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SYNTHESIS OF ALLYL AND BENZYL 4-*O*-(3,6-DI-*O*-METHYL-β-D-GLUCOPYRANOSYL)-2,3-DI-*O*-METHYL-α-L-RHAMNOPYRANOSIDE

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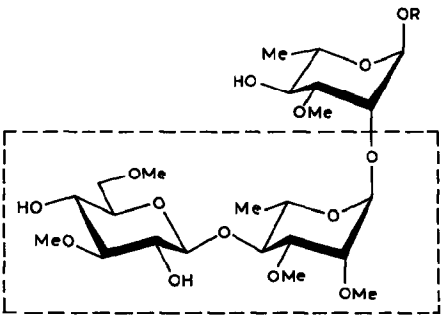
ABSTRACT

Condensation of 2,4-di-*O*-acetyl-3,6-di-*O*-methyl-α-D-glucopyranosyl bromide with either allyl or benzyl 2,4-di-*O*-methyl-α-L-rhamnopyranoside in the presence of mercuric cyanide, followed by *O*-deacetylation, gave the title oligosaccharides in excellent yields.



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INTRODUCTION

Mycobacterium leprae synthesizes a phenolic glycolipid which contains a unique carbohydrate portion consisting of a trisaccharide[1,2] (**1**). This component is the species-specific, antigenic determinant. It has a great value for the clinical diagnosis of leprosy and for differentiating the disease from tuberculosis and other infections caused by mycobacteria. The synthesis of the disaccharide indicated by dashed lines in **1** and of trisaccharide **1** was accomplished by two groups[3–9]. We report herein a simple route to disaccharide **3** as allyl, benzyl, or other glycosides.

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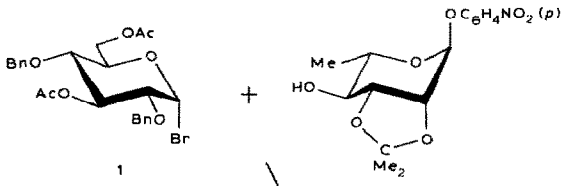

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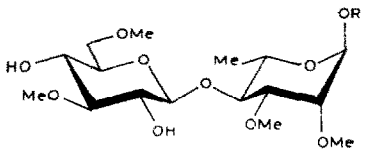

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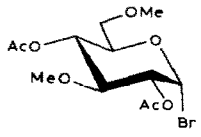

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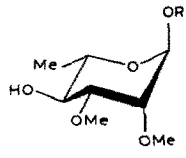

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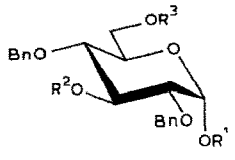
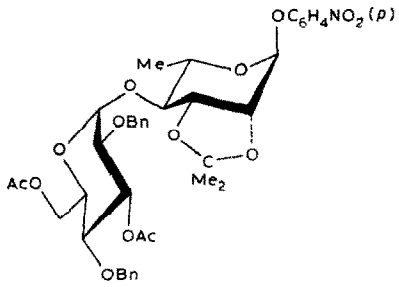


6 $R^1 = Me, R^2 = OH, R^3 = Bn$

7 $R^1 = R^2 = R^3 = Ac$



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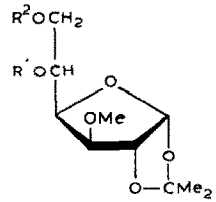
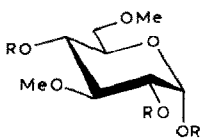


9 $R^1 = R^2 = H$

10 $R^1 = H, R^2 = Me$

11 $R^1 = Me, R^2 = H$

12 $R^1 = Me, R^2 = Bn$



13 R = H

14 R = Ac

RESULTS AND DISCUSSION

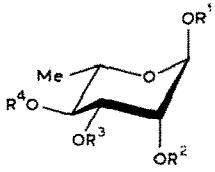
In a first approach, two different protective groups were used, permanent ones (benzyl) and temporary ones (acetyl and isopropylidene) to be replaced later

