

ABSTRACT OF DOCTORAL DISSERTATION

Organophosphorus compounds as therapeutics and markers in medical diagnostics

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Organophosphorus compounds have been the subject of intensive research for many years due to their versatile applications in organic synthesis and medicinal chemistry. An important subgroup of these compounds is 1-amino-1,1-bisphosphonates (ABPs). Their unique features, such as strong affinity for bone tissue and multidirectional biological activity have attracted great interest aimed at exploring their biological effects as well as developing efficient methods for their synthesis. Structural modifications of ABPs, as well as the synthesis of their conjugates with other biologically active molecules, also remain key areas of research, as these approaches can significantly enhance the therapeutic potential of the parent compounds.

The subject of this work focused on developing versatile synthetic strategies for 1-amino-1,1-bisphosphonate derivatives and their conjugates with biologically relevant molecules. Characterization of the synthesized compounds enabled the assessment of their therapeutic and diagnostic potential.

The study began with the synthesis of a wide range of structurally diverse *N*-protected derivatives of 1-aminoalkylidene-1,1-bisphosphonates *via* a multi-step procedure starting from ethyl imidoyl chlorides and proceeding through diethyl 1-ethoxyalkylphosphonates. This method was subsequently extended to obtain phosphonyl-phosphinoyl and phosphonyl-phosphinyl derivatives, establishing one of the few known universal sequential synthetic approaches for 1-amino-1,1-bisphosphonates. Effective conditions for deprotection and hydrolysis of symmetrical 1-amino-1,1-bisphosphonate derivatives were also described, along with the possibility of analogous transformations for phosphonyl-phosphinoyl ABPs derivatives.

Further efforts focused on structural modification of a selected ABP derivative. A simple and efficient method for coupling of tetraethyl 1-aminomethylidene-1,1-bisphosphonate with compounds such as mycophenolic acid, indomethacin, carboxyalkyltriphenylphosphonium bromides, and betulin derivatives was developed, based on amide bond formation assisted by ultrasound. This approach was successfully

applied both for minor structural modifications of ABP and for synthesizing conjugates with more complex biologically active molecules.

Furthermore, attempts were made to modify the structure of deferoxamine using a selected ABP derivative to obtain a ligand suitable for use as a diagnostic marker.

The final stage of the study involved the evaluation of the biological activity of selected 1-amino-1,1-bisphosphonate derivatives and their conjugates, including cytotoxicity and antibacterial properties. The research findings enabled identification of compounds with the most promising therapeutic applications.