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Note

A novel synthesis of methyl 2-*O*-methyl-α,β-L-fucofuranoside*

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Partially methylated 6-deoxy-L-hexoses are components[1] of immunologically active bacterial polysaccharides. Most of the syntheses of these compounds[2] have been based on naturally occurring but expensive 6-deoxy-L-hexoses. However, there is current interest[3] in routes to L sugars from readily accessible D-hexoses. This approach requires isomerisation at C-5 of a D-hexose; although this transformation can be achieved efficiently, many steps may be involved[4].

We have developed[5] a novel route to 2,6-dideoxy-L-hexoses, particularly for L-daunosamine from D-glucose, in which the epimerisation at C-5 was circumvented by converting C-1/6 of D-glucose into C-6/1 of L-hexose. As a part of a programme on the synthesis of the major phenolic glycolipid[6] [*O*-(2,6-dideoxy-4-*O*-methyl-α-D-*arabino*-hexopyranosyl)-(1→3)-*O*-(4-*O*-acetyl-2-*O*-methyl-α-L-fucosyl)-(1→3)-*O*-(2-*O*-methyl-α-L-rhamnosyl)-(1→3)-2,4-di-*O*-methyl-α-L-rhamnosyl-1-lipid] from *Mycobacterium kansasii*, we have reported[7] the synthesis of the terminal unit, namely, 2,6-dideoxy-4-*O*-methyl-D-*arabino*-hexopyranose. We now report the use of this strategy in a synthesis of methyl 2-*O*-methyl-α,β-L-fucofuranoside (**12**) from commercially available D-glucurono-6,3-lactone[8] (**1**).

The 1,2-*O*-isopropylidene-5-*O*-methyl derivative[9] (**2**) was heated with Amberlite IR-120 (H^+) resin in refluxing dry methanol to give the methyl glycoside **3**. Reaction of **3** with silver oxide and benzyl bromide gave 60% of the 2-*O*-benzyl derivative **4**, which, with an excess of ethanethiol in the presence of conc. hydrochloric acid, gave 71% of the diethyl dithioacetal **5**. Reduction of the lactone in **5** with di-isobutylaluminium hydride for 1 h at −78° gave the lactol **6** which, with Amberlite IR-120 (H^+) resin in boiling methanol, gave the methyl α,β-glycoside **7**. When **7** was stirred with freshly prepared W2 Raney nickel in ethanol for 48 h, the deoxy derivative **8** was obtained (58%). Inversion of the configuration at C-3 in **8** was achieved by treatment of the 3-mesylate **9** with sodium benzoate in *N,N*-dimethylformamide for 40 h at 110°, which gave 75% of the benzoate **10**. The signal (δ 5.31, dd, $J_{2,3}$ 1 Hz) for H-3 in the ^{1}H-n.m.r. spectrum of **10** indicated H-2,3 to be *trans*. *O*-Debenzoylation of **10** with methanolic sodium methoxide

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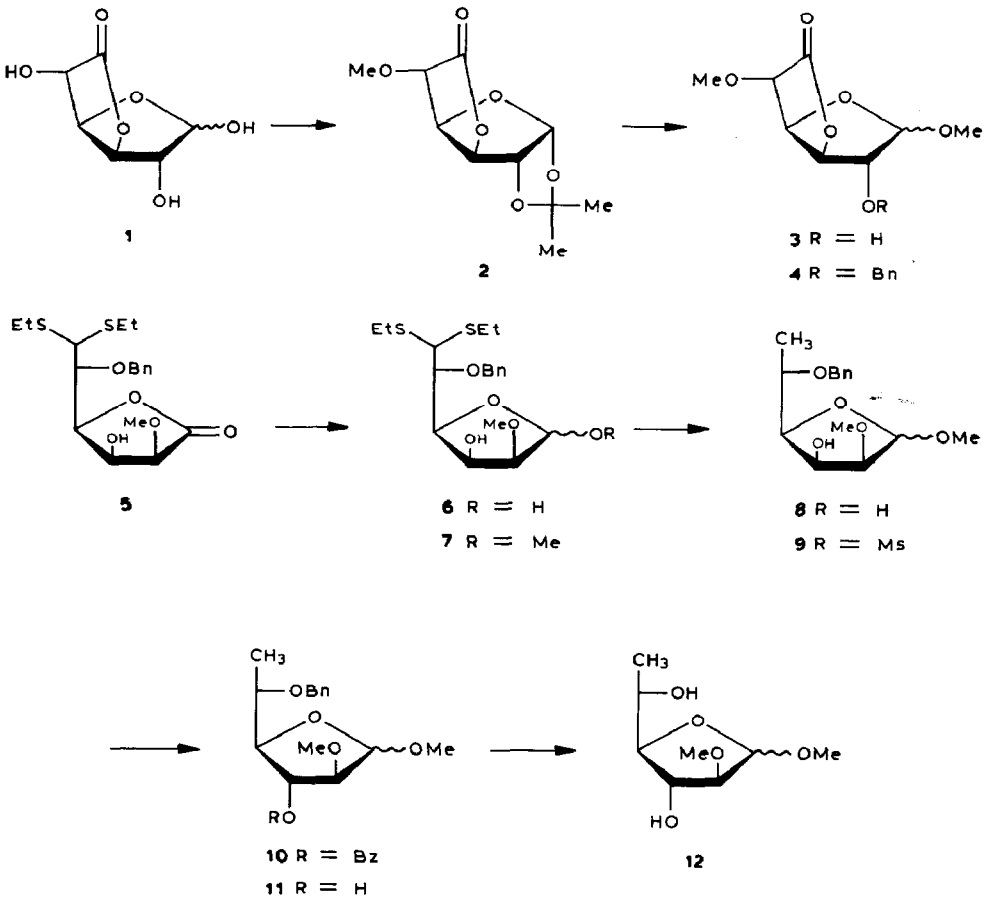

