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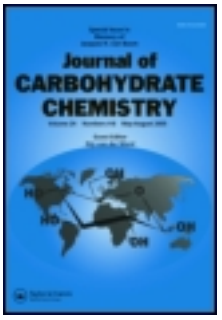

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Synthesis of a Neolactotetraose Glycoside Suitable for Enzymatic Elaboration to the Sialyl Lewis X Stage

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SYNTHESIS OF A NEOLACTOTETRAOSE GLYCOSIDE SUITABLE FOR ENZYMATIC ELABORATION TO THE SIALYL LEWIS X STAGE

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ABSTRACT

A tetrasaccharide glycoside comprising the core of the sialyl Lewis X structure was synthesized from "building-block" derivatives of the component sugar units. Initially 2-methyl-(3,4,6-tri-*O*-acetyl-1,2-dideoxy-α-D-glucopyrano)-[2',1':4,5]-2-oxazoline (**1**) was coupled to the known 2-(trimethylsilyl) ethyl 2,3,6,2',4',6'-hexa-*O*-benzyl-β-D-lactoside to give a trisaccharide glycoside (**3**) in 60% yield. De-*O*-acetylation, benzylidenation, benzylation, and reductive opening of the benzylidene acetal function of **6** gave a derivative having OH-4" open. This derivative was coupled with tetra-*O*-acetyl-α-D-galactosyl bromide to give a tetrasaccharide in 62% yield, and the product was de-*O*-acetylated and de-*O*-benzylated to give the target compound, 2-(trimethylsilyl)ethyl β-D-galactopyranosyl-(1→4)-2-acetamido-2-deoxy-β-D-glucopyranosyl-(1→3)-β-D-galactopyranosyl-(1→4)-β-D-glucopyranoside (**11**).

INTRODUCTION

The interaction of the hexasaccharide moiety of sialyl Lewis X ganglioside with the selectins, a family of glycoproteins involved in the recruitment of leukocytes to activated vascular endothelium,[1] is currently of intense medicinal chemical

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interest.[2-5] Recruitment by adhesion is an early step in pathophysiological phenomena such as thrombosis and leukocyte extravasation leading to inflammation.[6,7] Modulation of these and other cell-cell adhesion processes is thought to have broad therapeutic potential.

Chemical syntheses of the sialyl Lewis X ganglioside and related compounds have been described,[8-14] but these syntheses are laborious because of the complexity of the structure, and the necessity of incorporating sialic acid in a glycosidic linkage.[15,16] However, enzymatic glycosylation catalyzed by a sialyltransferase[17,18] is a viable alternative to the chemical construction[19-22] of this linkage, given the availability of a suitable acceptor substrate. We now describe a straightforward synthesis of 2-(trimethylsilyl)ethyl neolactotetraoside (**11**), a versatile intermediate for further elaboration by enzymatic sialylation and fucosylation.

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RESULTS AND DISCUSSION

The reaction sequence used for the preparation of the tetrasaccharide glycoside **11** is shown in the Scheme. Compound **11** was sequentially assembled from the four carbohydrate building blocks **1**,**2**,**7** and **8** by alternate coupling and partial deblocking reactions, with complete deblocking as the final step. In all the intermediates the benzyl ether group was used as the persistent protecting group and the acetyl group as the temporary protecting group.

2-(Trimethylsilyl)ethyl 2,4,6-tri-*O*-benzyl-β-D-galactopyranosyl-(1→4)-2,3,6-tri-*O*-benzyl-β-D-glucopyranoside (**2**) was chosen as the precursor of the reducing end segment of **11**. Lactoside **2**, earlier reported from Hasegawa's laboratory but not fully characterized,[23] has a hydroxyl group open for chain extension at position 3'. As the glucosaminyl donor in the initial coupling, we utilized 2-methyl (3,4,6-tri-*O*-acetyl-1,2-dideoxy-α-D-glucopyrano)-[2',1':4,5]-2-oxazoline[24] (**1**). The use of this donor instead of the corresponding *N*-phthaloylglucosyl bromide eliminates the need for the eventual replacement of the *N*-protecting group, which often proceeds with some difficulty. The reaction of **1** and **2** under conditions previously described by Nashed *et al.*[25] furnished the trisaccharide glycoside **3** in good yield. The ^{13}C NMR spectrum of **3** showed signals characteristic of both the donor and the acceptor

