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# Di- and tri-saccharide glycosyl donors for the synthesis of fragments of the O-specific antigen of *Shigella dysenteriae* type 1

Pavol Kováč

*NIDDK, National Institutes of Health, Bethesda, Maryland 20892 (USA)*

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## ABSTRACT

Methyl *O*-(2,4-di-*O*-benzoyl-3-*O*-bromoacetyl-α-L-rhamnopyranosyl)-(1 → 3)-2,4-di-*O*-benzoyl-α-L-rhamnopyranoside was treated with dichloromethyl methyl ether and $ZnCl_2$ to give *O*-(2,4-di-*O*-benzoyl-3-*O*-bromoacetyl-α-L-rhamnopyranosyl)-(1 → 3)-2,4-di-*O*-benzoyl-α-L-rhamnopyranosyl chloride. Similar treatment of methyl *O*-(3,4,6-tri-*O*-acetyl-2-azido-2-deoxy-α-D-glucopyranosyl)-(1 → 3)-2,4-di-*O*-benzoyl-α-L-rhamnopyranoside (**13**) gave crystalline *O*-(3,4,6-tri-*O*-acetyl-2-azido-2-deoxy-α-D-glucopyranosyl)-(1 → 3)-2,4-di-*O*-benzoyl-α-L-rhamnopyranosyl chloride (**14**), which was also obtained by treatment of methyl *O*-(3,4,6-tri-*O*-acetyl-2-azido-2-deoxoy-α-D-glucopyranosyl)-(1 → 3)-2,4-di-*O*-benzoyl-1-thio-α-L-rhamnopyranoside (**12**) with chlorine. In contrast to the conversion **12** → **14**, which was stereospecific, the reaction of methyl *O*-(3,4,6-tri-*O*-acetyl-2-azido-2-deoxy-α-D-glucopyranosyl)-(1 → 3)-(*O*-2,4-di-*O*-benzoyl-α-L-rhamnopyranosyl)-(1 → 3)-2,4-di-*O*-benzoyl-1-thio-α-L-rhamnopyranoside with chlorine gave a mixture of the corresponding α- (**16**) and β- (**17**) glycosyl chlorides. Condensation of the mixed chlorides **16** and **17** with 1,3,4,6-tetra-*O*-acetyl-α-D-galactopyranose, followed by reduction–acetylation of the product, gave a fully protected derivative of the tetrasaccharide α-D-Glc*p*NAc-(1 → 3)-α-L-Rha*p*-(1 → 3)-α-L-Rha*p*-(1 → 2)-α-D-Gal*p*.

## INTRODUCTION

The chemical repeating unit of the O-specific polysaccharide antigen of *Shigella dysenteriae* type 1 has been determined[2].

→ )-3-α-L-Rha*p*-(1 → 3)-α-L-Rha*p*-(1 → 2)-α-D-Gal*p*-(1 → 3)-α-D-Glc*p*NAc-(1 →
A B C D

In connection with our efforts aimed at the developing of a synthetic vaccine against the disease caused by Shiga's bacillus, this laboratory has been extensively

* Part 5 of the series Synthesis of ligands related to the O-Specific antigen of *Shigella dysenteriae* type 1. For Part 4, see ref 1.

involved in the synthesis of partial structures related to this O-antigen[1,3–5]. Others have also been active in that regard[6], and it has become evident that further efforts toward the synthesis of fragments of the polysaccharide would be facilitated by the availability of a wide selection of building blocks. Thus, in continuation of our work[4] on the preparation of glycosyl donor forms of fragments AB and ABC we now describe syntheses of additional donors. The reagents made include a donor derivative (**11**) of the AB sequence that allows extension of the oligosaccharide chain at position 3 of the nonreducing end-group, and protected DA and DAB fragments in both 1-thio-glycoside and glycosyl chloride form. The two alternatives were designed to provide flexibility in the choice of glycosylation strategies, some of which require the one anomeric leaving group and some the other.

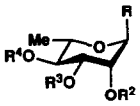
## RESULTS AND DISCUSSION

The AB sequence donor, glycosyl chloride **11**, was obtained readily by treatment[7] of the known[4] methyl glycoside **10** with dichloromethyl methyl ether (DCMME) in the presence of a catalytic amount of $ZnCl_2$.

To synthesize a glycosyl donor for the sequence DA in the form of a 1-thio-glycoside, a suitably protected derivative of an alkyl 1-thio-L-rhamnopyranoside had to be prepared first. In view of the previous successful use of methyl 2,4-di-*O*-benzoyl-α-L-rhamnopyranoside in syntheses of related oligosaccharides[3–5,8,9], we prepared the 1-thio analog **7** of the *O*-glycoside. This was accomplished via both 3-*O*-benzyl (**4**) and 3-*O*-(4-methoxybenzyl) (**6**) derivatives as intermediates. Thus, methyl 1-thio-α-L-rhamnopyranoside[10] (**1**) was regioselectively benzylated and 4-methoxybenzylated via stannylation methodology[11], as described for the corresponding methyl *O*-glycoside[4]. The 3-*O*-benzyl (**2**) and 3-*O*-(4-methoxybenzyl) (**5**) derivatives thus obtained were then benzoylated to give the fully protected thioglycosides **4** and **6**. Regeneration of HO-3 in **4** and **6**, by catalytic hydrogenolysis and by treatment with ceric ammonium nitrate, respectively, gave **7** *.

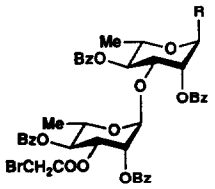
Condensation of **7** with 3,4,6-tri-*O*-acetyl-2-azido-2-deoxy-α-D-glucopyranosyl chloride[12] (**21**), now obtained in a more practical way than originally described (see Experimental), was promoted with silver perchlorate. Some of the side products of the condensation showed chromatographic properties similar to those of the major product, glycosyl donor **12**. This rendered purification of the latter difficult, so that it was obtained in only moderate yield (42%). A much more efficient preparation of a glycosyl donor for the same sequence was then developed starting with the previously described[3], readily obtainable, crystalline methyl glycoside **13**. Treatment of the latter with the DCMME–$ZnCl_2$ reagent[7] gave the crystalline glycosyl

* The two pathways **1** → **2** → **4** → **7** and **1** → **5** → **6** → **7** were tried in the hope that one would include an intermediate purifiable by crystallization, thus reducing the number of chromatographic separations required. This hope was realized by the isolation of crystalline **6**.

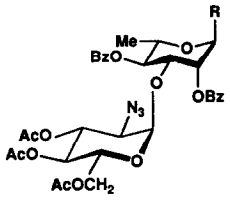


| | R | $R^2$ | $R^3$ | $R^4$ |
|---|---|---|---|---|
| 1 | SMe | H | H | H |
| 2 | SMe | H | Bn | H |
| 3 | SMe | Ac | Bn | Ac |
| 4 | SMe | Bz | Bn | Bz |
| 5 | SMe | H | MBn | H |
| 6 | SMe | Bz | MBn | Bz |
| 7 | SMe | Bz | H | Bz |
| 8 | OMe | Bz | $BrCH_2CO$ | Bz |
| 9 | Cl | Bz | $BrCH_2CO$ | Bz |

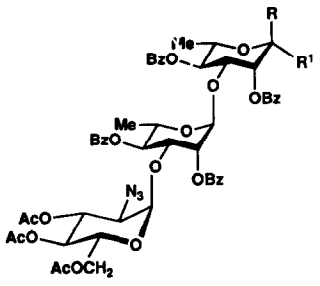
MBn = 4-methoxybenzyl



| | R |
|---|---|
| 10 | OMe |
| 11 | Cl |



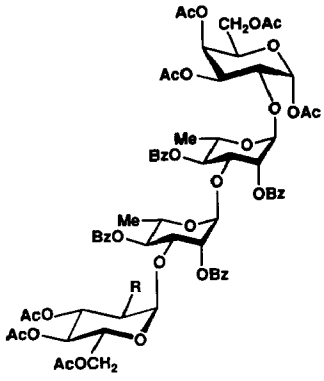
| | R |
|---|---|
| 12 | SMe |
| 13 | OMe |
| 14 | Cl |



| | R | $R^1$ |
|---|---|---|
| 15 | SMe | H |
| 16 | Cl | H |
| 17 | H | Cl |

chloride **14** in 85% yield. The same glycosyl chloride was obtained by the reaction of the disaccharide 1-thioglycoside **12** with chlorine. The reaction was monitored by $^1H$ NMR spectroscopy, which showed that the corresponding $\beta$-glycosyl chloride was not formed. Addition of an excess of the chlorine solution did not cause anomerization, and the material obtained on crystallization was identical with the above described **14**.

