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Capsular polysaccharide of *Streptococcus pneumoniae* type 19F: synthesis of the repeating unit

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Abstract

A new and more versatile synthesis of β-D-Man*p*NAc-(1→4)-α-D-Glc*p*-(1→2)-α-L-Rha*p*, the trisaccharide repeating unit of the *Streptococcus pneumoniae* type 19F capsular polysaccharide, is described. The present approach allows a simple access to different fragments containing the trisaccharide and the conjugation of the product(s) to a protein through the selective manipulation of the anomeric position at the reducing end and of the HO-4 function at the nonreducing end. The synthetic scheme shows an efficient application of the sulfoxide method for the stereoselective and high yielding formation of the glycosidic linkages. © 1998 Elsevier Science Ltd. All rights reserved

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1. Introduction

Pneumococcal capsular polysaccharides have recently attracted considerable attention because of their use in a multivalent vaccine against pneumococcal infections. The highly purified polysaccharide vaccines introduced in the seventies have been demonstrated to be efficacious in adults and older children but not significantly immunogenic in young infants. A new strategy has been then devised involving the use of glycoconjugates, where carbohydrate antigens and haptens are covalently linked to protein carriers working as T-helper dependent antigens [1].

Recent investigations [2] have been devoted to the assessment of the structure-activity relationship of capsular polysaccharides for different serotypes of *Streptococcus pneumoniae*.

In a project aimed at designing new semi-synthetic oligoglycoconjugate vaccines, we are interested in defining the minimal oligosaccharide sequence required for the production of antibodies against serotype 19F of *S. pneumoniae*. The synthesis of a repeating unit (→4)-β-D-Man*p*NAc-(1→4)-α-D-Glc*p*-(1→2)-α-L-Rha*p*-(1-PO_4^-→) of the

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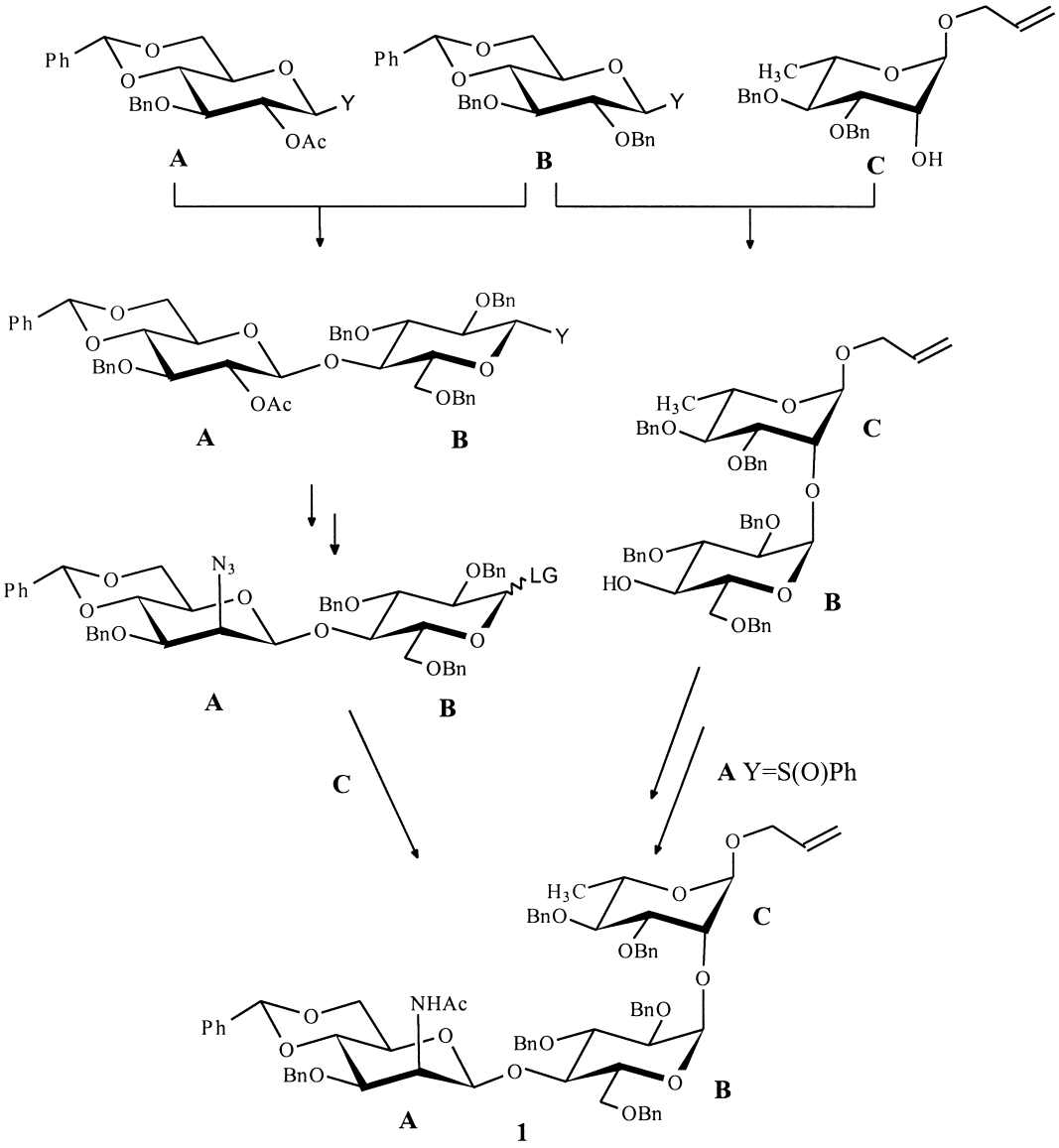
capsular polysaccharide of this serotype has already been described by us [3] and others [4].

In this paper we present a new and more versatile synthetic approach to the fully protected trisaccharide **1**, where the protecting groups strategy allows the formation of dimers or trimers through phosphate bridges and the introduction of a spacer arm for the conjugation to protein carriers. Different strategies were adopted to assemble the trisaccharide **1** (Scheme 1).

The strategy reported in Scheme 1 gave excellent results in the first coupling (A + B→AB), but low yields and stereoselectivity were obtained in the second glycosylation (AB + C→ABC), although different glycosyl donors (trichloroacetimidate, phenyl thioglycoside, phenyl sulfoxide) were used. These preliminary results suggested to change the synthetic strategy by inverting the joining order of the monosaccharide units. Thus, the formation of disaccharide B-C α-D-Glc*p*-(1→2)-α-L-Rha*p* followed by the glycosylation with a suitably protected donor and inversion at C-2″ using N_3^- as a nucleophile were planned to afford the trisaccharide **1** (Scheme 1).

2. Results and discussion

Phenyl 4,6-*O*-benzylidene-1-thio-β-D-glucopyranoside **2** [5] was used as a common precursor in



Scheme 1.

the synthesis of the *gluco* and *manno* moieties. Compound **2** was fully benzylated (→3), then careful oxidation with *m*-chloroperbenzoic acid gave sulfoxide donor **4**. Condensation of **4** with allyl 3,4-di-*O*-benzyl-α-L-rhamnopyranoside **5** using trifluoromethanesulfonic anhydride as a promoter and 2,6-di-*tert*-butyl-4-methyl pyridine as an acid scavenger at −60 °C [6] afforded disaccharide **6** in a good yield (80%). Only the α product was isolated, although small traces of by-products were detected on TLC. The α configuration of the newly formed glycosidic linkage was ascertained through ^{13}C NMR spectroscopy (C-1 and C-1′ exhibited signals at δ 97.31 and 98.56).

