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# Synthesis of a tetrasaccharide donor corresponding to the O-specific polysaccharide of *Shigella dysenteriae* type 1

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ABSTRACT

*O*-(2,4-Di-*O*-benzoyl-3-*O*-chloroacetyl-α-L-rhamnopyranosyl)-(1 → 2)-*O*-(3,4,6-tri-*O*-benzoyl-α-D-galactopyranosyl)-(1 → 3)-*O*-(2-acetamido-4,6-di-*O*-acetyl-2-deoxy-α-D-glucopyranosyl)-(1 → 3)-2,4-di-*O*-benzoyl-α-L-rhamnopyranosyl trichloroacetimidate (**1**) was synthesized in a stepwise manner, using the following monosaccharide units: 2-(trimethylsilyl)ethyl 2,4-di-*O*-benzoyl-α-L-rhamnopyranoside, 2-azido-4,6-*O*-benzylidene-3-*O*-chloroacetyl-2-deoxy-β-D-glucopyranosyl chloride, methyl 3,4,6-tri-*O*-benzoyl-2-*O*-(4-methoxybenzyl)-1-thio-β-D-galactopyranoside, and 2,4-di-*O*-benzoyl-3-*O*-chloroacetyl-α-L-rhamnopyranosyl chloride. Compound **1** corresponds to a complete tetrasaccharide repeating unit of the O-specific polysaccharide of the lipopolysaccharide of *Shigella dysenteriae* type 1.

## INTRODUCTION

The pathogenic bacilli of the genus *Shigella* are classified by Kauffmann[1] into four groups, A, B, C, and D. The most virulent of these is *Shigella dysenteriae* type 1 (Shiga's bacillus[2]), which belongs to group A. Infections of humans by *Sh. dysenteriae* type 1 may reach epidemic proportions in developing countries and are characterized by high rates of morbidity and mortality[3]. It was proposed by Robbins[4] that antibodies to the lipopolysaccharide (LPS) of *Sh. dysenteriae* type 1 may confer protective immunity against shigellosis. Indeed, synthetic vaccines in which the regular heteropolymer O-specific polysaccharide[5,6] (O-SP) of the LPS

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

O-SP

of *Sh. dysenteriae* type 1 was covalently linked to tetanus toxoid elicited high levels of IgG antibodies in mice[3].

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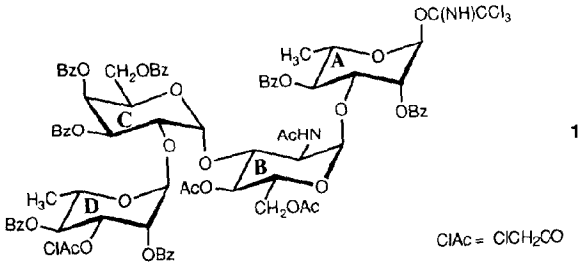


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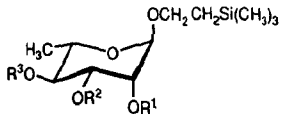
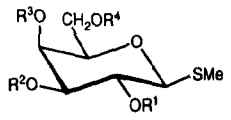
Conjugates to proteins of synthetic oligosaccharides, rather than the native polysaccharide, provide an alternative approach in the search for an efficient synthetic vaccine. This approach requires the availability of structurally defined oligosaccharides in a form that permits their covalent coupling to the proposed carrier. Such oligosaccharides would also be expected to mimic the conformation of the native polysaccharide. As part of our project aimed at developing synthetic vaccines against shigellosis, our current goal is to define the structural requirements for oligosaccharides that will elicit protective antibodies when linked to a protein. As another aspect of this project, we are using synthetic oligosaccharides[7,8] to probe the binding specificities of these compounds to antibodies directed against *Sh. dysenteriae* type 1 (ref 9). We here describe the synthesis of the fully protected tetrasaccharide building block **1**, which corresponds to the complete repeating unit sequence of the O-SP. Compound **1** complements another tetrasaccharide building block[8] corresponding to the O-SP, the difference being in a frame-shift of the four sugar residues of the repeating unit. The presence of the selectively removable *O*-chloroacetyl group[10] in the glycosyl donor **1** permits chain-extension at the nonreducing rhamnose terminus. This feature together with the trichloroacetimidoyl group at C-1 of the reducing-end residue make **1** a suitable building block for the synthesis of extended fragments of the O-SP.

## RESULTS AND DISCUSSION

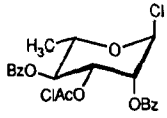
*The monosaccharide units.*—In the synthesis of **1** the key, reducing terminal residue was the 2-trimethylsilyl)ethyl glycoside **6**. 2-(Trimethylsilyl)ethyl glycosides were previously shown by Magnusson's group to be amenable to a variety of functional group manipulations and to be convertible into glycosyl halides and hemiacetals[11,12]. The treatment of the triol[8] **2** with 2,2-dimethoxypropane–$H^+$ (→ **3**, 95%) followed by benzoylation (BzCl–Py) gave **4** (91%). Acidolytic removal (AcOH–$H_2O$) of the acetal protecting group (→ **5**, 89%) followed by regioselective, *O*-benzoylation[13] [(i) $PhC(OCH_3)_3$–$H^+$; (ii) $H_3O^+$] afforded the dibenzoate **6** (82%), which is the presursor for residue A in the tetrasaccharide donor **1**. Treatment of **6** with chloroacetic anhydride in pyridine[14] afforded the fully




| | R1 | R2 | R3 |
|---|---|---|---|
| 2 | H | H | H |
| 3 | C(CH3)2 | | H |
| 4 | C(CH3)2 | | Bz |
| 5 | H | H | Bz |
| 6 | Bz | H | Bz |
| 7 | Bz | ClAc | Bz |




| | R1 | R2 | R3 | R4 |
|---|---|---|---|---|
| 9 | H | H | H | H |
| 10 | H | H | H | TBDPSi |
| 11 | H | C(CH3)2 | | TBDPSi |
| 12 | MBn | C(CH3)2 | | TBDPSi |
| 13 | MBn | C(CH3)2 | | H |
| 14 | MBn | H | H | H |
| 15 | MBn | Bz | Bz | Bz |

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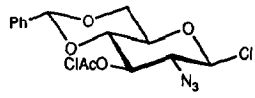


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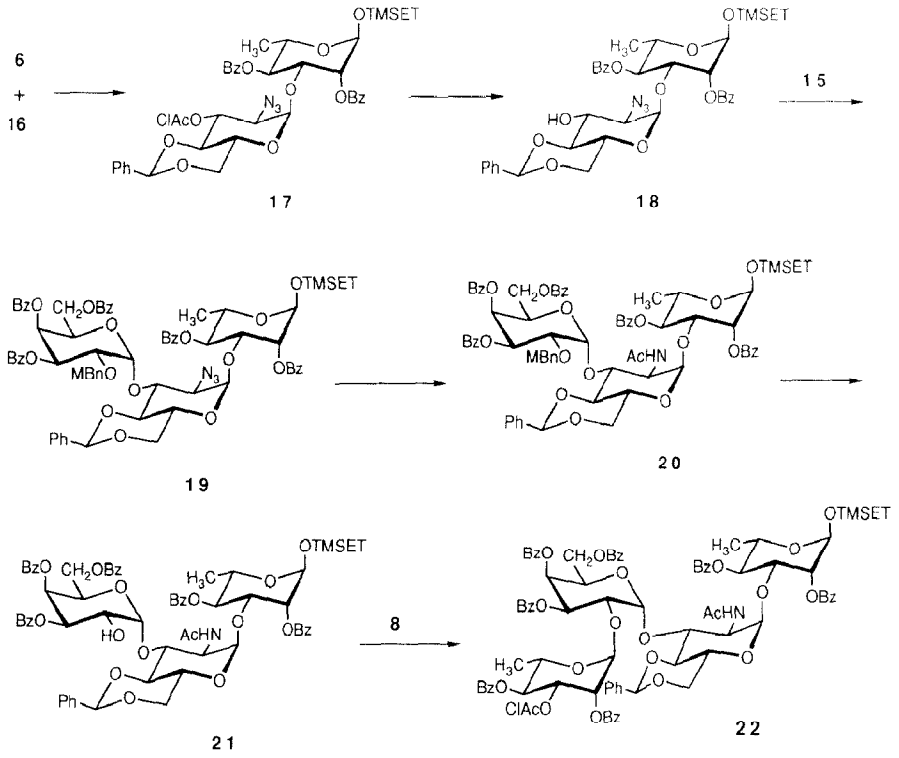
Bz = benzoyl
ClAc = chloroacetyl
MBn = 4-methoxybenzyl
TBDPSi = *tert*-butyldiphenylsilyl

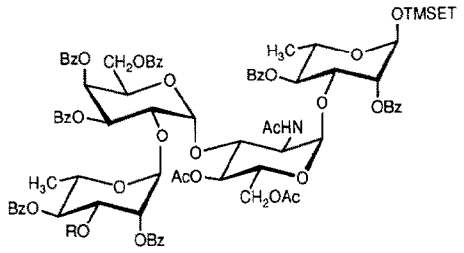
protected derivative **7** (86%). It is worth noting that this reaction proceeded without the appearance of dark-colored impurities, which frequently occur with the chloroacetyl chloride–pyridine reagent. Anomeric chlorination[12] of the trimethylsilylethyl glycoside **7** with 1,1-dichloromethyl methyl ether afforded rhamnosyl chloride **8** (84%), the precursor of the nonreducing terminal unit (residue D) of the target compound **1**.

