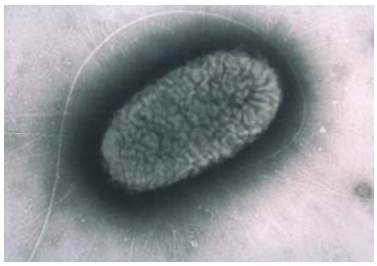

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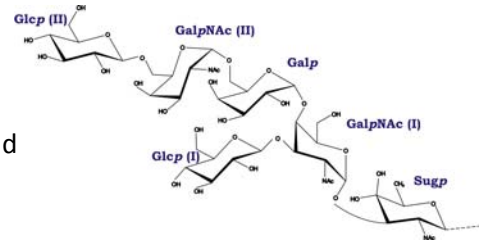

ABSTRACT - POSTER 26

In search of new antifungal agents. Synthesis of benzyl and thiophenyl 2-deoxy-6-*O*-diethylphosphonato-2-hydroxyimino-D-hexopyranosides

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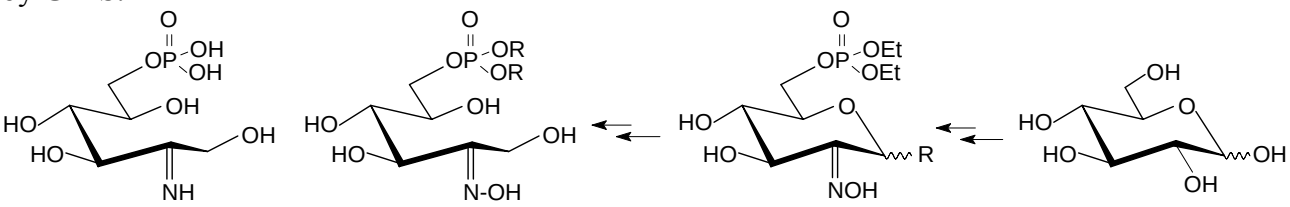
Emerging challenge of systemic fungal infections, especially in immunocompromised patients, and a limited repertoire of effective antifungals stimulate a search for novel targets and drug candidates. Enzymes involved in biosynthesis of the fungal cell wall components are of a special interest in this respect. One of them is GlcN-6P synthase (GlmS), enzyme catalyzing 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.

The reaction performed by GlmS is believed to proceed through the formation of intermediate **1**, a Schiff base created between the keto group of the sugar and the ammonia generated from the glutamine amide function.[3] Mechanism of the reaction catalyzed by PMI is similar to that catalyzed by GlmS.[4]



In the course of search of antifungal agents, we plan to synthesize 2-deoxy-2-hydroxyimino-6-*O*-phosphono-D-glucitol (**2**) and its diethyl ester (**3**), and explore their antifungal activity. Ethyl residues are incorporated into **2** to 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 **3** will be metabolized to **2** inside a cell.

Here, the first steps of our synthesis are presented. These involve the transformation of D-glucose into benzyl (**4**) and thiophenyl 2-deoxy-6-*O*-diethylphosphonato-2-hydroxyimino-D-hexopyranosides (**5**).

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