Carbohydrate Research, 241 (1993) 99–116
Elsevier Science Publishers B.V., Amsterdam

A new approach to the chemical synthesis of the trisaccharide, and the terminal di- and mono-saccharide units of the major, serologically active glycoplipid from *Mycobacterium leprae* *

Anikó Borbás and András Lipták **

Department of Biochemistry, L. Kossuth University, P.O. Box 55, H-4010 Debrecen (Hungary)

(Received March 19th, 1992; accepted August 22nd, 1992)

ABSTRACT

The key intermediates for the synthesis of *p*-trifluoroacetamidophenyl *O*-(3,6-di-*O*-methyl-β-D-glucopyranosyl)-(1 → 4)-*O*-(2,3-di-*O*-methyl-α-L-rhamnopyranosyl)-(1 → 2)-3-*O*-methyl-α-L-rhamnopyranoside (**15**), as well as *p*-trifluoroacetamidophenyl *O*-(3,6-di-*O*-methyl-β-D-glucopyranosyl)-(1 → 4)-2,3-di-*O*-methyl-α-L-rhamnopyranoside (**29**), were the methyl and ethyl *O*-(2-*O*-benzyl-4,6-*O*-benzylidene-3-*O*-methyl-β-D-glucopyranosyl)-(1 → 4)-2,3-*O*-diphenylmethylene-1-thio-α-L-rhamnopyranosides (**10** and **24**). Dichloroalane treatment of **10** and **24** removed the diphenylmethylene group, liberating HO-2 and HO-3 of the rhamnopyranoside residue, and opened the benzylidene acetal regioselectively to give the 4-*O*-benzyl-glucopyranosyl disaccharides. Methylation of the free OH groups resulted in the tetra-*O*-methyl 1-thio disaccharides (**12** and **26**), useful as glycosyl donors. Introduction of these temporary blocking groups allowed a drastic reduction in the number of synthetic steps to the target compounds.

INTRODUCTION

Mycobacterium leprae and tissues infected by the bacterium contain a phenolic glycolipid[1,2]. The aglycon is 29-(4-hydroxyphenyl)-3-methoxy-4-methyl-9,11-nonacosanediol 9,11-dimycocerosate, which is glycosylated with a trisaccharide, *O*-(3,6-di-*O*-methyl-β-D-glucopyranosyl)-(1 → 4)-*O*-(2,3-di-*O*-methyl-α-L-rhamnopyranosyl)-(1 → 2)-3-*O*-methyl-α-L-rhamnopyranose. Antibodies to the glycolipid, present in the sera of leprosy patients[2–5], are of interest as diagnostic agents for leprosy infection at an early stage of the disease[6–11]. Because this trisaccharide is the species-specific segment of the glycolipid, it inhibits interaction of the major glycolipid of *Mycobacterium leprae* with the Immunoglobulin M (IgM) antibody from human leprosy sera and, therefore, it can be used in the enzyme-linked

* Dedicated to Professor F.W. Lichtenthaler on the occasion of his 60th birthday.
** Corresponding author.

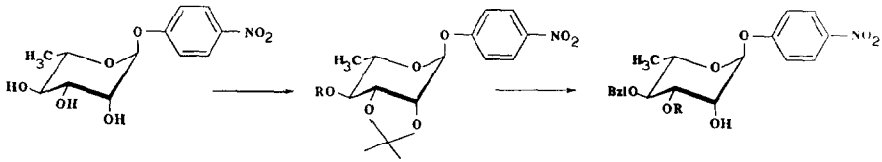
immunosorbent assay (ELISA). By conjugation of this trisaccharide with a protein, such as bovine serum albumin (BSA) using a suitable spacer, artificial antigens can be obtained to elicit specific antibodies. The prospect of a fully synthetic specific antigen for the worldwide serodiagnosis of leprosy has initiated much preparative work to synthesise the trisaccharide unit[8,12–16] or the disaccharide building blocks[8,9,17–21], and to study their conformation[22]. Now we report the synthesis of the trisaccharide, together with the terminal disaccharide and 3,6-di-*O*-methyl-D-glucose, in the form of their *p*-trifluoroacetamidophenyl glycosides, **15**, **29**, and **43**, respectively.

RESULTS AND DISCUSSION

Earlier syntheses of the trisaccharide hapten have employed a common strategy, namely, the partially methylated monosaccharide-type building blocks were synthesised and used either as glycosyl acceptor or glycosyl donor. The preparation of these partially methylated monosaccharide units required multistep synthesis, preparation of the trisaccharide, glycosidically linked to spacers, required as many as 30–37 steps. To reduce the number of steps, we developed the following strategy: (*i*) introduction of several methyl groups in one step, (*ii*) the use of benzyl or benzyl-equivalent blocking group(s), and (*iii*) synthesis of a spacer-containing trisaccharide hapten that could easily conjugate with BSA.

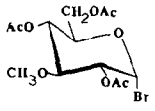
For the synthesis of the planned *p*-trifluoroacetamidophenyl *O*-(3,6-di-*O*-methyl-β-D-glucopyranosyl)-(1 → 4)-*O*-(2,3-di-*O*-methyl-α-L-rhamnopyranosyl)-(1 → 2)-3-*O*-methyl-α-L-rhamnopyranoside[21,23] (**15**), a 2 + 1 synthetic scheme was chosen. For the preparation of the glycosyl acceptor **4**, we started from *p*-nitrophenyl 2,3-*O*-isopropylidene-α-L-rhamnopyranoside[23] (**1**), but to improve the work-up procedure the 2,2-dimethoxypropane–*p*-toluenesulfonic acid[24] system was used without solvent, and crystallisation was achieved from cyclohexane. The acetal **1** was benzylated[25,26] to obtain **2**. The isopropylidene group from crystalline **2** was hydrolysed to obtain the amorphous diol **3**. By using the well-known procedure developed previously[27] for the alkylation of the equatorial hydroxy group of an axial–equatorial diol system, *p*-nitrophenyl 4-*O*-benzyl-α-L-rhamnopyranoside (**3**) was converted into the 2,3-*O*-dibutylstannylidene derivative by treatment with dibutyltin oxide in benzene with azeotropic removal of water. The stannylidene intermediate reacted in situ with methyl iodide in *N*,*N*-dimethylformamide, to yield crystalline *p*-nitrophenyl 4-*O*-benzyl-3-*O*-methyl-α-L-rhamnopyranoside (**4**) whose structure was verified by the chemical shift value of the anomeric carbon in the ^{13}C NMR spectrum.

As the disaccharide-type glycosyl donor, we selected a thioglycoside derivative. The recently prepared methyl 2,3-*O*-diphenylmethylene-1-thio-α-L-rhamnopyranoside[28] (**5**) was glycosylated with 2,4,6-tri-*O*-acetyl-3-*O*-methyl-α-D-glucopyranosyl bromide[8] (**6**) in dichloromethane–toluene, using silver triflate as the promoter. The resulting disaccharide (**7**) was methanolysed, using an equimolar amount of

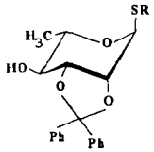


1 R = H
2 R = Bzl

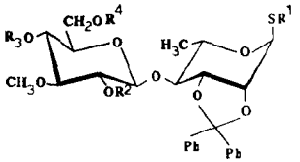
3 R = H
4 R = CH_3



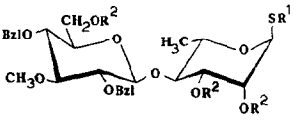
6



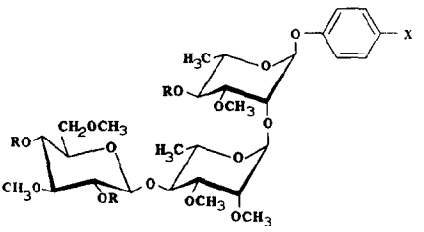
5 R = CH_3
20 R = CH_2-CH_3



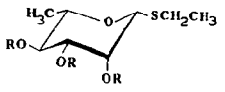
7 R^1 = CH_3; R^2 = R^3 = R^4 = Ac
8 R^1 = CH_3; R^2 = R^3 = R^4 = H
9 R^1 = CH_3; R^2 = H; R^3,R^4 = Ph-CH<
10 R^1 = CH_3; R^2 = Bzl; R^3,R^4 = Ph-CH<
21 R^1 = CH_2-CH_3; R^2 = R^3 = R^4 = Ac
22 R^1 = CH_2-CH_3; R^2 = R^3 = R^4 = H
23 R^1 = CH_2-CH_3; R^2 = H; R^3,R^4 = Ph-CH<
24 R^1 = CH_2-CH_3; R^2 = Bzl; R^3,R^4 = Ph-CH<



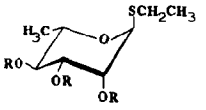
11 R^1 = CH_3; R^2 = H
12 R^1 = R^2 = CH_3
25 R^1 = CH_2-CH_3; R^2 = H
26 R^1 = CH_2-CH_3; R^2 = CH_3



13 X = NO_2; R = Bzl
14 X = NH-$COCF_3$; R = Bzl
15 X = NH-$COCF_3$; R = H



16 R = Ac
18 R = H



17 R = Ac
19 R = H

$NaOCH_3$ (since the 2′-OAc is extremely stable[29,30]), to obtain compound **8**. Benzylidenation of **8** gave **9**, which was benzylated to afford methyl *O*-(2-*O*-benzyl-4,6-*O*-benzylidene-3-*O*-methyl-β-D-glucopyranosyl)-(1 → 4)-2,3-*O*-diphenylmethylene-1-thio-α-L-rhamnopyranoside (**10**). This fully protected disaccharide derivative (**10**) contains two acetal rings (benzylidene and diphenylmethylene) which show

completely different reactivity towards $AlHCl_2$; the dioxane-type benzylidene ring is hydrogenolysed to a 4′-benzyl ether–6′-hydroxy derivative[31], but the diphenylmethylene acetal is removed completely and thus both hydroxyl groups are regenerated[32,33]. Treatment of **10** with dichloroalane ($LiAlH_4 + 3AlCl_3$) in ether–dichloromethane at reflux temperature gave two products in the ratio ~ 8:2. The major product proved to be the desired compound, methyl *O*-(2,4-di-*O*-benzyl-3-*O*-methyl-β-D-glucopyranosyl)-(1 → 4)-1-thio-α-L-rhamnopyranoside (**11**). Spectroscopic data showed the complete disappearance of both acetal rings, with the formation of three hydroxyl groups, one of which was assigned as HO-6′ (δ 62 ppm). The minor product, assumed to be the 6′-*O*-benzyl-4′-hydroxy isomer, was not isolated. The formation of compound **11** with three free OH groups fulfilled our expectation, because simple methylation of **11** allowed the introduction of three methyl groups into the desired positions, to give methyl *O*-(2,4-di-*O*-benzyl-3,6-di-*O*-methyl-β-D-glucopyranosyl)-(1 → 4)-2,3-di-*O*-methyl-1-thio-α-L-rhamnopyranoside (**12**). The advantage of **12** is not only the presence of all four methoxy groups, but being a thioglycoside it should also serve as a glycosyl donor. Methyl triflate activation[34] of **12** and coupling with the aglycon **4** resulted exclusively in a 1,2-*trans*, α-rhamnopyranosyl linkage, although a non-participating group (OCH_3) was present at position C-2. The trisaccharide derivative (**13**) contained only benzyl protecting groups, and the aglycon was substituted with a nitro group. Our original plan, that we could possibly remove all benzyl groups and reduce the aglycon to a *p*-aminophenyl moiety in one step, failed; the yield was extremely low and many degradation products were formed. Similar observations were reported by Ekborg et al.[35].