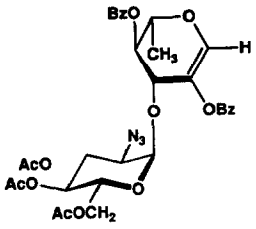
To prepare glycosyl donors of the sequence DAB, the glycosyl chloride **14** was treated with 1-thioglycoside **7** and silver trifluoromethanesulfonate (triflate). In this reaction, an excess of the more costly glycosyl donor was avoided. This notwithstanding, the amorphous trisaccharide 1-thioglycoside **15** was obtained in 83% yield. With the intention of isolating the $\beta$-linked trisaccharide, if it were present among the products of this reaction, two minor byproducts were collected during the purification of **15** by column chromatography. One of these was shown by NMR spectroscopy to be the glycoside **12**. A plausible cause for the formation of such a product in silver triflate-promoted condensations of glycosyl halides and




R

18 $N_3$

19 NHAc

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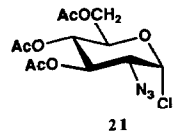


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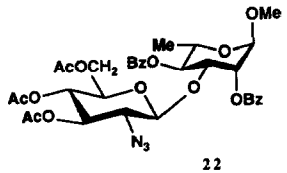


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1-thioglycosides has been discussed[13]. The other minor byproduct, not formed when the reaction was run at subambient temperature, was the olefinic disaccharide **20**.

To obtain a glycosyl chloride from **15**, the compound was treated with chlorine under the conditions of the conversion **12** → **14**. The reaction of **15** with chlorine, unlike that of **12** was however not stereospecific. Instead, both anomeric glycosyl chlorides (**16** and **17**) were formed. Their ratio in several preparations varied somewhat, as shown by $^1$H NMR spectroscopy of crude products, and could not be controlled. Each of the two glycosyl chlorides, obtained analytically pure by column chromatography, was characterized by specific optical rotation and $^1$H and $^{13}$C NMR spectroscopy. To test their glycosyl-donating ability, a mixture of **16** and **17** was treated with 1,3,4,6-tetra-*O*-acetyl-α-D-galactopyranose[14]. The fully protected tetrasaccharide **18** was obtained in ~ 76% yield. Catalytic hydrogenolysis in the presence of acetic anhydride converted **18** to the fully protected sequence α-D-Glc*p*NAc-(1 → 3)-α-L-Rha*p*-(1 → 3)-α-L-Rha*p*-(1 → 2)-α-D-Gal*p* (**19**).

## EXPERIMENTAL

*General methods.*—Thin-layer chromatography (TLC) was performed with solvent mixtures of appropriately adjusted polarity consisting of *A*, $CCl_4$–acetone; *B*, toluene–acetone; *C*, toluene–EtOAc; *D*, $CH_2Cl_2$–acetone; *E*, $CCl_4$–EtOAc; *F*,

hexane–EtOAc; and *G*, hexane–acetone. Carbohydrates were visualized by charring with 5% $H_2SO_4$ in EtOH and, when applicable, by UV light. For preparative chromatography of glycosyl chlorides, the silica gel used was dried at 160°C for 16 h. Reactions requiring anhydrous conditions were performed under Ar, and reagents and solvents were handled with gas-tight syringes. Silver perchlorate was prepared as described[15]. Silver trifluoromethanesulfonate (triflate, AgOTf), purchased from Aldrich Chemical Co., was dried at 140°C. The solution of chlorine in $CCl_4$ (~0.1 g/mL), used for conversions of 1-thioglycosides into glycosyl chlorides, was an older stock solution used in our previous preparations[15]. Optical rotations were measured at 25°C for solutions in $CHCl_3$, using a Perkin–Elmer, Model 241 MC. NMR spectra were obtained at 300 MHz for $^1H$ and 75 MHz for $^{13}C$. The measurements were done at 25°C, using the Varian XL 300 or the Varian Gemini spectrometer. The $^1H$ NMR chemical shifts were measured from the signal of internal $Me_4Si$, and $^{13}C$ shifts from internal $CDCl_3$ ($\delta$ 77.0). Assignments of NMR signals were made by first-order analysis of the spectra and by comparison with spectra of related substances. When possible, the assignments were supported by homonuclear decoupling experiments or homonuclear and heteronuclear 2-dimensional correlation spectroscopy done with commercial software. Sugar residues in oligosaccharides are serially numbered, beginning with the one bearing the aglycone, and identified by a superscript in listings of signal assignments. Chemical ionization mass spectra (CIMS) were measured using ammonia as the reactive gas. Fast-atom bombardment (FAB) mass spectra were obtained using *m*-nitrobenzyl alcohol as the matrix.

*Methyl* O-*(2,4-di-*O*-benzoyl-3-*O*-bromoacetyl-α-*L*-rhamnopyranosyl)-(1 → 3)-2,4-di-*O*-benzoyl-α-*L*-rhamnopyranoside* (**10**).—This compound was prepared essentially as previously described[3] (77% yield vs. a reported 60%), except that 2,6-di-*tert*-butyl-4-methylpyridine was used as the base, instead of 2,4,6-trimethylpyridine.

O-*(2,4-Di-*O*-benzoyl-3-*O*-bromoacetyl-α-*L*-rhamnopyranosyl)-(1 → 3)-2,4-di-*O*-benzoyl-α-*L*-rhamnopyranosyl chloride* (**11**).—A mixture of methyl *O*-(2,4-di-*O*-enzoyl-3-*O*-bromoacetyl-α-L-rhamnopyranosyl)-(1 → 3)-2,4-di-*O*-benzoyl-α-L-rhamnopyranoside (**10**, 2.3 g), DCMME (8 mL), and freshly fused $ZnCl_2$ (50 mg) in alcohol-free $CHCl_3$ (4 mL) was heated at 60°C with the exclusion of moisture until TLC (solvent *A*) showed that only traces of the starting material remained (2–2.5 h). One major product showing faster chromatographic mobility than **10** was formed. After the addition of dry toluene the mixture was concentrated, and the crude product was chromatographed to give pure **11** (1.87 g, 81%); $[\alpha]_D$ + 95° (*c* 1.1). $^1H$ NMR ($CDCl_3$): $\delta$ 6.24 (br s, 1 H, H-$1^1$), 5.66-5.60 [m, 2 H, consisting of signals for H-$4^1$ (t, 5.63) and H-$2^1$)], 5.38 (dd, partially overlapped, $J_{2,3}$ 3.1, $J_{3,4}$ 10.0 Hz, H-$3^2$), 5.33 (t, partially overlapped, H-$4^2$), 5.18–5.17 (m, 2 H, H-$1^2$,$2^2$), 4.75 (dd, 1 H, $J_{2,3}$ 3.4, $J_{3,4}$ 10.0 Hz, H-$3^1$), 4.39–4.30 (m, 1 H, H-$5^1$), 4.09–4.0 (m, 1 H, H-$5^2$), 3.50 and 3.46 (2 d, 2 H total, *J* 12.3 Hz, C$H_2$Br), 1.38 (d, 3 H, $J_{5,6}$ 6.3 Hz, H-$6^1$), and 1.15 (d, 3 H, $J_{5,6}$ 6.1 Hz, H-$6^2$); $^{13}C$ NMR ($CDCl_3$): $\delta$ 99.21 (C-$1^2$), 89.45 (C-$1^1$), 74.55 (C-$3^1$), 74.20 (C-$4^1$), 72.37 (C-$2^1$), 71.03 (C-$4^2$), 70.26 (C-$3^2$),

69.98, 69.86 (C-5$^1$,2$^1$), 67.65 (C-5$^2$), 24.97 ($CH_2Br$), 17.45 (C-6$^1$), and 17.39 (C-6$^2$); CIMS: $m/z$ 884 ([M + 18]$^+$). Anal. Calcd for $C_{42}H_{38}BrClO_{13}$: C, 58.24; H, 4.42. Found: C, 57.94; H, 4.38.