The galactose derivative **15** was prepared from methyl 1-thio-β-D-galactopyranoside[15] **9**. Previously[7,8], we have prepared compound **15** from the known methyl 3,4-*O*-isopropylidene-6-*O*-(1-methoxy-1-methylethyl)-1-thio-β-D-galactopyranoside[15]. However, the sensitivity of the 1-methoxy-1-methylethyl protecting group to acid necessitated slightly basic conditions during the handling of this compound, e.g., during chromatography, as reported earlier by Pozsgay and Jennings[15]. In this work we describe an alternative route to **15**. Treatment of **9** with *tert*-butyldiphenylsilyl chloride[16] afforded compound **10** (82%), which was acetonated with 2,2-dimethoxypropane–$H^+$ to give the alcohol **11** (92%). Subsequent alkylation at HO-2 with 4-methoxybenzyl chloride–NaH (→ **12**, 70%), followed by a two-step deprotection sequence [(i) $Bu_4NF$–THF[16] (→ **13**, 81%), (ii) $HBF_4$–MeOH[17] (94%)] afforded the triol[8] **14**, which was *O*-benzoylated as described[8] to afford compound **15**.

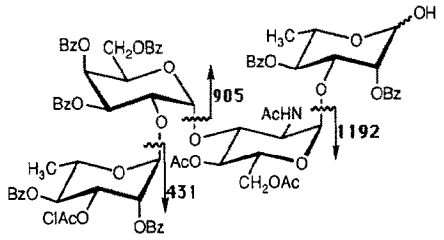



The glucosamine donor **16** corresponding to residue B in tetrasaccharide **1** was available from related work[8].

*Glycosylation reactions.*—Coupling of the donor **16** with the alcohol **6** (AgOTf–$CH_2Cl_2$) afforded the disaccharide **17** (71%). The 1,2-*cis* interglycosidic linkage in **17** was evidenced by the low value (3.8 Hz) configuration of the $^3J_{1,2}$ coupling constant for residue B. In this glycosylation reaction formation of the isomeric disaccharide having a 1,2-*trans* intersugar linkage could not be observed. Removal of the chloroacetyl group from **17** by thiourea[10] afforded nucleophile the **18** (83%). Reaction of thiogalactoside **15** with **18** in ether under activation[18] by methyl trifluoromethanesulfonate then afforded the trisaccharide **19**. The $\alpha$ linkage of the galactose residue was shown by its $^3J_{1,2}$ coupling constant (3.7 Hz). Again, the glycosidation reaction proceeded in a highly stereoselective manner, without the formation of the unwanted, *trans*-linked isomer. Next the azido group in **19** was converted into an acetamido group by reduction[19] with triphenylphosphine followed by *N*-acetylation ($Ac_2O$–Py) ($\rightarrow$ **20**, 84%). Oxidative removal of the 4-methoxybenzyl group by 2,3-dichloro-5,6-dicyano-1,4-benzoquinone[20] afforded the trisaccharide alcohol **21** (97%). Coupling of the rhamnose donor **8** with **21**




**23** R=ClAc
**24** R=Ac




**25**

($AgOTf–CH_2Cl_2$) yielded the fully protected tetrasaccharide **22** which contained ~ 10% of a cochromatographing impurity. Acidolytic removal ($AcOH–H_2O$) of the benzylidene group in **22** followed by acetylation ($Ac_2O$–Py) afforded two compounds in a ratio of ~ 3:2. The chromatographically faster-moving component proved to be the expected *O*-chloroacetylated tetrasaccharide **23**, on the basis of combined NMR and mass spectroscopic evidence. These include resonances in the NMR spectra indicative of a chloroacetyl group ($\delta_H$ 3.621 ppm for $CH_2Cl$ and $\delta_C$ 40.1 ppm for $CH_2Cl$), and peaks in the positive ion fast atom bombardment mass spectrum (FABMS) corresponding to the nonreducing terminal rhamnose fragment [$m/z$ 431, $(C_{22}H_{20}ClO_7)^+$] and to the molecular ion [$m/z$ 1664, $(M + 1)^+$]. The slower-moving compound (**24**) lacked a chloroacetyl group. Its structure was established by the presence in its NMR spectra of resonances corresponding to one *N*-acetyl and three *O*-acetyl groups. The FAB mass spectrum corroborated this assignment: the fragment ion at $m/z$ 397 corresponds to the 3-*O*-acetyl-2,3-di-*O*-benzoyl-L-rhamnopyranosyl residue and the ion at $m/z$ 1630 to the molecular ion.

Reaction[12] of the (trimethylsilyl)ethyl glycoside **23** with trifluoroacetic acid provided the tetrasaccharide hemiacetal **25**. The structure of **25** was indicated by its FAB mass spectrum displaying the molecular ion at $m/z$ 1564 and fragment ions resulting from cleavage of one of the three interglycosidic linkages as shown in formula **25**. The hemiacetal **25** was treated[21,22] with trichloroacetonitrile and 1,8-diazabicyclo[5.4.0]undec-7-ene in $CH_2Cl_2$ to afford the tetrasaccharide trichloroacetimidate **1** in 81% yield from **23**. The $\alpha$ configuration at C-1 of the reducing-end rhamnose residue was assigned on the basis of the $^1J_{C\text{-}1,H\text{-}1}$ coupling

constant, which equalled 180 Hz. The FAB mass spectrum of **1** is in agreement with the proposed structure. The peak at *m/z* 1729 corresponds to the ion $(M + Na)^+$. Loss of the trichloroacetimidate group gave rise to the ion at *m/z* 1546 $(M - C_2HCl_3NO)^+$. Ions at m/z 1192, 905, and 431 correspond to inter-residue cleavages as described for the fragmentation of hemiacetal **25**.

Experiments to utilize the donor **1** and related derivatives to build extended fragments of the O-specific polysaccharide of *Sh. dysenteriae* type 1 for use as molecular probes in the study of the specificities of carbohydrate–protein interactions and for the preparation of synthetic antigens are in progress in these laboratories.

## EXPERIMENTAL

*General methods.*—Column chromatography was performed on Silica Gel 60 (0.040–0.063 mm). All reagents and solvents were of commercial grade. Anhydrous solvents were purchased from Aldrich and were used as received. Melting points were measured with a Thomas–Hoover apparatus and are uncorrected. Optical rotations were measured in $CHCl_3$ at 22°C with a Perkin–Elmer type 241MC polarimeter, except where indicated otherwise. The NMR spectra were recorded on a Gemini-300 spectrometer (300 MHz for $^1H$ and 75 MHz for $^{13}C$), at 23–25°C. Internal references were tetramethylsilane (0.000 ppm for $^1H$) and $CDCl_3$ (77.00 ppm for $^{13}C$). Subscripts A–D refer to the individual sugar residues, with A standing for the reducing-end unit. Low resolution mass spectra were obtained by the chemical ionization techique (CIMS), using $NH_3$ as the ionizing gas, and by the positive-ion fast atom-bombardment technique (FABMS), using 3-nitrobenzyl alcohol as the matrix. Elemental analyses were performed by Atlantic Microlab, Inc., Norcross, GA.

