Solid state NMR GIPAW calculations and experimental of the lamivudine salicylate monohydrate: a case study.

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Abstract

Technical solids analysis, such as solid state NMR, may require additional techniques for structure determination. A comparison between experimental and theoretical data of NMR parameters of the drug lamivudine salicylate monohydrate showed a significant correlation for its characterization, thus allowing clearer and more accurate information.

Introduction

Solid dosage forms are the most widespread among pharmacists, due to its ease of handling and high adherence by patients, leading the growth of structural studies of drugs in this state. The technique of solid state NMR has gained increasingly space in analysis of drugs combined with other techniques, such as X- ray diffraction and infrared spectroscopy, besides having different types of computations as tools to aid structural characterization. The objective of this work is the characterization of the structure of the drug lamivudine salicylate monohydrate via technique of nuclear magnetic resonance in the solid state with the aid of computer calculations as a confirmatory tool. [1-3]

Results and discussion

The NMR experiments of a lamivudine salicylate monohydrate solid state were obtained in a spectrometer Bruker Avance III 11.75 T. The theoretical calculations Were Performed using GIPAW theory by computer program CASTEP. All calculations were performed with version 5.0.1 of the code CASTEP using ultrasoft pseudopotentials calculated in real time. [4-6]

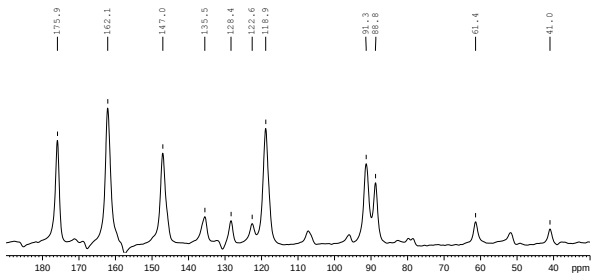
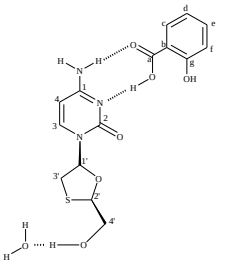


Figure 01. NMR Spectrum/CPTOSS ^{13}C NMR salicylate monohydrate lamivudine solid.

Table 1. NMR chemical shifts of ^{13}C (ppm) calculated experimental and for lamivudine salicylate monohydrate solid GIPAW/CASTEP.

Mono-hidrato de salicilato de lamivudina.	^{13}C	^{13}C EXP.	^{13}C (CASTEP)	Δδ
	C1	162,1	157,2	4,9
	C2	147,0	144,6	2,4
	C3	147,0	144,7	2,3
	C4	91,3	86,8	4,5
	C1'	88,7	87,6	1,1
	C3'	41,0	32,3	8,7
	C2'	52,0	46,7	5,3
	C4'	96,2	95,0	1,2
	Ca	175,9	177,7	1,8
	Cb	135,5	132,5	3,0
	Cc	118,9	114,7	4,2
	Cd	122,6	124,0	1,4
	Ce	162,1	163,7	1,6
	Cf	128,4	125,4	3,0
	Cg	107,3	115,8	8,5

The method GIPAW / CASTEP is significant studies to theoretical calculations in solid-state NMR, with values of R^2, SD and MD respectively, 0.99, 2.5 and 3.6.

After the analysis of the relation between theoretical and experimental chemical shifts through values of statistical parameters, it is observed that GIPAW calculation mode for the solid state is an important tool for elucidating the crystal structures previously unknown, or incomplete data.

Conclusions

The GIPAW method is effective for NMR studies in the solid state in the crystal structure determination and aid in assignments on low-resolution spectra, providing data which can not be obtained from NMR experiments. [3-4]

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[1] David E. Bugay. *Adv. Drug Deliv. Rev*. **2001**, 48, 43–65.
[2] Wainberg, M. A. *Nature*. **2011**, 469, 306–7.
[3] Singhal, D. Curatolo, W. *Adv. Drug Deliv. Rev*. **2004,** 56, 335–47.
[4] Gryff-Keller, A. *Concepts Magn. Reson*. **2011**, 38A, 289–307.
[5] Webber, A. L.; Emsley, L.; Claramunt, R. M. e Brown, S. P. *The journal of physical chemistry*. **2010**,114A, 10435–42.
[6] Pickard, C. e Mauri, F. *Physical Review*. **2001**, 63B, 245101.