*3,4,6-Tri-*O*-acetyl-2-azido-2-deoxy-α-*D*-glucopyranosyl chloride* (**21**).—This compound was obtained essentially as described[12]. It has been found, however, that in the conversion of 1,3,4,6-tetra-*O*-acetyl-β-D-mannopyranose into **21** the isolation of the intermediate 1,3,4,6-tetra-*O*-acetyl-2-*O*-trifluoromethylsulfonyl-β-D-mannopyranose is not necessary. Thus, the following modifications of the overall procedure should be noted. Trifluoromethanesulfonic anhydride was added portionwise to a stirred solution of 1,3,4,6-tetra-*O*-acetyl-β-D-mannopyranose[16,17] in pyridine at such a rate that the precipitate that formed dissolved before further addition of the reagent. When TLC (solvent *A*) showed that the reaction was complete (a few minutes after the addition of the last portion of reagent) the crude product, obtained by concentration, was rid of residual pyridine by concentration of its solution in acetone to which water had been added. After an addition and evaporation of toluene the residue was treated with sodium azide as described[12]. Purification of the crude displacement product by chromatography followed by crystallization gave 1,3,4,6-tetra-*O*-acetyl-2-azido-2-deoxy-β-D-glucopyranose (88%). In the subsequent conversion[12] of the latter compound with DCMME (3 mL/g of the starting 2-azido derivative) the use of the additional solvent, alcohol-free $CHCl_3$, was omitted. In this way, the reaction time was shortened to 1 h. The title compound (**21**), containing ~3–5% (TLC in solvent *B*, NMR) of the β anomer[12], was isolated by chromatography in ~95% yield. This mixed glycosyl chloride was used in subsequent glycosylations. The $^{13}C$ NMR signals of **21** in a spectrum taken in $C_6D_6$, were fully assigned by 2-dimensional heteronuclear correlation spectroscopy: δ 92.02 (C-1), 71.30 (C-5), 70.93 (C-3), 67.76 (C-4), 62.37 (C-2), and 61.10 (C-6).

*Methyl* O-*(3,4,6-tri-*O*-acetyl-2-azido-2-deoxy-α- and -β-*D*-glucopyranosyl)-(1 → 3)-2,4-di-*O*-benzoyl-α-*L*-rhamnopyranoside (respectively* **13** *and* **22**).—The preparation of the α anomer **13** was previously described[3]. Chromatography of the crude product obtained[3] from 3.5 mmol of methyl 2,4-di-*O*-benzoyl-α-L-rhamnopyranoside gave first **13** (2.46 g, 71%) and then a small amount of material (~60 mg, ~2.5%) that proved to be the β isomer **22**; $[\alpha]_D$ + 43° (*c* 0.5). $^1H$ NMR ($CDCl_3$): δ 5.57 (t, 1 H, *J* 9.8 Hz, H-4$^1$), 5.48 (dd, 1 H, $J_{1,2}$ 1.7, $J_{2,3}$ 3.5 Hz, H-2$^1$), 4.85 (m, partially overlapped, ~2 H, H-1$^1$,4$^2$), 4.78 (*t*, partially overlapped, ~1 H, *J* 9.5 Hz, H-3$^2$), 4.43 (d, 1 H, $J_{1,2}$ 8.1 Hz, H-1$^2$), 4.37 (dd, 1 H, $J_{3,4}$ 9.8 Hz, H-3$^1$), 4.14 (dd, 1 H, $J_{5,6a}$ 4.8, $J_{6a,6b}$ 12.2 Hz, H-6$^2$a), 4.07 (dd, partially overlapped, ~1 H, $J_{5,6b}$ 2.4 Hz, H-6$^2$b), 4.00 (m, partially overlapped, H-5$^1$), 3.60 (ddd, 1 H, $J_{4,5}$ 9.2 Hz, H-5$^2$), 3.45 (s, 3 H, $OCH_3$), 3.33 (t, *J* ~8.4 Hz, H-2$^2$), 1.95 (s, 9 H, 3 $COCH_3$), 1.31 (d, 3 H, $J_{5,6}$ 6.4 Hz, H-6); $^{13}C$ NMR ($CDCl_3$): δ 102.54 ($J_{C,H}$ 161.2 Hz, C-1$^2$), 98.24 ($J_{C,H}$ 170.9 Hz C-1$^1$), 76.84 (C-3$^1$), 72.71, 72.60 (C-4$^1$, 3$^2$), 72.18 (C-2$^1$), 71.44 (C-5$^2$), 68.15 (C-4$^2$), 66.42 (C-5$^1$), 63.84 (C-2$^2$), 61.67 (C-6$^2$), 55.23 ($OCH_3$), and 17.74 (C-6$^1$). CIMS: $m/z$ 717 ([M + 18]$^+$).

*Methyl 2,4,-di-O-acetyl-* (**3**) *and 2,4-di-O-benzoyl-3-O-benzyl-1-thio-α-L-rhamnopyranoside* (**4**).—A mixture of methyl 1-thio-α-L-rhamnopyranoside[10] (**1**, 1 g, 5.14 mmol) and dibutyltin oxide (1.28 g, 5.14 mmol) in toluene (25 mL) was refluxed for 2 h in a Soxhlet apparatus, the thimble of which contained 4A molecular sieves. Finely powdered cesium fluoride[11] (1.56 g, 10.3 mmol) was added, and the mixture was concentrated. The residue was suspended in DMF (25 mL), benzyl bromide (1.22 mL, 10.3 mmol) was added, and the mixture was stirred at room temperature for 18 h. TLC (solvent *B*) showed that only a trace of the starting material was present. After concentration, the residue was triturated with $CH_2Cl_2$, the mixture was filtered, and the solids were washed with $CH_2Cl_2$ (6 times). The collected filtrate was washed with aq NaCl, and the latter was backwashed with $CH_2Cl_2$. The $CH_2Cl_2$ solutions were combined and concentrated, and the residue was chromatographed to give amorphous[10] **2** (1.15 g, 78%). The material was sufficiently pure for the next steps and showed the reported[10] $^{13}C$ NMR characteristics. For further characterization, compound **2** (0.35 g) was treated at room temperature for 18 h with $Ac_2O$–pyridine (1:1, 5 mL). After conventional processing the crude product was chromatographed (solvent *C*) to give pure **3** (0.37 g, 83%); mp 77–78°C (from hexane); $[\alpha]_D$ – 60° (*c* 0.8); $^1H$ NMR ($CDCl_3$): δ 5.43 (dd, 1 H, $J_{1,2}$ 1.5, $J_{2,3}$ 3.4 Hz, H-2), 5.10 (br d, 1 H, H-1), 5.05 (t, 1 H, *J* 9.8 Hz, H-4). 4.62 and 4.4 (2 d, 2 H, $^2J$ 12.2 Hz, $CH_2Ph$), 4.06 (m, 1 H, H-5), 3.75 (dd, 1 H, H-3), 2.14 (s, 3 H, $SCH_3$), 2.13 and 2.01 (2 s, 6 H, 2 $COCH_3$), and 1.21 (d, 3 H, $J_{5,6}$ 6.2 Hz, H-6); $^{13}C$ NMR ($CDCl_3$): δ 83.61 (C-1), 74.81 (C-3), 72.50 (C-4), 71.29 ($CH_2Ph$), 69.85 (C-2), 67.00 (C-5), 21.11 and 20.97 ($COCH_3$), 17.52 (C-6), and 13.96 ($SCH_3$); CIMS: *m/z* 369 ($[M + 1]^+$) and 386 ($[M + 18]^+$). Anal. Calcd for $C_{18}H_{24}O_6S$: C, 58.67: H, 6.56; S, 8.70. Found: C, 58.77; H, 6.59; S, 8.60.

