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Note

Convenient syntheses of 2-*O*-methyl- and 3-*O*-methyl-D-galactose

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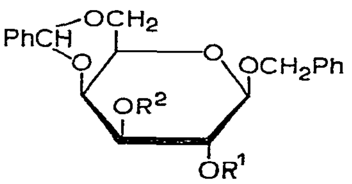
Samples of 2-*O*-methyl-D-galactose (1) and 3-*O*-methyl-D-galactose (2) were required as part of a study[1] of the structure of the mycelial wall of *Penicillium charlesii* G. Smith Previously reported syntheses of **1**[2,3] and **2**[3,4] from D-galactose are laborious, or often involve chromatographic purification, at many stages, with low overall yields. An improved procedure for the synthesis of **2** has been described[5]

Benzoylation of benzyl 4,6-*O*-benzylidene-β-D-galactopyranoside (3) with *N*-benzoylimidazole has been shown[6] to give the corresponding 3-benzoate **4** in excellent yield (89–93%). Treatment[7] of **4** with dilute alkali yields the corresponding 2-benzoate **5**, also in high yield Diazomethane, with boron trifluoride etherate as a catalyst[8], is an effective methylation reagent for partially acylated carbohydrate derivatives that are susceptible to acyl migration under mildly basic conditions. Convenient syntheses of **1** and **2**, in good yield from benzoates **4** and **5**, using this reagent, are now described.

Treatment of the 3-benzoate **4**, in dichloromethane, with excess diazomethane in the presence of boron trifluoride etherate at −5° gave compound **6** as a homogeneous syrup (t l c) This product was debenzoylated with lithium aluminium hydride in tetrahydrofuran to give 74% of benzyl 4,6-*O*-benzylidene-2-*O*-methyl-β-D-galactopyranoside (7) Exhaustive hydrogenation of **7** over a palladium catalyst gave crystalline 2-*O*-methyl-D-galactose (1), which was characterised as 2-*O*-methyl-*N*-phenyl-D-galactopyranosylamine



3 $R^1 = R^2 = H$
4 $R^1 = H, R^2 = Bz$
5 $R^1 = Bz, R^2 = H$
6 $R^1 = Me, R^2 = Bz$
7 $R^1 = Me, R^2 = H$
8 $R^1 = Bz, R^2 = Me$
9 $R^1 = H, R^2 = Me$

Similar methylation of the 2-benzoate **5** with the diazomethane reagent yielded 84–87% of benzyl 2-*O*-benzoyl-4,6-*O*-benzylidene-3-*O*-methyl-β-D-galactopyranoside (8) This product was debenzoylated with sodium methoxide in methanol to give benzyl 4,6-*O*-benzylidene-3-*O*-methyl-β-D-galactopyranoside (9), which, on catalytic hydrogenation over palladium oxide, yielded 3-*O*-methyl-α-D-galactose (2) The product was characterised as 3-*O*-methyl-D-*lyxo*-hexose phenylosazone

Methylation of compound **4** with methyl iodide–silver oxide in *N,N*-dimethylformamide yielded a mixture of four components (t l c), no attempt at separation was made Similar treatment of the 2-benzoate **5** gave compound **8** in 41% yield The product was difficult to purify due to the presence of the isomer **6**, presumably formed after migration of the O-2 benzoyl group in **5** to position 3 under the mildly alkaline conditions It has been shown[7] that, in the interconversion of **4** and **5** under homogeneous conditions, **5** was slightly the more-stable isomer

EXPERIMENTAL

Descending paper chromatography and t l c were performed as described previously[9] I r spectra were determined for Nujol mulls Dichloromethane was redistilled from phosphorus pentaoxide before use All melting points are uncorrected

*Benzyl 3-*O*-benzoyl-4,6-*O*-benzylidene-2-*O*-methyl-β-*D*-galactopyranoside* (**6**) — Compound **4**[6] (1.5 g) dissolved in dichloromethane (30 ml) at −5°, was treated with boron trifluoride etherate (0 05 ml) and, at the same temperature, diazomethane[8] in dichloromethane was then added until a faint yellow colour persisted in the solution for 10–15 sec After 1 h at 0°, polymethylene was filtered off, and the filtrate was washed successively with saturated, aqueous sodium hydrogen carbonate and water, dried (Na_2SO_4), and evaporated to yield **6** as a syrup (1 48 g, 96%), $[\alpha]_D^{24}$ +61 5° (*c* 1 06, dichloromethane), ν_{max} 1715 cm^{-1} (COPh) (Found C, 69 5, H, 5 5 $C_{28}H_{28}O_7$ calc · C, 70 6, H, 5 9%)