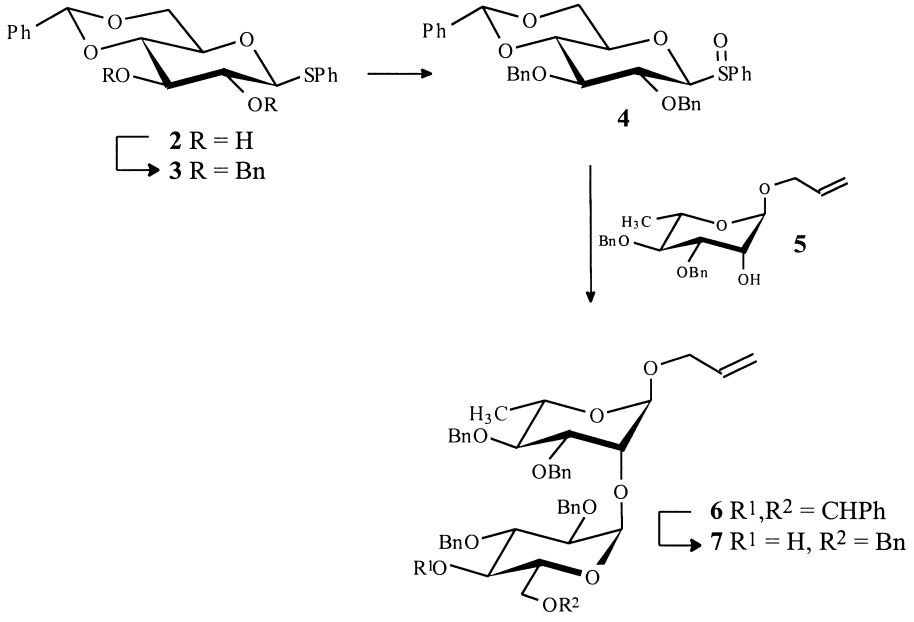
The benzylidene ring of disaccharide **6** was hydrolysed with aqueous 90% trifluoroacetic acid and the resulting diol was regioselectively 6′-*O*-benzylated via a stannylene acetal to give compound **7** in 80% yield (Scheme 2).

The second glucosyl donor was synthesized again from **2** through regioselective benzylation of HO-3 (→**8**) [7] followed by acetylation of HO-2 (→**9**) and oxidation of the thiophenyl glycoside to sulfoxide **10**. Condensation of **10** with acceptor **7**, performed as previously described [6], gave trisaccharide **11** in 77% yield (Scheme 3). Again, the stereochemistry of the newly synthesized glycosidic linkage was deduced by NMR analysis [^{13}C NMR, signals at δ 101.69 and 101.35 attributable to C-1″ and to C*H*Ph; ^{1}H NMR, H-1″β δ 4.34 ($J_{1'',2''}$ 7.9 Hz)].

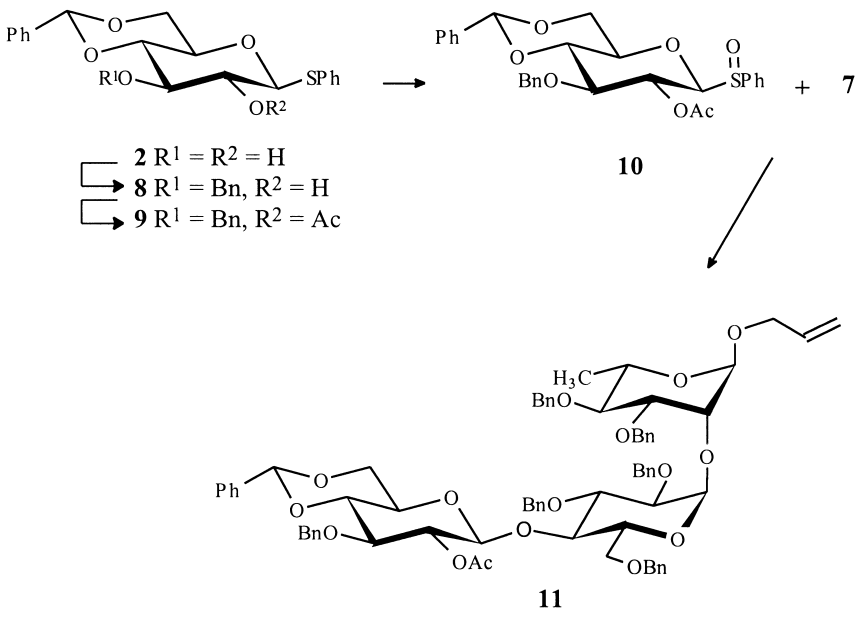
Zemplèn deacetylation of **11** (Scheme 4) gave trisaccharide **12** having the HO-2″ function available for the introduction of the azido group. Although the *gluco–manno* conversion through a S_N2 inversion was easily performed in the preparation of the disaccharide AB (Scheme 1), the same transformation on the trisaccharide **12** was difficult. Usual procedures (Mitsunobu reaction, triflate or mesylate formation followed by treatment with N_3^-, oxidation with pyridinium chlorochromate followed by treatment with hydroxylamine hydrochloride and subsequent reduction of the resulting oxime) were unsuccessful. Treating **12** with NaH and sulfonyl diimidazole in *N*,*N*-dimethylformamide at −40 °C [8], imidazoyl sulfate **13** was obtained in quantitative yield; then, reaction with tetrabutylammonium azide in toluene afforded trisaccharide **14** in almost quantitative yield.

The reduction of the azido group of **14** was also attempted in many different conditions (hydrogen sulfide–pyridine, dithiols, Staudinger reaction); the best results were obtained using a slightly modified recent literature procedure [9] which allows to obtain directly the acetamido group. Thus, compound **14** was treated with a Zn–Cu couple in tetrahydrofuran—acetic anhydride—acetic acid to afford compound **1** (84%).

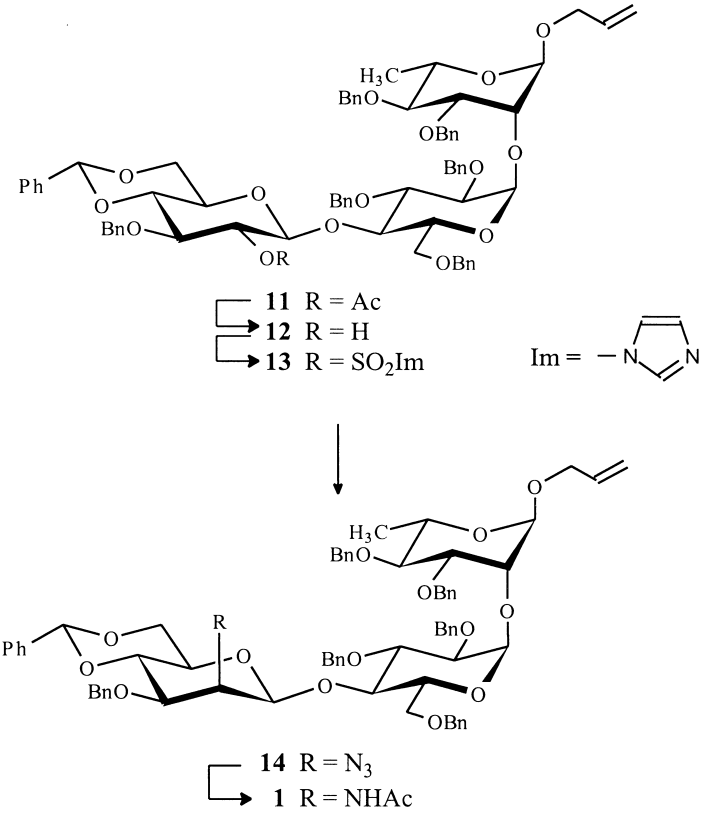
The trisaccharide repeating unit **1** was then alternatively deprotected at positions O-1 or O-4″. Reductive opening of the benzylidene ring of **1**



Scheme 2.

