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SYNTHESIS OF A DI-, TRI-, AND TETRA-SACCHARIDE UNIT OF THE GROUP B STREPTOCOCCAL COMMON ANTIGEN*†

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ABSTRACT

Condensation of methyl 2,3-*O*-isopropylidene-α-L-rhamnopyranoside with methyl 3,4,6-tri-*O*-acetyl-2-deoxy-2-phthalimido-1-thio-β-D-glucopyranoside activated by nitrosyl tetrafluoroborate gave an excellent yield of the protected disaccharide **9**, which was transformed into glycosyl acceptor **11**. Methyl 2,3,4,6-tetra-*O*-acetyl-1-thio-β-D-galactopyranoside, obtained from D-galactose pentaacetate and methyl trimethylsilyl sulfide, under catalysis by boron trifluoride etherate, was converted into glycosyl donor **25**, which was condensed with **11** under halide-ion catalysis to give the trisaccharide derivative **26**. Rhamnosylation with **28** of **27**, obtained by selective deprotection of **26**, gave the protected tetrasaccharide **29**. Deprotection of **10, 26,** and **29** gave di- (**2**), tri- (**3**) and tetra-saccharide (**4**) methyl glycosides which form part of the group-specific polysaccharide antigen of Group B *Streptococci*.

INTRODUCTION

Lancefield's serological studies[1] indicated that Group B Streptococci possess a common, group-specific polysaccharide antigen. Ongoing structural studies[2] in our laboratory provided proof for the structural identity of the Group B antigens obtained from the different serotypes and showed the presence of the octasaccharide **1** as one of the major structural units. The existence of the common polysaccharide could make it an ideal recognition marker for all members of the group and offers, in principle, the possibility of group-specific serodiagnosis of, and a single, synthetic human vaccine against, the different strains of Group B Streptococci.

In order to uncover the major, immunodominant region(s) of the common polysaccharide and thus provide haptens of well-defined structure to obtain totally synthetic antigens, we have started a synthesis program to obtain a series of oligo-

*Dedicated to Professor Bengt Lindberg.

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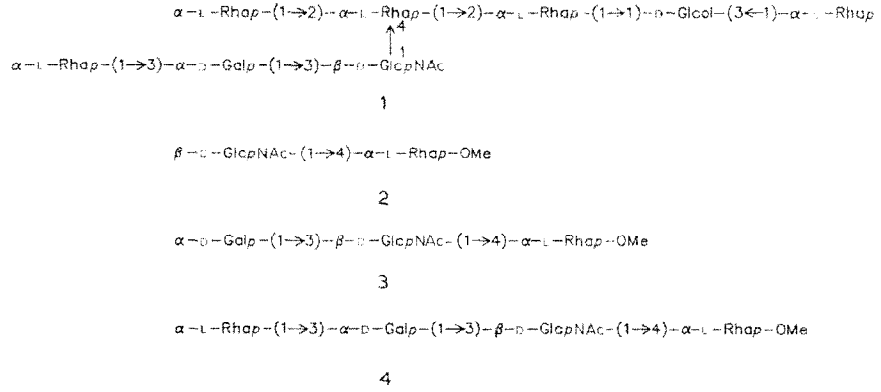
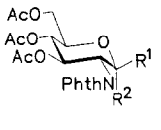
saccharides related to the common antigen. Recently, we reported[3] the synthesis of the methyl glycoside of the rhamnotriose unit. We now report the synthesis of the di- (**2**), tri- (**3**), and tetra-saccharide (**4**) as their methyl glycosides.



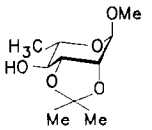
RESULTS AND DISCUSSION

Compounds **2**–**4** were synthesized in a stepwise fashion, starting at the reducing end. Reaction of glycosyl donor **5**[4–6] with methyl 2,3-*O*-isopropylidene-α-L-rhamnopyranoside[7,8] (**8**), using the procedure of Akiya and Osawa[9], gave the protected disaccharide **9** in 73.5% yield. In this study, **5** was obtained by brominolysis[10–12] of **7**[13,14] in 96% yield. The structure of **5** was unambiguously established by its elemental analysis and by its 500-MHz ^{1}H-n.m.r. and 125-MHz ^{13}C-n.m.r. spectra, which also supported evidence for the exclusive, 1,2-*trans* configuration of our preparation, the melting point (135–137°) of which agrees with that reported by Akiya and Osawa[5], but differs substantially from that (122–123°) reported by Baker *et al.*[4] and later by Lemieux *et al.*[6]. No correct elemental analytical data could be obtained for the former preparation whilst the latter one was not characterized by such data. In an alternative synthesis of **9**, the thioglycoside **7**[13,14] was envisaged as the glycosyl donor; **7** was prepared[14] from tetra-acetate **6**[4–6] by reaction with methyl trimethylsilyl sulfide under catalysis by boron trifluoride etherate, in 93.5% yield. Compound **7** was also obtained by reaction of **6** with MeSH under the conditions of Ferrier and Furneaux[15] in 55% yield. Compound **7** was synthesized earlier by Ogawa *et al.*[13] from **6** and methyl tributyltin sulfide. In the alternative route, glycosylation of acceptor **8** with thioglycoside **7** activated[16] by nitrosyl tetrafluoroborate, in dichloromethane, gave disaccharide **9** in 89.7% yield. This glycosylation reaction is thought to proceed through the intermediacy of a sulfonium species generated by electrophilic attack of the nitrosyl cation on the anomeric sulfur atom. It is thus similar, in principle, to the methods suggested by Nicolaou *et al.*[17], Lönn[18], and Fügedi and Garegg[19]. The reaction is fast and high yielding, and the activator nitrosyl salt is a commercially available solid which can be stored

indefinitely at 4° under anhydrous conditions. The configuration of the new, interglycosidic linkage in **9** was shown to be β-D by ^{13}C-n.m.r. spectroscopy: the $J_{C\text{-}1',H\text{-}1'}$ value for the C-1′ resonance at 97.8 p.p.m. is 168 Hz, which is characteristic[19] for this type of linkage.



5 R^1 = Br, R^2=H
6 R^1 = OAc, R^2=H
7 R^1 = SMe, R^2=H



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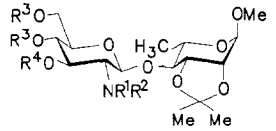


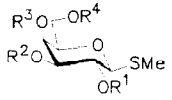
9 R^1,R^2=Phth, R^3=R^4=Ac
10 R^1=Ac, R^2=R^3=R^4=H
11 R^1=Ac, R^2=H, R^3=CH-(C$_6$H$_4$)-OMe, R^4=H

Removal of the *N*-phthaloyl group with $BuNH_2$ according to Durette *et al.*[20] followed by *N*-acetylation afforded **10**, the hydrolysis of which in aqueous acetic acid gave **2**. Compound **10** was transformed into glycosyl acceptor **11** by reaction with 4-methoxybenzaldehyde dimethyl acetal[21] in the presence of $TsOH \cdot H_2O$ in 91% yield.

As the glycosyl donor for reaction with acceptor **11**, compound **25** was selected; **25** contains a strategically positioned, temporary protecting group at HO-3, *i.e.*, the site of further chain extension. As a precursor to **25**, thioglycoside **13**[22,23] was used which allows a wide range of synthetic manipulations and can be converted into a glycosyl bromide under extremely mild conditions[10–12] after the desired transformations. Methyl 2,3,4,6-tetra-*O*-acetyl-1-thio-β-D-galactopyranoside[22,23] (**12**) was obtained[14] from 1,2,3,4,6-penta-*O*-acetyl-β-D-galactopyranose and methyl trimethylsilyl sulfide in 89% yield. Transesterification (Zemplén) of **12** gave **13**, the melting point of which (181–182°) is in agreement with the value reported by Helferich *et al.*[22] and is at variance with that (132–133°) given recently by Ogawa's group[23]. Attempts to selectively allylate HO-3 in **13**, by analogy[24] with the corresponding glycoside, were unsuccessful, which led us to resort to a multistep route to obtain intermediate **22**.