*Benzyl 4,6-*O*-benzylidene-2-*O*-methyl-β-*D*-galactopyranoside* (**7**) — A solution of **6** (1 1 g) in dry tetrahydrofuran (40 ml) was added dropwise with stirring to a mixture of lithium aluminium hydride (1 g) in tetrahydrofuran (30 ml), and the mixture was then heated under reflux for 3 h Cautious addition of water (6 ml) gave a gelatinous precipitate which was separated by filtration and washed well with hot dichloromethane (100 ml) The combined filtrate and washings were concentrated *in vacuo*, and the residue was recrystallised from propan-1-ol to give **7** (0 64 g, 74%), m p. 106–110°, $[\alpha]_D^{23}$ −41 2° (*c* 0 9, dichloromethane) (Found C, 67 6; H, 6 8 $C_{21}H_{24}O_6$ calc · C, 67 7, H, 6 5%)

*2-*O*-Methyl-*D*-galactose* (**1**) — Compound **7** (500 mg), in *p*-dioxane (30 ml), ethanol (30 ml), and glacial acetic acid (5 ml) was hydrogenated exhaustively in the presence of palladium (from 1 g of the oxide). The filtered mixture was concentrated *in vacuo*, and the residue was recrystallised from ethanol–ether to yield **1** (185 mg, 71%), m p 145–148°, $[\alpha]_D^{23}$ +81 4° (equil , *c* 1, water), R_{GAL} 1 70, lit [2] m p 147–149°, $[\alpha]_D$ +82 6° (equil)

A small portion of the product in methanol was treated with one equivalent of redistilled aniline, and the mixture was heated under reflux for 2 h. Evaporation of the solvent and recrystallization of the residue from acetone–light petroleum (60–80°) gave 2-*O*-methyl-*N*-phenyl-D-galactopyranosylamine, m p 162–164°, lit ^{3} m p 165°.

Benzyl 2-O-benzoyl-4,6-O-benzylidene-3-O-methyl-β-D-galactopyranoside (**8**) — A solution of compound 5^7 (2 0 g) in dichloromethane (40 ml) at $-5°$ was treated with diazomethane–boron trifluoride etherate and processed as described for compound **4** The product was recrystallized from propan-2-ol to yield **8** (1 73–1 8 g, 84–87%), m p 168–170°, $[\alpha]_D^{24}$ +42° (*c* 1, chloroform), ν_{max} 1719 cm^{-1} (COPh) (Found C, 70 3, H, 6 0 $C_{28}H_{28}O_7$ calc C 70 6, H, 5 9%)

A solution of compound **5** (1 0 g) in *N,N*-dimethylformamide (3 ml) and methyl iodide (5 ml) was treated with silver oxide (3 0 g), and the mixture was stirred for 56 h at room temperature in total darkness The solids were filtered off and washed with chloroform (100 ml), and the combined filtrate and washings were extracted with 5% aqueous sodium cyanide and water, dried (Na_2SO_4), and evaporated The semicrystalline residue, after five recrystallisations from propan-2-ol, yielded **8** (412 mg, 41%), m p 166–169°, $[\alpha]_D^{23}$ +41 6° (*c* 1 8, chloroform)

Benzyl 4,6-O-benzylidene-3-O-methyl-β-D-galactopyranoside (**9**) — A suspension of compound **8** (1 0 g) in methanol (100 ml) was treated with 2M methanolic sodium methoxide (1 5 ml) at room temperature for 65 h with stirring The homogeneous solution was neutralised with methanol-washed Dowex-50(H^+) resin, the solid was filtered off and washed with methanol, and the combined filtrate and washings were evaporated The crystalline residue was recrystallised from propan-2-ol–dichloromethane to give **9** (652 mg, 83 5%), m p 182–183°, $[\alpha]_D^{24}$ -44 2° (*c* 1 13, dichloromethane) (Found· C, 67 8, H, 6 8 $C_{21}H_{24}O_6$ calc · C, 67 7, H, 6 5%).

3-O-Methyl-D-galactose (**2**) — Compound **9** (500 mg) was hydrogenolysed in the same manner as described for compound **7** The residue crystallized from absolute ethanol, and recrystallization from the same solvent gave **2** (198 mg, 76%), m p 143–146°, $[\alpha]_D^{24}$ +108 2° (equil , *c* 0 8, water), R_{GAL} 1 55, lit.^{4} m p. 146–149°, $[\alpha]_D$ +82 6° (equil)

A solution of compound **2** (21 mg) in 20% aqueous acetic acid (3 0 ml) was heated for 5 h at 100° with freshly distilled phenylhydrazine (35 mg) in ethanol (0 2 ml) and sodium metabisulphite (2 mg) The yellow product, which precipitated on cooling, was recrystallised from water (charcoal treatment) to give 3-*O*-methyl-D-*lyxo*-hexose phenylosazone, m p 176–178°, lit ^{3} m p 176–179°

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