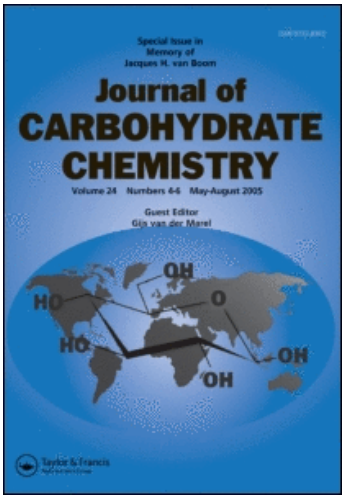

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The Allyl Group for Protection in Carbohydrate Chemistry, Part 14.[1] Synthesis of 2, 3-Di-O-Methyl-4-O-(3, 6-Di-O-Methyl-β-D-Glucopyranosyl)-L-Rhamnopyranose (and its α-Propyl Glycoside): A Haptenic Portion of the Major Glycolipid from *Mycobacterium Leprae*

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J. CARBOHYDRATE CHEMISTRY, 2(3), 207-223 (1983)

THE ALLYL GROUP FOR PROTECTION IN CARBOHYDRATE CHEMISTRY, PART 14.[1] SYNTHESIS OF 2,3-DI-O-METHYL-4-O-(3,6-DI-O-METHYL-β-D-GLUCOPYRANOSYL)-L-RHAMNOPYRANOSE (AND ITS α-PROPYL GLYCOSIDE): A HAPTENIC PORTION OF THE MAJOR GLYCOLIPID FROM *MYCOBACTERIUM LEPRAE*.

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ABSTRACT

3,6-Di-O-methyl-D-glucose was prepared *via* 5-O-allyl-1,2-O-isopropylidene-3-O-methyl-α-D-glucofuranose and was converted into 2,4-di-O-acetyl-3,6-di-O-methyl-D-glucopyranosyl chloride. Condensation of the chlorosugar with methanol or allyl 2,3-O-isopropylidene-α-L-rhamnopyranoside gave the corresponding crystalline β-glycosides. The allyl 4-O-(2,4-di-O-acetyl-3,6-di-O-methyl-β-D-glucopyranosyl)-2,3-O-isopropylidene-α-L-rhamnopyranoside was converted into the title compounds and into crystalline 2,3-di-O-acetyl-4-O-(2,4-di-O-benzyl-3,6-di-O-methyl-β-D-glucopyranosyl)-L-rhamnopyranosyl chloride which should serve as an intermediate for the synthesis of the trisaccharide portion of the major glycolipid of *Mycobacterium leprae*.

 0732-8303/83/0203-0207$3.50/0

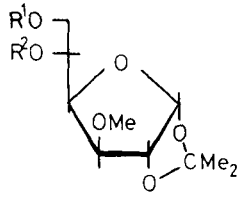
INTRODUCTION

Recently[2,3] it has been shown that *Mycobacterium leprae*, grown in the nine-banded armadillo, produces a unique phenolic glycolipid containing a trisaccharide with the sequence 3,6-di-O-methylglucose (1β4) 2,3-di-O-methylrhamnose (1α2) 3-O-methyl rhamnose. This glycolipid shows serological activity, interacting with antibodies in the sera of leprosy patients[3,4] and thus the synthesis of the oligosaccharide portion was considered to be of value for further immunological studies. Although the absolute configurations of the substituted glucose and rhamnose molecules were not established in the degradative work,[3] we have carried out our initial studies on the synthesis assuming that the glucose derivative has the D-configuration and the rhamnose derivatives have the L-configuration, and our synthetic propyl 2,3-di-O-methyl-4,O-(3,6-di-O-methyl-β-D-glucopyranosyl)-L-rhamnopyranoside (23) shows serological activity[5] toward antibodies prepared against the natural glycolipid.

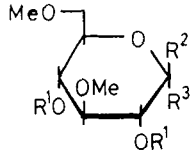
RESULTS AND DISCUSSION

We aimed for the disaccharide derivative 21, as a key intermediate in the synthesis, since this would give access to the title compounds 23 and 27, required for immunological studies, as well as the acetate 32 and hence the chloride 33 which should be a suitable intermediate for further condensation to give the complete trisaccharide which occurs as a component of the glycolipid from *Mycobacterium leprae*.

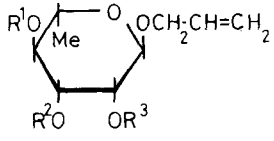
For this purpose, the chloride 10 derived from 3,6-di-O-methyl-D-glucose (8) was required. 3,6-Di-O-methyl-D-glucose (8) has been prepared *via* derivatives obtained (i) by methylation of the boric acid derivatives of methyl-D-glucopyranosides,[6] (ii) by methylation of 1,2-O-isopropylidene-α-D-glucofuranose 5-nitrate,[7] (iii) by the action of sodium methoxide on 1,2-O-isopropylidene-3-O-methyl-6-O-toluene ρ-sulphonyl-α-D-glucofuranose[7] and (iv) by



