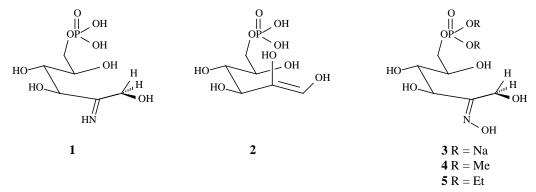
SYNTHESIS OF 2-DEOXY-2-HYDROXYIMINO-6-*O*-PHOSPHONO-D-GLUCITOLS AND THEIR ESTER ANALOGS AS NEW POTENTIAL ANTIFUNGAL AGENTS

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In search for new effective antifungals we focus on two enzymes involved in biosynthesis of the fungal cell wall. The first enzyme is glucosamine-6-phosphate synthase (GlmS), which catalyzes transformation of D-fructose-6-phosphate (Fru-6P) to D-glucosamine-6-phosphate (GlcN-6P) in the chitin biosynthesis pathway [1]. The second enzyme is phosphomannose isomerase (PMI) reported to play a crucial role in biosynthesis of many mannosylated structures, including cell wall components of fungi. PMI is aldose-ketose isomerase and catalyzes reversible isomerization of D-manno-6-phosphate (Man-6P) to D-fructose-6-phosphate (Fru-6P) [2]. Both enzymes are proposed as the targets for antifungal chemotherapy and a search for their selective inhibitors is continued.

Mechanisms of the reactions catalyzed by both enzymes are known and similar. The reaction performed by GlmS is believed to proceed through the formation of an imine intermediate 1 [3], whereas the reaction catalyzed by PMI proceeds *via* a *cis*-endiol intermediate 2 [4].



We synthesized 2-deoxy-2-hydroxyimino-6-O-phosphono-D-glucitol (3) and its ester analogs (4, 5) as potential antifungal agents. Their antifungal activity will be explored. Methyl and ethyl residues are incorporated into 3 to increase a lipophilicity of the molecule. It is supposed to be advantageous for better penetration of the derivatives through the cytoplasmic cell membrane. Probably, esters 4 and 5 will be metabolized to 3 inside a cell.

The syntheses involved transformation of D-fructose-6-phosphate disodium salt into 2-deoxy-2-hydroxyimino-6-*O*-phosphono-D-glucitol disodium salt (3). A subsequent esterification of 3 with diazomethane provided ester 4. 2-Deoxy-2-hydroxyimino-6-*O*-diethylphosphonate-D-glucitol (5) was obtained by a few steps transformation of D-glucose.

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