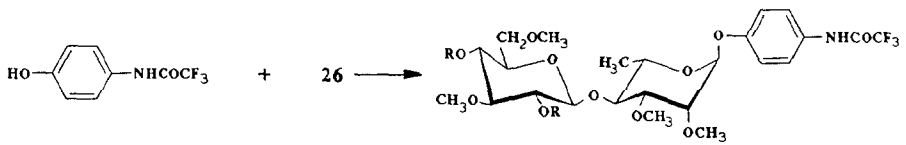
To overcome this difficulty, the nitro group in **13** was reduced using Adams' catalyst, and the resulting amino group was acylated with trifluoroacetic anhydride to obtain the *p*-trifluoroacetamidophenyl glycoside (**14**) of the blocked haptenic trisaccharide. In this case, removal of the benzyl groups from **14** proceeded very smoothly and the desired target compound (**15**) was obtained. The conjugation of these types of glycosides to proteins is well-documented[36].

The "bottle-neck" of the whole procedure is the preparation of compound **5**, because the isolation of the syrupy methyl 2,3,4-tri-*O*-acetyl-1-thio-α-L-rhamnopyranoside[28] requires chromatographic purification. At the same time, ethyl 1-thio-α-L-rhamnopyranoside derivatives[37–39] are easily obtainable. When 1,2,3,4-tetra-*O*-acetyl-α-L-rhamnopyranose was treated with ethanethiol in the presence of 1.0 equivalent of $SnCl_4$, a very fast reaction occurred, and two anomers were formed which could be separated by simple crystallisation. Thus, ethyl 2,3,4-tri-*O*-acetyl-1-thio-β-L-rhamnopyranoside (**16**) crystallised from ethanol, and crystalline ethyl 2,3,4-tri-*O*-acetyl-1-thio-α-L-rhamnopyranoside (**17**) was obtained from the filtrate in 60.9% yield after concentration; upon deacetylation, crystalline ethyl 1-thio-β-L- (**18**) and syrupy ethyl 1-thio-α-L-rhamnopyranoside (**19**) were prepared. Compound **19** was treated with dichlorodiphenylmethane in pyridine and crystalline ethyl 2,3-*O*-diphenylmethylene-1-thio-α-L-rhamnopyranoside (**20**) was iso-

lated. The acetal **20** was glycosylated with **6**, as described for the preparation of disaccharide **7**, to give compound **21**; deacetylation then gave **22**. Benzylidenation (→ **23**), benzylation (→ **24**), hydrogenolysis with dichloroalane (→ **25**), and methylation resulted in the glycosyl donor **26**. This glycosyl donor was also used for the preparation of compound **13**.

The introduction of the diphenylmethylene acetal function, as a temporary protecting group, and its simultaneous reduction together with the benzylidene ring drastically reduced the number of synthetic steps required for the preparation of the haptenic trisaccharide, demonstrating the importance of the protecting group strategy in the synthesis of complex oligosaccharides.

For comparative immunological investigations, we decided upon the synthesis of the terminal disaccharide, as well as of the terminal monosaccharide glycosides with the same spacer. For this reason, *p*-trifluoroacetamidophenol (**27**) was glycosylated with the thioglycoside **26** (activated by methyl triflate) to give **28** in 80% yield. The benzyl groups were removed by catalytic hydrogenation and the spacer-containing *p*-trifluoroacetamidophenyl *O*-(3,6-di-*O*-methyl-β-D-glucopyranosyl)-(1 → 4)-2,3-di-*O*-methyl-α-L-rhamnopyranoside (**29**) was obtained in nearly quantitative yield.

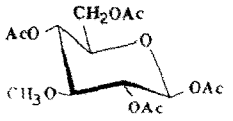


27

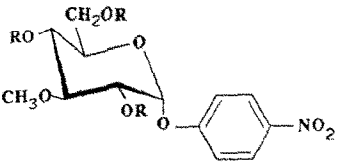
28 R=Bzl
29 R=H

For the synthesis of *p*-trifluoroacetamidophenyl 3,6-di-*O*-methyl-β-D-glucopyranoside (**43**), 1,2,4,6-tetra-*O*-acetyl-3-*O*-methyl-β-D-glucopyranose[40] (**30**) was selected as the starting compound. Coupling of **30** with *p*-nitrophenol was achieved using $SnCl_4$ as catalyst[41], and both isomers were isolated (in a ratio of 3:7) in favour of *p*-nitrophenyl 2,4,6-tri-*O*-acetyl-3-*O*-methyl-β-D-glucopyranoside (**32**). The corresponding α anomer (**31**) was also a crystalline compound. Both glycosides were *O*-deacetylated and the crystalline aromatic glycosides (**33** and **34**) were isolated and characterised. The β anomer (**34**) was treated with 0.9 equivalent of methyl iodide in *N*,*N*-dimethylformamide in the presence of powdered KOH, and the main product was isolated in a yield of 57%. Surprisingly, this compound proved to be *p*-nitrophenyl 2,3-di-*O*-methyl-β-D-glucopyranoside (**35**) instead of the desired 3,6-di-*O*-methyl derivative. A very similar product distribution was found when NaH was used instead of KOH. The unambiguous structure proof of **35** was based on ^{13}C and ^{1}H NMR spectroscopy, as well as on proton–carbon correlated spectra.

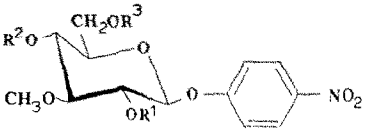
To overcome the unexpected high reactivity of HO-2 of **34**, it was isopropylidenated to obtain crystalline **36** (83%). The free HO-2 in **36** was benzylated (→ **37**),



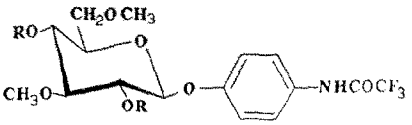
30



31 R = Ac
33 R = H



32 $R^1 = R^2 = R^3 = Ac$
34 $R^1 = R^2 = R^3 = H$
35 $R^1 = CH_3$; $R^2 = R^3 = H$
36 $R^1 = H$; $R^2, R^3 = >C(CH_3)_2$
37 $R^1 = Bzl$; $R^2, R^3 = >C(CH_3)_2$
38 $R^1 = Bzl$; $R^2 = R^3 = H$
39 $R^1 = Bzl$; $R^2 = CH_3$; $R^3 = H$
40 $R^1 = R^2 = Bzl$; $R^3 = H$
41 $R^1 = R^2 = Bzl$; $R^3 = CH_3$



42 R = Bzl
43 R = H

and the isopropylidene group was removed by acid hydrolysis, resulting in crystalline **38**. Methylation of the latter with 0.9 equivalent of methyl iodide gave a rather complex reaction mixture. The main product, isolated in a yield of 41%, was *p*-nitrophenyl 2-*O*-benzyl-3,4-di-*O*-methyl-β-D-glucopyranoside (**39**); the desired 3,6-di-*O*-methyl derivative was present in a yield of only 10–12%. In view of this unusual selectivity, **38** was benzylated and *p*-nitrophenyl 2,4-di-*O*-benzyl-**3**-*O*-methyl-β-D-glucopyranoside (**40**) was isolated in 39% yield. Methylation (→ **41**), reduction of the nitro group, and trifluoroacetylation of the resulting amine gave compound **42**, from which the benzyl groups were removed by catalytic reduction to afford the desired target compound (**43**) in crystalline form.

The unexpected low reactivity of HO-6 in the case of *p*-nitrophenyl β-D-glucopyranoside derivatives is under investigation.

EXPERIMENTAL

General methods.—Solutions were concentrated at 40°C (bath) under diminished pressure. Chromatography was performed on Kieselgel 60. Optical rotations were measured with a Perkin–Elmer 241 automatic polarimeter at room tempera-

ture in $CHCl_3$. The ^1H (200 and 400 MHz) and ^{13}C NMR (50.3 and 100 MHz) spectra were recorded with Bruker WP-200 SY and Varian XLA-400 spectrometers for solutions in $CDCl_3$ (internal Me_4Si). Melting points were determined on a Kofler apparatus and are uncorrected. TLC was performed on Kieselgel 60 F_{254} (Merck) with *A* 3:2, *B* 7:3, *C* 95:5, *D* 97:3, *E* 98:2 CH_2Cl_2–acetone; *F* 1:1, *G* 3:2, *H* 7:3, *I* 4:1 hexane–EtOAc; *K* 9:1 and *L* 95:5 CH_2Cl_2–MeOH; with detection by charring with H_2SO_4.

p-*Nitrophenyl 2,3-O-isopropylidene-α-*L*-rhamnopyranoside* (**1**).—*p*-Nitrophenyl α-L-rhamnopyranoside (5.4 g, 0.018 mol) was dissolved in 2,2-dimethoxypropane (35 mL, 0.28 mol), *p*-toluenesulfonic acid (20 mg) was added, and the mixture was stirred overnight. Then the mixture was diluted with CH_2Cl_2 (500 mL), neutralised with $NaHCO_3$ (200 mg), washed with water, dried (Na_2SO_4), and concentrated in vacuo. The residue (5.6 g) crystallised from cyclohexane (35 mL) to give **1** (4.8 g, 81.8%); mp 108–109°C, lit.[23] 107–108°C; $[\alpha]_D^{20}$ −124.6° (*c* 0.75); lit.[23] −128° (*c* 1.1); TLC (*C*): R_f 0.46. Anal. Calcd. for $C_{15}H_{19}NO_7$: C, 55.38; H, 5.88. Found: C, 55.43; H, 5.97.

p-*Nitrophenyl 4-O-benzyl-2,3-O-isopropylidene-α-*L*-rhamnopyranoside* (**2**).—To a stirred solution of **1** (4.2 g, 0.012 mol) in dry DMF (20 mL) were added 2 equiv of powdered KOH (2 g) and 1.2 equiv of benzyl bromide (2 mL, 2.86 g) at 0°C. After complete conversion (4 h), the mixture was diluted with CH_2Cl_2 (500 mL), the KOH was filtered off, and the filtrate was washed with water (3 × 80 mL), dried (Na_2SO_4), and concentrated in vacuo. The residue crystallised from 4:1 cyclohexane–n-hexane (25 mL) to give **2** (3.6 g, 72.2%); mp 89–90°C; $[\alpha]_D^{20}$ −109.05° (*c* 0.54); TLC (*C*): R_f 0.60; ^1H NMR: δ 8.21 and 7.14 (2 d, each 2 H, *p*-NO_2Ph), 7.38–7.25 (m, 5 H, Ph), 5.80 (s, 1 H, H-1), 4.92 and 4.65 (2 d, 2 H, J_{gem} 11.5 Hz, OCH_2Ph), 4.48–4.36 (m, 2 H), 3.72 (m, 1 H, H-5), 3.30 (dd, 1 H, $J_{3,4}$ 6.5, $J_{4,5}$ 10 Hz, H-4), 1.55 and 1.43 [2 s, each 3 H, C$(CH_3)_2$], and 1.22 (d, 3 H, $J_{5,6}$ 6 Hz, H-6). Anal. Calcd for $C_{22}H_{25}NO_7$: C, 63.60; H, 6.06. Found: C, 63.63, H, 6.11.