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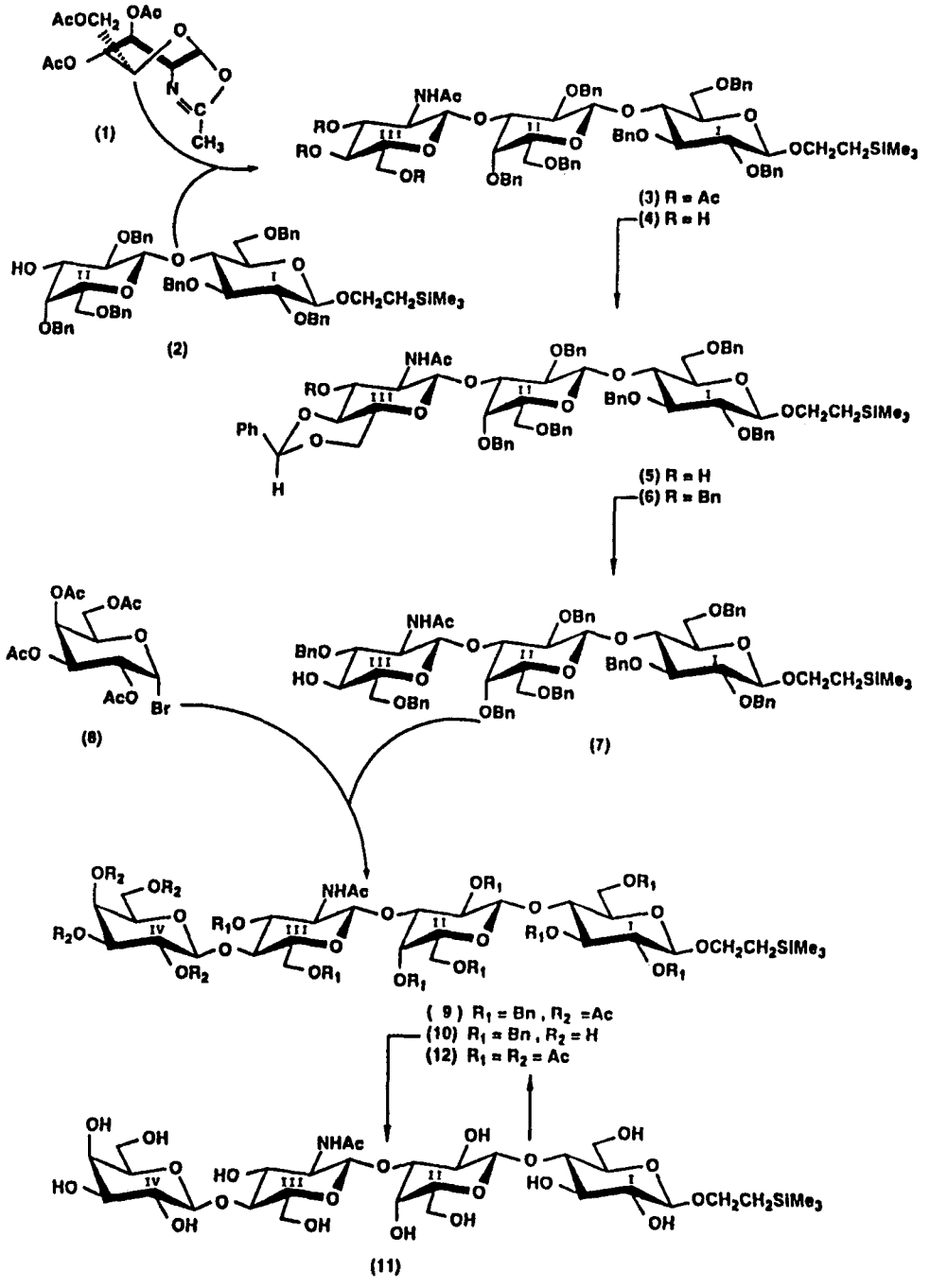

Scheme

moieties. These included signals at δ 171.35 (amide *C*O), 169.15-169.85(3 ester *C*O), and 102.01, 102.47, and 103.00 ppm. A signal at δ 22.60 was assigned to the *C*H_3 of the *N*-acetyl group, and one at δ 20.50 to three *O*-acetyl methyl carbons.

De-*O*-acetylation of **3** with sodium methoxide afforded 2-(trimethylsilyl)ethyl-2-acetamido-2-deoxy-β-D-glucopyranosyl-(1→3)-2,4,6-tri-*O*-benzyl-β-D-galactopyranosyl-(1→4)-2,3,6-tri-*O*-benzyl-β-D-glucopyranoside (**4**)[23] in almost quantitative yield. The ^{13}C NMR spectrum of **4** was similar to that of **3**, but it lacked the signals for *O*-acetyl carbonyl and *O*-acetyl methyl carbons.

