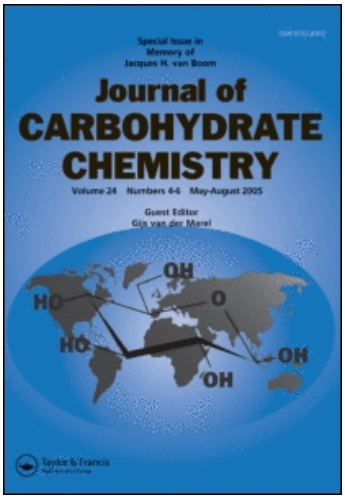

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OLIGOSACCHARIDE SYNTHESIS *VIA* ELECTROPHILE-INDUCED ACTIVATION OF GLYCOSYL-*N*-ALLYLCARBAMATES[1]

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ABSTRACT

Glycosyl-*N*-allyl carbamates, obtained by reaction of anomerically unprotected saccharides with allyl isocyanate, can be activated by an electrophile-induced cyclisation and reacted with glycosyl acceptors to form the corresponding oligosaccharides. By this method the mucin core 2 trisaccharide[2] has successfully been synthesized. Due to the mild glycosylation conditions even 1-*O*-acetyl protected glycosyl acceptors can be used. This was demonstrated in the synthesis of a 1,6-linked glucosyl trisaccharide whereby a reptitious glycosylation strategy could be applied.

INTRODUCTION

Carbohydrates and glycoconjugates are of significant importance in biological systems, e.g., as epitopes in cell-cell recognition, as tumor associated antigens or as linkers in infectious, immunological and inflammatory processes.[3] Therefore, these compounds are of particular interest in biochemical and pharmaceutical research. Glycoconjugates isolated from biological sources often are microheterogeneous so that pure compounds are difficult to obtain. For that reason the chemical synthesis of glycosides is a challenging task. In addition to established glycosylation methods like the Koenigs-Knorr glycosylation, the thioglycoside- or trichloroacetimidate-method[4] alternative procedures that start from stable compounds and proceed under mild activation conditions are still of interest. The observation of an unexpected

instability of the *N*-allyloxycarbonyl group[5] towards soft electrophiles in glycosylations of serine peptides using thioglycosides as glycosyl donors stimulated the development of a glycosylation method which is based on an electrophile-induced lactonisation of anomeric alkenoic esters.[6] The required soft electrophiles causing the remote activation of the alkene side chain are similar to those used by Fraser-Reid et al.[7] for the activation of pentenyl glycosides. In order to achieve a rapid, efficient access to glycosyl donors and to improve their activity, especially when 2-*O*-acyl compounds are employed, we have applied the anomeric *N*-allylcarbamates.[8] These compounds are readily obtained from anomerically unprotected carbohydrates by reaction with commercially available allyl isocyanate. The formation of *O*-glycosyl *N*-allylcarbamates is carried out in dichloromethane and requires catalysis by bases, such as *N*-ethyldiisopropylamine ("Hünig's base"). While the carbamates are stable compounds, they can be efficiently activated by soft electrophiles, e.g., methyl-bis(methylthio)-sulfonium hexachloroantimonate (TMTSB).[9] The addition of TMTSB to the allylic double bond results in the formation of a bridged thiiranium ion which attacks the carbonyl-oxygen and initiates intramolecular cyclisation. The so formed oxazolidinone behaves as an efficient leaving group and the remaining glycosyl cations react with glycosyl acceptors to give the corresponding glycosides. As a rule, *N*-allylcarbamates are less stable towards nucleophiles than pentenyl glycosides and thioglycosides. However, they are more easily activated by soft electrophiles, so that *O*-acetyl protected allylcarbamates are efficient glycosyl donors in stereoselective formations of 1,2-*trans*-glycosides.

We here describe the potential of this glycosylation method in the synthesis of the mucin core trisaccharide **15**. In this context a wide variety of protection groups, e.g. acetyl, benzyl, silyl, or benzylidene groups have been used without being affected during the glycosylation reactions.

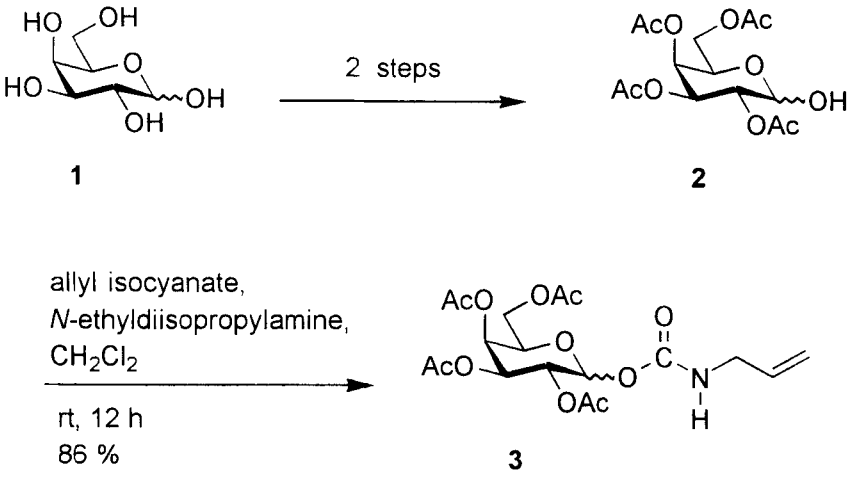
The easy preparation of the *O*-glycosyl *N*-allyl carbamates and the mild glycosylation conditions led to the idea of a repetitious glycosylation of 1-*O*-acyl acceptors. The so obtained 1-*O*-acyl saccharides can subsequently be transformed to *O*-glycosyl *N*-allyl carbamate donors for the next glycosylation. By use of hydrazine acetate anomerically unprotected carbohydrates are obtained, which are then transformed to glycosyl-*N*-allylcarbamates by base-catalyzed reaction with allyl isocyanate. This repetitious glycosylation method will be demonstrated in the synthesis of trisaccharide **20**.

Simple Synthesis of Methyl-Bis(methylthio)-Sulfonium Hexachloro-antimonate (TMTSB). TMTSB can be synthesized by two different methods.[9] The simplified procedure

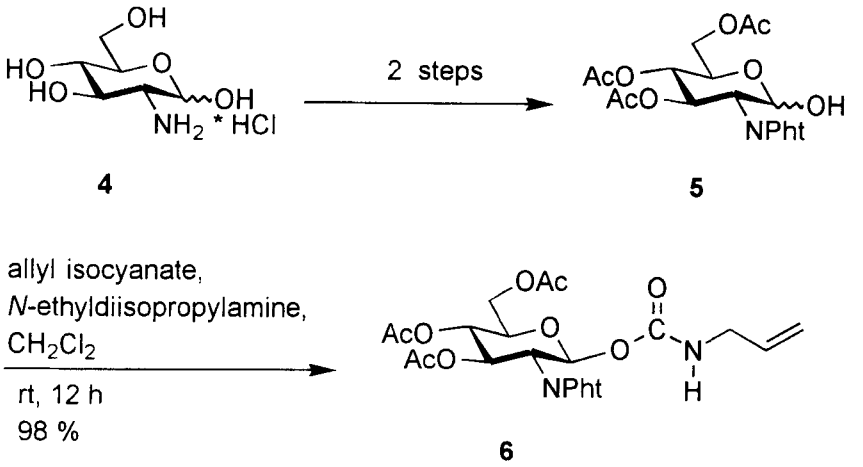
proposed by R. Weiss and C. Schlierf was modified for the synthesis of TMTSB used in the following glycosylation reactions: TMTSB was prepared from antimony pentachloride and dimethyl disulfide in a one pot reaction, whereby the *in situ*-formation of methanesulfenyl chloride is assumed. By addition of dry ether the product precipitated as slightly yellowish, fine crystals. To obtain a promotor with high activity, the precipitate was washed twice with dry diethyl ether and dried *in vacuo*. At -25 °C the activity of the electrophile is preserved for months.

Synthesis of the *O*-Glycosyl *N*-Allyl Carbamate Donors. 2,3,4,6-Tetra-*O*-acetyl-1-*O*-(*N*-allyl)carbamoyl-α/β-D-galactose **3** was synthesized from the anomerically unprotected galactose derivative **2**[10] by addition of allyl isocyanate under catalysis of *N*-ethyldiisopropylamine.[8] The anomerically deprotected galactose derivative **2** was obtained in high yield from peracetylated galactose by cleavage of the anomeric acetyl group with hydrazine acetate (Scheme 1). 3,4,6-Tri-*O*-acetyl-1-*O*-(*N*-allyl)carbamoyl-2-deoxy-2-phthalimido-β-D-glucopyranose **6** was synthesized from the 1,3,4,6-tetra-*O*-acetyl-2-deoxy-2-phthalimido-α/β-D-glucopyranose[11] by removal of the anomeric acetyl group with hydrazine acetate and subsequent reaction with allyl isocyanate (Scheme 2). 2,3,4-Tri-*O*-acetyl-1-*O*-(*N*-allyl)carbamoyl-6-*O*-benzyl-β-D-galactopyranose **8** was synthesized from 1,2,3,4-Tetra-*O*-acetyl-6-*O*-benzyl-α/β-D-galactopyranose[12] which can be obtained in four steps from galactose, by conversion to the diisopropylidene derivative, benzylation, subsequent hydrolysis of the isopropylidene protecting groups and acetylation with acetic anhydride in pyridine. The *O*-glycosyl *N*-allylcarbamate **8** was also obtained by reaction with hydrazine acetate and subsequent addition of allyl isocyanate (Scheme 3).

