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Computational protocol for predicting the Pt-195 NMR chemical shift in Pt(IV) derivatives of cisplatin and carboplatin

Milena de A. Pereira [1], Célia Fonseca Guerra[2], and Diego F. S. Paschoal[1]

[1]Núcleo de Química Teórica e Computacional de Macaé, Polo Ajuda, Instituto Multidisciplinar de Química, Centro Multidisciplinar UFRJ-Macaé, Universidade Federal do Rio de Janeiro, Macaé, RJ, Brazil.

[2]Department of Theoretical Chemistry, Amsterdam Institute of Molecular and Life Sciences (AIMMS), Amsterdam Center for Multiscale Modeling (ACMM), Vrije Universiteit Amsterdam, 1081 HV Amsterdam, The Netherlands.

E-mail: milenaaguiarj18@gmail.com; diegopaschoal01@gmail.com

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The computational prediction of the Pt-195 NMR chemical shift (δ^{195}Pt) in Pt(IV) complexes has been of great importance in understanding the coordination chemistry of these compounds, which have potential antitumor applications[1]. However, there are some gaps in the literature regarding the study of platinum(IV) complexes and their NMR parameters, especially with regard to a systematic evaluation of all the parameters that are indispensable for predicting the NMR properties of Pt(IV) complexes, i.e. geometry, basis sets, DFT functional, implicit/explicit solvent effects and relativistic effects[2]. In the present study, a computational protocol for predicting the Pt-195 NMR chemical shift in Pt(IV) derivatives of cisplatin and carboplatin using the new NMR-ZORA basis sets is proposed. Initially, two Pt(IV) complexes, *cis*-$[Pt(NH_3)_2Cl_4]$, analogue of cisplatin, and *cis,trans*-$[Pt(CBDCA)(NH_3)_3Cl_2]$, analogue of carboplatin, were selected and the role of the structure in predicting the δ^{195}Pt was assessed considering 100 protocols (20 DFT-functionals, 5 platinum basis sets – PTBS) for the structures, named as DFT-Functional/PTBS/def2-SVP/IEF-PCM(UFF) level – Gaussian 16 Rev. C.01 program. For each structure protocol, the δ^{195}Pt was calculated at GIAO-BP86-SC-ZORA/NMR-ZORA/CPCM level – ORCA 5.0.4 program. After, the DFT-functional for predicting the δ^{195}Pt was also assessed, considering a set of 13 functionals. The role of the explicit solvent and relativistic effects will also be evaluated. From the calculated results for the structures, all protocols presented a good description of the geometry of the two Pt(IV) complexes studied, with a mean relative deviation (MRD) below 2%. When δ^{195}Pt is considered at the GIAO-BP86-SC-ZORA/NMR-ZORA/CPCM level for the different 100 geometries obtained, the NMR sensitivity to the structure considered can be easily observed. The lowest MRD obtained was 8.5% with the structure obtained with LC-TPSS/def2-TZVPP/def2-SVP protocol. In general, the protocols that presented the lowest MRD were those that used functionals with long-range correction in GGA functionals (LC-BLYP, LC-BP86, LC-PBE, LC-TPSS, LC-wHPBE and LC-wPBE). Subsequently, the protocols will be applied in another set of Pt(IV) complexes for validation: *cis*,*cis*,*trans*-$[Pt(NH_3)_2Cl_2I_2]$ and *cis*,*cis*,*trans*-$[Pt(NH_3)_2Cl_2Br_2]$, cisplatin analogues with axial ligands iodine and bromine, respectively; *cis*,*trans*-$[Pt(CBDCA)(NH_3)_2I_2]$ and *cis*,*trans*-$[Pt(CBDCA)(NH_3)_2Br_2]$, carboplatin analogues with axial ligands iodine and bromine, respectively. Finally, the explicit solvent and relativistic effects will be considered for all six Pt(IV) complexes selected.

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