Compound **4** was used for the preparation of the trisaccharide acceptor **7** needed for the final coupling reaction. Treatment of **4** with benzaldehyde dimethyl acetal in DMF in the presence of *p*-toluenesulfonic acid monohydrate gave the 4,6-*O*-benzylidene derivative (**5**)[23] in excellent yield. The NMR data included new signals at δ_H 5.44 and δ_c 101.54, attributable to the arylmethine group (Ph*CH*).

Benzylation of the benzylidene derivative (**5**) with benzyl bromide in the presence of barium oxide and barium hydroxide octahydrate, according to the directions of Harrison and Fletcher,[26] yielded the fully protected trisaccharide (**6**), which on reductive ring-opening of the benzylidene group with sodium cyanoborohydride-hydrogen chloride in THF,[27] afforded **7** in 72% yield. The ^{13}C NMR spectrum was similar to that of compound **5** except for the disappearance of one singlet at δ 101.54 due to (Ph*C*H), and appearance of new signals at δ 73.60 and 73.64 attributable to the methylene carbons of the two newly added benzyl groups.

Proceeding to the addition of the fourth sugar unit, galactosyl bromide **8** was coupled to **7** under modified Koenigs-Knorr conditions to afford the tetrasaccharide **9**. Compound **9** carried only benzyl ether and acetyl ester protecting groups and hence could be deblocked in two operations. First, Zemplen de-*O*-acetylation gave the tetraol derivative (**10**) in quantitative yield. Second, catalytic hydrogenolysis (Pd-C) in MeOH gave the unprotected neolactotetraoside (**11**) in very good yield (78%). The ^{13}C NMR spectrum showed the resolution of the four anomeric carbons at δ 103.85, 105.22, 105.33, 105.39 and the disappearance of the signals due to the benzyl carbons, and the acetyl carbons.

For further characterization **11** was acetylated, and a 750 MHz NMR spectrum of the dodeca-*O*-acetyl (**12**) was recorded. The δ 4.3-5.5 region (Fig. 1)

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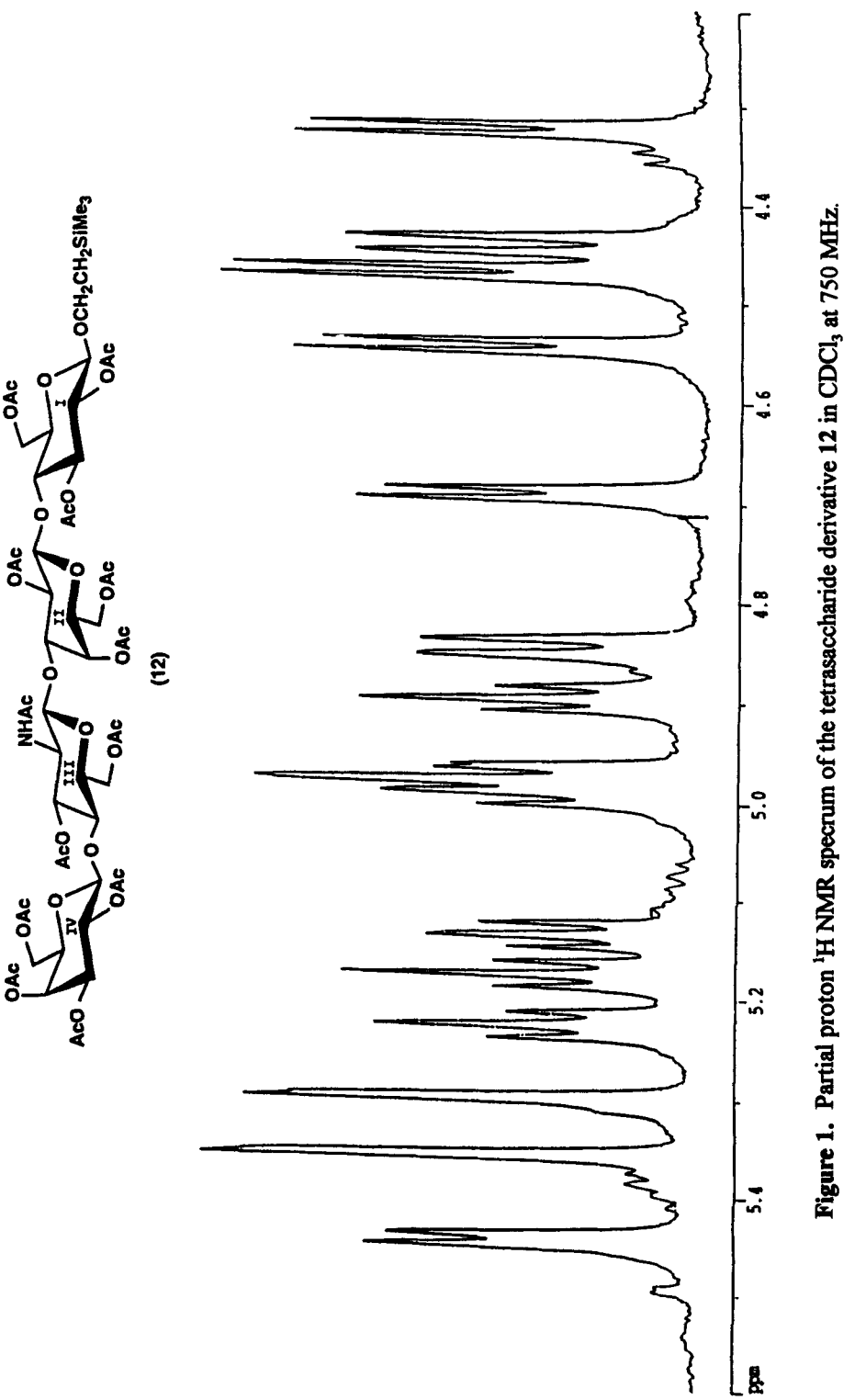

