Theoretical conformational analysis and vibrational spectral investigations of an anticancer drug, anastrozole

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Anastrozole (Arimidex) is a non-steroidal aromatase inhibitor, a drug that inhibits the aromatase enzyme and by that means lowers the level of the estradiol estrogen. Aromatase inhibitors are a class of antiestrogens. Since estrogens are responsible for many breast cancers and since most estrogen after menopause comes from the action of aromatase, aromatase inhibitors can therefore be used to treat estrogen-dependent tumors after the menopause.

To foster the understanding of the activity mechanism of a biological active molecule, it is useful to explore its conformational possibilities and determine its more stable conformers. Therefore in this study the conformational landscape of anastrozole has been investigated in its electronic ground state by exploring the scanning potential energy surface with Density Functional Theory (DFT) method. The possible conformers of anastrozole have been so identified.

A set of dihedral angles driving the conformational analysis has been used to provide the initial molecular structures necessary for geometry optimization calculations carried out with DFT (at B3LYP/6-31G(d,p) level). The vibrational normal modes of each conformer and the associated wavenumbers have been also calculated in the harmonic approximation at the same theory level. Furthermore, the electronic properties of low-energy conformers of anastrozole have been investigated by analysing the frontier molecular orbitals (MO).

In the experimental part of this study, the FT-IR and FT-Raman spectra of the molecule have been recorded and have been compared to the calculated spectra with the help of PED calculation. The results enabled us to determine the most probable structure of anastrozole at room temperature in solid phase.

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