p-*Nitrophenyl 4-O-benzyl-α-*L*-rhamnopyranoside* (**3**).—A solution of **2** (3.6 g, 9.6 mmol) in CH_2Cl_2 (100 mL) was treated at room temperature with trifluoroacetic acid (10 mL) containing 1% of water, and was monitored by TLC (*C*). After 30 min, disappearance of starting material indicated complete reaction. The solution was diluted with CH_2Cl_2 (400 mL), washed successively with aq 10% $NaHCO_3$ and water, dried (Na_2SO_4), and concentrated in vacuo. The residue was purified by column chromatography (*C*) to give **3** (2.0 g , 96.8%); $[\alpha]_D^{20}$ −130.67° (*c* 0.64); TLC (*C*): R_f 0.38; ^{13}C NMR: δ 97.54 (C-1), 80.94 (C-4), 75.02 (OCH_2Ph), 71.08 (C-3), 70.53 (C-2), 68.71 (C-5), and 17.88 (C-6). Anal. Calcd for $C_{19}H_{21}NO_7$: C, 60.79; H, 5.64. Found: C, 60.84; H, 5.68.

p-*Nitrophenyl 4-O-benzyl-3-O-methyl-α-*L*-rhamnopyranoside* (**4**).—A solution of **3** (2.0 g, 5.3 mmol) and dibutyltin oxide (6.0 mmol, 1.5 g) in benzene (20 mL) was refluxed in a Dean and Stark apparatus. After 3 h, the benzene was distilled off, DMF (20 mL) and MeI (2 mL, 0.03 mol) were added and the mixture was stirred overnight at 50°C, then diluted with water, and extracted with diethyl ether. The

extract was dried (K_2CO_3) and concentrated in vacuo. The residue was dissolved in solvent *E* (200 mL), filtered through a layer of Celite, and concentrated. The crude product was purified by column chromatography (*E*) to give **4** (1.2 g, 58.1%) (a by-product, *p*-nitrophenyl 4-*O*-benzyl-2-*O*-methyl-α-L-rhamnopyranoside was detected by TLC (R_f 0.20, ~5%), but was not isolated). Compound **4** had $[\alpha]_D^{20}$ −165.3° (*c* 0.72); TLC (*E*): R_f 0.30; ^{1}H NMR: δ 8.24–7.08 (m, 9 H, *p*-NO_2Ph and Ph), 5.67 (d, 1 H, $J_{1,2}$ 2 Hz, H-1), 4.88 and 4.64 (2 d, 2 H, J_{gem} 11 Hz, OCH_2Ph), 4.28 (dd, 1 H, $J_{2,3}$ 3.5 Hz, H-2), 3.77 (dd, 1 H, $J_{3,4}$ 9 Hz, H-3), 3.71 (m, 1 H, H-5), 3.59 (s, 3 H, OCH_3), 3.50 (t, 1 H, H-4), 2.90 (s, 1 H, OH), and 1.43 (d, 3 H, $J_{5,6}$ 6 Hz, H-6); ^{13}C NMR: δ 97.21 (C-1), 81.23, 79.35 (C-3,4), 75.33 (OCH_2Ph), 68.62, 67.51 (C-2,5), 57.70 (OCH_3), and 17.85 (C-6). Anal. Calcd for $C_{20}H_{23}NO_7$: C, 61.69; H, 5.95. Found: C, 61.67; H, 6.03.

Methyl 2,3-O-diphenylmethylene-4-O-(2,4,6-tri-O-acetyl-3-O-methyl-β-D-gluco-pyranosyl)-1-thio-α-L-rhamnopyranoside (**7**).—A solution of silver triflate (2.5 g, 10 mmol) in 3:2 CH_2Cl_2–toluene (30 mL) was added dropwise to a stirred mixture of **5** (1.2 g, 3.34 mmol), **6** (1.92 g, 5 mmol), and 4A molecular sieves (2 g) in toluene (20 mL) at −40°C under Ar. The mixture was stirred for 30 min in the dark, and TLC (*C*) then revealed the disappearance of **5**. Pyridine (5 mL) and CH_2Cl_2 (80 mL) were added, and the mixture was filtered through a layer of Celite. The filtrate was washed with aq 10% sodium thiosulfate (50 mL) and water (2 × 50 mL), dried (Na_2SO_4), and concentrated in vacuo. The residue was purified by column chromatography (*C*) to give **7** as a white foam (1.70 g, 77.0%); $[\alpha]_D^{20}$ −109.9° (*c* 0.85); TLC (*C*): R_f 0.61; ^{1}H NMR: δ 7.61–7.23 (m, 10 H, 2 Ph), 5.53 (s, 1 H, H-1), 4 .99 (t, 1 H, $J_{3',4'}$ 9 Hz, H-4'), 4.88 (t, 1 H, $J_{1',2'}$ 8 Hz, H-2'), 4.44 (d, 1 H, H-1'), 4.29 (dd, 1 H, $J_{2,3}$ 6, $J_{3,4}$ 8 Hz, H-3), 4.09 (d, 1 H, H-2), 4.00 (dd, 1 H, $J_{5',6a'}$ 7.5, J_{gem} 12 Hz, H-6a'), 3.91 (m, 1 H, H-5), 3.80 (dd, 1 H, $J_{5',6b'}$ 3 Hz, H-6b'), 3.47–3.31 (m, 2 H), 3.41 (s, 3 H, OCH_3), 3.06 (m, 1 H, H-5'), 2.22, 2.09, 2.07 and 2.01 (4 s, each 3 H, 3 OAc and SCH_3), and 1.17 (d, 3 H, $J_{5,6}$ 6 Hz, H-6); ^{13}C NMR: δ 170.41, 169.34, and 169.21 (CO), 109.03 (C-ac), 100.79 (C-1'), 80.68 (C-1), 58.41 (OCH_3), 20.94, 20.70, and 20.56 (COCH_3), 13.12 (SCH_3). Anal. Calcd for $C_{33}H_{40}O_{12}S$: C, 59.98; H, 6.10. Found: C, 60.01; H, 6.17.

Methyl 2,3-O-diphenylmethylene-4-O-(3-O-methyl-β-D-glucopyranosyl)-1-thio-α-L-rhamnopyranoside (**8**).—Sodium methoxide (50 mg) was added to a solution of **7** (1.6 g, 2.4 mmol) in MeOH (30 mL). The mixture was stirred overnight, then neutralised with Amberlite IR-120 (H^+) ion-exchange resin, filtered, and concentrated in vacuo. The residue was purified by column chromatography (*L*) to give **8** (1.3 g, 96%); $[\alpha]_D^{20}$ −165.3° (*c* 0.32); TLC (*L*): R_f 0.38; ^{1}H NMR: δ 7.58–7.20 (m, 10 H, 2 Ph), 5.56 (s, 1 H, H-1), 4.43 (m, 2 H, H-1', 3), 4.11 (d, 1 H, $J_{2,3}$ 6 Hz, H-2), 3.97 (m, 1 H, H-5), 3.67 (s, 3 H, OCH_3), 3.63–3.41 (m, 4 H), 3.34 (dd, 1 H, $J_{3,4}$ 8, $J_{4,5}$ 10 Hz, H-4), 3.11 (t, 1 H, $J_{2',3'}$ 9 Hz, H-3'), 2.92 (m, 1 H, H-5'), 2.11 (s, 3 H, SCH_3), 1.21 (d, 3 H, $J_{5,6}$ 6 Hz, H-6); ^{13}C NMR: δ 109.43 (C-ac), 102.10 (C-1'), 80.89 (C-1), 60.53 (OCH_3), and 13.16 (SCH_3). Anal. Calcd for $C_{27}H_{34}O_9S$: C, 60.66; H, 6.41. Found: C, 60.57; H, 6.33.

Methyl 4-O-(4,6-O-benzylidene-3-O-methyl-β-D-glucopyranosyl)-2,3-O-diphenylmethylene-1-thio-α-L-rhamnopyranoside (**9**).—A mixture of **8** (620 mg, 1.16 mmol), α,α-dimethoxytoluene (2 mL), and a catalytic amount of *p*-toluenesulfonic acid was stirred for 1 h, then diluted with CH_2Cl_2 (50 mL), $NaHCO_3$ (4 g) was added, and the mixture was stirred for an additional 2 h. The organic layer was washed with water (3 × 20 mL), dried (Na_2SO_4), and concentrated in vacuo. The residue was purified by column chromatography (*E*) to give **9** (600 mg, 83.0%); $[\alpha]_D^{20}$ −156.9° (*c* 0.31); TLC (*E*): R_f 0.46; ^{1}H NMR: δ 7.60–7.22 (m, 15 H, 3 Ph), 5.56 (s, 1 H, H-1), 5.49 (s, 1 H, H-ac), 4.62 (d, 1 H, $J_{1',2'}$ 8 Hz, H-1'), 4.48 (dd, 1 H, $J_{2,3}$ 6, $J_{3,4}$ 8 Hz, H-3), 4.13 (d, 1 H, H-2), 4.08–3.90 (m, 2 H), 3.68 (s, 3 H, OCH_3), 3.65–3.35 (m, 5 H), 3.04 (m, 1 H, H-5'), 2.78 (s, 1 H, OH), 2.10 (s, 3 H, SCH_3), and 1.20 (d, 3 H, $J_{5,6}$ 6 Hz, H-6); ^{13}C NMR: δ 102.20 (C-ac'), 101.32 (C-1'), 81.07 (C-1), 60.78 (OCH_3), and 13.23 (SCH_3). Anal. Calcd for $C_{34}H_{38}O_9S$: C, 65.58; H, 6.15. Found: C, 65.66; H, 6.10.

