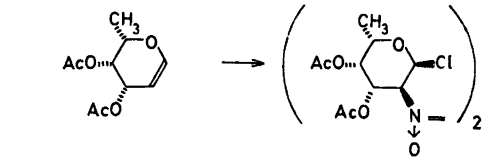
A Synthesis of a 2-Acetamido-2,6-dideoxy-L-galactose Derivative

PER J. GAREGG, BENGT LINDBERG and THOMAS NORBERG

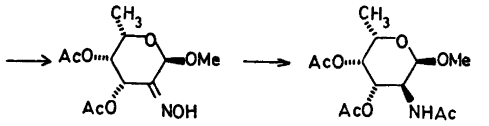
Department of Organic Chemistry, Arrhenius Laboratory, University of Stockholm, S-104 05 Stockholm, Sweden

In connection with studies of bacterial polysaccharides, 2-acetamido-2,6-dideoxy-L-galactose (*N*-acetyl-L-fucosamine) was needed. Different syntheses of this sugar, and of its enantiomer, have been described,[1-3] and the synthesis of this sugar *via* the corresponding acetylated glycal, a procedure devised by Serfontein,[4] Lemieux [5-7] and their coworkers, is now reported. The advantage of this procedure is that the desired epimer predominates in the final product and that it is simple.

3,4-Di-*O*-acetyl-1,2,6-trideoxy-L-*lyxo*-hex-1-enopyranose [8] (3,4-di-*O*-acetyl-L-fucal, I) and nitrosyl chloride gave the dimeric nitroso compound (II) in 86 % yield. Treatment of II



I II



III IV

with methanol and pyridine in tetrahydrofuran yielded the glycoside oxime (III) which, without purification, was treated with lithium aluminium hydride and acetylated. GLC of the product revealed the presence of two components (7:3), presumably the methyl 2-acetamido-3,4-di-*O*-acetyl-2,6-dideoxy-α-hexopyranosides with the L-*galacto*- and L-*talo*-configurations. The major component crystallized (20 % yield from II), m.p. 150 °C, $[\alpha]_D$ −144° (chloroform) and NMR spectroscopy in the presence of tris-(dipivaloylmethanoato)europium demonstrated that this was the *galacto*-isomer (IV). The spectral assignments of ring protons shown in Table 1 were confirmed by spin decoupling experiments.

Table 1. ^{1}H NMR data for methyl 2-acetamido-3,4-di-*O*-acetyl-2,6-dideoxy-α-L-*galacto*-hexoside (IV). δ values in ppm from tetramethylsilane (internal) in deuteriochloroform, coupling constants in Hz.

Proton	Compound IV	IV + Eu(DPM)$_3$[a]
H−1	[b]	5.62 ($J_{1,2}$3)
H−2	[b]	7.00 ($J_{2,3}$10)
H−3	[b]	6.15 ($J_{3,4}$ 3.5)
H−4	[b]	5.81 ($J_{4,5}$1)
H−5	4.08 ($J_{4,5}$1)	4.50 ($J_{5,6}$6)
H−6	1.17 ($J_{5,6}$6)	1.35
OCH_3	3.40	3.60 or 3.61
N*H*Ac	5.80	7.15
NHAc		3.61 or 3.60
OAc		2.32, 2.45
NH*Ac* or OAc	2.12 1.97 1.98	

[a] 0.2 mol Eu(DPM)$_3$/mol IV. [b] Unresolved at δ 4.4−5.4.

Experimental. Melting points are corrected. Concentrations were performed at reduced pressure. Optical rotations were recorded at room temperature (20−22 °C) using a Perkin-Elmer 141 instrument. NMR spectra were recorded for all new compounds using a Varian A60-A instrument and were invariably in agreement with the postulated structures. TLC was performed on silica gel F_{254} (Merck). Gas liquid chromatography was performed on a Perkin-Elmer Model 990 instrument at a nitrogen flow of 20 ml/min on an ECNSS column (3 % on Gas-Chrom Q).

