INTERACTION CISDDP WITH BASES OF DNA

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In previous study [1], two-bases (adenine-adenine, adenine-guanine and guanine-guanine) interactions with cisplatine were examined using ab initio methods. Current study represents further extention of that work including sugar-phosphate backbone which connects bases. Starting geometries of the studied systems (ApA, ApG and GpG) were based on X-ray Pt-GpG structure[2]. The optimizations were performed using density functional Becke3LYP with 6-31G* basis; for platinum and phosphor pseudopotential description was used. Single-point second order Moller-Plesset perturbation theory (MP2) was used for the DFT-optimized structures. Then sugar-phosphate chain was removed and B-Pt-B bridged systems (B=A and G) were calculated (also at MP2/6-31G* level). Using these calculations, bond dissociation energies (BDE) of two bonds between Pt and N_7 site at purine were determined for systems with and without sugar-phosphate string. Systems without sugar-phosphate string were also calculated at MP2/6-31+G* level, and BDE were determined for each Pt-B and Pt-NH_3. These data were compared with energies from study [1].

It was shown that close correspondence can be found between Pt-N_7 BDE's for systems optimized without ([1]) and with (this work) sugar-phosphate backbone when these backbones are not considered. Similar comparison can be done within current model where the role of sugar-phosphate string can be elucidated. Analogous Pt-N_7 BDE are additionally influenced mainly with coulomb interaction between negatively charged phosphate group and Pt cation. This causes an increase in BDE up to 40 kcal/mol in Pt-ApA complex.

1. J.V. Burda, J. Leszczynski: Deformation of the DNA helix: The influence of cisplatin as relead by ab initio study of platinum(II) bridged DNA purine bases, *J. Am. Chem. Soc*., submitted
2. P.M. Takahara, A.C. Rosenzweig, C.A. Frederick, S.J. Lippard, Crystal Structure of a Double-Stranded DNA Containing the Major Adduct of the Anticancer Drug Cisplatin, *Nature*, **377** (1995) pp. 649-652.