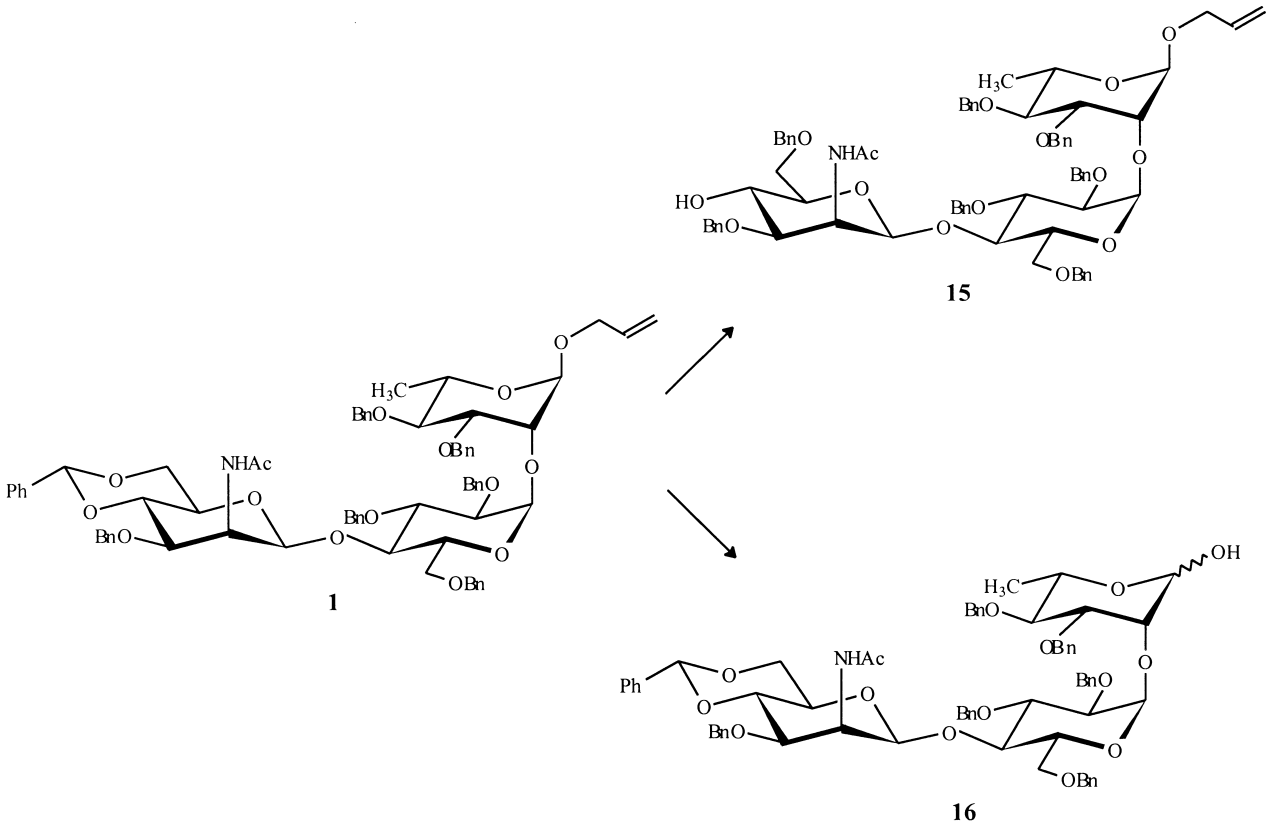


Scheme 3.



Scheme 4.

[10] (borane trimethylamine complex, boron trifluoride ethyl etherate) gave compound **15** (82% yield) with a HO-4″ group. On the other hand, the allyl group of **1** was isomerized to the corresponding 1-propenyl glycoside [11] which was finally hydrolyzed with iodine in tetrahydrofuran–water [12] to give **16** (96%) as an anomeric mixture (Scheme 5).



Scheme 5.

3. Experimental

General methods.—^{1}H NMR and ^{13}C NMR spectra were recorded on Bruker AC 300 and Bruker AC 200 spectrometers for solutions in $CDCl_3$. Melting points were determined with a Büchi apparatus and are not corrected. Optical rotations were measured at room temperature with a Perkin–Elmer 241 polarimeter. TLC was carried out on Merck Silica-gel 60 F_{254} plates (0.25 mm thickness), and spots were visualized by spraying with a solution containing H_2SO_4 (31 mL), ammonium molybdate (21 g) and $Ce(SO_4)_2$ (1 g) in 500 mL water, followed by heating at 110 °C for 5 min. Column chromatography was performed by the flash procedure using Merck Silica-gel 60 (230–400 mesh). IR spectra were recorded on a Perkin–Elmer 681 spectrometer. Elemental analyses were performed using the Carlo Erba elemental analyser 1108.

Phenyl 2,3-di-O-*benzyl-4,6*-O-*benzylidene-1-thio-β*-D-*glucopyranoside* (**3**).—Sodium hydride (10 g, 416.6 mmol) was added with stirring to a solution of phenyl 4,6-*O*-benzylidene-1-thio-β-D-glucopyranoside **2** (12.01 g, 33.32 mmol) in dry THF (200 mL) under N_2; the mixture was stirred for 10 min and after the dropwise addition of benzyl bromide (16 mL, 134.6 mmol) boiled under reflux overnight. The reaction was quenched with MeOH and the solution was partitioned between CH_2Cl_2 and aq NH_4Cl. The organic layer was washed with water, dried (Na_2SO_4), and concentrated. The residue was purified by crystallization from 1:1 hexane–EtOAc to give **3** (15.2 g, 96%); mp 155–156 °C; $[\alpha]_D$ −21.6° (*c* 1, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.70–7.20 (m, 20 H, ArH), 5.60 (s, 1 H, C*H*Ph), 4.98 (d, 1 H, J_{gem} 11.1 Hz, CH*H*Ph), 4.92–4.77 (m, 4 H, H-1, CH_2Ph and C*H*HPh), 4.41 (dd, 1 H, $J_{6a,6b}$ 12.9, $J_{6a,5}$ 5.0 Hz, H-6a), 3.90–3.80 (m, 2 H, H-2,6b), 3.73 (t, 1 H, $J_{4,3} = J_{4,5} = 9.2$ Hz, H-4), 3.58–3.46 (m, 2 H, H-3,5); ^{13}C NMR (75.46 MHz, $CDCl_3$): δ 101.79 (d, *C*HPh), 88.93 (d, C-1), 83.67, 82.11, 81.12, and 70.90 (4 d, C-2,3,4,5), 76.56, 75.98, and 69.35 (3 t, C-6 and 2 *C*H_2Ph). Anal. Calcd for $C_{33}H_{32}O_5S$: C, 73.31; H, 5.97. Found : C, 73.54; H, 6.12.

Phenyl 2,3-di-O-*benzyl-4,6*-O-*benzylidene-1-thio-β*-D-*glucopyranoside sulfoxide* (**4**).—A solution of **3** (7.0 g, 9.2 mmol) in dry CH_2Cl_2 (230 mL) was cooled at −60 °C, then 85% *m*-chloroperbenzoic

acid (2.88 g, 10.88 mmol) was added, and the mixture was allowed to warm up to 0 °C and stirred for 5 h. The reaction was quenched with aq 5% $FeSO_4$ and after extraction with CH_2Cl_2, the organic layer was washed with satd $NaHCO_3$ and water, dried (Na_2SO_4), and concentrated. The residue was crystallized from hexane–EtOAc to give **4** (5.1 g, 98%) as a mixture of diastereoisomers. A small amount (200 mg) was chromatographed (3:1 petroleum ether–EtOAc) to give pure analytical samples; the diastereoisomer with the higher R_f value was obtained as white crystals; mp 161–162 °C; $[\alpha]_D$ −19.8° (*c* 1, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.58–7.08 (m, 20 H, ArH), 5.51 (s, 1 H, C*H*Ph), 4.90 (d, 1 H, J_{gem} 11.0 Hz, C*H*HPh), 4.88 (d, 1 H, J_{gem} 10.9 Hz, C*H*HPh), 4.75 (d, 1 H, C*H*HPh), 4.69 (d, 1 H, C*H*HPh), 4.57 (d, 1 H, $J_{1,2}$ 9.3 Hz, H-1), 4.40 (dd, 1 H, $J_{6a,6b}$ 9.9, $J_{6a,5}$ 3.7 Hz, H-6a), 3.92 (t, 1 H, $J_{4,3}=J_{4,5}=8.1$ Hz, H-4), 3.81 (t, 1 H, $J_{3,2}$ 8.1 Hz, H-3), 3.68 (m, 1 H, H-5), 3.62–3.55 (m, 2 H, H-2,6b); ^{13}C NMR (75.46 MHz, $CDCl_3$): δ 101.95 (d, *C*HPh), 96.48 (d, C-1), 83.61, 81.77, 75.94, and 70.71 (4 d, C-2,3,4,5), 75.46 and 74.65 (2 t, 2 *C*H_2Ph), 69.05 (t, C-6); further elution gave the second diastereoisomer as white crystals; mp 148–149 °C; $[\alpha]_D$ −116.7° (*c* 1, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.65–7.20 (m, 20 H, ArH), 5.52 (s, 1 H, C*H*Ph), 5.04 and 4.95 (2 d, 2 H, J_{gem} 10.7 Hz, C*H*$_2$Ph), 4.98 and 4.82 (2 d, 2 H, J_{gem} 11.5 Hz, C*H*$_2$Ph), 4.15 (t, 1 H, $J_{2,3}$ 9.2 Hz, H-2), 4.02 (dd, 1 H, $J_{6a,6b}$ 11.6, $J_{6a,5}$ 4.8 Hz, H-6a), 4.01 (d, 1 H, $J_{1,2}$ 9.8 Hz, H-1), 3.91 (t, 1 H, $J_{3,4}$ 9.2 Hz, H-3), 3.79 (d, 1 H, H-6b), 3.74 (t, 1 H, H-4), 3.28 (m, 1 H, H-5); ^{13}C NMR (75.46 MHz, $CDCl_3$): δ 101.92 (d, *C*HPh), 94.38 (d, C-1), 83.32, 81.83, 76.88, and 71.59 (4 d, C-2,3,4,5), 76.72 and 75.54 (2 t, 2 *C*H_2Ph), 68.70 (t, C-6). Anal. Calcd for $C_{33}H_{32}O_6S$: C, 71.20; H, 5.79. Found: C, 70.85; H, 5.98.

