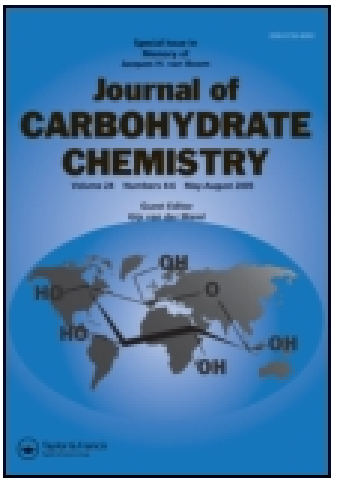

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Regiospecific Syntheses of N-Acetyllactosamine Derivatives and Application Toward a Highly Practical Synthesis of Lewis X Trisaccharide

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REGIOSPECIFIC SYNTHESES OF *N*-ACETYLLACTOSAMINE DERIVATIVES AND APPLICATION TOWARD A HIGHLY PRACTICAL SYNTHESIS OF LEWIS X TRISACCHARIDE

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ABSTRACT

An efficient methodology for regiospecific glycosylation was developed by using 6-*O*-*tert*-butyldiphenylsilyl *N*-acetylglucosamine derivatives **3** and **5** which bear two free hydroxyl groups as acceptors. The regiospecificity was attributed to the presence of the *tert*-butyldiphenylsilyl group at the *O*-6 position of the *N*-acetylglucosamine derivatives. Glycosylation of suitably protected galactoside donors **10-14** with acceptors **3** and **5** gave only β (1→4) linked disaccharides **15-19** in good yields. Fucosylation of disaccharide **18** led to Lewis X (Le^x) trisaccharide **21** in high yield.

INTRODUCTION

N-Acetyllactosamine [Galβ(1→4)GlcNAc, LacNAc] is well known as a biologically important disaccharide core structure which has been found in glycoproteins and glycolipids, and is widely distributed in many different human and animal tissues.[1,2] Furthermore, it is also a key intermediate of sialyl Lewis X (sLe^x)[3] and sulfo-Le^x,[4] identifi-

ed as a ligand for the endothelial leukocyte adhesion molecule-1 (ELAM-1) which mediates the early stage of adhesion of leukocytes to activated endothelial cells. Several chemical syntheses of *N*-acetyllactosamine derivatives have been developed by the glycosylations between galactose and *N*-acetylglucosamine derivatives.[5-10] The secondary hydroxyl group at C-4 of a hexopyranose with a $^4C_1$ conformation was particularly unreactive when the remaining hydroxyl groups were acylated.[11] This problem has been solved by using a non $^4C_1$ conformation precursor, such as 2-acetamido-1,6-anhydro-2-deoxy-β-D-glucopyranose with a $^1C_4$ conformation,[12] or an acyclic *N*-acetylglucosamine derivative.[13] Moreover, Sinaÿ et al.[5] demonstrated that OH-4 of a 2-acetamido-2-deoxy-D-glucose residue where the remaining hydroxyl groups were protected by benzyl groups was more reactive than the corresponding acyl counterpart under appropriate glycosylation conditions. However, the procedure often involved tedious multiple protection and deprotection steps. To overcome this drawback, a new strategy has been the use of "lightly protected" acceptors that have several hydroxyl groups unprotected, especially near the position where the glycosidic bond is formed. This "open" glycosylation in which one hydroxyl group is preferentially glycosylated in the presence of the other free hydroxyl group(s) may offer shorter and easier routes to oligosaccharide synthesis. The "lightly protected" acceptors, such as 6-*O*-benzyl or 6-*O*-pivaloyl-2-deoxy-2-phthalimido-β-D-glucopyranoside derivatives, were used as key intermediates in various glycosylations by Ogawa's group,[14] Sinaÿ's group,[15] and Matta's group.[16] The bulky phthalimido group which was chosen to protect N-2 was claimed to reduce the reactivity of OH-3 by steric hindrance. However, the regioselectivity was unsatisfactory in these cases. The yields of undesired β-(1→3) linked disaccharides were from 8% to 25%. More recently, Verez-Bencomo et al.[17] have reported a complete regiospecific galactosylation of a similar diol acceptor bearing a phthalimido protecting group by using a 4,6-benzylidene galactosyl donor. No 1→3 isomer was detected. The presence of both the phthalimido group of the acceptor and the rigidified bicyclic system of the galactosyl donor were crucial for the regiospecific galactosylation.

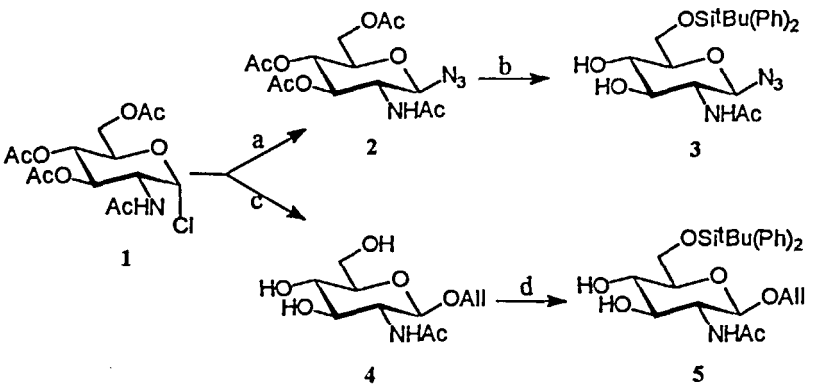
Recently, we found that an *O*-6 *tert*-butyldiphenylsilyl protecting group could also contribute to regiospecific glycosylation. We used *p*-nitrophenyl 2-phthalimido-6-*O*-*tert*-

butyldiphenylsilyl-2-deoxy-1-thio-β-D-glucopyranoside as the glycosyl acceptor and phenyl 2,3,4,6-tetra-*O*-benzoyl-1-thio-β-D-galactopyranoside as the donor to obtain only the corresponding β-(1→4) linked disaccharide in 74% yield.[18] The regiospecificity was attributed to the bulky 6-*O*-*tert*-butyldiphenylsilyl and phthalimido groups. In order to explore the possibility that the enhanced regioselectivity was not a combination of these two protecting groups, we chose the analogous 2-acetamido-6-*O*-*tert*-butyldiphenylsilyl-2-deoxy-β-D-glucopyranoside derivative as glycosyl acceptor to synthesize *N*-acetyllactosamine derivatives. Furthermore, we also used this strategy toward the synthesis of a Lewis X derivative.

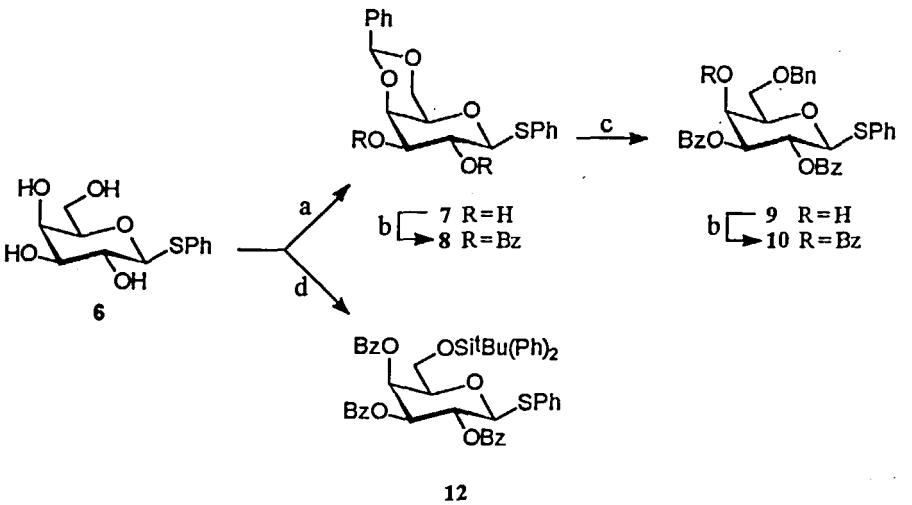
RESULTS AND DISCUSSION

Acetochloro-*N*-acetylglucosamine **1**[19] was treated with sodium azide under PTC conditions[20] to give glycosyl azide **2** in 94% yield. The compound had the β configuration as confirmed by ^{1}H NMR spectroscopy ($J_{1,2}$ = 9.3 Hz). Subsequent Zemplén deacetylation and selective silylation of OH-6 with *tert*-butylchlorodiphenylsilane in pyridine gave azide acceptor **3** in 88% overall yield. Compound **1** was also treated with a 1M solution of sodium allyloxide in allyl alcohol to afford allyl β-glycoside **4** ($J_{1,2}$ = 8.4 Hz, 80% yield) and simultaneous de-*O*-acetylation. No oxazoline byproduct formed under these conditions. Compared with other methods to prepare allyl β-glycosides, for example, via an oxazoline intermediate[21] or acetochloro-*N*-acetylglucosamine coupled with allyl alcohol,[22] this method was simpler and afforded a higher yield. Selective silylation of OH-6 with TBDPSCl yielded the allyl β-glycoside acceptor **5** (88%) (Scheme 1).