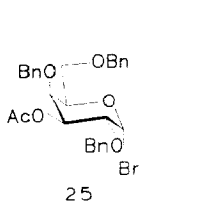
Reaction of **13** with 2,2-dimethoxypropane under $TsOH \cdot H_2O$ catalysis gave a mixture of compounds (**14–17**), the controlled hydrolysis of which afforded crystalline **16** in 91% yield without chromatography. Isomeric **17** could be obtained in 57% yield under reaction conditions[25] favouring kinetic control. Mixed acetal derivatives of galactopyranosides, similar to **15**, have been synthesized and characterized[26–28]. We were now able to isolate the extremely acid-labile, peracetalated derivative **14**. Formation of this type of tris-acetalated derivative was hitherto observed[28] with α-D-, but not with β-D-galactopyranosides. Mixtures of isomeric acetals **16** and **17** have been prepared by Garegg and Oscarson[29] and by Ogawa's group[23], but the isomers were not separated before further functionalization. Compound **16** was transformed into **22** in four steps: (*a*) BnBr–NaH–$HCONMe_2$; (*b*) HBF_4–H_2O–MeOH[27]; (*c*) Bu_2SnO–AllBr–C_6H_6[30]; (*d*) BnBr–NaH–$HCONMe_2$. De-

allylation (KO^tBu–Me_2SO[31]) of **22** followed by acetylation gave **24**, brominolysis[10–12] of which afforded a quantitative yield of syrupy glycosyl donor **25** in which the α-D configuration was ascertained by the presence in its ^{1}H-n.m.r. spectrum of the signal for H-1 at 6.479 p.p.m. with $J_{1,2}$ = 3.7 Hz.



12	$R^1=R^2=R^3=R^4=Ac$
13	$R^1=R^2=R^3=R^4=H$
14	$R^1=R^4=C(OMe)Me_2$, $R^2,R^3=CMe_2$
15	$R^1=H$, $R^2,R^3=CMe_2$, $R^4=C(OMe)Me_2$
16	$R^1=R^4=H$, $R^2,R^3=CMe_2$
17	$R^1=R^2=H$, $R^3,R^4=CMe_2$
18	$R^1=R^4=Ac$, $R^2,R^3=CMe_2$
19	$R^1=R^4=Bn$, $R^2,R^3=CMe_2$
20	$R^1=R^4=Bn$, $R^2=R^3=H$
21	$R^1=R^4=Bn$, $R^2=All$, $R^3=H$
22	$R^1=R^3=R^4=Bn$, $R^2=All$
23	$R^1=R^3=R^4=Bn$, $R^2=H$
24	$R^1=R^3=R^4=Bn$, $R^2=Ac$

Reaction of glycosyl donor **25** with the disaccharide acceptor **11** under conditions of halide-ion catalysed glycosidation[32] gave the protected trisaccharide **26** in 34.8% yield. Removal of the blocking groups from **26** in three steps [(*a*) NaOMe–MeOH; (*b*) HBF_4–MeOH[27]; (*c*) H_2–Pd/C–AcOH] gave the trisaccharide glycoside **3**. Transesterification (Zemplén) of **26** afforded acceptor **27**, which was glycosylated with rhamnosyl donor **28**[33] under Helferich conditions[34], followed by deacetylation (Zemplén) to give tetrasaccharide **29** in 67% yield. Deprotection of **29**, as described above, afforded the target tetrasaccharide glycoside **4**.



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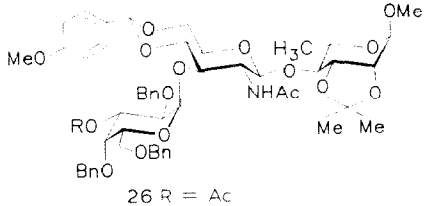
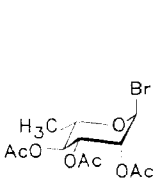


26 R = Ac

27 R = H



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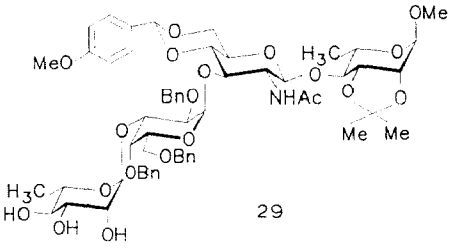

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The structures of the di- (**2**), tri- (**3**), and tetra-saccharide (**4**) methyl glycosides are supported by their ^{1}H- and ^{13}C-n.m.r. data (Tables I and II) obtained by combined application of one-dimensional measurements, and two-dimensional, homonuclear-correlated spectroscopy (COSY[35], RELAYED-COSY[36]) for protons.

TABLE I

^{1}H-N.M.R. DATA[a] FOR **2–4**

Chemical shifts (p.p.m.)				*Coupling constants[b] (Hz)*			
H atom	*Compound*			J_{H-H}[c]	*Compound*		
	2	**3**	**4**		**2**	**3**	**4**
1_A	4.663	4.674	4.676	1_A–2_A	1.9	1.9	2.2
2_A	3.857	3.868	3.870	2_A–3_A	3.5	3.5	3.4
3_A	3.776	3.785	3.795	3_A–4_A	9.4	9.3	9.4
4_A	3.584	3.606	3.610	4_A–5_A	9.4	9.3	9.4
5_A	3.695	3.702	3.706	5_A–6_A	6.2	6.2	6.2
6_A	1.330	1.338	1.340				
1_B	4.760	4.814	4.822	1_B–2_B	8.5	8.2	7.9
2_B	3.679	3.79	3.81	2_B–3_B	10.4		
3_B	3.540	3.75	3.78	3_B–4_B	8.4		
4_B	3.448	3.71	3.74	4_B–5_B	8.2	9.7	9.8
5_B	3.415	3.437	3.440	5_B–6_B	5.0	5.4	5.3
6_B	3.753	3.760	3.748	5_B–$6'_B$	2.1	2.3	2.6
$6'_B$	3.908	3.910	3.886	6_B–$6'_B$	12.4	12.4	12.5
1_C		5.437	5.486	1_C–2_C		3.4	4.0
2_C		3.795	3.915	2_C–3_C			9.9
3_C		3.77	3.816	3_C–4_C		2.8	3.6
4_C		3.984	4.052	4_C–5_C		1.2	<1
5_C		3.879	3.89	5_C–6_C		5.5	
6_C,$6'_C$		3.72	3.73	5_C–$6'_C$		6.8	
1_D			5.008	1_D–2_D			2.2
2_D			4.062	2_D–3_D			3.3
3_D			3.837	3_D–4_D			9.5
4_D			3.465	4_D–5_D			9.5
5_D			3.807	5_D–6_D			6.2
6_D			1.281				
CH_3O	3.369	3.378	3.379				
CH_3CO	2.032	2.055	2.064				

[a]At 500 MHz, in D_2O at 300 K. Other details are to be found in the Experimental. [b]Values obtained by first-order analysis. [c]Subscripts A–D refer to individual monosaccharide units, starting at the "reducing" end.

and CHORTLE[37] and two-dimensional, C–H heteronuclear-correlated spectroscopy[38] with a composite pulse sequence for carbons.

Serological experiments indicated that compounds **2–4** only poorly inhibit the reaction between the group-specific polysaccharide antigen and antibodies raised against it in mice. Details of this investigation will be published elsehwere[39].

