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Practical syntheses of B disaccharide and linear B type 2 trisaccharide—non-primate epitope markers recognized by human anti-α-Gal antibodies causing hyperacute rejection of xenotransplants

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Abstract—Synthetic protocols are presented for the elaboration of Galα1→3GalOR and Galα1→3Galβ1→4GlcNAcOR di- and trisaccharides that use a common Gal donor/acceptor unit, and are potentially adaptable to scale-up. © 2001 Elsevier Science Ltd. All rights reserved.

1. Introduction

The replacement of vital organs in humans (allotransplantation) is arguably one of the most dramatic scientific accomplishments in the annals of medical history. Through enormous advances and heroic efforts in the field of transplantation, such procedures are quasi routine today for a number of organs that include the heart, kidney, and liver for example. In spite of these monumental successes, the continued practice of one of the noblest of human life-saving procedures is severely jeopardized by the limited availability of suitable donors.[1]

A possible solution has been considered through xenotransplantation, where suitable animal donors would be used. Although phylogenetically close to man, non-human primates such as apes, monkeys and baboons are not suitable donors for various ethical and epidemiological reasons.[2] Pigs, however, appear to present a good alternative[3] since they can be bred in large numbers, even with genetically engineered variants.[4] Moreover, they are anatomically and physiologically similar to man with suitable heart sizes. In spite of this somewhat futuristic notion with obvious advantages if successfully implemented, the practice of xenotransplantation from pig to man is plagued by at least two major obstacles. Firstly, the phenomenon of rejection looms as a real threat, as discussed below.[5] Secondly, in the advent of a successful transplant, extreme care must be exercised to avoid the transfer, either directly or through a dormant genetic mechanism, of the porcine endogenous retrovirus and other retroviruses to man.[6] This socio-medical issue can, in principle, be resolved by breeding genetically modified pigs that do not encode for the virus, and its implications are outside the scope of this paper.

Of greater immediate concern, however, are the immunologic barriers to discordant xenotransplantation from pig to man.[5] A major cause for hyperacute rejection of a xenograft would be the result of binding anti-pig antibodies to antigens expressed on the endothelium of the donated organ. α-Gal containing epitopes on pig tissues are abundantly expressed, and recognized by anti-α-Gal antibodies, which constitute approximately 1% of circulating antibodies (IgG, IgM and IgA) in humans.[5,7] In fact, such antibodies bind to α-GalR containing oligosaccharide epitopes such as Galα1→3GalOR (B disaccharide antigen group) **1** and Galα1→3Galβ1→4GlcNAcOR (linear B type 2 antigen group) **2** among others[4,8] (Fig. 1).

Curiously, the Galα1→3Gal epitope is absent in all human tissue because α1→3Gal transferase[9] is not expressed except in certain malignancies.[5,10] They do however produce large amounts of anti-α-Gal antibodies as part of a natural class of immunoglobulins, perhaps as a preventive measure toward bacteria and cells of other species.[11] It is clear then why the binding of human anti-α-Gal antibodies to α-GalOR containing epitopes of vascularized organ