then gave **11**, which is being studied as a receptor for *O*-glycosylation. Treatment of **11** with lithium in liquid ammonia cleaved the benzyl group to afford methyl 2-*O*-methyl-α,β-L-fucofuranoside (**12**, 55%).

EXPERIMENTAL

General. — Solvents were evaporated at <45°. ^{1}H-N.m.r. spectra were obtained with Jeol PMX 90 and Varian FT-80A spectrometers. Mass spectra were obtained using Finnigan Mat 1020B (e.i.) and VG Micromass 7070H (c.i.) spectrometers. Optical rotations were determined with a JASCO DIP 360 polarimeter. Light petroleum refers to the fraction b.p. 60–80°. Silica gel was purchased from the Acme Chemical Company (India). T.l.c. was performed on silica gel (Merck).

Methyl 2-O-benzyl-5-O-methyl-α,β-D-glucofuranosidurono-6,3-lactone (**4**). — A mixture of **2** (ref. 9) (9.0 g, 39.1 mmol) and Amberlite IR-120 (H^+) resin (10.0 g) in dry methanol (100 mL) was heated under reflux for 4 h, then filtered, and concentrated to give **3** (6.7 g, 84%). A mixture of **3** (6.0 g, 29.4 mmol), silver oxide (8.2 g), benzyl bromide

(5.7 g, 33.3 mmol), and benzene (50 mL) was stirred vigorously overnight, then worked-up in the usual manner. Column chromatography (ethyl acetate–light petroleum, 1:3) of the product gave **4** (5.2 g, 60%), isolated as a syrup, $[\alpha]_D$ +6.1° (*c* 1.3, chloroform). ^{1}H-N.m.r. data ($CDCl_3$): δ 3.34, 3.56 (2 s, 6 H, 2 OMe), 4.0 (m, 2 H), 4.53 (s, 2 H, PhCH_2), 4.85 (m, 2 H), 5.00 (s, 1 H, H-1), 7.2 (s, 5 H, Ph). Mass spectrum: *m/z* 263 (M^+ − OMe), 203 (M^+ − Bn).

Anal. Calc. for $C_{15}H_{18}O_6$: C, 61.2; H, 6.1. Found: C, 61.2; H, 6.05.

*2-O-Benzyl-5-O-methyl-*D*-glucurono-6,3-lactone diethyl dithioacetal* (**5**). — A mixture of **4** (4.75 g, 16.1 mmol), ethanethiol (4 mL), and conc. hydrochloric acid (2 mL) was stirred at room temperature overnight, then neutralised with saturated aqueous sodium carbonate, and partitioned between chloroform and water; the chloroform layer was then dried and concentrated. Column chromatography (ethyl acetate–light petroleum, 1:3) of the residue gave **5** (4.45 g, 71%), $[\alpha]_D$ +36° (*c* 1.1, chloroform); ν_{max} 1790 cm^{-1} (lactone), 3500 cm^{-1} (OH). ^{1}H-N.m.r. data ($CDCl_3$): δ 1.23 (m, 6 H, 2 CH_3CH$_2$S), 2.5 (m, 4 H, 2 CH$_3$CH_2S), 3.46 (s, 3 H, OMe), 3.9 (m, 3 H), 4.3 (m, 2 H), 4.56 (ABq, 2 H, CH_2Ph), 7.2 (m, 5 H, Ph). High-resolution mass spectrum: *m/z* 386.1223 (calc. for $C_{18}H_{26}O_5S_2$: *m/z* 386.1221).

*Methyl 2-O-benzyl-5-O-methyl-α,β-*D*-gluco-hexodialdo-6,3-furanoside diethyl dithioacetal* (**7**). — To a solution of **5** (4.2 g, 10.8 mmol) in dry dichloromethane (25 mL) at −78° was added 20% di-isobutylaluminium hydride in hexane (10 mL). After 1 h at −78°, the mixture was worked-up in the usual manner and the product was heated under reflux with Amberlite IR-120 (H^+) resin (5 g) in dry methanol (35 mL) for 3 h. The mixture was filtered and concentrated. Column chromatography (ethyl acetate–light petroleum, 1:3) of the residue gave **7** (3.46 g, 79%), isolated as a syrup, $[\alpha]_D$ +68° (*c* 0.7, chloroform). ^{1}H-N.m.r. data ($CDCl_3$): δ 1.25 (m, 6 H, 2 CH_3CH$_2$S), 2.7 (m, 4 H, 2 CH$_3$CH_2S), 3.37, 3.46 (2 s, 6 H, 2 OMe), 3.7–5.0 (m, 6 H, H-1/6), 7.3 (m, 5 H, Ph).