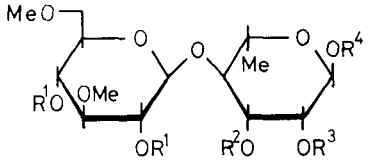
(1) $R^1 = R^2 = H$
(2) $R^1 = CPh_3$; $R^2 = H$
(3) $R^1 = CPh_3$; $R^2 = CH_2CH{=}CH_2$
(4) $R^1 = H$; $R^2 = CH_2CH{=}CH_2$
(5) $R^1 = Me$; $R^2 = CH_2CH{=}CH_2$
(6) $R^1 = Me$; $R^2 = CH{=}CH{\cdot}Me$
(7) $R^1 = Me$; $R^2 = H$



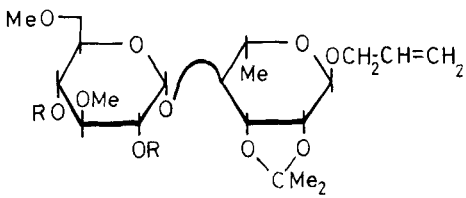
(8) $R^1 = H$; $R^2, R^3 = H, OH$
(9) $R^1 = Ac$; $R^2, R^3 = H, OAc$
(10) $R^1 = Ac$; $R^2 = H$; $R^3 = Cl$
(11) $R^1 = Ac$; $R^2 = OMe$; $R^3 = H$
(12) $R^1 = H$; $R^2 = OMe$; $R^3 = H$
(13) $R^1 = Bz$; $R^2 = OMe$; $R^3 = H$



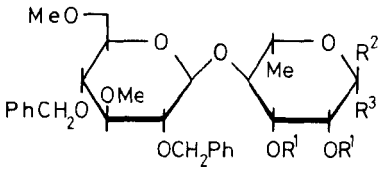
(14) $R^1 = R^2 = R^3 = H$
(15) $R^1 = H$; $R^2, R^3 = {>}CMe_2$
(16) $R^1 = CH_2Ph$; $R^2, R^3 = {>}CMe_2$
(17) $R^1 = CH_2Ph$; $R^2 = R^3 = H$



(18) $R^1 = Ac$; $R^2, R^3 = {>}CMe_2$; $R^4 = CH_2CH{=}CH_2$
(19) $R^1 = H$; $R^2, R^3 = {>}CMe_2$; $R^4 = CH_2CH{=}CH_2$
(20) $R^1 = CH_2Ph$; $R^2, R^3 = {>}CMe_2$; $R^4 = CH_2CH{=}CH_2$
(21) $R^1 = CH_2Ph$; $R^2 = R^3 = H$; $R^4 = CH_2CH{=}CH_2$
(22) $R^1 = CH_2Ph$; $R^2 = R^3 = Me$; $R^4 = CH_2CH{=}CH_2$
(23) $R^1 = H$; $R^2 = R^3 = Me$; $R^4 = CH_2CH_2Me$
(24) $R^1 = CH_2Ph$; $R^2 = R^3 = Me$; $R^4 = CH{=}CH{\cdot}Me$
(25) $R^1 = CH_2Ph$; $R^2 = R^3 = H$; $R^4 = CH{=}CH{\cdot}Me$
(26) $R^1 = CH_2Ph$; $R^2 = R^3 = Ac$; $R^4 = CH{=}CH{\cdot}Me$
(27) $R^1 = H$; $R^2 = R^3 = Me$; $R^4 = H$



(28) R = Ac
(29) R = H



(30) R^1=Me; R^2R^3=H,OH
(31) R^1=Ac; R^2R^3=H,OH
(32) R^1=Ac; R^2R^3=H,OAc
(33) R^1=Ac; R^2R^3=H,Cl

methylation of 5-O-benzyl-1,2-O-isopropylidene-α-D-glucofuranose.[8]

For the present synthesis we chose a different route to 3,6-di-O-methyl-D-glucose (8) *via* 1,2-O-isopropylidene-3-O-methyl-α-D-glucofuranose (1).[9] Compound 1 was converted into the trityl derivative 2 which gave the allyl ether 3. Hydrolysis of the trityl group from 3, in acidic aqueous-acetone, gave 5-O-allyl-1,2-O-isopropylidene-3-O-methyl-α-D-glucofuranose (4), which was methylated to give the dimethyl ether 5. Isomerisation[8] of the allyl group with potassium *tert*-butoxide in dimethyl sulphoxide gave the prop-1-enyl ether 6, which was converted into 8 either by direct acidic hydrolysis of both the prop-1-enyl and isopropylidene groups or stepwise by mercury(II) chloride hydrolysis[10] of the prop-1-enyl group to give 3,6-di-O-methyl-1,2-O-isopropylidene-α-D-glucofuranose (7),[7,8] followed by acidic hydrolysis of the isopropylidene group to give 8.

Acetylation of 8 with acetic anhydride-pyridine gave a crystalline mixture of anomers 9, one of which was obtained pure by recrystallisation. Treatment of the mixture of anomers 9 with a saturated solution of hydrogen chloride in glacial acetic acid gave the chloride 10.