Phenyl 1-thio-β-D-galactopyranoside **6** (Zemplén deacetylation from phenyl 2,3,4,6-tetra-*O*-acetyl-1-thio-β-D-galactopyranoside **13** which was prepared under PTC conditions[20]) was the precursor for the preparation of the galactosyl donors **10**, **11**[23] and **12**. Benzylidenation of **6** was accomplished with benzaldehyde dimethyl acetal under acid catalysis (*p*-TsOH) to give acetal **7** in 90% yield. Benzoylation of **7** with benzoyl chloride in pyridine afforded compound **8** in quantitative yield. The reductive ring opening of benzylidene acetal **8** with sodium cyanoborohydride provided galactosyl derivative **9**



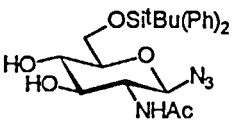
Scheme 1. *Reagents and conditions*: (a) NaN_3, TBAHS, 1M Na_2CO_3, 94%; (b) *i*: NaOMe/MeOH; *ii*: TBDPSCl, pyridine, 92%; (c) $NaOCH_2CH{=}CH_2/HOCH_2CH{=}CH_2$, 80%; (d) TBDPSCl, pyridine, 88%.



Scheme 2. *Reagents and conditions*: (a) $C_6H_5CH(OCH_3)_2$, *p*-TsOH, 90%; (b) BzCl, pyridine, 99%; (c) $NaBH_3CN$, HCl, 84%; (d) *i*: TBDPSCl, pyridine; *ii*: BzCl, 92%.

(84%). Finally, benzoylation of **9** finished the preparation of glycosyl donor **10**. Galactosyl donor **12** was easily available by a simple one pot, two step reaction from phenyl thiogalactoside **6**. Thus successive treatment of **6** with *tert*-butyldiphenylsilyl chloride and benzoyl chloride in dry pyridine gave galactosyl donor **12** in 92% overall yield (Scheme 2).

In order to study the regioselectivity/specificity of the *tert*-butyldiphenylsilyl protecting group in glycosylation, the two glycosyl acceptors **3**, **5** and the five



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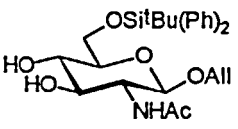

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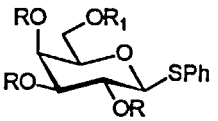
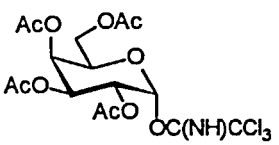


10 R = Bz, R_1 = Bn
11 R = Bz, R_1 = Bz
12 R = Bz, R_1 = $Si^tBu(Ph)_2$
13 R = Ac, R_1 = Ac



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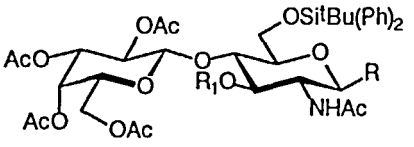
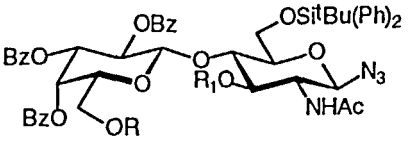
Scheme 3. Glycosyl acceptors **3**, **5** and donors **10-14**

functionalized glycosyl donors **10-14** (Scheme 3) were used as building blocks for the synthesis of *N*-acetyllactosamine derivatives.

Condensation of phenyl 2,3,4,6-tetra-*O*-acetyl-1-thio-β-D-galactopyranoside (**13**) with 6-*O*-*tert*-butyldiphenylsilyl acceptor **3** was performed using *N*-iodosuccinimide and trifluoromethanesulfonic acid as promoter in dichloromethane-acetonitrile (1:1) at -45 °C. The reaction afforded the desired β-(1→4)-linked disaccharide **15** in 73% yield (Δ C-4 +8.1 ppm). Very impressively, no β-(1→3)-linked regioisomer was detected during this coupling reaction. The β-configuration of the disaccharide **15** was deduced from the ^{1}H NMR spectrum which showed H-1' as a doublet at δ 4.69 ppm ($J_{1',2'}$ = 8.1 Hz). The regiochemistry of the newly introduced glycosidic linkage of **15** was further confirmed by converting **15** to its corresponding acetate **15a**. The signal of H-3 in the ^{1}H NMR spectrum of **15a** at 4.88 ppm was considerably deshielded in comparison to that of its precursor **15** (Δδ = +1.0 ppm). All the ^{1}H and ^{13}C signal assignments were unambiguously determined using 2-D COSY together with HMQC experiments.

It appears that the bulky 6-*O*-*tert*-butyldiphenylsilyl protecting group in acceptor **3** played a key role in controlling the regiospecificity. Under such reaction conditions, this





15 R=N_3, R_1=H
15a R=N_3, R_1=Ac
19 R=OAll, R_1=H
19a R=OAll, R_1=Ac

16 R=Bn, R_1=H
16a R=Bn, R_1=OAc
17 R=Bz, R_1=H
17a R=Bz, R_1=OAc
18 R=TBDPS, R_1=H
18a R=TBDPS, R_1=OAc

Scheme 4. *N*-Acetyllactosamine derivatives **15-19.**

very bulky protecting group could cover the top side (3,5-*cis*) of OH-3 of the acceptor **3** and block the approach of the glycosyl donor.

To test this hypothesis, other more bulky phenylthiogalactoside donors **10-12** were used to glycosylate acceptor **3.** The β-(1→4)-linked disaccharides **16-18** were obtained in 71-82% yield and no β-(1→3) coupling products were obtained as products of this reaction. The sites of glycosylation in **16-18** were identified by observation of significant deshieldings for the signals of their C-3 carbons as well as by the H-3 protons in the ^{1}H NMR spectra of their acetylated derivatives **16a, 17a,** and **18a.**

Boron trifluoride etherate was also used as the promoter for the glycosylation of acceptors **3** and **5** with *O*-(2,3,4,6-tetra-*O*-acetyl-α-D-galactopyranosyl)trichloroacetimidate **(14)** in dichloromethane to afford the disaccharides **15** and **19** in reasonable yields (Scheme 4). The results of the glycosidation reactions between donors **10-14** and acceptors **3** and **5** are summarized in Table 1.

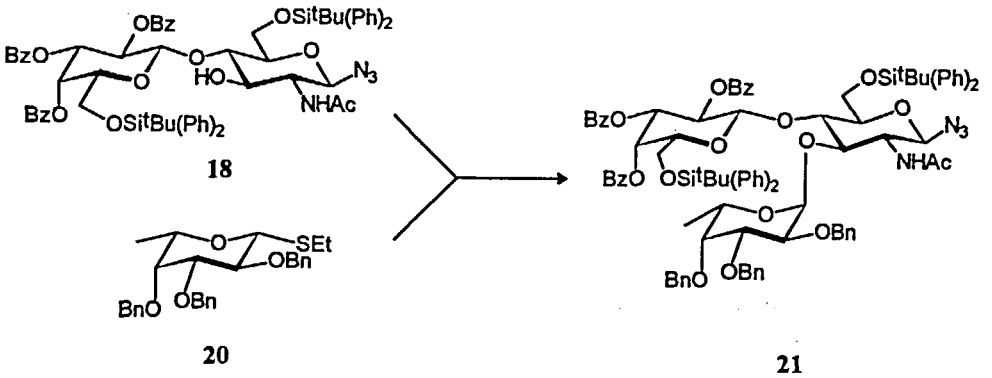
Further fucosylation of the *N*-acetyllactosamine derivative **18** with ethyl 2,3,4-tri-*O*-benzyl-1-thio-β-L-fucopyranoside **20** by using DMTST as promoter at 0 °C afforded Le^x derivative **21** in good yield (78%) (Scheme 5). The α configuration of the newly introduced anomeric center in compound **21** was assigned by ^{1}H NMR spectroscopy ($J_{1'',2''}$ = 3.5 Hz).