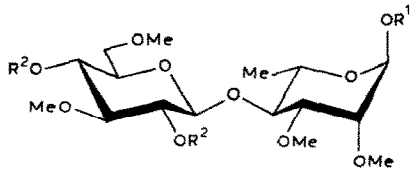
by methyl groups. The most important aspect of this route was the synthesis of the glycosyl donor **1** and its stereoselective coupling with **2**. 3,6-Di-*O*-acetyl-2,4-di-*O*-benzyl-α-D-glucopyranosyl bromide (**1**) was synthesized in three steps from methyl α-D-glucopyranoside which was partially benzylated[10,11] and acetolyzed[12] to afford the triacetate **7** as an α,β mixture in 35% yield. Treatment of **7** with hydrogen bromide in acetic acid–dichloromethane at 0° gave **1**, which was coupled with *p*-nitrophenyl 2,3-*O*-isopropylidene-α-L-rhamnopyranoside (**2**) in the presence of silver zeolite at room temperature in toluene; unexpectedly, only the α-D anomer **8** was isolated in 66% yield. The same stereoselectivity, but with a lower yield, was observed with silver silicate or silver carbonate as catalysts. This showed that the steric course of this reaction was independent of the nature of the insoluble silver salt used. The formation of a 1,2-*cis*-glucoside under the conditions employed was not surprising as van Boeckel *et al.*[13] had shown that the stereoselectivity of a glucosylation using a donor with a nonparticipating group at C-2 and silver silicate as promotor depends greatly on the protective groups at other positions. When the donor had an acyl group at O-3, a large proportion of 1,2-*cis*-glucoside was always obtained.

Consequently, the use of an acyl group at O-2 of the glycosyl donor was considered and methylation was performed before glycosylation. Several syntheses of 3,6-di-*O*-methyl-D-glucose are known, but in our hands all of them gave very poor yields*. Monomethylation of 1,2-*O*-isopropylidene-3-*O*-methyl-α-D-glucofuranose by the phase-transfer technique gave a 1:1 mixture of two compounds that was separated by flash chromatography. When this mixture was tritylated, only the second compound reacted so it was assigned the structure of the 5-*O*-methyl isomer **11**. Further evidence for structures **10** and **11** was obtained by ^{13}C-n.m.r.-spectrometry: for **10**, a characteristic down-field shift for C-6 of 13.2 p.p.m. was observed. To improve the selectivity of the methylation, other methods were investigated. Interestingly, methylation with diazomethane–stannous chloride, under the same conditions as described by Chittenden[15], failed to give pure **11** as was described, and instead a mixture of **10** and **11** was obtained in a 1.3:1 proportion. The best results were obtained when the methylation was carried out with diazomethane–boron trifluoride etherate, and a 1.6:1 mixture of **10** and **11** was obtained in a very high yield. In order to avoid a chromatographic separation of the closely-migrating compounds, the mixture of **10** and **11** was treated with benzoyl chloride–triethylamine in dichloromethane. After 24 h, only **11** had reacted and **10** was obtained in a 47% yield. Removal of the *O*-isopropylidene group afforded 3,6-di-*O*-methyl-D-glucose (**13**). Acetylation with acetic anhydride–pyridine gave **14** and bromination the glycosyl donor **1**.

The glycosyl acceptor **5** was obtained as benzyl or allyl glycoside starting from the corresponding rhamnosides **15** or **16**. *O*-Isopropylidenation with acetone–*p*-

*After submission of this manuscript, a facile synthesis of 3,6-di-*O*-methyl-D-glucose was published[14].





15 R^1 = Bn, R^2 = R^3 = R^4 = H
16 R^1 = All, R^2 = R^3 = R^4 = H
17 R^1 = Bn, R^2 = R^3 = Me_2C, R^4 = H
18 R^1 = All, R^2 = R^3 = Me_2C, R^4 = H
19 R^1 = Bn, R^2 = R^3 = Me_2C, R^4 = All
20 R^1 = All, R^2 = R^3 = Me_2C, R^4 = Bz
21 R^1 = Bn, R^2 = R^3 = H, R^4 = All
22 R^1 = All, R^2 = R^3 = H, R^4 = Bz
23 R^1 = Bn, R^2 = R^3 = Me, R^4 = All
24 R^1 = All, R^2 = R^3 = Me, R^4 = Bz
25 R^1 = Bn, R^2 = R^3 = Me, R^4 = H
26 R^1 = All, R^2 = R^3 = Me, R^4 = H