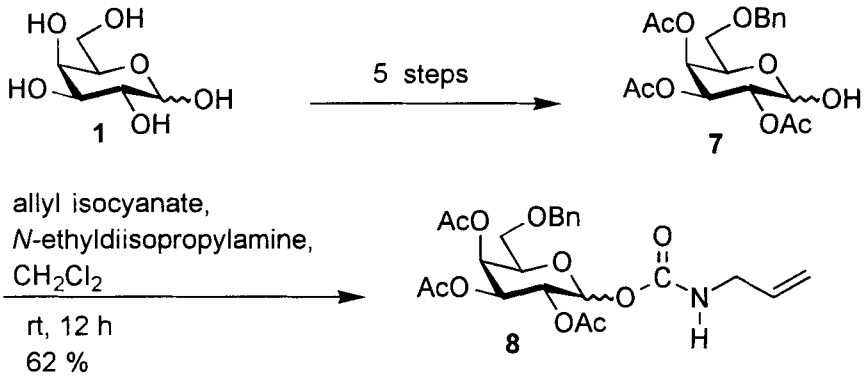
Synthesis of the Mucin Core Structure 15. The azidogalactose derivative **9**[13] was obtained from galactose by synthesis of galactal, subsequent azidonitration and hydrolysis of the anomeric nitrate with sodium nitrite in dioxane/water. Reaction of the anomerically unprotected azido galactose derivative **9** with thexyldimethylsilyl chloride led to azido-galactose derivative **10**. After Zemplén transesterification with sodium methanolate in methanol the deacetylated product **11** was isolated and subsequently converted into the benzylidene derivative **12** with benzaldehyde dimethyl acetal. This acceptor was glycosylated with *O*-glycosyl *N*-allyl carbamate donor **8** by addition of TMTSB in dry dichloromethane to the T-antigen disaccharide **13** in a yield of 67 %. It is necessary that the crude product is purified by flash chromatography immediately after work up. Otherwise the Lewis acidic conditions lead to a decrease in yield due to partial hydrolysis of the benzylidene group. By an



Scheme 1 . Synthesis of 2,3,4,6-Tetra-*O*-acetyl-1-*O*-(*N*-allyl)carbamoyl-α/β-D-galactopyranose



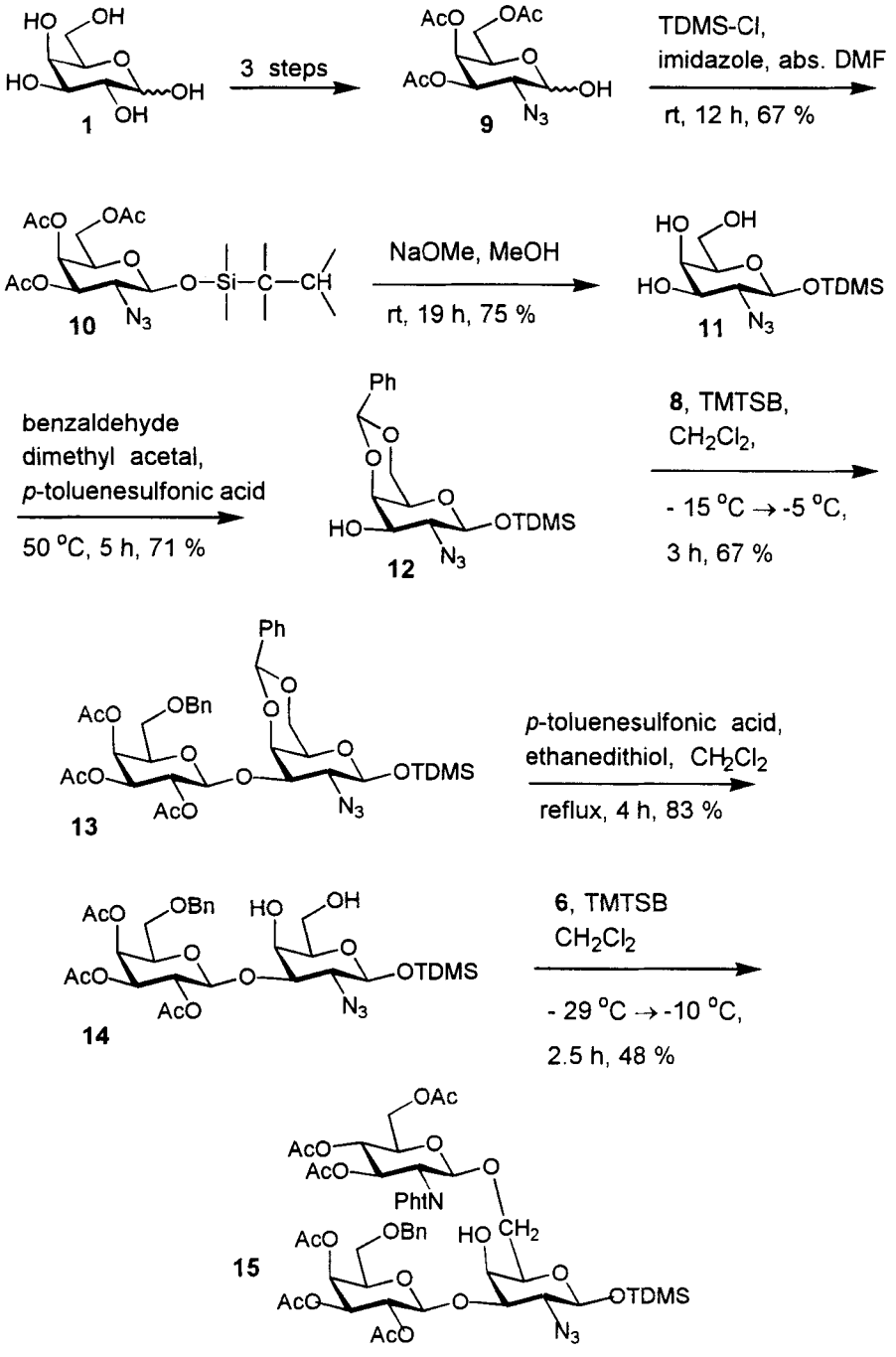
Scheme 2 . Synthesis of 3,4,6-Tri-*O*-acetyl-1-*O*-(*N*-allyl)carbamoyl-2-deoxy-2-phthalimido-β-D-glucopyranose