EXPERIMENTAL

General methods. — See ref. 27. Optical rotations were measured on solutions in $CHCl_3$ at 20°, unless stated otherwise, with a Perkin–Elmer 243 automatic polarimeter. ^{1}H-N.m.r. spectra (500 MHz) and ^{13}C-n.m.r. spectra (125 and 50

TABLE II

^{13}C-N.M.R. CHEMICAL SHIFTS[a,b] FOR **2–4** AND HETERONUCLEAR COUPLING CONSTANTS[c] FOR THE ANOMERIC CARBON ATOMS OF **4**

Carbon atoms	*Compound*		
	2[e]	**3**[f]	**4**[f]
1_A	101.37	101.40	101.41 (170.6, 4.7)
2_A	70.97	70.98	71.00
3_A	71.18	71.29[g]	71.26
4_A	80.92	80.93	80.97
5_A	67.58	67.59	67.60
6_A	17.78	17.81	17.81
1_B	102.32	102.23	102.19 (163.9, 6.7)
2_B	56.68	55.22	55.19
3_B	74.73	80.32	79.95
4_B	70.61	71.45	71.79
5_B	76.44	76.12	76.16
6_B	61.39	61.17	61.18
1_C		99.80	99.52 (175.1)
2_C		69.25	68.53
3_C		70.02[g]	77.93
4_C		69.77	70.89
5_C		71.65	71.47
6_C		61.33	61.28
1_D			103.13 (171.0, 5.0)
2_D			69.67
3_D			70.89
4_D			72.82
5_D			69.93
6_D			17.47
CH_3O	55.57	55.54	55.57
CH_3CO	23.08	23.19	23.22
CH_3CO	175.46	175.24	175.27

[a]In D_2O, at 300 K. [b]Assignments are based on one-dimensional, heteronuclear ^{13}C–^{1}H correlation spectroscopy (CHORTLE[37]), using ^{1}H-n.m.r. data as given in Table I. Other conditions are to be found in the Experimental. [c]The one-bond ^{13}C–^{1}H and three-bond, ^{13}C–O–C–^{1}H coupling constants (in Hz) are given in parentheses. [d]Subscripts A–D refer to individual monosaccharide units, starting at the "reducing" end. [e]At 50 MHz. [f]At 125 MHz. [g]Carbons 3_A and 3_C in **3** could not be differentiated by CHORTLE; the assignments given are based on comparison with the spectra of **2** and **3**.

MHz) were recorded with Bruker AM-500 and AM-200 instruments, respectively, for solutions in $CDCl_3$ at 300 K unless stated otherwise. Two-dimensional measurements were made using standard Bruker software DISNMR. Compounds **2–4** were lyophilized from 99.5% D_2O twice before n.m.r. measurements in 99.95% D_2O solutions. Spectra obtained for solutions in CD_3OD were referenced to internal Me_4Si ($\delta = 0$) for protons and to the central line of the CD_3 multiplet ($\delta = 49.9$) for carbons. ^{13}C-N.m.r. assignments given in Table II and for compounds **5, 7, 12–17, 20–22,** and **24** are definitive; others are tentative. Assignments with an asterisk may be interchanged. *MBn* stands for the 4-methoxybenzylidene group.

3,4,6-Tri-O-acetyl-2-deoxy-2-phthalimido-β-D-glucopyranosyl bromide (**5**). — A solution of compound **7**[13,14] (1.02 g, 2.2 mmol) in CH_2Cl_2 (12 mL) was cooled to 0°. Bromine (115 μL, 2.2 mmol) was added, the cooling bath was removed, and the mixture was left standing for 15 min at 20°, then successively extracted with ice-cold, aqueous 2% $NaHSO_3$ (5 mL) and water (5 mL), dried (Na_2SO_4), and concentrated. Crystallization of the residue from diethyl ether gave colorless **5** (1.05 g, 96%), m.p. 135–137°, $[\alpha]_D$ +46° (*c* 1.3 or 3.7); lit.[5] m.p. 136–137°, $[\alpha]_D^{15}$ +27° (chloroform), lit.[6] m.p. 122–123°, $[\alpha]_D^{24}$ +57.3° (chloroform); lit.[4] m.p. 120–121°; ^{1}H-n.m.r.: δ 7.89–7.88, 7.78–7.76 (2 m, each 2 H, aromatic protons), 6.412 (d, 1 H, $J_{1,2}$ 9.7 Hz, H-1), 5.769 (dd, 1 H, $J_{2,3}$ 10.5 Hz, H-3), 5.263 (dd, 1 H, $J_{3,4}$ 8.9, $J_{4,5}$ 10.4 Hz, H-4), 4.634 (t, 1 H, H-2), 4.330 (dd, 1 H, $J_{5,6}$ 4.7, $J_{6,6'}$ 12.5 Hz, H-6), 4.203 (dd, 1 H, $J_{5,6'}$ 2.2 Hz, H-6'), 3.967 (ddd, 1 H, H-5), 2.139, 2.042, 1.872 (3 s, each 3 H, 3 CH_3CO); ^{13}C-n.m.r.: δ 170.6, 169.9, 167.3 (3 $COCH_3$), 170.2 (2 C=O), 134.6 (aromatic carbons), 130.7 (aromatic quaternary carbons), 123.9 (aromatic carbons), 77.2 (C-1), 76.8 (C-5), 70.6 (C-3), 68.1 (C-4), 61.7 (C-6), 58.1 (C-2), 20.7, 20.6, 20.3 (3 CH_3CO).

Anal. Calc. for $C_{20}H_{20}BrNO_9$ (498.27): C, 48.21; H, 4.05; Br, 16.04; N, 2.81. Found: C, 47.98; H, 3.98; Br, 15.91; N, 2.71.

Methyl 3,4,6-tri-O-acetyl-2-deoxy-2-phthalimido-1-thio-β-D-glucopyranoside (**7**). — (*a*) A mixture of compound **6**[4–6] (430 mg), $(CH_3)_3SiSCH_3$ (500 μL), $(CH_3)_3SiOSO_2CF_3$ (200 μL), and CH_2Cl_2 (5 mL) was stirred for 2 days at 20°, then treated with *N,N*-diisopropylethylamine (0.5 mL), extracted with water, dried (Na_2SO_4), and concentrated. The resulting syrup crystallized on addition of ether, to give **7** (392 mg, 93.5%), m.p. 153–154°, $[\alpha]_D$ +47° (*c* 1.5); lit.[13] m.p. 154–155°, $[\alpha]_D$ +50.9° (chloroform); ^{1}H-n.m.r. (200 MHz): δ 7.73–7.91 (m, 4 H, aromatic protons), 5.871 (dd, 1 H, $J_{2,3}$ 10.3, $J_{3,4}$ 9.1 Hz, H-3), 5.406 (d, 1 H, $J_{1,2}$ 10.5 Hz, H-1), 5.195 (dd, 1 H, $J_{4,5}$ 10.2 Hz, H-4), 4.441 (t, 1 H, H-2), 4.268 (dd, 1 H, $J_{5,6}$ 4.7, $J_{6,6'}$ 12.4 Hz, H-6), 4.196 (dd, 1 H, $J_{5,6'}$ 2.3 Hz, H-6'), 3.946 (ddd, 1 H, H-5), 2.171 (s, 3 H, SCH_3), 2.111, 2.046, 1.873 (3 s, each 3 H, 3 CH_3CO); ^{13}C-n.m.r.: δ 170.5, 169.9, 169.4 ($COCH_3$), 167.6, 167.1 (2 C=O), 134.34, 134.27 (aromatic carbons), 131.5, 131.0 (aromatic quaternary carbons), 123.6 (2×) (aromatic carbons), 80.5 (C-1, $J_{C\text{-}1,H\text{-}1}$ 155.4 Hz), 75.9 (C-5), 71.4 (C-3), 68.7 (C-4), 62.1 (C-6), 52.9 (C-2), 20.6, 20.5, 20.3 (3 CH_3CO), 11.3 (SCH_3, $J_{CH_3,H\text{-}1}$ 5.5 Hz).

Anal. Calc. for $C_{21}H_{23}NO_9S$ (465.45): C, 54.19; H, 4.98; N, 3.01; S, 6.89. Found: C, 54.38; H, 4.96; N, 2.96; S, 6.79.

(*b*) A solution of **6** (74 g, 0.21 mol), $BF_3 \cdot Et_2O$ (100 mL), and CH_2Cl_2 (300 mL) at 0° was treated with MeSH (25 g, 0.52 mol). The solution was allowed to reach 20° during 4 h, then neutralized by extraction with ice-cold, aqueous $NaHCO_3$, washed with water, and concentrated. Spontaneous crystallization was completed by addition of ethyl acetate and ether, to give **7** (26.6 g). Concentration of the mother liquor followed by chromatography of the residue in 2:1 ether–hexane gave more **7** (28 g; total yield, 54.6 g, 54.7%). This product was indistinguishable from the preparation obtained in (*a*).