In conclusion, a very simple and efficient synthetic route towards *N*-acetyllactosamine derivatives was developed. This procedure takes advantage of a 6-*O*-

Table 1. Glycosidation reactions of donors **10-14** with acceptors **3** and **5**[a].

Entry	Donor	Acceptor	Promoter	Solvent	Product (yield%)[b]
1	**13** (1.5 eq)	**3**	NIS/TfOH	CH_2Cl_2/CH_3CN	**15** (73%)
2	**14** (1.5 eq)	**3**	$BF_3{\cdot}Et_2O$	CH_2Cl_2	**15** (70%)
3	**10** (1.3 eq)	**3**	NIS/TfOH	CH_2Cl_2/CH_3CN	**16** (78%)
4	**11** (1.3 eq)	**3**	NIS/TfOH	CH_2Cl_2/CH_3CN	**17** (71%)
5	**12** (1.3 eq)	**3**	NIS/TfOH	CH_2Cl_2/CH_3CN	**18** (82%)
6	**14** (1.5 eq)	**5**	$BF_3{\cdot}Et_2O$	CH_2Cl_2	**19** (68%)

a. Reactions were performed at -45 °C in the presence of 4Å molecular sieves.
b. After purification by column chromatography.



Scheme 5. *Reagents and conditions*: DMTST, benzene:CH_2Cl_2 5:1, 0 °C, 78%.

tert-butyldiphenylsilyl protected *N*-acetylglucosamine derivative, allowing the regiospecific introduction of a galactosyl moiety. In addition, this method constitutes a highly practical synthesis of Lewis X trisaccharide.

EXPERIMENTAL

General methods. Melting points were determined on a Gallenkamp apparatus and are uncorrected. ^1H and ^{13}C NMR spectra were recorded on Bruker AMX 500 or

Varian Gemini 200 NMR spectrometers. Proton chemical shifts (δ) were given relative to internal $CHCl_3$ (7.24 ppm) for $CDCl_3$ solutions and to internal HOD (4.76 ppm) for D_2O solutions. Carbon chemical shifts were given relative to $CDCl_3$ (77.0 ppm). All final signal assignments were made by means of 2-D COSY and HMQC experiments. Mass spectra were obtained using a Kratos II H instrument (FAB-glycerol) or VG 7070-E spectrometer (CI). Optical rotations were measured on a Perkin Elmer 241 polarimeter and were run at 23 °C. Thin layer chromatography (TLC) were performed on silica gel 60 F-254, and column chromatography was carried out on silica gel 60.

2-Acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-β-D-glucopyranosyl azide (2). To a solution of 2-acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-α-D-glucopyranosyl chloride **1** (10 g, 27.3 mmol), TBAHS (13.9 g, 41 mmol) and sodium azide (3.55 g, 54.6 mmol) in dichloromethane (100 mL) were added a 1M Na_2CO_3 solution (100 mL). The two phase reaction mixture was vigorously stirred at room temperature for 2 h. The organic phase was separated, washed with water, then dried over anhydrous sodium sulfate, and concentrated to give **2** (9.6 g, 94%). Compound **2** was crystallized from ethanol as colorless needles: mp 159-161 °C; $[\alpha]_D$ -45.7° (*c* 0.9, chloroform); ^{1}H NMR ($CDCl_3$) δ 5.77 (d, 1H, $J_{2,NH}$ = 8.9 Hz, NH), 5.23 (dd, 1H, $J_{3,4}$ = 9.8 Hz, H-3), 5.07 (dd, 1H, $J_{4,5}$ = 9.6 Hz, H-4), 4.74 (d, 1H, $J_{1,2}$ = 9.3 Hz, H-1), 4.24 (dd, 1H, $J_{6a,6b}$ = 12.5 Hz, H-6a), 4.13 (dd, 1H, $J_{5,6b}$ = 2.4 Hz, H-6b), 3.92 (dd, 1H, $J_{2,3}$ = 10.1 Hz, H-2), 3.72 (ddd, 1H, $J_{5,6b}$ = 4.7 Hz, H-5), 2.07, 2.02, 2.01, 1.96 (4s, 3 x OAc, NHAc).

2-Acetamido-6-*O*-*tert*-butyldiphenylsilyl-2-deoxy-β-D-glucopyranosyl azide (3). To a suspension of **2** (3.0 g, 8.04 mmol) in methanol (50 mL) was added 1M NaOMe/MeOH solution until the pH was 9-10. The mixture was stirred for 1 h at room temperature. TLC (ethanol/CH_2Cl_2, 1:4) showed that deacetylation was complete. The solution was neutralized with H^+ resin (Dowex 50W-X8), filtered, and concentrated. To the residue (1.7 g, 6.9 mmol) in dry pyridine (20 mL) was added *tert*-butylchlorodiphenyl-silane (2.15 mL, 8.28 mmol). The solution was stirred at room temperature for 6 h. The reaction mixture was poured into ice-water and extracted with dichloromethane (3 x 20 mL). The combined extracts were washed successively with 5% hydrochloric acid, saturated $NaHCO_3$ solution, and water. The organic extract was dried (Na_2SO_4), filtered, and concentrated. The crude product was subjected to column chromatography with

CH_2Cl_2-CH_3OH (15:1, v/v) as eluant to give **3** as a syrup (3.08 g, 92%): $[\alpha]_D$ -53.6° (*c* 1.0, chloroform); ^1H NMR ($CDCl_3$) δ 7.67-7.34 (m, 10H, aromatic), 6.14 (d, 1H, $J_{2,NH}$ = 7.1 Hz, NH), 4.61 (d, 1H, $J_{1,2}$ = 9.1 Hz, H-1), 3.88 (m, 2H, H-6, H-6'), 3.66 (dd, 1H, $J_{3,4}$ = 9.4 Hz, H-3), 3.60 (dd, 1H, $J_{4,5}$ = 9.1 Hz, H-4), 3.53 (dd, 1H, $J_{2,3}$ = 9.1 Hz, H-2), 3.44 (ddd, 1H, $J_{5,6a}$ = 4.3 Hz, $J_{5,6b}$ = 4.5 Hz, H-5), 2.02 (s, 3H, NHAc), 1.02 (s, 9H, $SiCMe_3$); ^{13}C NMR ($CDCl_3$)) δ 172.6 (C=O), 137.6-127.7 (12C, aromatic), 88.2 (C-1), 77.8 (C-5), 74.4 (C-3), 71.2 (C-4), 63.5 (C-6), 55.6 (C-2), 26.7 ($SiC(\underline{C}H_3)_3$), 23.3 (NHAc), 19.2 ($Si\underline{C}Me_3$).

Anal. Calcd for $C_{24}H_{32}N_4O_5Si$: C, 59.48; H, 6.66; N, 11.56. Found: C, 59.51; H, 6.55; N, 11.91.

Allyl 2-acetamido-2-deoxy-β-D-glucopyranoside (4). To a solution of 2-acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-α-D-glucopyranosyl chloride **1** (10 g, 27.3 mmol) dissolved in CH_2Cl_2 (25 mL) was added a solution of sodium allyloxide in allyl alcohol (1M, 54.6 mL). The mixture was stirred at room temperature for 30 min. The suspension was neutralized with Amberlite IR-120 (H^+ form) resin as judged by pH test paper, filtered, and the resin was washed with methanol (3 x 40 mL). The filtrate and washings were combined and concentrated to give the allyl β-glycoside **4** (6.79 g, 95%) as a solid. Crystallization from ethanol gave colorless crystalline **4** (5.71 g, 80%): mp 168-169 °C (lit.[22] 171-172 °C); $[\alpha]_D$ -23° (*c* 1.0, methanol) (lit.[22] $[\alpha]_D$ –33.9° (*c* 4.99, water); ^1H NMR (D_2O) δ 5.86 (m, 1H, -C$\underline{H}$=CH_2), 4.51 (d, 1H, $J_{1,2}$ = 8.4 Hz, H-1), 1.98 (s, 3H, NHAc).