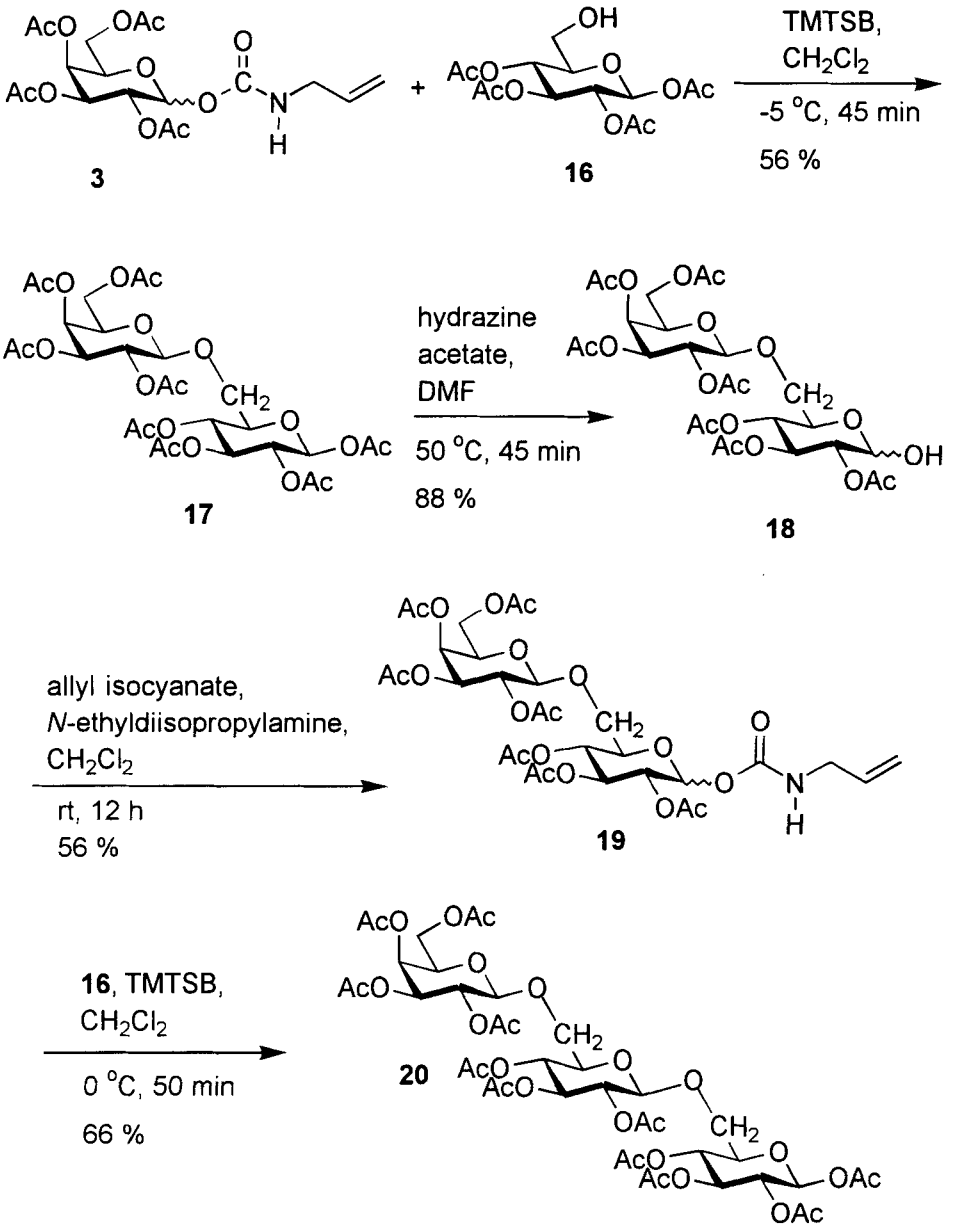
Scheme 3 . Synthesis of 3,4,6-Tri-*O*-acetyl-1-*O*-(*N*-allyl)carbamoyl-6-*O*-benzyl-α/β-D-galactopyranose

acid-catalyzed transacetalisation with 1,2-ethanedithiol in dichloromethane, the 4,6-*O*-benzylidene protecting group was cleaved in high yield. Although an excess of ethanedithiol was applied, a small amount of starting material was recovered. Glycosylation of the disaccharide acceptor **14** with *O*-glycosyl donor **6** by activation with TMTSB gave the mucin core structure **15** as target molecule in 48 % (Scheme 4). In all cases, the glycosylation reactions proceeded with complete stereo- and chemoselectivity. The reaction conditions were so mild that none of the various other functionalities were affected.

Repetitious Glycosylation to Yield the Trisaccharide 20. The 1,2,3,4-Tetra-*O*-acetyl-β-D-glucopyranose acceptor **16**[14] was synthesized from glucose by protecting the 6-OH group as a triphenylmethyl ether, subsequent acetylation with acetic anhydride in pyridine, and cleavage of the trityl group with HBr in glacial acetic acid. Glycosylation of the glucopyranose acceptor **16** with donor **3** under promotion by TMTSB gave disaccharide **17** in 56 % yield. Anomeric deprotection of **17** was carried out by cleavage of the 1-acetyl group with hydrazine acetate to give **18**. Subsequently, reaction of **18** with allyl isocyanate gave the disaccharide allyl carbamate donor **19** which was applied in the next glycosylation reaction. With 1,2,3,4-tetra-*O*-acetyl-β-D-glucopyranose **16** as acceptor, trisaccharide **20** synthesized in 66 % yield (Scheme 5). This sequence demonstrates that even 1-*O*-acetyl protected saccharides can be used as glycosyl acceptors in a repetitious synthesis of oligosaccharides if TMTSB promoted activation of anomeric *N*-allyl carbamates is used as the glycosylation method. Because of the mild reaction conditions a complicated pattern of different orthogonal protecting groups is not



Scheme 4 . Synthesis of Mucin Core Structure Trisaccharide 15



Scheme 5 . Synthesis of Trisaccharide 20

required. In this context it should be mentioned that *O*-glycosyl-*N*-allylcarbamates can also be activated using hard Lewis acids like boron trifluoride.[15] However, the repetitious glycosylation described here can only be achieved using the mild activation with the soft electrophile TMTSB which does not affect the 1-*O*-acetyl group. There is hardly any other glycosylation method known which tolerates 1-*O*-acetyl protection in the glycosyl acceptor.[16]

EXPERIMENTAL

General methods. Optical rotations were measured with a Perkin-Elmer-241 polarimeter. ^{1}H NMR (200 MHz) spectra and ^{13}C NMR (50.3 MHz) spectra were recorded on a Bruker-AC-200, ^{1}H NMR (400 MHz) and ^{13}C NMR (100.6 MHz) spectra on a Bruker-AM 400. Melting points are uncorrected. Flash chromatography was carried out on silica gel 30 - 60 μm purchased from J. T. Baker, Gross Gerau, Germany. Preparative reversed phase HPLC was performed on a Spherisorb ODS II, 250 x 40 mm column (Bischoff, Leonberg, Germany) with a flow rate of 20 mL min^{-1}. The FAB mass spectra were recorded on a Finnigan-MAT-95 with 3-nitrobenzyl alcohol (nba) as matrix. Analytical TLC plates (silica gel 60-F_{254}) were purchased from E. Merck, Darmstadt, Germany. Visualization was achieved by spraying with a solution of 0.2 % *p*-methoxyphenol in ethanol / 2 N H_2SO_4 (1/1, v/v) and heating. Dichloromethane was distilled from calcium hydride.

General Procedure I for the Cleavage of Anomeric Acetyl Protecting Groups with Hydrazine Acetate.[10] The 1-acetylated saccharide (10 mmol) was dissolved in 100 mL of dry DMF and 1.25 equiv of hydrazine acetate were added at 50 °C. The solution was stirred for 1 h at 50 °C (TLC-monitoring). After complete conversion of the starting material the mixture was diluted with 400 mL of ethyl acetate. The organic layer was washed three times with 100 mL of water, 100 mL of 0.2 mol HCl, 100 mL of saturated $NaHCO_3$ solution and 100 mL of water. The organic layer was dried with $MgSO_4$ and concentrated *in vacuo*. A small amount of the product was purified by flash chromatography and identified by NMR, the rest was used directly without further purification in the next reaction step.

General Procedure II for the Synthesis of *O*-Glycosyl *N*-Allyl Carbamates.[8] The anomerically unprotected saccharide derivative (10 mmol) was dissolved in 200 mL of dichloromethane, then 3 equiv of *N*-ethyldiisopropylamine and 2 equiv of allyl isocyanate were added. The reaction solution was stirred for 16 h (TLC-monitoring). Subsequently the solution was diluted with 200 mL of dichloromethane and the organic layer was washed three times

with 100 mL of water, 100 mL of 0.2 mol HCl, 100 mL of saturated $NaHCO_3$ solution and100 mL of water. The solution was dried with $MgSO_4$, concentrated *in vacuo*, and the crude product was purified by flash chromatography.

General Procedure III for the Glycoside Synthesis *via* TMTSB-Induced Activation of *N*-Allyl Carbamates. Under an argon atmosphere 2 mmol of the glycosyl donor and 1 mmol of the acceptor molecule were dissolved in 40 mL of dry dichloromethane, molecular sieves (4 Å, powder) were added and the mixture was stirred for 1 h at rt. Then 1.2 g (2.5 mmol) of TMTSB were added at the temperature quoted for each compound. The reaction mixture was warmed up slowly and the reaction was quenched after 1-2 h (TLC-control) by addition of 2 mL triethylamine. The molecular sieves were filtered off and the organic phase was diluted with 400 mL of chloroform. The organic layer was washed three times with 100 mL of water, 100 mL of 0.2 mol HCl, 100 mL of saturated $NaHCO_3$ and 100 mL of water. The organic phase was dried with $MgSO_4$ and concentrated *in vacuo*. The crude product was purified by flash chromatography.

2,3,4,6-Tetra-*O*-acetyl-α/β-D-galactopyranose (2).[10,17] General procedure I; eluent for flash chromatography: ethyl acetate/petroleum ether (2:1, v/v); yield 3.38 g (97 %).

3,4,6-Tri-*O*-acetyl-2-deoxy-2-phthalimido-α/β-D-glucopyranose (5).[18] General procedure I; eluent for flash chromatography: ethyl acetate/petroleum ether (1:2, v/v); yield 3.13 g (72 %).

2,3,4-Tri-*O*-acetyl-6-benzyl-α/β-D-galactopyranose (7). General procedure I; eluent for flash chromatography: ethyl acetate/petroleum ether (1:2, v/v); yield 2.54 g (64 %).