Methyl 2,3-O-isopropylidene-4-O-(3,4,6-tri-O-acetyl-2-deoxy-2-phthalimido-β-D-glucopyranosyl)-α-L-rhamnopyranoside (**9**). — (*a*) A mixture of **5** (4.8 g, 9.63 mmol), **8**[7,8] (4.2 g, 19.25 mmol), powdered molecular sieves (4A, 3 g), and dichloromethane (20 mL) was stirred for 1 h at 20°, and then Ag_2CO_3 (2.5 g) was added. The mixture was stirred overnight at 20° and filtered, and the filtrate was concentrated. Chromatography of the residue in 2:1 hexane–ethyl acetate gave **9** (4.5 g, 73.5%) as a syrup which crystallized on standing; m.p. 147–148°, $[\alpha]_D$ +8.5° (*c* 1); ^{13}C-n.m.r.: δ 170.6, 170.0, 169.5 (3 $COCH_3$), 167.8 (2×) (2 C=O), 133.8 (2×) (aromatic carbons), 123.3 (2×) (aromatic carbons), 109.1 [$C(CH_3)_2$], 99.4 (C-1, $J_{C\text{-}1,H\text{-}1}$ 165 Hz), 97.7 (C-1′, $J_{C\text{-}1',H\text{-}1'}$ 168 Hz), 83.7 (C-4), 77.4 (C-5′), 75.7 (C-3), 71.5 (C-3′), 70.4 (C-2), 69.3 (C-4′), 63.9 (C-5), 62.3 (C-6′), 55.0 (CH_3O), 54.7 (C-2′), 27.6, 25.6 [(CH_3)$_2$C], 20.6 (2×), 20.4 (3 CH_3CO), 17.3 (C-6).

Anal. Calc. for $C_{30}H_{37}NO_{14}$ (635.5): C, 56.69; H, 5.87; N, 2.20. Found: C, 56.48; H, 5.79; N, 2.11.

(*b*) A mixture of **5** (490 mg, 0.98 mmol), **8** (220 mg, 1.01 mmol), and powdered molecular sieves (4A, 1.5 g) in dichloromethane (5 mL) was stirred for 15 min at 20°. Nitrosyl tetrafluoroborate (120 mg, 1.03 mmol) was added and stirring was continued for 1.5 h. The mixture was filtered, the filtrate concentrated, and the residue chromatographed in 2:1 ether–hexane to give **9** (575 mg, 89.7%), identical to the product obtained in (*a*).

Methyl 4-O-(2-acetamido-2-deoxy-β-D-glucopyranosyl)-2,3-O-isopropylidene-α-L-rhamnopyranoside (**10**). — A solution of **9** (3.5 g, 5.5 mmol) in MeOH (60 mL) and $BuNH_2$ (10 mL) was boiled under reflux[20] for 3 h and then concentrated. $BuNH_2$ was removed by repeated addition and evaporation of MeOH. A solution of the residue in MeOH (50 mL) at 0° was treated with Ac_2O (10 mL) for 4 h. The solution was concentrated and the residue chromatographed in 8:1 ethyl acetate–methanol to give **10** (1.55 g, 66.8%) as an amorphous solid, $[\alpha]_D$ −42° (*c* 0.7); ^{13}C-n.m.r.: δ 173.8 (C=O), 109.5 [$C(CH_3)_2$], 101.9 (C-1′, $J_{C\text{-}1',H\text{-}1'}$ 159 Hz), 97.7 (C-1, $J_{C\text{-}1,H\text{-}1}$ 168 Hz), 82.2 (C-4), 78.0 (C-3), 76.0 (C-5′), 75.7 (C-3′), 75.5 (C-2), 70.4 (C-4′), 64.1 (C-5), 61.7 (C-6′), 56.8 (C-2′), 54.8 (OCH_3), 28.0, 26.2 [$C(CH_3)_2$], 23.1 (CH_3CO), 17.5 (C-6).

Methyl 4-O-[2-acetamido-2-deoxy-4,6-(4-O-methoxybenzylidene)-β-D-glucopyranosyl]-2,3-O-isopropylidene-α-L-rhamnopyranoside (**11**). — A solution of **10** (1.2 g, 2.85 mmol), TsOH · H_2O (50 mg), 4-methoxybenzaldehyde dimethyl acetal[21] (5 mL), and *N,N*-dimethylformamide (10 mL) was stirred for 12 h at 20°. $NaHCO_3$ (~200 mg) was added and stirring was continued for 1 h. The solution was concentrated, and the residue was solidified by stirring with water, to give **11** (1.4 g, 91.1%), m.p. 256–257° (from ethyl acetate), $[\alpha]_D$ −72° (*c* 0.7); ^{13}C-n.m.r.: δ 173.1 (C=O), 160.1 [C-4′ *(MBn)*], 127.6 (2×) [C-2,6 *(MBn)*], 113.5 (2×) [C-3,5 *(MBn)*], 109.8 [$C(CH_3)_2$], 102.9 [C-7, *(MBn)*], 101.6 (C-1′), 97.7 (C-1), 83.8 (C-4), 81.3 (C-4′), 78.1 (C-3′), 76.2 (C-3), 73.6 (C-2), 68.4 (C-6′), 66.5 (C-5′), 64.0 (C-5), 59.3 (C-2′), 55.2, 54.9 (2 CH_3O), 28.1, 26.2 [(CH_3)$_2$C], 22.9 (CH_3CO), 17.2 (C-6).

Anal. Calc. for $C_{26}H_{37}NO_{11}$ (539.56): C, 59.54; H, 6.91; N, 2.59. Found: C, 58.80; H, 6.97; N, 2.59.

Methyl 2,3,4,6-tetra-O-acetyl-1-thio-β-D-galactopyranoside (**12**). — A mixture of 1,2,3,4,6-penta-*O*-acetyl-β-D-galactopyranose (2 g, 5.12 mmol), $(CH_3)_3SiSCH_3$ (2 mL, 19.6 mmol), and powdered molecular sieves (4A, 2.5 g) in CH_2Cl_2 (20 mL) was stirred for 2 h at 20°, and then cooled to 0–5°. $BF_3 \cdot Et_2O$ (600 μL) was added and the mixture was further stirred for 36 h at 0–5°. $(CH_3)_3SiSCH_3$ (1 mL, 9.8 mmol) and $BF_3 \cdot Et_2O$ (400 μL) were added, and stirring was continued for a further 12 h at 0–5°. The mixture was filtered, and the filtrate was extracted with ice-cold, aqueous 2% $NaHCO_3$ and H_2O, and then concentrated. The residue crystallized from 96% EtOH to give **12** (1.55 g, 79.9%), m.p. 110–112°, $[\alpha]_D$ +2.4° (*c* 1.3); lit.[22] m.p. 108°, $[\alpha]_D$ +2.9° (chloroform); lit.[23] m.p. 113–115°, $[\alpha]_D$ +2.0° (chloroform). The mother liquor was concentrated, and the residue was purified by chromatography in 1:1 EtOAc–hexane, to give additional **12** (0.18 g, 9.3%); total yield of **12**, 89.2%. The ^{1}H-n.m.r. data are identical with those given in ref. 23, except for the value of $J_{H-4,H-5}$ which was 1.1 Hz as compared with the reported[23] value of 0.3 Hz. ^{13}C-N.m.r.: δ 170.0, 169.8, 169.6, 169.2 (4 $COCH_3$), 82.9 (C-1, $J_{C-1,H-1}$ 153.5 Hz), 74.1 (C-5), 71.5 (C-3), 67.0 (C-4), 66.2 (C-2), 61.1 (C-6), 20.4, 20.3 (3×) (4 CH_3CO), 11.0 (SCH_3, $J_{CH_3,H-1}$ 4.2 Hz).

Anal. Calc. for $C_{15}H_{22}O_9S$ (378.39): C, 47.61; H, 5.86; S, 8.47. Found: C, 47.40; H, 5.78; S, 8.19.

