3-a1</b>	<b>3-a2</b>	<b>3-e1</b>	<b>3-e2</b>
HF/6-31G(d)	-498.703311 (0.03) 28.5%	-498.703327 (0.02) 29.1%	-498.703355 (0) 30.0%	-498.702586 (0.48) 12.3%
+ZPVE	-498.469487 (0.03) 28.4%	-498.469459 (0.04) 27.5%	-498.469529 (0) 29.9%	-498.468873 (0.41) 14.1%
SCI-PCM	-498.708810 (0.08) 23.7%	-498.708936 (0) 27.6%	-498.708882 <sup>a</sup> (0.03) 25.9%	-498.708770 (0.10) 22.6%
MP2/6-31G(d)	-500.265666 (0) 45.0%	-500.265520 (0.09) 38.3%	-500.264408 (0.79) 10.4%	-500.263959 (1.07) 6.3%
B3LYP/6-31G(d)	-501.842427 (0.23) 28.7%	-501.842370 (0.26) 27.0%	-501.842792 (0) 44.2%	— <sup>b</sup>
PBE0/6-31G(d)	-501.261429 (0.47) 22.9%	-501.261397 (0.49) 22.4%	-501.262174 (0) 54.6%	— <sup>b</sup>
+ZPVE	-501.041563 (0.51) 21.5%	-501.041618 (0.48) 23.2%	-501.042375 (0) 55.2%	— <sup>b</sup>
SCI-PCM	-501.266027 (0.45) 23.5%	-501.266026 (0.45) 23.0%	-501.266744 (0) 53.5%	— <sup>b</sup>
SCI-PCM opt.	— <sup>c</sup>	— <sup>c</sup>	-501.266799 (0)	-501.266626 (0.11)

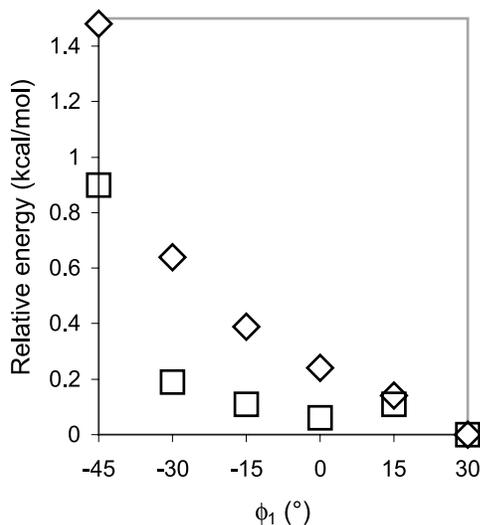
**Note:** Relative energies (kcal/mol) in parentheses, equilibrium populations at 273 K.

<sup>a</sup>Total energy from an optimization that includes solvent at this level is -498.708974 hartrees.

<sup>b</sup>Not a stationary point.

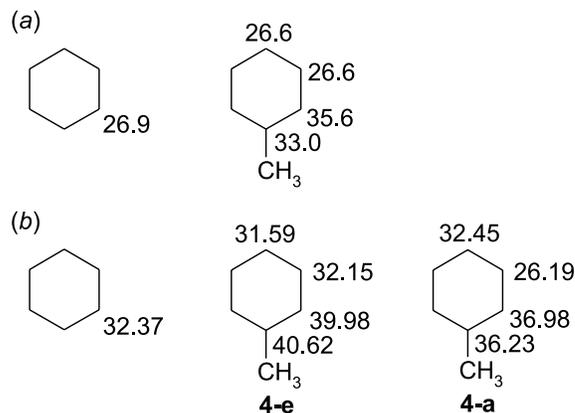
<sup>c</sup>Could not be determined.

**Fig. 4.** Torsional energy profile for  $\phi_1$  in **3** with the substituent in equatorial orientation (with  $\phi_2$  at about  $0^\circ$ , relaxed scan). Shown are energies for gas phase geometries from B3LYP/6-31G(d) ( $\diamond$ ) and solvent-optimized geometries from PBE0/6-31G(d) ( $\square$ ).



rotamers with a negative  $\phi$  (or  $\phi_1$ ) than for rotamers with a positive value for this torsion angle. This also holds for our estimated value of **3-e2**. We have estimated the  $\gamma$ -effect

**Fig. 5.** (a) Experimental and (b) calculated (B3LYP/6-311+G(d,p)/B3LYP/6-31G(d))  $^{13}\text{C}$  chemical shifts for the ring carbon atoms of cyclohexane and methylcyclohexane in ppm.



from separately weighted averages of axial and equatorial conformers. In this way, the  $\gamma$ -effect ( $\delta_{\text{eq}} - \delta_{\text{ax}}$ ) for **1** is about 5 ppm, for **2** about 4.5 ppm, and for **3** about 4 ppm, the actual values depending little on the specific energy differences used in the weighting. This reduction in the  $\gamma$ -effect results from a progressively more shielded averaged chemical shift for the equatorial species (for example, 30.80 ppm in **1**, 30.35 ppm in **2**, 29.73 ppm in **3**, from the PBE0 solvent

**Table 4.** Chemical shifts (ppm) for C<sup>4</sup> in conformers of **1–3** from B3LYP/6-311+G(d,p)//B3LYP/6-31G(d).

<b>1-a1</b>	<b>1-a2</b>	<b>1-e1</b>	<b>1-e2</b>
25.88	25.24	31.04	30.18
<b>2-a1</b>	<b>2-a2</b>	<b>2-a3</b>	<b>2-a4</b>
25.77	25.94	25.45	24.81
<b>2-e1</b>	<b>2-e2</b>	<b>2-e3</b>	<b>2-e4</b>
30.76	29.69	30.61	30.05
<b>3-a1</b>	<b>3-a2</b>	<b>3-e1</b>	<b>3-e2</b>
26.09	25.74	29.73	30.46 <sup>a</sup>

<sup>a</sup>Value estimated as described in the text.**Table 5.** Calculated (weighted average at 273 K) and experimental chemical shifts  $\delta_m$  (ppm) for C<sup>4</sup> in **1–3**.