Methyl 4-O-(2-O-benzyl-4,6-O-benzylidene-3-O-methyl-β-D-glucopyranosyl)-2,3-O-diphenylmethylene-1-thio-α-L-rhamnopyranoside (**10**).—To a stirred solution of **9** (600 mg, 0.96 mmol) in dry DMF (2 mL) were added 4 equiv of powdered KOH (220 mg) and 2 equiv of benzyl bromide (0.17 mL). After 2 h the mixture was diluted with CH_2Cl_2 (80 mL), the KOH was filtered off, and the filtrate was washed with water until neutral, dried (Na_2SO_4), and concentrated in vacuo. The crude product was purified by column chromatography (*I*) to give **10** as a yellow foam (520 mg, 75.9%); $[\alpha]_D^{20}$ −114.25° (*c* 0.41); TLC (*I*): R_f 0.43; ^{1}H NMR; δ 7.59–7.20 (m, 20 H, 4 Ph), 5.56 (s, 1 H, H-1), 5.49 (s, 1 H, H-ac), 4.94 and 4.75 (2 d, 2 H, J_{gem} 11 Hz, OCH_2Ph), 4.83 (d, 1 H, $J_{1',2'}$ 8 Hz, H-1'), 4.39 (dd, 1 H, $J_{2,3}$ 6, $J_{3,4}$ 8 Hz, H-3), 4.18–4.08 (m, 2 H, H-2,5), 4.03–3.90 (m, 2 H), 3.64 (s, 3 H, OCH_3), 3.62–3.40 (m, 3 H), 3.24 (t, 1 H), 3.01 (m, 1 H, H-5'), 2.13 (s, 3 H, SCH_3), and 1.21 (d, 3 H, $J_{5,6}$ 6 Hz, H-6). Anal. Calcd for $C_{41}H_{44}O_9S$: C, 69.08; H, 6.22. Found: C, 69.13; H, 6.14.

Methyl 4-O-(2,4-di-O-benzyl-3-O-methyl-β-D-glucopyranosyl)-1-thio-α-L-rhamnopyranoside (**11**).—To a stirred solution of **10** (800 mg, 1.12 mmol) in 1:1 diethyl ether–CH_2Cl_2 (40 mL) were added 4 equiv of $LiAlH_4$ (180 mg) and 12 equiv of $AlCl_3$ (1.8 g). The mixture was refluxed for 2 h, then diluted with diethyl ether (30 mL), and the excess of $LiAlH_4$ was decomposed by successive addition of EtOAc and water. The organic layer was washed with water (30 mL), dried (Na_2SO_4), and concentrated in vacuo. The residue was purified by column chromatography (*B*) to give **11** (400 mg, 64.9%); $[\alpha]_D^{20}$ −98.7° (*c* 0.23); TLC (*B*): R_f 0.52; ^{1}H NMR: δ 7.42–7.23 (m, 10 H, 2 PH), 5.10 (s, 1 H, H-1), 4.94–4.55 (m, 5 H, H-1' and 2 OCH_2Ph), 4.02–3.21 (m, 10 H), 3.67 (s, 3 H, OCH_3), 2.60 (s, 3 H, 3 OH), 2.12 (s, 3 H, SCH_3), and 1.30 (d, 3 H, $J_{5,6}$ 6 Hz, H-6); ^{13}C NMR: δ 103.49 (C-1'), 82.26 (C-1), 75.43 and 74.96 (2 OCH_2Ph), 61.80 (C-6'), 60.93 (OCH_3), and 13.48 (SCH_3). Anal. Calcd for $C_{28}H_{38}O_9S$: C, 61.10; H, 6.95. Found: C, 61.03; H, 6.88.

Methyl 4-O-(2,4-di-O-benzyl-3,6-di-O-methyl-β-D-glucopyranosyl)-2,3-di-O-methyl-1-thio-α-L-rhamnopyranoside (**12**).—To a stirred solution of **11** (400 mg,

0.73 mmol) in dry DMF were added powdered KOH (370 mg) and MeI (0.45 mL). After 5 h TLC (*C*) indicated complete conversion. The mixture was diluted with CH_2Cl_2 (80 mL), washed with water until neutral, dried (Na_2SO_4), and concentrated in vacuo. The residue was purified by column chromatography (*C*) to give **12** (290 mg, 67.3%); $[\alpha]_D^{20}$ −79.3° (*c* 0.11); TLC (*C*): R_f 0.45; ^{1}H NMR: δ 7.43–7.21 (m, 10 H, 2 Ph), 5.29 (s, 1 H, H-1), 4.97-4.58 (m, 5 H, H-1′ and 2 OCH_2Ph), 4.11 (m, 1 H, H-5), 3.87–3.21 (m, 9 H), 3.64, 3.48, 3.37, and 3.32 (4 s, each 3 H, 4 OCH_3), 2.11 (s, 3 H, SCH_3), and 1.35 (d, 3 H, $J_{5,6}$ 6 Hz, H-6); ^{13}C NMR: δ 102.96 (C-1′), 81.28 (C-1), 74.70 and 74.50 (2 OCH_2Ph), 61.04, 59.50, 58.14, and 56.97 (4 OCH_3), and 13.75 (SCH_3). Anal. Calcd for $C_{31}H_{44}O_9S$: C, 62.81; H, 7.48. Found: C, 62.87; H, 7.56.

p-*Nitrophenyl 4-O-benzyl-2-O-[4-O-(2,4-di-O-benzyl-3,6-di-O-methyl-β-*D*-glucopyranosyl)-2,3-di-O-methyl-α-*L*-rhamnopyranosyl]-3-O-methyl-α-*L*-rhamnopyranoside* (**13**).—To a stirred mixture of **12** (200 mg, 0.32 mmol), **4** (140 mg 0.34 mmol), and 4A molecular sieves (1.5 g) in dry CH_2Cl_2 (20 mL) were added 10 equiv of methyl triflate (0.36 mL) under Ar. After 20 h, TLC (*C*) indicated disappearance of **12**. Triethylamine (0.5 mL) was then added, and the mixture was diluted with CH_2Cl_2 (80 mL), filtered through a layer of Celite, and concentrated in vacuo. The residue was purified by column chromatography (*C*) to give **13** (180 mg, 56.7%); mp 186–188°C (from EtOH); $[\alpha]_D^{20}$ −73.5° (*c* 0.20); TLC (*C*): R_f 0.48; ^{1}H NMR: δ 8.22 and 7.17 (2 d, each 2 H, *p*-NO_2Ph), 7.40–7.23 (m, 15 H, 3 Ph), 5.64 (s, 1 H, H-1), 5.18 (s, 1 H, H-1′), 4.95–4.58 (m, 7 H, H-1″ and 3 OCH_2Ph), 4.23 (dd, 1 H), 3.90–3.10 (m, 13 H), 3.63, 3.58, 3.37, 3.31, and 3.24 (5 s, each 3 H, 5 OCH_3), 1.39 and 1.29 (2 d, each 3 H, H-6,6′); ^{13}C NMR: δ 102.69 (C-1″), 99.05 (C-1′), 97.28 (C-1), 61.10, 59.50, 58.95, 58.12, and 57.24 (5 OCH_3).

The coupling reaction starting from compounds **4** and **26**, using the above method, gave **13** with the same yield. Anal. Calcd for $C_{50}H_{63}NO_{16}$: C, 64.29; H, 6.79. Found: C, 64.37; H, 6.87.

p-*Trifluoroacetamidophenyl 4-O-benzyl-2-O-[4-O-(2,4-di-O-benzyl-3,6-di-O-methyl-β-*D*-glucopyranosyl)-2,3-di-O-methyl-α-*L*-rhamnopyranosyl]-3-O-methyl-α-*L*-rhamnopyranoside* (**14**).—A solution of **13** (150 mg, 0.16 mol) in EtOAc (10 mL) was hydrogenated over Adams' catalyst (30 mg) at room temperature and atmospheric pressure. After 1 h, the reduction of the nitro group was complete (TLC in *C*, R_f 0.45), then trifluoroacetic anhydride (0.2 mL) and pyridine (0.5 mL) were added, and the reaction mixture was kept at 60°C for 30 min, filtered, and concentrated in vacuo. A solution of the residue in CH_2Cl_2 (70 mL) was washed with water, dried (Na_2SO_4), and concentrated to give syrupy **14** (150 mg), which was used for the next step without any purification.

p-*Trifluoroacetamidophenyl 2-O-[4-O-(3,6-di-O-methyl-β-*D*-glucopyranosyl)-2,3-di-O-methyl-α-*L*-rhamnopyranosyl]-3-O-methyl-α-*L*-rhamnopyranoside* (**15**).—A solution of **14** (150 mg) in EtOH (10 mL) was hydrogenated at room temperature and atmospheric pressure over 10% Pd–C (30 mg). When TLC (*A*) indicated complete conversion (10 h), the mixture was filtered and concentrated in vacuo. The residue

was purified by column chromatography (*A*) to give **15** (87 mg, 75.3% for two steps); $[\alpha]_D^{20}$ −62.87° (*c* 0.62); TLC (*A*): R_f 0.27; ^{1}H NMR: δ 8.19 (s, 1 H, NH), 7.52 and 7.07 (2 d, each 2 H, *p*-NHCOCF$_3$Ph), 5.46 (d, 1 H, $J_{1,2}$ 2 Hz, H-1), 5.10 (d, 1 H, $J_{1',2'}$ 1.5 Hz, H-1'), 4.41 (d, 1 H, $J_{1'',2''}$ 8 Hz, H-1''), 3.78–3.17 (m, 13 H), 3.68, 3.54, 3.51, 3.50, and 3.38 (5 s, each 3 H, 5 OCH$_3$), 3.17 (t, 1 H), 1.34 and 1.27 (2 d, each 3 H, H-6,6'); ^{13}C NMR: δ 105.49 (C-1''), 98.57 (C-1'), 97.38 (C-1), 60.38, 59.49, 58.96, 57.63, and 56.49 (5 OCH$_3$). Anal. Calcd for $C_{31}H_{46}F_3NO_{15}$: C, 51.03; H, 6.35. Found: C, 51.07; H, 6.28.

*Ethyl 2,3,4-tri-*O*-acetyl-1-thio-β- and -α-*L*-rhamnopyranoside* (**16** *and* **17**).—Ethanethiol (7.2 mL, 0.10 mol) and $SnCl_4$ (11.5 mL, 0.10 mol) were added to a stirred solution of 1,2,3,4-tetra-*O*-acetyl-α-L-rhamnopyranose (30.5 g, 0.09 mol) in CH_2Cl_2 (20 mL) at 0°C. After 30 min, TLC (*H*) indicated 90% conversion and the presence of a mixture **16** and **17** in the ratio 1:5. The mixture was diluted with CH_2Cl_2 (500 mL), washed successively with water and aq 10% $NaHCO_3$ until neutral, dried (Na_2SO_4), and concentrated in vacuo. The residue crystallised from EtOH (40 mL) to give **16** (4.3 g, 14.0%); mp 166–167°C, lit.[38] 163–164°C; $[\alpha]_D^{20}$ +70.5° (*c* 0.71), lit.[38] $[\alpha]_D^{25}$ +70.5° (*c* 0.9); TLC (*H*): R_f 0.34; ^{1}H NMR: δ 5.50 (dd, 1 H, $J_{1,2}$ 1, $J_{2,3}$ 3 Hz, H-2), 5.10 (t, 1 H, $J_{3,4}$ 9 Hz, H-4), 5.02 (dd, 1 H, H-3), 4.76 (d, 1 H, H-1), 3.56 (m, 1 H, H-5), 2.74 (q, 2 H, SCH_2CH$_3$), 2.19, 2.06, 1.98 (3 s, each 3 H, 3 OAc), 1.32 (d, 3 H, $J_{5,6}$ 6 Hz, H-6), and 1.28 (t, 3 H, SCH$_2$CH_3).