27 R^1 = Bn, R^2 = Ac
28 R^1 = Bn, R^2 = H
29 R^1 = All, R^2 = Ac
30 R^1 = All, R^2 = H

toluenesulfonic acid provided **17** and **18**, respectively. The benzyl rhamnoside **16** was allylated to give **18**, and the *O*-isopropylidene group removed to afford **21** in a 90% yield. Methylation was followed by treatment with palladium–charcoal in refluxing acetic acid to remove the allyl group. Thus, the glycosyl acceptor **4** was obtained in 80% overall yield from **15**.

The synthesis of the glycosyl acceptor as the allyl rhamnoside **26** was similar. The method differed only in that the benzoyl group was selected for protection of OH-4 and the methylation was effected with diazomethane–boron trifluoride etherate.

Condensation of **25** with the glycosyl donor **4** was performed by the Helferich variant of the Koenigs–Knorr reaction, in acetonitrile in the presence of mercury cyanide. In order to avoid decomposition of **4**, the reaction was done in a high-vacuum system. Disaccharide **27** was obtained in 86% yield. The same condensation of **4** with **26** gave similar results. Deacetylation provided disaccharides **28** and **30**. The preparation of a synthetic antigen with the easily available allyl disaccharide **30** and the synthesis of allyl trisaccharide is reported elsewhere[16].

EXPERIMENTAL

General methods. — Melting points are uncorrected. Optical rotations were determined with a Polamat A automatic polarimeter (DDR) for 1% solution in chloroform at 25°, unless otherwise stated. ^{1}H-N.m.r. spectra were recorded at 100 MHz (Tesla BS487) and ^{13}C-n.m.r. spectra at 22.5 MHz (Jeol FX90Q). Unless

otherwise stated, (^{2}H)chloroform was used as a solvent and internal tetramethylsilane as a standard. Thin-layer chromatograms were developed on Silica gel G and the spots detected by spraying with 20% H_2SO_4 in ethanol, followed by heating. A 1% solution of $KMnO_4$ in 2M Na_2CO_3 was used for detection of compounds containing allyl groups.

1,3,6-Tri-O-acetyl-2,4-di-O-benzyl-α,β-D-glucopyranose (**7**). — To a solution of methyl 2,4,6-tri-*O*-benzyl-α-D-glucopyranoside (**6**; 1 g) in 1:1 (v/v) acetic anhyride–acetic acid (6 mL) was added a solution of H_2SO_4 (14 drops) in acetic anhydride (2%) with cooling. The solution was stirred for 24 h at room temperature. Ice–water was added, and the mixture was stirred for 4 h and then extracted with chloroform (3 × 15 mL). The organic layer was washed with a saturated solution of $NaHCO_3$ and then water, dried, and evaporated. Column chromatography of the residue afforded **7** in a 35% yield, $[\alpha]_D^{25}$ +50° (*c* 1, chloroform); ^{13}C-n.m.r.: δ 170.3, 169.6, 169.0 (C=O), 93.8 (C-1β), 89.2 (C-1α), 20.9, 20.7, and 20.5 (Ac); lit.[12] $[\alpha]_D$ +51.5°.

p-*Nitrophenyl 2,3-O-isopropylidene-α-L-rhamnopyranoside* (**2**). — This compound was obtained from *p*-nitrophenyl α-L-rhamnopyranoside and acetone in the presence of anhydrous $CuSO_4$ and a catalytic amount of H_2SO_4, yield 67%, m.p. 101–104°, $[\alpha]_D^{25}$ −118° (*c* 1, chloroform); ^{13}C-n.m.r.: δ 160.9, 142.6, 125.8, 116.3 (Ph), 110.1 (Me_2C), 95.8 (C-1), 78.6, 75.7, 74.3 (C-2,3,4), 67.2 (C-5), 28.0, 26.2 [$(CH_3)_2C$], and 17.2 (C-6).