Figure 1. Partial proton ^{1}H NMR specrum of the tetrasaccharide derivative **12** in $CDCl_3$ at 750 MHz.

showed the down field shifted proton signals required by the proposed structure. The anomeric protons gave rise to four doublets having J values (8.1-8.0 Hz), characteristic of β-glycosidic linkages. The remaining signals, arising from methine protons geminal to acetoxy groups, comprised five triplets having J ~ 9.8 Hz (H-2^{I}, 3^{I}, 2^{II}, 3^{III}, and 2^{IV}), one doublet of doublets with J 11.2 Hz and 2.9 Hz (H-3^{IV}), and two doublets having the small J values (~2.8 Hz) characteristic of H-4 of galactose (H-4^{II}, 4^{IV}). The numerical data are listed in the experimental section.

EXPERIMENTAL

General method. Optical rotations were determined at 22 °C with a Perkin-Elmer Model 241 polarimeter. ^{1}H NMR spectra were recorded at Glycomed, Inc. Alameda, California with a Varian Gemini 300 MHz spectrometer, and Department of Biochemistry, University of Wisconsin-Madison at 750 MHz (Bruker DMX 750) spectrometer at ambient temperature. ^{13}C NMR spectra were recorded with a Varian Gemini 300 MHz instrument operating at 75.50 MHz. Chemical shifts are referenced to $CDCl_3$(δ 77.00 ppm) or internal acetone (δ 30.50 ppm). The assignment of ^{13}C peaks was supported by the attached proton test experiments (APT), and by carbon-proton shift correlation experiments. The following common signals for the 2-(trimethylsilyl)ethyl aglycon were observed in $CDCl_3$ solution; ^{1}H NMR: δ 0.05 [s,9H,Si(CH_3)$_3$], 1.05 (dt, 2H, Me_3SiCH_2); ^{13}C NMR: δ 0.10 [Si(CH_3)$_3$], 18.15 [CH_2Si(CH_3)$_3$], 68.38 [OCH_2CH_2Si(CH_3)$_3$]. Liquid secondary ion mass spectrometry (LSIMS) was performed on a Finnigan MATTSQ-70, triple-stage quadrupole mass spectrometer equipped with an Antek cesium ion gun. Glycerol or 3-nitrobenzyl alcohol (*m*-NBA, Aldrich) was employed as the sample matrix. Separations were accomplished by open-column chromatography on Merck silica gel 60 (70-230 mesh). TLC was performed on silica gel plates (250 μm, Merck). The following solvent combinations (v/v) were utilized for thin-layer and column chromatography: A, 19.5:0.5 $CHCl_3$-MeOH; B, 19:1 $CHCl_3$-MeOH; C, $CHCl_3$; D, 18.5:1.5 $CHCl_3$-MeOH; E, 3:3:1 EtOAc-2-propanol-H_2O. Elemental analyses were performed at the Galbraith Laboratories, Inc., Knoxville, TN 37821.

