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Note

A synthesis of 2-amino-2,6-dideoxy-L-mannose (L-rhamnosamine) and 2-amino-2,6-dideoxy-L-glucose (L-quinovosamine)*

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2-Amino-2,6-dideoxyhexoses were required in order to develop new methods for their analysis and for the preparation of reference methyl ether derivatives needed for structural studies on polysaccharides isolated from *Pseudomonas* species Although the syntheses of many of these glycoses have been reported, we have found it convenient to make them by a direct and general procedure involving the addition of nitromethane to readily available 5-deoxypentoses to yield 1,6-dideoxy-1-nitrohexitols which, after acetylation and treatment with methanolic ammonia, gave 2-acetamido-1,2,6-trideoxy-1-nitrohexitols These, under modified conditions of the Nef reaction[1,2] gave the expected 2-acetamido-2,6-dideoxyhexoses[3] This note records the successful synthesis of 2-amino-2,6-dideoxy-L-mannose (L-rhamnosamine) and 2-amino-2,6-dideoxy-L-glucose (L-quinovosamine) from 5-deoxy-L-arabinose by the nitromethane addition-method

Since we failed to obtain crystalline intermediates, the synthesis was performed without their isolation in pure form

5-Deoxy-L-arabinose, obtained by the degradation of L-rhamnose diethyl dithioacetal[4], on base-catalyzed addition of nitromethane. gave a mixture of 1,6-dideoxy-1-nitro-L-mannitol and 1,6-dideoxy-1-nitro-L-glucitol (*ca* 1 0 7) Acetylation of the mixture afforded the corresponding 2,3,4,5-tetra-*O*-acetyl derivatives of the 1,6-dideoxy-1-nitrohexitols, and treatment of the product with methanolic ammonia afforded a mixture of 2-acetamido-1,2,6-trideoxy-1-nitro-L-mannitol and 2-acetamido-1,2,6-trideoxy-1-nitro-L-glucitol (*ca* 2 1) The mixed 2-acetamido-1,2,6-trideoxy-1-nitrohexitols, treated under the modified Nef conditions[2] gave a mixture of 2-acetamido-2,6-dideoxy-L-mannose and 2-acetamido-2,6-dideoxy-L-glucose The latter, on hydrolysis with hot, dilute hydrochloric acid afforded a mixture of the corresponding 2-amino-2,6-dideoxyhexose hydrochlorides

The 2-amino-2,6-dideoxyhexose hydrochlorides were easily separated by cellulose-column chromatography to give pure 2-amino-2,6-dideoxy-L-mannose hydrochloride and 2-amino-2,6-dideoxy-L-glucose hydrochloride in 17 9% and 9 2% yield, respectively, based on the 5-deoxy-L-arabinose used The 2-amino-2,6-dideoxy-L-mannose crystallized readily, but the 2-amino-2,6-dideoxy-L-glucose derivative

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could not be induced to crystallize It was therefore converted, in good yield, into crystalline 2-acetamido-2,6-dideoxy-L-glucose

EXPERIMENTAL

General methods — Paper chromatography was performed by the descending method[5] on Whatman No 1 filter paper with either (*A*) pyridine–ethyl acetate–water (2 5 5 v/v, top layer) or (*B*) butyl alcohol–ethanol–water (4 1 5 v/v, top layer) as the mobile phase Glycoses were detected with either (*a*) 2% silver nitrate in acetone followed by 3% sodium hydroxide in ethanol[6], (*b*) 2% *p*-anisidine hydrochloride in ethanol[7], or (*c*) 2% ninhydrin in acetone The rates of migration of the glycoses are quoted relative to D-galactose (R_{Gal}) or to 2-amino-2-deoxy-D-glucose hydrochloride (R_{GN})

Gas–liquid partition chromatography was carried out by using a Hewlett–Packard Model 402 chromatograph with a hydrogen-flame detector and fitted with glass U-tubes (1 3 m × 6 mm × 3 mm internal diameter) packed with either (*A*) 10% neopentylglycol sebacate polyester on 80–100 mesh acid-washed Chromosorb W or (*B*) 3% ECNSS-M on 100–120 mesh Gas-Chrom Q (Applied Science Labs , State College, Pennsylvania) Retention times of the compounds are quoted relative to 2-acetamido-2-deoxy-1,3,4,5,6-penta-*O*-(trimethylsilyl)-D-glucitol[8] (T_{GN}), or to penta-*O*-acetyl-L-arabinitol[9] (T_A)

