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Title: Pentacyclic Triterpenes isomers ^{13}C NMR Chemical Shift Prediction Using GIAO-mPW1PW91/3-21G//PM7 Level of Theory

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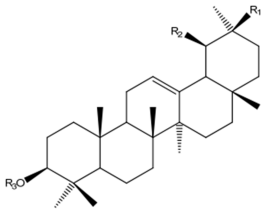
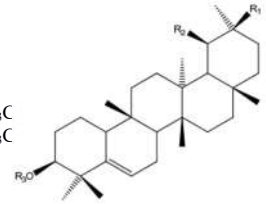
Abstract: Triterpenes are a class of natural products with great importance due to their biological and pharmacological activities [1]. These molecules may have complex structures, which makes their structural characterization through routine analytical techniques a difficult task. Despite the recent advances in spectroscopic techniques, cases of revision of erroneously established natural product structures are still to be found in the literature [2]. Therefore, it is necessary to develop quantum calculation protocols aimed in the structural determination of these compounds. In order to spread its applicability to different time-demanding tasks, a protocol should have the bigger cost-effectiveness radio as possible. In this work we intend to test the robustness of a scaling factor based on GIAO//semi-empirical (mPW1PW91/3-21G//PM7) [3] calculations to determine the^{13}C NMR chemical shifts (δ) of 6 pentacyclic triterpenes [4] (2 pairs of regioisomers), i.e., α-amyrin (**I**) – β-amyrin (**II**) and α-amyrin acetate (**III**) – β-amyrin acetate (**IV**), glutinol (**V**) and glutinol acetate (**VI**), see figure 1. It's worth to note that, the compounds **I**, **II** and **V** are diastereoisomers ($C_{30}H_{50}O$) as well as the compounds **III**, **IV** and **VI** ($C_{32}H_{52}O_2$). The δ are obtained as $\delta_{calc} = \sigma_{TMS} - \sigma$, where σ_{TMS} is the isotropic shielding constant of the reference compound, tetramethysinale (TMS), calculate at the same level of theory. The scaled δ (δ_{scal}) were obtained u the equation: $\delta_{scal} = 1.14.\delta_{calc} - 4.70$ (**1**).



	R1	R2	R3
I	H	Me	H
II	Me	H	H
III	H	Me	CH_3C
IV	Me	H	CH_3C



	R1	R2	R3
V	Me	H	H
VI	Me	H	CH_3CO

Figure 1. pentacyclic triterpenes: α-amyrin (**I**), β-amyrin (**II**), α-amyrin acetate (**III**), β-amyrin acetate (**IV**), glutinol (**V**) and glutinol acetate (**VI**).

The 6 triterpenes were submitted to randomized conformational searches using Monte Carlo method and MMFF force field, as implemented in SPARTAN08 [5]. For complete conformational analysis and the conformer's selection protocol, see Giacomello *et alli* [6]. All DFT quantum mechanical calculations were performed in gas phase, using Gaussian 09 software package [7], PM7 calculations were performed using MOPAC2012 [8]. Table 1 shows for the 6 pentacyclic triterpenes, the Mean Absolute Deviation (MAD) and the Root Mean Square Deviation (RMSD), in ppm, before and after (in parenthesis) the application of the equation **1**.

Table 1. Statistics parameters MAD and RMS, in ppm, for the 6 triterpenes.

Statistics/Molecules	**(I)**	**(II)**	**(III)**	**(IV)**	**(V)**	**(VI)**
MAD_{calc} (MAD_{scal})	2.65 (1.11)	2.97 (1.66)	3.10 (1.25)	3.25 (1.33)	2.51 (1.56)	3.25 (1.89)
RMS_{calc} (RMS_{scal})	3.75 (1.34)	4.73 (3.11)	4.93 (1.43)	4.96 (1.56)	3.78 (1.92)	4.99 (2.33)

The results showed that at the mPW1PW91/3-21G//PM7 level of theory it was able to reproduce the experimental data with small errors. After the application of the scaling factor (which intend to cancel systematic errors), the MAD and RMD errors became significantly smaller (almost 50% for all molecules). This means that even low-levels of theory can be used to cancel systematic errors. Thus, we conclude that the level of theory GIAO-mPW1PW91/3-21G together with the use of the scaling factor represented by the linear equation $\delta_{scal} = 1.14.\ \delta_{calc} - 4.7$ shows an efficient and low cost tool for the calculation of ^{13}C NMR chemical shifts and triterpenes.

Key-words: Triterpenos; Ressonância Magnética Nuclear ^{13}C; Modelagem Molecular.
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