*2-(Trimethylsilyl)ethyl 2,3-O-isopropylidene-α-L-rhamnopyranoside* (**3**).—A solution of the triol[8] **2** (1.6 g) in 2,2-dimethoxypropane (20 mL) was treated with a catalytic amount of 10-camphorsulfonic acid at 25°C for 1 h. Triethylamine (0.5 mL) was added and the solution was concentrated. The residue was partitioned between $CHCl_3$ and $H_2O$. The $CHCl_3$ phase was dried ($Na_2SO_4$) and concentrated to give **3** as a syrup (1.75 g, 95%); $[\alpha]_D$ −35° (*c* 0.6). NMR ($CDCl_3$): $^1H$, $\delta$ 4.963 (br s, 1 H, H-1), 4.068–4.126 (m, 2 H, H-2,3), 3.666 (dq, 1 H, H-5), 3.397 (dd, 1 H, $J_{3,4}$ 6.1, $J_{4,5}$ 8.8 Hz, H-4), 1.528 and 1.355 [2 s, 6 H, $(CH_3)_2C$], 1.296 (d, 3 H, $J_{5,6}$ 6.3 Hz, H-6), and 0.029 [s, 9 H, $(CH_3)_3Si$]; $^{13}C$, $\delta$ 109.4 [$C(CH_3)_2$], 96.5 (C-1), 78.4, 75.9 (C-2,3), 74.3 (C-4), 65.9 (C-5), 64.9 ($OCH_2CH_2$), 27.9 and 26.1 [$(CH_3)_2C$], 17.8 ($CH_2Si$), 17.5 (C-6), and −1.4 [$(CH_3)_3Si$]. CIMS: *m/z* 204 [$(M - Me_3SiCH_2CH_2OH + 18)^+$], 322 [$(M + 18)^+$]. Anal. Calcd for $C_{14}H_{28}O_5Si$: C, 55.23; H, 9.27. Found: C, 55.33; H, 9.31.

*2-(Trimethylsilyl)ethyl 4-O-benzoyl-2,3-O-isopropylidene-α-L-rhamnopyranoside* (**4**).—A solution of **3** (1.4 g) in pyridine (2 mL) was treated at 0°C with benzoyl chloride (2 mL). The solution was allowed to reach 25°C in 1 h and was then

recooled to 0°C, and treated with MeOH (2 mL). Removal of the volatiles followed by column chromatographic purification (8:1 hexane–EtOAc) gave **4** as a syrup (1.72 g, 91%); $[\alpha]_D$ −16° (*c* 0.9). NMR ($CDCl_3$): $^1H$, δ 8.4–8.18 and 7.6–7.4 (aromatic), 5.133 (dd, 1 H, $J_{3,4}$ 7.8, $J_{4,5}$ 10.2 Hz, H-4), 5.072 (br s, 1 H, H-1), 4.337 (dd, 1 H, $J_{2,3}$ 5.4 Hz, H-3), 4.180 (br d, 1 H, H-2), 3.896 (dq, 1 H, H-5), 1.625 and 1.356 [2 s, 6 H, $(CH_3)_2C$], 1.218 (d, 3 H, $J_{5,6}$ 6.3 Hz, H-6), and 0.050 [s, 9 H, $(CH_3)_3Si$]; $^{13}C$, δ 165.7 (*C*=O), 133.1, 129.7, and 128.3 (aromatic), 109.7 [$C(CH_3)_2$], 96.4 (C-1), 76.2 (C-2), 75.9 (C-3), 75.1 (C-4), 65.0 ($OCH_2CH_2$), 64.0 (C-5), 27.7 and 26.4 [$(CH_3)_2C$], 17.9 ($CH_2Si$), 17.1 (C-6), and −1.4 [$(CH_3)_3Si$]. CIMS: *m/z* 291 [$(M - Me_3SiCH_2CH_2OH + 1)^+$], 308 [$(M - Me_3SiCH_2CH_2OH + 18)^+$], 409 [$(M + 1)^+$], and 426 [$(M + 18)^+$]. Anal. Calcd for $C_{21}H_{32}O_6Si$: C, 61.74; H, 7.89. Found: 61.56; H, 8.08.

*2-(Trimethylsilyl)ethyl 4-O-benzoyl-α-L-rhamnopyranoside* (**5**).—A solution of **4** (1.5 g) in 5:1 AcOH–$H_2O$ (12 mL) was warmed at 80°C with stirring until all starting material disappeared (TLC, 3:1 hexane–EtOAc). The volatiles were then removed under vacuum. Column chromatography (2:1 hexane–EtOAc) of the residue afforded **5** as a syrup (1.2 g, 89%); $[\alpha]_D$ −91° (*c* 0.8). NMR ($CDCl_3$): $^1H$, δ 8.08–8.02 and 7.6–7.4 (aromatic), 5.090 (t, 1 H, $J_{3,4} = J_{4,5} = 9.6$ Hz, H-4), 4.867 (d, 1 H, H-1), 4.015 (dd, 1 H, $J_{2,3}$ 3.4 Hz, H-3), 3.97 (H-2), 3.958 (H-5), 1.260 (d, 1 H, $J_{5,6}$ 6.3 Hz, H-6), and 0.040 [s, 9 H, $(CH_3)_3Si$]; $^{13}C$, δ 167.2 (*C*=O), 133.3, 129.8, 129.5, and 128.4 (aromatic), 99.0 (C-1), 75.9 (C-4), 71.0, 70.1 (C-2,3), 65.7 (C-5), 65.2 ($OCH_2CH_2$), 17.9 $CH_2Si$), 17.5 (C-6), and −1.4 [$(CH_3)_3Si$]. CIMS: *m/z* 386 [$(M + 18)^+$]. Anal. Calcd for $C_{18}H_{28}O_6Si$: C, 58.67; H, 7.66. Found: C, 58.77; H, 7.71.

*2-(Trimethylsilyl)ethyl 2,4-di-O-benzoyl-α-L-rhamnopyranoside* (**6**).—To a stirred solution of **5** (500 mg) in $CH_2Cl_2$ (5 mL) was added trimethyl orthobenzoate (2 mL). The mixture was treated with a catalytic amount of 10-camphorsulfonic acid then the reaction flask was evacuated (water aspirator). After 15 min aq 80% AcOH (10 mL) was added followed by the removal of the volatiles under vacuum. The residue was partitioned between $CHCl_3$ and $H_2O$. The $CHCl_3$ phase was concentrated and the residue purified by column chromatography (8:1 hexane–EtOAc) to give **6** (526 mg, 82%); mp 134–136°C, lit.[8] 133–134°C; $[\alpha]_D$ +30° (*c* 0.8), lit.[8] +31°. For NMR data see ref 8.

*2-(Trimethylsilyl)ethyl 2,4-di-O-benzoyl-3-O-chloroacetyl-α-L-rhamnopyranoside* (**7**).—To a solution of **6** (9.5 g) in pyridine (80 mL) at 0°C was added chloroacetic anhydride (5.0 g) under stirring. After 10 min $H_2O$ (10 mL) was added and the solution was concentrated. Column chromatography (8:1 hexane–EtOAc) of the residue afforded syrupy **7** (9.5 g, 86%) which crystallized on standing; mp 72–74°C; $[\alpha]_D$ +55° (*c* 0.7). NMR ($CDCl_3$): $^1H$, δ 8.14–8.0 and 7.65–7.42 (aromatic), 5.691 (dd, 1 H, $J_{2,3}$ 3.4, $J_{3,4}$ 10.1 Hz, H-3), 5.526 (dd, 1 H, H-2), 5.486 (t, 1 H, $J_{4,5}$ 9.9 Hz, H-4), 4.972 (d, 1 H, $J_{1,2}$ 1.7 Hz, H-1), 4.133 (dq, 1 H, H-5), 3.891 and 3.818 (2 d, 2 H, *J* 15 Hz, $CH_2Cl$), 1.338 (d, 1 H, $J_{5,6}$ 6.2 Hz, H-6), and 0.078 [s, 9 H, $(CH_3)_3Si$]; $^{13}C$, δ 166.6 (C=O of ClAc), 165.69 and 165.63 (*C*=O of Bz), 133.5–128.5 (aromatic),

96.9 (C-1), 71.6 (C-4), 71.3 (C-3), 70.5 (C-2), 66.6 (C-5), 65.8 ($OCH_2CH_2$), 40.5 ($CH_2Cl$), 17.9 ($CH_2Si$), 17.6 (C-6), and −1.4 [$(CH_3)_3Si$]. CIMS: *m/z* 566 [(M + 18)$^+$]. Anal. Calcd for $C_{27}H_{33}ClO_8Si$: C, 59.06; H, 6.06; Cl, 6.46. Found: C, 59.17; H, 6.06; Cl, 6.42.

*2,4-Di-O-benzoyl-3-O-chloroacetyl-α-*L*-rhamnopyranosyl chloride* (**8**).—A stirred solution of **7** and 1,1-dichloromethyl methyl ether (1.9 mL) in $CH_2Cl_2$ was treated with a catalytic amount of freshly fused $ZnCl_2$ at 25°C for 24 h. The mixture was cooled to 0°C and extracted with ice-cold, aq $NaHCO_3$, then $H_2O$, followed by concentration. Column chromatography (15:1 hexane–EtOAc) of the residue afforded **8** as a syrup[8] (765 mg, 84%); $[\alpha]_D$ +73°, lit.[8] +52°. For NMR and CIMS data see ref 8.