2,3,4,6-Tetra-*O*-acetyl-1-*O*-(*N*-allyl)carbamoyl-α/β-D-galactopyranose (3). General procedure II; eluent for flash chromatography: ethyl acetate/petroleum ether (1:2, v/v); yield 3.71 g (86 %), (α:β = 1:4.2); colorless crystals; mp 124 °C; $[\alpha]^{22}_D$ +14.7° (*c* 0.94, MeOH); R_f = 0.18 (ethyl acetate/petroleum ether = 2:1); 400 MHz ^{1}H NMR ($CDCl_3$) [β-anomer] δ 5.89 - 5.69 (m, 1H, C<u>H</u>=CH_2), 5.62 (d, 1H, $J_{1,2}$ = 8.2 Hz, 1-Hβ), 5.39 (d, 1H, $J_{4,3}$ = 3.2 Hz, 4-H), 5.33 - 5.02 (m, 5H, 2-H, 3-H, NH, CH=C<u>H</u>$_2$), 4.16 - 4.00 (m, 3H, 5-H, 6-Ha, 6-Hb), 3.79 (m, 2H, NH-C<u>H</u>$_2$-), 2.13, 2.02, 2.01, 1.96 (4s, 12 H, -CH_3); [α-anomer] δ = 6.22 (s, 1H, 1-Hα), 5.76 (m, 1H, C<u>H</u>=CH_2), 5.24 (m, 6H, 2-H, 3-H, 4-H, NH, CH=C<u>H</u>$_2$), 4.01 (m, 5H, 5-H, 6-Ha, 6-Hb, NH-C<u>H</u>$_2$-), 2.09, 1.97, 1.93 (3s, 12H, 4 -CH_3); 100.6 MHz ^{13}C NMR ($CDCl_3$) [β-anomer] δ 170.27, 170.07, 169.88, 169.55 (C=O), 153.54 (carbamate), 133.47 (<u>C</u>H=CH_2), 116.55 (CH=<u>C</u>H$_2$), 93.18 (C-1β), 71.29, 72.74, 67.76, 66.73 (C-2, C-3, C-4, C-

5), 60.87 (C-6), 43.38 (NH-CH_2-), 20.65, 20.58, 20.47 (-CH_3); [α-anomer] δ 170.19, 170.01, 169.95, 169.68 (C=O), 153.76 (carbamate), 133.77 (C$\underline{H}$=CH_2), 116.26 (CH=C$\underline{H}_2$), 90.42 (C-1α), 68.28, 67.45, 67.35, 66.49, (C-2, C-3, C-4, C-5), 61.22 (C-6), 43.29 (NH-CH_2-), 20.41 (-CH_3).

Anal.Calcd for $C_{14}H_{25}NO_{11}$: C, 50.12; H, 5.84; N, 3.25. Found: C, 50.38; H, 5.75; N, 3.38.

3,4,6-Tri-*O*-acetyl-1-*O*-(*N*-allyl)carbamoyl-2-deoxy-2-phthalimido-β-D-glucopyranose (6). General procedure II; eluent for flash chromatography: ethyl acetate/petroleum ether (1:4, v/v); yield 5.08 g (98 %); colorless amorphous solid; $[\alpha]^{22}_D$ +45.3° (*c* 1.0, $CHCl_3$); R_f = 0.51 (ethyl acetate/petroleum ether = 1:1); 400 MHz ^{1}H NMR ($CDCl_3$) δ 7.83 - 7.24 (m, 4H, Ar-H), 6.41 (d, 1H, $J_{1,2}$ = 8.9 Hz, 1-H), 5.88 (dd, 1H, $J_{2,3}$ = 10.5 Hz, $J_{3,4}$ = 9.2 Hz, 3-H), 5.70 - 5.60 (m, 1H, C$\underline{H}$=CH_2), 5.17 (t, 1H, $J_{4,3}$ = 9.5 Hz, $J_{4,5}$ = 9.8 Hz, 4-H), 5.04 - 4.97 (m, 2H, J_{trans} = 17.5 Hz, J_{cis} = 10.4 Hz, J_{gem} = 1.1 Hz, CH=C$\underline{H}_{2trans}$, CH=C$\underline{H}_{2cis}$), 4.93 (t, 1H, J_{vic} = 5.8 Hz, NH), 4.40 (dd, 1H, $J_{1,2}$ = 9.0 Hz, $J_{2,3}$ = 10.6 Hz, 2-H), 4.34 (dd, 1H, $J_{6a,5}$ = 4.2 Hz, $J_{6a,6b}$ = 12.5 Hz, 6-Ha), 4.10 (dd, 1H, $J_{6b,5}$ = 1.8 Hz, $J_{6a,6b}$ = 12.4 Hz, 6-Hb), 3.99 (m, 1H, 5-H), 3.71 - 3.59 (m, 2H, NH-C$\underline{H}_2$-), 2.06, 1.99, 1.82 (3s, 9H, -CH_3); 100.6 MHz ^{13}C NMR δ 170.41, 169.73, 169.31, 167.17 (C=O), 153.12 (carbamate), 134.23, 133.49 (Ar-C, C$\underline{H}$=CH_2), 131.02 (ipso-C), 123.53 (Ar-C), 116.26 (CH=C$\underline{H}_2$), 90.56 (C-1), 72.08, 70.21, 68.15 (C-3, C-4, C-5), 62.34 (C-6), 53.33 (C-2), 43.16 (NH-CH_2-), 20.48, 20.38, 20.17 (-CH_3).

Anal.Calcd for $C_{24}H_{26}N_2O_{11}$: C, 55.60; H, 5.05; N, 5.40. Found: C, 55.60; H, 5.02; N, 5.27.

2,3,4-Tri-*O*-acetyl-1-*O*-(*N*-allyl)carbamoyl-6-*O*-benzyl-β-D-galactopyranose (8). General procedure II; eluent for flash chromatography: ethyl acetate/petroleum ether (1:4, v/v); yield 2.97 g (62 %, 50 % β-anomer, 12 % α-anomer); β-anomer: colorless crystals; mp 140 °C; $[\alpha]^{22}_D$ -14.7° (*c* 1.00, $CHCl_3$); R_f = 0.61 (ethyl acetate/petroleum ether = 1:1); 400 MHz ^{1}H NMR ($CDCl_3$) δ 7.31 - 7.22 (m, 5H, Ar-H), 6.24 (d, 1H, $J_{1,2}$ = 2.9 Hz, 1-H), 5.85 - 5.75 (m, 1H, C$\underline{H}$=CH_2), 5.52 (s, 1H, 4-H), 5.27 - 5.30 (m, 2H, 2-H, 3-H), 5.17 (dd, 1H, J_{trans} = 17.0 Hz, J_{gem} = 1.5 Hz, CH=C$\underline{H}_{2trans}$), 5.11 (dd, 1H, J_{cis} = 10.3 Hz, J_{gem} = 1.2 Hz, CH=C$\underline{H}_{2cis}$), 5.04 (t, 1H, J_{vic} = 5.9 Hz, NH), 4.50 (d, 1H, J_{gem} = 12.0 Hz, -CH_{2a}-Ar), 4.35 (d, 1H, J_{gem} = 12.0, -CH_{2b}-Ar), 4.24 (t, 1H, $J_{5,6a}$ = 6.3 Hz, $J_{5,6b}$ = 6.3 Hz, 5-H), 3.80 - 3.73 (m, 2H, NH-C$\underline{H}_2$-), 3.40 (dd, 1H, $J_{6a,6b}$ = 9.4 Hz, $J_{6a,5}$ = 7.3 Hz, 6-Ha), 3.47 (dd, 1H, $J_{6b,6a}$ = 9.4 Hz, $J_{6b,5}$ = 5.7 Hz, 6-Hb), 2.01, 1,98, 1.96 (3s, 9H, -CH_3). 100.6 MHz ^{13}C NMR ($CDCl_3$) δ 170.01, 169.82

(C=O), 153.97 (carbamate), 137.48 (ipso-C), 133.85 (CH=CH_2), 128.40, 127.91, 127.79 (Ar-C), 116.47 (CH=CH_2), 90.69 (C-1), 73.54 (-CH_2-Ar), 69.74, 68.04, 67.69, 67.35, 66.81 (C-2, C-3, C-4, C-5, C-6), 43.41 (NH-CH_2-), 20.58, 20.52, 20.49 (-CH_3).

Anal.Calcd for $C_{23}H_{29}NO_{10}$: C, 57.61; H, 6.10; N, 2.92. Found : C, 57.56; H, 6.15; N, 2.95.

