Carbohydrate Research, 31 (1973) 131–134
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Note

A synthesis of 2-acetamido-2,6-dideoxy-D-allose and 2-acetamido-2,6-dideoxy-D-altrose*

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(Received March 16th, 1973, accepted, in revised form, May 14th, 1973)

The base-catalyzed addition of nitromethane to 5-deoxy-D-ribose[1,2] gave a mixture of 1,6-dideoxy-1-nitro-D-allitol and 1,6-dideoxy-1-nitro-D-altritol A portion of this product underwent a modified Nef reaction[3,4] to yield 6-deoxy-D-allose and 6-deoxy-D-altrose (*allo altro ca* 2 3), which were obtained pure by cellulose-column chromatographic separation

The mixture of 1,6-dideoxy-1-nitro-D-allitol and 1,6-dideoxy-1-nitro-D-altritol was acetylated to yield the corresponding 2,3,4,5-tetra-*O*-acetyl-1,6-dideoxy-1-nitro-D-allitol and 2,3,4,5-tetra-*O*-acetyl-1,6-dideoxy-1-nitro-D-altritol derivatives which, without separation, were treated with methanolic ammonia to yield a mixture of 2-acetamido-1,2,6-trideoxy-1-nitro-D-allitol and 2-acetamido-1,2,6-trideoxy-1-nitro-D-altritol These derivatives, without separation, were subjected to the modified Nef reaction[3] to yield 2-acetamido-2,6-dideoxy-D-allose and 2-acetamido-2,6-dideoxy-D-altrose (*allo altro ca* 2 1)

The final mixture was fractionated by cellulose-column chromatography to yield the chromatographically pure glycoses 2-Acetamido-2,6-dideoxy-D-altrose, previously undescribed, remained a syrup, and its hydrochloride underwent degradation with ninhydrin to give 5-deoxy-D-ribose 2-Acetamido-2,6-dideoxy-D-allose was readily obtained crystalline and was converted by hydrolysis with hydrochloric acid into crystalline 2-amino-2,6-dideoxy-D-allose hydrochloride, which had physical properties in close agreement with those previously recorded for the compound[5].

EXPERIMENTAL

General — Paper chromatography was performed by the descending method[6] on Whatman No 1 filter paper by using either (*A*) pyridine–ethyl acetate–water (2 5 5 *v/v*, top layer) or (*B*) 1-butanol–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[7], (*b*) 2% *p*-anisidine hydrochloride in ethanol[8], or (*c*) 2% ninhydrin in acetone The rates of migration of the glycoses are

*Issued as N R.C C. No 13273.

quoted relative to D-galactose (R_{Gal}) or to 2-amino-2-deoxy-D-glucose hydrochloride (R_{GN})

Gas–liquid partition chromatography was performed with a Hewlett–Packard model 402 gas chromatograph equipped with a hydrogen-flame detector and fitted with glass U-tubes (1 3 m × 6 mm × 3 mm internal diameter) packed with 3% ECNSS-M on 100–120 mesh Gas–Chrom Q (Applied Science Labs State College, Pa) Retention times are quoted relative to penta-*O*-acetyl-L-arabinitol (T_A) or 2-acetamido-1,3,4,5,6-penta-*O*-acetyl-2-deoxy-D-glucitol (T_{GNolAc})

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

Addition of nitromethane to 5-deoxy-D-ribose — 5-Deoxy-D-ribose[1,2] (5 g), dissolved in a mixture of dry methanol (60 ml) and nitromethane (18 ml), was treated with freshly prepared 1 7M sodium methoxide in methanol (26 ml) and the stirred solution was kept for 18 h at 20° Following the addition of ether (200 ml), the resulting precipitate was collected by filtration, and washed with a little cold methanol followed by ether The product (*ca* 6 g) was dissolved in water (60 ml) and the solution was deionized by passing it down a column of Rexyn 101 (H^+) ion-exchange resin (60 ml). The eluate and water washings from the column were concentrated to a syrup (4 9 g)