Methyl 1-thio-β-D-galactopyranoside (**13**). — To a stirred mixture of **12** (24 g) in MeOH (60 mL) was added a catalytic amount of NaOMe. The mixture was stirred for 10 min at 20° and was left standing for 12 h at 0–4°. Scratching of the wall induced rapid crystallization, to give **13** (11.0 g, 82%), m.p. 181–182°, $[\alpha]_D$ +10.7° (*c* 1.2, water), $[\alpha]_D$ −2.9° (*c* 0.58, methanol); lit.[22] m.p. 174–175°, $[\alpha]_D$ +10.7° (water); lit.[23] m.p. 132–133°, $[\alpha]_D$ −5.1° (methanol). The ^{1}H-n.m.r. data are identical to those in ref. 23. ^{13}C-N.m.r. (CD_3OD): δ 88.8 (C-1), 81.6 (C-5), 77.1 (C-3), 71.7 (C-2), 71.4 (C-4), 63.5 (C-6), 12.9 (SCH_3).

Anal. Calc. for $C_7H_{14}O_5S$ (210.24): C, 39.99; H, 6.71; S, 15.25. Found: C, 39.76; H, 6.56; S, 15.11.

Methyl 3,4-O-isopropylidene-2,6-di-O-(1-methoxy-1-methylethyl)-1-thio-β-D-galactopyranoside (**14**), *methyl 3,4-O-isopropylidene-6-O-(1-methoxy-1-methylethyl)-1-thio-β-D-galactopyranoside* (**15**), *methyl 3,4-O-isopropylidene-1-thio-β-D-galactopyranoside* (**16**), *and methyl 4,6-O-isopropylidene-1-thio-β-D-galactopyranoside* (**17**). — (*a*) A mixture of **13** (2.55 g, 12.1 mmol), 2,2-dimethoxypropane (100 mL, 1.13 mol), and $TsOH \cdot H_2O$ (200 mg) was stirred for 8 h at 20°, then treated with Et_3N (2 mL), and concentrated. Chromatography of the residue in 1:1 hexane–ethyl acetate, containing 1% of Et_3N, gave, first, syrupy **14** (85 mg, 1.8%), $[\alpha]_D$ −17.2° (*c* 0.9); ^{1}H-n.m.r.: δ 4.522 (d, 1 H, $J_{1,2}$ 5.7 Hz, H-1), 4.252 (dd, 1 H, $J_{3,4}$ 6.6, $J_{4,5}$ 1.9 Hz, H-4), 4.221 (dd, 1 H, $J_{2,3}$ 4.3 Hz, H-3), 3.949 (dd, 1 H, H-2), 3.817 (ddd, 1 H, H-5), 3.651 (dd, 1 H, $J_{5,6}$ 6.5, $J_{6,6'}$ 9.9 Hz, H-6), 3.622 (dd, 1 H, $J_{5,6'}$ 5.8 Hz, H-6'), 3.27, 3.23 (2 s, each 3 H, 2 CH_3O), 2.209 (s, 3 H, CH_3S), 1.523, 1.417, 1.401, 1.358, 1.353, 1.329 [6 s, each 3 H, 2 $(CH_3)_2C(OCH_3)$ and $(CH_3)_2C$]; ^{13}C-n.m.r.: δ 109.5 [$C(CH_3)_2$], 101.4, 99.9 [2 $C(CH_3)_2(OCH_3)$], 85.8 (C-1), 77.3

(C-3), 74.7 (C-5), 73.0 (C-4), 70.7 (C-2), 60.3 (C-6), 49.5, 48.3, (2 CH_3O), 26.8 25.6, 25.4, 25.0, 24.3 (2×) [$C(CH_3)_2$ and 2 $C(CH_3)_2(OCH_3)$], 13.7 SCH_3.

Subsequent elution gave **15** (2.9 g, 74.2%), m.p. 58–60°, softens at 50–55°, $[\alpha]_D$ +20.6° (*c* 1.3); ^{1}H-n.m.r.: δ 4.226 (dd, 1 H, $J_{3,4}$ 5.4, $J_{4,5}$ 2.2 Hz, H-4), 4.185 (d, 1 H, $J_{1,2}$ 10.1 Hz, H-1), 4.070 (dd, 1 H, $J_{2,3}$ 7.0 Hz, H-3), 3.822 (ddd, 1 H, H-5), 3.702 (dd, 1 H, $J_{5,6}$ 6.3, $J_{6,6'}$ 9.8 Hz, H-6), 3.674 (dd, 1 H, $J_{5,6'}$ 6.0 Hz, H-6'), 3.582 (m, 1 H, H-2), 3.233 (s, 3 H, OCH_3), 2.204 (s, 3 H, SCH_3), 1.524, 1.365, 1.356, 1.348 [4 s, each 3 H, $(CH_3)_2C$ and $(CH_3)_2C(OCH_3)$]; ^{13}C-n.m.r.: δ 109.6 [$C(CH_3)_2$], 100.1 [$C(CH_3)_2(OCH_3)$], 84.9 (C-1), 79.1 (C-3), 75.8 (C-5), 73.7 (C-4), 71.4 (C-2), 60.3 (C-6), 48.4 (OCH_3), 28.1, 26.0, 24.2 [$C(CH_3)_2$ and $C(CH_3)_2(OCH_3)$], 11.4 (SCH_3).

Anal. Calc. for $C_{14}H_{26}O_6S$ (322.41): C, 52.15; H, 8.13; S, 9.94. Found: C, 52.01; H, 8.32; S, 10.01.

Further elution with ethyl acetate gave **16** (370 mg, 12.8%), m.p. 136–138° (from ether), $[\alpha]_D$ +44.8° (*c* 1); ^{1}H-n.m.r.: δ 4.243 (dd, 1 H, $J_{3,4}$ 5.4 Hz, $J_{4,5}$ 2.2 Hz, H-4), 4.220 (d, 1 H, $J_{1,2}$ 10.0 Hz, H-1), 4.006 (dd, 1 H, $J_{2,3}$ 7.8 Hz, H-3), 3.849 (ddd, 1 H, H-5), 3.773 (dd, 1 H, $J_{5,6}$ 7.2, $J_{6,6'}$ 11.5 Hz, H-6), 3.719 (dd, 1 H, $J_{5,6'}$ 5.0 Hz, H-6'), 3.469 (dd, 1 H, H-2), 2.184 (s, 3 H, SCH_3), 1.471, 1.329 [2 s, each 3 H, $(CH_3)_2C$]; ^{13}C-n.m.r. (CD_3OD): δ 111.8 [$C(CH_3)_2$], 87.6 (C-1), 82.0 (C-3), 79.4 (C-5), 76.2 (C-4), 73.8 (C-2), 63.5 (C-6), 29.4, 27.4 [$C(CH_3)_2$], 12.6 (SCH_3).

Anal Calc. for $C_{10}H_{18}O_5S$ (250.30): C, 47.98; H, 7.25; S, 12.81. Found: C, 48.02; H, 7.39; S, 12.59.

Finally, elution with 10:1 ethyl acetate–methanol gave **17** (85 mg, 2.9%), m.p. 108–110° (from ether–hexane), $[\alpha]_D$ −9.5° (*c* 1.5); ^{1}H-n.m.r. (CD_3OD): δ 4.219 (d, 1 H, $J_{1,2}$ 9.5 Hz, H-1), 4.210 (dd, 1 H, $J_{3,4}$ 3.6, $J_{4,5}$ 1.2 Hz, H-4), 4.098 (dd, 1 H, $J_{5,6}$ 2.0 Hz, H-6), 3.821 (dd, 1 H, $J_{5,6'}$ 1.7, $J_{6,6'}$ 12.8 Hz, H-6'), 3.650 (t, 1 H, $J_{2,3}$ 9.4 Hz, H-2), 3.520 (dd, 1 H, H-3), 3.419 (ddd, 1 H, H-5), 2.186 (s, 3 H, SCH_3), 1.462, 1.381 [2 s, each 3 H, $(CH_3)_2C$]: ^{13}C-n.m.r. (CD_3OD): δ 100.8 [$C(CH_3)_2$], 87.6 (C-1), 75.6 (C-3), 71.9 (C-5), 71.1 (C-4), 70.7 (C-2), 64.8 (C-6), 30.4, 19.7 [$(CH_3)_2C$], 12.4 (SCH_3).