To confirm the suitability of the chloride 10 for the preparation of the required glycosides, it was allowed to react with methanol in the presence of silver carbonate to give crystalline methyl 2,4-di-O-acetyl-3,6-di-O-methyl-β-D-gluco-

pyranoside (11). The anomeric configuration of 11 was confirmed by ^{1}H NMR spectroscopy and by further conversion, *via* methyl 3,6-di-O-methyl-β-D-glucopyranoside (12)(also required for immunological studies), into the known,[6] crystalline methyl 2,4-di-O-benzoyl-3,6-di-O-methyl-β-D-glucopyranoside (13).

The aglycone required for condensation with the chloride 10, for the disaccharide synthesis, was allyl 2,3-O-isopropylidene-α-L-rhamnopyranoside (15). This was obtained by acetonation of the crude allyl α-L-rhamnopyranoside (14), prepared by Fischer glycosidation of L-rhamnose in allyl alcohol, followed by chromatography to remove the small amount of β-isomer also formed. For future work, on the synthesis of the trisaccharide, the benzyl ether 17 was required. Benzylation of 15 and subsequent acidic hydrolysis of the isopropylidene group gave the crystalline allyl 4-O-benzyl-α-L-rhamnopyranoside (17).

Condensation of the chloride 10 with the alcohol 15 under Helferich conditions, using mercury(II) cyanide in acetonitrile, gave the crystalline disaccharide 18 together with a small amount of the corresponding α-linked disaccharide 28. The anomeric configurations of the products were readily established by comparison of the ^{1}H NMR spectra of the corresponding diols 19 and 29 prepared by basic hydrolysis of 18 and 28. Benzylation of the diol 19 gave 20, which on acidic hydrolysis to remove the isopropylidene group, gave the key intermediate 21.

Methylation of 21 gave the tetramethyl ether 22, which on hydrogenation over Pd-C gave propyl 2,3-di-O-methyl-4-O-(3,6-di-O-methyl-β-D-glucopyranosyl)-α-L-rhamnopyranoside (23). Compound 23 inhibited the interaction of the intact major glycolipid of *Mycobacterium leprae* with the antibody, produced against the glycolipid, in the enzyme-linked immunosorbent assay ('ELISA').[5]

Isomerisation[8] of the allyl group in compound 22 gave the prop-1-enyl glycoside 24, which on depropenylation with mercury(II) chloride[10] gave crystalline 2,3-di-O-methyl-4-O-(2,4-di-O-benzyl-

3,6-di-O-methyl-β-D-glucopyranosyl)-L-rhamnose (30). Hydrogenolysis of 30 over Pd-C gave the syrupy disaccharide 27, also required for immunological studies.

For the preparation of the chloride 33, compound 21 was isomerised[8] with potassium *tert*-butoxide in dimethyl sulphoxide to give the prop-1-enyl glycoside 25 which was acetylated to give the diacetate 26. Hydrolysis of the prop-1-enyl group with mercury(II) chloride[10] gave crystalline 2,3-di-O-acetyl-4-O-(2,4-di-O-benzyl-3,6-di-O-methyl-β-D-glucopyranosyl)-L-rhamnose (31), and this on acetylation gave an anomeric mixture of the acetates 32 from which a pure isomer was obtained by recrystallisation. Treatment of the anomeric mixture of acetates 32 with a saturated solution of hydrogen chloride in glacial acetic acid gave the crystalline chloro-derivative 33 which should be a suitable intermediate for further condensations to give the trisaccharide portion of the glycolipid.

EXPERIMENTAL

General Procedures. Light petroleum had bp 40-60 °C, and TLC was carried out on microscope slides coated with silica gel G (Merck) unless otherwise stated. Solvents were evaporated under reduced pressure, and rotations were measured with a Bendix automatic polarimeter. ^{1}H NMR spectra were recorded with a Bruker WH-270 spectrometer, and fully decoupled ^{13}C NMR spectra were recorded at 50MHz with a Bruker WM-200 spectrometer, both in $CDCl_3$ using tetramethylsilane as an internal standard.

5-O-Allyl-1,2-O-isopropylidene-3-O-methyl-α-D-glucofuranose (4). A solution of 1,2-O-isopropylidene-3-O-methyl-α-D-glucofuranose (1)[9] (20 g, 85.4 mmol) and triphenylmethyl chloride (28 g, 100.4 mmol) in pyridine (200 mL) was kept at 20° C for 24 h. Methanol (10 mL) was added, and after 2 h at 20 °C, potassium carbonate (10 g) was added in portions, and the pyridine was evaporated. Toluene was evaporated from the residue to remove the last traces of pyridine, and the crude product 2