p-*Nitrophenyl 4-O-(3,6-di-O-acetyl-2,4-di-O-benzyl-α-D-glucopyranosyl)-2,3-O-isopropylidene-α-L-rhamnopyranoside* (**8**). — Compound **7** (600 mg) was dissolved in dry dichloromethane (16 mL) and the solution cooled to 0°. A 40% solution of HBr in acetic acid was added and the mixture stirred for 30 min at 0°. The reaction was stopped by addition of ice–water. The organic layer was washed with ice-cooled water, dried, and evaporated. The syrupy residue and **2** (337 mg) were dissolved in dry toluene (40 mL). The solution was evaporated to one half of its volume under Ar. Molecular sieves 4A were added to the cooled solution and it was stirred for 30 min. The catalyst (silver zeolite, silicate, or carbonate) was added with exclusion of light, and the mixture was stirred for 12 h, filtered, and evaporated. The product was purified by column chromatography in 15:1 toluene–acetone, $[\alpha]_D^{25}$ −90° (*c* 1, chloroform); ^{13}C-n.m.r.: δ 170.8, 169.9 (C=O), 109.8 (Me_2C), 97.9 (C-1′α), 95.3 (C-1), 30.0, 26.7 [$(CH_3)_2C$], 21.0, 20.8 (Ac), and 17.3 (C-6).

Anal. Calc. for $C_{38}H_{45}O_{14}$: C, 62.89; H, 6.25. Found: C, 62.70; H, 6.00.

1,2-O-Isopropylidene-3-O-methyl-α-D-glucofuranose (**9**). — To a solution of 1,2,5,6-di-*O*-isopropylidene-α-D-glucofuranose (11 g) in dimethyl sulfoxide (28 mL) was added pulverized KOH (9.8 g). The suspension was mechanically stirred for 30 min and then cooled, and methyl iodide (7 mL) was added dropwise and stirring continued for 1 h. Chloroform (300 mL) and water (50 mL) were added, and the organic extract was washed several times with water, dried, and evaporated. The residue, homogeneous by t.l.c. in 1:3 ethyl acetate–hexane, was

dissolved in 80% acetic acid (100 mL). The hydrolysis of the 5,6-*O*-isopropylidene group proceeded within 1–2 days at room temperature (t.l.c. in 4:1 chloroform–acetone). The solution was cooled and made neutral with 50% KOH. Minor impurities were removed by extraction with toluene and then continuous extraction with ethyl acetate afforded **9** (9.5 g, 96%), $[\alpha]_D^{25}$ −54° (*c* 1, ethyl acetate); lit.[18] $[\alpha]_D$ −52°.

1,2-O-Isopropylidene-3,6-di-O-methyl-α-D-glucofuranoside (**10**) *and 1,2-O-isopropylidene-3,5-di-O-methyl-α-D-glucofuranoside* (**11**). — To a solution of **9** (1 g) in dry dichloromethane (20 mL), cooled to −5°, was added boron trifluoride etherate (50 μL) and dropwise a solution of diazomethane in ether (prepared from 4 g of 1-methyl-3-nitro-1-nitrosoguanidine). A second, identical portion of diazomethane was added and, after 15 min of each addition, the reaction was monitored by t.l.c. (6:1 chloroform–acetone). After all **3** had reacted, the mixture was filtered and the filtrate evaporated. Column chromatography of the residue in 30:1 chloroform–acetone gave **10** and **11** as major compounds.

Compound **10**. Yield 11 mg (50%), $[\alpha]_D^{25}$ −48.6° (*c* 1, chloroform); ^{13}C-n.m.r.: δ 11.7 (Me_2C), 105.3 (C-1), 74.9 (C-6), 67.7 (C-5), 59.1, 58.0 (Me), 26.9 and 26.4 [(CH_3)$_2$C]; lit.[19] $[\alpha]_D$ −46°, lit.[20] $[\alpha]_D$ −46.5°.

Compound **11**. Yield 332 mg (31%), $[\alpha]_D^{25}$ −31° (*c* 1, chloroform); ^{13}C-n.m.r.: δ 111.9 (Me_2C), 105.2 (C-1), 77.8 (C-5), 61.7 (C-6), 57.9, 57.6 (Me), 26.9, and 26.4 [(CH_3)$_2$C]; lit.[21] $[\alpha]_D$ −26°.