3,4,6-Tri-*O*-acetyl-2-azido-2-deoxy-1-*O*-thexyldimethylsilyl-β-D-galactopyranose (10). A solution of 208 mg (0.628 mmol) of anomeric unprotected galactose derivative **9**[13] in 15 mL of dry DMF was cooled to 0 °C, 450 mg (2.50 mmol) of thexyldimethylsilyl chloride and 166 mg (2.43 mmol) of imidazole were added and the mixture was warmed to room temperature under continuous stirring. After 12 h (TLC-monitoring) 60 mL of water were added, the solution was stirred for further 10 min and the crude product was extracted two times with dichloromethane. The organic layer was dried with $MgSO_4$ and the solvent was evaporated under reduced pressure. The crude product was purified by flash chromatography (ethyl acetate/petroleum ether (1:10, v/v)); yield 198 mg (67 %); colorless crystals; mp 73 °C; $[\alpha]^{22}_D$ -19.4° (*c* 1.01, $CHCl_3$); R_f = 0.42 (ethyl acetate/petroleum ether = 1:4); 400 MHz $^1H,^1H$-COSY-NMR ($CDCl_3$) δ 5.26 (dd, 1H,$J_{4,3}$ = 3.5 Hz, $J_{4,5}$ = 0.9 Hz, 4-H), 4.71 (dd, 1H, $J_{3,2}$ = 11.0 Hz, $J_{3,4}$ = 3.4 Hz, 3-H), 4.52 (d, 1H, $J_{1,2}$ = 7.6 Hz, 1-H), 4.09 (dd, 1H, $J_{6a,6b}$ = 11.3 Hz, $J_{6a,5}$ = 7.2 Hz, 6-Ha), 4.03 (dd, 1H, $J_{6b,6a}$ = 11.3 Hz, $J_{6b,5}$ = 6.0 Hz, 6-Hb), 3.79 (m, 1H, $J_{5,6a}$ = 7.1 Hz, $J_{5,6b}$ = 7.1 Hz, $J_{5,4}$ = 0.9 Hz, 5-H), 3.54 (dd, 1H, $J_{2,1}$ = 7.6 Hz, $J_{2,3}$ = 10.9 Hz, 2-H), 2.11, 2.00, 1.99 (3s, 9H, -CH_3 Ac), 1.63 (m, 1H, -C<u>H</u>(CH_3)$_2$), 0.87 (d, J_{vic} = 6.7 Hz, 6H, -CH(C<u>H</u>$_3$)$_2$), 0.85 (2s, 6H, -C(C<u>H</u>$_3$)$_2$-), 0.16 (2s, 6H, -Si(C<u>H</u>$_3$)$_2$-). 100.6 MHz $^1H,^{13}C$-COSY-NMR ($CDCl_3$) δ 170.22, 170.00, 169.66 (C=O), 97.22 (C-1), 70.92 (C-3), 70.83 (C-5), 66.59 (C-4), 63.34 (C-2), 61.60 (C-6), 33.89 (-<u>C</u>H(CH_3)$_2$), 24.87 (-<u>C</u>(CH_3)$_2$-), 20.50, 20.47 (-<u>C</u>H$_3$ Ac), 19.90, 19.82 (-C(<u>C</u>H$_3$)$_2$-), 18.42, 18.34 (-CH(<u>C</u>H$_3$)$_2$), -2.18, -3.26 (-Si(<u>C</u>H$_3$)$_2$-).

Anal.Calcd for $C_{20}H_{35}N_3O_8Si$: C, 50.72; H, 7.45; N, 8.87. Found: C, 50.81; H, 7.40; N, 8.81.

2-Azido-2-deoxy-1-*O*-thexyldimethylsilyl-β-D-galatopyranose (11). The 2-azido-galactopyranosyl derivative **10** (15.3 g, 32.3 mmol) was dissolved in 225 mL of dry MeOH and 3 mL of 1% NaOMe/MeOH were added. After complete deacetylation (19 h, TLC-monitoring, chloroform : methanol = 9:1, [v/v]) the reaction mixture was neutralized with Amberlite® IR 120, filtered off and the solvent was evaporated *in vacuo*. The residue was recrystallised from ether/petroleum ether. (yield : 8.41 g; 75 %, mp 59 °C). The product was directly used in the next reaction step without further purification and characterization.

2-Azido-4,6-*O*-benzylidene-2-deoxy-1-*O*-thexyldimethylsilyl-β-D-galactopyranose (12). *p*-Toluenesulfonic acid (75 mg, 0.35 mmol) was added to a solution of 6.2 g (17.85 mmol) of deacetylated saccharide compound **11** and 7.5 g (49.28 mmol) of benzaldehyde dimethyl acetal in 150 mL of dry DMF. This reaction mixture was stirred at 50 °C for 5 h. After complete conversion the solution was cooled to rt and 0.38 mL of triethylamine were added. The solvent was distilled off under vacuum, and the crude product was purified by flash chromatography (ethyl acetate/petroleum ether (1:4, v/v)); yield 5.5 g (71 %); colorless gelatinous solid; $[\alpha]^{22}_D$ -11.0° (*c* 1.00, $CHCl_3$); R_f = 0.49 (ethyl acetate/petroleum ether = 1:1); 200 MHz ^{1}H NMR ($CDCl_3$) δ 7.52 - 7.33 (m, 5H, Ar-H), 5.52 (s, 1H, Ph-CH-), 4.51 (d, 1H, $J_{1,2}$ = 7.3 Hz, 1-H), 4.25 (dd, 1H, $J_{6a,5}$ = 1.6 Hz, $J_{6a,6b}$ = 12.2 Hz, 6-Ha), 4.11 (d, 1H, $J_{4,3}$ = 1.5 Hz, 4-H), 4.02 (dd, 1H, $J_{6b,5}$ = 1.7 Hz, $J_{6b,6a}$ = 12.4 Hz, 6-Hb), 3.51 - 3.45 (m, 2H, 2-H, 3-H), 3.37 (s, 1H, 5-H), 2.56 (s, broad, -OH), 1.69 (m, 1H, -C<u>H</u>$(CH_3)_2$), 0.90 (d, 6H, J_{vic} = 6.4 Hz, -CH(C<u>H</u>$_3)_2$), 0.90, 0.89 (2s, 6H, -C(C<u>H</u>$_3)_2$-), 0.22, 0.20 (2s, 6H, -Si(C<u>H</u>$_3)_2$-). 100.6 MHz ^{13}C NMR ($CDCl_3$) δ 135.58 (ipso-C), 129.38, 128.36, 126.47 (Ar-C), 101.42 (Ph-CH-), 97.00 (C-1), 74.61, 71.18, 69.16, 66.59, 66.45 (C-2, C-3, C-4, C-5, C-6), 33.96 (-<u>C</u>H$(CH_3)_2$), 24.91 (-<u>C</u>$(CH_3)_2$), 20.09, 19.98 ((-C(<u>C</u>H$_3)_2$-), 18.56, 18.46 (-C(<u>C</u>H$_3)_2$-), -1.90, -2.84 (-Si(<u>C</u>H$_3)_2$-).

Anal.Calcd for $C_{21}H_{33}N_3O_5Si$: C, 57.90; H, 7.64; N, 9.65. Found : C, 57.88; H, 7.66; N, 9.72.

3-*O*-(2′,3′,4′-Tri-*O*-acetyl-6′-*O*-benzyl-β-D-galactopyranosyl)-2-azido-4,6-*O*-benzylidene-2-deoxy-1-*O*-thexyldimethylsilyl-β-D-galactopyranose (13). At -13 °C 2.05 g (4.31 mmol) of TMTSB were added to a solution of 2.10 g (4.37 mmol) of glycosyl donor **8** and 1.04 g (2.39 mmol) of acceptor **12** in dry dichloromethane. Within 2 h the slightly yellowish reaction mixture was warmed up to -5 °C. Triethylamine was added and the solution was worked up as described in general procedure III. Washing of the organic phase with hydrochloric acid was avoided. Eluent of flash chromatography: ethyl acetate/petroleum ether (1:4, v/v); yield 1.30 g (67 %); colorless crystals; mp 168 °C; $[\alpha]^{22}_D$ +1.4° (*c* 1.00, $CHCl_3$); R_f = 0.42 (ethyl acetate/petroleum ether = 1:2); 400 MHz ^{1}H NMR ($CDCl_3$) δ 7.53-7.22 (m, 9H, Ar), 5.45 (s, 1H, Ph-C<u>H</u>-), 5.41 (dd, 1H, $J_{4',5'}$ = 0.9 Hz, $J_{4',3'}$ = 3.5 Hz, 4'-H), 5.23 (dd, 1H, $J_{2',1'}$ = 7.9 Hz, $J_{2',3'}$ = 10.6 Hz, 2'-H), 5.00 (dd, 1H, $J_{3',2'}$ = 10.3 Hz, $J_{3',4'}$ = 3.5 Hz, 3'-H), 4.73 (d, 1H, $J_{1',2'}$ = 7.9 Hz, 1'-H), 4.49 (d, 1H, J_{gem} = 11.7 Hz, -CH_{2a}-Ar), 4.47 (d, 1H, $J_{1,2}$ = 7.3 Hz, 1-H), 4.43 (d, 1H, J_{gem} = 11.7 Hz, -CH_{2b}-Ar), 4.17 (dd, 1H, $J_{6a,6b}$ = 12.0 Hz, $J_{6a,5}$ = 1.2 Hz, 6-Ha), 4.17 (d, 1H, $J_{4,3}$ = 3.5 Hz, 4-H), 3.86 (dd, 1H, $J_{6b,6a}$ = 12.2 Hz, $J_{6b,5}$ = 1.2 Hz, 6-Hb), 3.85 (s, 1H, 5'-H), 3.67 (dd, 1H, $J_{2,1}$ = 7.6 Hz, $J_{2,3}$ = 10.6 Hz, 2-H), 3.53 (dd, 1H, $J_{6a',6b'}$