(contaminated with methyl triphenylmethyl ether) was extracted from the residue with chloroform. The crude product was dissolved in N,N-dimethylformamide (250 mL) containing allyl bromide (10 mL, 115.5 mmol), and sodium hydride-oil (7 g, 146 mmol, 50% sodium hydride) was added in portions with stirring. After 2 h at 20 °C, TLC (ether-light petroleum, 1:1) showed complete conversion of the alcohol 2 (R_f 0.4) into the allyl ether 3 (R_f 0.8). Methanol (10 mL) was added slowly to decompose the excess of sodium hydride, and the solution was diluted with water (300 mL) and extracted with ether. The extract was washed with saturated potassium chloride solution and dried (K_2CO_3) and evaporated to give crude 3. This was added to acetone (400 mL) and N-hydrochloric acid (50 mL), and the mixture was heated under reflux for 2 h when TLC (as above) showed complete conversion of 3 (R_f 0.8) into the product 4 (R_f 0.25), together with triphenylcarbinol and oil (solvent front) and some deacetonation product (origin). Sodium hydrogen carbonate (10 g) was added in portions to the cooled solution, and the solvents were evaporated off. The crude product 4 was extracted from the residue with chloroform and the extract dried (K_2CO_3) and evaporated. The residue was chromatographed on basic alumina (800 g) in ether, which eluted the oil and triphenylcarbinol, and subsequent elution with ether-methanol (24:1) gave the product 4 (16 g, 68%) as a syrup contaminated with traces of more mobile tritylated by-products. For analysis a portion was chromatographed on silica gel to give pure 4, $[\alpha]_D^{23}$ -38.7° (c 1, $CHCl_3$).

Anal. Calcd for $C_{13}H_{22}O_6$: C, 56.92; H, 8.08. Found: C, 56.88; H, 8.02.

5-O-Allyl-1,2-O-isopropylidene-3,6-di-O-methyl-α-D-glucofuranose (5). 5-O-Allyl-1,2-O-isopropylidene-3-O-methyl-α-D-glucofuranose (4) (15 g, 54.7 mmol) was dissolved in dry toluene (100 mL) containing methyl iodide (10 mL, 160.6 mmol). Sodium hydride (2 g, 83.3 mmol) was added, and the mixture was stirred at 100 °C for 6 h when TLC (ether-light petroleum, 1:1) showed

complete conversion of 4 (R_f 0.25) into the methyl ether 5 (R_f 0.7). Methanol (10 mL) was added slowly to the cooled solution, and after adding solid carbon dioxide, the solvent was evaporated. The product was extracted from the residue with ether to give 5 (15 g, 95%) as a syrup. For analysis a portion was chromatographed on silica gel to give pure 5, $[\alpha]_D^{25}$ -31.8° (c 1, $CHCl_3$).

Anal. Calcd for $C_{14}H_{24}O_6$: C, 58.31; H, 8.39. Found: C, 58.61; H, 8.16.

1,2-O-Isopropylidene-3,6-di-O-methyl-α-D-glucofuranose (7).[7,8] Potassium *tert*-butoxide (5 g, 44.6 mmol) was added to a solution of compound 5 (14 g, 48.5 mmol) in dry dimethyl sulphoxide (50 mL). After 2 h at 20 °C, TLC (ether-light petroleum, 1:2) showed complete conversion of the allyl ether 5 (R_f 0.5) into the prop-1-enyl ether 6 (R_f 0.6). Ice-water (100 mL) was added, and the mixture was extracted with ether (3 x 100 mL); the extract was dried (K_2CO_3) and evaporated to give 6 (13 g). Compound 6 was dissolved in acetone-water (9:1, 100 mL) and mercury(II) oxide (10 g) and mercury(II) chloride (10 g)[10] were added to the stirred solution. After 15 min, TLC (as above) showed complete conversion of 6 into 7 (R_f 0.1). The mixture was filtered through Celite, the residue washed with acetone and the combined filtrates were evaporated to dryness. The residue was taken into dichloromethane (100 mL) and stirred with saturated potassium iodide solution (100 mL) to extract the mercury salts. The organic layer was separated and dried (K_2CO_3) and evaporated to give 7 (11 g, 91%) as a syrup. A portion was chromatographed on silica gel to give pure 7, $[\alpha]_D^{23}$ -48° (c 1, $CHCl_3$) {lit.[7] $[\alpha]_D^{20}$ -45.9° (c 5, $CHCl_3$); lit.[8] $[\alpha]_D^{22}$ -46.5° (c 2, $CHCl_3$)}.

3,6-Di-O-methyl-D-glucose (8).[6,7,8] (a) A solution of compound 7 (10 g, 40.3 mmol) in dioxane (60 mL) and N-hydrochloric acid (60 mL) was heated under reflux for 1 h. Sodium hydrogen carbonate (5 g) was added in portions to the cooled

solution, and the solution was then concentrated to near dryness on the rotatory evaporator. Hot ethyl acetate (200 mL) and magnesium sulphate (20 g) were added to the residue, and the extract was filtered and evaporated to a small volume. The product 8 (7 g, 83.5%) crystallised, mp 114-116 °C, $[\alpha]_D^{23}$+60° (c 1,H_2O, final value) {lit.[7] mp 113-116 °C, $[\alpha]_D^{18}$+102.5 → 61.52°; lit.,[8] mp 114-117 °C $[\alpha]_D^{22}$+89° (5 min) → 60° (c 1,H_2O)}.