*Methyl 6-O-(*tert*-butyldiphenylsilyl)-1-thio-β-*D*-galactopyranoside* (**10**).—A solution of **9** (ref 15) (2.0 g), imidazole (2 g), and *tert*-butyldiphenylsilyl chloride (6 mL) in pyridine (20 mL) was stirred at 25°C for 48 h. The volatiles were evaporated under reduced pressure. The residue was partitioned between $CHCl_3$ and $H_2O$. The $CHCl_3$ phase was dried ($Na_2SO_4$) and concentrated. Column chromatography (2:1 EtOAc–hexane) of the residue afforded **10** as a syrup (3.5 g, 82%); $[\alpha]_D$ +0.1° (*c* 0.8). NMR (20:1 $CDCl_3$–$D_2O$): $^1$H, $\delta$ 7.72–7.64 and 7.44–7.33 (aromatic), 4.210 (d, 1 H, $J_{1,2}$ 9.5 Hz, H-1), 4.091 (dd, 1 H, $J_{3,4}$ 3.4, $J_{4,5} < 1$ Hz, H-4), 3.912 (dd, 1 H, $J_{5,6}$ 5.8, $J_{6,6'}$ 11.4 Hz, H-6), 3.865 (dd, 1 H, $J_{5,6'}$ 5.3 Hz, H-6'), 3.734 (br t, 1 H, H-2), 3.563 (dd, 1 H, $J_{2,3}$ 9.3 Hz, H-3), 3.533 (m, 1 H, H-5), 2.158 (s, 3 H, $CH_3S$), and 1.040 [s, 9 H, $(CH_3)_3C$]; $^{13}$C, $\delta$ 135.6, 135.5, 133.0, 132.9, 129.8, and 127.7 (aromatic), 86.0 (C-1), 78.2 (C-5), 74.8 (C-3), 69.6 (C-2), 69.2 (C-4), 63.3 (C-6), 26.7 [$(CH_3)_3C$], 19.1 [$C(CH_3)_3$], and 11.9 ($CH_3S$). CIMS: *m/z* 466 [(M + 18)$^+$]. Anal. Calcd for $C_{23}H_{32}O_5SSi$: 61.57; H, 7.19; S, 7.15. Found: C, 61.32; H, 7.25; S, 7.06.

*Methyl 6-O-(*tert*-butyldiphenylsilyl)-3,4-O-isopropylidene-1-thio-β-*D*-galacto-pyranoside* (**11**).—A solution of the triol **10** (10 g) in 2,2-dimethoxypropane (120 mL) was treated with a catalytic amount of 10-camphorsulfonic acid for 2 h. Triethylamine (2 mL) was added and the solution was concentrated. The residue was partitioned between $CHCl_3$ and $H_2O$. The $CHCl_3$ phase was dried and concentrated. The residual syrup crystallized spontaneously to give **11** (10.6 g, 97%); mp 134–136°C; $[\alpha]_D$ +18° (*c* 1.2). NMR ($CDCl_3$): $^1$H, $\delta$ 7.74–7.66 and 7.46–7.32 (aromatic), 4.350 (dd, 1 H, $J_{3,4}$ 5.4, $J_{4,5}$ 1.5 Hz, H-4), 4.140 (d, 1 H, $J_{1,2}$ 10.1 Hz, H-1), 4.072 (dd, 1 H, $J_{2,3}$ 6.9 Hz, H-3), 3.97–3.88 (m, 3 H, H-5,6,6'), 3.572 (ddd, 1 H, H-2), 2.505 (d, 1 H, $J_{H\text{-}2,HO}$ 2.0 Hz, *HO*), 2.171 (s, 3 H, $CH_3S$), 1.517 and 1.371 [2 s, 6 H, $(CH_3)_2C$], and 1.056 [s, 9 H, $(CH_3)_3C$]; $^{13}$C, $\delta$ 135.6, 133.3, 133.2, 129.6, 127.6, and 127.5 (aromatic), 109.9 [$C(CH_3)_2$], 85.3 (C-1), 79.0 (C-3), 77.0 (C-5), 73.3 (C-4), 71.6 (C-2), 62.6 (C-6), 28.3 and 26.2 [$(CH_3)_2C$], 26.7 [$(CH_3)_3C$], 19.2 [$C(CH_3)_3$], and 11.6 ($CH_3S$). CIMS: *m/z* 506 [(M + 18)$^+$]. Anal. Calcd for $C_{26}H_{36}O_5SSi$: C, 63.90; H, 7.42; S, 6.56. Found: C, 63.88; H, 7.44; S, 6.65.

*Methyl 6-O-(*tert*-butyldiphenylsilyl)-3,4-O-isopropylidene-2-O-(4-methoxybenzyl)-*

*1-thio-β-D-galactopyranoside* (**12**).—To a stirred solution of **11** (2.0 g) in DMF (20 mL) at 0°C was added NaH (0.18 g, 60% suspension in oil) followed by 4-methoxybenzyl chloride (1 mL). After 1 h MeOH (1 mL) was added and the mixture was concentrated. The residue was partitioned between $CHCl_3$ and $H_2O$. The $CHCl_3$ phase was concentrated. Column chromatography (8:1 hexane–EtOAc) of the residue afforded **12** as a syrup (1.74 g, 70%); $[\alpha]_D$ −4° (*c* 0.7). NMR ($CDCl_3$): $^1H$, δ 7.72–7.67, 7.45–7.23, and 6.90–6.83 (aromatic), 4.789 and 4.675 (2 d, 2 H, *J* 11 Hz, C$H_2$ of MBn), 4.307 (dd, 1 H, $J_{3,4}$ 5.5, $J_{4,5}$ 2.0 Hz, H-4), 4.265 (d, 1 H, $J_{1,2}$ 9.8 Hz, H-1), 4.205 (t, 1 H, H-3), 3.92 (m, 2 H, H-6,6′), 3.813 (m, 1 H, H-5), 3.777 (s, 3 H, C$H_3$O), 3.426 (dd, 1 H, $J_{2,3}$ 6.6 Hz, H-2), 2.144 (s, 3 H, C$H_3$S), 1.443 and 1.356 [2 s, 6 H, (C$H_3$)$_2$C], and 1.050 [s, 9 H, (C$H_3$)$_3$C]; $^{13}C$, δ 159.2, 135.6, 135.5, 133.3, 129.9. 129.6, 127.6, 127.5, and 113.6 (aromatic), 109.7 [*C*(CH$_3$)$_2$], 84.5 (C-1), 79.7 (C-3), 78.5 (C-2), 76.7 (C-5), 73.4 (C-4), 73.0 (*C*H$_2$ of MBn), 62.7 (C-6), 55.2 (*C*H$_3$O), 28.0 and 26.3 [(*C*H$_3$)$_2$C], 26.7 [(*C*H$_3$)$_3$C], 19.1 [*C*(CH$_3$)$_3$], and 12.6 (*C*H$_3$S). CIMS: *m/z* 626 [(M + 18)$^+$]. Anal. Calcd for $C_{34}H_{44}O_6SSi$: 6, 67.07; H, 7.28; S, 5.27. Found: C, 67.59; H, 7.48; S, 5.10.

*Methyl 3,4-O-isopropylidene-2-O-(4-methoxybenzyl)-1-thio-β-D-galactopyranoside* (**13**).—A solution of **12** (1.3 g) in tetrahydrofuran (10 mL) was treated with $Bu_4NF$ (2 mL of a 0.1 M solution in tetrahydrofuran) for 4 h at 25°C. Concentration of the solution followed by purification by column chromatography (3:1 hexane–EtOAc) afforded syrupy **13** (650 mg, 81%); $[\alpha]_D$ +2° (*c* 1). NMR $CDCl_3$): $^1H$, δ 4.779 and 4.676 (2 d, 2 H, *J* 11 Hz, $CH_2$ of MBn), 4.309 (d, 1 H, $J_{1,2}$ 9.6 Hz, H-1), 4.241 (t, 1 H, H-3), 4.190 (dd, 1 H, $J_{3,4}$ 5.6, $J_{4,5}$ 1.7 Hz, H-4), 3.94 (m, 1 H, H-6), 3.84–3.74 (m, 2 H, H-5,6′), 3.793 (s, 3 H, C$H_3$O), 2.185 (s, 3 H, C$H_3$S), 1.456 and 1.355 [2 s, 6 H, (C$H_3$)$_2$C]; $^{13}C$, δ 159.2, 129.9, and 113.6 (aromatic), 110.0 [*C*(CH$_3$)$_2$], 84.4 (C-1), 79.7 (C-3), 78.2 (C-2), 76.7 (C-5), 74.0 (C-4), 73.0 (*C*H$_2$ of MBn), 62.4 (C-6), 55.2 (*C*H$_3$O), 27.8 and 26.2 [(*C*H$_3$)$_2$C], and 12.8 (*C*H$_3$S). CIMS: *m/z* 388 [(M + 18)$^+$]. Anal. Calcd for $C_{18}H_{26}O_6S$: C, 58.36; H, 7.07; S, 8.65. Found: C, 59.45; H, 7.31; S, 8.38.