Anal. Calc. for $C_{19}H_{30}O_5S_2$: C, 56.7; H, 7.5. Found: C, 56.6; H, 7.5.

*Methyl 5-O-benzyl-6-deoxy-3-O-mesyl-2-O-methyl-α,β-*L*-gulofuranoside* (**9**). — A mixture of **7** (3.2 g, 7.9 mmol), freshly prepared W2 Raney nickel (10 g), and ethanol (50 mL) was stirred vigorously for 48 h, then filtered, and concentrated. Column chromatography (ethyl acetate–light petroleum, 1:3) of the residue gave **8** (1.3 g, 58%). Mass spectrum: *m/z* 191 (M^+ − Bn).

Compound **8** (0.80 g, 2.8 mmol) was treated with methanesulfonyl chloride–pyridine for 4 h at room temperature to give **9** (0.74 g, 72%), $[\alpha]_D$ +53° (*c* 1, chloroform). ^{1}H-N.m.r. data ($CDCl_3$): δ 1.28 (d, 3 H, *J* 6.5 Hz, H-6,6,6), 3.12 (s, 3 H, Ms), 3.43, 3.46 (2 s, 6 H, 2 OMe), 3.9 (m, 3 H, H-2,4,5), 4.7–4.9 (m, 3 H, CH_2Ph and H-1), 5.12 (dd, 1 H, *J* 3 and 4.5 Hz, H-3), 7.25 (s, 5 H, Ph). C.i.-mass spectrum: *m/z* 360 (M^+), 329 (M^+ − MeO).

Anal. Calc. for $C_{16}H_{24}O_7S$: C, 53.3; H, 6.7. Found: C, 53.0; H, 6.8.

*Methyl 5-O-benzyl-2-O-methyl-α,β-*L*-fucofuranoside* (**11**). — A mixture of **9** (0.70 g, 1.9 mmol), sodium benzoate (0.7 g), and *N,N*-dimethylformamide (10 mL) was stirred for 40 h at 110°, then diluted with water, and extracted with ether. The extract was washed with water, dried, and concentrated. Column chromatography (ethyl acetate–

light petroleum, 1:3) of the residue gave **10** (0.54 g, 75%). ^{1}H-N.m.r. data ($CDCl_3$): δ 1.28 (d, 3 H, J 6 Hz, H-6,6,6), 3.40, 3.46 (2 s, 6 H, 2 OMe), 4.0 (m, 3 H, H-2,4,5), 4.56 (s, 2 H, PhCH_2), 4.90 (s, 1 H, H-1), 5.31 (dd, 1 H, J 1 and 4.5 Hz, H-3), 7.8 (m, 10 H, 2 Ph).

Compound **10** (0.5 g, 1.3 mmol) was debenzoylated conventionally with methanolic M sodium methoxide. Column chromatography (light petroleum–ethyl acetate, 1:3) of the product gave **11** (0.28 g, 73%), isolated as a syrup, $[\alpha]_D$ +59° (c 0.7, chloroform). ^{1}H-N.m.r. data ($CDCl_3$): δ 1.25 (d, 3 H, J 6.5 Hz, H-6,6,6), 2.12 (s, 1 H, OH), 3.37 (s, 6 H, 2 OMe), 3.8 (m, 4 H, H-2,3,4,5), 4.59 (ABq, 2 H, CH_2Ph), 4.87 (s, 1 H, H-1), 7.25 (s, 5 H, Ph).

Anal. Calc. for $C_{15}H_{22}O_5$: C, 63.8; H, 7.85. Found: C, 63.7; H, 7.7.

Methyl 2-O-methyl-α,β-L-fucofuranoside (**12**). — To liquid ammonia (50 mL) was added a solution of **11** (0.24 g, 0.85 mmol) in dry tetrahydrofuran (5 mL) at −33°. Lithium metal (20 mg) was introduced and the mixture was kept for 2 h at −33°. Solid ammonium chloride (2 g) was added, the mixture was kept at room temperature overnight and then partitioned between water and ethyl acetate, and the ethyl acetate layer was dried and concentrated. Column chromatography (ethyl acetate–light petroleum, 1:1) of the residue gave **12** (0.09 g, 55%), isolated as a syrup, $[\alpha]_D$ +47° (c 4, chloroform). ^{1}H-N.m.r. data ($CDCl_3$) (4:1 αβ-mixture): δ 1.28 (d, 3 H, J 6.5 Hz, H-6,6,6), 2.43 (bs, 1 H, OH), 3.43 (s, 6 H, 2 OMe), 4.0 (m, 4 H, H-2,3,4,5), 5.0 (s, 1 H, H-1). Mass spectrum: m/z 161 (M^+ − MeOH), 147 (M^+ − EtO).

Anal. Calc. for $C_8H_{16}O_5$: C, 50.0; H, 8.3. Found: C, 49.7; H, 8.1.

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