The mother liquid was concentrated and the residue recrystallised from EtOH (10 mL) to give **17** (18.7 g, 60.9%); mp 66-68°C, lit.[38] 69–70°C; $[\alpha]_D^{20}$ −113.5° (*c* 0.78), lit.[38] $[\alpha]_D^{25}$ −115° (*c* 2); TLC (*H*): R_f 0.44; ^{1}H NMR: δ 5.34 (dd, 1 H, $J_{1,2}$ 1.5, $J_{2,3}$ 3.5 Hz, H-2), 5.28–5.19 (m, 2 H, H-1,3), 5.10 (t, 1 H, $J_{3,4}$ 9.5 Hz, H-4), 4.24 (m, 1 H, H-5), 2.64 (m, 2 H, SCH_2CH$_3$), 2.17, 2.16, 1.98 (3 s, each 3 H, 3 OAc), 1.30 (t, 3 H, SCH$_2$CH_3), and 1.24 (d, 3 H, $J_{5,6}$ 6 Hz, H-6). Anal. Calcd for $C_{14}H_{22}O_7S$: C, 50.28; H, 6.63. Found: C, 50.21; H, 6.55.

*Ethyl 1-thio-β-*L*-rhamnopyranoside* (**18**).—A stirred solution of **16** (2.0 g, 5.98 mmol) in MeOH (20 mL) was treated with NaOMe (20 mg). After complete conversion (TLC in *K*), the solution was neutralised with Amberlite IR-120 (H^+) ion-exchange resin, filtered, and concentrated in vacuo. The residue crystallised from EtOH to give **18** (1.1 g, 88.3%); mp 145–146°C, lit.[38] 145°C; $[\alpha]_D^{20}$ +130.5° (*c* 1.18, MeOH), lit.[38] $[\alpha]_D^{25}$ +123.5° (*c* 0.8, MeOH); TLC (*K*): R_f 0.36; ^{1}H NMR (D_2O): δ 4.85 (s, 1 H, H-1), 4.03 (d, 1 H, $J_{2,3}$ 3.5 Hz, H-2), 3.62 (dd, 1 H, $J_{3,4}$ 9 Hz, H-3), 3.52–3.33 (m, 2 H), 2.75 (q, 2 H, SCH_2CH$_3$), and 1.34–1.23 (m, 6 H, H-6 and SCH$_2$CH_3). Anal. Calcd for $C_8H_{16}O_4S$: C, 46.13; H, 7.74. Found: C, 46.04; H, 7.79.

*Ethyl 1-thio-α-*L*-rhamnopyranoside* (**19**).—Compound **19** was prepared from **17** by the above method used for conversion of **16** into **18**, with 89.7% yield. The syrupy **19** had $[\alpha]_D^{20}$ −223.4° (*c* 0.75, MeOH), lit.[38] $[\alpha]_D^{25}$ −229.5° (*c* 1.3, MeOH); TLC (*K*): R_f 0.41; ^{1}H NMR (D_2O): δ 5.25 (s, 1 H, H-1), 4.12–3.97 (m, 2 H), 3.75 (dd, 1 H, $J_{2,3}$ 3, $J_{3,4}$ 9 Hz, H-3), 3.42 (t, 1 H, H-4), 2.68 (m, 2 H, SCH_2CH$_3$), and

1.34–1.23 (m, 6 H, H-6 and SCH_2CH_3). Sugar analysis, as described above for **18**, gave the same results for **19**.

Ethyl 2,3-O-diphenylmethylene-1-thio-α-L-rhamnopyranoside (**20**).—To a solution of **19** (3.1 g, 0.015 mol) in dry pyridine (20 mL) were added 2 equiv of dichlorodiphenylmethane (5.7 mL). The mixture was stirred for 4 days at 110°C (TLC, solvent *C*). The dark-red solution was then poured onto crushed ice, and, after 1 h, the residue was diluted with CH_2Cl_2, washed with 0.5 M H_2SO_4, then with water until neutral, dried (Na_2SO_4), and concentrated. The dark-red residue was passed through a short column of silica gel (*E*). The appropriate fractions were combined and concentrated to give **20** (73%); mp 99–100°C (from cyclohexane); $[\alpha]_D^{20}$ −188.3° (*c* 0.52); TLC (*C*): R_f 0.63; ^{1}H NMR: δ 7.58–7.24 (m, 10 H, 2 Ph), 5.70 (s, 1 H, H-1), 4.28 (dd, 1 H, $J_{2,3}$ 6, $J_{3,4}$ 7.5 Hz, H-3), 4.0 (d, 1 H, H-2), 4.00 (m, 1 H, H-5), 3.40 (dd, 1 H, $J_{4,5}$ 10 Hz, H-4), 2.60 (m, 2 H, SCH_2CH_3), 1.30 (t, 3 H, SCH_2CH_3), and 1.24 (d, 3 H, $J_{5,6}$ 6.5 Hz, H-6); ^{13}C NMR: δ 143.11–125.76 (2 Ph), 109.48 (C-ac), 79.42 (C-1), 79.09 (C-3), 77.17 (C-2), 74.78 (C-4), 66.08 (C-5), 24.47 (SCH_2CH_3), 17.18 (C-6), and 14.61 (SCH_2CH_3). Anal. Calcd for $C_{21}H_{24}O_4S$: C, 67.72; H, 6.49. Found: C, 67.80; H, 6.51.

Ethyl 2,3-O-diphenylmethylene-4-O-(2,4,6-tri-O-acetyl-3-O-methyl-β-D-glucopyranosyl)-1-thio-α-L-rhamnopyranoside (**21**).—The method used for the synthesis of **7** was applied to couple **6** to **20**, to give **21**. Compound **21** (85.7%) had $[\alpha]_D^{20}$ −138.7° (*c* 0.64); TLC (*E*): R_f 0.28; ^{1}H NMR: δ 7.61–7.24 (m, 10 H, 2 Ph), 5.67 (s, 1 H, H-1), 4.96 (t, 1 H, $J_{3',4'}$ 9.5 Hz, H-4'), 4.91 (t, 1 H, $J_{1',2'}$ 8 Hz, H-2'), 4.43 (d, 1 H, H-1'), 4.28 (dd, 1 H, $J_{2,3}$ 5.5, $J_{3,4}$ 8 Hz, H-3), 4.10 (d, 1 H, H-2), 4.04 (dd, 1 H, $J_{5',6a'}$ 5, J_{gem} 12 Hz, H-6a'), 3.96 (dd, 1 H, $J_{4,5}$ 10, $J_{5,6}$ 6.5 Hz, H-5), 3.79 (dd, 1 H, $J_{5',6b'}$ 2.5 Hz, H-6b'), 3.47–3.31 (m, 2 H, H-3' and H-4), 3.41 (s, 3 H, OCH_3), 3.05 (m, 1 H, H-5'), 2.57 (m, 2 H, SCH_2CH_3), 2.23, 2.08, and 2.01 (3 s, each 3 H, 3 OAc), 1.28 (t, 3 H, SCH_2CH_3), and 1.17 (d, 3 H, H-6). Anal. Calcd for: $C_{34}H_{42}O_{12}S$: C, 60.52; H, 6.27. Found: C, 60.57; H, 6.19.

Ethyl 2,3-O-diphenylmethylene-4-O-(3-O-methyl-β-D-glucopyranosyl)-1-thio-α-L-rhamnopyranoside (**22**).—The method used for the conversion of **7** into **8** was applied to **21**, to give **22**. Compound **22** (91.3%) had $[\alpha]_D^{20}$ −162.3° (*c* 0.74); TLC (*B*): R_f 0.35; ^{1}H NMR: δ 7.60–7.24 (m, 10 H, 2 Ph), 5.68 (s, 1 H, H-1), 4.44 (d, 1 H, $J_{1',2'}$ 8 Hz, H-1'), 4.43 (dd, 1 H, $J_{2,3}$ 6, $J_{3,4}$ 8 Hz, H-3), 4.12 (d, 1 H, H-2), 4.01 (m, 1 H, H-5), 3.67 (s, 3 H, OCH_3), 3.62–3.45 (m, 4 H), 3.34 (dd, 1 H, $J_{4,5}$ 10 Hz, H-4), 3.12 (t, 1 H, $J_{2',3'}$ 9 Hz, H-3'), 2.92 (m, 1 H, H-5'), 2.59 (m, 2 H, SCH_2CH_3), 1.29 (t, 3 H, SCH_2CH_3), and 1.20 (d, 3 H, $J_{5,6}$ 6 Hz, H-6). Anal. Calcd for $C_{28}H_{36}O_9S$: C, 61.29; H, 6.61. Found: C, 61.37; H, 6.55.

Ethyl 4-O-(4,6-O-benzylidene-3-O-methyl-β-D-glucopyranosyl)-2,3-O-diphenylmethylene-1-thio-α-L-rhamnopyranoside (**23**).—The method used for the conversion of **8** into **9** was applied to **22**, to give **23**. Compound **23** (87.4%) had $[\alpha]_D^{20}$ −162.9° (*c* 0.95); TLC (*H*): R_f 0.41; ^{1}H NMR; δ 7.60–7.25 (m, 15 H, 3 Ph), 5.69 (s, 1 H, H-1), 5.49 (s, 1 H, H-ac), 4.62 (d, 1 H, $J_{1',2'}$ 7.5 Hz, H-1'), 4.47 (dd, 1 H, $J_{2,3}$ 6 Hz, $J_{3,4}$ 8 Hz, H-3), 4.13 (d, 1 H, H-2), 4.09–3.91 (m, 2 H), 3.68 (s, 3 H, OCH_3),

3.65–3.36 (m, 5 H), 3.03 (m, 1 H, H-5′), 2.59 (m, 3 H, SCH_2CH_3 and OH), 1.29 (t, 3 H, SCH_2CH_3), and 1.20 (d, 3 H, $J_{5,6}$ 6 Hz, H-6). Anal. Calcd for $C_{35}H_{40}O_9S$: C, 66.02; H, 6.33. Found: C, 66.13; H, 6.37.

Ethyl 4-O-(2-O-benzyl-4,6-O-benzylidene-3-O-methyl-β-D-glucopyranosyl)-2,3-O-diphenylmethylene-1-thio-α-L-rhamnopyranoside (**24**).—The method used for the conversion of **9** into **10** was applied to **23**, to give **24**. Compound **24** (84.7%) had $[\alpha]_D^{20}$ −139.3° (*c* 0.79); TLC (*H*): R_f 0.62; ^{1}H NMR: δ 7.59–7.23 (m, 20 H, 4 Ph), 5.69 (s, 1 H, H-1), 5.49 (s, 1 H, H-ac), 4.93 and 4.77 (2 d, 2 H, J_{gem} 11 Hz, OCH_2Ph), 4.84 (d, 1 H, $J_{1',2'}$ 8 Hz, H-1′), 4.39 (t, 1 H, $J_{2,3}$ 6, $J_{3,4}$ 8 Hz, H-3), 4.10 (d, 1 H, H-2), 4.05–3.90 (m, 2 H), 3.64 (s, 3 H, OCH_3), 3.62–3.42 (m, 4 H), 3.26 (t, 1 H), 3.01 (m, 1 H, H-5′), 2.60 (m, 2 H, SCH_2CH_3), 1.30 (t, 3 H, SCH_2CH_3), and 1.19 (d, 3 H, $J_{5,6}$ 6 Hz, H-6). Anal. Calcd for $C_{42}H_{46}O_9S$: C, 69.40; H, 6.38. Found: C, 69.46; H, 6.44.