2-(Trimethylsilyl)ethyl 2-Acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-β-D-glucopyranosyl-(1→3)-2,4,6-tri-*O*-benzyl-β-D-galactopyranosyl-(1→4)-2,3,6-tri-*O*-benzyl-

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β-D-glucopyranoside (3). Compound **2** was prepared according to Hasegawa *et al.*[23]: ^{1}H NMR ($CDCl_3$) δ 2.18 (bd, 1H, D_2O-exchangeable, O*H*-3'), 3.30-5.05 (m, 28H, PhCH_2, OCH_2, sugar C*H*, and CH_2), 7.10-7.33 (m, 30H, 6 Ph); ^{13}C NMR ($CDCl_3$) δ 67.35, 67.89 (C-6^I, 6^{II}), 73.09, 73.32, 74.93, 75.06, 75.31, (6 PhCH_2), 73.14, 74.07, 75.13, 75.86, 76.86, 80.60, 81.87, 82.92, (8 *C*H of sugar), and 102.69, 103.13 (C-1^I, 1^{II}).

A mixture of compound **2** (2.0 g, 2.0 mmol), the oxazoline derivative **1** (1.4 g, 4.2 mmol), *p*-toluenesulfonic acid (30 mg), and powdered 4Å activated molecular sieves (1g) in a round-bottomed flask was equipped with a magnetic bar dried under vacuum for 4-6 h, then dry 1,2-dichloroethane (15 mL) was added. The reaction mixture was stirred at 80 °C until TLC (solvent A) showed complete reaction. The reaction mixture was diluted with CH_2Cl_2, filtered, and the filtrate was washed with $NaHCO_3$ solution, and water. The organic layer was dried over anhydrous sodium sulphate, and concentrated to dryness under reduced pressure. Chromatography (solvent A) of the residue on a column of silica gel afforded (1.6 g, 60%) of **3**: $[\alpha]_D$ -13.4°, $[\alpha]_{578}$ -13.6°, $[\alpha]_{546}$ -15.1°, $[\alpha]_{436}$ -26.0°, $[\alpha]_{365}$ -40.8° (*c* 1.06, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 1.45 (s, 3H, NHCOCH_3), 1.95, 2.05 (2s, 9H, 3 COCH_3), 3.28-5.10 (m, 35H, PhCH_2, OCH_2, sugar C*H* and CH_2), and 7.10-7.45 (m, 31H, N*H*CO, 6 Ph); ^{13}C NMR ($CDCl_3$) δ 20.50 (3 COCH_3), 22.60 (NHCOCH_3), 54.25 (C-2^{III}), 67.20, 68.00, 68.14 (C-6^I, 6^{II}, 6^{III}), 73.11, 73.22, 74.26, 74.74, 74.83, 75.28 (6 PhCH_2), 68.50, 71.58, 72.72, 73.15, 74.97, 75.93, 76.50, 79.84, 81.72, 81.97, 82.74 (11 *C*H of sugar), 102.01, 102.47, 103.00 (C-1^I, 1^{II}, 1^{III}), 126.10-128.60 (aromatic carbons), 138.10-139.10 (6 aromatic carbons), 169.15-169.85 (3 *C*OCH_3), and 171.35 (NH*C*O); positive-ion LSIMS: *m/z* 1335.2 $(M+Na)^+$, 1244.3 $(M+Na - PhCH_2)^+$, 762.1 (M - reducing moiety).

Anal. Calcd for $C_{73}H_{89}NO_{19}Si$ (1312.59): C, 66.80; H, 6.83; N, 1.07. Found: C, 67.15; H, 6.73; N, 1.12.

2-(Trimethylsilyl)ethyl 2-Acetamido-2-deoxy-β-D-glucopyranosyl-(1→3)-2,4,6-tri-*O*-benzyl-β-D-galactopyranosyl-(1→4)-2,3,6-tri-*O*-benzyl-β-D-glucopyranoside(4). A solution of compound **3** (2.0 g, 1.52 mmol) in MeOH (15 mL) was stirred with methanolic M sodium methoxide (3 mL) for 2 h at room temperature, whereupon results from TLC (solvent B) indicated that the reaction was complete. The reaction

