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Note

Synthesis of 6-*O*-β-D-galactopyranosyl-D-galactose and isolation of a (1→6)-linked D-galactan*†

ELIZABETH E. LEE, GAY KEAVENEY, ANGELA HARTIGAN, AND PROINNSIAS S. O'COLLA
Chemistry Department, University College, Galway (Ireland)
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A new route towards the synthesis of regular β-D-glucans by zinc chloride-catalysed polycondensation of partially acetylated D-glucopyranose derivatives has been reported[1,2]. Similar polymerisation of α (and β)-D-mannose 1,2,3,4-tetra-acetates yielded two polysaccharide preparations which were shown to be mainly (1→6)-α-D-linked polymers[3]. A further application of the technique to the polymerisation of 1,2,3,4-tetra-*O*-acetyl-β-D-galactopyranose is now reported.

Hydrogenolysis of tetra-*O*-acetyl-6-*O*-benzyl-β-D-galactopyranose (**1**), prepared from 6-*O*-benzyl-α-D-galactose[4], gave crystalline 1,2,3,4-tetra-*O*-acetyl-β-D-galactopyranose (**2**). When compound **2** was methylated with diazomethane–boron trifluoride etherate[5] and the product deacetylated, crystalline 6-*O*-methyl-D-galactose was the only sugar isolated (49%), and a useful preparation of this methyl sugar is thereby provided. Compound **2** yielded a crystalline 6-phenylcarbamate. The synthesis of 1,2,3,4-tetra-*O*-acetyl-D-galactopyranose[6,7] (*via* 1,2,3,4-tetra-*O*-acetyl-6-*O*-trityl-β-D-galactopyranose[8]) has been reported, but no physical constants were given.

Chromatography indicated that, in the melt-polymerisation of 1,2,3,4-tetra-*O*-acetyl-β-D-galactopyranose with 5% of zinc chloride, oligo- and poly-saccharides were readily formed. A polygalactose {6.6%, $[\alpha]_D$ +13° (water)} was isolated after polymerisation (at 125–130° for 20 min), deacetylation, and dialysis. Fractionation of a portion of the dialysate on Whatmann 3MM paper gave syrupy 6-*O*-β-D-galactopyranosyl-D-galactopyranose. The optical rotation of the polymer was taken as evidence for a preponderance of β-D linkages, in accordance with the probable reaction mechanism[2]. Synthetic galactans prepared by non-specific procedures are highly branched and have rotations[9,10] of +42° to +70°. The polygalactose contained no chromatographically mobile sugars, and yielded galactose on acid hydrolysis. Methylation analysis showed that the polygalactose was mainly (1→6)-linked. 2,3,6-Tri-*O*-methylgalactose (characterised as the methyl glycoside by g.l.c.)

*Dedicated to the memory of Professor Edward J. Bourne.
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was a minor product in the methylation analysis, and the proportion of tri- to tetra-*O*-methylgalactose was ~1:8.

EXPERIMENTAL

The standard methods have been described[1,3] except that optical rotations were determined with a Perkin–Elmer Model 241 Polarimeter. Paper chromatography was performed as described[3], except that solvent *C* was ethyl acetate–pyridine–water (10:4:3). The polymerisation technique is described in Part I.

1,2,3,4-Tetra-O-*acetyl-6*-O-*benzyl-β*-D-*galactopyranose* (**1**). — 6-*O*-Benzyl-α-D-galactose (2 g), M_G 0.76, was treated with acetic anhydride (20 ml) and anhydrous sodium acetate (1 g). The mixture was heated under reflux for 1 h and then poured into ice–water, and **1** was isolated in the usual way as a syrup (2.84 g), a portion of which (0.70 g) was fractionated on a column (22 × 2 cm) of silica gel. Fractions (25 ml) were collected and concentrated, and the residues were examined by t.l.c. Fractions 5–23, eluted with ether–benzene (5:95), were concentrated to a syrup, $[\alpha]_D$ +3.6° (*c* 1.01, chloroform), which crystallised from ethanol on long standing, giving **1**, m.p. 104–106°.

Anal. Calc. for $C_{21}H_{26}O_{10}$: C, 57.53; H, 5.94. Found: C, 56.41; H, 5.82.

1,2,3,4-Tetra-O-*acetyl-β*-D-*galactopyranose* (**2**). — A solution of compound **1** (2.4 g) in ethanol (100 ml) was hydrogenated over 10% palladium-on-charcoal (1 g) at atmospheric pressure. Consumption of hydrogen had ceased after 18 h. The catalyst was removed, and the filtrate was concentrated to a syrup (1.85 g, 97%) that crystallised from isopropyl ether–ethanol, giving **2** as rectangular crystals, m.p. 142–143°, $[\alpha]_D$ +33° (*c* 1.2, chloroform). N.m.r. data ($CDCl_3$): τ 4.30 (d, $J_{1,2}$ 7 Hz, H-1); 4.62 (t, $J_{1,2}$ 7, $J_{2,3}$ 8 Hz, H-2); 5.00 (doublet of doublets, $J_{3,2}$ 8, $J_{3,4}$ 3.5 Hz, H-3); 5.70 (m, H-6); 5.90 (overlapping doublets, $J_{4,3}$ 3.5, $J_{4,5}$ <1.5 Hz, H-4); 6.13 (t, $J_{5,6}$ 6 Hz, $J_{4,5}$ <1.5 Hz caused broadening of t peaks, H-5); 7.90–8.00 (12 H, overlapping signals, 4 AcO).

Anal. Calc. for $C_{14}H_{20}O_{10}$: C, 48.28; H, 5.75. Found: C, 47.95; H, 5.78.

