Theoretical study on the Solvent Effects for Chemical Reactions using the QM/MC/FEP method

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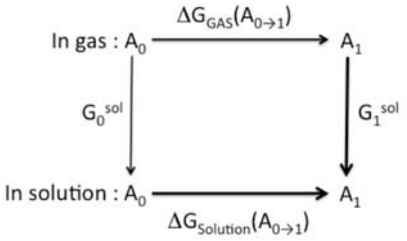
Molecular simulation such as Monte Carlo (MC) simulations or Molecular Dynamics (MD) simulations is a useful approach to understand micro-scopic dynamics of complex many-body systems of molecular assembly. We have been developing the QM/MC simulation using quantum mechanical (QM) calculations in order to investigate solvent effects for chemical reactions. The QM/MC method is Monte Carlo simulations with fully Quantum Mechanical calculations. Fully quantum calculations makes possible to get high accurate results and geometries between solutes and solvents as coordinates with no parameters.

We developed a program[1] which calculates difference of free energy of solvation, ΔG(solv), using the QM/MC method connected with free energy perturbation (FEP) calculations according to Eq. (1), i.e., the QM/MC/FEP simulation.

$$\Delta G_{1-0} = G_1 - G_0 = -k_B T \ln \left\langle \exp\left(-\frac{E_1^{sol} - E_0^{sol}}{k_B T} \right) \right\rangle_0 \qquad (1)$$

$\Delta G^{\ddagger}$ in solution can be calculated by adding $\Delta G^{\ddagger}$ in the gas phase to ΔΔG(solv) between the Transition State (TS) and the reactant in solution. The QM/MC/FEP calculations use the thermodynamic cycle shown in Scheme 1. We adopted he droplet model that includes a solute molecule in its center and have solvent molecules around the solute within a radius depending on the sides of solvent molecules. The solute has structures optimized using quantum mechanical calculations.
The QM/MC/FEP simulation was applied to calculate ΔΔG(solv) between the reactant and TS, between TS and the product by dividing differences between the structures by 50 points. Detailed applications will be reported.



Scheme 1 : Thermodynamic cycle

[†] http://www.tstcl.jp/

[1] K. Hori et al., *J. Comp. Chem.*, **32**, 778-786 (2011).