6-Deoxy-D-allose and 6-deoxy-D-altrose — A portion (1 g) of the preceding syrup, dissolved in a solution of $Ba(OH)_2$ $8H_2O$ (1 2 g) in water (20 ml), was added dropwise with stirring to a solution of concentrated sulfuric acid (1 15 ml) in water (10 ml) After 18 h at room temperature, the reaction mixture was neutralized ($BaCO_3$), filtered, and the filtrate, after deionization with Rexyn 101 (H^+) and RG6 (OH^-) ion-exchange resins (10 ml), was concentrated to a syrup (0.62 g) Paper-chromatographic examination of the syrup (solvent *A*) revealed two components having R_{Gal} 3 52 and 4 63, corresponding in mobility and color reactions to 6-deoxy-D-allose and 6-deoxy-D-altrose, respectively

A portion of the mixed 6-deoxyhexoses (10 mg) was reduced ($NaBH_4$) and acetylated[9]. On g l p c (170°), the product gave two peaks having T_A 0 55 and 0 61 (ratio 2 3), corresponding in retention times to authentic 1,2,3,4,5-penta-*O*-acetyl-6-deoxy-D-allitol and 1,2,3,4,5-penta-*O*-acetyl-6-deoxy-D-altritol, respectively

The mixed 6-deoxyhexoses (0 5 g) were separated by cellulose-column chromatography (35 × 2 5 cm) with 1-butanol–water (10 1 *v/v*) as the mobile phase, to give the following chromatographically pure products

6-Deoxy-D-altrose 6-Deoxy-D-altrose (0 26 g) was obtained as a syrup that gave a single spot on paper chromatography (R_{Gal} 4 63, solvent *A*); it had $[\alpha]_D$ +15° (*c* 1 9, water) [lit [10] $[\alpha]_D$ +20° (water)] The glycose (0 1 g), on reduction ($NaBH_4$), afforded crystalline 6-deoxy-D-altritol having m p 120° (lit [10] m p. 117–120° and[11] m p 116–119°).

6-Deoxy-D-allose The second component to be eluted from the column (0 15 g) was 6-deoxy-D-altrose, which gave a single spot on paper chromatography (R_{Gal} 3.52)

and had $[\alpha]_D$ −1 2° (*c* 1 6, water) [lit [12] $[\alpha]_D$ +1 2° (water)] The glycose, on treatment with phenylhydrazine, afforded 6-deoxy-D-*ribo*-hexose phenylosazone having m p and mixture m.p 182–184° (decomp) (lit [12] m p 184–185°) and had an i r spectrum (KBr disc) identical with that of an authentic derivative

*2-Acetamido-2,6-dideoxy-*D*-allose and 2-acetamido-2,6-dideoxy-*D*-altrose* — The mixed 1,6-dideoxy-1-nitro-D-allitol and 1 6-dideoxy-1-nitro-D-altritol (3 8 g) from the first experiment, in acetic anhydride (40 ml), was treated with one drop of concentrated sulfuric acid and the mixture was heated for 30 min on a boiling water-bath The cooled mixture was poured onto crushed ice (200 ml) and after one h the water was decanted from the oily product The latter was then taken up in chloroform (300 ml) The chloroform extract was washed with water (3 × 50 ml), dried (anhyd Na_2SO_4), and concentrated to a syrup (5 8 g) containing 2,3,4,5-tetra-*O*-acetyl-1,6-dideoxy-1-nitro-D-allitol and 2,3,4,5-tetra-*O*-acetyl-1,6-dideoxy-1-nitro-D-altritol

