MP2 and DFT calculations of the interaction energies between boronated aromatic molecules and small DNA models: applications to cancer therapy

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Boronated molecules are increasingly used in pharmacological applications including cancer therapy. In boron-neutron capture therapy, boronated molecules localized in tumor cells are bombarded with slow neutrons in order to induce cell death. Thus, the ability of boronated molecules to target specific areas in the body is crucial. Previous research in our group examined how boronated aromatic molecules interact with other small molecule models and solvents. This work examines possible localization of boronated molecules in DNA by examining the differences in interaction energies between boronated and non-boronated small molecule ligands with nucleic acid models. We have created complexes of boronated and non-boronated aromatic ligands with different nucleic acid sequences (AA, TT, GG, etc.) and optimized their structures. Counterpoise corrected interaction energies have been calculated using MP2 and various DFT functionals (local, GGA, and meta-GGA) and the 6-31+g* and 6-311+g* basis sets. Results show consistent differences in binding between boronated molecules and non-boronated molecules to nucleic acids within single-stranded DNA complexes. CCSD calculations were performed using select complexes to confirm whether MP2 or DFT calculations were most accurate. Current work includes MP2 interaction energy calculations for boronated and non-boronated ligands within double-stranded DNA complexes. ONIOM is used in these calculations to allow the DNA backbones to be modeled with a lower-level method.

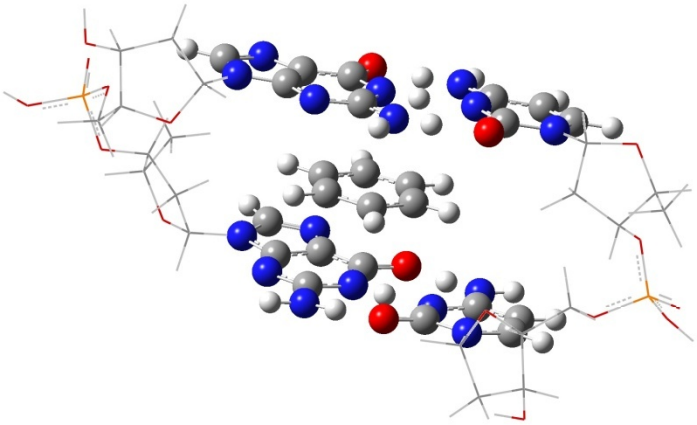

Figure 1. Benzene sandwiched between a GG strand and its complementary CC strand. In this ONIOM model, the upper level is shown in ball-and-bond format and the lower level is shown in wire frame.