Streszczenie rozprawy doktorskiej – mgr Mateusz Klarek

Tytuł pracy: Synteza i transformacje halogenowanych pochodnych estrów kwasów *β*-imino oraz *β*-aminofosfonowych

Tytuł pracy w języku angielskim: Synthesis and transformations of halogenated *β*-imino and *β*-aminophosphonic acid esters derivatives

The literature part includes three important topics directly related to the research part of this doctoral thesis. The first concerns halogenated imine transformation, both by reductive cyclization, leading to aziridines, and by the base-catalyzed [1,3] proton shift reaction. Undoubtedly, one of the leading theme of this doctoral dissertation is the three-membered heterocyclic compounds - aziridines. These compounds, which are nitrogen analogs of epoxides, are an excellent source of a wide range of amine derivatives due to their extremely reactive three-membered ring. In this literature review, special attention was paid to aziridines substituted with heteroatoms (halogen atoms and a phosphonate group) - both from a synthetic perspective and a discussion of their reactivity. A coherent element ending the literature part is a discussion on aminophosphonic acids and their esters, which are analogues of amino acids, in the context of their biological applications.

In the results section, the topic of the synthesis and transformation of *α,α*-halofluorinated *β*-imino- and *β*-aminophosphonates was discussed. The efficient one-pot halofluorination of a *β*-enaminophosphonate/*β*-iminophosphonate tautomeric mixture resulting in *α*,*α*-halofluorinated *β*-iminophosphonates is reported. Subsequent imine reduction gave the corresponding *β*-aminophosphonates as a racemic mixture or with high diastereoselectivity. The proposed protocol is the first example of a synthesis of *N*-inactivated aziridines substituted by a fluorine and phosphonate moiety on the same carbon atom. Based on spectroscopic and theoretical studies, we determined the *cis*/*trans* geometry of the resulting fluorinated aziridine-2-phosphonate. Our procedure, involving the reduction of *cis/trans*-fluoroaziridine mixture allows us to isolate chiral *trans*-aziridines as well as *cis*-aziridines that do not contain a fluorine atom. We also investigated the influence of the fluorine atom on the reactivity of aziridine through an acid-catalyzed regioselective ring-opening reaction.

The research was complemented by examining the possibility of substituting the bromine (or chlorine) atom with *β*-imino and *β*-aminophosphonates in the reaction with nucleophiles. It was

found out that the substitution of the halogen atom (Br or Cl) occurred only in the case of reaction with NaN_3, and the nucleophilic substitution reaction was accompanied by hydrolysis of one of the ethoxy groups from the phosphonate moiety. The use of anhydrous reaction conditions resulted in a [1,3]-proton shift and the dehydrohalogenation reaction of *α,α*-halofluorinated *β*-iminophosphonate, leading to a product with a conjugated C=N-C=C bond system.

An important element of the work was the use of *N*-deprotected *α,α*-halofluorinated *β*-aminophosphonates in the reaction with *N*-Boc amino acids, leading to obtain the phosphonate analogues of dipeptides, which are an interesting target in the biological point of view.

The concluding part of the doctoral thesis contains a description of the experiments performed, spectroscopic characteristics of the synthesized compounds, a set of spectra, and a bibliography.