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Note

Synthesis of benzyl 2,3,4-tri-acetamido-2,3,4,6-tetradeoxy-α-D-galacto-pyranoside

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In connection with other work pursued in our laboratory, a sample of 2,3,4-triacetamido-2,3,4,6-tetradeoxyhexitol was required; the compound with the D-*galacto* configuration (**6**) was prepared as follows. Treatment of benzyl 2-acetamido-2-deoxy-α-D-allopyranoside[1] (**1**) with methanesulfonyl chloride in pyridine gave the tri-*O*-mesyl derivative **2**, which was converted by reduction with sodium borohydride[2] into benzyl 2-acetamido-2,6-dideoxy-3,4-di-*O*-methylsulfonyl-α-D-allopyranoside (**3**). The dimethanesulfonate **3** was transformed into benzyl 2,3,4-triacetamido-2,3,4,6-tetradeoxy-α-D-galactopyranoside (**5**) *via* the diazido derivative **4** by catalytic reduction of the latter, followed by *N*-acetylation. The ^{1}H-n.m.r. spectrum (400 MHz) of the glycoside **5** was in agreement with the assigned structure ($J_{2,3}$ 12, $J_{3,4}$ 3.6, and $J_{4,5}$ 1 Hz). To obtain the alditol **6**, the aglycon was removed from **5** by hydrogenation, and the free sugar was reduced by treatment with borohydride; after acetylation, it gave, upon g.l.c., a single peak whose mass spectrum was determined.

EXPERIMENTAL

General methods. — Evaporations were carried out *in vacuo* at 40°. Melting points were determined with a Kofler hot-plate. Optical rotations were measured with a Perkin–Elmer 141 polarimeter. ^{1}H-N.m.r. spectra were recorded at 60 MHz with a Varian T 60 instrument with chloroform-*d* (containing 1% of Me_4Si as internal standard) as the solvent; those at 400 MHz were recorded with an instrument built by Dr. E. Kan and his colleagues at the Institut d'Électronique, Université de Paris-Sud, Centre d'Orsay, France. ^{13}C-N.m.r. spectra were recorded with a Varian CFT 20 spectrometer operating at 20 MHz in the Fourier-transform mode. T.l.c. was performed on silica gel (F-1500 LS_{254}, Schleicher and Schüll); compounds were located by spraying with 10% sulfuric acid in ethanol and heating. Gas–liquid chromatography was performed on a column (3.2 × 1500 mm, stainless

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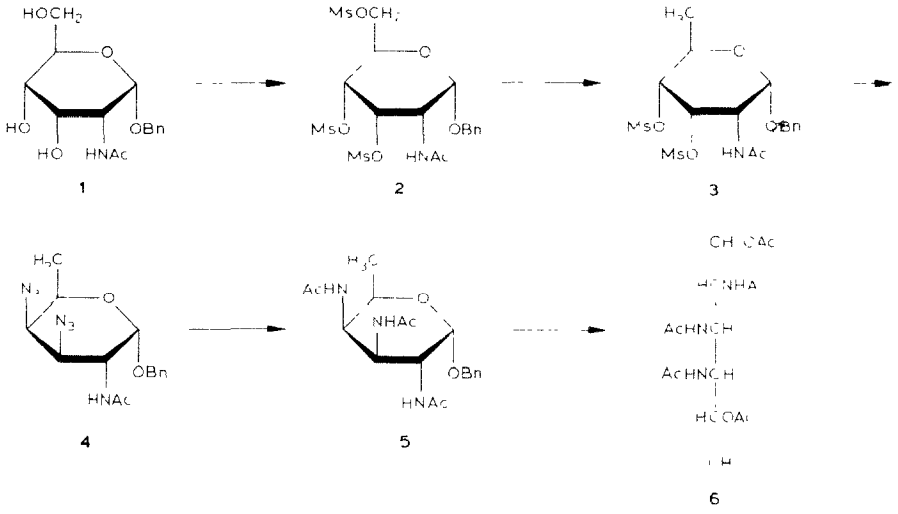


steel) packed with 3% of methyl silicone SE 30 on Varaport (100–200 mesh) at 250° (isothermal) in a Varian Aerograph, Model 2700, instrument coupled to a DuPont 21-492 double-focusing, medium-resolution, mass spectrometer, with nitrogen as carrier gas, an injector temp. of 165°, and a detector temp. of 280°.

Benzyl 2-acetamido-2-deoxy-3,4,6-tri-O-methylsulfonyl-α-D-allopyranoside (**2**). — Methanesulfonyl chloride (47 mL) was added to a cooled solution (0°) of benzyl 2-acetamido-2-deoxy-α-D-allopyranoside[1] (**1**, 19 g) in anhydrous pyridine (250 mL); the mixture was kept for 2 days at 0°, and then poured under constant stirring into ice–water. The precipitate formed was filtered off, dissolved in dichloromethane, and the dried (Na_2SO_4) solution concentrated to a yellow syrup (22 g, 66%). A sample (0.2 g) crystallized from methanol after purification by l.c. under elevated pressure (silica gel, 10:1, v/v, ethyl acetate–hexane), m.p. 169–170°, $[\alpha]_D^{20}$ +95° (*c* 0.3, chloroform); ^{1}H-n.m.r. (60 MHz): δ 7.33 (s, 5 H, arom.), 3.16, 3.13, 3.06 (3 s, 9 H, 3 SO_2CH_3), and 1.96 (s, 3 H, $NHCOCH_3$).