Melting points were determined on a Fisher–Johns apparatus and are corrected Solutions were concentrated under diminished pressure below 40° Optical rotations were determined at 20° with a Perkin–Elmer 141 polarimeter

Addition of nitromethane to 5-deoxy-L-arabinose — 5-Deoxy-L-arabinose[4] (18 6 g), dissolved in a mixture of dry methanol (230 ml) and nitromethane (65 ml), was treated with freshly prepared 1 7M sodium methoxide in methanol (96 ml) and the stirred solution was kept for 2 h at 20° and for a further 14 h at 5° Following the addition of ether (800 ml), the resulting precipitated product was collected by filtration and washed with a little cold methanol followed by ether The air-dried product, dissolved in water (200 ml), was passed down a column of Rexyn-101 (H^+) ion-exchange resin (*ca* 500 ml) and the eluate and water washings were concentrated to a syrup (25 1 g)

A portion of the product (40 mg) in 2M sodium hydroxide was added to a solution of cold 3M sulfuric acid (0 6 ml) and the mixture was then kept for 5 h at 20° The diluted mixture was neutralized ($BaCO_3$) and deionized [Rexyn-101 (H^+) and RG6 (OH^-) resins, 5 ml] and was concentrated to a syrup (*ca* 30 mg) Paper-chromatographic examination of the syrup (solvent *A*) showed two components having R_{Gal} 2 58 and 2 81, corresponding in mobility and color reactions with authentic 6-deoxy-L-glucose and 6-deoxy-L-mannose, respectively Gas–liquid partition chromatography (column B, 180°) of the reduced ($NaBH_4$) and acetylated[9] Nef-reaction product gave two peaks corresponding with penta-*O*-acetyl-6-deoxy-L-mannitol (T_A 0 58, 58%) and penta-*O*-acetyl-6-deoxy-L-glucitol (T_A 0 84, 42%)

Acetylation of 1,6-dideoxy-1-nitro-L-mannitol and 1,6-dideoxy-1-nitro-L-glucitol — The mixed 1,6-dideoxy-1-nitrohexitols (25 g) (from the preceding experiment), dissolved in acetic anhydride (225 ml), were treated with two drops of concentrated sulfuric acid and, after the initial reaction, the mixture was heated for 30 min on a boiling water-bath The cooled mixture was poured into stirred ice–water (1 6 liters) and after 1 h the water was decanted from the oily product, which was then taken up in chloroform (350 ml) The chloroform solution was washed with cold water (2 × 70 ml), dried (anhydrous Na_2SO_4), and concentrated to give a mixture of 2,3,4,5-tetra-*O*-acetyl-1,6-dideoxy-1-nitro-L-mannitol and 2,3,4,5-tetra-*O*-acetyl-1,6-dideoxy-1-nitro-L-glucitol (45 5 g)

Treatment of the mixture of 2,3,4,5-tetra-O-acetyl-1,6-dideoxy-1-nitro-L-mannitol and -L-glucitol with methanolic ammonia — The mixed 2,3,4,5-tetra-*O*-acetyl derivatives of 1,6-dideoxy-1-nitro-L-mannitol and 1,6-dideoxy-1-nitro-L-glucitol (45 g) (from the preceding experiment) were dissolved in dry methanol (900 ml) and the solution, cooled externally in ice, was saturated with ammonia gas and then kept for 14 h at 5° The reaction mixture was concentrated to a syrup which, following trituration with hot chloroform (4 × 100 ml) to remove acetamide, left a residual mixture of 2-acetamido-1,2,6-trideoxy-1-nitro-L-mannitol and 2-acetamido-1,2,6-trideoxy-1-nitro-L-glucitol (27 1 g)

2-Acetamido-2,6-dideoxy-L-mannose and -L-glucose — The mixture of 2-acetamido-1,2,6-trideoxy-1-nitro-L-mannitol and 2-acetamido-1,2,6-trideoxy-1-nitro-L-glucitol (26 g) (from the preceding experiment) was dissolved in a solution of $Ba(OH)_2\ 8H_2O$ (32 g) in water (520 ml) and the solution was added dropwise with stirring to a cooled solution of concentrated sulfuric acid (30 ml) in water (300 ml), and the mixture was kept for 14 h at 20° The reaction mixture was neutralized ($BaCO_3$), filtered, passed through Rexyn-101 (H^+) and RG6 (OH^-) (20 ml) ion-exchange resins, and concentrated to a syrup (20 g)

