

Conformational analysis of 8-oxabicyclo[3.2.1]oct-6-en-3-one derivatives by NMR and theoretical calculations*.

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Introdução

In our research on the synthesis of compounds with herbicidal and/or plant growth regulating activity, it was studied the synthesis and biological activities of the 2a,4a-di-methyl-6,7-exo-isopropylidenedioxy-8-oxabicyclo[3.2.1]octan-3a-ol (**3**) and -3b-ol (**4**), as well as 1,2a,4a,5-tetramethyl-6,7-exo-isopropylidene dioxy-8-oxabicyclo[3.2.1]octan-3a-ol (**5**) and -3b-ol (**6**), obtained from the reduction of 2a,4a-dimethyl- and 1,2a,4a,5-tetra-methyl-6,7-exo-isopropylidenedioxy-8-oxabicyclo[3.2.1]octan-3-one (**1**) and (**2**), respectively.

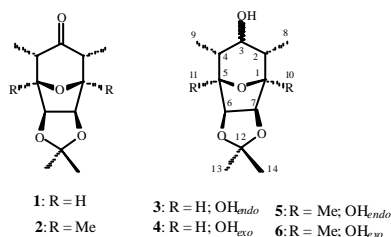


Fig. 1. 8-oxabicyclo[3.2.1]octane derivatives.

To unravel the structure-biological activity relationship of **3** to **6**, it is interesting to develop studies of their conformational properties as these compounds may show different activities. These studies may be performed by combining experimental NMR data and theoretical calculations. As will be shown later, NMR (¹H and ¹³C) studies and theoretical calculations using the semi-empirical (AM1), *ab initio* Hartree-Fock (HF) and Density Functional Theory (DFT) quantum chemical methods for **3** to **6** yielded very interesting information on their conformational analysis.

Theoretical studies were carried out using the Gaussian03W software package. The geometry optimizations were performed using AM1, HF, and DFT with the BLYP functional and the 6-31G* basis set. The solvent effect (CHCl₃) in the geometry optimizations was assessed using the Polarizable Continuum Model. For the hydrogen (*d_H*) and carbon (*d_C*) chemical shift calculations the DFT/B3LYP/6-311++G**(PCM, CHCl₃) optimized geometries were used. DFT/B3LYP/6-31G* calculations were performed relative to TMS (*d_H* 32.09 and *d_C* 190.90).

Resultados e Discussão

The ¹H NMR data of these compounds suggests predominance in the chair conformation for hydroxyl ring of **3**, **4**, and **5** but boat conformations for this ring of **6**.

The AM1, HF/6-31G* and DFT/B3LYP/6-31G* optimized geometries of **3** to **6** in the chair conformation present energies lower than the corresponding geometries in the boat conformation. Similarly, DFT/B3LYP/6-311++G**(PCM(CHCl₃)) geometry optimizations and the DFT/B3LYP/6-31G* conformational population calculations also indicate a lower relative energy of the **6_{chair}** conformation.

DFT/B3LYP/6-31G* values of *d_C* and *d_H* of the **8_{boat}** and **8_{chair}** were calculated with geometries optimized at the DFT/B3LYP/6-311++G**(PCM,CHCl₃) level. The *d_C* and *d_H* calculated values of conformations **8_{boat}** and **8_{chair}** show some discrepancies in relation to the experimental *d_C* and *d_H* of **8**. However, it can be observed that **8_{boat}** presents smaller discrepancies than **8_{chair}**.

Conclusões

The chair conformation stability explains the NMR results for alcohols **3** to **5**, but not for **6**. Therefore, it may be concluded that for this last compound the theoretical calculations of the energy-balance do not take into account the increase in stability contributed by the formation of hydrogen bond. In such a case, the unfavorable van der Waals spatial interactions between the neighbor methyl groups at C-1 and C-5 of **6_{boat}** may be favorably compensated by the 1-4 hydrogen bond between the OH and the ring oxygen.

HF/6-31G* and DFT/B3LYP/6-31G* calculations of *d_C* and *d_H* of **6_{boat}** are closer to the experimentally derived values of **6**. Therefore, although not so frequently used, calculations of the *d_C* and *d_H* chemical shifts showed to be more adequate than the thermodynamic calculations for the conformational analysis of **6**.

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