	Calculated	Experimental
<b>1</b>		
HF/6-31G(d)	26.53	22.6
+ZPVE	26.66	
SCI-PCM	27.18	
B3LYP/6-31G(d)	26.65	
PBE0/6-31G(d)	26.84	
+ZPVE	26.89	
SCI-PCM	27.46	
<b>2</b>		
HF/6-31G(d)	27.40 (0.9) <sup>a</sup>	23.3 (0.7) <sup>a</sup>
+ZPVE	27.45 (0.8) <sup>a</sup>	
SCI-PCM	27.85 (0.7) <sup>a</sup>	
B3LYP/6-31G(d)	27.86 (1.2) <sup>a</sup>	
PBE0/6-31G(d)	28.31 (0.5) <sup>a</sup>	
+ZPVE	28.33 (0.4) <sup>a</sup>	
SCI-PCM	28.68 (1.2) <sup>a</sup>	
<b>3</b>		
HF/6-31G(d)	27.59 (0.2) <sup>b</sup>	23.9 (0.6) <sup>b</sup>
+ZPVE	27.67 (0.2) <sup>b</sup>	
SCI-PCM	27.87 (0.0) <sup>b</sup>	
MP2/6-31G(d)	26.61	
B3LYP/6-31G(d)	27.58 (−0.3) <sup>b</sup>	
PBE0/6-31G(d)	27.97 (−0.3) <sup>b</sup>	
+ZPVE	27.99 (−0.3) <sup>b</sup>	
SCI-PCM	27.96 (−0.7) <sup>b</sup>	
SCI-PCM opt.	28.68	

<sup>a</sup>Difference to **1**.<sup>b</sup>Difference to **2**.

calculations) and an essentially stable chemical shift for the axial species (25.86 ppm in **1**, 25.76 ppm in **2**, 25.92 ppm in **3**).

The weighted averages  $\delta_m$  for an equilibrium consisting of all axial and equatorial species at 0°C and the experimental chemical shifts at this temperature are listed in Table 5. The difference  $\Delta\delta_m$  that results from a change of substituent at C<sup>2</sup> is also given. Replacing methoxy at C<sup>2</sup> with vinyloxy leads to an experimentally observed  $\Delta\delta_m$  of 0.7 ppm, and this is reproduced well with all model chemistries. If we also consider that the difference between experimental and calculated values  $\delta$  for cyclohexane and methylcyclohexane is about 5.5 ppm, the chemical shifts determined using relative energies from PBE0 solvent calculations give the best agree-

ment with experiment for both **1** and **2**. The experimentally observed deshielding of 0.6 ppm as vinyloxy is exchanged for acetoxy, on the other hand, is not reproduced by any of the model chemistries listed (Table 5). Instead, the calculated  $\delta_m$  for **2** and **3** is about the same (or even slightly smaller) at all levels, as can be seen from the  $\Delta\delta_m$  in Table 5. This of course is in accord with the calculated equilibrium composition for **2** and **3**, which is also similar and lies, for the equatorial conformers, at about 60% at the DFT level.

As discussed above, for **3**, the observed equatorial preference is only reproduced with PBE0, and the equilibrium is estimated to contain about 67% equatorial conformers when the solvent-optimized conformers are considered. The estimated  $\delta_m$  of 28.68 ppm reflects the fact that even this equilibrium is not rich enough in equatorial conformers.

## Conclusions

The unexpected increase in equatorial conformer upon introducing unsaturation in the 2-substituent of methylenecyclohexanes that was observed experimentally (**1** 41% eq, **2** 61% eq, and **3** 80% eq in CHFC1<sub>2</sub>-CD<sub>2</sub>Cl<sub>2</sub> at 0°C) and was termed the “unsaturation effect” was qualitatively reproduced. For **1** (methoxy substituent), the equilibrium was well described already at the HF level when relative energies from single-point solvent calculations were employed. For **2** (vinyloxy substituent), to reproduce the observed equatorial preference, PBE0 had to be employed, and again single-point solvent calculations gave the best results. Agreement with the large equatorial preference in the equilibrium of **3** (acetoxy substituent) was only obtained with relative energies from solvent-optimized conformers at the PBE0 level, even though the equilibrium composition could only be estimated because of the lack of data for the axial conformers. <sup>13</sup>C chemical shifts for C<sup>4</sup> (in  $\gamma$ -position to the substituent), which were calculated as weighted averages from all equilibrium species, confirmed the progressively increased deshielding in the methoxy–vinyloxy–acetoxy series that was observed experimentally.

In this study, we have shown that the experimentally observed “unsaturation effect” can indeed be reproduced computationally. We will now focus on studies towards an explanation of this effect.

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