Compound **2** (0.6 g) was treated at 50°C for 18 h with benzoyl chloride–pyridine (1:2, 6 mL). After conventional processing the crude product was chromatographed (solvent *C*) to give pure, amorphous **4** (0.93 g, 90%); $[\alpha]_D$ + 33.5° (*c* 1.5); $^1H$ NMR ($CDCl_3$): δ 5.70 (dd, 1 H, $J_{1,2}$ 1.3, $J_{2,3}$ 3.4 Hz, H-2), 5.48 (t, 1 H, *J* 9.8 Hz, H-4), 5.30 (br d, 1 H, H-1), 4.67 and 4.44 (2 d, 2 H, $^2J$ 12.6 Hz, $CH_2Ph$), 4.28 (m, 1 H, H-5), 4.00 (dd, 1 H, H-3), 2.18 (s, 3 H, $SCH_3$), and 1.31 (d, 3 H, $J_{5,6}$ 6.1 Hz, H-6); $^{13}C$ NMR ($CDCl_3$): δ 83.75 (C-1), 74.45 (C-3), 73.19 (C-4), 70.94 ($CH_2Ph$), 70.44 (C-2), 67.27 (C-5), 17.75 (C-6), and 14.07 ($SCH_3$); CIMS: *m/z* 493 ($[M + 1]^+$), 510 ($[M + 18]^+$). Anal. Calcd for $C_{28}H_{28}O_6S$: C, 68.27; H, 5.72; S 6.50, Found: C, 68.35; H, 5.73; S, 6.55.

*Methyl 2,4-di-O-benzoyl-3-O-(4-methoxybenzyl)-1-thio-α-L-rhamnopyranoside* (**6**). —The thiorhamnoside **1** (5.83 g, 30 mmol) was treated with dibutyltin oxide as described for the preparation of **2**. Cesium fluoride[11] (9.11 g, 60 mmol) was added, the mixture was concentrated, the residue was suspended in DMF (150 mL), and 4-methoxybenzyl chloride (8.17 mL, 60 mmol) and KI (9.96 g, 60 mmol) were added. The mixture was stirred at room temperature for 18 h. One major and several minor products were formed, as shown by TLC (solvents *B* and *D*), and the products in the zone containing the monosubstituted derivatives of methyl

1-thio-α-L-rhamnopyranoside were difficult to separate. After processing, as described above, the crude product was chromatographed on a column of silica gel to give some pure **5** (0.9 g, 2.86 mmol); $[\alpha]_D$ −111° (*c* 1.3). Anal. Calcd for $C_{15}H_{22}O_5S$: C, 57.30; H, 7.05; S 10.19. Found: C, 57.23; H, 7.08; S, 10.27.

The remainder of the monosubstituted fraction was dissolved in pyridine and treated with benzoyl chloride, as described above for the preparation of **4**. After conventional processing, chromatography (solvent *C*) gave **6** (7.31 g, 14 mmol); mp 94–95°C (from isopropyl ether); $[\alpha]_D$ + 40° (*c* 1.5); $^1$H NMR ($CDCl_3$): δ 5.70 (dd, 1 H, $J_{1,2}$ 1.3, $J_{2,3}$ 3.4 Hz, H-2), 5.44 (t, 1 H, *J* 9.6 Hz, H-4), 5.30 (br d, 1 H, H-1), 4.55 and 4.38 (2 d, 2 H, $^2J$ 12.2 Hz, $CH_2Ph$), 4.25 (m, 1 H, H-5), 3.98 (dd, 1 H, H-3), 3.72 (s, 3 H, $OCH_3$), 2.18 (s, 3 H, $SCH_3$), and 1.30 (d, 3 H, $J_{5,6}$ 6.2 Hz, H-6); $^{13}$C NMR ($CDCl_3$): δ 83.79 (C-1), 73.87 (C-3), 73.19 (C-4), 70.51 ($CH_2Ph$), 70.45 (C-2), 67.29 (C-5), 55.14 ($OCH_3$), 17.77 (C-6), and 14.08 ($SCH_3$); CIMS: *m/z* 540 ($[M + 18]^+$). Anal. Calcd for $C_{29}H_{30}O_7S$: C, 66.64; H, 5.78; S, 6.13. Found: C, 66.38; H, 5.72; S, 6.00.

The combined yield of **5** and **6** was 56% (from **1**), and this figure did not increase significantly when KBr, instead of KI, was used in the 4-methoxybenzylation of **1**.

*Methyl 2,4-di-O-benzoyl-1-thio-α-L-rhamnopyranoside* (**7**).—(*a*) A solution of compound **4** (850 mg) in 2-methoxyethanol containing 5% Pd–C (0.5 g) was stirred overnight at room temperature under an $H_2$ atmosphere. TLC (solvent *A*) showed that ~60% of the starting material was still present. Only a little progress was noted when, after conventional processing of the partially hydrogenolyzed material, the treatment with $H_2$ was continued for 18 h with fresh catalyst, in DMF as the solvent. However, complete conversion of the starting material was achieved when the mixture was again processed, and hydrogenolysis was continued with another portion of fresh catalyst for 18 h, in a mixture of DMF and 2-methoxyethanol. The crude product, chromatographed on a column of silica gel to remove catalyst debris and a more polar byproduct, gave pure **7** (450 mg, 65%); $[\alpha]_D$ − 30° (*c* 1.1); $^1$H NMR ($CDCl_3$): δ 5.49 (dd, 1 H, $J_{1,2}$ 1.2, $J_{2,3}$ 3.6 Hz, H-2), 5.33 (br s, 1 H, H-1), 5.29 (t, 1 H, *J* 9.7 Hz, H-4), 4.38 (m, 1 H, H-5), 4.27 (m, 1 H, H-3), 2.59 (d, 1 H, $J_{3,OH}$ 7.4 Hz, O*H*), 2.20 (s, 3 H, $SCH_3$), and 1.34 (d, 3 H, $J_{5,6}$ 6.2 Hz, H-6); $^{13}$C NMR ($CDCl_3$): δ 83.47 (C-1), 75.71 (C-4), 74.66 (C-2), 69.58 (C-3), 66.78 (C-5), 17.70 (C-6), and 14.09 ($SCH_3$); CIMS; *m/z* 403 ($[M + 1]^+$), 420 ($[M + 18]^+$). Anal. Calcd for $C_{21}H_{22}O_6S$: C, 62.66; H, 5.51; S 7.96. Found: C, 62.46; H, 5.52; S, 7.88.

(*b*) Ceric ammonium nitrate (12.6 g, 23 mmol) was added with stirring to a solution of compound **6** (6 g, 11.5 mmol) in MeCN–$H_2O$ (10:1, 66 mL). After 20 min, TLC (solvent *A*) showed that only little starting material remained. Solid $NaHCO_3$ (8 g) was added, the mixture was stirred for 10 min, then concentrated to remove most of MeCN, and the residue was partitioned between $CH_2Cl_2$ and aq NaCl (a little dilute acetic acid was added, to aid the separation of phases). The organic phase was dried, concentrated, and chromatographed. Eluted first was

some unchanged **6** (0.6 g, 1.15 mmol), then 4-methoxybenzaldehyde, and finally compound **7** (4.15 g, 10.3 mmol, 80% based on the amount of transformed starting material), identical (TLC, NMR) with the substance described above.