Anal. Calc. for $C_{10}H_{18}O_5S$ (250.30): C, 47.98; H, 7.25; S, 12.81. Found: C, 47.68; H, 7.38; S, 12.88.

(*b*) A mixture of **13** (15 g), $TsOH \cdot H_2O$ (250 mg), and 2,2-dimethoxypropane (300 mL) was stirred for 12 h at 20°. Et_3N (1 mL) was added and the solution was concentrated. A solution of the residue in CH_2Cl_2 (150 mL) was stirred with aqueous 50% trifluoroacetic acid (2 mL) for 15 min at 20°, then treated with Et_3N (3 mL), and concentrated. Crystallization (ether) gave **16** (16.3 g, 91.2%). The product was identical to **16** obtained in (*a*).

(*c*) A mixture of **13** (500 mg, 2.38 mmol), *N,N*-dimethylformamide (5 mL), 2,2-dimethoxypropane (1 mL), and $TsOH \cdot H_2O$ (85 mg) was stirred for 2 h at 0°. Et_3N (0.5 mL) was added and the mixture was concentrated. Chromatography of the residue in ethyl acetate gave **15** (10 mg, 1.3%), **16** (95 mg, 15.9%), and **17** (340 mg, 57.1%).

Methyl 2,6-di-O-acetyl-3,4-O-isopropylidene-1-thio-β-D-galactopyranoside (**18**). — A solution of **16** (100 mg) in pyridine (1 mL) and Ac_2O (1 mL) was kept for 14 h at 20°. Concentration followed by recrystallization from ether–hexane gave **18** (119 mg, 89.1%), m.p. 102–104°, $[\alpha]_D$ +74° (*c* 0.8); ^{1}H-n.m.r.: δ 5.031 (dd, 1 H, $J_{2,3}$ 6.8 Hz, H-2), 4.368 (dd, 1 H, $J_{5,6}$ 4.6, $J_{6,6'}$ 11.8 Hz, H-6), 4.327 (dd, 1 H, $J_{5,6'}$ 7.3 Hz, H-6'), 4.18–4.25 (m, 2 H, H-3,4), 4.016 (ddd, 1 H, $J_{4,5}$ 2 Hz, H-5), 2.164 (s, 3 H, SCH_3), 2.118, 2.098 (2 s, each 3 H, 2 CH_3CO), 1.556, 1.348 [2 s, each 3 H, $(CH_3)_2C$]; ^{13}C-n.m.r.: δ 170.7, 169.6 (2 C=O), 110.6 [$C(CH_3)_2$], 82.0 (C-1), 77.0 (C-3*), 74.3 (C-5), 73.6 (C-4*), 70.5 (C-2), 63.5 (C-6), 27.6, 26.2 [$(CH_3)_2C$], 20.9, 20.8 (2 CH_3CO), 11.3 (SCH_3).

Anal. Calc. for $C_{14}H_{22}O_7S$ (334.38): C, 50.28; H, 6.58; S, 9.59. Found: C, 50.53; H, 6.72; S, 9.40.

Methyl 2,6-di-O-benzyl-3,4-O-isopropylidene-1-thio-β-D-galactopyranoside (**19**). — NaH (8 g) was added in small portions to a solution of **16** (12 g, 47.9 mmol) in *N,N*-dimethylformamide (100 mL) under stirring and cooling with ice–water. After addition, the mixture was stirred for 30 min, then benzyl bromide (28 mL, 114.5 mmol) was added dropwise, and the mixture was stirred for 12 h at 20°. The excess of NaH was decomposed by dropwise addition of MeOH (10 mL) and then H_2O (10 mL). The mixture was diluted with $CHCl_3$ (200 mL), extracted with H_2O (3 × 100 mL), dried, and concentrated to give syrupy **19** (18.7 g, 90.6%). A portion of the syrup, further purified by chromatography in 3:1 hexane–ethyl acetate, had $[\alpha]_D$ −5° (*c* 0.6); lit.[23] $[\alpha]_D$ −15.7° (*c* 1, chloroform). For the ^{1}H-n.m.r. data, see ref. 23. ^{13}C-N.m.r.: δ 137.9, 137.5 (aromatic quaternary carbons), 128.0, 127.4, 127.3 (aromatic carbons), 109.6 [$C(CH_3)_2$], 84.1 (C-1), 79.2 (C-3*), 78.5 (C-2), 75.4 (C-5), 73.6 (C-4*), 73.2, 73.0 [2 CH_2 (Bn)], 69.3 (C-6), 27.6, 26.0 [$C(CH_3)_2$], 12.5 (SCH_3).

Methyl 2,6-di-O-benzyl-1-thio-β-D-galactopyranoside (**20**). — A solution of **19** (18 g, 41.8 mmol) in MeOH (250 mL) and 50% aqueous HBF_4 (4 mL) was stirred[27] for 2 h at 20°, $NaHCO_3$ (5 g) was added, and the mixture was stirred for 1 h and then concentrated. The residue was partitioned between CH_2Cl_2 (200 mL) and H_2O (3 × 50 mL), and the organic phase was dried (Na_2SO_4) and concentrated, to give **19** (13.8 g, 84.6%), m.p. 90–91°, $[\alpha]_D$ +8.1° (*c* 0.7); lit.[23] m.p. 91–92°, $[\alpha]_D$ +6.3° (*c* 0.6, chloroform). The ^{1}H-n.m.r. data agreed with those published in ref. 23, except for the following: δ 4.032 (dd, 1 H, $J_{3,4}$ 3.3, $J_{4,5}$ 1.1 Hz, H-4), 3.617 (dd, 1 H, H-3). ^{13}C-N.m.r.: δ 137.9, 137.6 (aromatic quaternary carbons), 128.3, 128.1, 127.8, 127.6 (aromatic carbons), 85.2 (C-1), 78.3 (C-2), 76.8 (C-5), 75.1 [CH_2 (Bn)], 74.7 (C-3), 73.5 [CH_2 (Bn)], 69.39 (C-4), 69.34 (C-6), 12.7 (SCH_3).

Anal. Calc. for $C_{21}H_{26}O_5S$ (390.48): C, 64.59; H, 6.71; S, 8.21. Found: C, 64.19; H, 6.52; S, 8.00.

Methyl 3-O-allyl-2,6-di-O-benzyl-1-thio-β-D-galactopyranoside (**21**). — A mixture of **20** (13.0 g, 33.3 mmol), Bu_2SnO (12.1 g, 34.9 mmol), and benzene (250 mL) was stirred under reflux, using a Dean–Stark trap, for 8 h. Benzene (150 mL) was then removed by distillation, and the reaction mixture was cooled to ~45°.

Bu_4NBr (6.5 g, 34.9 mmol) and allyl bromide (5 mL, 57.6 mmol) were added, and the mixture was stirred for 5 h at ~45° and then concentrated. The residue was partitioned between CH_2Cl_2 (200 mL) and H_2O (3 × 50 mL), and the CH_2Cl_2 layer was dried (Na_2SO_4) and concentrated. Chromatography of the residue in 1:1 ether–hexane gave **21** (11.5 g, 80.3%) as a syrup, $[\alpha]_D$ −21.5° (*c* 2); ^{1}H-n.m.r.: δ 7.4–7.26 (m, 10 H, aromatic protons), 5.94 [m, 1 H, CH= (allyl)], 5.31, 5.20 [2 m, each 1 H, CH_2= (allyl)], 4.83, 4.76 [2 d, each 1 H, CH_2 (Bn)], 4.75 [s, 2 H, CH_2 (Bn)], 4.319 (d, 1 H, $J_{1,2}$ 9.7 Hz, H-1), 4.19 [m, 2 H, CH_2 (allyl)], 4.10 (m, 1 H, H-4), 3.791 (dd, 1 H, $J_{5,6}$ 6.1, $J_{6,6'}$ 10.0 Hz, H-6), 3.735 (dd, 1 H, H-6'), 3.649 (t, 1 H, H-2), 3.592 (dt, 1 H, $J_{4,5}$ 1.0 Hz, H-5), 3.460 (dd, 1 H, $J_{2,3}$ 9.0 Hz, H-3), 1.223 (s, 3 H, SCH_3); ^{13}C-n.m.r.: δ 138.0, 137.8 (aromatic quaternary carbons), 134.4 [*C*H= (allyl)], 128.3, 127.7 (aromatic carbons), 117.4 [CH_2= (allyl)], 85.2 (C-1), 82.1 (C-3), 77.2 (C-2), 76.8 (C-5), 75.6, 73.6 [2 CH_2 (Bn)], 71.0 [CH_2 (allyl)], 69.2 (C-6), 66.9 (C-4), 12.5 (SCH_3).