Allyl 3,4-di-O-*benzyl*-α-L-*rhamnopyranoside* (**5**).—3,4-Di-*O*-benzyl-1,2-*O*-(1-methoxyethylidene)-β-L-rhamnopyranose [13] (2.37 g, 5.91 mmol) was dissolved in dry CH_2Cl_2 (45 mL) and powdered 4 Å molecular sieves, allyl alcohol (8.9 mL, 130 mmol) and TMSOTf (244 μL, 1.353 mmol) were added at room temperature. After stirring for 15 min, the mixture was diluted with CH_2Cl_2 and filtered over a Celite pad. The filtrate was successively washed with satd $NaHCO_3$ and water, dried (Na_2SO_4), and concentrated. The residue was purified by flash chromatography (9:1 hexane–EtOAc) to give allyl 2-*O*-acetyl-3,4-di-*O*-benzyl-α-L-rhamnopyranoside, isolated as a syrup (2.44 g, 97%); $[\alpha]_D$ −21.3° (*c* 1, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.40–7.20 (m, 10 H, ArH), 5.81 (m, 1 H, $OCH_2CH=CH_2$), 5.34 (t, 1 H, $J_{2,3}$ 1.6 Hz, H-2), 5.12–5.24 (m, 2 H, $OCH_2CH=CH_2$), 4.86 (d, 1 H, J_{gem} 11.0 Hz, C*H*HPh), 4.72 (d, 1 H, $J_{1,2}$ 1.6 Hz, H-1), 4.65 (d, 1 H, J_{gem} 11.0, C*H*HPh), 4.56 (d, 1 H, C*H*HPh), 4.48 (d, 1 H, C*H*HPh), 4.09 (m, 1 H, OC*H*HCH $=CH_2$), 3.94–3.87 (m, 2 H, OCH*H*CH$=CH_2$ and H-3), 3.72 (m, 1 H, H-5), 3.38 (t, 1 H, $J_{4,3}=J_{4,5}=9.8$ Hz, H-4), 2.10 (s, 3 H, CH_3CO), 1.28 (d, 3 H, $J_{6,5}$ 5.9 Hz, H-6). Anal. Calcd for $C_{25}H_{30}O_6$: C, 70.40; H, 7.09. Found: C, 70.35; H, 6.98.

Allyl glycoside (2.34 g, 5.48 mmol) was dissolved in a solution of NaOH (440 mg, 11.0 mmol) in EtOH (73 mL) and kept for 2 h under stirring at room temperature. The mixture was concentrated to a small volume, then diluted with CH_2Cl_2 (50 mL), washed with aq 5% HCl, satd $NaHCO_3$, and water, dried (Na_2SO_4), and concentrated to afford **5**, isolated as a syrup (1.93 g, 92%); $[\alpha]_D$ −43.6° (*c* 1, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.42–7.28 (m, 10 H, ArH), 5.87 (m, 1 H, $OCH_2CH=CH_2$), 5.29–5.15 (m, 2 H, $OCH_2CH=CH_2$), 4.88 (d, 1 H, J_{gem} 10.9 Hz, C*H*HPh), 4.84 (brd, 1 H, H-1), 4.68 (brs, 2 H, C*H*$_2$Ph), 4.63 (d, 1 H, C*H*HPh), 4.16 (m, 1 H, OC*H*HCH$=CH_2$), 4.05 (brt, 1 H, H-2), 3.96 (m, 1 H, OCH*H*CH$=CH_2$), 3.86 (dd, 1 H, $J_{3,2}$ 3.7 Hz, H-3), 3.74 (m, 1 H, H-5), 3.45 (t, 1 H, $J_{4,3}=J_{4,5}=9.2$ Hz, H-4), 2.48 (d, 1 H, OH), 1.35 (d, 3 H, $J_{6,5}$ 6.0 Hz, H-6); ^{13}C NMR (75.46 MHz, $CDCl_3$): δ 134.46 (d, $OCH_2CH=CH_2$), 117.97 (t, $OCH_2CH=CH_2$), 98.85 (d, C-1), 80.71, 80.62, 69.23, and 68.03 (4 d, C-2,3,4,5), 76.03, 72.67, and 68.48 (3 t, 2 *C*H_2Ph and *C*H_2CH$=CH_2$), 18.52 (q, C-6); Anal. Calcd for $C_{23}H_{28}O_5$: C, 71.85; H, 7.34. Found: C, 72.00; H, 7.25.

Allyl (2,3-di-O-*benzyl-4,6*-O-*benzylidene*-α-D-*glucopyranosyl)-(1→2)-3,4-di*-O-*benzyl*-α-L-*rhamnopyranoside* (**6**).—Compound **4** (1.96 g, 3.53 mmol) was dissolved in 1:1 dry CH_2Cl_2–dry Et_2O containing freshly activated powdered 4 Å molecular sieves. After being cooled at −78 °C, Tf_2O (580 μL, 3.53 mmol) was added with stirring for 30 min, then a solution of **5** (905 mg, 2.353 mmol) and 2,6-di-^{t}butyl-4-methylpyridine (725 mg, 3.53 mmol) in 1:1 CH_2Cl_2–Et_2O (15 mL) was added under N_2 and the mixture was stirred for 5 h at −60 °C. The mixture was filtered through Celite, and the filtrate was washed with satd $NaHCO_3$ and water, dried (Na_2SO_4), and concentrated. The residue was purified by flash chromatography with 8:2

hexane–EtOAc to give **6**, isolated as a syrup (1.61 g, 84%); $[\alpha]_D$ +34.0° (*c* 1, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$): δ 7.60–7.10 (m, 25 H, ArH), 5.86 (m, 1 H, $OCH_2CH=CH_2$), 5.53 (s, 1 H, CHPh), 5.28–5.14 (m, 2 H, $OCH_2CH=CH_2$), 4.95–4.61 (m, 10 H, 4 CH_2Ph and H-1,1′), 4.23 (m, 1 H, H-5′), 4.20–3.85 (m, 6 H, H-2,3,3′,6′a and $OCH_2CH=CH_2$), 3.74 (m, 1 H, H-5), 3.66–3.51 (m, 4 H, H-2′,4,4′,6′b), 1.35 (d, 3 H, $J_{6,5}$ 6.0 Hz, H-6); ^{13}C NMR (75.46 MHz, $CDCl_3$): δ 134.66 (d, $OCH_2CH=CH_2$), 117.70 (t, $OCH_2CH=CH_2$), 101.88 (d, CHPh), 98.56 and 97.31 (2 d, C-1,1′), 83.14, 80.84, 80.15, 79.66, 78.93, 75.89, 69.00, and 63.42 (8 d, C-2,3,4,5,2′,3′,4′,5′), 75.78, 75.65, 73.50, 72.92, 69.71, and 68.44 (6 t, 4 CH_2Ph, C-6′ and $OCH_2CH=CH_2$), 18.63 (q, C-6). Anal. Calcd for $C_{50}H_{54}O_{10}$: C, 73.69; H, 6.68. Found: C, 73.31; H, 6.82.

