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EFAVIRENZ, A CALCULATED CHEMICAL SHIFT OF ^{13}C

Authors: Gustavo da Silva do Prado[a], Leonardo Buss Wulff[a], Thaís Forest Giacomello[a], Agnes Jalowitzki Silva[a], Leandro Leal Rocha De Oliveira[a], Sara Sâmitha Souza[a], Antônio Maia de Jesus Chaves Neto[b], Gunar Vingre Da Silva Mota[b], Fabio Luiz Paranhos Costa[a*],

Address: a Departament of Chemistry, Federal University of Goiás, REJ Jataí 75801-615, Brasil.
b Natural Science Faculty, Federal University of Pará, ICEN UFPA Belém 66075-110, Brasil
***flpcosta@ufg.br**

Abstract

One of the most widely used non-nucleoside reverse transcriptase inhibitors (NNRTIs) in the treatment of adults and children infected with the human immunodeficiency virus (HIV) is efavirenz (Figure 1) [1]. In this work, we aim to evaluate the ability of our protocol to calculate the chemical shift (δ) ^{13}C NMR to reproduce the experimental data obtained in the solid NMR state (SSNMR) for the efavirenz molecule. The chemical shift ^{13}C RNM calculation of efavirenz was obtained through the theory level GIAOmPW1PW91/6-31G(d)//mPW1PW91/6-31G(d). Through the Spartan'08 performed conformational analysis and Single Point to know and confirm the most stable conformers. Now with the most stable conformer Gaussian'09 calculates geometry optimization and vibrational frequency. After we know the lowest relative energy conformer, we calculate the chemical shift of ^{13}C, taking into account the Boltzmann distribution. The calculations of chemical shift are obtained with the equation $\delta_{calc} = \sigma_{TMS} - \sigma_{nuclei}$, where σ_{TMS} is the isotropic of the shielding constant of the reference compound TMS (tetramethylsilane) calculated at the same theory level and σ_{nuclei} is the isotropic of the shielding constant of the nuclei of the molecule. The scaled data chemical shift (δ_{scal}) are obtained according to the equation $\delta_{scal} = 1.05.\delta calc -1.22$ (1)[2]. It was possible to obtain good results, since the scaling factor used, obtained a good accuracy of the GIAO-HDFT method, which implies a very good statistical result of MAD (average absolute deviation) and RMSD (mean square error). Thus before (after), in ppm, the application of the scaling factor are MAD = 6.00 (3.64) and RMSD = 7.62 (4.82). We showed that even using the GIAO method, we obtained good results (since it is not the ideal procedure for this calculation), the method was able to have a good reproduction of the experimental data of the SSNMR. We can also deduce that the use of a scaling factor, made from a linear regression between experimental and calculated chemical shift data at the GIAOmPW1PW91/6-31G(d) level, is an efficient and low computational tool to minimize errors in the reproduction of ^{13}C SSNMR chemical shifts.

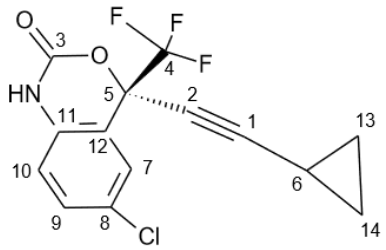

Figure 1: Efavirenz molecule.

[1]CAVALCANTE, G. I. T. et al. HIV antiretroviral drug Efavirenz induces anxiety-like and depression-like behavior in rats: evaluation of neurotransmitter alterations in the striatum. **Eur. J. Pharmacology,** 2017.
[2]GIACOMELLO, T. F. et al. Protocol for Calculating 13 C Nuclear Magnetic Resonance Chemical Shifts of Flexible Organic Molecules. **Advanced Science, Eng and Medicine**, v. 9, n. 8, p. 640–647, 1 ago. 2017.

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