(b) A solution of the prop-1-enyl ether 6 (5 g, 17.3 mmol) in dioxane (30 mL and N-hydrochloric acid (30 mL) was heated under reflux for 1 h allowing some of the solvents to evaporate slowly (to remove the propionaldehyde formed from the hydrolysis of the prop-1-enyl ether and thus prevent acetal formation[11]). Sodium hydrogen carbonate (2.5 g) was added in portions to the cooled solution which was then concentrated to near dryness, and the product 8 was isolated as described in (a) above.

1,2,4-Tri-O-acetyl-3,6-di-O-methyl-D-glucopyranose (9). A solution of 3,6-di-O-methyl-D-glucose (8) (2.5 g, 12 mmol) in acetic anhydride-pyridine (1:2, 30 mL) was kept at 20 °C for 12 h. Iced-water (200 mL) was added, and the product was extracted with dichloromethane. The extract was washed with saturated potassium chloride solution, 3N-hydrochloric acid and saturated sodium hydrogen carbonate solution and dried ($MgSO_4$) and evaporated to give a mixture of the anomers of the acetate 9 (3.9 g, 97%) which crystallised on standing. One of the anomers, mp 64-66 °C, $[\alpha]_D^{25}$+49.7° (c 1, $CHCl_3$) was obtained pure by recrystallisation from ether-light petroleum.

Anal. Calcd for $C_{14}H_{22}O_9$: C,50.29; H, 6.63. Found: C, 50.21; H, 6.78.

2,4-Di-O-acetyl-3,6-di-O-methyl-α-D-glucopyranosyl chloride (10). A solution of the mixed anomers 9 (14.6 g, 43.7 mmol) in a saturated solution of hydrogen chloride in glacial acetic acid (300 mL) was kept at 20 °C for 3 days when TLC (ether) showed conversion of the acetate 9 (R_f 0.6) into the chloride 10 (R_f 0.8), together with some hydrolysis product of the chloride (R_f 0.45-0.5). The solution was added slowly with vigorous

stirring to a mixture of dichloromethane (1 L), water (1 L) and sodium hydrogen carbonate (750 g). The dichloromethane layer was separated and dried ($MgSO_4$) and evaporated to give the crude chloride 10 (13.7 g) which was purified by chromatography on silica gel in ether-light petroleum (1:1). Yield 8 g (59%).

Methyl 2,4-Di-O-acetyl-3,6-di-O-methyl-β-D-glucopyranoside (11). The chloride 10 (500 mg, 1.6 mmol) was added to a stirred mixture of dry methanol (10 mL) and silver carbonate (200 mg). After 30 min at 20 °C, the silver salts were filtered off and the solution was evaporated to dryness. The crude crystalline product was chromatographed on silica gel to give the pure methyl glycoside 11, (360 mg, 73%), mp 100-101 °C, (from light petroleum, bp 60-80 °C), $[\alpha]_D^{23}$-30.5° (c 0.97, $CHCl_3$). ^1H NMR δ 4.97 (m, H-2, H-4), 4.34 (d, H-1, $J_{1,2}$ = 7.69 Hz), 3.49 (s, C-1 OCH_3) 3.39 and 3.36 (each s, C-3 and C-6 OCH_3), 2.10 and 2.09 (each s, C-2 and C-4 $COCH_3$); ^{13}C NMR δ 102.08 (C-1); 81.56; 73.88; 72.32; 72.10; 70.27; 59.85, 58.70, 56.97 (O-CH_3).

Anal. Calcd for $C_{13}H_{22}O_8$: C, 50.97; H, 7.24. Found: C, 51.29; H, 6.98.

Methyl 2,4-Di-O-benzoyl-3,6-di-O-methyl-β-D-glucopyranoside (13).[6] A solution of the acetate 11 (600 mg, 1.96 mmol) in methanol (10 mL) containing sodium hydroxide (400 mg) was kept at 20 °C for 1 h. Solid carbon dioxide was added, and the solution was evaporated to dryness. The diol 12 was extracted from the residue with dichloromethane and treated with an excess of benzyl chloride in pyridine and the product isolated in the usual way to give the benzoate 13, mp 159-160 °C (from ether-light petroleum), $[\alpha]_D^{27}$-12.5° (c 1, $CHCl_3$) {lit.[6] mp 155-156 °C, $[\alpha]_D^{19}$-11.65° (c 3, $CHCl_3$)}.

Allyl 2,3-O-Isopropylidene-α-L-rhamnopyranoside (15). L-Rhamnose monohydrate (23 g, 126.3 mmol) was added to a solution of hydrogen chloride (6.5 g, 178.3 mmol) in allyl alcohol (200 mL), and the mixture was heated under reflux for 2 h. An excess of sodium hydrogen carbonate was added to the cooled solution, and

the allyl alcohol was evaporated off. The crude allyl glycoside 14 was extracted from the residue with chloroform, and the extract was evaporated. Toluene was evaporated from the crude product to remove the last traces of allyl alcohol, and it was then added to a solution of toluene p-sulphonic acid monohydrate (2 g, 10.5 mmol) in dry acetone (400 mL). After 4 h at 20 °C, triethylamine (3 mL) and sodium hydrogen carbonate (2 g) were added, and the acetone was evaporated off. The residue was chromatographed on basic alumina (800 g), and the product 15 (TLC in toluene-acetone, 2:1, R_f 0.65)(21 g, 68%), contaminated with a small amount of the β-anomer (R_f 0.55), was eluted with ether-methanol (97:3) free from more polar by-products. Chromatography on silica gel in ether-light petroleum (4:1) gave pure 15 as a syrup, $[\alpha]_D^{24}$-36.6° (c 1, $CHCl_3$), ^1H NMR δ 5.01 (s, H-1), 1.53, 1.36 {each s, $C(OCH_3)_2$}, 1.30 (d, H-6).