In a large-scale preparation of **10**, the crude mixture of **10** and **11** was treated with benzoyl chloride (0.25 mL) and triethylamine (0.5 mL) in acetone to give the 5-benzoate **12** and unreacted **11**. Separation of this mixture and saponification gave **10** in 47% yield.

3,6-Di-O-methyl-D-glucose (**13**). — A solution of **10** in 1:1 1,4-dioxane–M HCl (22 mL) was heated at reflux for 1 h. The mixture was cooled, made neutral with $NaHCO_3$ (1.2 g), and lyophilized. The residue was extracted with hot ethyl acetate. After concentration, **13** crystallized (yield 1.5 g, 90%), m.p. 112–115°; lit.[4], m.p. 114–116°.

1,2,4-Tri-O-acetyl-3,6-di-O-methyl-D-glucopyranose (**14**). — Conventional acetylation of **13** with acetic anhydride–pyridine gave **14** (qualitative yield), $[\alpha]_D^{25}$ +50° (*c* 1, chloroform); lit.[4] $[\alpha]_D$ +49.7°; ^{13}C-n.m.r.: δ 169.7, 169.4, 169.2 (C–O), 92.1 (C-1β), 89.5 (C-1α), 59.1, 59.0 (MeO), and 20.9 (Ac).

Benzyl 2,3-O-isopropylidene-α-L-rhamnopyranoside (**17**). — Benzyl 2,3,4-tri-*O*-acetyl-α-L-rhamnopyranoside was obtained from 1,2,3,4-tetra-*O*-acetyl-α,β-L-rhamnopyranose and benzyl alcohol in the presence of $SnCl_2$[22]. It was deacetylated with sodium methoxide in methanol to give a syrup which was dried *in vacuo* (6 g), dissolved in acetone (120 mL), and stirred with *p*-toluenesulfonic acid (0.6 g) at room temperature for 4 h. The solution was made neutral with triethylamine (1 mL) and K_2CO_3 (0.6 g). The mixture was filtered, the filtrate evaporated, and the residue taken up in chloroform, washed with water, dried, and evaporated to a syrup that crystallized slowly from cyclohexane (yield 5.1 g, 79%), m.p. 68–70°, $[\alpha]_D^{25}$ −63° (*c* 1, chloroform); lit.[23] m.p. 72°.

Benzyl 4-O-allyl-2,3-O-isopropylidene-α-L-rhamnopyranoside (**19**). — Compound **17** (5 g, 17 mmol) was dissolved in *N,N*-dimethylformamide (60 mL). To this solution was added NaH (2.6 g) and the mixture was stirred for 30 min, cooled to 0°, and allyl chloride (2.2 mL) added dropwise. The mixture was stirred overnight and then methanol (1 mL) was added. *N,N*-Dimethylformamide was distilled off in high vacuum and the residue dissolved in chloroform, washed with water, dried, and evaporated to a syrup (yield 5.2 g, 100%), $[\alpha]_D^{25}$ −65° (*c* 1, chloroform); ^{1}H-n.m.r.: δ 7.31 (m, $C_6H_5CH_2$), 5.90 (m, CH=), 5.20 (d, t, CH_2=), 5.04 (s, 1 H), 4.57 (dd, $C_6H_4CH_2$), 4.20 (m, 4 H), 3.73 (m, H-5), 3.18 (m, H-4), 1.53 (s, 3 H, H_3-6), and 1.30 (d, 3 H, Me).

Anal. Calc. for $C_{19}H_{26}O_5$: C, 68.24; H, 7.83. Found: C, 68.22, H, 8.10.

