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# 4th February 2015

Dear Prof. Schlegel,

Please consider the submitted manuscript entitled “Comparison of the Effective Fragment Potential Method with Symmetry-Adapted Perturbation Theory for the Calculation of Interaction Energies for Ionic Liquids” for publication as a full paper in *Journal of Chemical Theory and Computation*. I am the corresponding author of the paper; my co-author has seen and formally approved the MS.

Ionic liquids have been heralded “electrolytes and solvents of the future”. In the move to afford large-scale calculations of this promising class of electrolytes, cheaper alternatives to higher-correlated levels such as MP2 needed. This MS analyses the performance of the Effective Fragment Potential (EFP) method for studying interaction energies of semi-Coulombic systems such as typical ionic liquids *for the first time*. The EFP method in combination with three basis sets was applied to an extensive series of single ion pairs of ionic liquids (over 170 cation-anion combinations altogether) and compared with the state-of-the-art method for studying intermolecular interactions, SAPT2+3. Absolute errors for each individual energetic component such as electrostatic, exchange-repulsion, induction and dispersion were found to be substantial, falling in the range of -63 to 70 kJ mol-1, which is well beyond chemical accuracy. Contrary to this finding, the analysis of the relative errors revealed that these fell within 20% on average (except charge transfer) of the corresponding SAPT components and hence, were comparable to those observed for the S22 and S66 datasets introduced by Pavel Hobza. This clearly highlights that EFP errors are not ionic liquid (*i.e.* charge) specific as previously suggested. Large absolute errors were attributed to the significantly larger magnitude of intermolecular forces occurring between ionic liquid ions compared to those between neutral complexes. For example, electrostatics can contribute up to -480 kJ mol-1 to the interaction energy in some ionic liquids and hence, even 5% would already make the error increase to 25 kJ mol-1. Exclusion of higher-order terms in the exchange-repulsion energy within the EFP formulation was identified as the main source of error in the prediction of energetics of ion pairs of ionic liquids, which is also in good agreement with similar findings for intermolecular complexes from the S22 and S66 databases.

As was expected, the largest relative deviations were observed for the charge transfer component - 40% on average. No clear correlation between the net charge transfer and either the charge-transfer energy or the induction energy was found (the net charge transfer was calculated from fitted atomic charges in the geodesic scheme).

Excellent linear correlations were established when fitting induction and dispersion components in EFP to reproduce SAPT2+3. Significant improvement in absolute errors was observed falling in a much narrower range of 1 to 11 kJ mol-1 on average. This finding supports our conclusion that there is huge potential in improving the EFP formulation to treat these two important forces in ionic liquids in intermolecular potentials for molecular dynamics simulations.

We believe that our MS represents a strong contribution to the field of theoretical chemistry as it showcases large errors of the EFP method for the prediction of intermolecular interactions in charged systems such as ionic liquids and identifies the deficiency of the EFP formulation that are not charge-specific.

I look forward to hearing from you soon.

Signed electronically

Best Regards

Ekaterina Izgorodina