Anal. Calc. for $C_{18}H_{27}NO_{12}S_3$: C, 39.63; H, 4.98; N, 2.57. Found: C, 39.44; H, 4.94; N, 3.03.

Benzyl 2-acetamido-2,6-dideoxy-3,4-di-O-methylsulfonyl-α-D-allopyranoside (**3**). — Sodium borohydride was added to a solution of **2** (21 g) in dimethyl sulfoxide[3] (110 mL), and the reaction mixture stirred for 2 h at 85°. The cooled mixture was poured into ice–water (200 mL) and made neutral with 1% aqueous acetic acid. The resulting brown, gummy precipitate was filtered off and dissolved in dichloromethane, and the solution washed with 1% aqueous acetic acid and water, dried (Na_2SO_4), and concentrated to a syrup. Chromatography on silica gel (10:1, v/v, ethyl acetate–hexane) gave, after evaporation of the solvent, a clear syrup (9.5 g, 54%), $[\alpha]_D^{20}$ +99° (*c* 0.58, chloroform); ^{1}H-n.m.r. (60 MHz): δ 7.41 (s, 5 H, arom.), 3.13 (s, 6 H, SO_2CH_3), 2.0 (s, 3 H, $NHCOCH_3$), and 1.28 (d, 3 H, H_3-6).

Anal. Calc. for $C_{17}H_{25}NO_9S_2$: C, 45.23; H, 5.58; N, 3.10. Found: C, 45.66; H, 5.69; N, 3.20.

*Benzyl 2-acetamido-3,4-diazido-2,3,4,6-tetradeoxy-α-*D*-galactopyranoside* (**4**). — A suspension of **3** (1.45 g) and sodium azide (3 g) in freshly distilled dimethyl sulfoxide (15 mL) was heated for 2 h to 170° under nitrogen. The mixture was cooled and poured into water (70 mL). The solution was extracted with dichloromethane, and the organic layer washed with water, dried (Na_2SO_4), and evaporated to dryness. The residue (620 mg, 56%) crystallized from ethyl acetate, m.p. 204–206°, $[\alpha]_D^{20}$ +78° (*c* 0.535, chloroform); ^{1}H-n.m.r. (60 MHz): δ 7.38 (s, 5 H, arom.), 1.96 (s, 3 H, NHAc), and 1.27 (d, 3 H, H_3-6).

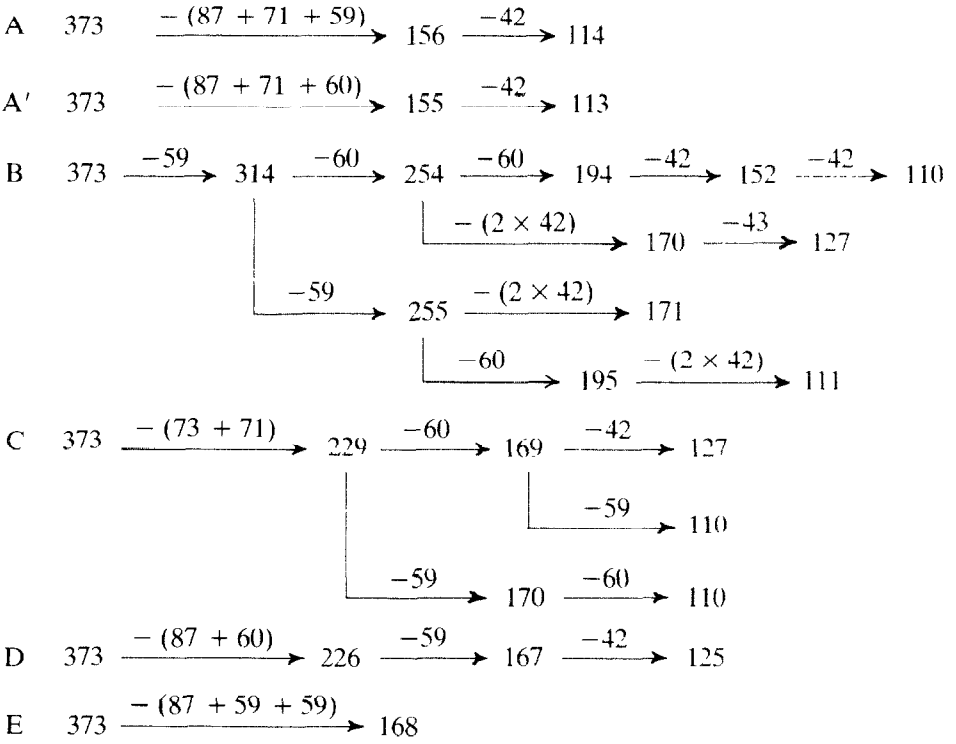
Anal. Calc. for $C_{15}H_{19}N_7O_3$: C, 52.17; H, 5.54; N, 28.40. Found: C, 52.28; H, 5.61; N, 28.29.