Benzyl 4-O-allyl-α-L-rhamnopyranoside (**21**). — Compound **19** was dissolved in ethanol (45 mL). To this solution was added 0.05M HCl in ethanol (45 mL). The solution was boiled at reflux for 1 h, cooled, made neutral with a saturated solution of $NaHCO_3$, and evaporated. The residue was dissolved in hexane and washed with water, dried, and evaporated to give **21** (2.8 g, 70%), m.p. 50–52°, $[\alpha]_D^{25}$ −73° (*c* 1, chloroform); ^{1}H-n.m.r.: δ 7.36 (m, 5 H, $C_6H_5CH_2$), 5.90 (m, CH=), 5.20 (t, CH_2=), 4.92 (s, H-1), 4.55 (dd, 2 H, $C_6H_5CH_2$), 4.20 (m, CH_2), 3.94 (s, 2 H, OH), 3.75 (m, H-5), 3.25 (m, H-2,3,4), and 1.31 (d, 3 H, H_3-6); lit.[24] m.p. 56°; $[\alpha]_D$ −67°.

Benzyl 4-O-allyl-2,3-di-O-methyl-α-L-rhamnopyranoside (**23**). — To a solution of **21** (1 g) in *N,N*-dimethylformamide (18 mL) was added NaH (0.5 g) and the mixture was stirred for 30 min at room temperature. To the cooled suspension was added methyl iodide (2.5 mL) dropwise and the mixture was stirred overnight. The excess of reagent was removed with methanol. The mixture was diluted with chloroform, washed with water, dried, and evaporated. The residue was dried in high vacuum (yield, 100%), $[\alpha]_D^{25}$ −61° (*c* 1, chloroform); ^{1}H-n.m.r.: δ 7.30 (m, 5 H, $C_6H_5CH_2$), 5.92 (m, CH=), 5.10 (m, 2 H, CH_2=), 4.91 (s, H-1), 4.56 (dd, 2 H, $C_6H_5CH_2$), 4.20 (m 2 H, CH_2), 3.61 (s, 3 H, Me), 3.49 (s, 3 H, Me), 3.8–3.2 (m, H-2,3,4,5), and 1.32 (d, 3 H, H-6).

Anal. Calc. for $C_{18}H_{26}O_5$: C, 67.05; H, 8.12. Found: C, 67.27; H, 8.09.

Benzyl 2,3-di-O-methyl-α-L-rhamnopyranoside (**25**). — Compound **23** (0.5 g) was dissolved in 1:1:0.5 (v/v) ethanol–acetic acid–water. To this solution was added 5% Pd–C (0.1 g), the mixture was stirred at 80–90° for 3 days, and then filtered, and the solution evaporated, coevaporated with toluene, dried, and chromatographied on silica gel with 10:1 chloroform–acetone, yield 0.4 g (91%), $[\alpha]_D^{25}$ −70° (*c* 1, chloroform); ^{1}H-n.m.r.: δ 7.34 (m, 5 H, $C_6H_5CH_2$), 4.95 (s, H-1), 4.60 (dd, 2 H, $C_6H_5CH_2$), 3.47 (s, 6 H, 2 MeO), 2.80 (s, OH), and 1.33 (d, 3 H, H_3-6).

Anal. Calc. for $C_{15}H_{22}O_5$: C, 63.81; H, 7.85. Found: C, 64.08; H, 7.46.

Allyl 2,3-O-isopropylidene-α-L-rhamnopyranoside (**18**). — Allyl 2,3,4-tri-*O*-acetyl-α-L-rhamnopyranose, obtained from the peracetate and allyl alcohol in the presence of $SnCl_2$, was deacetylated by the conventional procedure. The resulting syrup was dried *in vacuo* (2.5 g), and stirred with acetone (50 mL) and *p*-toluenesulfonic acid (0.25 g). After 4 h, the mixture was made neutral with K_2CO_3 (0.25

g) and triethylamine, and acetone evaporated off. The residue was dissolved in toluene, and the solution washed with water, dried, and evaporated (yield 1.6 g, 53%), $[\alpha]_D^{25}$ −26° (*c* 1, chloroform); lit.[4] $[\alpha]_D$ −36.6°; ^{1}H-n.m.r.: δ 5.90 (m, CH=), 5.25 (m, 2 H, CH_2=), 5.00 (s, H-1), 4.10 (m, 4 H, H-2,3, OCH), 3.66 (dt, H-5), 3.34 (m, 2 H, H-4, OH), 1.56 (s, 3 H, Me), 1.40 (s, 3 H, H_3-6), and 1.33 (d, 3 H, H_3-6).