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mixture was neutralized with Amberlite IR-120 (H^+) resin and concentrated to give the pure title compound **4** as a syrup in almost quantitative yield: $[\alpha]_D$ -8.1°(*c* 0.50, CH_2Cl_2), lit.[23] $[\alpha]_D$ -7.3°; ^1H NMR ($CDCl_3$) δ 1.45 (s, 3H, NHCOC*H*$_3$), 2.30 (bs, 2H, D_2O-exchangeable, 2O*H*), 3.20-5.00 (m, 35H, PhC*H*$_2$, OC*H*$_2$, sugar C*H* and C*H*$_2$), 5.50 (bs, 1H, D_2O-exchangeable, O*H*), 5.82 (d, 1H, J=6.9 Hz, D_2O-exchangeable, N*H*CO), and 7.10-7.39 (m, 30H, 6 Ph); ^{13}C NMR ($CDCl_3$) δ 22.64 (NHCOC*H*$_3$), 57.38 (C-2^{III}) 62.03 (OC*H*$_2$), 67.31, 68.00, 68.13 (C-6^I, 6^{II}, 6^{III}), 73.22, 73.32, 74.20, 74.73, 74.93, 75.39 (6 PhC*H*$_2$), 70.84, 73.11, 74.98, 75.35, 75.39, 75.63, 76.20, 76.34, 79.76, 81.75, 82.79 (11 *C*H of sugar), 102.35, 102.47, 103.06 (C-1^I, 1^{II}, 1^{III}), 125.87-128.97 (aromatic carbons), 137.57-139.27(6 aromatic carbines), and 172.57 (NH*C*O).

2-(Trimethylsilyl)ethyl 2-Acetamido-4,6-*O*-benzylidene-2-deoxy-β-D-glucopyranosyl-(1→3)-2,*4*,6-tri-*O*-benzyl-β-D-galactopyranosyl-(1→4)-2,3,6-tri-*O*-benzyl-β-D-glucopyranoside (5). To a solution of compound **4** (1.5 g, 1.26 mmol) in DMF (8 mL), benzaldehyde dimethyl acetal (400 μL, 2.67 mmol) and *p*-toluenesulfonic acid (20 mg) and Drierite (1.5 g) were added. The reaction mixture was stirred at room temperature and monitored by TLC (solvent A) until complete reaction, then neutralized with Amberlite IR-410 (OH^-) resin. The solvent was concentrated and the residue was chromatographed on a column of silica gel (using CH_2Cl_2 as an eluent), to furnish (1.32 g, 84%) of the pure title compound (**5**) as a syrup: $[\alpha]_D$ -22.5° (*c* 1.0, CH_2Cl_2), lit.[23] $[\alpha]_D$ -23°; ^1H NMR ($CDCl_3$) δ 1.47 (s, 3H, NHCOC*H*$_3$), 3.20-5.06 (m, 36H, PhC*H*$_2$, OC*H*$_2$, O*H*, sugar C*H*, and C*H*$_2$), 5.44 (s, 1H, PhC*H*), 5.80 (bs, 1H, D_2O-exchangeable, N*H*CO), and 7.09-7.50 (m, 35H, 7Ph); ^{13}C NMR ($CDCl_3$) was similar to that of compound **4** except for the appearance of a new signal at δ 101.54 (PhC*H*); positive-ion LSIMS: *m/z* 1274.1 $(M+H)^+$, 1296.1 $(M+Na)^+$, 1405.9 $(M+Cs)^+$.

Anal. Calcd for $C_{74}H_{87}NO_{16}Si$(1274.6): C, 69.73; H, 6.89; N, 1.10. Found: C, 69.78; H, 6.50; N, 1.03.

2-(Trimethylsilyl)ethyl 2-Acetamido-3-*O*-benzyl-4,6-*O*-benzylidene-2-deoxy-β-D-glucopyranosyl-(1→3)-2,*4*,6-tri-*O*-benzyl-β-D-galactopyranosyl-(1→4)-2,3,6-tri-*O*-benzyl-β-D-glucopyranoside (6). To a solution of the benzylidene derivative **5** (0.7 g, 0.55 mmol), in DMF, barium oxide (0.6 g, 3.91 mmol), barium hydroxide octahydrate (0.25 g, 0.79 mmol) and benzyl bromide (0.4 mL, 3.3 mmol) were added. The