Ethyl 4-O-(2,4-di-O-benzyl-3-O-methyl-β-D-glucopyranosyl)-1-thio-α-L-rhamnopyranoside (**25**).—The method used for the conversion of **10** into **11** was applied to **24**, to give **25**. Compound **25** (72.5%) had $[\alpha]_D^{20}$ −120.3° (*c* 0.53); TLC (*B*): R_f 0.51; ^{1}H NMR: δ 7.41–7.26 (m, 10 H, 2 Ph), 5.22 (s, 1 H, H-1), 4.95–4.56 (m, 5 H, H-1′ and 2 OCH_2Ph), 4.09–3.20 (m, 10 H), 3.67 (s, 3 H, OCH_3). 2.80 (s, 1 H, OH), 2.60 (m, 2 H, SCH_2CH_3), 1.90 (s, 2 H, 2 OH), 1.31 (d, 3 H, $J_{5,6}$ 6 Hz, H-6), and 1.29 (t, 3 H, SCH_2CH_3). Anal. Calcd for $C_{29}H_{40}O_9S$: C, 61.71; H, 7.12. Found: C, 61.73; H, 7.12.

Ethyl 4-O-(2,4-di-O-benzyl-3,6-di-O-methyl-β-D-glucopyranosyl)-2,3-di-O-methyl-1-thio-α-L-rhamnopyranoside (**26**).—The method used for the conversion of **11** into **12** was applied to **25**, to give **26**. Compound **26** (88.7%) had $[\alpha]_D^{20}$ −74.6° (*c* 0.83); TLC (*H*): R_f 0.32; ^{1}H NMR: δ 7.44–7.24 (m, 10 H, 2 Ph), 5.40 (s, 1 H, H-1), 4.95–4.58 (m, 5 H, H-1′ and 2 OCH_2Ph), 4.00 (m, 1 H), 3.79–3.23 (m, 9 H), 3.63, 3.52, 3.47, and 3.36 (4 s, each 3 H, 4 OCH_3), 2.67 (m, 2 H, SCH_2CH_3), 1.30 (t, 3 H, SCH_2CH_3), and 1.28 (d, 3 H, $J_{5,6}$ 6 Hz, H-6). Anal. Calcd for $C_{32}H_{46}O_9S$: C, 63.34; H, 7.64. Found: C, 63.38; H, 7.67.

p-*Trifluoroacetamidophenol* (**27**).—A solution of *p*-nitrophenol (5 g, 0.036 mol) in abs EtOH (50 mL) was hydrogenated over Pd–C (400 mg) at room temperature and atmospheric pressure. After 3 h, the mixture was filtered through a layer of Celite under Ar, and the filtrate was concentrated in vacuo under Ar. The solid residue was treated with 2 equiv of trifluoroacetic anhydride (5.4 mL) in trifluoroacetic acid (7.5 mL). The mixture was stirred; after 1 h, the crystalline product had precipitated. The mixture was poured onto crushed ice, and the precipitate was filtered off and washed with water. The crude product was recrystallised from water (35 mL) to give **27** (3.8 g, 51.5%) as white needles, mp 167–169°C. Anal. Calcd for $C_8H_6F_3NO_2$: C, 46.84; H, 2.95. Found: C, 46.89; H, 2.88.

p-*Trifluoroacetamidophenyl 4-O-(2,4-di-O-benzyl-3,6-di-O-methyl-β-D-glucopyranosyl)-2,3-di-O-methyl-α-L-rhamnopyranoside* (**28**).—To a stirred solution of **26** (300 mg, 0.49 mmol), **27** (150 mg, 0.74 mmol), and 4A molecular sieves (500 mg) in dry CH_2Cl_2 (10 mL) were added 10 equiv of methyl triflate (0.60 mL) under Ar.

After complete conversion (5 h), triethylamine (0.5 mL) was added, and the mixture was diluted with CH_2Cl_2 (50 mL), filtered through a layer of Celite, and concentrated in vacuo. The residue was purified by column chromatography (*H*) to give **28** (306 mg, 84%); $[\alpha]_D^{20}$ −60.6° (*c* 0.56); TLC (*H*): R_f 0.20; ^{1}H NMR: δ 8.20 (s, 1 H, NH), 7.54–7.10 (m, 14 H, *p*-NHCOCF$_3$Ph and 2 Ph), 5.54 (d, 1 H, $J_{1,2}$ 1.5 Hz, H-1), 4.93, 4.82, 4.73, and 4.61 (4 d, 4 H, each J_{gem} 11 Hz, 2 OCH_2Ph), 4.76 (d, 1 H, $J_{1',2'}$ 7.5 Hz, H-1') 3.78–3.19 (m, 10 H), 3.63, 3.54, 3.40, and 3.37 (4 s, each 3 H, 4 OCH$_3$), and 1.29 (d, 3 H, $J_{5,6}$ 6 Hz, H-6). Anal. Calcd for $C_{38}H_{46}F_3NO_{11}$: C, 61.28; H, 6.22. Found: C, 61.19; H, 6.28.

p-*Trifluoroacetamidophenyl 4-*O*-(3,6-di-*O*-methyl-β-*D*-glucopyranosyl)-2,3-di-*O*-methyl-α-*L*-rhamnopyranoside* (**29**).—A solution of **28** (100 mg, 0.13 mmol) in EtOH (10 mL) was hydrogenated over 10% Pd–C (20 mg) at room temperature and atmospheric pressure. After 10 h, TLC (*B*) indicated complete conversion, and the mixture was filtered through a layer of Celite and concentrated in vacuo. The residue was purified by column chromatography (*B*) to give **29** as a syrup (70 mg, 92%); $[\alpha]_D^{20}$ −70.8° (*c* 0.51); TLC (*B*): R_f 0.33; ^{1}H NMR: δ 8.48 (s, 1 H, NH), 7.52 and 7.05 (2 d, each 2 H, *p*-NHCOCF$_3$Ph), 5.54 (s, 1 H, H-1), 4.45 (d, 1 H, $J_{1',2'}$ 7.5 Hz, H-1'), 3.90–3.40 (m, 9 H), 3.67, 3.57, 3.54, and 3.38 (4 s, each 3 H, 4 OCH$_3$), 3.18 (t, 1 H), 2.21 (s, 2 H, 2 OH), and 1.29 (d, 3 H, $J_{5,6}$ 6 Hz, H-6). Anal. Calcd for $C_{24}H_{34}F_3NO_{11}$: C, 51.06; H, 6.07. Found: C, 51.12; H, 6.14.

p-*Nitrophenyl 2,4,6-tri-*O*-acetyl-3-*O*-methyl-α- and -β-*D*-glucopyranoside* (**31** *and* **32**).—*p*-Nitrophenol (3.28 g, 0.023 mol) and $SnCl_4$ (2.76 mL, 0.023 mol) were added to a stirred solution of **30** (8.5 g, 0.023 mol) in CH_2Cl_2 (25 mL) at room temperature. After 2 h, TLC (*F*) indicated complete conversion and the presence of an α:β anomeric mixture in the ratio 1:5. The solution was diluted with CH_2Cl_2 (500 mL), washed successively with aq 10% $NaHCO_3$ and water until neutral, dried (Na_2SO_4), and concentrated in vacuo. The anomeric mixture was fractionated by column chromatography (*G*) to give **31** and **32**.

Compound **31** (1.4 g, 13.8%) had mp 123–124°C (form cyclohexane); $[\alpha]_D^{20}$ +185.8° (*c* 1.11); TLC (*F*): R_f 0.57; ^{1}H NMR: δ 8.23 and 7.20 (2 d, each 2 H, *p*-NO$_2$Ph), 5.83 (d, 1 H, $J_{1,2}$ 3.5 Hz, H-1), 5.10 (t, 1 H, $J_{3,4}$ 10 Hz, H-4), 4.97 (dd, 1 H, $J_{2,3}$ 10 Hz, H-2), 4.19 (dd, 1 H, $J_{5,6a}$ 5, J_{gem} 12.5 Hz, H-6a), 4.02 (dd, 1 H, $J_{5,6b}$ 2 Hz, H-6b), 3.94 (m, 1 H, H-5), 3.92 (t, 1 H, H-3), 3.55 (s, 3 H, OCH$_3$), 2.13, 2.12, and 2.01 (3 s, each 3 H, 3 OAc). Anal. Calcd for $C_{19}H_{23}NO_{11}$: C, 51.70; H, 5.25. Found: C, 51.78; H, 5.33.

Compound **32** (6.8 g, 65.6%) had mp 120–122°C (from cyclohexane); $[\alpha]_D^{20}$ −58.2° (*c* 0.60); TLC (*F*): R_f 0.42; ^{1}H NMR: δ 8.21 and 7.06 (2 m, each 2 H, *p*-NO$_2$Ph), 5.30 (dd, 1 H, $J_{1,2}$ 7.5, $J_{2,3}$ 9.5 Hz, H-2), 5.15 (t, 1 H, $J_{3,4}$ 9.5 Hz, H-4), 5.12 (d, 1 H, H-1), 4.24 (dd, 1 H, $J_{5,6a}$ 6, J_{gem} 12.5 Hz, H-6a), 4.16 (dd, 1 H, $J_{5,6b}$ 3 Hz, H-6b), 3.83 (m, 1 H, H-5), 3.61 (t, 1 H, H-3), 3.46 (s, 3 H, OCH$_3$), 2.07–2.12 (3 s, each 3 H, 3 OAc). Sugar analysis, as described above for **31**, gave the same results for **32**.

p-*Nitrophenyl 3-*O*-methyl-α-*D*-glucopyranoside* (**33**).—A solution of **31** (1.1 g, 2.4

mmol) in MeOH (20 mL) was treated with NaOMe (50 mg) at 50°C for 1 h. The reaction mixture was neutralised with Amberlite IR-120 (H^+) ion-exchange resin and concentrated in vacuo. The solid residue was recrystallised from 4:1 cyclohexane–EtOAc (10 mL) to give **33** (610 mg, 80.6%); mp 160–161°C; $[\alpha]_D^{20}$ +217.7° (*c* 0.65, MeOH); TLC (*K*): R_f 0.16; ^{1}H NMR (D_2O): δ 8.20 and 7.28 (2 d, each 2 H, *p*-NO_2Ph), 5.79 (d, 1 H, $J_{1,2}$ 3.5 Hz, H-1), 3.90–3.48 (m, 6 H), and 3.72 (s, 3 H, OCH_3). Anal. Calcd for $C_{13}H_{17}NO_8$: C, 49.68; H, 5.43. Found: C, 49.74; H, 5.49.

