Synteza fosfonowych i fosfonianowych pochodnych hydroksyimino-D-alditoli

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Emerging challenge of systemic fungal infections, especially in immunocompromised patients, and a limited repertoire of effective antifungals stimulate a search for novel targets and drug candidates. Enzymes involved in biosynthesis of the fungal cell wall components are of a special interest in this respect. One of them is GlcN-6P synthase, enzyme catalysing the first committed step in chitin biosynthesis pathway, that is transformation of D-fructose-6-phosphate (Fru-6P) to D-glucosamine-6-phosphate (GlcN-6P).[1] Another one is phosphomannose isomerase (PMI), that catalyses the reversible isomerization of D-mannose-6-phosphate (Man-6P) and D-fructose-6-phosphate (Fru-6P). PMI is reported to play a crucial role in the biosynthesis of many mannosylated structures, including the cell wall components of fungi.[2] Both enzymes are proposed as the targets for antifungal chemotherapy and a search for their selective inhibitors has been continued.

In the course of search of antifungal agents, I plan to synthesise hydroxyimino-6-*O*-phosphono-D-alditols and their dimehtyl and diethyl ester, and explore their antifungal activity. Synthesized compounds will by the mimetics of intermediates which are formated in the reaction catalysed by GlcN-6P synthase and PMI. Methyl and ethyl residues located at phosphono group are incorporated intoto increase a lipophilicity of the molecule, which is supposed to be advantageous for better penetration of the derivative through the cytoplasmic cell membrane. Probably, diethyl ester will be metabolised to inside a cell.[1]

Referencje

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