Allyl 4-O-benzoyl-2,3-O-isopropylidene-α-L-rhamnopyranoside (**20**). — A solution of **18** (1.3 g, 5.3 mmol) in pyridine (6.5 mL) was cooled to 0°. Freshly distilled benzoyl chloride (0 mL) was added dropwise. After 3 h, the reaction was quenched with cold water and the solution extracted with chloroform (2 × 25 mL). The organic layer was washed with M HCl, saturated $NaHCO_3$ solution, and water, dried, and evaporated (yield 1.85 g, 95%), $[\alpha]_D^{25}$ −10° (*c* 1, chloroform); ^{1}H-n.m.r.: δ 7.80 (m, 2 H, Ph), 7.30 (m, 3 H, Ph), 5.92 (m, CH=), 5.20 (m, 3 H, CH_2=, H-4), 5.11 (s, H-1), 4.40–3.80 (m, 5 H, H-2,3,5, OCH_2), 1.63 (s, 3 H, Me), 1.36 (s, 3 H, Me), and 1.23 (d, 3 H, H_3-6).

Allyl 4-O-benzoyl-α-L-rhamnopyranoside (**22**). — Compound **20** (1 g, 00 mmol) was dissolved in 90% trifluoroacetic acid (10 mL) and the solution stirred at room temperature. Trifluoroacetic acid was evaporated after addition of toluene (yield, 0.88 g), m.p. 52–54°, $[\alpha]_D^{25}$ −80° (*c* 1, chloroform); ^{1}H-n.m.r.: δ 7.85 (m, 2 H, Ph), 7.25 (m, 3 H, Ph), 5.92 (m, CH=), 5.20 (m, 3 H, H-4, CH=), 4.90 (s, H-1), 4.10 (m, H-2,3,5, OCH, OH), and 1.25 (d, 3 H, H_3-6).

Anal. Calc. for $C_{16}H_{20}O_6$: C, 62.32; H, 6.54. Found: C, 62.49; H, 6.90.

Allyl 4-O-benzoyl-2,3-di-O-methyl-α-L-rhamnopyranoside (**24**). — Compound **22** (1.1 g) was dissolved in dry dichloromethane (16 mL). To this solution, cooled to −10°, was added BF_3 etherate (57 μL) and a solution of diazomethane in ether until a yellow color persisted. The mixture was stirred overnight. Polymethylene formed was filtered off and the solution evaporated to give **24** (1.0 g, 83%), $[\alpha]_D^{25}$ −50° (*c* 1, chloroform).

Anal. Calc. for $C_{18}H_{24}O_6$: C, 64.27; H, 7.19. Found: C, 64.34; H, 7.47.

Allyl 2,3-di-O-methyl-α-L-rhamnopyranoside (**26**). — Compound **24** (1 g) was debenzoylated with sodium methoxide in methanol for 24 h. The resulting solution was made neutral with Amberlite IR-120 (H^+) anion-exchange resin, filtered, and evaporated. Purification by column chromatography in 10:1 (v/v) chloroform–acetone afforded **26** (0.63 g, 92%), $[\alpha]_D^{25}$ −45° (*c* 1, chloroform); ^{1}H-n.m.r.: δ 5.80 (m, CH=), 5.20 (m, CH_2=), 4.78 (d, *J* 1.5 Hz, H-1), 4.05 (dd, OCH_2), 3.46 (s, OMe), 3.50 (s, OMe), 3.00 (s, OH), and 1.30 (d, 3 H, H_3-6).

Anal. Calc. for $C_{11}H_{20}O_5$: C, 56.88; H, 8.68. Found: C, 56.99; H, 8.52.