*Methyl 3-O-allyl-2,4,6-tri-O-benzyl-1-thio-β-*D*-galactopyranoside* (**22**). — Compound **21** was benzylated as described for **19**. Chromatography in 3:1 hexane–ether gave **22** as a syrup (72%), $[\alpha]_D$ −7.8° (*c* 0.9); ^{1}H-n.m.r.: δ 7.45–7.24 (m, 15 H, aromatic protons), 5.95 [m, 1 H, CH= (allyl)], 5.33, 5.19 (2 m, each 1 H, CH_2 (allyl)], 4.95, 4.84, 4.80, 4.61, 4.47, 4.42 [6 d, each 1 H, 3 CH_2 (Bn)], 4.314 (d, 1 H, $J_{1,2}$ 9.6 Hz, H-1), 4.19 [m, 2 H, CH_2 (allyl)], 3.929 (dd, 1 H, $J_{3,4}$ 2.9, $J_{4,5}$ 0.8 Hz, H-4), 3.784 (t, 1 H, H-2), 3.95–3.55 (m, 3 H, H-5,6,6'), 3.464 (dd, 1 H, $J_{2,3}$ 9.3 Hz, H-3), 2.195 (s, 3 H, SCH_3); ^{13}C-n.m.r.: δ 138.8, 138.3, 137.8 (aromatic quaternary carbons), 134.8 [CH= (allyl)], 128.4–127.4 (aromatic carbons), 116.7 [CH_2= (allyl)], 85.6 (C-1), 83.7 (C-3), 77.8 (C-2), 77.1 (C-5), 75.7, 74.3, 73.6 (3 CH_2 (Bn)], 73.4 (C-4), 71.4 [CH_2 (allyl)], 68.6 (C-6), 12.7 (SCH_3).

*Methyl 2,4,6-tri-O-benzyl-1-thio-β-*D*-galactopyranoside* (**23**). — A solution of **22** (4.4 g, 8.4 mmol) in Me_2SO (40 mL) was treated with KO^{t}Bu (3 g, 26.7 mmol) for 20 min at 80°. The solution was cooled to 20°, diluted with H_2O (200 mL), and extracted with $CHCl_3$ (5 × 100 mL). The $CHCl_3$ solutions were combined, washed with H_2O (2 × 100 mL), and concentrated. Chromatography of the residue in 2:1 hexane–ether gave **23** (3.2 g, 78.8%) as an oil, $[\alpha]_D$ +7.2° (*c* 0.7); ^{1}H-n.m.r.: δ 7.2–7.4 (m, 15 H, aromatic protons), 4.911, 4.731, 4.688, 4.641, 4.498, 4.440 {6 d, 6 H, J_{gem} 11–12 Hz [3 CH_2 (Bn)]}, 4.292 (d, 1 H, $J_{1,2}$ 9.4 Hz, H-1), 3.872 (d, 1 H, $J_{3,4}$ 3.2 Hz, H-4), 3.6–3.7 (m, 4 H, H-3,5,6,6'), 3.565 (t, 1 H, $J_{2,3}$ 9.3 Hz, H-2), 2.211 (s, 3 H, SCH_3); ^{13}C-n.m.r.: δ 138.4, 138.0, 137.7 (quaternary aromatic carbons), 128.4–127.6 (aromatic carbons), 85.3 (C-1), 78.9 (C-2), 77.1 (C-5*), 76.1 (C-4), 75.4 (C-3*), 75.2, 74.9, 73.4 [3 CH_2 (Bn)], 68.4 (C-6), 12.8 (SCH_3).

*Methyl 3-O-acetyl-2,4,6-tri-O-benzyl-1-thio-β-*D*-galactopyranoside* (**24**). — A solution of **23** (3.0 g, 6.2 mmol) in pyridine (10 mL) and Ac_2O (10 mL) was kept for 12 h at 20° and then concentrated. A solution of the residue in $CHCl_3$ (50 mL) was successively washed with aqueous 5% $NaHCO_3$, H_2O, aqueous HCl (5%), and H_2O, dried, and concentrated to give **24** (3.1 g, 95%) as a syrup, $[\alpha]_D$ +30.7° (*c* 0.7); ^{1}H-n.m.r.: 7.22–7.34 (m, 15 H, aromatic protons), 4.973 (dd, 1 H, $J_{2,3}$ 9.7, $J_{3,4}$

3.1 Hz, H-3), 4.855, 4.618, 4.601, 4.517, 4.480, 4.405 [6 d, 6 H, J ~11 Hz, 3 CH_2 (Bn)], 4.378 (d, 1 H, $J_{1,2}$ 9.6 Hz, H-1), 4.016 (dd, 1 H, $J_{4,5}$ 0.9 Hz, H-4), 3.832 (t, 1 H, H-2), 3.702 (ddd, 1 H, $J_{5,6}$ ~$J_{5,6'}$ 5.6 Hz, H-5), 3.607 (dd, 1 H, H-6), 3.585 (dd, 1 H, $J_{6,6'}$ 7.8 Hz, H-6'), 2.203 (s, 3 H, SCH_3), 1.869 (s, 3 H, CH_3CO); ^{13}C-n.m.r.: δ 170.1 (C=O), 138.2, 137.9, 137.7 (aromatic quaternary carbons), 128.2–127.7 (aromatic carbons), 85.5 (C-1, $J_{C\text{-}1,H\text{-}1}$ 155.6 Hz), 76.6 (C-3,5), 76.0 (C-2), 75.1, 74.7, 73.3 [3 CH_2 (Bn)], 74.5 (C-4), 67.9 (C-6), 20.7 (CH_3CO), 12.7 (SCH_3).

3-O-Acetyl-2,4,6-tri-O-benzyl-α-D-galactopyranosyl bromide (**25**). — A mixture of **24** (1.16 g, 2.22 mmol), CH_2Cl_2 (10 mL), and bromine (140 μL, 2.72 mmol) was stirred for 20 min at 0° and then concentrated. Toluene (3 × 5 mL) was evaporated from the residue to give syrupy **25** (1.25 g, quantitative); ^{1}H-n.m.r.: δ 7.1–7.4 (m, 15 H, aromatic protons), 6.479 (d, 1 H, $J_{1,2}$ 3.7 Hz, H-1), 5.267 (dd, 1 H, $J_{2,3}$ 10.2, $J_{3,4}$ 2.9 Hz, H-3), 4.7–4.4 [5 d, 6 H, J_{gem} 11–12 Hz, 3 CH_2(Bn)], 4.321 (dt, 1 H, H-5), 4.110 (dd, 1 H, $J_{4,5}$ ~1 Hz, H-4), 9.543 (dd, 1 H, H-2), 3.576 (d, 1 H, $J_{5,6}$ 7.1 Hz, H-6), 3.563 (d, 1 H, $J_{5,6'}$ 6.2 Hz, H-6'), 1.980 (s, 3 H, CH_3CO).