*Methyl 2-O-(4-methoxybenzyl)-1-thio-β-D-galactopyranoside* (**14**).—A solution of **13** (200 mg) in MeOH (3 mL) was treated with aq 50% $HBF_4$ (30 μL) at 0°C for 3 h. Filtration of the mixture afforded crystalline **14** (168 mg, 94%). A portion was recrystallized from MeOH; mp 170–172°C, lit.[8] 173–175°C; $[\alpha]_D$ −5° (*c* 0.8, MeOH), lit.[8] −3° (MeOH). For NMR data see ref 8.

*2-(Trimethylsilyl)ethyl O-(2-azido-4,6-O-benzylidene-3-O-chloroacetyl-2-deoxy-α-D-glucopyranosyl)-(1 → 3)-2,4-di-O-benzoyl-α-L-rhamnopyranoside* (**17**).—A mixture of 2-(trimethylsilyl)ethyl 2,4-di-*O*-benzoyl-α-L-rhamnopyranoside[8] (**6** 2.3 g), 2-azido-4,6-*O*-benzylidene-3-*O*-chloroacetyl-2-deoxy-β-D-glucopyranosyl chloride[8] (**16**, 1.9 g), 2,6-di-*tert*-butyl-4-methylpyridine (950 mg), 4A molecular sieves (1 g), and dry $CH_2Cl_2$ (50 mL) was stirred for 1 h then cooled to −50°C. Silver trifluoromethanesulfonate (1.9 g) was added. The stirred mixture wavs allowed to reach 20°C in 1 h. Ice-cold, aq $NaHCO_3$ was added and the mixture was filtered. The organic phase was separated and concentrated. Column chromatography (6:1

hexane–EtOAc) of the residue afforded **17** as an amorphous solid (2.88 g, 71%); $[\alpha]_D$ +130° (*c* 0.7). NMR ($CDCl_3$): $^1H$, $\delta$ 5.626 (dd, 1 H, $J_{2,3}$ 3.2 Hz, H-$2_A$), 5.579 (t, 1 H, $J_{3,4} = J_{4,5} = 9.9$ Hz, H-$4_A$), 5.249 (s, 2 H, C*H*Ph), 5.231 (d, 1 H, $J_{1,2}$ 3.8 Hz, H-$1_B$), 5 .214 (t, 1 H, H-$3_B$), 4.985 (d, 1 H, $J_{1,2}$ 1.7 Hz, H-$1_A$), 4.455 (dd, 1 H, H-$3_A$), 4.102 (dq, 1 H, H-$5_A$), 4.095 (dd, 1 H, $J_{5,6}$ 4.1, $J_{6,6'}$ 10 Hz, H-$6_B$), 3.964 (s, 2 H, C$H_2$Cl), 3.707 (ddd, 1 H, H-$5_B$), 3.550 (t, 1 H, $J_{5,6'} = J_{6,6'} = 10$ Hz, H-$6_A$), 3.461 (t, 1 H, $J_{3,4}$ 9.5 Hz, H-$4_A$), 3.149 (dd, 1 H, $J_{2,3}$ 10.2 Hz, H-$2_B$), 1.346 (d, 1 H, $J_{5,6}$ 6.2 Hz, H-$6_A$), and 0.075 [t, 9 H, (C$H_3$)$_3$Si]; $^{13}C$, $\delta$ 166.1, 165.7, and 165.3 (*C*=O), 136.6–126.2 (aromatic), 101.1 (*C*HPh), 97.1 (C-$1_A$), 94.7 (C-$1_B$), 78.6 (C-$4_B$), 72.1 (C-$4_A$), 71.7 (C-$3_A$), 70.6 (C-$3_B$), 68.2 (C-$6_B$), 67.8 (C-$2_A$), 66.6 (C-$5_A$), 65.7 (O*C*H$_2$CH$_2$), 62.7 (C-$5_B$), 61.0 (C-$2_B$), 40.4 (*C*H$_2$Cl), 17.9 (*C*H$_2$Si), 17.6 (C-$6_A$), and −1.3 [(*C*H$_3$)$_3$Si]. CIMS: *m/z* 841 [(M + 1)$^+$]. Anal. Calcd for $C_{40}H_{46}ClN_3O_{12}Si$: C, 58.28; H, 5.62; N, 5. 10; Cl, 4.30. Found: C, 58.69; H, 5.78; N, 5.06; Cl, 4.44.

*2-(Trimethylsilyl)ethyl* O-*(2-azido-4,6-*O*-benzylidene-2-deoxy-α-*D*-glucopyranosyl)-(1 → 3)-2,4-di-*O*-benzoyl-α-*L*-rhamnopyranoside* (**18**).—A solution of compound **17** (2 g) and thiourea[10] (1 g) in EtOH (50 mL) was stirred at 25°C for 48 h. The solution was concentrated and the residue was equilibrated between $CHCl_3$ and aq $NaHCO_3$. The $CHCl_3$ phase was extracted with $H_2O$ and concentrated. Column chromatography (5 : 1 hexane–EtOAc) of the residue afforded amorphous **18** (1.5 g, 83%); $[\alpha]_D$ +113° (*c* 0.7). NMR ($CDCl_3$): $^1H$, $\delta$ 8.20–8.07, 7.63–7.22, and 7.06–7.00 (aromatic), 5.605 (dd, 1 H, H-$2_A$), 5.556 (t, 1 H, $J_{3,4} = J_{4,5} = 9.8$ Hz, H-$4_A$), 5.288 (s, 1 H, C*H*Ph), 5.104 (d, 1 H, $J_{1,2}$ 3.7 Hz, H-$1_B$), 4.982 (d, 1 H, $J_{1,2}$ 1.5 Hz, H-$1_A$), 4.431 (dd, 1 H, $J_{2,3}$ 3.3 Hz, H-$3_A$), 4.074 (dq, 1 H, H-$5_A$), 4.029 (dd, 1 H, $J_{5,6}$ 5.4, $J_{6,6'}$ 10 Hz, H-$6_A$), 3.895 (ddd, 1 H, H-$3_B$), 3.694 (dd, 1 H, H-$5_B$), 3.523 (t, 1 H, H-$6'_A$), 3.305 (t, 1 H, $J_{3,4} = J_{4,5} = 9.2$ Hz, H-$4_B$), 3.145 (dd, 1 H, $J_{2,3}$ 10 Hz, H-$2_B$), 2.385 (s, 1 H, $J_{H\text{-}3,OH}$ 2.7 Hz, O*H*), 1.324 (d, 3 H, H-$6_A$), and 0.073 [s, 9 H, (C$H_3$)$_3$Si]; $^{13}C$, $\delta$ 166.0 and 165.4 (C=O), 136.7–126.8 (aromatic), 101.8 (*C*HPh), 97.1 (C-$1_A$), 94.9 (C-$1_B$), 81.3 (C-$4_B$), 72.5 (C-$4_A$), 71.9 (C-$3_A$), 68.4 (C-$3_B$,$6_B$), 68.1 (C-$2_A$), 66.5 (C-$5_A$), 65.7 (O*C*H$_2$CH$_2$), 62.8, 62.6 (C-$2_B$,$5_B$), 18.0 (*C*H$_2$Si), 17.6 (C-$6_A$), and −1.3 [(CH$_3$)$_3$Si]. CIMS: *m/z* 765 [(M + 18)$^+$]. Anal. Calcd for $C_{38}H_{45}N_3O_{11}Si$: C, 61.03; H, 6.06; N, 5.62. Found: C, 61.45; H, 6.28; N, 5.44.

