Comparison of electrostatic approaches to halogen bonding description

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Recently, the phenomenon of favorable interaction between heavy halogen atom (Cl, Br, I) and Lewis bases was rediscovered. It is called halogen bonding (XB) and attracts much attention [1,2] for several reasons. First, it is found in many different systems such as organic crystals, liquid crystals, polymers, biological macromolecules and their complexes. Second, the interaction energy is comparable to traditional hydrogen bonding energies. Third, it is able to form directional interactions in hydrophobic environment and complement [2] identified previously and widely used interaction patterns, such as hydrogen bonding, electrostatic interactions, dispersion interactions, hydrophobic interactions, aromatic stacking. At last, XB contradicts traditional conception of halogen in molecule being only a Lewis base.
Although the nature of XB is still under investigation, the main hypothesis states that electrostatic interaction is the main factor determining its energetics [3]. Despite several models for empirical description of XB were reported earlier, none became a scheme of common choice, due to lack of systematic investigation comparing different approaches. Moreover, development of fast empirical models capable of reliable description of XB is of crucial significance to progress in its better understanding and its successful application.

We conducted a systematic study of different approaches to description of molecular electrostatic potential (MEP) anisotropy for a set of halogen-containing organic molecules and Lewis bases (hydrides, fluorides, methyl and trifluoromethylderivatives of Cl, Br, I as XB donor and ammonia as XB acceptor). We studied extra-point charge and distributed atom-centered multipole expansion approaches. Both MEP and potential energy surface (PES) reproduction were investigated. $MP2_{cp}$/aug-cc-pVTZ level of theory was used as *ab initio* reference. Both models performed well in describing halogen bonding by combining enhanced electrostatics with van-der-waals potentials from widely used force fields. It is shown that multipolar approach is more prospective for further development, however it is less convenient for applied modeling.

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[2] Y. Lu, Y. Liu, Zh. Xu, H. Li, H. Liu, W. Zhu, *Exp. Opin. Drug Disc.*, **2012**, *7(5)*, 375-383.
[3] P. Politzer, J.S. Murray, T. Clark., *Phys. Chem. Chem. Phys.*, **2010**, *12*, 7748-7757.