Allyl 2-acetamido-6-*O*-*tert*-butyldiphenylsilyl-2-deoxy-β-D-glucopyranoside (5). To a solution of compound **4** (1 g, 3.83 mmol) in dry pyridine (15 mL) was added *tert*-butylchlorodiphenylsilane (1.30 mL, 4.98 mmol). The solution was stirred at room temperature for 6 h. The reaction mixture was poured into ice-water and extracted with CH_2Cl_2 (3 x 20 mL). The combined extracts were washed successively with 5% hydrochloric acid, saturated $NaHCO_3$ solution, and water. The organic extract was dried (Na_2SO_4), filtered, and concentrated. The crude product was subjected to column chromatography with CH_2Cl_2-CH_3OH (15:1, v/v) as eluant to give **5** as a syrup (1.68 g, 88%): $[\alpha]_D$ -42.6° (*c* 1.0, chloroform); ^1H NMR ($CDCl_3$) δ 7.70-7.24 (m, 10H, aromatic), 6.83 (br, 1H, NH), 5.91-5.83 (m, 1H, -C$\underline{H}$=CH_2), 4.48 (d, 1H, $J_{1,2}$ = 7.6 Hz, H-1), 3.94 (dd, 1H, $J_{5,6a}$ = 2.8 Hz, $J_{6a,6b}$ = 11.0 Hz , H-6a), 3.84 (dd, 1H, $J_{5,6b}$ = 5.5 Hz, H-6b), 3.68-

3.61 (m, 2H, H-2, H-3), 3.47 (dd, 1H, $J_{3,4}$ = 9.4 Hz, $J_{4,5}$ = 8.2 Hz, H-4), 3.39 (ddd, 1H, H-5), 1.99 (s, 3H, NHAc), 1.01 (s, 9H, $SiCMe_3$); ^{13}C NMR ($CDCl_3$)) δ 172.6 (C=O), 135.5-127.6 (12C, aromatic), 134.1 (-$\underline{C}H$=CH_2), 117.4 (-CH=$\underline{C}H_2$), 99.7 (C-1), 76.1 (C-5), 74.7 (C-3), 71.3 (C-4), 69.5 (O-$\underline{C}H_2$CH=), 63.9 (C-6), 56.2 (C-2), 26.7 ($SiC(\underline{C}H_3)_3$), 23.2 (NHAc), 19.1 ($Si\underline{C}Me_3$).

Anal. Calcd for $C_{27}H_{37}NO_6Si$: C, 64.90; H, 7.46; N, 2.80. Found: C, 64.88; H, 7.44; N, 3.06.

Phenyl 4,6-*O*-benzylidene-1-thio-β-D-galactopyranoside (7). Phenyl 1-thio-β-D-galactopyranoside **6** (1 g, 3.67 mmol) in acetonitrile (10 mL) was heated at 60 °C until the starting material was completely dissolved. The solution was then cooled to room temperature, benzaldehyde dimethyl acetal (1.65 mL, 11 mmol) and *p*-toluenesulfonic acid monohydrate (catalytic amount) were then added. The mixture was stirred for 4 h at room temperature, neutralized with triethylamine, and concentrated under reduced pressure. The residue was then purified by column chromatography using MeOH-CH_2Cl_2 (1:10, v/v) as eluant to give 7 as a syrup (1.17 g, 90%): $[\alpha]_D$ -24.0° (*c* 1.0, chloroform); ^1H NMR ($CDCl_3$) δ 7.70-7.10 (m, 10H, aromatic), 5.41 (s, 1H, PhCH), 4.39 (d, 1H, $J_{1,2}$ = 9.2 Hz, H-1), 4.29 (dd, 1H, $J_{5,6a}$ = 1.4 Hz, $J_{6a,6b}$ = 12.4 Hz, H-6a), 4.11 (d, 1H, $J_{3,4}$ < 1.0 Hz, H-4), 3.94 (dd, 1H, $J_{5,6b}$ = 1.7 Hz, H-6b), 3.58 (m, 2H, H-2, H-3), 3.46 (m, 1H, H-5).

Anal. Calcd for $C_{19}H_{20}O_5S$: C, 63.32; H, 5.59. Found: C, 63.51; H, 5.31.

Phenyl 2,3-di-*O*-benzoyl-4,6-*O*-benzylidene-1-thio-β-D-galactopyranoside (8). To a solution of 7 (1 g, 2.77 mmol) in dry pyridine (15 mL) at 0 °C was added benzoyl chloride (0.81 mL, 7 mmol) slowly. The solution was then stirred at room temperature for 2 h. TLC showed the reaction was complete. Methanol (1 mL) was added and stirred for additional 15 min. The mixture was concentrated under reduced pressure. The crude product was purified by column chromatography using ethyl acetate-hexane (1:4, v/v) as eluant to give **8** as a syrup (1.54 g, 97%): $[\alpha]_D$ +54.9° (*c* 1.0, chloroform); ^1H NMR ($CDCl_3$) δ 7.95-7.10 (m, 20H, aromatic), 5.66 (dd, 1H, $J_{2,3}$ = 10.0 Hz, H-2), 5.41 (s, 1H, PhCH), 5.22 (dd, 1H, $J_{3,4}$ = 3.2 Hz, H-3), 4.84 (d, 1H, $J_{1,2}$ = 9.7 Hz, H-1), 4.50 (d, 1H, $J_{4,5}$ < 1.0 Hz, H-4), 3.87-3.67 (m, 3H, H-6a, H-6b, H-5).

Anal. Calcd for $C_{33}H_{28}O_7S$: C, 69.70; H, 4.96. Found: C, 69.82; H, 4.90.

Phenyl 2,3-di-*O*-benzoyl-6-*O*-benzyl-1-thio-β-D-galactopyranoside (9). To a solution of **8** (1 g, 1.76 mmol) in dry THF (10 mL) was added powdered molecular sieves

(4 Å, 1 g). The mixture was stirred for 2 h at room temperature, and sodium cyanoborohydride (1.5 g, 23.9 mmol) was gradually added. After the reagent had dissolved, a saturated solution of hydrogen chloride in ether was added dropwise at room temperature until the evolution of gas ceased. TLC (EtOAc/Hexane 2:3) indicated that the starting material **8** (Rf = 0.46) had been converted to product **9** (Rf = 0.54) after 10 min. The reaction mixture was diluted with dichloromethane and filtered. The organic phase was washed with saturated $NaHCO_3$ solution and water. The solution was dried (Na_2SO_4), filtered, and concentrated. Column chromatography on silica gel using ethyl acetate-hexane (1:3, v/v) as eluant gave **9** as a syrup (0.85 g, 84%): $[\alpha]_D$ +77.0° (*c* 1.0, chloroform); ^1H NMR ($CDCl_3$) δ 7.99-7.20 (m, 20H, aromatic), 5.75 (dd, 1H, $J_{2,3}$ = 9.8 Hz, H-2), 5.29 (dd, 1H, $J_{3,4}$ = 3.2 Hz, H-3), 4.91 (d, 1H, $J_{1,2}$ = 9.9 Hz, H-1), 4.56 (AB pattern, 2H, CH_2Ph), 4.41 (ddd, 1H, $J_{4,OH}$ = 1.4 Hz, $J_{4,5}$ < 1.0 Hz, H-4), 3.91-3.83 (m, 3H, H-5, H-6a, H-6b), 2.67 (d, 1H, OH).

Anal. Calcd for $C_{33}H_{30}O_7S$: C, 69.46; H, 5.30. Found: C, 69.32; H, 5.23.

Phenyl 2,3,4-tri-*O*-benzoyl-6-*O*-benzyl-1-thio-β-D-galactopyranoside (10). Compound **9** was treated as was **7** for the synthesis of **8**. Column chromatography of the residue on silica gel using methanol-dichloromethane (1%, v/v) gave **10** in 97% yield as an amorphous mass: $[\alpha]_D$ +113.5° (*c* 1.0, chloroform); ^1H NMR ($CDCl_3$) δ 7.96-7.10 (m, 25H, aromatic), 5.94 (dd, 1H, $J_{4,5}$ < 1.0 Hz, H-4), 5.68 (dd, 1H, $J_{2,3}$ = 9.8 Hz, H-2), 5.53 (dd, 1H, $J_{3,4}$ = 3.0 Hz, H-3), 4.98 (d, 1H, $J_{1,2}$ = 9.9 Hz, H-1), 4.52 (AB pattern, 1H, J = 11.8 Hz, H-A of CH_2Ph), 4.45 (AB pattern, 1H, H-B of CH_2Ph), 4.19 (m, 1H, H-5), 3.73 (dd, 1H, $J_{5,6a}$ = 6.3 Hz, $J_{6a,6b}$ = 9.8 Hz, H-6a), 3.62 (dd, 1H, $J_{5,6b}$ = 6.3 Hz, H-6b).

Anal. Calcd for $C_{40}H_{34}O_8S$: C, 71.20; H, 5.08. Found: C, 71.28; H, 4.96.