*2-(Trimethylsilyl)ethyl* O-*[3,4,6-tri-*O*-benzoyl-2-*O*-(4-methoxybenzyl)-α-*D*-galactopyranosyl]-(1 → 3)-*O*-(2-azido-4,6-*O*-benzylidene-2-deoxy-α-*D*-glucopyranosyl)-(1 → 3)-2,4-di-*O*-benzoyl-α-*L*-rhamnopyranoside* (**19**).—A mixture of **18** (1.3 g ), methyl 3,4,6-tri-*O*-benzoyl-2-*O*-(4-methoxybenzyl)-1-thio-α-D-galactopyranoside[8] (**15**, 2.33 g), 2,6-di-*tert*-butyl-4-methylpyridine (0.9 g), and 4A molecular sieves (3 g) in dry ether (60 mL) was stirred for 2 h at 25°C. Methyl trifluoromethanesulfonate[18] (600 μL) was added and stirring was continued for 36 h. The mixture was filtered and the filtrate was concentrated. Column chromatography (5 : 1 hexane–EtOAc) of the residue afforded amorphous **19** (2.1 g, 90%); $[\alpha]_D$ + 130° (*c* 0.9). NMR ($CDCl_3$): $^1H$, $\delta$ 8.18–6.42 (aromatic), 5.800 (dd, 1 H, $J_{3,4}$ 3.3, $J_{4,5}$ 1.2 Hz, H-$4_C$),

5.662 (dd, 1 H, H-$2_A$), 5.651 (dd, 1 H $J_{2,3}$ 10 Hz, H-$3_C$), 5.600 (t, 1 H, $J_{3,4} = J_{4,5} = 9.7$ Hz, H-$4_A$), 5.430 (d, 1 H, $J_{1,2}$ 3.7 Hz, H-$1_C$), 5.277 (s, 1 H, C*H*Ph), 5.243 (d, 1 H, $J_{1,2}$ 3.8 Hz, H-$1_B$), 4.993 (d, 1 H, $J_{1,2}$ 1.6 Hz, H-$1_A$), 4.587 (ddd, 1 H, H-$5_C$), 4.498 (dd, 1 H, $J_{2,3}$ 3.4 Hz, H-$3_A$), 3.862 (dd, 1 H, H-$2_C$), 3.656 (s, 3 H, C$H_3$O), 3.258 (dd, 1 H, $J_{2,3}$ 10 Hz, H-$2_B$), 1.346 (d, 1 H, $J_{5,6}$ 6.2 Hz, H-$6_A$), and 0.077 [s, 9 H, (C$H_3$)$_3$Si]; $^{13}$C, δ, 166.1, 165.6, and 165.3 (2 C), 165.1 (*C*=O), 158.9, 137–126.5, and 113.3 (aromatic), 102.2 (*C*HPh), 97.1 (C-$1_A$,$1_C$), 95.0 (C-$1_B$), 82.2 (C-$4_B$), 72.5 and 72.4 (C-$2_A$,$4_A$), 71.9 (C-$3_A$), 71.0 (C-$2_B$), 70.5 (*C*H$_2$ of MBn), 69.1, 69.0 and 68.0 (C-$2_C$,$3_C$,$4_C$), 68.6 (C-$6_B$), 66.7, and 66.6 (C-$5_A$,$5_C$), 65.8 (O*C*H$_2$CH$_2$), 62.4 (C-$2_B$), 61.7 (C-$6_C$), 61.5 (C-$5_B$), 55.0 (*C*H$_3$O), 18.0 (*C*H$_2$Si), 17.7 (C-$6_A$), and −1.3 [(*C*H$_3$)$_3$Si]. FABMS: *m/z* 595 [(C$_{35}$H$_{31}$O$_9$)$^+$] and 1314 [(M + 1 − N$_2$)$^+$]. Anal. Calcd for C$_{73}$H$_{75}$N$_3$O$_{20}$Si: C, 65.31; H, 5.63; N, 3.13. Found: C, 65.33; H, 6.67; N, 3.13.

*2-(Trimethylsilyl)ethyl O-[3,4,6-tri-O-benzoyl-2-O-(4-methoxybenzyl)-α-D-galactopyranosyl]-(1 → 3)-O-(2-acetamido-4,6-O-benzylidene-2-deoxy-α-D-glucopyranosyl)-(1 → 3)-2,4-di-O-benzoyl-α-L-rhamnopyranoside* (**20**).—A solution of **19** (1.3 g) and triphenylphosphine[19] (0.7 g) in dry $CH_2Cl_2$ (60 mL) was stirred at 35–40°C for 24 h. More triphenylphospine (0.5 g) was added and stirring was continued for an additional 6 h. Water (10 mL) was added and stirring was continued at 35–40°C for 36 h. The solution was concentrated. The syrupy residue was dried by the addition and distillation of toluene thrice, then dissolved in pyridine (5 mL). Acetic anhydride (2 mL) was added and the solution was kept at 25°C for 3 h, then concentrated. Column chromatography (2:1 hexane–EtOAc) of the residue afforded amorphous **20** (1.11 g, 84%); $[\alpha]_D$ +99° (*c* 0.4). NMR ($CDCl_3$): $^1$H, δ 8.24–6.44 (aromatic), 5.895 (dd, 1 H, $J_{3,4}$ 3.5, $J_{4,5}$ 1.1 Hz, H-$4_C$), 5.646 (dd, 1 H, $J_{2,3}$ 10.7 Hz, H-$3_C$), 5.439 (dd, 1 H, $J_{2,3}$ 3.2 Hz, H-$2_A$), 5.436 (t, 1 H, $J_{3,4} = J_{4,5} = 9.6$ Hz, H-$4_A$), 5.376 (d, 1 H, $J_{1,2}$ 3.7 Hz, H-$1_C$), 5.235 (s, 1 H, C*H*Ph), 4.995 (d, 1 H, $J_{1,2}$ 3.9 Hz, H-$1_B$), 4.953 (d, 1 H, $J_{1,2}$ 1.5 Hz, H-$1_A$), 4.824 (dd, 1 H, $J_{5,6}$ 5.0, $J_{6,6'}$ 11 Hz, H-$6_B$), 4.628 (ddd, 1 H, H-$5_B$), 4.389 (dd, 1 H, H-$2_B$), 4.327 (H-6), 4.036 (dq, 1 H, H-$5_A$), 3.745 (H-$3_B$), 3.655 (s, 3 H, C$H_3$O), 1.849 (s, 3 H, C$H_3$CO), 1.33 (d, 3 H, $J_{5,6}$ 6.3 Hz, H-$6_A$), and 0.064 [s, 9 H, (C$H_3$)$_3$Si]; $^{13}$C, δ 170.1 (C=O of Ac), 166.9, 165.9, 165.7, 165.4, and 165.0 (C = O of Bz), 158.8, 137.1, 134–126.5, and 113.3 (aromatic), 102.0 (*C*HPh), 100.0 (C-$1_B$), 97.2 (C-$1_A$), 97.1 (C-$1_C$), 82.2 (C-$4_B$), 77.6 (C-$3_A$), 73.5 (C-$3_B$), 73.3 (C-$4_A$), 71.2 (C-$2_C$), 70.8 (C-$2_A$), 70.3 (*C*H$_2$ of MBn), 69.1 (C-$3_C$,$4_C$), 68.3 (C-$6_B$), 66.5 (C-$5_A$), 66.3 (C-$5_C$), 65.7 (OCH$_2$CH$_2$), 63.2 (C-$5_B$), 61.1 (C-$6_C$), 55.0 (*C*H$_3$O), 51.9 (C-$2_B$), 22.7 (*C*H$_3$CO), 17.9 (*C*H$_2$Si), 17.6 (C-$6_A$), and −1.3 [(*C*H$_3$)$_3$Si]. FABMS: *m/z* 1358 [(M + 1)$^+$]. Anal. Calcd for C$_{75}$H$_{79}$NO$_{21}$Si: C, 66.31; H, 5.86; N, 1.03. Found: C, 66.23; H, 6.22; N, 1.02.

