A Theoretical Conformational Analysis and Vibrational Spectroscopic Investigation on Niflumic Acid

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Niflumic acid is a selective inhibitor of COX-2 enzyme. It provides potent analgesic and anti-pyretic properties and is widely used as a drug for joint and muscular pain. Theoretically possible stable conformers of niflumic acid molecule in electronic ground state were carefully examined by means of both molecular dynamics calculations using molecular mechanics AMBER force field and potential energy surface scan calculations carried out at B3LYP/3-21g(d) level of theory. The equilibrium geometrical parameters for the determined stable conformers of the free molecule were obtained through geometry optimizations carried out using B3LYP hybrid DFT and MP2 ab-initio methods with 6-31G(d), 6-31++G(d,p), 6-311++G(d,p) and aug-cc-pvTZ basis sets. The vibrational normal modes and corresponding frequencies, IR and Raman intensities of each determined stable conformers of the molecule were obtained through frequency calculations performed at the same levels of theory as used in the geometry optimizations in both "harmonic oscillator" and "anharmonic oscillator" approaches, separately.

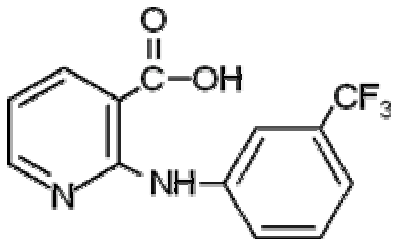

Fig. 1: Chemical structure of niflumic acid molecule.

In fitting of the calculated harmonic wavenumbers to the experimental ones, two different scaling procedures referred to as "Scaled Quantum Mechanical Force Field (SQM FF) methodology" [1, 2] and "Scaling wavenumbers with dual scale factors" [3] were proceeded, independently. The frequencies and associated Raman and IR intensities calculated for each normal mode of the molecule were compared with the corresponding experimental data ; the theoretical results have been found to be in rather good agreement with our experimental assignments proposed as the fundamental bands of the molecule.

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[3] M.D. Halls, J. Velkovski, H.B. Schlegel, Theor. Chem. Acc. 105 (2001) 413.