Phenyl 2,3,4-tri-*O*-benzoyl-6-*O*-*tert*-butyldiphenylsilyl-1-thio-β-D-galacto-pyranoside (12). To a solution of compound **6** (3.3 g, 12.1 mmol) in dry pyridine (15 mL) was added *tert*-butyldiphenylsilyl chloride (TBDPSCl, 3.5 mL, 13.3 mmol). The reaction mixture was stirred for 4 h at room temperature. TLC showed complete conversion of **6**. The mixture was cooled to 0 °C, and benzoyl chloride (5.0 mL, 44 mmol) was added. The mixture was stirred at room temperature for 1 h and then poured into ice. The solution was extracted with chloroform. The extracts were washed successively with 5% hydrochloric acid, saturated $NaHCO_3$ solution, and water. The organic extract was dried (Na_2SO_4),

filtered, and concentrated. The crude product was subjected to column chromatography with ethyl acetate/hexane (1:4, v/v) as eluant to give **12** as a syrup (9.2 g, 92%): $[\alpha]_D$ +110° (*c* 1.0, chloroform); M.S. (C.I. ether) (*m/z*): 823.3 ($[M+1]^+$, 3.6%); ^{1}H NMR ($CDCl_3$) δ 7.98-7.14 (m, 30H, aromatic), 6.06 (dd, 1H, $J_{4,5}$ < 1 Hz, H-4), 5.66 (dd, 1H, $J_{2,3}$ = 9.8 Hz, H-2), 5.60 (dd, 1H, $J_{3,4}$ = 3.1 Hz, H-3), 4.98 (d, 1H, $J_{1,2}$ = 9.8 Hz, H-1), 4.14 (m, 1H, H-5), 3.90 (dd, 1H, $J_{5,6a}$ = 6.1 Hz, $J_{6a,6b}$ = 10.3 Hz, H-6a), 3.79 (dd, 1H, $J_{5,6b}$ = 7.6 Hz, H-6b), 1.02 (s, 9H, $SiCMe_3$).

***O*-(2,3,4,6-Tetra-*O*-acetyl-β-D-galactopyranosyl)-(1→4)-2-acetamido-6-*O*-*tert*-butyldiphenylsilyl-2-deoxy-β-D-glucopyranosyl azide (15).** Method A: To a solution of compound **3** (200 mg, 0.41 mmol) and phenyl 2,3,4,6-tetra-*O*-acetyl-1-thio-β-D-galactopyranoside **13** (273 mg, 0.62 mmol) in 10 mL of dry acetonitrile and dichloromethane (1:1, v/v) under nitrogen was added powdered molecular sieves (4 Å, 0.5 g). The mixture was stirred for 2 h at room temperature, then cooled to -45 °C. *N*-iodosuccinimide (186 mg, 0.83 mmol) and trifluoromethanesulfonic acid (36 μL, 0.41 mmol) were added. After 1 h the mixture was diluted with dichloromethane (10 mL), filtered through celite, and washed with dichloromethane. The combined filtrate and washings were washed successively with 10% $Na_2S_2O_3$ and sat. $NaHCO_3$ solution. The dried (Na_2SO_4) solution was concentrated under vaccum. The syrupy residue was purified by silica gel chromatography using methanol-dichloromethane as eluant (1:30, v/v) to afford disaccharide **15** (246 mg, 73%).

Method B: To a solution of compound **3** (200 mg, 0.41 mmol) and 2,3,4,6-tetra-*O*-acetyl-α-D-galactopyranosyl trichloroacetimidate **14** (305 mg, 0.62 mmol) in 10 mL of dry dichloromethane under nitrogen was added powdered molecular sieves (4 Å, 0.5 g). The mixture was stirred for 2 h at room temperature, then cooled to -45 °C. $BF_3{\cdot}Et_2O$ (50 μL, 0.41 mmol) was added dropwise. After 1 h the mixture was neutralized with triethylamine, diluted with dichloromethane (10 mL), filtered through celite, and washed with dichloromethane. The combined filtrate and washings were dried with Na_2SO_4, filtered, and concentrated. The syrupy residue was purified by silica gel chromatography using methanol-dichloromethane (1:30, v/v) as eluant to give **15** (235 mg, 70%): mp 160-161 °C; $[\alpha]_D$ -11.6° (*c* 1.0, chloroform); FAB-MS (glycerol) gave *m/z* (ion, relative intensity): 815.3 ($[M+1]^+$, 6.1%), 772.3 ($[M-N_3]^+$, 25.5%); ^{1}H NMR ($CDCl_3$) δ 7.72-7.33 (m, 10H,

aromatic), 6.08 (d, 1H, $J_{2,NH}$ = 8.4 Hz, NH), 5.33 (d, 1H, $J_{3',4'}$ = 3.4 Hz, H-4'), 5.15 (dd, 1H, $J_{2',3'}$ = 10.5 Hz, H-2'), 4.93 (dd, 1H, H-3'), 4.69 (d, 1H, $J_{1',2'}$ = 8.1 Hz, H-1'), 4.67 (d, 1H, $J_{1,2}$ = 9.3 Hz, H-1), 4.17-4.06 (m, 2H, H-6a', H-6b'), 3.94 (dd, 1H, $J_{5,6a}$ = 1.2 Hz, $J_{6a,6b}$ = 10.9 Hz, H-6a), 3.89-3.77 (m, 4H, H-3, H-4, H-6b, H-5'), 3.64 (ddd, 1H, $J_{2,3}$ = 9.1 Hz, H-2), 3.43 (m, 1H, H-5), 2.10, 2.02, 2.00, 1.95, 1.70 (5s, 15H, 4 x OAc, NHAc), 1.05 (s, 9H, $SiCMe_3$); ^{13}C NMR ($CDCl_3$) δ 170.8, 170.4, 170.0, 169.8, 169.1 (5 x C=O), 135.8-127.6 (12C, aromatic), 100.9 (C-1'), 87.8 (C-1), 79.3 (C-4), 76.6 (C-5), 71.6 (C-3), 71.4 (C-5'), 70.7 (C-3'), 68.7 (C-2'), 66.9 (C-4'), 61.3 (C-6), 61.1 (C-6'), 55.9 (C-2), 26.8 ($SiC(\underline{C}H_3)_3$), 23.5 (NHAc), 20.6, 20.5, 20.4, 20.3 (4 x OAc), 19.3 ($Si\underline{C}Me_3$).

Anal. Calcd for $C_{38}H_{50}N_4O_{14}Si$: C, 56.01; H, 6.18; N, 6.88. Found: C, 56.29; H, 6.16; N, 6.81.

***O*-(2,3,4-Tri-*O*-benzoyl-6-*O*-benzyl-β-D-galactopyranosyl)-(1→4)-2-acetamido-6-*O*-*tert*-butyldiphenylsilyl-2-deoxy-β-D-glucopyranosyl azide (16).** Compound **3** (100 mg, 0.21 mmol) was glycosylated with **10** (181 mg, 0.27 mmol) as described in method A to give **16** (168 mg, 78%) as an amorphous mass: $[\alpha]_D$ +56.5° (*c* 1.0, chloroform); FAB-MS (glycerol) gave *m/z* (ion, relative intensity): 1049.4 ($[M+1]^+$, 4.8%); ^1H NMR ($CDCl_3$) δ 8.01-7.12 (m, 30H, aromatic), 5.91 (d, 1H, H-4'), 5.73 (dd, 1H, $J_{2',3'}$ = 10.5 Hz, H-2'), 5.57 (d, 1H, $J_{2,NH}$ = 8.1 Hz, NH), 5.51 (dd, 1H, $J_{3',4'}$ = 3.4 Hz, H-3'), 5.02 (d, 1H, $J_{1',2'}$ = 8.1 Hz, H-1'), 4.74 (d, 1H, $J_{1,2}$ = 9.3 Hz, H-1), 4.52 (AB pattern, 1H, J = 11.8 Hz, H-A of CH_2Ph), 4.40 (AB pattern, 1H, H-B of CH_2Ph), 4.15 (dd, 1H, $J_{5',6a'}$ = 6.3 Hz, $J_{5',6b'}$ = 6.5 Hz, H-5'), 4.03-4.00 (m, 2H, H-3, H-4), 3.79 (dd, 1H, $J_{5,6a}$ = 1.4 Hz, $J_{6a,6b}$ = 11.8 Hz, H- = 1.4 Hz, $J_{6a,6b}$ = 11.8 Hz, H-6a), 3.72-3.67 (m, 2H, H-6b, H-6a'), 3.61 (dd, 1H, $J_{6a',6b'}$ = 9.5 Hz, H-6b'), 3.52 (ddd, 1H, $J_{2,3}$ = 8.9 Hz, H-2), 3.36 (m, 1H, H-5), 2.01 (s, 3H, NHAc), 1.06 (s, 9H, $SiCMe_3$); ^{13}C NMR ($CDCl_3$) δ 170.6, 165.4, 165.4 and 165.1 (4 x C=O), 137.2-127.8 (24C, Aromatic), 100.9 (C-1'), 87.6 (C-1), 78.6 (C-4), 76.6 (C-5), 73.7 ($\underline{C}H_2Ph$), 73.0 (C-5'), 71.6 (C-3'), 71.4 (C-3), 68.8 (C-2'), 68.1 (C-4'), 67.3 (C-6'), 61.5 (C-6), 56.5 (C-2), 26.9 ($SiC(\underline{C}H_3)_3$), 23.6 (NHAc), 19.5 ($Si\underline{C}Me_3$).