*2-(Trimethylsilyl)ethyl O-(3,4,6-tri-O-benzoyl-α-D-galactopyranosyl)-(1 → 3)-O-(2-acetamido-4,6-O-benzylidene-2-deoxy-α-D-glucopyranosyl)-(1 → 3)-2,4-di-O-benzoyl-α-L-rhamnopyranoside* (**21**).—A mixture of **20** (1.0 g), 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (1.5 g), $CH_2Cl_2$ (40 mL), and $H_2O$ (5 mL) was stirred at 25°C for 4 h. The mixture was extracted with aq $NaHCO_3$ and $H_2O$. The organic phase

was concentrated. Column chromatography (2:1 hexane–EtOAc) of the residue afforded amorphous **21** (890 mg, 97%); $[\alpha]_D$ +73° (*c* 0.8). NMR ($CDCl_3$): $^1H$, $\delta$ 8.2–7.22 (aromatic), 6.620 (d, 1 H, $J_{H\text{-}2A,HN}$ 9.8 Hz, N*H*), 5.902 (br d, 1 H, H-$4_C$), 5.550 (dd, 1 H, H-$2_A$), 5.540 (dd, 1 H, $J_{2,3}$ 10.4, $J_{2,3}$ 3,4 Hz, H-$3_C$), 5.440 (t, 1 H, $J_{3,4} = J_{4,5} = 9.7$ Hz, H-$4_A$), 5.353 (s, 1 H, C*H*Ph), 5.147 (d, 1 H, $J_{1,2}$ 3.7 Hz, H-$1_C$), 4.989 (d, 1 H, $J_{1,2}$ 3.7 Hz, H-$1_B$), 4.959 (d, 1 H, $J_{1,2}$ 1.5 Hz, H-$1_A$), 4.150 (ddd, 1 H, $J_{2,3}$ 10.4 Hz, H-$2_C$), 4.065 (dq, 1 H, H-$5_A$), 2.650 (d, 1 H, $J_{H-3c,HO}$ 11.3 Hz, O*H*), 1.786 (s, 3 H, C$H_3$CO), 1.347 (d, 3 H, H-$6_A$), and 0.073 [s, 9 H, (C$H_3$)$_3$]; $^{13}C$, $\delta$ 170.3 (*C*=O of Ac), 166.6, 165.87, 165.85 and 165.4 (*C*=O of Bz), 136.4–126.0 (aromatic), 101.3 (*C*HPh), 101.0 (C-$1_C$), 99.0 (C-$1_B$), 97.1 (C-$1_A$), 81.1 (C-$4_B$), 77.3 (C-$3_A$), 76.2 (C-$3_B$), 73.0 (C-$4_A$), 70.9, 70.2 (C-$2_A$,$3_C$), 69.0 (C-$4_C$), 68.2, 67.5 (C-$2_C$,$5_C$), 68.1 (C-$6_B$), 66.5 (C-$5_A$), 65.7 (O*C*$H_2$C$H_2$), 63.3 (C-$5_B$), 61.3 (C-$6_C$), 52.1 (C-$2_B$), 22.7 (*C*$H_3$CO), 17.9 (*C*$H_2$Si), 17.6 (C-$6_A$), and −1.3 [(*C*$H_3$)$_3$Si]. FABMS: *m/z* 1239 [(M + 1)$^+$]. Anal. Calcd for $C_{67}H_{71}NO_{20}Si$: C, 64.98; H, 5.78; N, 1.13. Found: C, 65.28; H, 6.10; N, 1.04.

*2-(Trimethylsilyl)ethyl O-(2,4-di-O-benzoyl-3-O-chloroacetyl-α-*L*-rhamnopyranosyl)-(1 → 2)-O-(3,4,6-tri-O-benzoyl-α-*D*-galactopyranosyl)-(1 → 3)-O-(2-acetamido-4,6-di-O-acetyl-2-deoxy-α-*D*-glucopyranosyl)-(1 → 3)-2,4-di-O-benzoyl-α-*L*-rhamnopyranoside* (**23**) *and 2-(trimethylsilyl)ethyl O-(3-O-acetyl-2,4-di-O-benzoyl-α-*L*-rhamnopyranosyl)-(1 → 2)-O-(3,4,6-tri-O-benzoyl-α-*D*-galactopyranosyl)-(1 → 3)-O-(2-acetamido-4,6-di-O-acetyl-2-deoxy-α-*D*-glucopyranosyl)-(1 → 3)-2,4-di-O-benzoyl-α-*L*-rhamnopyranoside* (**24**).—A mixture of **21** (0.8 g), **8** (1.4 g), 2,6-di-tert-butyl-4-methylpyridine (0.6 g), 4A molecular sieves (0.3 g), and $CH_2Cl_2$ (30 mL) was stirred for 1 h then cooled to −40°C. Silver trifluoromethanesulfonate (1 g) was added, the mixture was further stirred for 30 min at −40°C, then allowed to reach 25°C in 20 min. Stirring was continued another 20 min. Tetraethylammonium bromide (1 g ) was added followed by ice-cold, aq $NaHCO_3$. The mixture was filtered. The organic phase was extracted with $H_2O$, then concentrated. Column chromatography (2:1 hexane–EtOAc) of the residue afforded **22** (840 mg, containing < 10% of a cochromatographing impurity). FABMS: *m/z* 1669 [(M + 1)$^+$].

A solution of **22** (770 mg) in 10:1 AcOH–$H_2O$ (5.5 mL) was stirred at 80°C until reaction was complete. The mixture was concentrated, and the residue was dried by the repeated addition and distillation of toluene. A solution of the residue in pyridine (5 mL) was then treated with acetic anhydride (3 mL) and a catalytic amount of 4-dimethylaminopyridine at 25°C for 3 h. The volatiles were removed under reduced pressure. Column chromatography (2:1 hexane–EtOAc) of the residue afforded first **23** as a syrup (320 mg); $[\alpha]_D$ +112° (*c* 0.4). NMR ($CDCl_3$): $^1H$, $\delta$ 5.963 (br d, 1 H, H-$4_C$), 5.690 (dd, 1 H, $J_{2,3}$ 10.6, $J_{3,4}$ 3.2 Hz, H-$3_C$), 5.579 (dd, 1 H, $J_{2,3}$ 3.4, $J_{3,4}$ 10 Hz, H-$3_D$), 5.543 (dd, 1 H, H-$2_A$), 5.453 (t, 1 H, $J_{3,4} = J_{4,5} = 9.8$ Hz, H-$4_A$), 5.33–5.26 (m, 2 H, H-$2_D$, $4_D$), 5.217 (d, 1 H, $J_{1,2}$ 1.8 Hz, H-$1_D$), 5.202 (d, 1 H, $J_{1,2}$ 3.5 Hz, H-$1_C$), 5.043 (d, 1 H, $J_{1,2}$ 3.4 Hz, H-$1_B$), 4.957 (d, 1 H, $J_{1,2}$ 1.4 Hz, H-$1_A$), 3.621 (s, 2 H, C$H_2$Cl), 1.980, 1.839, and 1.755 (C$H_3$CO),

1.309 and 1.017 (2 d, 6 H, $J$ 6.2 Hz, H-$6_A$,$6_B$), and 0.060 [s, 9 H, $(CH_3)_3Si$]; $^{13}C$, $\delta$ 171.0, 170.7, 170.1, and 168.9 (C=O of Ac and ClAc), 166.2–164.7 (C=O of Bz), 133.8–132.6 and 130–128 (aromatic), 97.9 (C-$1_D$), 97.7 (C-$1_C$), 97.6 (C-$1_B$), 97.0 (C-$1_A$), 75.1 (C-$3_A$), 74.1 (C-$3_B$), 74.0 (C-$2_C$), 72.7 (C-$4_A$), 71.6 (C-$4_D$), 70.2, 69.6 (C-$2_D$,$4_B$), 70.1 (C-$2_A$), 69.9 (C-$3_D$), 68.9 (C-$3_C$), 68.6 (C-$4_C$,$5_B$), 67.3 (C-$5_D$), 66.5 (C-$5_A$), 66.6 (C-$5_C$), 65.8 ($OCH_2CH_2$), 60.9 (C-$6_C$), 60.3 (C-$6_B$), 51.5 (C-$2_B$), 40.1 ($CH_2Cl$), 22.6 ($CH_3CON$), 20.6 and 20.5 ($CH_3COO$), 17.9 ($CH_2Si$), 17.6 and 17.4 (C-$6_A$,$6_D$), and −1.4 [$(CH_3)_3Si$]. FABMS: $m/z$ 431 [$(C_{22}H_{20}ClO_7)^+$] and 1664 [$(M+1)^+$]. Anal. Calcd for $C_{86}H_{90}ClNO_{29}Si$: C, 62.03; H, 5.45; N, 0.84; Cl, 2.13. Found: C, 62.41; H, 5.84; N, 0.72; Cl, 2.09.