Gas–liquid partition chromatography (column *A*, 190°) of the trimethylsilylated product[8] showed a composition of peaks corresponding to 2-acetamido-2,6-dideoxy-L-mannose (68%, peaks T_{GN} 0 76 and 0 92) and 2-acetamido-2,6-dideoxy-L-glucose (32%, peaks T_{GN} 1 38 and 2 14)

2-Amino-2,6-dideoxy-L mannose and -L-glucose hydrochlorides — The mixture of 2-acetamido-2,6-dideoxy-L-mannose and 2-acetamido-2,6-dideoxy-L-glucose (19 6 g) (from the preceding preparation) in 3M hydrochloric acid (400 ml) was heated for 3 h on a boiling water-bath, and was then concentrated to a syrup (17 g) The product was divided into two equal portions, and each was fractionated on a cellulose column (6 × 50 cm) with butyl alcohol–water (10.1 v/v) as the mobile phase Fractions collected (20 ml each) were examined by paper chromatography (solvent *B*) The first component eluted was 2-amino-2,6-dideoxy-L-glucose, and concentration of the combined fractions containing this glycose gave a syrup that was taken up in M hydrochloric acid (50 ml), and extracted with chloroform (30 ml) and ether (30 ml) Following reconcentration, the product was kept under vacuum over potassium hydroxide The 2-amino-2,6-dideoxy-L-glucose hydrochloride, on paper chromato-

graphy, gave a single ninhydrin-positive spot having R_{GN} 1 74 (solvent *B*) and had $[\alpha]_D$ −50° (*c* 1.1, water) (lit [10] $[\alpha]_D$ −53° in water)

Anal Calc for $C_6H_{14}ClNO_4$. C, 36 10, H, 7 07, N, 7 02 Found C, 36 21, H, 7 11, N, 7 00

The second component eluted from the column was 2-amino-2,6-dideoxy-L-mannose, which was purified in the manner already described to yield a syrup (4 94 g) 2-Amino-2,6-dideoxy-L-mannose hydrochloride (4 4 g), obtained crystalline from a methanol–acetone–water mixture, gave on paper chromatography a single ninhydrin-positive spot having R_{GN} 1 50 (solvent *B*) and had m p 170–175° (decomp), $[\alpha]_D$ +25 5° (*c* 0 4, water) lit [11] m p 180° (decomp), for the D enantiomorph[12] m p 175° (decomp), $[\alpha]_D$ −23° in water)

Anal Calc for $C_6H_{14}ClNO_4$ C, 36 10, H, 7 07, N, 7 02 Found C, 36 06, H, 7 16, N, 7 10

A portion of the *N*-acetylated and trimethylsilylated crystalline 2-amino-2,6-dideoxy-L-mannose hydrochloride[8], on gas–liquid partition chromatography (column *A*, 190°), gave two peaks having T_{GN} 0 76 (72%) and 0 92 (28%)

2-Acetamido-2,6-dideoxy-L-glucose — The syrup of 2-amino-2,6-dideoxy-L-glucose hydrochloride (2 g) was *N*-acetylated[13] The product (2-acetamido-2,6-dideoxy-L-glucose), obtained crystalline from ethanol solution, gave on paper chromatography a single spot having R_{Gal} 3 20 (solvent *A*), m p 215–218°, $[\alpha]_D$ −68°→−8 6° (*c* 0 5, water) (lit [10] m p 201–204°, $[\alpha]_D$ −54→−14° (water), for the D- enantiomorph[10] m p 209–211°, $[\alpha]_D$ +63→+15° (water), m p 210–211°, $[\alpha]_D$ +15 3° (water) (ref 4)

Anal Calc for $C_8H_{15}NO_5$ C, 46 82, H, 7 37, N, 6 83 Found C, 46 71, H, 7 21, N, 6 62

The trimethylsilylated[8] crystalline 2-acetamido-2,6-dideoxy-L-glucose, on gas–liquid partition chromatography (column A, 190°), gave a single peak having T_{GN} 1 38, whereas the trimethysilylated product prepared from the aminoglycose equilibrated in water gave two peaks having T_{GN} 1 38 (72%) and 2 14 (28%)

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