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SYNTHESIS OF 2-ACETAMIDO-2-DEOXY-α-D-GLYCOSYL PHOSPHATES *VIA* 2-METHYL-GLYCO[2',1':4,5]-2-OXAZOLINES

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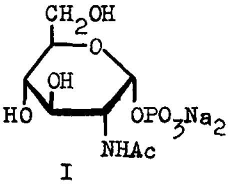
Synthesis of 1,2-*trans*-2-acetamido-2-deoxyglycosides including oligosaccharides *via* 2-methyl-glyco[2',1':4,5]-2-oxazolines had been shown to be characterized by its simplicity and efficiency[1]. Recently Salo and Fletcher[2] have reported the glycosylation of dibenzyl hydrogen phosphate (DBP) with 2-methyl-(3',4',6'-tri-O-acetyl-1,2-dideoxy-β-D-mannopyrano)-[2',1':4,5]-2-oxazoline which gives rise to 2-acetamido-2-deoxy-α-D-mannopyranosyl phosphate. This synthesis however gave no possibility to conclude the stereochemical course of glycosylation of disubstituted phosphates with other glyco[2',1':4,5]-2-oxazolines.

We found that interaction of 2-methyl-(3',4',6'-tri-O-acetyl-1,2-dideoxy-α-D-glucopyrano)[2',1':4,5]-2-oxazoline[3] with slight excess of DBP in dry toluene at 20 - 25° for 20 hr yielded a single product (tlc) from which the benzyl groups were removed by catalytic hydrogenolysis over Pd on carbon in methanol solution. Following de-O-acetylation with 0.1*M* sodium methoxide (pH 10-11) and crystallization of the resulting solid from aqueous ethanol gave the chromatographically pure hygroscopic 2-acetamido-2-deoxy-α-D-glucopyranosyl disodium phosphate (I) in 49% yield; $[\alpha]_D$ +62° (*c* 1.54, water); *anal*. for $C_8H_{14}NO_9PNa_2 \cdot H_2O$. NMR spectrum (in D_2O, TMS as internal reference, 100 MHz) included signals at δ 2.06 (singlet, 3 H, NAc), 3.88 (singlet, H-6), and 5.34 (quartet, H-1, $J_{1,2}$ = 2.7 Hz, $J_{1,P}$ = 7.5 Hz) (*cf.*[4]).

The treatment of 2-methyl-[4'-O-(2'-acetamido-3',4',6'-tri-O-acetyl-2'-deoxy-β-D-glucopyranosyl)-3',6'-di-O-acetyl-1,2-dideoxy-α-D-glucopyrano][2',1':4,5]-2-oxazoline[3] with diphenyl hydrogen phosphate in toluene-nitromethane (1:1) mixture for 24 hr at room temperature gives the crystalline tlc-pure 2-acetamido-4-O-(2-acetamido-3,4,6-tri-O-acetyl-2-deoxy-β-D-glucopyranosyl)-3,6-di-O-acetyl-2-deoxy-α-D-glucopyranosyl diphenyl phosphate (II) in 64% yield; m.p. 140 - 142° (dec.), $[\alpha]_D$ +55° (*c* 0.2, methanol), $[M]_D$ +477° (*cf*. $[M]_D$ +372° for α-chitobioside octaacetate[5] and $[M]_D$ -279° for methyl β-chitobioside heptaacetate[6]); λ_{max}^{MeOH} 264 nm; anal. for $C_{38}H_{47}N_2O_{19}P$.



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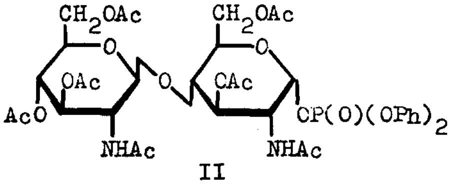

II

It should be noted that formation of α-phosphates (I) and (II) is the first example of uncommon stereochemical course of glycosylation with glyco-oxazolines. This phenomenon seems to be explained by S_N1 mechanism of the glycosylation of hydrogen phosphates in which phosphate anions attack the intermediate cation in *cis*-position leading to the thermodynamically more stable α-anomers.

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