

Electronic and Conformational Structure of Ortho-Aminobenzoic Acid in Solution Combining the Sequential QM/MM and the Free Energy Gradient Methods

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INTRODUCTION

In the last years, the use of an iterative Sequential QM/MM method with an average solvent field as electrostatic embedding [1] together with the Free Energy Gradient method [2], called the ASEC-FEG method, has provided interesting results for the conformational structure and properties of molecules in solution. In this work, we make use of that methodology to investigate the electronic structure of the ortho-aminobenzoic acid (o-Abz) in water, acetonitrile and cyclohexane. The o-Abz molecule has a considerably broad absorption band in the UV region and a long fluorescence lifetime. Therefore, o-Abz is frequently used as a fluorescent label in peptides whereas some derivatives are used in membranes. The o-Abz has two rotamers in gas-phase which differ by 180° rotation of the carboxylic group. We studied the solvent effect in the geometry of the neutral, anionic and cationic species.

METHODS

In each step of the iterative geometry optimization process, we generate an ensemble using Monte Carlo Metropolis simulations at room temperature with empirical Lennard-Jones-Coulomb potential, and we select hundreds of uncorrelated configurations. Then, we superpose all configurations with scaled charges to include the solvent average field in the solute's Hamiltonian. We perform only one quantum mechanics calculation of the atomic forces and an approximate Hessian to obtain a new geometry through the Newton-Raphson method. Lastly, a calculation of the charge distribution in the new geometry in the presence of the solvent is performed. With the new geometry and atomic charges, the next step of the simulation is initiated.

RESULTS AND DISCUSSION

In gas phase, we found two stable rotamers differing by 2.9 kcal/mol for the neutral species. Vibrational frequencies for the rotamer I (more stable) are in good agreement with the experimentally observed values. We also found that protonation occurs preferentially in the amino group, while deprotonation occurs in the carboxylic group. The cation also has two stable rotamers whereas in the anion they are the same rotamer.

In solution, the polarizable continuum model predicts no significant difference in the geometry of the o-Abz species. In contrast, using the ASEC-FEG method, we found remarkable structural changes in aqueous solution. The pyramidalization of the amino group is further increased (~20°) in the two rotamers of the neutral species. In rotamer II, the internal hydrogen bond is broken, in favour of intermolecular bonds with water, whereas it is maintained in rotamer I. In the anionic species, the hydrogen bond is also broken. In the cationic species, only one minimum was found, related to the rotamer I.

CONCLUSIONS

The results obtained indicate that the ASEC-FEG method is capable of describing accurately the structure of the molecules in solution.

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¹ K. Coutinho, H. C. Georg, T. L. Fonseca, V. Ludwig, S. Canuto. *Chem. Phys. Lett.* **437**, 148 (2007).

² N. Okuyama-Yoshida, M. Nagaoka, T. Yamabe. *Int. J. Quantum Chem.* **70**, 95 (1998).