Parameterization of the hpCADD NDDO-based Polarizable Force Field: The NDDO Hamiltonian

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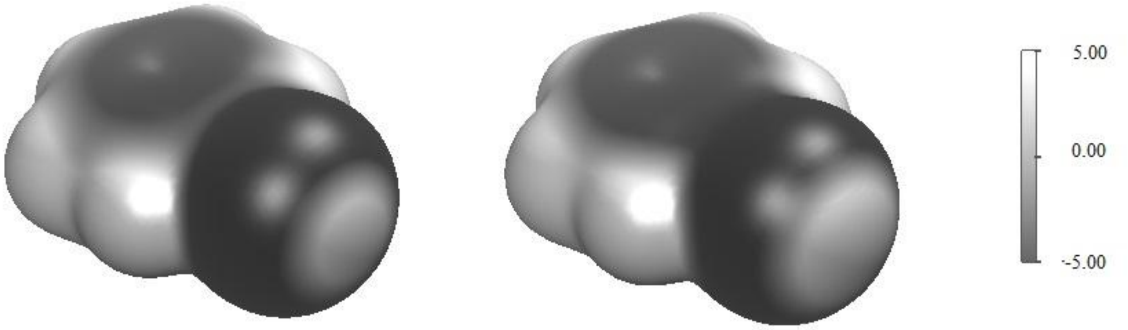
In Computer-Aided-Drug-Design (CADD), the electrostatic interactions contribute significantly to the interaction between the drug-molecule and the target. Further, it is a crucial term for calculating the electrostatic contribution to the solvation energy. In spite of this, conventional Force Fields use the obsolete physical concept of atom-centred point-monopoles and thus, are not able to represent the molecular electrostatic potential (MEP) accurately. They are especially in error for atoms that have positively and negatively charged areas on their surface, such as most halogens [1]. A far better way to describe the MEP is to use atom-centred multipoles derived from semiempirical MO-theory [2,3].

For the parameterization of the polarizable hpCADD Force Field, the two techniques are combined to obtain the MEP from the NDDO wavefunction and structures and energies from a combination of the NDDO-electrostatics with classical force-field potentials. Additionally, distinguishing between different atom types for some elements allows the electronic properties to be reproduced more accurately. This is important for reproducing phenomena such as halogen bonding [4].



Iodobenzene
Gaussian09
MP2/aug-cc-pVDZ

Iodobenzene
hpCADD

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