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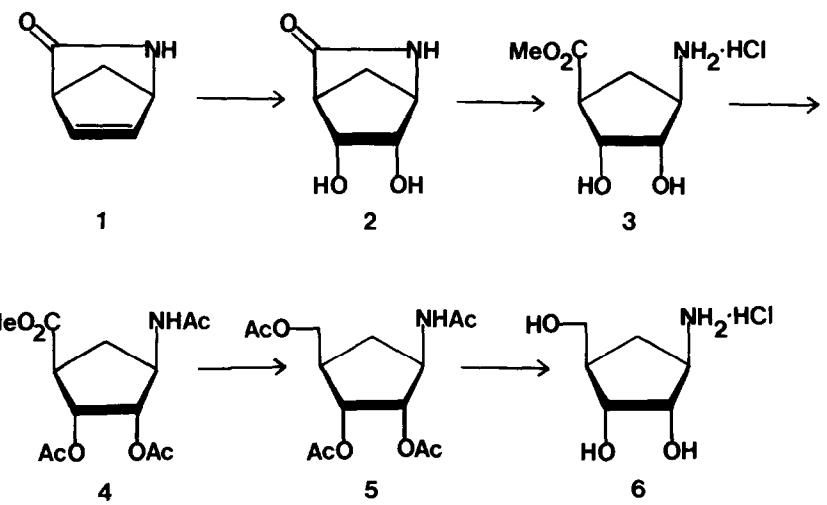
(±) 4β-AMINO-2α,3α-DIHYDROXY-1β-CYCLOPENTANEMETHANOL HYDROCHLORIDE. CARBOCYCLIC RIBOFURANOSYLAMINE FOR THE SYNTHESIS OF CARBOCYCLIC NUCLEOSIDES.

Richard C. Cermak and Robert Vince*
Department of Medicinal Chemistry, College of Pharmacy
University of Minnesota, Minneapolis, MN 55455

Abstract. Carbocyclic ribofuranosylamine, a key intermediate for the synthesis of carbocycli ribonucleosides, was synthesized by a facile route from the lactam, 2-azabicyclo[2.2.1]hept-5-ene-3-one.

Carbocyclic analogues of purine and pyrimidine nucleosides, in which a cyclopentane ring replaces the furanose moiety, have been the object of the synthetic efforts of a number of groups.[1] The antitumor,[2] antimicrobial,[3,4] and antiviral[4] properties have generated considerable interest in the biological properties of carbocyclic nucleosides. Carbocyclic ribofuranosylamine (6) is the key intermediate for the synthesis of carbocyclic ribonucleosides.[1a,4b] Present procedures for the synthesis of 6 are either long and tedious,[5] or require the separation of isomers.[6] The present account represents a facile direct route to carbocyclic ribonucleosides.

A catalytic osmium tetroxide cis dihydroxylation of 2-azabicyclo[2.2.1]hept-5-ene-3-one (1)[4b,7] was employed using N-methylmorpholine N-oxide[8] to regenerate OsO_4 during glycolization (t-butyl alcohol/H_2O, 50°C). The glycolization product 2 (mp 173-180°C dec.)



was esterified (methanol/HCl) and gave methyl (±)-4β-amino-2α,3α-dihydroxy-1β-cyclopentanecarboxylate hydrochloride (3) (80% from 1), mp 151-153°. Acetylation of 3 with acetic ahydride in pyridine gave methyl (±)-4β-acetamido-2α,3α-diacetoxy-1β-cyclopentylcarboxylate (4) (89% from ethyl acetate-hexane, mp 116-117°, lit.[5] mp 116°). Reduction of the methyl ester of 5 with $Ca(BH_4)_2$ (THF, rt, 18 hr) gave, after acetylation, (±) 4β-acetamido-2α,2α-diacetoxy-1β-cyclopentanemethyl acetate (5) (78% from ethyl acetate-hexane, mp 94-95°). Acid hydrolysis of 5 gave the aminetriol (±) 4β-amino-2α,3α-dihydroxy-1β-cyclopentanemethanol hydrochloride (6) which is easily converted to carbocyclic nucleosides as previously described.[5,6]

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