1,2,3,4-Tetra-O-*acetyl-6*-O-*methyl-β*-D-*galactopyranose* (**3**). — A solution of **2** (490 mg) in dichloromethane (12 ml) was cooled to −5°. Boron trifluoride etherate (0.02 ml) was added and the solution was kept at −5° during the addition of excess of diazomethane in dichloromethane. The mixture was then kept for 1 h to allow all colour to discharge. T.l.c. then showed 50% conversion into the faster-moving product. Polymethylene was filtered off, and the filtrate concentrated. A solution of the syrupy residue in benzene (20 ml) was extracted with water (5 × 10 ml) to remove unchanged starting material, and then concentrated to give **3** as a syrup (0.30 g) that showed only one component on t.l.c., had $[\alpha]_D$ +27° (*c* 1.56, chloroform), and showed no i.r. absorption for hydroxyl.

Anal. Calc. for $C_{15}H_{22}O_{10}$: C, 49.72; H, 6.08. Found: C, 49.23; H, 6.33.

6-O-*Methyl*-D-*galactose.* — A solution of **3** (115 mg) in methanol (2 ml) was treated with 0.1M methanolic sodium methoxide (1 ml) for 4 h at room temperature.

Cations were removed with Amberlite IR-120(H^+) resin, and the solution was then evaporated to give the title compound (62 mg), which was crystallised from ethanol; m.p. 118–122°, $[\alpha]_D$ +75° (*c* 0.24, water); lit.[11] m.p. 123°, $[\alpha]_D$ +66° (water).

*1,2,3,4-Tetra-*O*-acetyl-6-*O*-phenylcarbamoyl-β-*D*-galactopyranose* (**4**). — To a solution of **2** (200 mg) in dry toluene (4 ml), phenyl isocyanate (0.5 ml) and dry pyridine (0.75 ml) were added. After 24 h at room temperature, t.l.c. showed 90% conversion into a faster-moving product. The solution was treated with water to decompose excess of phenyl isocyanate, kept for 1 h at room temperature, filtered, and concentrated to a syrup that was extracted with chloroform (30 ml). The extract was filtered, washed to remove pyridine, dried, and concentrated to a syrup, $[\alpha]_D$ +21° (*c* 0.86, chloroform), which was fractionated on a column (24 × 2 cm) of silica gel. First, penta-*O*-acetyl-β-D-galactopyranose was eluted with benzene, and then compound **4** with ether–benzene (1:9 → 15:85). After crystallisation from absolute alcohol, **4** had m.p. 158–161°.

Anal. Calc. for $C_{21}H_{25}NO_{11}$: C, 53.96; H, 5.35; N, 2.99. Found: C, 52.75; H, 5.07; N, 2.92.

*Polymerisation of 1,2,3,4-tetra-*O*-acetyl-β-D-galactopyranose.* — The tetra-acetate (15 g) with zinc chloride (750 mg) was heated for 20 min at 125°/20 mmHg. The melt was deacetylated, and the water-soluble material was isolated as a syrup that was redissolved in water (100 ml). The solution was filtered, and dialysed in cellophane against frequent changes of distilled water for 48 h. The dialysate obtained during the first 16 h was concentrated, and deionised with Biodeminrolit. A portion of the derived neutral material was separated by chromatography on Whatman No. 1 paper (solvent *C*). A plot of log $(1/R_F - 1)$ against presumed d.p. gave a straight line for the main sugars resolved. The residual material (0.9 g) was fractionated by preparative chromatography on Whatman 3MM paper (solvent *C*) The disaccharide 6-*O*-β-D-galactopyranosyl-D-galactopyranose was isolated as a syrup (170 mg) having a chromatographic mobility identical with that of authentic material provided by Dr. G. A. Adams. The disaccharide had $[\alpha]_D$ +29° (*c* 0.72, water), R_{GAL} 0.32 and 0.35 (solvents *B* and *C*, respectively), and M_G 0.80; lit.[12] $[\alpha]_D$ +34°, R_{GAL} 0.30 and 0.37 (solvents *B* and *C*); lit.[13] M_G 0.83.

The polymer solution was further dialysed against running tap-water for 30 h, concentrated to ~15 ml, and treated with a six-fold volume of ethanol. The gelatinous precipitate settled on the addition of acetone, and was collected on a sintered-glass funnel as an off-white powder (500 mg), $[\alpha]_D$ +13° (*c* 0.085, water). The galactan was non-mobile on development for 48 h in solvent *A*, and, on hydrolysis, gave galactose only.

Methylation analysis of the galactan. — The method consisted of two Haworth methylations, and one Kuhn and Baer methylation. The infrared spectrum of the product showed no absorption peak at 3400 cm^{-1} (OH). P.c. (solvent *D*) of a hydrolysate of the methylated material revealed 2,3,4,6-tetra-*O*-methyl-D-galactose (R_G 0.86; lit.[14] R_G 0.88) and 2,3,4-tri-*O*-methyl-D-galactose (red spot, R_G 0.71; lit.[14] 0.74). A third spot having R_G 0.80 indicated the presence of 2,3,6-tri-*O*-methyl-

D-galactose, which has an R_G value higher than those of the other pyranose isomers[15]. G.l.c. of the derived methyl galactosides indicated the presence of 2,3,4,6-tetra-*O*-methyl-D-galactose (T value 1.62; lit.[14] 1.64), 2,3,4-tri-*O*-methyl-D-galactose (T 5.23s; lit.[14] 5.14), and 2,3,6-tri-*O*-methyl-D-galactose (T 2.47, 3.33, 3.90; lit.[16] 2.30, 3.10, 3.58). The respective areas of the peaks given by the methyl tetra and tri-*O*-methyl-galactosides indicated a ratio of 1:8.

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