Allyl (2,3,6-tri-O-*benzyl-α*-D-*glucopyranosyl)-(1→2)-3,4-di*-O-*benzyl-α*-L-*rhamnopyranoside* (**7**).—To a stirred solution of **6** (500 mg, 0.6 mmol) in dry CH_2Cl_2 (20 mL) cooled at 0 °C was added aq 90% CF_3CO_2H. The reaction was complete within 1 h at 0 °C. The reaction was quenched with satd $NaHCO_3$, and the mixture extracted with CH_2Cl_2. The organic phase was washed with satd $NaHCO_3$ and brine, dried (Na_2SO_4), and concentrated. ^1H NMR analysis of the crude residue showed the disappearance of the signal at δ 5.53 corresponding to the benzylidene acetal group. The crude residue, dibutyltin oxide (224 mg, 0.9 mmol) and benzene (60 mL) were placed in a two-necked flask equipped with a Dean–Stark separator. The mixture was boiled under reflux for 3 h, then concentrated to half its initial volume and cooled at 50 °C. Then Bu_4NBr (290 mg, 0.28 mmol) and benzyl bromide (1.8 mmol, 214 μL) were added, and the mixture was stirred for 18 h at 90 °C. After completion, the solvent was evaporated, and the residue was purified by flash chromatography (8:2 hexane–EtOAc) yielding compound **7**, isolated as an oil (392 mg, 80%); $[\alpha]_D$ +13.4° (*c* 1, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$): δ 7.40–7.20 (m, 25 H, ArH), 5.86 (m, 1 H, $OCH_2CH=CH_2$), 5.26–5.13 (m, 2 H, $OCH_2CH=CH_2$), 4.93 (brd, 1 H, H-1′), 4.81 (d, 1 H, $J_{1,2}$ 2.2 Hz, H-1), 4.98–4.52 (m, 8 H, 4 CH_2Ph), 4.45 and 4.36 (2 d, 2 H, J_{gem} 12.2 Hz, CH_2Ph), 4.13 (m, 1 H, $OCHCH=CH_2$), 4.09–4.03 (m, 2 H, H-2,5′), 3.96–3.85 (m, 3 H, H-3,3′ and $OCHCH=CH_2$), 3.72 (dq, 1 H, $J_{5,4}$ 9.2, $J_{5,6}$ 6.1 Hz, H-5), 3.64 (t, 1 H, $J_{4',3'}=J_{4',5'}=9.5$ Hz, H-4′), 3.57 (t, 1 H, $J_{4,3}=J_{4,5}=9.2$ Hz, H-4), 3.54 (dd, 1 H, $J_{2',1'}$ 3.5, $J_{2',3'}$ 9.8 Hz, H-2′), 3.44 (dd, 1 H, $J_{5,6'a}$ 4.1 Hz, H-6′a), 3.36 (dd, 1 H, $J_{6'a,6'b}$ 10.0, $J_{5,6'b}$ 3.1 Hz, H-6′b), 2.30 (brs, 1 H, OH), 1.35 (d, 3 H, $J_{6,5}$ 6.0 Hz, H-6); ^{13}C NMR (75.46 MHz, $CDCl_3$): δ 134.57 (d, $OCH_2CH=CH_2$), 117.74 (t, $OCH_2CH=CH_2$), 96.94 (d, C-1,1′), 81.47, 80.90, 80.25, 79.56, 74.66, 71.43, 70.90, and 68.93 (8 d, C-2,3,4,5,2′,3′,4′,5′), 75.81, 75.63, 74.14, 72.88, 72.52, 69.89, and 68.46 (7 t, 5 CH_2Ph, C-6′, and $OCH_2CH=CH_2$), 18.68 (q, C-6). Anal. Calcd for $C_{50}H_{56}O_{10}$: C, 73.51; H, 6.91. Found: C, 73.12; H, 6.98.

Phenyl 3-O-*benzyl-4,6*-O-*benzylidene-1-thio-β*-D-*glucopyranoside* (**8**).—Compound **2** (5.0 g, 13.87 mmol) was stirred with sodium hydride (1.5 g, 36.5 mmol) in dry Me_2NCHO (50 mL) at room temperature. When the evolution of hydrogen was ceased, anhydrous cupric chloride (2.25 g, 18.26 mmol) was added and the mixture was stirred for 10 min. Then, benzyl bromide (5.0 mL, 41.5 mmol) was added. The reaction was heated for 4 h at 70 °C, then MeOH was added and the mixture was diluted with EtOAc, washed with water, dried (Na_2SO_4), and concentrated. The residue was purified on a short silica gel column (8:2 hexane–EtOAc) affording compound **8** (4.5 g, 72%) as a powder; mp 136–137 °C; $[\alpha]_D$ −46.8° (*c* 1, $CHCl_3$); ^1H NMR (200 MHz, $CDCl_3$): δ 7.57–7.26 (m, 15 H, ArH), 5.57 (s, 1 H, CHPh), 4.95 and 4.78 (2 d, each 1 H, J_{gem} 11.5 Hz, CH_2Ph), 4.64 (d, 1 H, $J_{1,2}$ 9.5 Hz, H-1), 4.39 (dd, 1 H, $J_{6a,5}$ 4.8, $J_{6a,6b}$ 10.4 Hz, H-6a), 3.85–3.61 (m, 4 H, H-2,3,4,6b), 3.53 (m, 1 H, H-5), 2.55 (d, 1 H, OH); ^{13}C NMR (50.29 MHz, $CDCl_3$): δ 101.95 (d, CHPh), 89.20 (d, C-1), 82.36, 81.77, 73.02, and 71.40 (4 d, C-2,3,4,5), 75.40 and 69.27 (2 t, C-6 and CH_2Ph). Anal. Calcd for $C_{26}H_{26}O_5S$: C, 69.31; H, 5.82. Found: C, 69.14; H, 5.98.

Phenyl 2-O-*acetyl-3*-O-*benzyl-4,6*-O-*benzylidene-1-thio-β*-D-*glucopyranoside* (**9**).—To a solution of **8** (2.03 g, 4.5 mmol) in dry CH_2Cl_2 (60 mL) were added dry pyridine (4.5 mL) and Ac_2O (3.0 mL). The mixture was kept for 5 h at room temperature, then diluted with CH_2Cl_2 (50 mL), washed with aq 5% HCl, satd $NaHCO_3$, and water, dried (Na_2SO_4), and concentrated to afford **9** (2.04 g, 93%) as a white solid; mp 177–179 °C; $[\alpha]_D$ +1.4° (*c* 1, $CHCl_3$); ^1H NMR (200 MHz, $CDCl_3$): δ 7.54–7.20 (m, 10 H, ArH), 5.60 (s, 1 H, CHPh), 5.05 (m, 1 H, H-2), 4.88 (d, 1 H, J_{gem} 11.9 Hz, CHHPh), 4.73 (d, 1 H, $J_{1,2}$ 10.6 Hz, H-1), 4.67 (d, 1 H, CHHPh), 4.42 (dd, 1 H, $J_{6a,6b}$ 10.8, $J_{6a,5}$ 5.0 Hz, H-6a), 3.88–3.74 (m, 3 H, H-3,4,6b), 3.57

(m, 1 H, H-5), 2.10 (s, 3 H, CH_3CO); ^{13}C NMR (75.46 MHz, $CDCl_3$): δ 169.19 (s, CO), 101.20 (d, *C*HPh), 86.76 (d, C-1), 81.27, 79.77, 71.39, and 70.49 (4 d, C-2,3,4,5), 74.29 and 68.51 (2 t, C-6 and *C*H_2Ph), 20.91 (q, *C*H_3CO). Anal. Calcd for $C_{28}H_{28}O_6S$: C, 68.27; H, 5.73. Found: C, 68.54; H, 5.92.