Dimeric-3,4-di-O-acetyl-2,6-dideoxy-2-nitroso-α-L-galacto-hexopyranosyl chloride (II). 3,4-Di-*O*-acetyl-1,2,6-trideoxy-L-*lyxo*-hex-1-enopyranose (I) ("di-*O*-acetyl-L-fucal") was obtained in a 52 % yield from L-fucose essentially as described by Iselin and Reichstein [8] who report a 30 % yield for this transformation. The higher yield in the present synthesis may be due to the lower temperature (−10 to −20 °C) used in the reductive 1,2-elimination, the shorter reaction time (1 h against 3 h) or the use of extremely finely powdered zinc. The glycal I (1.42 g, m.p. 48−50 °C, in agreement with the literature value) in ethyl acetate (60 ml) was cooled to −40 °C with stirring while air in the reaction vessel was displaced with nitrogen. Nitrosyl chloride was then passed through the solution at −40 °C for about 20 min. Excess nitrosyl chloride was displaced by nitrogen and the solution was allowed to attain room temperature. Concentration and recrystallization from

chloroform – hexane gave 1.60 g of II, m.p. 147 °C (decomp.), $[\alpha]_D$ −183° (*c* 0.5, in chloroform). (Found: C 42.8; H 4.94; N 4.88; O 34.4; Cl 12.9. $C_{10}H_{14}NO_6Cl$ requires C 42.9; H 5.05; N 5.01; O 34.3; Cl 12.7.)

*Methyl 2-acetamido-3,4-di-*O*-acetyl-2,6-dideoxy-α-*L*-galacto-hexoside (IV).* The above nitrosyl chloride adduct II (1.40 g) was refluxed with methanol (0.32 g) and pyridine (0.79 g) in dry tetrahydrofuran (40 ml) for 1 h and concentrated. The residue was taken up in chloroform and the chloroform solution shaken with water, dried over magnesium sulfate, filtered and concentrated to yield III as a colourless syrup (1.38 g) which was used directly in the next step. The oxime III (1.38 g) in tetrahydrofuran (35 ml) was refluxed under nitrogen with lithium aluminium hydride (0.66 g) for 3 h. Excess hydride was decomposed by adding, in turn, ethyl acetate and 50 % aqueous methanol (135 ml). The mixture was filtered, the filtrate was neutralized (HCl) to pH 4.5, low-boiling solvents were removed by evaporation and the residual water solution was freeze-dried. The product was acetylated overnight at room temperature with acetic anhydride (8 ml) and pyridine (20 ml). The solution was poured into ice-water and the mixture extracted with chloroform. The combined chloroform phases were washed with ice-cold 1 M sulfuric acid, saturated aqueous sodium hydrogen carbonate and finally water, dried over magnesium sulfate, filtered and concentrated to yield 1.44 g of crude product. GLC at 200 °C showed the presence of two components in an approximate ratio of 7:3. The major component crystallized from diethyl ether – hexane to yield 0.31 g of IV, m.p. 150 °C, $[\alpha]_D$ −144° (*c* 0.25, chloroform). (Found: C 51.7; H 6.91; N 4.82. $C_{13}H_{21}NO_7$ requires C 51.5; H 6.98; N 4.62.)

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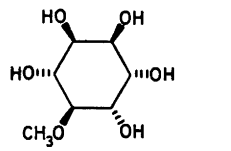
Synthesis of 3-Deuterio-2,3-diphospho-D-glyceric Acid

BERTIL ERBING, PER J. GAREGG and BENGT LINDBERG

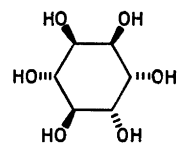
Department of Organic Chemistry, Arrhenius Laboratory, University of Stockholm, S-104 05 Stockholm, Sweden

2,3-Diphospho-D-glyceric acid, labelled with deuterium at C-3, was required for NMR studies of its association with hemoglobin [1] and the present paper describes the synthesis of this substance. The key intermediate, 2,3:4,5-di-*O*-cyclohexylidene-D-*manno*-hexodialdose (III) was obtained in a manner similar to that described by Angyal and Hoskinson for the synthesis of 2,3:4,5-di-*O*-isopropylidene-L-*manno*-hexodialdose, an intermediate in the synthesis of L-mannitol from quebrachitol.[2]

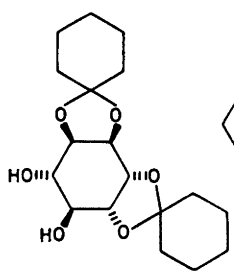
D-*chiro*-Inositol (I), obtained by demethylation of pinitol, was converted into the 1,2:5,6-dicyclohexylidene derivative (II) as described by Angyal and co-workers for the enantiomer.[3]



Pinitol



I



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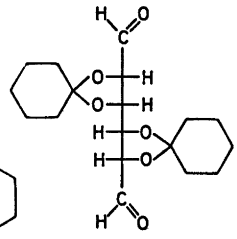
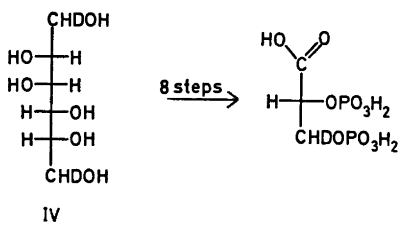


III



IV