= 9.7 Hz, $J_{6a',5'}$ = 6.8 Hz, 6'-Ha), 3.48 (dd, 1H, $J_{6b',6a'}$ = 9.7 Hz, $J_{6b',5'}$ = 5.9 Hz, 6'-Hb), 3.39 (dd, 1H, $J_{3,2}$ = 10.6 Hz, $J_{3,4}$ = 3.5 Hz, 3-H), 3.23 (s, 1H, 5-H), 2.06, 2.05, 1.96 (3s, 9H, -C$\underline{H}_3$ Ac), 1.66 (m, 1H, -C$\underline{H}$(CH$_3$)$_2$), 0.89 - 0.86 (m, 12H, -C(C$\underline{H}_3$)$_2$-CH(C$\underline{H}_3$)$_2$), 0.18, 0.17 (2s, 6H, -Si(C$\underline{H}_3$)$_2$-); 100.6 MHz ^{13}C NMR ($CDCl_3$), δ 170.25, 170.07, 169.34 (C=O), 138.02 (ipso-C Ph-CH-), 137.65 (ipso-C Bzl); 128.79, 128.49, 128.10, 127.93, 127.73, 126.28 (Ar-C),102.51 (C-1'), 100.69 (Ph-$\underline{C}$H-), 97.25 (C-1), 78.76 (C-3), 75.01 (C-4), 73.59 (-$\underline{C}$H$_2$-Ar), 72.42 (C-5'), 71.26 (C-3'), 69.06, 69.03 (C-6, C-6'), 68.26 (C-2'), 67.76 (C-4'), 66.60 (C-5), 64.82 (C-2), 33.96 (-$\underline{C}$H(CH$_3$)$_2$), 24.90 (-$\underline{C}$(CH$_3$)$_2$), 20.64, 20.54 (-$\underline{C}$H$_3$ Ac), 20.05, 19.95 (-C(C$\underline{H}_3$)$_2$-), 18.50, 18.42 (-CH(C$\underline{H}_3$)$_2$), -1.86, -2.92 (-Si(C$\underline{H}_3$)$_2$-).

Anal.Calcd for $C_{40}H_{55}O_{13}N_3Si$: C, 59.02; H, 6.81; N, 5.16. Found: C, 59.10 ; H, 6.84; N, 5.19.

3-*O*-(2',3',4'-Tri-*O*-acetyl-6'-*O*-benzyl-β-D-galactopyranosyl)-2-azido-2-deoxy-1-*O*-thexyldimethylsilyl-β-D-galactopyranose (14). A solution of 342 mg (0.42 mmol) of the benzylidene protected disaccharide **13**, 250 μL of ethanedithiol (2.37 mmol) and 4.3 mg of *p*-toluenesulfonic acid in dry dichloromethane (70 mL) was heated to gentle reflux for 4 h. The reaction mixture was cooled to rt, diluted with 100 mL of chloroform and extracted with 20 mL of saturated sodium hydrogencarbonate solution and 20 mL of water. The aqueous phases were reextracted with 30 mL of chloroform, respectively. The combined organic extracts were dried with $MgSO_4$ and concentrated *in vacuo*. The oily residue was purified by flash chromatography (ethyl acetate/petroleum ether (1:4, v/v)); yield 254 mg (83 %); colorless foam; $[\alpha]^{22}_D$ -6.2° (*c* 0.93, $CHCl_3$); R_f = 0.38 (ethyl acetate/petroleum ether = 1:1); 400 MHz ^{1}H NMR ($CDCl_3$) δ 7.34 - 7.22 (m, 5H, Aryl), 5.40 (d, 1H, $J_{4',3'}$ = 3.3 Hz, 4'-H), 5.20 (dd, 1H, $J_{2',1'}$ = 8.3 Hz, $J_{2',3'}$ = 10.3 Hz, 2'-H), 4.99 (dd, 1H, $J_{3',2'}$ = 10.3 Hz, $J_{3',4'}$ = 3.3 Hz, 3'-H), 4.61 (d, 1H, $J_{1',2'}$ = 7.8 Hz, 1'-H), 4.47 (d, 1H, J_{gem} = 11.8 Hz, -C$\underline{H}_{2a}$-Ar), 4.41 (d, 1H, $J_{1,2}$ = 7.8 Hz, 1-H), 4.40 (d, 1H, J_{gem} = 11.8 Hz, -C$\underline{H}_{2b}$-Ar), 3.96 (d, 1H, $J_{4,3}$ = 3.3 Hz, 4-H), 3.87 - 3.82 (m, 2H, $J_{6a',6b'}$ = 11.5 Hz, $J_{6a',5'}$ = 6.6 Hz, $J_{5',6a'}$ = 6.6 Hz, $J_{5',6b'}$ = 4.9 Hz, 6'-Ha, 5'-H), 3.65 (dd, 1H, $J_{6b',6a'}$ = 11.5 Hz, $J_{6b',5'}$ = 4.9 Hz, 6'-Hb), 3.51 - 3.42 (m, 3H, $J_{6a,5}$ = 5.8 Hz, $J_{6a,6b}$ = 9.9 Hz, 2-H, 6-Ha, 6-Hb), 3.38 (t, 1H, $J_{5,6a}$ = 5.8 Hz, $J_{5,6b}$ = 5.8 Hz, 5-H), 3.32 (dd, 1H, $J_{3,2}$ = 10.3 Hz, $J_{3,4}$ = 3.3 Hz, 3-H), 2.06, 2.05, 1.96 (3s, 9H, -CH$_3$ Ac), 1.63 (m, 1H, -C$\underline{H}$(CH$_3$)$_2$), 0.86 (d, 6H, J_{vic} = 5.8 Hz, -CH(C$\underline{H}_3$)$_2$), 0.85 (s, 6H, -C(CH$_3$)$_2$-), 0.15 (s, 6H, -Si(CH$_3$)$_2$-). 100.6 MHz ^{13}C NMR ($CDCl_3$) δ 170.06, 169.95, 169.54 (C=O), 137.41 (ipso-C), 128.50, 127.97, 127.75 (Ar-C), 102.17 (C-1'), 97.16 (C-1), 81.16 (C-3), 74.19 (C-4), 73.59 (-$\underline{C}$H$_2$-Ar), 72.60 (C-5'), 70.78, 68.76, 67.93, 67.84, 67.52 (C-2', C-3', C-4', C-6, C-6'), 65.12 (C-

5), 62.10 (C-2), 33.88 ((-CH(CH$_3$)$_2$), 24.81 (-C(CH$_3$)$_2$-), 20.52, 20.48 (-CH$_3$ Ac), 19.97, 19.84 (-C(CH$_3$)$_2$), 18.46, 18.35 (-CH(CH$_3$)$_2$), -1.90, -3.19 (-Si(CH$_3$)$_2$-).

Anal.Calcd for $C_{33}H_{51}N_3O_{13}Si$: C, 54.61; H, 7.08; N, 5.79. Found : C, 54.95 ; H, 7.01; N, 5.49. FAB-MS (nba, pos + LiCl), *m/z*: 733.0 (M + Li$^+$, 100 %, Calcd. 732.4).

