DETERMINATION OF THE SUPRAMOLECULAR ARCHITECTURE OF SOME *N*-(2-BROMO-PHENYL)-2-HYDROXY-BENZAMIDE INCLUSION COMPLEXES

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Abstract

Three structures of the N-(2-bromo-phenyl)-2-hydroxy-benzamide derivatives (ethyl ester EE, hydrazide HD, hydrazone HN) were optimized at B3LYP/6-311+G level of theory [1]. The graphical representation of the frontier molecular orbitals HOMO/LUMO has been performed and the energy difference between the orbitals was employed for the evaluation of the stability of the compounds. The results suggest a higher stability for both the EE and HD, the HOMO orbitals are located on the 2-bromo-phenyl moiety, while the LUMO orbitals are delocalized over the two aromatic cycles. For hydrazone, where a decrease in the HOMO energy and an increase in the LUMO energy was observed, the HOMO orbitals are present over the benzaldehyde moiety, not on the 2-bromo-phenyl moiety. Also, the LUMO orbitals of the HN are located on the two aromatic rings of the salicylanilide structure.

The logP, polarizability, polar surface area and steric parameters like ovality, molecular area and volume were computed [2]. Similarities of properties like ovality, molecular area and volume for the EE and the HD were observed. Larger values of the polar surface area were obtained for HD and HN, compounds with free amine and hydroxyl groups. All compounds are hydrophobic, a larger logP value being obtained for HN with three phenyl rings.

The molecular docking and visualization of the ligand–receptor (β-cyclodextrin β-CD) interactions have been performed with AutoDock Vina [3]. To calculate the variation in energy associated with the formation of the β-cyclodextrin–ligand inclusion complexes, single-point energy calculation was performed for the inclusion complexes of β-CD with the best conformation of the ligands, and for the ligands and receptor alone, at the B3LYP/6-31G level of theory. The size of β-CD cavity allows the partial inclusion of the compounds. The best binding affinities were obtained for HN (−5.59 kcal/mol). Regarding the interaction between the compounds and β-CD, atoms in close contact were present, and only in case of HN, one hydrogen bond is formed. These results suggest the partial inclusion of the compounds within the β-CD cavity. Molecular docking computations also suggested that hydrazone, characterized by the largest area, volume and polarizability within the series, has the highest binding affinity towards β-CD.

References

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