Allyl 4-O-(2,4-di-O-acetyl-3,6-di-O-methyl-β-D-glucopyranosyl)-2,3-di-O-methyl-α-L-rhamnopyranoside (**28**). — The triacetate **14** (375 mg) was dried *in vacuo* and dissolved in dry dichloromethane (5 mL). To the cooled solution was added a 45% solution of HBr in acetic acid. The solution was maintained at 0° for 30 min, and then diluted with dichloromethane (5 mL) and washed with ice–water (3 mL). The organic layer was washed with ice–water (2 × 3 mL) and dried

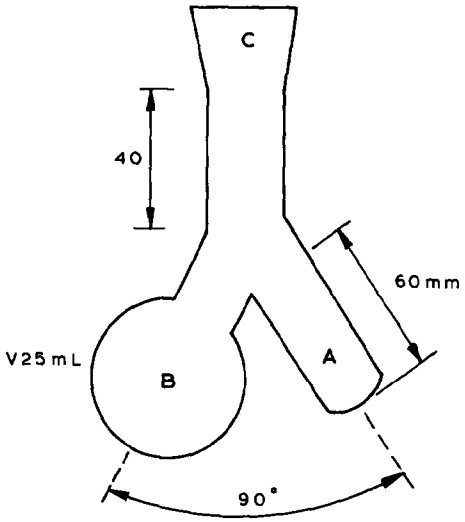


Fig. 1. Condensation vessel.

(Na_2SO_4). This solution of bromide **4** was evaporated *in high vacuum* directly into arm A of the two-armed reaction vessel illustrated in Fig. 1*. Previously, compound **26** (150 mg) and $Hg(CN_2)$ (240 mg) had been placed in arm B, and the equipment was connected to high vacuum through neck C. The content was dried for 2 h (0.1 Pa). Acetonitrile (stored in high vacuum over CaH_2) was distilled into both arms and the equipment was disconnected from the vacuum under positive Ar pressure. The content of side A was added to side B, and the mixture stirred for several hours and evaporated. The residue was dissolved in chloroform, and the solution washed with KI solution, $NaHCO_3$ solution, water, dried, and evaporated. Column chromatography of the residue (10:1 chloroform–acetone) afforded **28** in a 73% yield, $[\alpha]_D^{25}$ −40° (*c* 1, chloroform); ^{13}C-n.m.r.: δ 169.6, 169.3 (C=O), 133.8 (CH=), 117.7 (CH_2), 101.0 (C-1′β), 95.9 (C-1α), 59.6, 59.0, 58.3, 57.1 (Me), 20.9 (Ac), and 17.8 (C-6).

Anal. Calc. for $C_{23}H_{38}O_{12}$: C, 54.68; H, 7.58. Found: C, 54.37; H, 7.41.

Benzyl 4-O-(2,4-di-O-acetyl-3,6-di-O-methyl-β-D-glucopyranosyl)-2,3-di-O-methyl-α-L-rhamnopyranoside (**27**). — This compound was obtained from bromide **4** and **25** similarly to the preparation of **28**, yield 86%, $[\alpha]_D^{25}$ −38° (*c* 1, chloroform); ^{13}C-n.m.r.: δ 169.6 (C=O), 128.5, 128.2, 127.9 ($C_6H_5CH_2$), 101.0 (C-1′β), 96.1 (C-1α), 59.6, 59.0, 58.2, 57.2 (Me), 20.9 (Ac), and 17.8 (C-6).

Anal. Calc. for $C_{27}H_{40}O_{12}$: C, 58.26; H, 7.24. Found: C, 57.98; H, 7.34.

Allyl 4-O-(3,6-di-O-methyl-β-D-glucopyranosyl)-2,3-di-O-methyl-α-L-rhamnopyranoside (**30**). — Disaccharide **29** (95 mg) was deacetylated with sodium

*The procedure is similar to that used by Nashed and Anderson[25].

methoxide in methanol for 24 h, yield 79 mg (100%), $[\alpha]_D^{25}$ −39° (*c* 1, chloroform).

Anal. Calc. for $C_{19}H_{34}O_{10}$: C, 64.27; H, 7.19. Found: C, 64.60; H, 7.14.

Benzyl 4-O-(3,6-di-O-methyl-β-D-glucopyranosyl)-2,3-di-O-methyl-α-L-rhamnopyranoside (**29**). — This compound was synthesized similarly to **30**, yield 85%, $[\alpha]_D^{25}$ −33° (*c* 1, ethyl acetate).

Anal. Calc. for $C_{23}H_{36}O_{10}$: C, 58.49; H, 7.68. Found: C, 58.61; H, 8.02.

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