Further elution gave 230 mg of a syrup consisting mainly (> 80%) of **24**. NMR ($CDCl_3$): $^1H$, $\delta$ 6.605 (d, 1 H N*H*), 5.953 (dd, 1 H, H-$4_C$), 5.679 (dd, 1 H, $J_{2,3}$ 10.7, $J_{3,4}$ 3.4 Hz, H-$3_C$), 5.522 (d, 1 H, H-$1_D$), 5.502 (dd, 1 H, $J_{2,3}$ 3.4 Hz, H-$3_D$), 5.441 (t, 1 H, $J_{3,4} = J_{4,5} = 9.9$ Hz, H-$4_A$), 5.200 (d, 1 H, $J_{1,2}$ 3.6 Hz, H-$1_B$), 4.950 (d, 1 H, $J_{1,2}$ 1.5 Hz, H-$1_A$), 2.020, 1.879, 1.788, and 1.647 (4 s, 12 H, 4 C*H*$_3$CO), 1.325 and 1.030 (2 d, 6 H, H-$6_A$,$6_B$), and 0.066 [s, 9 H, $(CH_3)_3Si$]; $^{13}C$, $\delta$ 170.8, 170.2, 169.1 and 169.0 (*C*=O of Ac), 165.9–164.8 (*C*=O of Bz), 134–128 (aromatic), 98.3 (C-$1_D$), 98.0 C-$1_C$), 97.8 (C-$1_B$), 97.1 (C-$1_A$), 75.4 (C-$3_A$), 74.6 (C-$3_B$), 74.4 (C-$2_C$), 72.8 (C-$4_A$), 72.0, 70.6, 70.3, and 69.5 (C-$2_A$,$2_D$,$4_B$,$4_D$), 68.9 (C-$3_C$), 68.6 (C-$4_C$,$5_B$), 68.0 (C-$3_D$), 67.4 and 66.7 (C-$5_A$,$5_D$), 66.8 (C-$5_C$), 65.8 ($OCH_2CH_2$), 51.6 (C-$2_B$), 22.7 ($CH_3CON$), 20.7, 20.6, and 20.3 ($CH_3COO$), 18.0 ($CH_2Si$), 17.6, 17.5 (C-$6_A$,$6_D$), and −1.4 [$(CH_3)_2Si$]. FABMS: $m/z$ 397 [$(C_{22}H_{21}O_7)^+$] and 1630 [$(M+1)^+$].

O-*(2,4-Di*-O-*benzoyl-3*-O-*chloroacetyl-α*-L-*rhamnopyranosyl)-(1 → 2)*-O-*(3,4,6-tri*-O-*benzoyl-α*-D-*galactopyranosyl)-(1 → 3)*-O-*(2-acetamido-4,6-di*-O-*acetyl-2-deoxy-α*-D-*glucopyranosyl)-(1 → 3)-2,4-di*-O-*benzoyl-α*-L-*rhamnopyranosyl trichloroacetimidate* (**1**).—A solution of **23** (300 mg) in a 1:1 mixture of $CH_2Cl_2$ and trifluoroacetic acid (5 mL) was kept at 25°C for 30 h then the volatiles were removed. Toluene (3 × 5 mL) was added and evaporated from the residue. The solid residue {**25**, FABMS: $m/z$ 431 [$(C_{22}H_{20}ClO_7)^+$], 905 [$(C_{49}H_{42}ClO_{15})^+$], 1192 [$(C_{61}H_{59}ClNO_{22})^+$], and 1564 [$(M+1)^+$]} was dissolved in $CH_2Cl_2$ (2 mL) and the solution was cooled to −20°C. Then $CCl_3CN$ (0.8 mL) and 1,8-diazabicyclo[5.4.0]undec-7-ene (80 μL) were added. The solution was stirred at −20°C for 1 h and then was allowed to reach ~20°C in 1 h. Removal of the volatiles followed by purification by column chromatography (2:1 hexane–EtOAc) gave **1** as an amorphous solid (250 mg, 81%); $[\alpha]_D$ + 100° ($c$ 0.6). NMR ($CDCl_3$): $^1H$, $\delta$ 8.823 (s, 1 H, C=N*H*), 8.2–7.2 (aromatic), 6.538 (d, 1 H, $J_{H\text{-}2B,NH}$ 9.8 Hz, N*H*Ac), 6.411 (d, 1 H $J_{1,2}$ 1.6 Hz, H-$1_A$), 5.951 (dd, 1 H $J_{3,4}$ 3.4, $J_{4,5}$ 1.6 Hz, H-$4_C$), 5.782 (dd, 1 H, $J_{2,3}$ 3.3 Hz, H-$2_A$), 5.671 (dd, 1 H, $J_{2,3}$ 10.6 Hz, H-$3_C$), 5.579 (dd, 1 H, $J_{2,3}$ 3.4 Hz, $J_{3,4}$ 9.9 Hz, H-$3_D$), 5.564 (t, 1 H, $J_{3,4} = J_{4,5} = 9.7$ Hz, H-$4_A$), 5.305 (t, 1 H, $J_{3,4} = J_{4,5} = 9.5$ Hz, H-$4_B$), 5.295 (dd, 1 H, H-$2_D$), 5.288 (t, 1 H, $J_{3,4} = J_{4,5} = 9.6$ Hz, H-$4_D$), 5.230 (d, 1 H, $J_{1,2}$ 1.2 Hz, H-$1_D$), 5.214 (d, 1 H, $J_{1,2}$ 3.5 Hz, H-$1_C$), 5086 (d, 1 H, $J_{1,2}$ 3.4 Hz, H-$1_B$), 4.776 (dd, 1 H, $J_{5,6}$ 5.0, $J_{6,6'}$ 10.5 Hz, H-$6_C$), 4.673 (ddd, 1 H, $J_{5,6'}$ 9.6 Hz, H-$5_C$), 4.570 (dt, 1 H, $J_{2,3}$ 10 Hz, H-$2_B$), 4.430

(dd, 1 H, H-$3_A$), 4.404 (dd, 1 H, H-$2_C$), 4.286 (dq, 1 H, H-$5_A$), 4.284 (dd, 1 H, H-$6_C$), 4.078 (dq, 1 H, H-$5_D$), 3.908 (dd, 1 H, H-$3_B$), 3.792 (dd, 1 H, $J_{5,6}$ 3.3, $J_{6,6'}$ 12.4 Hz, H-$6_B$), 3.682 and 3.631 (2 d, 2 H, $J$ 14.8 Hz, $CH_2Cl$), 3.623 (m, 1 H, H-$5_B$), 3.470 (dd, 1 H, $J_{5,6'}$ 1.8 Hz, H-$6'_B$), 2.000, 1.859, and 1.785 (3 s, 9 H, 3 $CH_3CO$), 1.385 (d, 3 H, $J_{5,6}$ 6.2 Hz, H-$6_A$), and 1.025 (d, 3 H, $J_{5,6}$ 6.2 Hz, H-$6_D$); $^{13}C$, $\delta$ 170.7, 170.1, and 168.9 (*C*=O of 3 Ac), 166.0–168.4 (8 C, *C*=O) of ClAc and 7 Bz), 159.9 (*C*=NH), 134.1–132.8 and 130.2–128.1 (aromatic), 98.0 ($^1J_{H\text{-}1,C\text{-}1}$ 172 Hz, C-$1_B$), 97.8 ($^1J_{H\text{-}1,C\text{-}1}$ 172 Hz, C-$1_D$), 97.6 ($^1J_{H\text{-}1,C\text{-}1}$ 171 Hz, C-$1_C$), 95.0 ($^1J_{H\text{-}1,C\text{-}1}$ 180 Hz, C-$1_A$), 75.0 (C-$3_A$), 73.8 (C-$2_C$,$3_B$), 72.0 (C-$4_A$), 71.6 (C-$4_D$), 70.2 (C-$2_D$), 70.0 (C-$3_D$), 69.8 (C-$4_B$), 69.7 (C-$5_A$), 68.91, (C-$3_C$), 68.87 (C-$5_B$), 68.6 (C-$4_C$), 68.4 (C-$2_A$), 67.4, (C-$5_D$), 66.7 (C-$5_C$), 61.0 (C-$6_B$), 60.9 (C-$6_C$), 51.5 (C-$2_B$), 40.2 ($CH_2Cl$), 22.6 ($CH_3CON$), 20.7 and 20.6 ($CH_3COO$), 17.7 and 17.5 (C-$6_A$,$6_D$). FABMS: $m/z$ 431 $[(C_{22}H_{20}ClO_7)^+]$, 905 $[(C_{49}H_{42}ClO_{15})^+]$, 1192 $[(C_{61}H_{59}ClNO_{22})^+]$, 1546 $[(M - C_2HCl_3NO)^+]$, and 1729 $[(M + 23)^+]$. Anal. Calcd for $C_{83}H_{78}Cl_4N_2O_{29}$: C, 58.32; H, 4.60; N, 1.64; Cl, 8.30 Found: C, 58.09; H, 4.66; N, 1.59; Cl, 8.20.

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