p-*Nitrophenyl 3-*O*-methyl-β-*D*-glucopyranoside* (**34**).—Compound **34** was prepared from **32** by the above method, with 85.2% yield. Compound **34** had mp 139.5–140°C (from MeOH); $[\alpha]_D^{20}$ −78.2° (*c* 0.51, MeOH); TLC (*K*): R_f 0.19; ^{1}H NMR (D_2O): δ 8.26 and 7.24 (2 d, each 2 H, *p*-NO_2Ph), 5.28 (d, 1 H, $J_{1,2}$ 7.5 Hz, H-1), 3.99–3.40 (m, 6 H), and 3.68 (OCH_3). Sugar analysis, as described above for **33**, gave the same results for **34**.

p-*Nitrophenyl 2,3-di-*O*-methyl-β-*D*-glucopyranoside* (**35**).—A stirred solution of **34** in dry DMF (5 mL) was cooled in an ice–water bath, and 80% NaH (0.9 equiv, 77 mg) and MeI (0.9 equiv, 0.16 mL) were added. After 10 min, the mixture was diluted with EtOAc, washed with water until neutral, dried (Na_2SO_4), and concentrated in vacuo. TLC patterns (*B*): 60% of **35**, 10% of starting material, and 30% of by-products. The crude product was purified by column chromatography (*B*) to give **35** (535 mg, 57%); mp 155–156°C (from EtOAc–n-hexane); $[\alpha]_D^{20}$ −94.0° (*c* 0.40); TLC (*B*): R_f 0.37; ^{1}H NMR (400 MHz): δ 8.18 and 7.20 (2 d, each 2 H, *p*-NO_2Ph), 5.04 (d, 1 H, $J_{1,2}$ 7.5 Hz, H-1), 4.42 (d, 1 H, $J_{4,OH}$ 4.5 Hz, HO-4), 3.85 (m, 2 H, H_2-6), 3.67 and 3.64 (2 s, each 3 H, 2 OCH_3), 3.61 (m, 1 H, H-4), 3.47 (m, 1 H, H-5), 3.44 (t, 1 H, $J_{6,OH}$ 6.5 Hz), 3.33 (dd, 1 H, $J_{2,3}$ 9 Hz, H-2), and 3.26 (t, 1 H, $J_{3,4}$ 9 Hz, H-3); ^{13}C NMR (100 MHz): δ 161.92, 142.60, 125.77 and 116.40 (*p*-NO_2Ph), 100.60 (C-1), 85.59 (C-2), 83.12 (C-3), 76.28 (C-5), 69.82 (C-4), 61.83 (C-6), 61.03 (OCH_3-3), and 60.59 (OCH_3-2). Anal. Calcd for $C_{14}H_{19}NO_8$: C, 51.06; H, 5.81. Found: C, 51.11; H, 5.87.

p-*Nitrophenyl 4,6-*O*-isopropylidene-3-*O*-methyl-β-*D*-glucopyranoside* (**36**).—A mixture of **33** (1.46 g, 4.63 mmol), 2,2-dimethoxypropane (40 mL), and *p*-toluenesulfonic acid (30 mg) was stirred overnight, then diluted with CH_2Cl_2 (200 mL), washed with water until neutral, dried (Na_2SO_4), and concentrated in vacuo. The residue crystallised from EtOAc–n-hexane to give **36** (1.38 g, 83.9%); mp 139–140°C; $[\alpha]_D^{20}$ −75.8° (*c* 0.82); TLC (*C*): R_f 0.30; ^{1}H NMR: δ 8.21 and 7.10 (2 m, each 2 H, *p*-NO_2Ph), 5.11 (d, 1 H, $J_{1,2}$ 7.5 Hz, H-1), 3.98 (dd, 1 H, $J_{5,6a}$ 5.5, J_{gem} 11 Hz, H-6a), 3.97–3.70 (m, 3 H), 3.66 (s, 3 H, OCH_3), 3.49 (m, 1 H, H-5), 3.39 (t, 1 H, $J_{2,3}$ 9 Hz, H-3), 2.82 (d, 1 H, $J_{2,OH}$ 3 Hz, OH), 1.53 and 1.45 (2 s, each 3 H, $C(CH_3)_2$). Anal. Calcd for $C_{16}H_{21}NO_8$: C, 54.08; H, 5.95. Found: C, 54.12; H, 5.98.

p-*Nitrophenyl 2-*O*-benzyl-4,6-*O*-isopropylidene-3-*O*-methyl-β-*D*-glucopyranoside* (**37**).—A stirred solution of **36** (1.5 g, 4.2 mmol) in dry DMF (5 mL) was cooled in an ice–water bath, and 80% NaH (1 equiv, 130 mg) and benzyl bromide (1.1 equiv, 0.55 mL) were added. After 10 min, the mixture was diluted with EtOAc (200 mL),

washed with water until neutral, dried (Na_2SO_4), and concentrated in vacuo. The residue was purified by column chromatography (*I*) to give **37** as a yellow syrup (1.6 g, 85.5%); $[\alpha]_D$ −53.3° (*c* 0.76); TLC (*I*): R_f 0.31; ^{1}H NMR: δ 8.24–7.03 (m, 9 H, *p*-NO_2Ph and Ph), 5.15 (d, 1 H, $J_{5,6a}$ 7.5, J_{gem} 10.5 Hz, H-6a), 4.85 (s, 2 H, OCH_2Ph), 3.98 (dd, 1 H, $J_{3,4}$ 9.5, $J_{4,5}$ 5.5 Hz, H-4), 3.85–3.72 (m, 2 H, H-2,4), 3.70 (dd, 1 H, $J_{5,6b}$ 2.5 Hz, H-6b), 3.64 (s, 3 H, OCH_3), 3.50–3.37 (m, 2 H, H-3,5), 1.52 and 1.45 (2 s, each 3 H, C(CH_3)$_2$). Anal. Calcd f or $C_{23}H_{27}NO_8$: C, 62.01; H, 6.10. Found: C, 62.10; H, 6.15.

p-*Nitrophenyl 2-O-benzyl-3-O-methyl-β-*D*-glucopyranoside* (**38**).—A stirred solution of **37** (0.90 g , 2.02 mmol) in CH_2Cl_2 (50 mL) was treated at room temperature with trifluoroacetic acid (5 mL) containing 1% of water. After 10 min, the solution was concentrated in vacuo. The solid residue (0.7 g) crystallised from EtOH (15 mL) to give **38** (0.68 g, 83%); mp 188–190°C; $[\alpha]_D$ −74.3° (0.28, MeOH); TLC (*B*): R_f 0.46; ^{1}H NMR: δ 8.26–7.04 (m, 9 H, *p*-NO_2Ph and Ph), 5.16 (d, 1 H, $J_{1,2}$ 7.5 Hz, H-1), 4.94 and 4.81 (2 d, 2 H, J_{gem} 11 Hz, OCH_2Ph), 3.96 (dd, 1 H, $J_{5,6a}$ 3, J_{gem} 12 Hz, H-6a), 3.82 (dd 1 H, $J_{5,6b}$ 4.5 Hz, H-6b), 3.69 (s, 3 H, OCH_3), 3.65–3.51 (m, 4H), 3.36 (m, 1 H, H-5), 2.61 and 1.95 (2 s, 2 H, 2 OH). Anal. Calcd for $C_{20}H_{23}NO_8$: C, 59.25; H, 5.72. Found: C, 59.32; H, 5.76.

p-*Nitrophenyl 2-O-benzyl-3,4-di-O-methyl-β-*D*-glucopyranoside* (**39**).—A stirred solution of **38** (280 mg, 0.69 mmol) in dry DMF (3 mL) was cooled in an ice–water bath, and 80% NaH (0.9 equiv, 18 mg) and MeI (0.9 equiv, 0.038 mL) were added. After 10 min, the mixture was diluted with EtOAc, washed with water until neutral, dried (Na_2SO_4), and concentrated in vacuo. The crude product crystallised from EtOAc–cyclohexane to give white crystalline **39** (120 mg, 41%); mp 178–179°C; $[\alpha]_D^{20}$ −67.5° (*c* 0.64); TLC (*G*): R_f 0.25; ^{1}H NMR: δ 8.24–7.00 (m, 9 H, *p*-NO_2Ph and Ph), 5.09 (d, 1 H, $J_{1,2}$ 7.5 Hz, H-1), 4.90 and 4.82 (2 d, 2 H, J_{gem} 11 Hz, OCH_2PH), 3.93 (ddd, 1 H, $J_{5,6a}$ 3, $J_{6a,OH}$ 6, J_{gem} 12 Hz, H-6a), 3.77 (ddd, 1 H, $J_{5,6b}$ 4.5, $J_{6b,OH}$ 8 Hz , H-6b), 3.69 and 3.60 (2 s, each 3 H, 2 OCH_3), 3.59 (dd, 1 H, $J_{2,3}$ 9 Hz, H-2), 3.45 (m, 1 H, H-5), 3.39 (t, 1 H, $J_{3,4}$ 9 Hz), 3.27 (t, 1 H, H-3), and 1.86 (dd, 1 H, HO-6). Anal. Calcd for $C_{21}H_{25}NO_8$: C, 60.13; H, 6.00. Found: C, 60.11; H, 6.03.

p-*Nitrophenyl 2,4-di-O-benzyl-3-O-methyl-β-*D*-glucopyranoside* (**40**).—A stirred solution of **38** (380 mg, 0.94 mmol) in dry DMF (5 mL) was cooled in an ice–water bath, and 80% NaH (0.9 equiv, 25 mg) and benzyl bromide (0.9 equiv, 0.10 mL) were added. After 5 min, the mixture was diluted with EtOAc, washed with water until neutral, dried (Na_2SO_4), and concentrated in vacuo. The crude product was purified by column chromatography (*E*) to give **40** (180 mg, 39%); mp 172–174°C (from EtOH); $[\alpha]_D^{20}$ −56.4° (*c* 0.07); TLC (*E*): R_f 0.36; ^{1}H NMR: δ 8.25–7.00 (m, 14 H, *p*-NO_2Ph and 2 Ph), 5.11 (d, 1 H, $J_{1,2}$ 7.5 Hz, H-1), 4.92, 4.90, 4.83, and 4.68 (4 d, 4 H, each J_{gem} 11 Hz, 2 OCH_2Ph), 3.89 (ddd, 1 H, $J_{5,6a}$ 2.5, $J_{6a,OH}$ 6, J_{gem} 12 Hz, H-6a), 3.71 (ddd, 1 H, $J_{5,6b}$ 4.5, $J_{6b,OH}$ 8 Hz, H-6b), 3.70 (s, 3 H, OCH_3), 3.64–3.43 (m, 4 H), and 1.76 (dd, 1 H, OH). Anal. Calcd for $C_{27}H_{29}NO_8$: C, 65.45; H, 8.34. Found: C, 65.43; H, 8.31.

