FT-IR and FT-Raman spectra of the anti-HIV nucleoside analogue d4T (Stavudine). Solid state simulation by DFT methods

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A theoretical and experimental vibrational study of the anti-HIV d4T (stavudine or Zerit) Nucleoside Analogue was carried out, Fig. 1. Its bio-activity can be explained due to the absence of the hydroxyl group (O3'-H group) [1–3]. The predicted spectra in the two most stable conformers of d4T in the biological active anti-form were determined at three DFT levels, especially by B3LYP/6-31G(d,p), B3LYP/6-311++G(2d,p) and X3LYP/6-31G(d,p). Comparison of the conformers with those of the natural nucleos–ide thymidine was carried out. The calculated spectra were scaled by using the linear scaling equation procedure (LSE) [4] and the polynomic equation. The crystal unit cell of the different polymorphism forms were simulated through dimer forms by using DFT methods. The scaled spectra of these dimer forms were compared with the FT-IR and FT-Raman spectra recorded in the solid state. All the vibrational bands were analyzed and assigned to different normal modes of vibration.

The most important findings of this study are the following: 1.- In the isolated state the stability trend of the five first optimum conformers is the same by several methods and levels. The spectra corresponding to the monomers C1 and C3 are very similar, with the exception of the modes corresponding to the O5'-H groups, due to their different orientations. 2.- The simulated spectra are in accordance to the experimental ones. The stretching bands corresponding to N-H modes in dimer G and I (Fig. 2) appear at lower wavenumbers than those corresponding to monomer C1 and dimer V. This fact is due to these G and I dimers are stabilized by two N-H···O=C intermolecular H-bonds. 3.- The scaled wavenumbers with the polynomic equations slightly improved the values that with LSE. The scaled values with the X3LYP method are slightly better than by B3LYP.

Keywords: d4T; scaling; simulated spectra

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References