3-*O*-(2′,3′,4′-Tri-*O*-acetyl-6′-*O*-benzyl-β-D-galactopyranosyl)-6-*O*-(3′′,4′′,6′′-tri-*O*-acetyl-2′′-deoxy-2′′-phthalimido-β-D-glucopyranosyl)-2-azido-2-deoxy-1-*O*-thexyldimethylsilyl-β-D-galactopyranose (15). At -29 °C, 904 mg (1.90 mmol) of TMTSB was added to a solution of 1.03 g (1.98 mmol) of glucosyl donor **6** and 0.80 g (1.10 mmol) disaccharide acceptor **14** in dry dichloromethane (80 mL). The red colored reaction mixture was warmed to -10 °C within 2.5 h. At the same time the intense color disappeared. The batch was quenched and worked up as described in general procedure III. After flash chromatography with ethyl acetate/petroleum ether (1:1, v/v) the product, which was still soiled by little amounts of byproducts, was cleaned by preparative reversed phase HPLC (gradient elution: 30 % CH_3CN, 70 % H_2O → 100 % CH_3CN within 60 min, UV-detection at 222 nm, retention time: 39.5 min). yield 605 mg (48 %); colorless amorphous solid.; $[\alpha]^{22}_D$ +7.7° (*c* 0.97, $CHCl_3$); R_f = 0.37 (ethyl acetate/petroleum ether = 1:1); 400 MHz ^{1}H,^{1}H-COSY-NMR ($CDCl_3$) δ 7.84 - 7.69 (m, 4H, Pht-H), 7.34 - 7.23 (m, 5H, Bzl-H), 5.67 (dd, 1H, $J_{3'',2''}$ = 10.6 Hz, $J_{3'',4''}$ = 9.0 Hz, 3''-H), 5.42 (d, 1H, $J_{1'',2''}$ = 8.6 Hz, 1''-H), 5.37 (d, 1H, $J_{4',3'}$ = 2.8 Hz, 4'-H), 5.15 (dd, 1H, $J_{2',1'}$ = 8.2 Hz, $J_{2',3'}$ = 10.4 Hz, 2'-H), 5.11 (t, 1H, $J_{4'',3''}$ = 9.0 Hz, $J_{4'',5''}$ = 9.0 Hz, 4''-H), 4.94 (dd, 1H, $J_{3',4'}$ = 3.1 Hz, $J_{3',2'}$ = 10.4 Hz, 3'-H), 4.51 (d, 1H, $J_{1',2'}$ = 8.2 Hz, 1'-H), 4.49 (d, 1H, J_{gem} = 12.1 Hz, -CH$_{2a}$-Bzl), 4.40 (d, 1H, J_{gem} = 12.1 Hz, -CH$_{2b}$-Bzl), 4.25 (dd, 1H, $J_{2'',1''}$ = 8.6 Hz, $J_{2'',3''}$ = 10.6 Hz, 2''-H), 4.25 (d, 1H, $J_{1,2}$ = 7.5 Hz, 1-H), 4.23 (dd, 1H, $J_{6b'',6a''}$ = 12.1 Hz, $J_{6b'',5''}$ = 4.7 Hz, 6''-Hb), 4.10 (dd, 1H, $J_{6a'',6''}$ = 12.1 Hz, $J_{6a'',5''}$ = 4.7 Hz, 6''-Ha), 3.93 (dd, 1H, $J_{6a,6b}$ = 10.4 Hz, $J_{6a,5}$ = 3.9 Hz, 6-Ha), 3.84 (d, 1H, $J_{4,3}$ = 2.7 Hz, 4-H), 3.79 (ddd, 1H, $J_{5'',4''}$ = 10.2 Hz, $J_{5'',6a''}$ = 2.4 Hz, $J_{5'',6b''}$ = 4.7 Hz, 5''-H), 3.74 - 3.69 (m, 2H, 5'-H, 6-Hb), 3.37 - 3.34 (m, 3H, 5-H, 6-Ha', 6-Hb'), 3.36 (dd, 1H, $J_{2,3}$ = 10.2 Hz, $J_{2,1}$ = 7.8 Hz, 2-H), 3.20 (dd, 1H, $J_{3,2}$ = 10.2 Hz, $J_{3,4}$ = 3.1 Hz, 3-H), 2.05, 2.03, 1.99, 1.94, 1.80 (5s, 18H, -CH$_3$ Ac), 1.45 (m, 1H, -CH(CH$_3$)$_2$), 0.74 (d, J_{vic} = 7.04, 6H, -CH(CH$_3$)$_2$), 0.68 (s, 6H, -C(CH$_3$)$_2$-), -0.09, -0.26 (2s, 6H, -Si(CH$_3$)$_2$). 100.6 MHz ^{1}H,^{13}C-COSY-NMR ($CDCl_3$) δ 170.48, 170.02, 169.99, 169.92, 169.41, 169.35 (C=O Ac), 167.42 (C=O Pht), 137.43 (ipso-Bzl), 134.21, 131.58, 123.5 (Ar-C Pht), 128.51, 127.90, 127.81 (Ar-C Bzl), 102.10 (C-1'), 98.02 (C-1''), 96.90 (C-1), 80.83 (C-3), 73.55 (-CH$_2$-Ar), 73.00 (C-5), 72.45 (C-5'), 71.93 (C-5''), 70.95 (C-3''), 70.76 (C-3'), 69.01 (C-6), 68.96 (C-4''),

68.72 (C-2'), 67.77 (C-4), 67.60 (C-6'), 67.40 (C-4'), 64.93 (C-2), 61.95 (C-6''), 54.66 (C-2''), 33.81 (-$\underline{C}H(CH_3)_2$), 24.60 (-$\underline{C}(CH_3)_2$-), 20.64, 20.51, 20.47, 20.27 (-$\underline{C}H_3$ Ac), 19.80, 19.69 (-C($\underline{C}H_3)_2$-), 18.36, 18.26 (-CH($\underline{C}H_3)_2$), -2.18, -3.84 (-Si($CH_3)_2$-).

Anal.Calcd for $C_{53}H_{70}N_4O_{22}Si{\cdot}H_2O$: C, 54.82; H, 6.25; N, 4.82. Found: C, 54.54 ; H, 6.52; N, 4.90. FAB-MS (nba, pos + LiBr), *m/z*: 1150.8 ($M + Li^+$, 66 %, Calcd. 1150.2).

1,2,3,4-Tetra-*O*-acetyl-6-*O*-(2′,3′,4′,6′-tetra-*O*-acetyl-β-D-galactopyranosyl)-β-D-glucopyranose (17). Glucosyl acceptor **16** (345 mg, 1 mmol) and galactosyl donor **3** (857 mg, 2 mmol) were reacted as described in general procedure III; the reaction temperature was -5 °C; eluent for flash chromatography: ethyl acetate/petroleum ether (1:4, v/v); yield 380 mg (56 %); colorless amorphous solid; $[\alpha]^{22}_D$ +0.4° (*c* 1.00, $CHCl_3$); R_f = 0.30 (toluene/acetone = 4:1); 400 MHz ^{1}H NMR ($CDCl_3$) δ 5.64 (d, 1H, $J_{1,2}$ = 8.3 Hz, 1-H), 5.33 (d, 1H, $J_{4',3'}$ = 2.9 Hz, 4′-H), 5.20 (t, 1H, $J_{3,4}$ = 9.5 Hz, $J_{3,2}$ = 9.5 Hz, 3-H), 5.18 (dd, 1H, $J_{2',1'}$ = 7.9 Hz, $J_{2',3'}$ = 10.5 Hz, 2′-H), 5.05 (dd, 1H, $J_{2,1}$ = 8.4 Hz, $J_{2,3}$ = 9.5 Hz, 2-H), 4.96 (dd, 1H, $J_{3',4'}$ = 3.0 Hz, $J_{3',2'}$ = 10.7 Hz, 3′-H), 4.95 (t, 1H, $J_{4,5}$ = 9.7 Hz, $J_{4,3}$ = 9.7 Hz, 4-H), 4.47 (d, 1H, $J_{1',2'}$ = 7.9 Hz, 1′-H), 4.13 (dd, 1H, $J_{6'a,6'b}$ = 11.3 Hz, $J_{6'a,5'}$ = 6.6 Hz, 6′-Ha), 4.08 (dd, 1H, $J_{6'b,5'}$ = 6.7 Hz, $J_{6'b,6'a}$ = 11.3 Hz, 6′-Hb), 3.90 (dd, 1H, $J_{6a,6b}$ = 11.5 Hz, $J_{6a,5}$ = 2.2 Hz, 6-Ha), 3.84 (t, 1H, $J_{5',6'a}$ = 6.7 Hz, $J_{5',6'b}$ = 6.7 Hz, 5′-H), 3.60 (ddd, 1H, $J_{5,4}$ = 10.1 Hz, $J_{5,6a}$ = 2.2 Hz, $J_{5,6b}$ = 5.8 Hz, 5-H), 3.54 (dd, 1H, $J_{6b,6a}$ = 11.5 Hz, $J_{6b,5}$ = 5.8 Hz, 6-Hb), 2.11, 2.08, 2.06, 2.02, 2.01, 1.99, 1.97, 1.94 (8s, 24 H, -CH_3); 100.6 MHz ^{13}C NMR ($CDCl_3$) δ 170.33, 170.16, 170.06, 170.02, 169.56, 169.38, 169.17, 168.76 (C=O), 101.06 (C-1), 91.63 (C-1′), 74.08 (C-5), 72.87, 70.89, 70.79, 68.52, 68.52 (C′-2, C′-5, C-2, C-3, C-4), 70.34 (C′-3), 67.44 (C-6), 67.05 (C′-4), 61.24 (C′-6), 20.71, 20.57, 20.53, 20.49 (-CH_3).

Anal.Calcd for $C_{28}H_{38}O_{19}$: C, 49.56; H, 5.64. Found : C, 49.69 H, 5.57.

2,3,4-Tri-*O*-acetyl-6-*O*-(2′,3′,4′,6′-tetra-*O*-acetyl-β-D-galactopyranosyl)-α/β-D-glucopyranose (18). Disaccharide **17** (339 mg, 0.5 mmol) was transformed to the anomeric deprotected derivative **18** as described in general procedure I. 280 mg (88 %) of the crude product were obtained as a colorless oil.