p-*Nitrophenyl 2,4-di-*O*-benzyl-3,6-di-*O*-methyl-β-*D*-glucopyranoside* (**41**).—A stirred solution of **40** (150 mg, 0.25 mmol) in dry DMF (3 mL) was cooled in an ice–water bath, and 80% NaH (2 equiv, 18 mg) and MeI (2 equiv, 0.037 mL) were added. After 5 min, TLC (*I*) indicated complete conversion. The excess of NaH was decomposed by addition of MeOH, and the mixture was diluted with EtOAc, washed with water until neutral, dried (Na_2SO_4), and concentrated in vacuo. The residue crystallised from EtOH (8 mL) to give **41** (130 mg, 81.2%); mp 160–162°C; $[\alpha]_D^{20}$ −43.6° (*c* 0.23); TLC (*I*): R_f 0.32; ^{1}H NMR: δ 8.23–7.01 (m, 14 H, *p*-NO_2Ph and 2 Ph), 5.04 (d, 1 H, $J_{1,2}$ 7.5 Hz, H-1), 4.92, 4.89, 4.83, and 4.64 (4 d, 4 H, each J_{gem} 11 Hz, 2 OCH_2Ph), 3.70 (s, 3 H, OCH_3-3), 3.68–3.40 (m, 6 H), and 3.34 (s, 3 H, OCH_3-6); ^{13}C NMR: δ 161.89, 142.75, 125.73, and 116.40 (*p*-NO_2Ph), 100.59 (C-1), 86.51–81.53 (C-2,3,4), 77.05 (C-5), 74.97 (2 O*C*H_2Ph), 70.86 (C-6), 61.35, and 59.32 (2 OCH_3). Anal. Calcd for $C_{28}H_{31}NO_8$: C, 66.00; H, 6.13. Found: C, 66.07; H, 6.15.

p-*Trifluoroacetamidophenyl 2,4-di-*O*-benzyl-3,6-di-*O*-methyl-β-*D*-glucopyranoside* (**42**).—A solution of **41** (100 mg, 0.20 mol) in EtOAc (10 mL) was hydrogenated over Adams' catalyst (30 mg) at room temperature and atmospheric pressure. After 1 h, reduction of the nitro group was complete (TLC in *C*, R_f 0.23), then trifluoroacetic anhydride (10 equiv, 0.28 mL) and pyridine (0.6 mL) were added, and the mixture was kept at 60°C for 1 h, then filtered, and concentrated in vacuo. A solution of the residue in CH_2Cl_2 (70 mL) was washed with water, dried (Na_2SO_4), and concentrated. The solid, brown residue was purified by column chromatography (*H*) to give white crystalline **42** (110 mg, 95.5%); mp 178–180°C (from EtOH); $[\alpha]_D^{20}$ −15.7° (*c* 0.76); TLC (*H*): R_f 0.44; ^{1}H NMR: δ 7.97 (s, 1 H, NH), 7.48–6.97 (m, 14 H, *p*-$NHCOCF_3$Ph and 2 Ph), 4.96, 4.88, 4.80, and 4.63 (4 d, 4 H, each J_{gem} 11 Hz, 2 OCH_2Ph), 4.93 (d, 1 H, $J_{1,2}$ 7.5 Hz, H-1), 3.68 (s, 3 H, OCH_3-3), 3.65–3.38 (m, 6 H), and 3.34 (s, 3 H, OCH_3-6). Anal. Calcd for $C_{30}H_{32}F_3NO_7$: C, 62.60; H, 5.60. Found: C, 62.64; H, 5.65.

p-*Trifluoroacetamidophenyl 3,6-di-*O*-methyl-β-*D*-glucopyranoside* (**43**).—A solution of **42** (70 mg, 0.12 mmol) in EtOH (8 mL) was hydrogenated over 10% Pd–C (20 mg) at room temperature and atmospheric pressure. After 10 h, TLC (*B*) indicated complete conversion, and the mixture was filtered through a layer of Celite and concentrated in vacuo. The residue was purified by column chromatography (*B*) to give crystalline **43** (44 mg, 93%); mp 188–189°C (from EtOAC–n-hexane); $[\alpha]_D^{20}$ −46.8° (*c* 0.45, MeOH); TLC (*B*): R_f 0.31; ^{1}H NMR: δ 7.92 (s, 1 H, NH), 7.62 and 7.05 (2 m, each 2 H, *p*-NO_2Ph), 4.86 (d, 1 H, $J_{1,2}$ 7.5 Hz, H-1), 3.70 (s, 3 H, OCH_3-3), 3.68–3.50 (m, 5 H), 3.38 (s, 3 H, OCH_3-6), 3.25 (t, 1 H, $J_{2,3}$ 9 Hz, H-3), 2.30 and 2.00 (2 s, 2 H, 2 OH). Anal. Calcd for $C_{15}H_{20}F_3NO_7$: C, 48.61; H, 5.09. Found: C, 48.67; H, 5.12.

ACKNOWLEDGMENT

The authors acknowledge Financial support from the National Science Foundation (OTKA 1666).

REFERENCES

1 S.W. Hunter and P.J. Brennan, *J. Bacteriol.*, 147 (1981) 728–735.
2 S.W. Hunter, T. Fujiwara, and P.J. Brennan, *J. Biol. Chem.*, 257 (1982) 15072–15078.
3 S.N. Payne, P. Draper, and R.J.W. Rees, *Int. J. Lepr.*, 50 (1982) 220–221.
4 S.J. Brett, P. Draper, S.N. Payne, and R.J.W. Rees, *Clin. Exp. Immunol.*, 52 (1983) 271–279.
5 D.B. Young, S. Dissanayake, R.A. Miller, S.R. Khanolkar, and T.M. Buchanan, *J. Infect. Dis.*, 149 (1984) 870–873.
6 D.B. Young and T.M. Buchanan, *Science*, 221 (1983) 1057–1059.
7 T.M. Buchanan, D.B. Young, R.A. Miller, and S.R. Khanolkar, *Int. J. Lepr.*, 51 (1983) 524–530.
8 T. Fujiwara, S.W. Hunter, S.-N. Cho, G.O. Aspinall, and P.J. Brennan, *Infect Immun.*, 43 (1984) 245–252.
9 S.-N. Cho, T. Fujiwara, S.W. Hunter, T.H. Rhea, R.H. Gelber, and P.J. Brennan, *J. Infect. Dis.*, 50 (1984) 311–322.
10 S.J. Brett, S.N. Payne, J. Gigg, P. Burgess, and R. Gigg, *Clin. Exp. Immunol.*, 64 (1986) 476–483.
11 S.-N. Cho, D.L. Yanagihara, S.W. Hunter R.H. Gelber, and P.J. Brennan, *Infect. Immun.*, 41 (1983) 1077–1083.
12 J. Gigg, R. Gigg, S. Payne, and R. Conant, *Chem. Phys. Lipids*, 35 (1985) 299–307.
13 T. Fujiwara, G.O. Aspinall, S.W. Hunter, and P.J. Brennan, *Carbohydr. Res.*, 163 (1987) 41–52.
14 T. Fujiwara and S. Izumi, *Agric. Biol. Chem.*, 51 (1987) 2539–2547.
15 D. Chatterjee, S.-N. Cho, C. Stewart, J.T. Douglas, T. Fujiwara, and P.J. Brennan, *Carbohydr. Res.*, 183 (1988) 241–260.
16 J. Marino-Albernas, V. Verez-Bencomo, L. Gonzalez-Rodriguez, C.S. Perez-Martinez, E. Gonzalez-Abreu Castell, and A. Gonzalez-Segredo, *Carbohydr. Res.*, 183 (1988) 175–182.
17 R. Gigg, S. Payne, and R. Conant, *J. Carbohydr. Chem.*, 2 (1983) 207–223.
18 J. Gigg, R. Gigg, S. Payne, and R. Conant, *Carbohydr. Res.*, 141 (1985) 91–97.
19 T. Fujiwara, S. Izumi, and P.J. Brennan, *Agric. Biol. Chem.*, 49 (1985) 2301–2308.
20 T. Fujiwara, S.W. Hunter, and P.J. Brennan, *Carbohydr. Res.*, 148 (1986) 287–298.
21 J. Marino-Albernas, V. Verez-Bencomo, L. Gonzalez-Rodriguez, and C.S. Perez-Martinez, *Carbohydr. Res.*, 165 (1987) 197–206.
22 K. Bock, T. Hvidt, J. Marino-Albernas, and V. Verez-Bencomo, *Carbohydr. Res.*, 200 (1990) 33–45.
23 P.J. Garegg, T. Norberg, P. Konradsson, and S.C.T. Svensson, *Carbohydr. Res.*, 122 (1983) 165–167.
24 A. Lipták, J. Imre, and P. Nánási, *Carbohydr. Res.*, 92 (1981) 154–156.
25 G. Medgyes, I. Pelczer, and J. Kuszmann, *Carbohydr. Res.*, 96 (1981) 306–311.
26 P. Fügedi and P. Nánási, *J. Carbohydr., Nucleosides, Nucleotides*, 8 (1981) 547–555.
27 C. Augé, S. David, and A. Veyrieres, *J. Chem. Soc., Chem. Commun.*, (1976) 375–376.
28 A. Lipták, L. Szabó, and J. Harangi, *J. Carbohydr. Chem.*, 7 (1988) 687–699.
29 Z. Szurmai and A. Lipták, *Carbohydr. Res.*, 107 (1982) 33–41.
30 Z. Szurmai, A. Lipták, and G. Snatzke, *Carbohydr. Res.*, 200 (1990) 201–208.
31 A. Lipták, I. Jodál, and P. Nánási, *Carbohydr. Res.*, 44 (1975) 1–11.
32 A. Borbás, J. Hajkó, and A. Lipták, *J. Carbohydr. Chem.*, submitted.
33 J. Hajkó, A. Borbás, A. Lipták, and M. Kajtàr-Peredy, *Carbohydr. Res.*, 216 (1991) 413–420.
34 H. Lönn, *Carbohydr. Res.*, 139 (1985) 105–113.
35 G. Ekborg, P.J. Garegg, and B. Gotthammar, *Acta Chem. Scand., Ser. B*, 29 (1975) 765–771.
36 K. Eklind, P.J. Garegg, and B. Gotthammar, *Acta Chem. Scand., Ser. B*, 30 (1976) 305–308.
37 G.H. Veeneman, L.F.J. Gomes, and J.H. van Boom, *Tetrahedron*, 45 (1989) 7433–7448.
38 J. Kihlberg, D.A. Leigh, and D.R. Bundle, *J. Org. Chem.*, 55 (1990) 2860-2863; F.-I. Auzanneau and D.R. Bundle, *Carbohydr. Res.*, 212 (1991) 13–24.
39 A. Lipták, A. Borbás, J. Kerékgyártó, and I. Bajza, *J. Carbohydr. Chem.*, submitted.
40 K. Freudenberg and R. Hixon, *Ber.*, 56 (1923) 2125–2127.
41 P.J. Garegg and T. Norberg, *J. Chem. Soc., Perkin Trans. 1*, (1982) 2973–2982.