Toward Accurate Potentials for Condensed-Phase Chemical Reactions: Electrostatically Embedded Multi-Configuration Molecular Mechanics

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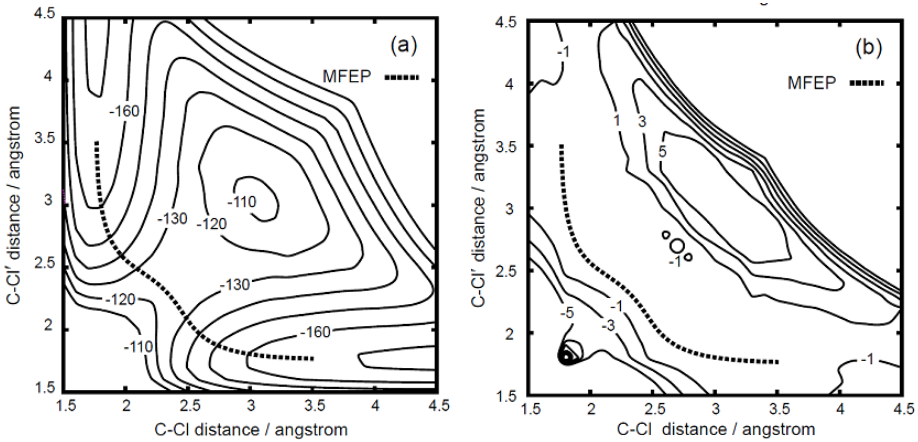
Combined quantum mechanical and molecular mechanical (QM/MM) methods have provided powerful means for studying chemical reactions in condensed phases such as liquids, enzymes, and solids. In these approaches, the reaction center is described quantum mechanically, while the surroundings are treated by using a molecular mechanics force field. However, the high computational cost of quantum mechanical (QM) calculations prevents carrying out QM/MM molecular dynamics simulations with reliable accuracy and adequate sampling.

In order to reduce the computational cost of the QM calculation, we* have developed a new method called electrostatically embedded multi-configuration molecular mechanics (EE-MCMM) for generating global potential energy surfaces (PESs) in the presence of an electrostatic potential. MCMM describes the global PES of a condensed-phase reaction with electronic structure information, in particular energies and partial charge distributions, obtained in the gas phase at selected geometries. Because this new method is efficient, high-level QM calculations can be used in QM/MM methods.

The result is a key step toward studying chemical reactions in condensed phases with high accuracy.



(a) Equipotential contours of the PES of the

$$Cl^- + CH_3Cl \rightarrow ClCH_3 + Cl^-$$

reaction in aqueous solution calculated by the EE-MCMM method. The minimum free energy path is shown as a dashed curve.

(b) Equipotential contours of the difference between the PESs calculated by the EE-MCMM and direct methods. Notice that the EE-MCMM representation obtained from gas-phase calculations is accurate for this liquid-phase reaction to 1 kcal/mol or better over a wide swath.

Figure provided by Masahiro Higashi and Donald G. Truhlar, Department of Chemistry and Supercomputing Institute, University of Minnesota.

*Masahiro Higashi and Donald G. Truhlar, "Electrostatically Embedded Multiconfiguration Molecular Mechanics Based on the Combined Density Functional and Molecular Mechanical Method," *Journal of Chemical Theory and Computation,* to be published.