SYNTHESIS OF QUATERNARY AMMONIUM DERIVATIVES OF BIOLOGICALLY ACTIVE HEXITOLS

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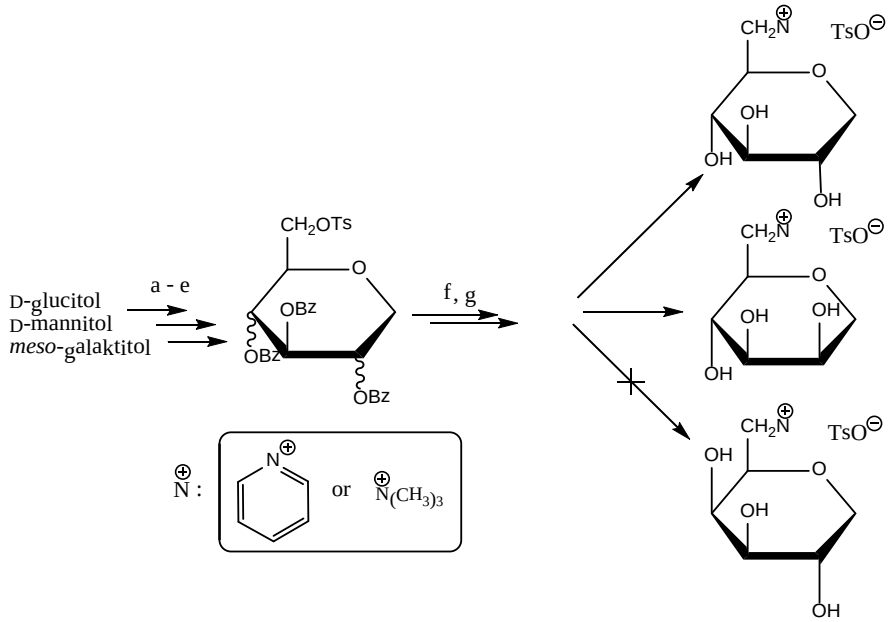
Alditols and anhydroalditols are widespread in both animal and plant kingdoms. They are used in pharmaceutics, as sweeteners, inhibitors and in organic synthesis. Levels of 1,5-anhydro-D-glucitol in human blood are the first symptoms of many diseases, e.g. type 2 diabetes or cardiovascular disease. Currently chemists and biologists are concentrated in synthesizing nucleoside mimetics where a sugar moiety is substituted with an anhydroalditol, e.g. 1,4-anhydro or 1,5-anhydro. There is information about inhibitory properties of alditol derivatives against HIV-1 retrovirus proteases [1].

Quaternary ammonium salts (QAS) are a group of cationic surfactants which are used in many fields of everyday life such as: pharmaceutics, disinfectants, corrosion inhibitors, fungicides or pesticides. They exhibit antibacterial and antifungal activities employed in many antimicrobial drugs. Typical QAS contain a hydrophilic, cationic head and a hydrophobic alkyl chain. The amphiphilic character allows these compounds to bind to the cell membranes. For model QAS the optimal activity was achieved when the alkyl chain is between 10 and 14 carbons long [2].

In view of this information, we synthesized compounds combining properties of these two groups of chemicals. A simplified scheme of the synthesis is presented beneath.



Scheme 1: Reagents and conditions; a: 5% H_2SO_4, 200°C, 0.5h; b: TrCl/Py, 6h, 60°C; c: BzCl/Py 1h 0°C, 3h RT; d: CH_3COOH/H_2O; e: TsCl/Py 1h 0°C, 4h RT; f: Py 70°C 14 days or $N(CH_3)_3$ in EtOH 70°C 7 days; g: MeONa/MeOH 96h RT

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1. V. Glacon, M. Benazza, A. El Anzi, D. Beaupere. *J. Carbohydr. Chem.* 23: 95-110, 2004.
2. T. Abel, J. I. Cohen, R. Engel, M. Filshtinskaya, A. Melkonian, K. Melkonian. *Carbohydr. Res.* 337: 2495-2499, 2002.