Anal. Calcd for $C_{12}H_{20}O_5$: C, 59.0; H, 8.26. Found: C, 59.22; H, 8.26.

Allyl 4-O-Benzyl-α-L-rhamnopyranoside (17). The alcohol 15 (1 g, 4.1 mmol), benzyl bromide (0.75 mL, 6.3 mmol) and sodium hydride (300 mg, 12.5 mmol) were stirred in dry N,N-dimethylformamide (25 mL) at 20 °C for 3 h when TLC (ether-light petroleum, 1:2) showed complete conversion of 15 (R_f 0.1) into the benzyl ether 16 (R_f 0.7). Methanol and water were added, and the product was extracted with ether. The crude product 16 (containing benzylation by-products) was heated under reflux for 30 min in methanol (135 mL) and N-hydrochloric acid (15 mL) when TLC (as above) showed complete conversion of 16 into the diol 17 (R_f 0.15). An excess of sodium hydrogen carbonate was added and the solvents were evaporated off. The crude product was chromatographed on silica gel to give pure 17 (1 g, 83%), mp 68-70 °C (from light petroleum, bp 60-80 °C, $[\alpha]_D^{25}$-71.5° (c 1, $CHCl_3$).

Anal. Calcd for $C_{16}H_{22}O_5$: C, 65.28; H, 7.53. Found: C, 65.19; H, 7.20.

Allyl 4-O-(2,4-Di-O-acetyl-3,6-di-O-methyl-β-D-glucopyranosyl)-2,3-O-isopropylidene-α-L-rhamnopyranoside (18). A solution of the chloride 10 (7.53 g, 24.2 mmol), mercury(II) cyanide (4.32 g, 17 mmol) and the alcohol 15 (4.7 g, 19.2 mmol) in dry acetonitrile (40 mL) was heated under reflux for 1 h when TLC (toluene-acetone, 2:1) showed complete conversion of the alcohol 15 (R_f 0.65) into a product (R_f 0.7) (with the same mobility as the chloride 10), together with some hydrolysis product of the chloride (R_f 0.4). The mixture was evaporated to dryness, and the product was extracted with ether. The extract was washed with saturated potassium iodide solution (to remove mercury salts), dried ($MgSO_4$) and evaporated. Chromatography on silica gel in ether-light petroleum gave the product (7.9 g) which partially crystallised on standing and recrystallisation from light petroleum (bp 60-80 °C) gave the pure disaccharide 18 (5.3 g, 42% from the chloride 10), mp 84-85 °C, $[\alpha]_D^{23}$-49.4° (c 1, $CHCl_3$), ^{1}H NMR δ 5.00 (s, H-1, rhamnose), 3.39, 3.34 (each s, OCH_3), 2.11, 2.08 (each s, $COCH_3$), 1.53, 1.35 (each s, $C(CH_3)_2$), 1.25 (d, H-6, rhamnose). ^{13}C NMR δ 133.98 (O-CH=) 118.26 (CH_2=CH-), 109.62 (Me_2C), 100.2 (C-1, glucose), 96.36 (C-1, rhamnose) 81.61; 73.80; 72.61; 72.45; 70.57; 59.87; 58.68 (O-CH_3); 28.16, 26.67 (C-$(CH_3)_2$).

Anal. Calcd for $C_{24}H_{38}O_{12}$: C, 55.59; H, 7.39. Found: C, 56.04; H, 7.98.

Allyl 4-O-(3,6-Di-O-methyl-β-D-glucopyranosyl)-2,3-O-isopropylidene-α-L-rhamnopyranoside (19) and Allyl 4-O-(3,6-di-O-methyl-α-D-glucopyranosyl)-2,3-O-isopropylidene-α-L-rhamnopyranoside (29). A solution of the crystalline disaccharide 18 (100 mg, 0.2 mmol) and sodium hydroxide (100 mg, 2.5 mmol) in methanol (20 mL) was kept at 20 °C for 2 h when TLC (ether) showed complete conversion of 18 (R_f 0.85) into the product 19 (R_f 0.5). Solid carbon dioxide was added, and the solution was evaporated to dryness. Extraction with ether gave the product 19 (80 mg, 95%) as a syrup, $[\alpha]_D^{27}$-50.3° (c 1, $CHCl_3$), ^{1}H NMR δ

5.00 (s, H-1, rhamnose) 4.57 (d, $J_{1,2}$ = 7.2 Hz, H-1, glucose), 3.66, 3.39 (each s, OCH_3), 1.52, 1.34 each s, $C(CH_3)_2$, 1.28 (d, H-6, rhamnose).