Phenyl 2-O-*acetyl-3*-O-*benzyl-4,6*-O-*benzylidene-1-thio-β*-D-*glucopyranoside sulfoxide* (**10**).—This compound was prepared as described for compound **4**. Compound **9** (3.18 g, 6.45 mmol) gave sulfoxide **10** (3.12 g, 95%) as a mixture of diastereoisomers. A small amount (100 mg) was chromatographed (7:3 petroleum ether–EtOAc) to give pure analytical samples. The diastereoisomer with the higher R_f value was obtained as an amorphous mass; $[\alpha]_D$ −11.6° (*c* 1, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$): δ 7.70–7.20 (m, 15 H, ArH), 5.50 (s, 1 H, C*H*Ph), 5.18 (dd, 1 H, $J_{2,3}$ 8.3 Hz, H-2), 4.83 and 4.63 (2 d, each 1 H, J_{gem} 11.8 Hz, CH_2Ph), 4.50 (d, 1 H, $J_{1,2}$ 9.7 Hz, H-1), 4.33 (dd, 1 H, $J_{6a,6b}$ 8.9, $J_{6a,5}$ 2.5 Hz, H-6a), 3.80 (t, 1 H, $J_{3,4}$ 8.3 Hz, H-3), 3.65–3.48 (m, 3 H, H-4,5,6b), 1.90 (s, 3 H, CH_3CO); ^{13}C NMR (75.46 MHz, $CDCl_3$): δ 169.25 (s, CO), 101.32 (d, *C*HPh), 93.30 (d, C-1), 80.72, 79.44, 70.48, and 68.48 (4 d, C-2,3,4,5), 74.35 and 68.06 (2 t, C-6 and *C*H_2Ph), 20.72 (q, CH_3CO). Further elution gave the second diastereoisomer as an amorphous mass; $[\alpha]_D$ −63.2° (*c* 0.5, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$): δ 7.70–7.20 (m, 15 H, ArH), 5.52 (s, 1 H, C*H*Ph), 5.39 (t, 1 H, $J_{2,3}$ 9.0 Hz, H-2), 4.85 and 4.64 (2 d, each 1 H, J_{gem} 12.0 Hz, CH_2Ph), 4.21 (d, 1 H, $J_{1,2}$ 9.0 Hz, H-1), 4.17 (dd, 1 H, $J_{6a,6b}$ 10.6, $J_{6a,5}$ 5.0 Hz, H-6a), 3.83–3.71 (m, 3 H, H-3,4,6b), 3.42 (dt, 1 H, $J_{5,6b} = J_{5,4} = 9.2$ Hz, H-5), 2.00 (s, 3 H, CH_3CO); ^{13}C NMR (75.46 MHz, $CDCl_3$): δ 169.78 (s, CO), 101.24 (d, *C*HPh), 91.39 (d, C-1), 80.62, 79.37, 70.76, and 68.34 (4 d, C-2,3,4,5), 74.10 and 67.97 (2 t, C-6 and *C*H_2Ph), 20.69 (q, CH_3). Anal. Calcd for $C_{28}H_{28}O_7S$: C, 66.13; H, 5.55. Found: C, 65.90; H, 5.71.

Allyl (2-O-*acetyl-3*-O-*benzyl-4,6*-O-*benzylidene-β*-D-*glucopyranosyl)-(1→4)-(2,3,6-tri*-O-*benzyl-α*-D-*glucopyranosyl)-(1→2)-3,4-di*-O-*benzyl-α*-L-*rhamnopyranoside* (**11**).—To a mixture of **10** (1.108 g, 2.179 mmol) in dry 1:1 CH_2Cl_2–Et_2O (15 mL) containing freshly activated powdered 4 Å molecular sieves, cooled at −78 °C, was added Tf_2O (357 μL, 2.179 mmol). After stirring for 30 min, a solution of **7** (1.187 g, 1.452 mmol) and 2,6-di-^{t}butyl-4-methylpyridine (447 mg, 2.179 mmol) in dry 1:1 CH_2Cl_2–Et_2O (27 mL) was added under N_2 and the mixture was stirred for 3 h at −60 °C. Then the mixture was neutralized with satd $NaHCO_3$, diluted with CH_2Cl_2, filtered through Celite, and the filtrate was washed with water, dried (Na_2SO_4), and concentrated. The residue was purified by flash chromatography (95:5 toluene–EtOAc) to afford **11** (1.34 g, 77%) as a powder; mp 122–125 °C; $[\alpha]_D$ +32.8° (*c* 1, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$): δ 7.50–7.11 (m, 35 H, ArH), 5.87 (m, 1 H, $OCH_2CH=CH_2$), 5.45 (s, 1 H, C*H*Ph), 5.26–5.13 (m, 2 H, $OCH_2CH=CH_2$), 4.95–4.56 (m, 15 H, H-1,1′,2″ and 6 CH_2Ph), 4.33 (d, 1 H, $J_{1'',2''}$ 7.9 Hz, H-1″), 4.18–4.09 (m, 3 H, OCH*H*CH=CH_2 and H-6″a,5′), 3.99–3.82 (m, 5 H, H-2,3,3′,6′a and OCH*H*CH=CH_2), 3.78–3.35 (m, 7 H, H-2′,3″,4,4′,4″, 5,6″b), 3.19 (brdd, 1 H, H-6′b), 3.07 (dt, 1 H, $J_{5'',6''a}$ 4.8, $J_{5'',6''b} = J_{5'',4''} = 9.7$ Hz, H-5″), 1.70 (s, 3 H, CH_3CO), 1.35 (d, 3 H, H-6); ^{13}C NMR (75.46 MHz, $CDCl_3$): δ 169.51 (s, CO), 134.57 (d, $OCH_2CH=CH_2$), 117.80 (t, $OCH_2CH=CH_2$), 101.69, 101.35, 100.70, and 98.70 (4 d, C-1,1′,1″ and *C*HPh), 82.30, 80.85, 80.12, 79.70, 79.19, 77.49, 76.75, 73.93, 71.04, 69.00, and 66.54 (11 d, C-2,2′,2″,3,3′,3″,4,4′,4″,5,5′,5″), 75.82, 75.66, 74.54, 74.15, 73.41, 72.61, 69.29, 68.35, and 67.80 (9 t, C-6′,6″, 6 *C*H_2Ph, and O*C*H_2CH=CH_2), 21.28 (q, *C*H_3CO), 18.62 (q, C-6). Anal. Calcd for $C_{72}H_{78}O_{16}$: C, 72.10; H, 6.55. Found: C, 72.31; H, 6.39.

Allyl (3-O-*benzyl-4,6*-O-*benzylidene-β*-D-*glucopyranosyl)-(1→4)-(2,3,6-tri*-O-*benzyl-α*-D-*glucopyranosyl)-(1→2)-3,4-di*-O-*benzyl-α*-L-*rhamnopyranoside* (**12**).—Compound **11** (846 mg, 0.705 mmol) was dissolved in dry MeOH (40 mL) and treated with a catalytic amount of NaOMe, then stirred overnight at room temperature. The mixture was concentrated, diluted with CH_2Cl_2 and washed with aq 5% HCl, satd $NaHCO_3$, and water. The organic layer was dried (Na_2SO_4) and concentrated. Flash chromatography of the residue (8:2 hexane–EtOAc) gave **12** as an amorphous mass (800 mg, 98%); $[\alpha]_D$ +41.8° (*c* 1, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$): δ 7.50–7.20 (m, 35 H, ArH), 5.87 (m, 1 H, $OCH_2CH=CH_2$), 5.45 (s, 1 H, C*H*Ph), 5.27–5.14 (m, 2 H, $OCH_2CH=CH_2$), 4.92–4.49 (m, 14 H, H-1,1′,1″, 5 CH_2Ph and CHHPh), 4.31 (d, 1 H, J_{gem} 12.1 Hz, CH*H*Ph), 4.16–3.85 (m, 8 H, H-2,3,3′,5′,6′a,6″a and O*C*H_2CH=CH_2), 3.76–3.40 (m, 8 H, H-2′,2″, 3″,4,4′,4″,5,6″b), 3.26 (brd, 1 H, H-6′b), 3.05 (dt, 1 H, $J_{5'',6''a}$ 4.8, $J_{5'',6''b} = J_{5'',4''} = 9.6$ Hz, H-5″), 2.95 (d, 1 H, *J* 1.5 Hz, OH), 1.35 (d, 3 H, $J_{6,5}$ 6.0 Hz, H-6); ^{13}C NMR (75.46 MHz, $CDCl_3$): δ 134.67 (d,

$CH_2CH=CH_2$), 117.84 (t, $OCH_2CH=CH_2$), 104.50, 101.90, 97.33, and 97.22 (4 d, *C*HPh and C-1,1′,1″), 81.92, 81.09, 80.46, 79.83, 77.99, 76.23, 75.38, 70.71, and 67.03 (9 d, C-2,2′,2″,3,3′,3″, 4,4′,4″,5,5′,5″), 75.92, 75.51, 75.16, 74.31, 73.37, 72.79, 69.43, and 68.52 (8 t, C-6′,6″, 6 CH_2Ph, and $OCH_2CH=CH_2$), 18.72 (q, C-6). Anal. Calcd for $C_{70}H_{76}O_{15}$: C, 72.65; H, 6.62. Found: C, 72.48; H, 6.83.