Methyl 4-O-[2-acetamido-3-O-(3-O-acetyl-2,4,6-tri-O-benzyl-α-D-galactopyranosyl)-2-deoxy-4,6-O-(4-methoxybenzylidene)-β-D-glucopyranosyl]-2,3-O-isopropylidene-α-L-rhamnopyranoside (**26**). — A mixture of **11** (600 mg, 1.1 mmol), bromide **25** (obtained from **24**; 1.16 g, 2.2 mmol), Et_4NBr (500 mg, 2.4 mmol), powdered molecular sieves (4A, 2 g), *N,N*-dimethylformamide (6 mL), and CH_2Cl_2 (10 mL) was stirred for 3 days at 20°. The mixture was filtered and the filtrate concentrated. The residue was partitioned between $CHCl_3$ (120 mL) and H_2O (2 × 30 mL), the organic layer was concentrated, and the residue was chromatographed in 1:1 ethyl acetate–hexane to give **26** (392 mg, 34.8%) as an amorphous solid, $[\alpha]_D$ +21° (*c* 0.3); ^{13}C-n.m.r.: δ 170.2, 169.8 (2 C=O), 160.0 [C-4 *(MBn)*], 137.7 (2×), 137.4 (aromatic quaternary carbons), 129.4–126.8 (aromatic carbons), 113.4 (2×) [C-3,5 *(MBn)*], 108.8 [$C(CH_3)_2$], 101.3 [C-7 *(MBn)*], 101.0 (C-1', $J_{C\text{-}1',H\text{-}1'}$ 162 Hz), 97.5 (C-1, $J_{C\text{-}1,H\text{-}1}$ 170 Hz), 96.2 (C-1'', $J_{C\text{-}1'',H\text{-}1''}$ 173 Hz), 82.4 (C-4), 74.7, 73.4, 70.1 [CH_2 (Bn)], 69.0 (C-6''), 68.4 (C-6'), 54.9, 54.3 (2 CH_3O), 27.6, 26.0 [$(CH_3)_2C$], 22.9 (CH_3CON), 20.6 (CH_3COO), 17.3 (C-6).

Anal. Calc. for $C_{55}H_{67}NO_{17}$ (1014.09): C, 65.14; H, 6.66; N, 1.38. Found: C, 64.88; H, 6.50; N, 1.23.

Methyl 4-O-[2-acetamido-2-deoxy-4,6-O-(4-methoxybenzylidene)-3-O-(2,4,6-tri-O-benzyl-α-D-galactopyranosyl)-β-D-glucopyranosyl]-2,3-O-isopropylidene-α-L-rhamnopyranoside (**27**). — A solution of **26** (345 mg, 0.35 mmol) in MeOH (15 mL) was treated with a catalytic amount of NaOMe and left standing for 12 h at 20°. Neutralization [Dowex 50W (H^+) resin] followed by removal of solvent left **27** (318 mg, 96.1%) as an amorphous solid, $[\alpha]_D$ +11° (*c* 0.8); ^{13}C-n.m.r.: δ 170.3 (C=O), 160.2 [C-4 *(MBn)*], 138.3, 137.9, 137.5 (aromatic quaternary carbons), 129.4–127.1 (aromatic carbons), 113.5 (2×) [C-3,5 *(MBn)*], 109.1 [$C(CH_3)_2$], 101.8 [C-7 *(MBn)*], 101.7 (C-1'), 97.7 (C-1), 96.3 (C-1''), 82.3 (C-4), 74.7, 73.9, 70.6 [3 CH_2 (Bn)], 70.4 (C-6''), 68.7 (C-6'), 55.2 (C-2'), 54.6, 54.5 (2 CH_3O), 27.9, 26.3 [$(CH_3)_2C$], 23.1 (CH_3CO), 17.4 (C-6).

Anal. Calc. for $C_{53}H_{65}NO_{16}$ (972.08): C, 65.48; H, 6.74; N, 1.44. Found: C, 65.20; H, 6.56; N, 1.34.

Methyl 4-O-{2-acetamido-2-deoxy-4,6-O-(4-methoxybenzylidene)-3-O-[2,4,6-tri-O-benzyl-3-O-(α-L-rhamnopyranosyl)-α-D-galactopyranosyl]-β-D-glucopyranosyl}-2,3-O-isopropylidene-α-L-rhamnopyranoside (**29**). — A mixture of **27** (240 mg, 0.25 mmol), **28** (250 mg, 0.71 mmol), $Hg(CN)_2$ (200 mg, 0.79 mmol), powdered molecular sieves (4A, 1.5 g), CH_3NO_2 (5 mL), and CH_2Cl_2 (5 mL) was stirred for 12 h at 20°. Compound **28** (300 mg, 0.85 mmol) was then added and stirring was continued for 24 h at 20°. The mixture was filtered, and the solution was extracted with aqueous 5% KI and then H_2O, dried (Na_2SO_4), and concentrated. A solution of the residue in MeOH (10 mL) was *O*-deacetylated as described for **26**. Chromatography of the residue in ethyl acetate gave **29** as an amorphous solid (185 mg, 67.0%), $[\alpha]_D$ −12.0° (*c* 0.2); ^{13}C-n.m.r.: δ 171.0 (C=O), 160.2 [C-4 *(MBn)*], 138.1, 137.7, 137.4 (aromatic quaternary carbons), 129.4–127.2 (aromatic carbons), 113.6 (2 ×) [C-3,5 *(MBn)*], 109.1 [$C(CH_3)_2$], 101.7 [C-7 *(MBn)*], 101.5 (2×) (C-1′,1‴), 97.7 (C-1), 96.4 (C-1″), 82.1 (C-4), 74.6, 73.9, 70.3 [3 CH_2 (Bn)], 70.3 (C-6″), 68.5 (C-6′), 55.2 (C-2′), 54.7 (2×) (2 CH_3O), 27.8, 26.3 [$(CH_3)_2C$], 23.1 (CH_3CO), 17.6, 17.3 (C-6,6‴).

Methyl 4-O-(2-acetamido-2-deoxy-β-D-glucopyranosyl)-α-L-rhamnopyranoside (**2**). — A solution of **10** (28 mg) in aqueous 70% CH_3COOH (5 mL) was stirred for 4 h at 70°. Concentration followed by gel filtration on Sephadex G-10 (H_2O) gave **2** as an amorphous solid (21 mg, 83%) after freeze-drying; $[\alpha]_D$ −42.5° (*c* 0.8, water). For ^{1}H- and ^{13}C-n.m.r. data, see Tables I and II, respectively.

Anal. Calc. for $C_{15}H_{27}NO_{10}$ (381.37): C, 47.24; H, 7.13; N, 3.67. Found: C, 46.97; H, 6.92; N, 3.49.

Methyl 4-O-[2-acetamido-2-deoxy-3-O-(α-D-galactopyranosyl)-β-D-glucopyranosyl]-α-L-rhamnopyranoside (**3**). A solution of **26** (250 mg, 0.25 mmol) in MeOH (40 mL) was treated with a catalytic amount of NaOMe and left standing for 12 h at 20°, aqueous 50% HBF_4 (8 mL) was added, and the solution was kept for 8 h at 20° and then its pH was adjusted to ~7 by addition of solid $NaHCO_3$. MeOH was removed by distillation, and the residue was partitioned between $CHCl_3$ (50 mL) and H_2O (20 mL). The $CHCl_3$ layer was concentrated and the residue was hydrogenated in 1:1 ethanol–acetic acid (10 mL) over 10% Pd/C (200 mg) under atmospheric pressure for 12 h at 20°. Purification of the product on a column of Sephadex G-15 with H_2O gave amorphous **3** (72 mg, 51.7%), after freeze-drying; $[\alpha]_D$ +34.3° (*c* 0.7, water). For ^{1}H- and ^{13}C-n.m.r. data, see Tables I and II, respectively.

Anal. Calc. for $C_{21}H_{35}NO_{15}$ (541.49): C, 46.58; H, 6.52; N, 2.58. Found: C, 46.29; H, 6.46; N, 2.29.

Methyl 4-O-{2-acetamido-2-deoxy-3-O-[3-O-(α-L-rhamnopyranosyl)-α-D-galactopyranosyl]-β-D-glucopyranosyl}-α-L-rhamnopyranoside (**4**). — Compound **29** (85 mg) was deprotected, essentially as described for **26**, to give, after purification through a column of Sephadex G-15 (H_2O), amorphous **4** (22 mg, 44.4%), $[\alpha]_D$ +14° (*c* 0.5, water). For ^{1}H- and ^{13}C-n.m.r. data, see Tables I and II, respectively.

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