*Methyl O-(3,4,6-tri-O-acetyl-2-azido-2-deoxy-α-D-glucopyranosyl)-(1 → 3)-2,4-di-O-benzoyl-1-thio-α-L-rhamnopyranoside* (**12**).—A solution of the glycosyl chloride **21** (0.63 g, 1.8 mmol), nucleophile **7** (0.6 g, 1.5 mmol), and 2,4,6-trimethylpyridine (0.25 mL, 1.9 mmol) in $CH_2Cl_2$ (10 mL) was added at 0°C to a suspension of silver perchlorate (0.415 g, 2 mmol) in $CH_2Cl_2$ (10 mL). Cooling was terminated after 30 min, and after an additional 30 min TLC (solvents *E* and *F*) showed that both starting materials were consumed. In addition to the major product **12** several minor products were formed, some of which showed chromatographic mobility very similar to that of **12**. The mixture was filtered through a Celite pad, the filtrate was washed with a mixture of aq $Na_2S_2O_3$ and $NaHCO_3$, dried, and concentrated. The residue was chromatographed to give pure **12** (450 mg, 42%); $[\alpha]_D$ + 140.5° (*c* 1.1); $^1$H NMR ($CDCl_3$): δ 5.74 (dd, 1 H, $J_{1,2}$ 1.5 Hz, H-1$^1$), 5.58 (t, 1 H, *J* 9.8 Hz, H-4$^1$), 5.33 (d, H-1$^1$), 5.18 (d, 1 H, $J_{1,2}$ 3.4 Hz, H-1$^2$), 5.05 (t, 1 H, *J* 9.3 Hz, H-3$^2$), 4.78 (t, 1 H, *J* 10 Hz, H-4$^2$), 4.41 (m, 1 H, H-5$^1$), 4.34 (dd, 1 H, $J_{2,3}$ 3.4, $J_{3,4}$ 9.8 Hz, H-3$^1$), 3.87 (m, 2 H, H-6$^2$a,b), 3.77 (m, 1 H, H-5$^2$), 3.24 (dd, 1 H, $J_{2,3}$ 10.5 Hz, H-2$^2$), 2.08, 1.92, and 1.61 (3 s, 9 H, 3 COC*H*$_3$), 2.22 (s 3 H, SC*H*$_3$), and 1.38 (d, 3 H, $J_{5,6}$ 6.3 Hz, H-6$^1$); $^{13}$C NMR ($CDCl_3$): δ 93.64 (C-1$^2$), 83.60 (C-1$^1$), 72.34 (C-4$^1$), 71.92 (C-3$^1$), 70.07 (C-3$^2$), 68.98 (C-2$^1$), 67.85 (C-4$^2$), 67.46 (C-5$^2$), 67.06 (C-5$^1$), 61.33 (C-6$^2$), 60.40 (C-2$^2$), 20.77, 20.69, and 20.36 (3 CO*C*H$_3$), 17.71 (S*C*H$_3$), and 14.13 (C-6$^1$); CIMS: *m/z* 733 ([M + 18]$^+$). Anal. Calcd for $C_{33}H_{37}N_3O_{13}S$: C, 55.37; H, 5.21; N, 5.87; S, 4.48. Found: C, 55.38; H, 5.24; N, 5.93; S, 4.55.

Also obtained was an impure fraction consisting of **12** contaminated with by products.

*O-(3,4,6-Tri-O-acetyl-2-azido-2-dexoy-α-D-glucopyranosyl)-(1 → 3)-2,4-di-O-benzoyl-α-L-rhamnopyranosyl chloride* (**14**).—(*a*) Freshly fused $ZnCl_2$ (0.1 g) was added to a solution of the glycoside **13** (2.77 g) in a mixture of DCMME and alcohol-free $CHCl_3$ (1:1, 16 mL). The mixture, in a flask equipped with a guard tube containing Drierite, was stirred at 50–55°C until TLC (solvent *E*) showed complete conversion of the starting material into a faster moving product (6–7 h). After the addition of dry toluene the mixture was filtered, and the filtrate was concentrated to dryness. The residue was chromatographed to give **14** as a foam; $[\alpha]_D$ + 164° (*c* 0.8). Crystallization from isopropyl ether gave material (2.37 g, 85%) showing mp 129–130°C and $[\alpha]_D$ + 167° (c 0.8). $^1$H NMR ($CDCl_3$): δ 6.20 (br s, 1 H, H-1$^1$), 5.76 (dd, 1 H, $J_{1,2}$ 1.9, $J_{2,3}$ 3.2 Hz, H-2$^1$), 5.62 (t, 1 H, *J* 10.0 Hz, H-4$^1$), 5.17 (d, 1 H, $J_{1,2}$ 3.4 Hz, H-1$^2$), 5.05 (t, 1 H, *J* 9.5 Hz, H-3$^2$), 4.80 (t, 1 H, *J* 9.8 Hz, H-4$^2$), 4.67 (dd, 1 H, $J_{3,4}$ 10.0 Hz, H-3$^1$), 4.42–4.32 (m, 1 H, H-5$^1$), 3.90–3.83 (m, 2 H, H-6$^2$a,b), 3.79–3.74 (m, 1 H, H-5$^2$), 3.28 (dd, 1 H, $J_{2,3}$ 10.5 Hz, H-2$^2$), 2.07, 1.92, and 1.63 (3 s, 9 H, 3 COC*H*$_3$), and 1.40 (d, 3 H, $J_{5,6}$ 6.4 Hz, H-6$^1$); $^{13}$C NMR ($CDCl_3$): δ 93.92 (C-1$^2$), 89.65 (C-1$^1$), 71.35 (C-4$^1$), 70.41 (C-3$^1$), 70.09 (C-3$^2$), 69.85

(C-$2^1$), 69.61 (C-$5^1$), 67.79 (C-$4^2$), 67.59 (C-$5^2$), 61.25 (C-$6^2$), 60.41 (C-$2^2$), and 17.38 (C-$6^1$). Anal. Calcd for $C_{32}H_{34}ClN_3O_{13}$: C, 54.58; H, 4.86; Cl, 5.03; N, 5.96. Found: C, 54.63; H, 4.89; Cl, 5.13; N, 5.86.

(*b*) A solution of chlorine in $CCl_4$ was added to a sample of **12** (36 mg, 0.05 mmol) in $CDCl_3$, contained in an NMR tube, until a faint yellow color persisted (~ 35 μL, ~ 0.05 mmol). The $^1H$ NMR spectrum taken at that point showed that the conversion was complete and that the α-glycosyl chloride **14** was formed stereospecifically. Addition of a further amount of the chlorine solution (25 μL) did not cause a noticeable change in the composition of the mixture, as shown by its spectrum. The mixture was poured into $CCl_4$ and concentrated to dryness, leaving **14** which crystallized on the addition of diisopropyl ether, mp 129–130°C.