2,3,4-Tri-*O*-acetyl-6-*O*-(2′,3′,4′,6′-tetra-*O*-acetyl-β-D-galactopyranosyl)-1-*O*-(*N*-allyl)carbamoyl-α/β-D-glucopyranose (19). The anomeric deprotected disaccharide **18** was subsequently reacted, without further purification, to the *O*-glycosyl *N*-allyl carbamate **19** as described in general procedure II. Eluent for flash chromatography: ethyl acetate/petroleum ether (1:4, v/v); yield 177 mg (56 %); colorless amorphous solid; $[\alpha]^{22}_D$ -0.3° (*c* 1.33, $CHCl_3$);

R_f = 0.21 (toluene/acetone = 4:1); 400 MHz ^{1}H NMR ($CDCl_3$) [β-anomer] δ 5.79 (m, 1H, C<u>H</u>=CH_2), 5.61 (d, 1H, $J_{1,2}$ = 8.2 Hz, 1-H), 5.32 (d, 1H, $J_{4',3'}$ = 2.8 Hz, 4′-H), 5.19 (t, 1H, $J_{3,4}$ = 9.4 Hz, $J_{3,2}$ = 9.4 Hz, 3-H), 5.15 - 5.10 (m, 3H, CH=C<u>H</u>$_2$, 2′-H), 5.02 (dd, 1H, $J_{2,3}$ = 9.4 Hz, $J_{2,1}$ = 8.3 Hz, 2-H), 4.97 (t, 1H, $J_{4,3}$ = 9.6 Hz, $J_{4,5}$ = 9.6 Hz, 4-H), 4.95 (dd, 1H, $J_{3',2'}$ = 10.7, $J_{3',4'}$ = 2.9 Hz, 3′-H), 4.48 (d, 1H, $J_{1',2'}$ = 8.0 Hz, 1′-H), 4.14 (dd, 1H, $J_{6a,6'b}$ = 11.2 Hz, $J_{6a',5'}$ = 6.6 Hz, 6′-Ha), 4.06 (dd, 1H, $J_{6b',6a'}$ = 11.2 Hz, $J_{6'b,5'}$ = 6.9 Hz, 6′-Hb), 3.91 (dd, 1H, $J_{6a,6b}$ = 11.6 Hz, $J_{6a,5}$ = 2.2 Hz, 6-Ha), 3.83 (t, 1H, $J_{5',6a'}$ = 6.7 Hz, $J_{5',6b'}$ = 6.7 Hz, 5′-H), 3.79 - 3.74 (m, 3H, 5-H, NH-C<u>H</u>$_2$-), 3.56 (dd, 1H, $J_{6b,6a}$ = 11.6 Hz, $J_{6b,5}$ = 5.2 Hz, 6-Hb), 2.10, 2.06, 2.01, 2.00, 1.99, 1.96, 1.94 (7s, 21H, -CH_3); 100.6 MHz ^{13}C NMR ($CDCl_3$) δ 170.38, 170.17, 170.03, 169.99, 169.69, 169.38 (C=O), 153.61 (carbamate), 133.64 (<u>C</u>H=CH_2), 116.62 (CH=<u>C</u>H_2), 101.11 (C-1′), 92.73 (C-1), 73.78 (C-5), 72.90, 70.93, 70.71, 70.34, 68.57 (C-2, C-3, C-4, C-2', C-3', C-5'), 67.40 (C-6), 67.06 (C-4'), 61.21 (C-6'), 43.45 (NH-<u>C</u>H_2-), 20.61, 20.56, 20.54, 20.49 (-CH_3).

Anal.Calcd for $C_{30}H_{41}NO_{19}$: C, 50.07; H, 5.74; N, 1.95. Found : C, 50.02; H, 5.80; N, 2.06.

.1,2,3,4-Tetra-*O*-acetyl-6-*O*-[2′,3′,4′-tri-*O*-acetyl-6′-*O*-(1′′,2′′,3′′,4′′-tetra-*O*-acetyl-β-D-galactopyranosyl)-β-D-glucopyranosyl]-β-D-glucopyranose (20). Disaccharide donor **19** (115 mg, 0.16 mmol) and glucosyl acceptor **16** (73 mg, 0.21 mmol) were transformed into trisaccharide **20** as described in general procedure III. Eluent for flash chromatography: ethyl acetate/petroleum ether (1:4, v/v); yield 102 mg (66 %); colorless crystals; mp 197 °C; $[\alpha]^{22}_D$ -5.9° (*c* 1.00, $CHCl_3$); R_f = 0.24 (toluene/acetone = 2:1); 400 MHz ^{1}H,^{1}H-COSY-NMR ($CDCl_3$) δ 5.61 (d, 1H, $J_{1,2}$ = 8.2 Hz, 1-H), 5.34 (dd, 1H, $J_{4'',5''}$ = 0.5 Hz, $J_{4'',3''}$ = 3.0 Hz, 4′′-H), 5.17 (t, 1H, $J_{3,2}$ = 9.5 Hz, $J_{3,4}$ = 9.5 Hz, 3-H), 5.13 (dd, 1H, $J_{2'',3''}$ = 10.7 Hz, $J_{2'',1''}$ = 8.1 Hz, 2′′-H), 5.11 (t, 1H, $J_{3',4'}$ = 9.5 Hz, $J_{3',2'}$ = 9.5 Hz, 3′-H), 5.04 (dd, 1H, $J_{2,3}$ = 9.5 Hz, $J_{2,1}$ = 8.3 Hz, 2-H), 5.00 (t, 1H, $J_{4,3}$ = 9.6 Hz, $J_{4,5}$ = 9.6 Hz, 4-H), 4.99 (dd, 1H, $J_{3'',2''}$ = 10.3 Hz, $J_{3'',4''}$ = 3.7 Hz, 3′′-H), 4.89 (dd, 1H, $J_{2',1'}$ = 8.0 Hz, $J_{2',3'}$ = 9.6 Hz, 2′-H), 4.82 (t, 1H, $J_{4',3'}$ = 9.6 Hz, $J_{4',5'}$ = 9.6 Hz, 4′-H), 4.51 (d, 1H, $J_{1'',2''}$ = 8.0 Hz, 1′′-H), 4.43 (d, 1H, $J_{1',2'}$ = 8.0 Hz, 1′-H), 4.10 (dd, 1H, $J_{6a'',6b''}$ = 11.2 Hz, $J_{6a'',5''}$ = 6.7 Hz, 6′′-Ha), 4.06 (dd, 1H, $J_{6b'',6a''}$ = 11.2 Hz, $J_{6b'',5''}$ = 6.7 Hz, 6′′-Hb), 3.97 (dd, 1H, $J_{6a,6b}$ = 11.2 Hz, $J_{6a,5}$ = 2.6 Hz, 6-Ha), 3.85 (t, 1H, $J_{5'',6a''}$ = 6.9 Hz, $J_{5'',6b''}$ = 6.9 Hz, 5′′-H), 3.81 (dd, 1H, $J_{6a',6b'}$ = 10.7 Hz, $J_{6a',5'}$ = 0.5 Hz, 6′-Ha), 3.73 (ddd, 1H, $J_{5,6a}$ = 2.7 Hz, $J_{5,6b}$ = 4.5 Hz, $J_{5,4}$ = 10.0 Hz, 5-H), 3.61 (m, 1H, $J_{5',6a'}$ = 1.6 Hz, $J_{5',6b'}$ = 8.1 Hz, $J_{5',4'}$ = 8.1 Hz, 5′-H), 3.51 (dd, 1H, $J_{6b',6a'}$ = 10.7 Hz, $J_{6b',5'}$ = 7.3 Hz, 6′-Hb), 3.49 (dd, 1H, $J_{6b,6a}$ = 11.2 Hz, $J_{6b,5}$ = 4.7 Hz, 6-Hb), 2.09,

2.04, 2.02, 2.00, 2.00, 1.98, 1.97, 1.96, 1.95, 1.94, 1.93 (11s, 33H, -CH_3); 100.6 MHz ^{13}C NMR ($CDCl_3$) δ 170.21, 170.04, 169.98, 169.85, 169.43, 169.29, 169.20, 169.06, 168.73 (C=O), 101.11 (C-1′′), 100.43 (C-1′), 91.69 (C-1), 73.65, 73.44, 72.84, 72.73, 70.93, 70.83, 70.74, 70.27, 69.04, 68.76 (C-2, C-3, C-4, C-5, C-3′, C-5′, C-2′′,C-3′′, C-4′′, C-5′′), 68.37 (C-2′), 67.15 (C-4′), 67.95 (C-6), 67.26 (C-6′), 61.24 (C-6′′), 20.67, 20.65, 20.44 (-CH_3).

Anal.Calcd for $C_{40}H_{54}O_{27}$: C, 49.69; H, 5.63. Found: C, 49.63; H, 5.44.

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