reaction mixture was stirred for 1 h at room temperature and monitored by TLC (solvent C) until complete reaction. The excess benzyl bromide was decomposed by the addition of MeOH, then the product was extracted with CH_2Cl_2, the organic layer washed three times with water, and dried over anhydrous sodium sulphate. The solvent was concentrated to dryness under diminished pressure and the residue was chromatographed on a column of silica gel (solvent C) to give (0.54 g, 72%) of the pure compound **6** as a syrup: $[\alpha]_D$ -4.4°, $[\alpha]_{578}$ -4.5°, $[\alpha]_{546}$ -5.1°, $[\alpha]_{436}$ -8.5°, $[\alpha]_{365}$ -12.7°, (*c* 2.3, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 1.46 (s, 3H, NHCOC*H*$_3$), 3.25-5.00 (m, 37H, 7PhC*H*$_2$, OC*H*$_2$, sugar C*H* and C*H*$_2$), 5.58 (s, 1H, PhC*H*), 6.18 (bd, 1H, D_2O-exchangeable, N*H*COCH$_3$), and 7.10-7.50 (m, 40H, 8 Ph); ^{13}C NMR ($CDCl_3$) was similar to that of compound **5** except for the appearance of signal at 74.41 due to the carbene of the additional benzyl group; positive-ion LSIMS: *m/z*. 1364.1 $(M+H)^+$, 1496.5 $(M+Cs)^+$, negative-ion LSIMS: *m/z* 1362.4 $(M-H)^-$, 1515.3 (M-H+*m*-NBA)$^-$.

Anal. Calcd for $C_{81}H_{93}NO_{16}Si.H_2O$ (1382.72): C, 70.30; H, 6.78; N, 1.01. Found: C, 70.64; H, 6.79; N, 0.74.

2-(Trimethylsilyl)ethyl 2-Acetamido-3,6-di-*O*-benzyl-2-deoxy-β-D-glucopyranosyl-(1→3)-2,4,6-tri-*O*-benzyl-β-D-galactopyranosyl-(1→4)-2,3,6-tri-*O*-benzyl-β-D-glucopyranoside (7). To a solution of compound **6** (0.9 g, 0.66 mmol) in dry THF (20 mL), powdered molecular sieves 3Å (2.0 g) was added, the mixture was stirred for 4 h at room temperature, then sodium cyanoborohydride (0.9 g) was gradually added. After the reagent had dissolved, hydrogen chloride in dry ether was added dropwise at room temperature until the evolution of gas ceased. TLC (solvent A) indicated that the reaction was complete after 15 min. The reaction mixture was diluted with CH_2Cl_2 (50 mL) and water (10 mL), then filtered over a Celite-bed, the filtrate was washed with $NaHCO_3$, water, dried over anhydrous sodium sulphate, and the solvents were evaporated under reduced pressure to dryness. Column chromatography (solvent A) of the residue on silica gel afforded (0.65 g, 72%) of **7** as a syrup. ^{1}H NMR ($CDCl_3$) was similar to that of the compound **6** except for the disappearance of one signal at δ 5.44 due to (PhC*H*); ^{13}C NMR was similar to that of the compound **6** except for the disappearance of one signal at δ 101.54 due to (PhCH), and appearance of new signal at δ 73.64 for the additional benzyl group PhC*H*$_2$, and a downfield shifted of (C-6^{III}) to 70.53. Positive-ion LSIMS: *m/z* 1366.5

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$(M+H)^+$, 1498.2 $(M+Cs)^+$, negative-ion LSIMS: *m/z* 1364.4 $(M-H)^-$, 1519.4 (M-H+*m*-NBA)$^-$.

Anal. Calcd for $C_{81}H_{95}NO_{16}Si$ (1366.73): C, 71.18; H, 7.01; N, 1.02. Found: C, 70.94; H, 7.32; N, 0.95.

2-(Trimethylsilyl)ethyl β-D-Galactopyranosyl-(1→4)-2-acetamido-3,6-di-*O*-benzyl-2-deoxy-β-D-glucopyranosyl-(1→3)-2,4,6-tri-*O*-benzyl-β-D-galactopyranosyl-(1→4)-2,3,6-tri-*O*-benzyl-β-D-glucopyranoside (10). The galactosyl bromide **8** (360 mg, 0.87 mmol) was dissolved in 40 mL of 1:1 (v/v) benzene-nitromethane containing the trisaccharide acceptor **7** (550 mg, 0.43 mmol) and mercuric cyanide (1.30 g, 5.14 mmol). The solution was stirred at 60 °C under anhydrous conditions. After vigorous stirring for 16 h, the reaction mixture was washed with saturated $NaHCO_3$, and then with water. The benzene phase was dried with magnesium sulphate anhydrous and evaporated to a syrup under diminished pressure. Column chromatography (solvent B) of the residue on silica gel afforded, 2-(trimethylsilyl)ethyl 2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl-(1→4)-2-acetamido-3,6-di-*O*-benzyl-2-deoxy-β-D-glucopyranosyl-(1→3)-2,4,6-tri-*O*-benzyl-β-D-galactopyranosyl-(1→4)-2,3,6-tri-*O*-benzyl-β-D-glucopyranoside (**9**) as a syrup (423 mg, 62%).