*Methyl O-(3,4,6-tri-O-acetyl-2-azido-2-deoxy-α-D-glucopyranosyl)-(1 → 3)-O-(2,4-di-O-benzoyl-α-L-rhamnopyranosyl)-(1 → 3)-2,4-di-O-benzoyl-1-thio-α-L-rhamnopyranoside* (**15**).—A solution of the glycosyl chloride **14** (1.96 g, 2.79 mmol), the nucleophile **7** (1.12 g, 2.79 mmol), and 2,4,6-trimethylpyridine (0.33 mL, 2.5 mmol) in $CH_2Cl_2$ (25 mL) was added with stirring, at 0°C, to a suspension of silver triflate (0.82 g, 3.19 mmol) in $CH_2Cl_2$ (25 mL). The mixture was stirred at 0°C for 10 min, and then at room temperature for an additional 30 min. TLC (solvent *E*) showed that the glycosyl donor was no longer present and that some **7** remained. One major product was formed. The mixture was processed as described for the preparation of **12**, and the crude product was chromatographed. This gave first a small amount (~ 10 mg) of material shown by $^1H$ and $^{13}C$ NMR spectroscopy to be the thioglycoside **12**, then the amorphous trisaccharide **15** (2.5 g, 83.7%); $[\alpha]_D$ +229° (*c* 0.65); $^1H$ NMR ($CDCl_3$): δ 5.64 (dd, 1 H, $J_{1,2}$ 1.1, $J_{1,2}$ 3.0 Hz, H-$2^1$), 5.57 (t, 1 H, *J* 9.8 Hz, H-$4^1$), 5.35 (t, partially overlapped, *J* 9.8 Hz, H-$4^2$), 5.33 (br d, partially overlapped, H-$1^1$), 5.17 (br dd, 1 H, H-$2^2$), 5.14 (br d, 1 H, H-$1^2$), 4.95 (t, 1 H, *J* 9.3 Hz, H-$3^3$), 4.73 (t, 1 H, *J* 10 Hz, H-$4^3$), 4.67 (d, 1 H, $J_{1,2}$ 3.5 Hz, H-$1^3$), 4.42–4.33 (m, 2 H, H-$3^1$,$5^1$), 4.08 (dd, partially overlapped, $J_{2,3}$ 3.4, $J_{3,4}$ 9.8 Hz, H-$3^2$), 4.06–3.98 (m, partially overlapped, H-$5^2$), 3.75 (dd, 1 H, $J_{5,6a}$ 3.0 Hz, $J_{6a,6b}$ 12.3 Hz, H-$6^3$a), 3.53 (d of br t, 1 H, H-$5^3$), 3.46 (dd, 1 H, $J_{5,6b}$ 2.0 Hz, H-$6^3$b), 3.04 (dd, 1 H, $J_{2,3}$ 10.5 Hz, H-$2^3$), 2.24 (s, 3 H, SC$H_3$), 2.01, 1.87, and 1.60 (3 s, 9 H, 3 COC$H_3$), 1.36 (d, 3 H, $J_{5,6}$ 6.3 Hz, H-$6^1$), and 1.14 (d, 3 H, $J_{5,6}$ 6.3 Hz, H-$6^2$); $^{13}C$ NMR ($CDCl_3$): δ 99.18 (C-$1^2$), 93.87 (C-$1^3$), 83.46 (C-$1^1$), 76.44 (C-$3^1$), 73.48, 73.34 (C-$2^1$, $4^1$), 71.74 (C-$4^2$), 71.65 (C-$3^2$), 70.21 (C-$3^3$), 67.65 (C-$2^2$), 67.47 (2 C, C-$5^2$, $4^3$), 67.30 (C-$5^1$), 67.18 (C-$5^3$), 60.85 (C-$6^3$), 60.33 (C-$2^3$), 17.76 (C-$6^1$), 17.40 (C-$6^2$), and 14.11 (SC$H_3$); FABMS, *m/z* 1070 ($[MH]^+$), 1044 ($[MH - 26]^+$)[18]. Anal. Calcd for $C_{53}H_{55}N_3O_{19}S$: C, 59.48; H, 5.18; N, 3.92; S, 2.99. Found: C, 59.53; H, 5.20; N, 3.90; S, 3.04.

When the reaction was conducted at room temperature the crude product contained a trace of material moving faster than **15**. In view of the possible presence of the β-linked trisaccharide the material was isolated, but analysis of its NMR spectra, ordinary FAB mass spectrum, and high resolution FAB mass spectrum showed it to be the olefin **20**, formed by a side reaction from the glycosyl

donor: $^1$H NMR ($CDCl_3$): δ 6.79 (s, 1 H, H-1), 5.44-5.37 (m, 2 H, H-4$^1$,3$^2$), 5.12 (d, 1 H, $J_{1,2}$ 3.5 H, H-1$^2$), 4.95 (t, 1 H, *J* 9.5 Hz, H-4$^2$), 4.76 (d, 1 H, $J_{3,4}$ 4.2 Hz, H-3$^1$), 4.44 (m, 1 H, H-5$^1$), 4.12-4.07 (m, 2 H, H-5$^2$,6$^2$a), 3.86 (dd, 1 H, $J_{5,6b}$ 3.9, $J_{6a,6b}$ 13.7 Hz, H-6$^2$b), 3.36 (dd, 1 H, $J_{2,3}$ 10.5 Hz, H-2$^2$), 2.18, 2.00, and 1.95 (3 s, 9 H, 3 COC$H_3$), and 1.49 (d, 3 H, $J_{5,6}$ 6.8 Hz, H-6$^1$); $^{13}$C NMR ($CDCl_3$): δ 138.9 (C-1$^1$), 98.23 (C-1$^2$), 73.17 (C-4$^1$), 73.02 (C-3$^1$), 72.88 (C-5$^1$), 70.65 (C-3$^2$), 68.45 (C-5$^2$), 68.13 (C-4$^2$), 61.41 (C-6$^2$), 61.10 (C-2$^2$), and 16.21 (C-6$^1$). The signal for the disubstituted olefinic carbon C-2$^1$ could not be unambiguously identified. FABMS, *m/z* 668 ([MH]$^+$), 642 ([MH − 26]$^+$)[18]; HRFAB, *m/z* 668.2114. $C_{32}H_{34}N_3O_{13}$ (MH) requires 668.6343.

O-*(3,4,6-Tri-*O*-acetyl-2-azido-2-deoxy-α-*D*-glucopyranosyl)-(1 → 3)-*O*-(2,4-di-*O*-benzoyl-α-*L*-rhamnopyranosyl)-(1 → 3)-2,4-di-*O*-benzoyl-α-* (**16**) *and -β-*L*-rhamnopyranosyl chloride* (**17**).—A solution of **15** (170 mg) in $CCl_4$ (1 mL) was treated with chlorine in $CCl_4$, as described for the preparation of **14**. A sample was withdrawn and added to $CDCl_3$ in an NMR tube. Examination by $^1$H NMR spectroscopy showed that the reaction was complete and that two products were formed. Their ratio remained unchanged upon addition of another portion of the chlorine solution ($^1$H NMR, TLC in solvent *G*). The mixture was concentrated and dried at 45°C/133 Pa, and the residue was chromatographed to give first the α anomer **16** as an amorphous white solid (68 mg, 40%); $[\alpha_D]$ + 156° (*c* 0.8); $^1$HNMR ($CDCl_3$): δ 6.20 (br s, 1 H, H-1$^1$), 5.67 (dd, 1 H, $J_{1,2}$ 1.7, $J_{2,3}$ 3.2 Hz, H-2$^1$), 5.61 (t, 1 H, *J* 10.0 Hz, H-4$^1$), 5.36 (t, 1 H, *J* 9.8 Hz, H-4$^2$), 5.18 (br s 2 H, H-1$^2$,2$^2$), 4.95 (t, 1 H, *J* 9.3 Hz, H-3$^3$), 4.74 (dd, partially overlapped, H-3$^1$), 4.73 (t, partially overlapped, H-4$^3$), 4.67 (d, 1 H, $J_{1,2}$ 3.5 Hz, H-1$^3$), 4.08 (dd, 1 H, $J_{2,3}$ 2.4, $J_{3,4}$ 9.8 Hz, H-3$^2$), 4.01 (m, 1 H, H-5$^2$), 3.75 (dd, 1 H, $J_{5,6a}$ 3.2, $J_{6a,6b}$ 12.5 Hz, H-6$^3$a), 3.54 (m, 1 H, H-5$^3$), 3.46 (dd, 1 H, $J_{5,6b}$ 2.0 Hz, H-6$^3$b), 3.04 (dd, 1 H, H-2$^3$), 2.016, 1.88, and 1.61 (3 s, 9 H, 3 COC$H_3$), 1.40 (d, 3 H, $J_{5,6}$ 6.1 Hz, H-6$^1$), and 1.16 (d, 3 H, $J_{5,6}$ 6.1 Hz, H-6$^2$); $^{13}$ C NMR ($CDCl_3$): δ 99.35 (C-1$^2$, $J_{C,H}$ 170.6 Hz), 93.98 (C-1$^3$, $J_{C,H}$ 170.6 Hz), 89.43 (C-1$^1$, $J_{C,H}$ 184.4 Hz), 74.54 (C-3$^1$), 74.08 (C-2$^1$), 72.41 (C-4$^1$), 71.70 (2 C, C-3$^2$,4$^2$), 70.23 (C-3$^3$), 69.89 (C-5$^1$), 67.65 (C-2$^2$), 67.56, 67.48 (C-5$^2$, 4$^3$), 67.24 (C-5$^3$), 60.86 (C-6$^3$), 60.35 (C-2$^3$), and 17.45 (2 C, C-6$^1$, 6$^2$); FABMS, *m/z* 1058 ([MH]$^+$), 1032 ([MH − 26]$^+$)[18], 1022 ([MH − HCl]$^+$). Anal. Calcd for $C_{52}H_{52}ClN_3O_{19}$: C, 59.00; H, 4.95; Cl, 3.34; N, 3.97. Found: C, 58.94; H, 4.98; Cl, 3.09; N, 3.92.