Anal. Calcd for $C_{58}H_{60}N_4O_{13}Si$: C, 66.40; H, 5.76; N, 5.34. Found: C, 66.11; H, 5.68; N, 5.32.

***O*-(2,3,4,6-Tetra-*O*-benzoyl-β-D-galactopyranosyl)-(1→4)-2-acetamido-6-*O*-*tert*-butyldiphenylsilyl-2-deoxy-β-D-glucopyranosyl azide (17).** Compound **3** (100 mg, 0.21 mmol) was glycosylated with **11** (185 mg, 0.27 mmol) as described in method A to

give **17** (156 mg, 71%) as an amorphous mass: $[\alpha]_D$ +67° (*c* 1.0, chloroform); FAB-MS (glycerol) gave *m/z* (ion, relative intensity): 1063.3 ($[M+1]^+$, 0.2 %), 1021.3 ($[M-N_3]^+$, 0.2%);^{1}H NMR ($CDCl_3$) δ 8.09-7.14 (m, 30H, aromatic), 5.97 (d, 1H, H-4'), 5.85 (dd, 1H, $J_{2',3'}$ = 10.5 Hz, H-2'), 5.85-5.75 (b, 1H, NH), 5.58 (dd, 1H, $J_{3',4'}$ = 3.5 Hz, H-3'), 5.12 (d, 1H, $J_{1',2'}$ = 8.1 Hz, H-1'), 4.65 (d, 1H, $J_{1,2}$ = 9.1 Hz, H-1), 4.64 (dd, 1H, $J_{5',6a'}$ = 5.0 Hz, H-6a'), 4.49 (dd, 1H, $J_{5',6b'}$ =8.0 Hz, $J_{6a',6b'}$ = 11.6 Hz, H-6b'), 4.15 (dd, 1H, H-5'), 4.10 (dd, 1H, $J_{3,4}$ = 8.9 Hz, H-4), 3.97 (dd, 1H, $J_{2,3}$ = 9.3 Hz, H-3), 3.80 (dd, 1H, $J_{5,6a}$ = 1.3 Hz, H-6a), 3.75 (dd, 1H, $J_{5,6b}$ = 2.2 Hz, $J_{6a,6b}$ = 11.8 Hz, H-6b), 3.64 (ddd, 1H, $J_{2,NH}$ = 8.4 Hz, H-2), 3.35 (ddd, 1H, $J_{4,5}$ = 9.6 Hz, H-5), 2.02 (s, 3H, NHAc), 0.98 (s, 9H, $SiCMe_3$); ^{13}C NMR ($CDCl_3$) δ 170.7, 166.0, 165.4, 165.3, 165.0 (5 x C=O), 135.8-127.8 (36C, Aromatic), 100.8 (C-1'), 87.8 (C-1), 78.2 (C-4), 76.5 (C-5), 72.4 (C-5'), 71.4 (2C, C-3, C-3'), 69.6 (C-2'), 68.1 (C-4'), 62.1 (C-6'), 61.1 (C-6), 56.2 (C-2), 26.7 ($SiC(\underline{C}H_3)_3$), 23.4 (NHAc), 19.3 ($Si\underline{C}Me_3$).

Anal. Calcd for $C_{58}H_{58}N_4O_{14}Si$: C, 65.52; H, 5.50; N, 5.27. Found: C, 65.22; H, 5.47; N, 5.10.

***O*-(2,3,4-Tri-*O*-benzoyl-6-*O*-*tert*-butyldiphenylsilyl-β-D-galactopyranosyl)-(1→4)-2-acetamido-6-*O*-*tert*-butyldiphenylsilyl-2-deoxy-β-D-glucopyranosyl azide (18).** Compound **3**(100 mg, 0.21 mmol) was glycosylated with **12** (220 mg, 0.27 mmol) as described in method A to give **18** as colorless needles (203 mg, 82%): mp 108-110 °C; $[\alpha]_D$ +45.2° (*c* 1.0, chloroform); FAB-MS (glycerol) gave *m/z* (ion, relative intensity): 1154.5 ($[M-HN_3]^+$, 3.2 %); ^{1}H NMR ($CDCl_3$) δ 7.99-7.10 (m, 35H, aromatic), 6.03 (d, 1H, H-4'), 5.73 (dd, 1H, $J_{2',3'}$ = 10.5 Hz, H-2'), 5.61 (d, 1H, $J_{3,NH}$ = 8.3 Hz, NH), 5.59 (dd, 1H, $J_{3',4'}$ = 3.3 Hz, H-3'), 5.06 (d, 1H, $J_{1',2'}$ = 8.0 Hz, H-1'), 4.70 (d, 1H, $J_{1,2}$ = 9.2 Hz, H-1), 4.07 (m, 1H, H-5'), 4.04 (dd, 1H, $J_{4,5}$ = 9.5 Hz, H-4), 3.94 (dd, 1H, $J_{3,4}$ = 8.4 Hz, H-3), 3.88 (dd, 1H, $J_{5',6a'}$ = 6.3 Hz, $J_{6a',6b'}$ = 10.1 Hz, H-6a'), 3.82-3.76 (m, 2H, H-6b', H-6a), 3.74 (dd, 1H, $J_{5,6b}$ = 2.3 Hz, $J_{6a,6b}$ = 11.6 Hz, H-6b), 3.54 (ddd, 1H, $J_{2,3}$ = 9.4 Hz, H-2), 3.32 (m, 1H, H-5), 1.98 (s, 3H, NHAc), 1.11, 1.01 (2s, 18H, 2 x $SiCMe_3$); ^{13}C NMR ($CDCl_3$) δ 170.6, 165.4, 165.3, 165.2 (4 x C=O), 135.9-127.7 (42C, Aromatic), 100.8 (C-1'), 87.7 (C-1), 77.9 (C-4), 76.7 (C-5), 74.3 (C-5'), 71.6 (C-3'), 71.3 (C-3), 69.9 (C-2'), 67.6 (C-4'), 61.3 (C-6), 60.9 (C-6'), 56.4 (C-2), 27.0 ($SiC(\underline{C}H_3)_3$), 26.7 ($SiC(\underline{C}H_3)_3$), 23.5 (NHAc), 19.5 ($Si\underline{C}Me_3$), 19.0 ($Si\underline{C}Me_3$).

Anal. Calcd for $C_{67}H_{72}N_4O_{13}Si_2$: C, 67.20; H, 6.06; N, 4.68. Found: C, 66.46; H, 6.01; N, 4.71.