Allyl (3-O-*benzyl-2*-O-*(*N-*imidazolyl-sulfonyl)-4,6*-O-*benzylidene-β*-D-*glucopyranosyl)-(1→4)-(2,3,6-tri*-O-*benzyl-α*-D-*glucopyranosyl)-(1→2)-3,4-di*-O-*benzyl-α*-L-*rhamnopyranoside* (**13**).—A mixture of **12** (152 mg, 0.131 mmol) and 60% NaH in oil (32 mg, 0.8 mmol) in dry Me_2NCHO (10 mL) was stirred for 1 h, then cooled at −40 °C. Sulfonyldiimidazole (266 mg, 134 mmol) was added, and the stirring was continued for 5 h at −40 °C. The reaction was quenched with MeOH, then the mixture was extracted with CH_2Cl_2, and the organic layer was washed with water, dried (Na_2SO_4), and concentrated. The residue was purified by flash chromatography (8:2 hexane–EtOAc) to give **13** (168 mg, 99%); $[\alpha]_D$ +28.0° (*c* 1, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.80 (s, 1 H, H-a imidazole), 7.50–7.10 (m, 35 H, ArH), 7.07 and 7.00 (2 s, each 1 H, H-b,c imidazole), 5.87 (m, 1 H, $OCH_2CH=CH_2$), 5.43 (s, 1 H, C*H*Ph), 5.27–5.15 (m, 2 H, $OCH_2CH=CH_2$), 5.00 (d, 1 H, J_{gem} 11.2 Hz, C*H*HPh), 4.90–4.59 (m, 13 H, H-1,1′,1″ and 5 CH_2Ph), 4.50 (d, 1 H, J_{gem} 11.4 Hz, CH*H*Ph), 4.36 (t, 1 H, $J_{2'',3''}=J_{2'',1''}=8.3$ Hz, H-2″), 4.26–3.30 (m, 15 H, H-2,2′,3,3′,3″,4,4′,4″,5,5′,6′a,6″a,6″b and $OCH_2CH=CH_2$), 3.25 (brdd, 1 H, H-6′b), 2.96 (m, 1 H, H-5″), 1.35 (d, 3 H, H-6); ^{13}C NMR (75.46 MHz, $CDCl_3$): δ 134.57 (d, $OCH_2CH=CH_2$), 117.74 (t, $OCH_2CH=CH_2$), 102.02 (d, *C*HPh), 99.10, 98.90, and 97.81 (3 d, C-1,1′,1″), 85.58, 82.57, 81.14, 79.84, 77.52, 77.32, 76.41, 70.29, and 66.35 (9 d, C-2,2′,2″,3,3′,3″,4,4′,4″, 5,5′,5″), 75.78, 74.84, 74.13, 73.50, 72.77, 68.34, and 67.96 (7 t, C-6′,6″, 6 CH_2Ph, and $OCH_2CH=CH_2$), 18.63 (q, C-6). Anal. Calcd for $C_{73}H_{78}N_2O_{17}S$: C, 68.04; H, 6.05; N, 2.17; S, 2.48. Found: C, 68.32; H, 6.13, N, 2.01; S, 2.25.

Allyl (2-azido-3-O-*benzyl-4,6*-O-*benzylidene-2-deoxy-β*-D-*mannopyranosyl)-(1→4)-(2,3,6-tri*-O-*benzyl-α*-D-*glucopyranosyl)-(1→2)-3,4-di*-O-*benzyl-α*-L-*rhamnopyranoside* (**14**).—To a stirred solution of **13** (700 mg, 0.54 mmol) in dry toluene (80 mL) under N_2, was added 0.42 M Bu_4NN_3 in dry toluene (6.6 mL, 0.138 mmol). The mixture was boiled under reflux for 3 h at 130 °C using a Dean–Stark apparatus, then cooled at room temperature, diluted with water and extracted with CH_2Cl_2. The extract was washed with water, dried (Na_2SO_4), and concentrated. Flash chromatography of the residue (8:2 hexane–EtOAc) gave **14** as a glass (620 mg, 97%); $[\alpha]_D$ +21.8° (*c* 1, $CHCl_3$); IR (KBr): υ 2110 ($N=N^+=N^-$); ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.50–7.10 (m, 35 H, ArH), 5.86 (m, 1 H, $OCH_2=CHCH_2$), 5.40 (s, 1 H, C*H*Ph), 5.28–5.15 (m, 2 H, $OCH_2CH=CH_2$), 5.01–4.51 (m, 14 H, H-1,1′ and 6 CH_2Ph), 4.39 (brs, 1 H, H-1″), 4.18–3.48 (m, 13 H, H-2,2′,2″,3,3′,4,4′,4″,5′,6″a,6″b and $OCH_2CH=CH_2$), 3.73 (dq, 1 H, $J_{5,6}$ 6.0, $J_{5,4}$ 9.1 Hz, H-5), 3.31 (dd, 1 H, $J_{3'',2''}$ 3.6, $J_{3'',4''}$ 9.5 Hz, H-3″), 3.15 and 3.08 (2 brd, each 1 H, $J_{6'a,6'b}$ 10.7 Hz, H-6′a,6′b), 2.93 (dt, 1 H, $J_{5'',6''a}=J_{5'',4''}=9.5$, $J_{5'',6''b}$ 4.6 Hz, H-5″), 1.35 (d, 3 H, H-6); ^{13}C NMR (75.46 MHz, $CDCl_3$): δ 134.50 (d, $OCH_2=CHCH_2$), 117.84 (t, $OCH_2CH=CH_2$), 102.07 (d, *C*HPh), 100.93, 97.54, and 97.17 (3 d, C-1,1′,1″), 80.93, 80.55, 79.94, 79.83, 79.09, 77.93, 77.05, 75.48, 70.13, 67.71, and 64.11 (11 d, C-2,2′,2″,3,3′,3″,4,4′,4″,5,5′,5″), 75.97, 75.62, 74.07, 73.31, 73.19, 72.73, 69.05, 68.53, and 68.36 (9 t, C-6,6′, $OCH_2CH=CH_2$, and 6 CH_2Ph), 18.55 (q, C-6). Anal. Calcd for $C_{70}H_{75}N_3O_{14}$: C, 71.11; H, 6.39; N, 3.55. Found: C, 71.23; H, 6.54; N, 3.71.

Allyl (2-acetamido-3-O-*benzyl-4,6*-O-*benzylidene-2-deoxy-β*-D-*mannopyranosyl)-(1→4)-(2,3,6-tri*-O-*benzyl-α*-D-*glucopyranosyl)-(1→2)-3,4-di*-O-*benzyl-α*-L-*rhamnopyranoside* (**1**).—A mixture of **14** (1.5 g, 1.2 mmol) and zinc (5.0 g) activated with aq 2% $CuSO_4$ in 6:4:2 THF–Ac_2O–HOAc (48 mL) was stirred for 2 h at 35 °C. After dilution with EtOAc and filtration through Celite, the solution was washed with satd $NaHCO_3$ and water, dried (Na_2SO_4), and concentrated. The residue was purified by flash chromatography (7:3 hexane–EtOAc) to give **1** isolated as a glass (1.2 g, 84%); $[\alpha]_D$ +14.4° (*c* 0.7, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.55–7.15 (m, 35 H, ArH), 5.85 (m, 1 H, $OCH_2CH=CH_2$), 5.50 (d, 1 H, *J* 9.5 Hz, NH), 5.46 (s, 1 H, C*H*Ph), 5.27–5.14 (m, 2 H, $OCH_2CH=CH_2$), 4.99–4.45 (m, 14 H, H-1,1′,1″, 5 CH_2Ph, and C*H*HPh), 4.24 (d, 1 H, J_{gem} 12.0 Hz, CH*H*Ph), 4.18–3.47 (m, 13 H, H-2,2′,2″,3,3′,4,4′,4″,5′,6″a,6″b and $OCH_2CH=CH_2$), 3.73 (dq, 1 H, $J_{5,6}$ 6.0, $J_{5,4}$ 9.1 Hz, H-5), 3.35–3.29 (m, 2 H, H-6′a,3″), 3.19 (brd, 1 H, $J_{6'a,6'b}$ 10.8 Hz, H-6′b), 3.05 (dt, 1 H, $J_{5'',6''a}=J_{5'',4''}=9.5$, $J_{5'',6''b}$ 4.7 Hz, H-5″), 1.75 (s, 3 H, CH_3CO), 1.35 (d, 3 H, H-6); ^{13}C NMR