A solution of compound **9** in MeOH (5 mL) was stirred with sodium methoxide (30 mg) for 2 h at room temperature. The mixture was treated with Amberlite IR-120 (H^+) resin and concentrated, afforded the title compound **10** in quantitive yield. ^1H NMR ($CDCl_3$) δ 1.38 (s, 3H, $NHCOCH_3$), 3.12-5.30 (51H, OCH_2, $8PhCH_2$, 4O*H*, N*H*, sugar C*H*, and CH_2), 7.10-7.38(m, 40H, 8Ph); ^{13}C NMR ($CDCl_3$) was similar to that of compound **7** except for the appearance of a new signal at δ 103.70 due to the additional anomeric carbon, and the appearance of five new signals for the galactose moiety. Positive-ion LSIMS:*m/z* 1527.9 $(M+H)^+$, 1550.0 $(M+Na)^+$, 1660.1 $(M+Cs)^+$, negative-ion LSIMS: *m/z* 1525.9 $(M-H)^-$, 1680.4 (M-H+*m*-NBA)$^-$.

Anal. Calcd for $C_{87}H_{105}NO_{21}Si$ (1528.87): C, 68.34; H, 6.93; N, 0.92. Found: C, 68.52; H, 6.84; N, 1.01.

2-(Trimethylsilyl)ethyl β-D-Galactopyranosyl-(1→4)-2-acetamido-2-deoxy-β-D-glucopyranosyl-(1→3)-β-D-galactopyranosyl-(1→4)-β-D-glucopyranoside (11). Compound **10** (200 mg. 0.13 mmol) was catalytically hydrogenolyzed in MeOH (15

mL), in the presence of 10% palladium-on-charcoal (50 mg), the reaction mixture was stirred overnight at room temperature and atmospheric pressure and monitored by TLC (solvent E). The catalyst was filtered off, and the filtrate was concentrated under reduced pressure to dryness to yield (83 mg, 78%) of compound **11**. ^{1}H NMR (D_2O) of **11** was similar to that of compound **10** except for the disappearance of the signals in the aromatic region at δ (7.10-7.38) due to the absence of the benzyl groups. The four anomeric protons were clearly resolved at δ 4.41 (d, 1H, J = 7.9 Hz), 4.45 (d, 1H, J= 7.3 Hz), 4.48 (d, 1H, J= 7.7 Hz), and 4.68 (d, 1H, J=7.8 Hz). The ^{13}C NMR (D_2O) spectrum of **11** was similar to that of compound **10** except for the absence of the carbon atoms of the benzyl groups. The four anomeric carbons appeared at δ 103.85, 105.22, 105.33, and 105.39 ppm. Negative-ion LSIMS: *m/z* 806.2 $(M-H)^-$.

Anal. Calcd for $C_{31}H_{57}NO_{21}Si.\ 2H_2O$ (843.88): C, 44.12; H, 7.29; N, 1.66. Found: C, 43.58; H, 7.04; N, 1.54.

Acetylation of **11** with Ac_2O in pyridine gave 2-(trimethylsilyl)ethyl 2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl-(1→4)-2-acetamido-3,6-di-*O*-acetyl-2-deoxy-β-D-glucopyranosyl-(1→3)-2,4,6-tri-*O*-acetyl-β-D-galactopyranosyl-(1→4)-2,3,6-tri-*O*-acetyl-β-D-glucopyranoside (**12**): ^{1}H NMR (750 MHz, $CDCl_3$) δ 4.33 (d, 1H, J= 8.0 Hz, H-1), 4.47 (d, 1H, J = 8.0 Hz, H-1), 4.65 (d, 1H, J= 8.1 Hz, H-1), 4.70 (d, 1H, J= 8.0 Hz, H-1), 4.90 (t, 1H, J= 9.3 Hz), 4.97 (dd, 1H, $J_{2,3}$= 11.2 Hz and $J_{3,4}$= 2.9 Hz, H-3^{IV}), 4.99 (t, 1H, J= 8.8 Hz), 5.14 (t, 1H, J = 9.8 Hz), 5.18 (t, 1H, J= 9.5 Hz), 5.23 (t, 1H, J = 9.9 Hz), 5.30 (d, 1H, $J_{3,4}$= 2.8 Hz, H-4), 5.36 (d, 1H, $J_{3,4}$= 2.9 Hz, H-4), and 5.44 (d, 1H, $J_{NH,H-2}$= 8.1 Hz, D_2O-exchangeable, N*H*).

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