Exploring Nucleoside Boranephosphonate Chemistry – Mechanistic and Synthetic Studies

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Nucleoside boranephosphonates are an important class of nucleotide analogues in which one of the non-bridging oxygen atom has been replaced by a borane moiety (-BH_3). The significant structural similarity to natural nucleotides and their higher stability in the cell medium make these analogues extremely useful in biological research. In contrast to their chemical and biological properties, reactivity of the borane group itself in these compounds has been poorly explored so far. From the chemistry point of view, modifying and carrying out transformations within this group opens new possibilities for application of boranephosphonate derivatives, *e.g*., as masking groups, chemical markers in post-synthetic modifications of oligonucleotides, or a new type of pharmacophores. These stimulated my interest in this class of compounds and ultimately, the reactivity of the borane group of nucleoside boranephosphonate under oxidative conditions with diverse *N*-nucleophiles became subject of my PhD thesis.

Using a stereochemical correlation analysis I determined the correct stereochemistry of the transformation of nucleoside boranephosphonates into phosphoramidates with 1 ° and 2 ° amines in the presence of iodine, and proposed a new mechanism for this reaction, consistent with all the experimental data. I also studied the reaction of boranephosphonate diesters with 3° and heteroaromatic amines in the presence of iodine, which led to a modification on the boron center in the form of the P-B-N bond system. I have shown that both reactions most probably occur *via* a common mechanism involving the same initial reaction steps and that formation of different products was determined by stability of the P-B bond in the intermediate compound, a corresponding aminoboranephosphonate. An additional insight into the mechanism provided experiments with differing solvents, which showed that the type of solvent used was crucial for the reactivity of boranephosphonates. I was able to identify and study the reactivity of new, so far not reported in the literature, boranephosphonate derivatives *e.g*., iodoboranephosphonate, adducts with acetonitrile (ACN-λ^3-boranophosphonate), and tetrahydrofuran (THF-λ^3-boranophosphonate). I have also demonstrated that it is possible to further modify adducts of amines with boranephosphonates at the borane center, and I have synthesized a boranephosphonate diester with two pyridine molecules at the borane center, as the first example of such derivatives.

To sum up, the research that I have carried out as a part of my doctoral thesis allowed me to discover new synthetic possibilities of boranephosphonate, both in the aspect of a formal substitution of the -BH_3 group with another group of atoms and in the functionalization of the borane group itself. The mechanistic studies helped to get deeper understanding of reactivity of boranephosphonate towards various types of *N*-nucleophiles that was also of synthetic importance. I believe that the acquired knowledge has a high cognitive value and can be a starting point for further basic research on this class of compounds and on the design of new boranephosphonate analogues of potential biological or therapeutic significance.