Eluted next was the β-glycosyl chloride **17** (87 mg, 51%); $[\alpha]_D$ + 240° (*c* 0.7). $^1$H NMR ($CDCl_3$): δ 5.84 (br d, 1 H, $J_{3,4}$ 2.5 Hz, H-2$^1$), 5.66 (br s, 1 H, $J_{1,2}$ < 0.5 Hz, H-1$^1$), 5.52 (t, 1 H, *J* 9.7 Hz, H-4$^1$), 5.41 (t, 1 H, *J* 9.8 Hz, H-4$^2$), 5.19 (dd, 1 H, $J_{1,2}$ 2.0, $J_{3,4}$ 3.2 Hz, H-2$^2$), 5.11 (br d, 1 H, H-1$^2$), 4.96 (dd, 1 H, $J_{3,4}$ 9.3, $J_{2,3}$ 10.3 Hz, H-3$^3$), 4.75–4.68 (m, 2 H, H-1$^3$, 4$^3$), 4.29–4.23 (m, 2 H, H-3$^1$, 5$^2$), 4.06 (dd, 1 H, $J_{2,3}$ 3.4, $J_{3,4}$ 9.7 Hz, H-3$^2$), 3.86–3.81 (m, partially overlapped, H-5$^1$), 3.77 (dd, partially overlapped, $J_{5,6}$ 2.6, $J_{6a,6b}$ 12.5 Hz, H-6$^3$a), 3.58–3.52 (m, 1 H, H-5$^3$), 3.33 (dd, 1 H, $J_{5,6}$ 2.0 Hz, H-6$^3$b), 3.03 (dd, 1 H, $J_{1,2}$ 3.7 Hz, H-2$^3$), 1.97, 1.87, and 1.61 (3 s, 9 H, 3 COC$H_3$), 1.46 (d, 3 H, $J_{5,6}$ 6.3 Hz, H-6$^1$) 1.33 (d, 3 H, $J_{5,6}$ 6.2 Hz, H-6$^2$); $^{13}$C

NMR ($CDCl_3$): δ 99.17 ($J_{C,H}$ 171.7 Hz, C-1$^2$), 93.71 ($J_{C,H}$ 174.1, C-1$^3$), 86.21 ($J_{C,H}$ 164.7, C-1$^1$), 76.48 (C-3$^1$), 74.91 (C-5$^1$), 72.69 (C-2$^1$), 72.56 (C-4$^1$), 71.71 (C-4$^2$), 71.18 (C-3$^2$), 70.12 (C-3$^3$), 67.51 (C-5$^2$), 67.30 (2 C, C-2$^2$,4$^3$), 67.17 (C-5$^3$), 60.63 (C-6$^3$), 60.25 (C-2$^3$), 17.81, and 17.69 (C-6$^1$,6$^2$); FABMS, *m/z* 1058 ([MH]$^+$), 1032 ([MH − 26]$^+$)[18], and 1022 ([MH − HCl]$^+$). Anal. Calcd for $C_{52}H_{52}ClN_3O_{19}$: C, 59.00; H, 4.95; Cl, 3.34; N, 3.97. Found: C, 58.77; H, 5.00; Cl, 3.09; N, 3.17.

*O-(3,4,6-Tri-O-acetyl-2-azido-2-deoxy-α-D-glucopyranosyl)-(1 → 3)-O-(2,4-di-O-benzoyl-α-L-rhamnopyranosyl)-(1 → 3)-O-(2,4-di-O-benzoyl-α-L-rhamnopyranosyl)-(1 → 2)-1,3,4,6-tetra-O-acetyl-α-D-galactopyranose* (**18**).—A solution of the mixed glycosyl chlorides **16** and **17** (1.3 g, 1.22 mmol), 1,3,4,6-tetra-*O*-acetyl-α-D-galactopyranose[14] (0.427 g, 1.22 mmol), and 2,6-di-*tert*-butyl-4-methylpyridine (0.41 g, 2 mmol) in $CH_2Cl_2$ (15 mL) was added at room temperature to a stirred suspension of silver triflate (0.385 g, 1.5 mmol) in $CH_2Cl_2$ (15 mL). After 30 min, the mixture was processed as described for the preparation of **12**, and chromatography (solvent *D*) gave the major product **18** (1.28, g 76.6%) as an amorphous solid; $[\alpha]_D$ + 198° (*c* 0.76); $^1$H NMR ($CDCl_3$): δ 6.40 (d, 1 H, $J_{1,2}$ 3.7 Hz, H-1$^1$), 5.52 (t, partially overlapped, *J* 9.9 Hz, H-4$^2$), 5.52 (br d, partially overlapped, H-4$^1$), 5.39–5.35 (m, partially overlapped, H-3$^1$,2$^2$), 5.34 (t, partially overlapped, *J* 9.8 Hz, H-4$^3$), 5.17 (m, 2 H, H-1$^2$,2$^3$), 5.11 (br d, 1-H, $J_{1,2}$ 1.5 Hz, H-1$^3$), 4.94 (t, 1 H, *J* 9.3 Hz, H-3$^4$), 4.73 (t, 1 H, *J* 9.7 Hz, H-4$^4$), 4.65 (d, 1 H, $J_{1,2}$ 3.5 Hz, H-1$^4$), 4.34 (br t, 1 H, $J_{4,5}$ < 1, $J_{5,6}$ 6.8 Hz, H-5$^1$), 4.25 (dd, partially overlapped, $J_{2,3}$ 10.5 Hz, H-2$^1$), 4.22 (dd, partially overlapped, $J_{2,3}$ 3.7 Hz, H-3$^2$), 4.13–4.05 (m, 4 H, H-3$^3$,5$^2$,6$^1$a,6$^1$b), 3.93 (m, 1 H, H-5$^3$), 3.73 (dd, 1 H, $J_{5,6}$ 2.9, $J_{6a,6b}$ 12.2 Hz, H-6$^4$a), 3.52 (m, partially overlapped, H-5$^4$), 3.47 (dd, partially overlapped, $J_{5,6}$ 1.9 Hz, H-6$^4$b), 3.04 (dd, 1 H, H-2$^4$), 2.27, 2.15, 2.14, 2.05, 2.02, 1.87, and 1.60 (7 s, 21 H, COC$H_3$), 1.34 (d, 3 H, $J_{5,6}$ 6.2 Hz, H-6$^2$), and 1.08 (d, 3 H, $J_{5,6}$ 6.2 Hz, H-6$^3$); $^{13}$C-NMR ($CDCl_3$): δ 99.17 (C-1$^3$), 98.80 (C-1$^2$), 93.93 (C-1$^4$), 90.84 (C-1$^1$), 75.91 (C-3$^2$), 72.52 (C-4$^1$), 71.73, 71.61 (3 C, 1 C, C-2$^1$,2$^2$,3$^3$,4$^3$), 70.20 (C-3$^4$), 69.42 (C-3$^1$), 68.70 (C-5$^1$), 67.71 (2 C), 67.60, 67.84, 67.36 (C-2$^3$,4$^2$,5$^2$,5$^3$,4$^4$), 67.20 (C-5$^4$), 61.16 (C-6$^1$), 60.85 (C-6$^4$), 60.33 (C-2$^4$), 17.70 (C-6$^2$), and 17.37 (C-6$^3$); FABMS, *m/z* 1370 ([MH]$^+$), 1344 ([MH − 26]$^+$)[18], 1311 ([M − $CH_3$COOH]$^+$). Anal. Calcd for $C_{66}H_{71}N_3O_{29}$: C, 57.84; H, 5.22; N, 3.06. Found: C, 57.86; H, 5.25; N, 2.99.