The foregoing mixture of penta-*O*-acetyl-1,6-dideoxy-1-nitrohexitols (5 5 g) was dissolved in dry methanol (60 ml) and the solution, cooled externally in ice, was saturated with dry ammonia gas, and the mixture was then kept for 18 h at 20° The concentrated reaction-mixture was triturated with hot chloroform (3 × 30 ml) to remove acetamide, and the residual syrup (3 g), dissolved in a solution of $Ba(OH)_2$ $8H_2O$ (3 7 g) in water (60 ml), was added dropwise with stirring to a solution of concentrated sulfuric acid (3 5 ml) in water (30 ml) After 18 h at room temperature, the reaction mixture was neutralized ($BaCO_3$), filtered, and the filtrate was passed down a column of mixed Rexyn 101 (H^+) and RG6 (OH^-) ion-exchange resins (25 ml) Concentration of the eluate and water washings afforded a syrup (1 4 g) which, on paper chromatography (solvent *A*), revealed two spots having R_{Gal} 3 13 and 3 34, corresponding to 2-acetamido-2,6-dideoxy-D-allose and 2-acetamido-2,6-dideoxy-D-altrose, respectively (visual ratio 2 1) A portion of the product (3 mg), after reduction ($NaBH_4$) and acetylation[13], on g l p c. (210°) gave two peaks having T_{GNolAc} 0 22 and 0 27, corresponding to 2-acetamido-1,3,4,5-tetra-*O*-acetyl-2,6-dideoxy-D-allitol (64 5%) and 2-acetamido-1,3,4,5-tetra-*O*-acetyl-2,6-dideoxy-D-altritol (35 5%), respectively

The foregoing, mixed 2-acetamido-2,6-dideoxyhexoses (1 3 g) were separated by cellulose-column chromatography (65 × 3 cm) with 1-butanol–water (10 1 *v/v*) as the mobile phase to give the following products

*2-Acetamido-2,6-dideoxy-*D*-altrose* The first compound to be eluted from the column was 2-acetamido-2,6-dideoxy-D-altrose (0 38 g), which remained a syrup, $[\alpha]_D$ −12° (*c* 1, water) On paper chromatography it gave a single spot having R_{Gal} 3 34 (solvent *A*)

Anal Calc for $C_8H_{15}NO_5$ C, 46 82; H, 7 37, N, 6 83 Found. C, 46 90, H, 7 42, N, 6 99

The reduced and acetylated glycose[13], on g l p c (210°) gave a single peak having T_{GNolAc} 0 27 A portion of the glycose (10 mg) was hydrolyzed with 1 5M hydrochloric acid (1 ml) for 1 h at 95° and the concentrated product, on degradation

with ninhydrin[14] gave 5-deoxy-D-ribose, identified by paper chromatography and by g l p.c [15]

2-Acetamido-2,6-dideoxy-D-allose The second component eluted from the column was 2-acetamido-2,6-dideoxy-D-allose (0 74 g), which was readily crystallized from ethanol The crystalline 2-acetamido-2,6-dideoxy-D-allose had m p 169—170° and $[\alpha]_D$ −88 5→ −76 5° (*c* 0 4, water) unchanged after further recrystallization

Anal. Calc for $C_8H_{15}NO_5$. C, 46 82, H, 7.37; N, 6 83 Found C, 46 66, H, 7 53, N, 6 66

On paper chromatography the glycose gave a single spot having R_{Gal} 3 13 (solvent *A*), and g l.p.c. (210°) of the reduced and acetylated glycose[13] gave a single peak having T_{GNolAc} 0 22, corresponding to 2-acetamido-1,3,4,5-tetra-*O*-acetyl-2,6-dideoxy-D-allitol.

2-Amino-2,6-dideoxy-D-allose hydrochloride 2-Acetamido-2,6-dideoxy-D-allose (0.12 g) was hydrolyzed with 3M hydrochloric acid (5 ml) for 3 h at 100°. Concentration of the solution gave 2-amino-2,6-dideoxy-D-allose hydrochloride (98 mg) which, after recrystallization from a methanol –acetone mixture, had m p 133° (decomp), $[\alpha]_D$ +4° (*c* 0 9, water) [lit[5] m p 135° (decomp), $[\alpha]_D$ +2° (water)]

Anal. Calc for $C_6H_{14}ClNO_4$ C, 36 09, H, 7 07, N, 7 01 Found C, 36 30, H, 7 13; N, 6 93

On paper chromatography, the glycose gave a single ninhydrin-positive spot having R_{GN} 1.73 (solvent *B*)

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