*Benzyl 2,3,4-triacetamido-2,3,4,6-tetradeoxy-α-*D*-galactopyranoside* (**5**). — The diazido derivative **4** (150 mg) was dissolved in warm methanol (10 mL), and hydrogen was bubbled for 90 min through the cooled (20°) and stirred solution, to which 10% palladium-on-carbon catalyst (100 mg) had been added. The catalyst was filtered off and acetic anhydride (2 mL) added. The mixture was evaporated to dryness by codistillation with toluene. Purification of the residue on a column of silica gel (1:1, v/v, ethanol–ethyl acetate) gave the crystalline triacetamido derivative **5** (105 mg, 64%), m.p. 233°, $[\alpha]_D^{20}$ +158° (*c* 0.54, ethanol); ^{1}H-n.m.r. (400 MHz), δ 7.31 (m, 5 H, arom.), 6.78 (d, 1 H, $J_{NH,H-4}$ 10 Hz, NH–C-4), 6.55 (dd, 2 H, $J_{NH,H-2}$ 8, $J_{NH,H-3}$ 8 Hz, NH–C-2 and –C-3), 4.91 (d, 1 H, $J_{1,2}$ 3.6 Hz, H-1), 4.72 (d, 1 H, $J_{vic.}$ 11.75 Hz, PhCH_2), 4.59 (m, 1 H, $J_{3,4}$ 3.6 Hz, H-3), 4.52 (d, 1 H, $J_{vic.}$ 11.75 Hz, PhCH_2), 4.31 (m, 1 H, $J_{4,5}$ 1 Hz, H-4), 4.24 (dd, 1 H, $J_{5,6}$ 6.6 Hz, H-5), 4.18 (m, 1 H, $J_{2,3}$ 12, $J_{NH,H-2}$ 8 Hz), 2.18 (s, 3 H, NHCOCH_3), 2.0 (s, 6 H, 2 NHCOCH_3), and 1.14 (d, 3 H, $J_{6,5}$ 6.6 Hz, H_3-6); ^{13}C-n.m.r. ($CDCl_3$): δ 172.16, 171.42, 170.85 (C–O), 137.02 (quaternary arom.), 128.29, 127.74, 127.53 (arom. CH), 96.28 (C-1), 69.51 CH_2-Ph), 65.50 (C-5), 51.62, 49.69, 49.11 (C-2, -3, and -4), 22.91, 22.80 (CH_3CO), and 16.38 (C-6).

Anal. Calc. for $C_{19}H_{27}O_5N_3$: C, 60.46; H, 7.20; N, 11.14; Found: C, 60.52; H, 7.23; N, 11.69.

*Triacetamido-1,5-di-*O*-acetyl-2,3,4-2,3,4,6-tetradeoxy-*D*-galactitol* (**6**). — A solution of **5** (15 mg) in methanol (10 mL) was hydrogenated for 48 h in the presence of 10% palladium-on-carbon catalyst (50 mg), the progress of the reaction being monitored by t.l.c. (1:1, v/v, ethanol–ethyl acetate). After removal of the catalyst, an aqueous solution (5 mL) of sodium borohydride (5 mg) was added, and the mixture kept for 2 h at room temperature. Cations were removed with Dowex 50 (H^+) resin, the resin was filtered off, the filtrate evaporated to dryness, and methanol (5 mL) evaporated three times from the residue. Pyridine (5 mL) and acetic anhydride (2 mL) were added, and the solution was kept for 20 h at 20°. The solvents were removed, and the residue, dissolved in ethyl acetate (200 μL), was analyzed by g.l.c.–m.s.; m.s. (% of base peak): *m/z* 314 (6), 255 (6), 254 (12), 230 (5), 229 (25), 226 (5), 195 (5), 194 (13), 170 (33), 168 (18), 156 (53), 155 (76), 152 (7), 151 (7), 142 (10), 139 (12), 137 (7), 135 (5), 128 (8), 127 (31), 125 (22), 114 (11), 113 (59), 111 (10), 110 (27), 109 (31), 101 (9), 100 (8), 99 (20), 98 (20), 97

(17), 96 (34), 95 (12), 85 (26), 84 (21), 83 (23), 74 (15), 71 (12), 70 (15), 69 (76), 68 (12), 60 (14), 59 (9), 58 (12), 57 (26), 56 (19), and 43 (100)); all peaks > 5% of the base peak are listed. The main fragmentation pathways (A and A′, see Scheme 1) appear to be due to loss of the fragment C-4–C-5–C-6 (15 + 72 + 71) and acetic acid (60) or acetamide (59), leading to the most intense peaks *m/z* 155 and 156 of the spectrum (the base peak is, as expected, *m/z* 43), from which *m/z* 113 and 114 were formed by loss of ketene. Other fragments seem to arise by patterns indicated in Scheme 1. The fragmentation pattern was not checked by precise mass measurements and should, therefore, be considered as tentative.



Scheme 1 Suggested fragmentation pathways of **6**, M = 373

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