In a preliminary experiment, a small amount of compound **18** was hydrogenated in the presence of $Ac_2O$ as previously described[3], to give *O*-(3,4,6-tri-*O*-acetyl-2-acetamido-2-deoxy-α-D-glucopyranosyl)-(1 → 3)-*O*-(2,4-di-*O*-benozyl-α-L-rhamno-*O*-pyranosyl)-(1 → 3)-*O*(2,4-di-*O*-benzoyl-α L-rhamnopyranosyl)-(1 → 2)-1,2,46-tet ra-acetyl-α-D-galactopyranose (**19**); $[\alpha]_D$ + 143° (*c* 1); $^1$H NMR ($CDCl_3$): δ 6.40 (1 H, $J_{1,2}$ 3.7 Hz, H-1$^1$), 5.65 (d, 1 H, $J_{2,NH}$ 9.8 Hz, N*H*), 5.54–5.48 (m, 2 H, H-4$^1$,4$^2$), 5.40–5.35 (m, 2 H, H-2$^2$,3$^1$), 5.27 (t, 1 H, *J* 9.8, H-4$^3$), 5.18 (br s, 1 H, H-1$^2$), 5.12 (br d, 1 H, H-2$^3$), 5.06 (br d, 1 H, H-1$^3$), 4.85 (t, 1 H, *J* 9.8, H-4$^4$), 4.70 (t, 1 H, *J* 10.5, H-3$^4$), 4.50 (d, 1 H, $J_{1,2}$ 3.7 Hz, H-1$^4$), 4.35 (br t, 1 H, $J_{4,5}$ < 1, $J_{5,6}$ 6.6 Hz, H-5$^1$), 4.26 (dd, $J_{2,3}$ 10.5 Hz, H-2$^1$), 4.20 (dd, 1 H, $J_{2,3}$ 3.4, $J_{3,4}$ 10.0 Hz, H-3$^2$), 4.14–4.03 (m, 5 H, H-2$^4$,3$^3$,5$^2$,6$^1$a,6$^1$b), 3.93 (m, 1 H, H-5$^3$), 3.67 (dd, 1 H, $J_{5,6}$ 2.7,

$J_{6a,6b}$ 12.5 Hz, H-6$^4$a), 3.46-3.38 (m, 2 H, H-5$^4$,6$^4$b), 2.26 (s, NCOC$H_3$), 2.15, 2.14, 2.04, 2.00, 1.85, and 1.61 (6 s, 18 H, OCOC$H_3$), 1.34 (s, partially overlapped, OCOC$H_3$), 1.33 (d, partially overlapped, H-6$^2$), and 1.10 (d, 1 H, $J$ 6.3 Hz, H-6$^3$); $^{13}$C NMR ($CDCl_3$): $\delta$ 99.17 (C-1$^3$), 98.75 (C-1$^2$), 95.67 (C-1$^4$), 90.83 (C-1$^1$), 75.92 (C-3$^2$), 73.01 (C-3$^3$), 72.48 (C-4$^1$), 71.92 (C-4$^3$), 71.71 (C-2$^2$), 71.51 (C-2$^1$), 70.84 (C-3$^4$), 69.37 (C-3$^1$), 68.66 (C-5$^1$), 68.50 (C-2$^3$), 67.61 (C-4$^2$), 67.56, 67.50, 67.38 (C-5$^2$,5$^3$,5$^4$), 67.02 (C-4$^4$), 61.09 (C-6$^1$), 60.77 (C-6$^4$), 50.80 (C-2$^4$), 22.14 (NCO$C$H$_3$), 17.52 (C-6$^2$), and 17.25 (C-6$^3$). FABMS, $m/z$ 1386 ([MH]$^+$), 1326 ([M − AcOH]$^+$. Anal. Calcd for $C_{68}H_{75}NO_{30}$: C, 58.91; H, 5.45; N, 1.01. Found: C, 58.72; H, 5.42; N, 1.00.

## REFERENCES


1 P. Kováč, *J. Carbohydr. Chem.*, 11 (1992) 999–1014.
2 B.A. Dmitriev, Yu. A. Knirel, and N.K. Kochetkov, *Eur. J. Biochem.*, 66 (1976) 559–566.
3 V. Pavliak, P. Kováč, and C.P.J. Glaudemans, *Carbohydr. Res.*, 229 (1991) 103–116.
4 P. Kováč and K.J. Edgar, *J. Org. Chem.*, 57 (1992) 2455–2467.
5 V. Pozsgay, C.P.J. Glaudemans, J.B. Robbins, and R. Schneerson, *Bioorg. Med. Chem. Lett.*, 2 (1992) 255–260.
6 P.J. Garegg and C. Hällgren, *J. Carbohydr. Chem.*, 11 (1992) 445–461.
7 H. Gross, I. Farkas, and R. Bognár, *Z. Chem.*, 18 (1978) 201–210.
8 H.P. Wessel and D.R. Bundle, *Carbohydr. Res.*, 124 (1983) 301–311.
9 J.O. Kihlberg, D.A. Leigh, and D.R. Bundle, *J. Org. Chem.*, 55 (1990) 2860–2863.
10 A. Lipták, L. Szabó, and J. Harangi, *J. Carbohydr. Chem.*, 7 (1988) 687–699.
11 N. Nagashima and M. Ohno, *Chem. Lett.*, (1987) 141–144.
12 V. Pavliak and P. Kováč, *Carbohydr. Res.*, 210 (1991) 333–337.
13 J. Kihlberg, E. Eichler, and D.R. Bundle, *Carbohydr. Res.*, 211 (1991) 59–75.
14 G.J.F. Chittenden, *Carbohydr. Res.*, 183 (1988) 140–143.
15 P. Kováč and L. Lerner, *Carbohydr. Res.*, 184 (1988) 87–112.
16 N.V. Bovin, S.E. Zurabyan, and A.Ya. Khorlin, *Izv. Akad. Nauk, Ser. Khim.*, (1981) 1638–1641.
17 J.O. Deferrari, E.G. Gros, and I.O. Mastronardi, *Carbohydr. Res.*, 4 (1967) 432–434.
18 J.M. Peltier, R.W. Smith, D.B. MacLean, and W.A. Szarek, *Carbohydr. Res.*, 207 (1990) 1–10.