Towards the understanding of the structure and formation of Deep Eutectic Solvents using classical molecular dynamics and fragmentation simulations

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Résumé

Introduction

Since their conception Deep Eutectic Solvents (DES) have been a constant subject of interest for researchers working on tailor-made solvents for various applications including catalysis, biomass conversion and drug delivery. The presence of diverse type of constituent molecules that make up these solvents and a spectrum of non-covalent interactions between these constituents help in designing solvents for particular applications by fine-tuning the functional groups of the molecules. The experiments developed to understand the nature of DES are generally accompanied by a computational study to aid in interpretation of the experimental results. In this thesis, we set out to understand the structure and formation of two types of DES using classical molecular dynamics, quantum mechanical calculations and fragmentation simulations of non-covalent clusters. The first part of this work involved parameterization of non-bonding parameters of GAFF v2.11 forcefield for molecular dynamics simulations of Urea : Choline Chloride (2:1 molar ratio) (named Reline) to accurately represent the thermophysical properties (density, diffusion coefficients and viscosity) and the structure of the solvent relative to the experimental results. The quantum mechanical calculations involving DFT and semi-empirical methods were used in the second part of this work for thermochemical calculations of non-covalent clusters of Reline and Evernic/Usinic acid to corrobarate the stability results observed in the soft-ionisation mass spectrometric experiments. Finally a major part of this thesis involves adopting and adapting the algorithm for molecular fragmentation simulations (M_3C) to make the computational study of fragmentation of non-covalent in mass spectrometry computationally tractable. Despite the initial computational bottleneck of the fragmentation simulations, with a combination of semi-empirical methods and density functional approximations methods we are able to finalize a workflow that can be employed in calculating the breaking curves of the chemical systems at the scale of supramolecular assemblies in mass spectrometry on a high-performance computing (HPC) cluster.

Keywords

Deep Eutectic Solvents, Molecular Dynamics, Collision-induced dissociation, Fragmentation, Parametrization

Results and Discussion

Forcefield parametrization for Reline

Since it was demonstrated that the incorporation of empirical charge-scaling can be avoided in molecular dynamic simulations by parametrization of Lennard-Jones(LJ) parameters of GAFF v2.11 forcefield in certain deep eutectic systems, this project started with adopting that approach for Reline system. The additional parametrization required for this specific system is the LJ parameters of Hydrogen and Nitrogen atoms of urea that participate in interactions extensively. After surveying the parameter hyperspace and incorporating the non-linear structure of urea in Reline, we were able to simulate a system with resonable agreement with experimental density (3.5 % relative error). The structure of the simulated system determined by the radial distribution functions (RDFs) also show resonable agreement with the experimental RDFs. (Figure 1 and Figure 2 show the comparison between experimental and calculated RDFs of Urea-Chloride and Choline-Chloride interactions)

Since the choice of partial-charge calculation scheme for electrostatic interactions also play a significant role in the accuracy of the simulations, we compared the RESP charge assignment scheme with DDEC6 scheme which is a density-partitioning protocol.

Thermochemical calculations of non-covalent clusters

The second part of this thesis involved a collaboration with the mass-spectrometric experimental project. Along with the normal mass-spectra, the other form experimental information of non-covalent clusters available for intrepretation of the stability of certain clusters with theoretical calculations is the variation of these cluster-ion intensities at a range of orifice 1 (OR1) voltages.

Two forms of comparison can be made based on the available experimental breaking curves: (i) cross-species comparison and (ii) intra-sample comparison. (i) The cross-species comparison involves comparing the experimental stability of urea-containing clusters and corresponding thiourea-containing clusters. (ii) The intra-sample comparison between different cluster species observed in the same experiment. This is a straight-forward comparison between the fraction of ion intensities of each species at a range of OR1 voltages.

The preliminary approach to understand the stability of certain clusters against the in-source collision-induced dissociation was calculating the interaction energies of these clusters using quantum chemical methods. In this work we started with the B3LYP level of theory using 6-311++G(d,p) basis set and D3 dispersion correction to keep the calculations consistent with the literature on QM calculations of Reline. For the thiourea-containing clusters we also studied the effect of change in basis set to diffuse def2-TZVP on the interaction energies. Other quantum chemical tools like NBO and QTAIM analysis were also used to understand the nature of interactions in these clusters. Starting from the cross-species comparison, comparing the interaction energies of urea-containing clusters with the corresponding thiourea-containing, we observed that the thiourea-containing clusters are more stable than the corresponding urea-containing clusters. This is in agreement with the cross-species comparison from the experiments. We identify that the structure of thiourea-containing clustes lend to larger extent of interactions between the sulphur atom (hydrogen-bond acceptor) and the electropositive hydrogens of the postively-charged choline.

Fragmentation simulations of non-covalent clusters

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