(75.46 MHz, $CDCl_3$): δ 171.00 (s, CO), 134.54 (d, $OCH_2CH=CH_2$), 117.95 (t, $OCH_2CH=CH_2$), 102.33 (d, *C*HPh), 100.34, 97.82, and 97.36 (3 d, C-1,1′,1″), 80.95, 80.24, 79.70, 79.24, 76.60, 76.36, 70.54, 69.03, and 67.80 (9 d, C-2,2′,3,3′,3″, 4,4′,4″,5,5′,5″), 75.39, 74.11, 73.54, 72.87, 71.88, 69.35, and 68.53 (7 t, C-6′,6″, 6 CH_2Ph and $OCH_2CH=CH_2$), 51.14 (d, C-2″), 23.84 (q, CH_3CO), 18.66 (q, C-6). Anal. Calcd for $C_{72}H_{79}NO_{15}$: C, 72.16; H, 6.64; N, 1.17. Found: C, 72.24; H, 6.84; N, 1.30.

Allyl (2-acetamido-3,6-di-O-*benzyl-2-deoxy-β*-D-*mannopyranosyl)-(1→4)-(2,3,6-tri*-O-*benzyl-α*-D-*glucopyranosyl)-(1→2)-3,4-di*-O-*benzyl-α*-L-*rhamnopyranoside* (**15**).—To a stirred solution of **1** (33 mg, 0.027 mmol) in dry CH_3CN (5 mL) was added $BH_3{\cdot}Me_3N$ (15 mg, 0.2 mmol). The reaction was cooled at 0 °C, then freshly distilled $BF_3{\cdot}Et_2O$ (60 μL) was added under N_2. The reaction was completed within 30 min, and the mixture was concentrated, diluted with CH_2Cl_2 (10 mL), washed with satd $NaHCO_3$ and water, and concentrated. The residue was purified on a short silica-gel column (7:4 petroleum ether–EtOAc) affording trisaccharide **15** isolated as a glass (27 mg, 82%); $[\alpha]_D$ +2.8° (*c* 2.5, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.50–7.15 (m, 35 H, ArH), 5.86 (m, 1 H, $OCH_2CH=CH_2$), 5.59 (d, 1 H, *J* 9.6 Hz, NH), 5.26–5.13 (m, 2 H, $OCH_2CH=CH_2$), 4.96–4.48 (m, 16 H, H-1,1′,1″,2″, 2 C*H*HPh, and 5 CH_2Ph), 4.37 (d, 1 H, J_{gem} 11.9 Hz, CH*H*Ph), 4.24 (d, 1 H, J_{gem} 11.1 Hz, CH*H*Ph), 4.16–3.85 (m, 7 H, H-2,3,3′,4′,5′ and $OCH_2CH=CH_2$), 3.72 (dq, 1 H, $J_{5,6}$ 6.0 Hz, H-5), 3.60 (t, 1 H, $J_{4,5}=J_{4,3}=9.3$ Hz, H-4), 3.56–3.50 (m, 4 H, H-2′,4″,6″a,6″b), 3.40 (dd, 1 H, $J_{6'a,5'}$ 2.1, $J_{6'a,6'b}$ 11.1 Hz, H-6′a), 3.27 (brd, 1 H, H-6′b), 3.15–3.07 (m, 2 H, H-3″,5″), 2.40 (brs, 1 H, OH), 1.75 (s, 3 H, CH_3CONH), 1.35 (d, 3 H, H-6); ^{13}C NMR (75.46 MHz, $CDCl_3$): δ 170.40 (s, CO), 139.91 (d, $OCH_2CH=CH_2$), 117.15 (t, $OCH_2CH=CH_2$), 99.77, 96.92, and 96.58, (3 d, C-1,1′,1″), 80.64, 80.24, 79.67, 79.01, 75.83, 75.02, 69.77, 68.32, and 67.35 (9 d, C-2,2′,3,3′,3″, 4,4′,4″,5,5′,5″), 75.27, 74.73, 73.53, 73.18, 72.62, 72.05, 70.99, 69.28, 68.20, and 67.76 (10 t, C-6′,6″, $OCH_2CH=CH_2$, and 7 CH_2Ph), 49.37 (d, C-2″), 23.14 and 18.01 (2 q, CH_3CO and C-6). Anal. Calcd for $C_{72}H_{81}NO_{15}$: C, 72.04; H, 6.80; N, 1.17. Found: C, 72.21; H, 6.64; N, 1.22.

(2-Acetamido-3-O-*benzyl-4,6*-O-*benzylidene-2-deoxy-β*-D-*mannopyranosyl)-(1→4)-(2,3,6-tri*-O-*benzyl-α*-D-*glucopyranosyl)-(1→2)-3,4-di*-O-*benzyl-α,β*-L-*rhamnopyranose* (**16**).—To a solution of **1** (30 mg, 0.025 mmol) in dry THF (5 mL) was added a catalytic amount of 1,5-cyclooctadiene-bis-[methyldiphenylphosphine]iridium hexafluorophosphate. The stirred solution was degassed by freezing the solvent and allowing it to warm to room temperature under vacuum and then placed under H_2 to activate the catalyst (the slightly red suspension became pale yellow). After 2 min, the solution was degassed once more and stirred at room temperature under N_2. After 2 h, TLC analysis showed a complete conversion of the allyl ether into the 1-propenyl ether. The hydrolysis was accomplished by adding water (2 mL) and I_2 (5 mg), and stirring the mixture for 5 min at room temperature. The mixture was diluted with water and extracted with CH_2Cl_2. The excess of iodine was destroyed by washing the organic phase with freshly prepared aq 5% $NaHSO_3$. After drying (Na_2SO_4) and concentration, the residue was purified by flash chromatography (7:3 petroleum ether–EtOAc) to give **16** (28 mg, 96%) as an oil (α,β mixture); $[\alpha]_D$ +3.0° (*c* 2.5, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$), major anomer: δ 7.60–7.00 (m, 35 H, ArH), 5.80 (d, 1 H, *J* 12.9 Hz, OH), 5.47 (s, 1 H, C*H*Ph), 5.43 (d, 1 H, *J* 9.7 Hz, NH), 5.02–4.42 (m, 16 H, H-1,1′,1″,2″ and 6 CH_2Ph), 4.12 (dd, 1 H, $J_{6''a,6''b}$ 10.7, $J_{6''a,5''}$ 4.7 Hz, H-6″a), 4.08–3.85 (m, 4 H, H-2,3′,4′,6″b), 3.64–3.32 (m, 7 H, H-3,4,5,2′,5′,4″,6′a), 3.28 (dd, 1 H, $J_{3'',2''}$ 4.3, $J_{3'',4''}$ 9.8 Hz, H-3″), 3.09–3.01 (m, 2 H, H-6′b,5″), 1.80 (s, 3 H, CH_3CO), 1.45 (d, 3 H, $J_{6,5}$ 6.0 Hz, H-6); ^{13}C NMR (75.46 MHz, $CDCl_3$), major anomer: δ 170.45 (s, CO), 102.47, 101.70, 99.41, and 93.96 (4 d, *C*HPh and C-1,1′,1″), 81.51, 81.27, 81.11, 79.78, 78.83, 78.51, 75.84, 71.44, 70.47, 67.17, and 50.53 (11 d, C-2,2′,2″, 3,3′,3″,4,4′,4″,5,5′,5″), 74.86, 74.46, 73.39, 71.67, 71.08, 68.63, and 67.52 (7 t, C-6′,6″ and 6 CH_2Ph), 23.21 and 18.07 (2 q, CH_3CO and C-6). Anal. Calcd for $C_{69}H_{75}NO_{15}$: C, 71.55; H, 6.53; N, 1.21. Found: C, 71.82; H, 6.78; N, 1.42.

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