Allyl *O*-(2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl)-(1→4)-2-acetamido-6-*O*-*tert*-butyldiphenylsilyl-2-deoxy-β-D-glucopyranoside (19). Compound **5** (200 mg, 0.40 mmol) was glycosylated with **14** (296 mg, 0.60 mmol) as described in method B to give **19** as a semi-crystalline solid (226 mg, 68%): mp 179-180 °C; $[\alpha]_D$ -3.1° (*c* 1.0, chloroform); FAB-MS (glycerol) gave *m/z* (ion, relative intensity): 830.4 ($[M+1]^+$, 0.7%); ^{1}H NMR ($CDCl_3$) δ 7.70-7.30 (m, 10H, aromatic), 6.06 (d, 1H, $J_{2,NH}$ = 8.2 Hz, NH), 5.90-5.83 (m, 1H, $CH_2C\underline{H}=CH_2$), 5.32 (d, 1H, $J_{3',4'}$ = 3.4 Hz, H-4'), 5.21 (dd, 1H, J_{gem} = 1.5 Hz, J_{trans} = 17.1 Hz, $CH_2CH=C\underline{H}_2$), 5.15-5.11 (m, 2H, H-2', $CH_2CH=C\underline{H}_2$), 4.93 (dd, 1H, $J_{2',3'}$ = 10.4 Hz, H-3'), 4.74 (d, 1H, $J_{1,2}$ = 7.9 Hz, H-1), 4.68 (d, 1H, $J_{1',2'}$ = 8.1 Hz, H-1'), 4.29 (dd, 1H, J = 5.1 Hz, J = 12.9 Hz, $OC\underline{H}_2CH=$), 4.12 (d, 2H, $J_{5',6'}$ = 6.6 Hz, H-6a', H-6b'), 4.03 (dd, 1H, $OC\underline{H}_2CH=$), 3.98 (dd, 1H, $J_{3,4}$ = 8.6 Hz, H-3), 3.92-3.82 (m, 2H, H-5', H-6a), 3.80-3.78 (m, 2H, H-4, H-6b), 3.53 (ddd, 1H, $J_{2,3}$ = 9.3 Hz, H-2), 3.40 (m, 1H, H-5), 2.13, 2.03, 2.01, 1.96, 1.69 (5s, 15H, 4 x OAc, NHAc), 1.05 (s, 9H, $SiCMe_3$); ^{13}C NMR ($CDCl_3$) δ 170.6, 170.3, 170.0, 169.8, 169.0 (5 x C=O), 135.9-127.6 (12C, aromatic), 133.9 ($-\underline{C}H=CH_2$), 117.2 ($-CH=\underline{C}H_2$), 100.9 (C-1'), 99.0 (C-1), 79.8 (C-4), 74.5 (C-5), 71.4 (C-3), 71.2 (C-5'), 70.7 (C-3'),69.1 ($-O\underline{C}H_2CH=$), 68.8 (C-2'), 66.9 (C-4'), 61.7 (C-6'), 61.1 (C-6), 56.4 (C-2), 26.8 ($SiC(\underline{C}H_3)_3$), 23.5 (NHAc), 20.6, 20.5, 20.4, 20.2 (4 x OAc), 19.3 ($Si\underline{C}Me_3$).

Anal. Calcd for $C_{41}H_{55}NO_{15}Si$: C, 59.33; H, 6.88; N, 1.69. Found: C, 59.10; H, 6.64; N, 1.81.

General procedure for the acetylation of disaccharides 15-19. Disaccharide (100 mg) was dissolved in pyridine (1 mL) and acetic anhydride (0.75 mL) was added. The reaction solution was stirred at room temperature for 2 h. The mixture was concentrated under reduced pressure. The crude product was purified by column chromatography using methanol-dichloromethane (3%, v/v) as eluant to give 3-*O*-acetyl disaccharide quantitatively.

***O*-(2,3,4,6-Tetra-*O*-acetyl-β-D-galactopyranosyl)-(1→4)-2-acetamido-3-*O*-acetyl-6-*O*-*tert*-butyldiphenylsilyl-2-deoxy-β-D-glucopyranosyl azide (15a).** $[\alpha]_D$ -31° (*c* 1.0, chloroform); ^{1}H NMR ($CDCl_3$) δ 7.71-7.34 (m, 10H, aromatic), 5.97 (d, 1H, $J_{2,NH}$ =

9.4 Hz, NH), 5.29 (d, 1H, $J_{3',4'}$ = 3.5 Hz, H-4'), 5.02-4.97 (m, 2H, H-2', H-3), 4.88 (dd, 1H, $J_{2',3'}$ = 10.3 Hz, H-3'), 4.76 (d, 1H, $J_{1',2'}$ = 8.0 Hz, H-1'), 4.44 (d, 1H, $J_{1,2}$ = 9.2 Hz, H-1), 4.17 (dd, 1H, $J_{3,4}$ = 9.3 Hz, H-4), 4.13-4.05 (m, 3H, H-2, H-6a', H-6b'), 3.95 (dd, 1H, $J_{5,6a}$ = 1.2 Hz, $J_{6a,6b}$ = 11.6 Hz, H-6a), 3.87 (dd, 1H, $J_{5,6b}$ = 2.3 Hz, H-6b), 3.73 (dd, 1H, $J_{5',6a'}$ = $J_{5',6b'}$ = 6.6 Hz, H-5'), 3.37 (ddd, 1H, $J_{4,5}$ = 9.5 Hz, H-5), 2.11, 2.05, 2.04, 1.97, 1.95, 1.74 (6s, 18H, 5 x OAc, NHAc), 1.06 (s, 9H, $SiCMe_3$).

***O*-(2,3,4-Tri-*O*-benzoyl-6-*O*-benzyl-β-D-galactopyranosyl)-(1→4)-2-acetamido-3-*O*-acetyl-6-*O*-*tert*-butyldiphenylsilyl-2-deoxy-β-D-glucopyranosyl azide (16a).** $[\alpha]_D$ +20.2° (*c* 1.0, chloroform); ^{1}H NMR ($CDCl_3$) δ 8.10-6.63 (m, 30H, aromatic), 6.86 (d, 1H, $J_{2,NH}$ = 9.7 Hz, NH), 5.92 (d, 1H, $J_{3',4'}$ = 3.3 Hz, H-4'), 5.62 (dd, 1H, $J_{2',3'}$ = 10.4 Hz, H-2'), 5.32 (dd, 1H, H-3'), 5.13 (dd, 1H, $J_{2,3}$ = 10.4 Hz, H-3), 5.07 (d, 1H, $J_{1',2'}$ = 8.1 Hz, H-1'), 4.72 (d, 1H, $J_{1,2}$ = 9.3 Hz, H-1), 4.53 (AB pattern, 1H, J = 11.8 Hz, H-A of CH_2Ph), 4.47 (AB pattern, 1H, H-B of CH_2Ph), 4.36 (dd, 1H, $J_{4,5}$ = 9.4 Hz, H-4), 4.24 (ddd, 1H, H-2), 4.01 (dd, 1H, $J_{5',6a'}$ = $J_{5',6b'}$ = 6.6 Hz, H-5'), 3.70-3.56 (m, 4H, H-6a, H-6b, H-6a', H-6b'), 2.95 (ddd, 1H, $J_{5,6a}$ < 1 Hz, $J_{5,6b}$ < 1 Hz, $J_{4,5}$ = 9.7 Hz, H-5), 2.03, 2.00 (2s, 6H, OAc, NHAc), 1.11 (s, 9H, $SiCMe_3$).

***O*-(2,3,4,6-Tetra-*O*-benzoyl-β-D-galactopyranosyl)-(1→4)-2-acetamido-3-*O*-acetyl-6-*O*-*tert*-butyldiphenylsilyl-2-deoxy-β-D-glucopyranosyl azide (17a).** $[\alpha]_D$ +24.4° (*c* 1.0, chloroform); ^{1}H NMR ($CDCl_3$) δ 8.12-6.64 (m, 30H, aromatic), 6.78 (d, 1H, $J_{2,NH}$ = 9.5 Hz, NH), 5.91 (d, 1H, $J_{3',4'}$ = 3.4 Hz, H-4'), 5.71 (dd, 1H, $J_{2',3'}$ = 10.4 Hz, H-2'), 5.38 (dd, 1H, H-3'), 5.20 (dd, 1H, $J_{2,3}$ = 10.5 Hz, H-3), 5.12 (d, 1H, $J_{1',2'}$ = 8.1 Hz, H-1'), 4.72 (d, 1H, $J_{1,2}$ = 9.4 Hz, H-1), 4.64 (dd, 1H, $J_{5',6a'}$ = 5.1 Hz, $J_{6a',6b'}$ = 11.6 Hz, H-6a'), 4.39-4.34 (m, 2H, H-4, H-6b'), 4.23 (ddd, 1H, H-2), 4.16 (dd, 1H, $J_{5',6b'}$ = 8.1 Hz, H-5'), 3.63 (dd, 1H, $J_{5,6a}$ < 1 Hz, $J_{6a,6b}$ = 11.3 Hz, H-6a), 3.53 (dd, 1H, $J_{5,6b}$ = 1.6 Hz, H-6b), 2.99 (ddd, 1H, $J_{4,5}$ = 9.7 Hz, H-5), 2.12, 2.03 (2s, 6H, OAc, NHAc), 0.97 (s, 9H, $SiCMe_3$).