Similar hydrolysis of a portion (200 mg) of the material from the mother liquors of the recrystallisation of 18 showed two products on TLC (as above), with R_f 0.5 and R_f 0.4, in approximately equal proportions. These were separated by chromatography on silica gel to give 19 (75 mg, 45%)(R_f 0.5) and 29 (70 mg, 42%)(R_f 0.4) as a syrup, $[\alpha]_D^{28}$+55.6° (c 1, $CHCl_3$), ^{1}H NMR δ 5.00 (s, H-1, rhamnose), 4.97 (d, $J_{1,2}$ = 4.1 Hz, H-1, glucose), 3.67, 3.41 (each s, OCH_3), 1.53, 1.33 each s, $C(CH_3)_2$, 1.26 (H-6, rhamnose).

Allyl 4-O-(2,4-Di-O-benzyl-3,6-di-O-methyl-β-D-glucopyranosyl)-2,3-O-isopropylidene-α-L-rhamnopyranoside (20). The diol 19 (2g, 4.6 mmol) obtained from the crystalline disaccharide 18 by hydrolysis as described above, was benzylated with benzyl bromide (2ml, 16.7 mmol) and sodium hydride (500 mg, 21 mmol) in N,N-dimethylformamide (25 mL) and the product was isolated as described above for the preparation of compound 17.

Chromatography of the crude product on silica gel gave pure 20 (2.5 g, 88%) as a syrup, $[\alpha]_D^{26}$-25.9° (c 0.7, $CHCl_3$).

Anal. Calcd for $C_{34}H_{46}O_{10}$: C, 66.43; H, 7.54. Found: C, 66.62; H, 7.34.

Allyl 4-O-(2,4-Di-O-benzyl-3,6-di-O-methyl-β-D-glucopyranosyl)-α-L-rhamnopyranoside (21). A solution of the isopropylidene derivative 20 (5.7 g, 9.3 mmol) in methanol (99 mL) and 10 N-hydrochloric acid (1 mL) was heated under reflux for 30 min when TLC (ether-light petroleum, 1:1) showed complete hydrolysis of 20 (R_f 0.8) into the diol 21 (R_f 0). An excess of sodium hydrogen carbonate was added to the cooled solution, and the methanol was evaporated off. The crude product was chromatographed on silica gel to give pure 21 (5 g, 94%) as a syrup, $[\alpha]_D^{26}$-41.9° (c 0.86, $CHCl_3$).

Anal. Calcd for $C_{31}H_{42}O_{10}$: C, 64.79; H, 7.37. Found: C, 64.50; H, 7.52.

Allyl 4-O-(2,4-Di-O-benzyl-3,6-di-O-methyl-β-D-glucopyranosyl)-2,3-di-O-methyl-α-L-rhamnopyranoside (22). Compound 21 (2 g, 3.5 mmol), sodium hydride (500 mg, 20.8 mmol) and methyl iodide (2 mL, 32 mmol) in N,N-dimethylformamide (50 mL) were kept at 20 °C for 2 h when TLC (ether) showed complete conversion of 21 (R_f 0.45) into a product (R_f 0.75). Methanol and water were added and the product (1.9 g, 90%) was extracted with ether. For analysis a portion was chromatographed on silica gel to give pure 22 as a syrup, $[\alpha]_D^{26}$ -29.7° (c 1, $CHCl_3$).

Anal. Calcd for $C_{33}H_{46}O_{10}$: C, 65.76; H, 7.69. Found: C, 65.53; H, 7.43.

Propyl 4-O-(3,6-Di-O-methyl-β-D-glucopyranosyl)-2,3-di-O-methyl-α-L-rhamnopyranoside (23). A solution of compound 22 (600 mg, 1 mmol) in ethanol (20 mL) containing Pd-C (Fluka 10%, 300 mg) was stirred in the presence of hydrogen at atmospheric pressure for 12 h. The catalyst was filtered off, and the solvent was evaporated to give 23 (360 mg, 85%) as a syrup, $[\alpha]_D^{26}$ -46.1° (c 1.22, $CHCl_3$), ^1H NMR δ 4.83 (s, H-1, rhamnose), 4.41 (d, $J_{1,2}$ = 7.2 Hz, H-1, glucose), 3.87, 3.82, 3.49, 3.47, 3.39 (OCH_3 and $O\text{-}CH_2\text{-}CH_2\text{-}CH_3$), 1.35 (d, H-6, rhamnose), 0.92 (t, $OCH_2CH_2CH_3$); ^{13}C NMR, δ 105.88, 97.05, 85.80, 82.10, 80.90, 76.22, 75.25, 74.28, 73.08, 71.46, 69.50, 67.71, 60.61, 59.73, 59.14, 56.56.

Anal. Calcd for $C_{19}H_{36}O_{10}$: C, 53.76; H, 8.55. Found: C, 53.41; H, 8.48.