***O*-(2,3,4-Tri-*O*-benzoyl- 6 - *O* - *tert*-butyldiphenylsilyl-β-D-galactopyranosyl)-(1→4)-2-acetamido-3-*O*-acetyl-6-*O*-*tert*-butyldiphenylsilyl-2-deoxy-β-D-glucopyranosyl azide (18a).** $[\alpha]_D$ +26.2° (*c* 1.0, chloroform); ^{1}H NMR ($CDCl_3$) δ 7.98-6.88 (m, 35H, aromatic), 6.07 (d, 1H, $J_{2,NH}$ = 8.1 Hz, NH), 6.06 (d, 1H, H-4'), 5.57 (dd, 1H, $J_{2',3'}$ = 10.4 Hz, H-2'), 5.46 (dd, 1H, $J_{3',4'}$ = 3.4 Hz, H-3'), 5.03 (d, 1H, $J_{1',2'}$ = 8.0 Hz, H-1'), 4.98 (dd, 1H, $J_{3,4}$ = 9.2 Hz, H-3), 4.46 (d, 1H, $J_{1,2}$ = 9.2 Hz, H-1), 4.25 (dd, 1H, $J_{4,5}$ = 9.5 Hz, H-4),

4.06 (ddd, 1H, $J_{2,3}$ = 10.1 Hz, H-2), 3.96 (dd, 1H, $J_{5',6a'}$ = 5.5 Hz, $J_{5',6b'}$ = 8.8 Hz, H-5'), 3.78 (dd, 1H, $J_{6a',6b'}$ = 9.7 Hz, H-6a'), 3.70 (dd, 1H, $J_{5,6a}$ = 1.4 Hz, $J_{6a,6b}$ = 12.0 Hz, H-6a), 3.64-3.60 (m, 2H, H-6b', H-6b), 3.06 (m, 1H, H-5), 1.96, 1,76 (2s, 6H, OAc, NHAc), 1.11, 0.99 (2s, 18H, 2 x $SiCMe_3$).

Allyl *O*-(2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl)-(1→4)-2-acetamido-3-*O*-acetyl-6-*O*-*tert*-butyldiphenylsilyl-2-deoxy-β-D-glucopyranoside (19a). $[\alpha]_D$ -16.2° (*c* 1.0, chloroform); ^1H NMR ($CDCl_3$) δ 7.74-7.34 (m, 10H, aromatic), 5.87-5.80 (m, 1H, C<u>H</u>=CH_2), 5.59 (d, 1H, $J_{2,NH}$ = 9.4 Hz, NH), 5.30 (d, 1H, $J_{3',4'}$ = 3.2 Hz, H-4'), 5.23 (dd, 1H, J_{gem} = 1.5 Hz, J_{trans} = 17.3 Hz, -CH=C<u>H</u>$_2$), 5.15 (dd, 1H, J_{cis} = 11.4 Hz, -CH=C<u>H</u>$_2$), 5.04 (dd, 1H, $J_{2',3'}$ = 10.3 Hz, H-2'), 4.99 (dd, 1H, $J_{2,3}$ = 9.7 Hz, $J_{3,4}$ = 8.8 Hz, H-3), 4.92 (dd, 1H, H-3'), 4.74 (d, 1H, $J_{1',2'}$ = 8.0 Hz, H-1'), 4.41 (d, 1H, $J_{1,2}$ = 7.8 Hz, H-1), 4.41-4.05 (m, 4H, H-2, H-4, H-6a', H-6b'), 3.94 (dd, 1H, $J_{5,6a}$ = 2.3 Hz, $J_{6a,6b}$ = 11.8 Hz, H-6a), 3.88 (dd, 1H, $J_{5,6b}$ = 0.8 Hz, H-6b), 3.75 (dd, 1H, $J_{5',6a'}$ = $J_{5',6b'}$ = 6.7 Hz, H-5'), 3.31 (ddd, 1H, $J_{4,5}$ = 8.7 Hz, H-5), 2.12, 2.04, 2.03, 1.96, 1.96, 1.78 (6s, 18H, 5 x OAc, NHAc), 1.06 (s, 9H, $SiCMe_3$).

***O*-(2,3,4-Tri-*O*-benzoyl – 6 - *O*-*tert*-butyldiphenylsilyl-β-D-galactopyranosyl)-(1→4)-*O*-[(2,3,4-tri-*O*-benzyl-α-L-fucopuranosyl)-(1→3)] - 2-acetamido-6-*O*-*tert*-butyl-diphenylsilyl-2-deoxy-β-D-glucopyranosyl azide (21).** To a solution of **18** (100 mg, 0.084 mmol) and ethyl 2,3,4-tri-*O*-benzyl-1-thio-α-L-fucopyranoside **20** (60 mg, 0.125 mmol) in 5 mL of 5:1 benzene/dichloromethane was added powdered molecular sieves (4Å, 100 mg). The mixture was stirred for 2 h at room temperature under nitrogen. DMTST (70 mg, 0.342 mmol) was added to the stirred mixture at 0 °C. After 1 h, TLC (2% MeOH in CH_2Cl_2) showed complete conversion of the donor. Then triethylamine (100 μL) and methanol (200 μL) were added to the reaction mixture which was stirred for an additional 25 min. The reaction mixture was filtered through celite, and washed with dichloromethane. The combined filtrate and washings were successively washed with saturated sodium bicarbonate solution, dried (Na_2SO_4), filtered, and concentrated. The residue was purified by silica gel chromatography using methanol-dichloromethane as eluant (1:30, v/v) to afford trisaccharide **21** (105 mg, 78%): $[\alpha]_D$ -15.1° (*c* 1.0, chloroform); FAB-MS (glycerol) gave *m/z* (ion, relative intensity): 1571.7 ($[M+1-N_3]^+$, 4.8 %); ^1H NMR ($CDCl_3$) δ (ppm): 8.04-6.82 (m, 50H, aromatic H), 6.13 (dd, 1H, $J_{4',5'}$ = 0.9

Hz, H-4'), 5.95 (d, 1H, $J_{2,NH}$ = 7.9 Hz, NH), 5.65 (dd, 1H, $J_{2',3'}$ = 10.5 Hz, H-2'), 5.59 (dd, 1H, $J_{3',4'}$ = 2.4 Hz, H-3'), 5.25 (d, 1H, $J_{1'',2''}$ = 3.5 Hz, H-1''), 5.09 (d, 1H, $J_{1',2'}$ = 7.8 Hz, H-1'), 4.91-4.50 (m, 4H, 2 x CH_2Ph), 4.42 (s, 2H, CH_2Ph), 4.28 (m, 2H, $J_{1,2}$ = 9.0 Hz, H-1, H-5''), 4.21 (dd, 1H, $J_{4,5}$ = 8.0 Hz, H-4), 4.08 (dd, 1H, $J_{2'',3''}$ = 10.2 Hz, H-2''), 4.02-3.95 (m, 2H, H-5', H-3), 3.90 (dd, 1H, $J_{5,6a}$ = 2.4 Hz, $J_{6a,6b}$ = 11.7 Hz, H-6a), 3.86-3.84 (m, 2H, H-6a', H-6b'), 3.85-3.75 (m, 2H, H-6b, H-3''), 3.64 (dd, 1H, $J_{2,3}$ = 9.0 Hz, H-2), 3.61 (d, 1H, $J_{4'',5''}$ < 1.0 Hz, H-4''), 3.04 (m, 1H, H-5), 1.76 (s, 3H, NHAc), 1.12 (s, 9H, $SiCMe_3$), 1.07 (d, 3H, $J_{5'',6''}$ = 6.6 Hz, H-6''), 0.95 (s, 9H, $SiCMe_3$); ^{13}CNMR ($CDCl_3$) δ (ppm): 170.3, 165.5, 165.3, 165.2 (4 x C=O), 138.9-127.2 (60C, aromatic), 99.6 (C-1'), 97.4 (C-1''), 88.1 (C-1), 79.8 (C-3''), 78.3 (C-4''), 77.5 (2C, C-5, C-2''), 75.3 (CH_2Ph), 75.1 (C-5'), 74.2 (CH_2Ph), 73.7 (C-4), 73.5 (C-3), 72.2 (CH_2Ph), 71.6 (C-3'), 70.3 (C-2'), 67.5 (C-4), 67.0 (C-5''), 61.5 (C-6), 60.3 (C-6'), 55.2 (C-2), 26.9 ($SiC(\underline{C}H_3)_3$), 26.6 ($SiC(\underline{C}H_3)_3$), 23.2 (NHAc), 19.3 ($Si\underline{C}Me_3$), 18.9 ($Si\underline{C}Me_3$), 16.9 (C-6'').

Anal. Calcd for $C_{94}H_{100}N_4O_{17}Si_2$: C, 69.95; H, 6.24; N, 3.47. Found: C, 69.84; H, 6.27; N, 3.71.

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