4-O-(2,4-Di-O-benzyl-3,6-di-O-methyl-β-D-glucopyranosyl)-2,3-di-O-methyl-L-rhamnopyranose (30). A solution of compound 22 (200 mg, 0.33 mmol) in dry dimethyl sulphoxide (20 mL) containing potassium *tert*-butoxide (500 mg, 4.4 mmol) was kept at 20 °C for 3 h when TLC (ether-light petroleum, 2:1) showed complete conversion of the allyl glycoside 22 (R_f 0.6) into the prop-1-enyl glycoside 24 (R_f 0.65). Ice-water was added, and the product 24 was extracted with ether. The prop-1-enyl group was hydrolysed from 24 by mercury(II) chloride-mercury(II) oxide, as described above for the preparation of compound 7, and the

crude product was recrystallised from light petroleum (bp 60-80 °C)-ethyl acetate to give 30 (140 mg, 75%), mp 104-104.5 °C, $[\alpha]_D^{26}$-3.8° (c 0.92, $CHCl_3$, final value).

Anal. Calcd for $C_{30}H_{42}O_{10}$: C, 64.04; H, 7.52. Found: C, 64.09; H, 7.59.

4-O-(3,6-Di-O-methyl-β-D-glucopyranosyl)-2,3-di-O-methyl-L-rhamnopyranose (27). Compound 30 (120 mg, 0.2 mmol) was treated with hydrogen over Pd-C (as described above for the preparation of compound 23) and the product 27 (75 mg, 92%) was obtained as a syrup, $[\alpha]_D^{24}$-23.2° (c 1.18, $CHCl_3$, final value).

Anal. Calcd for $C_{16}H_{30}O_{10}$: C, 50.25; H, 7.91. Found: C, 50.13; H, 7.90.

2,3-Di-O-acetyl-4-O-(2,4-di-O-benzyl-3,6-di-O-methyl-β-D-glucopyranosyl)-L-rhamnopyranose (31). A solution of compound 21 (840 mg, 1.5 mmol) in dry dimethyl sulphoxide (25 mL) containing potassium *tert*-butoxide (2 g, 17.8 mmol) was kept at 50°C for 5 h when TLC [ether, Kieselgel-60 plates (Merck No. 5721)] showed complete conversion of the allyl glycoside 21 (R_f 0.5) into the prop-1-enyl glycoside 25 (R_f 0.55). Ice-water was added, and the product was extracted with ether. The product 25 was acetylated with acetic anhydride-pyridine (1:2) at 50 °C for 2 h, and the product was isolated in the usual way to give the acetate 26 TLC (ether), R_f 0.9 . The prop-1-enyl group was hydrolysed with mercury(II) chloride-mercury(II) oxide (as described above for the preparation of compound 7) and the crude product was crystallised from light petroleum (bp 60-80 °C) -ethyl acetate to give 31 (600 mg, 66%), mp 170-170.5 °C, $[\alpha]_D^{25}$+4.5° (c 1, $CHCl_3$, final value). TLC (ether) R_f 0.75 and 0.7 for the two anomers.

Anal. Calcd for $C_{32}H_{42}O_{12}$: C, 62.12; H, 6.84. Found: C, 62.65; H, 6.80.

1,2,3-Tri-O-acetyl-4-O-(2,4-di-O-benzyl-3,6-di-O-methyl-β-D-glucopyranosyl)-L-rhamnopyranose (32). Compound 31 was acetylated with acetic anhydride-pyridine (1:2) at 50 °C for 2h, and the product isolated in the usual way. TLC (ether-light petrol-

eum, 3:1) showed a major anomer (R_f 0.65) and a minor anomer (R_f 0.6). Crystallisation from light petroleum (bp 60-80 °C) - ethyl acetate gave the major anomer of 32, mp 112-112.5 °C, $[\alpha]_D^{25}$-30.0° (c 1, $CHCl_3$).

Anal. Calcd for $C_{34}H_{44}O_{13}$: C, 61.80; H, 6.71. Found: C, 62.39; H, 6.71.

2,3-Di-O-acetyl-4-O-(2,4-di-O-benzyl-3,6-di-O-methyl-β-D-glucopyranosyl)-L-rhamnopyranosyl chloride (33). The mixed anomers 32 (300 mg, 0.45 mmol) were kept in a saturated solution of hydrogen chloride in glacial acetic acid (20 mL) for 18 h at 20 °C when TLC (ether-light petroleum, 2:1) showed complete conversion of the acetates 32 (R_f 0.6, 0.65) into the chloride 33 (R_f 0.7), together with a small amount of 31 (R_f 0.25-0.3)(from hydrolysis of the chloride). The product was isolated as described for compound 10 and crystallised on standing. Recrystallisation from light petroleum (bp 60-80 °C) - ethyl acetate gave the chloride 33, mp 102-103 °C, $[\alpha]_D^{25}$-58.5° (c 1, CH_2Cl_2).

Anal. Calcd for $C_{32}H_{41}ClO_{10}$: C, 60.32; H, 6.49; Cl, 5.56: Found: C, 60.09; H, 6.80; Cl, 5.18.

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