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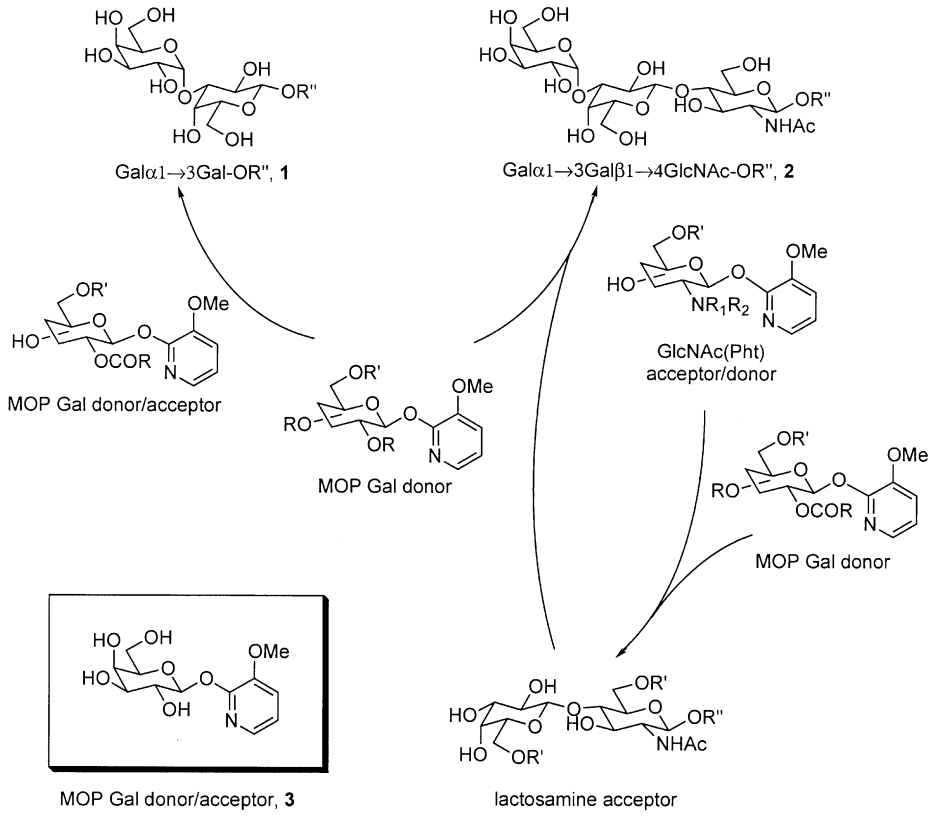


Figure 1.

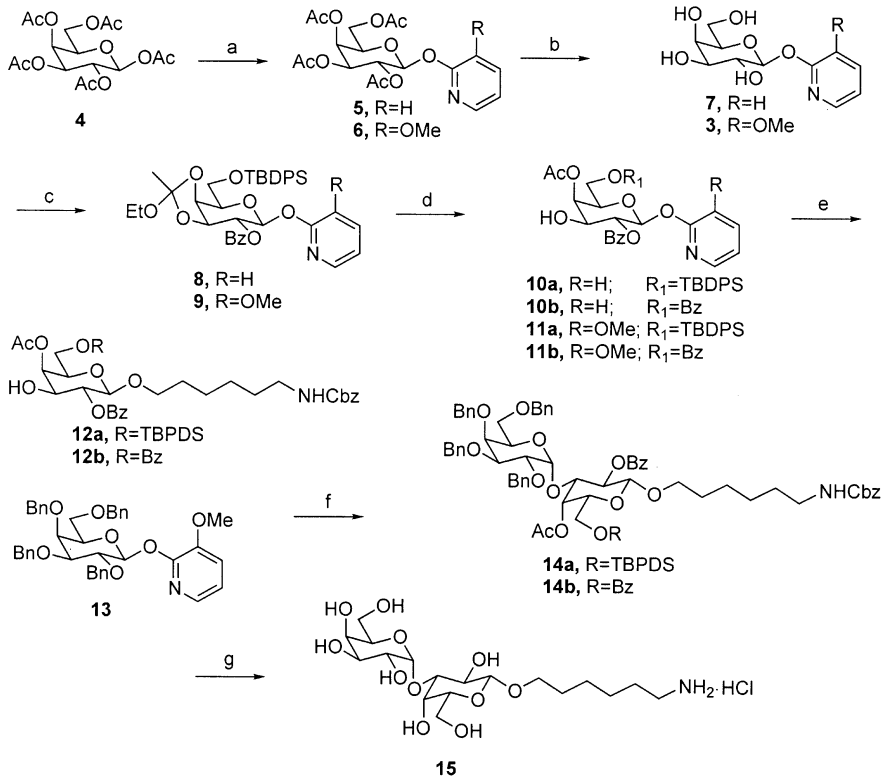
tissues results in hyperacute rejection. To achieve successful 'accommodation'[12] (adaptation, anergy) of the transplant, one must deplete the anti-α-Gal antibodies from the recipient before the new organ is placed.[5] Although there are other barriers to successful xenotransplantation even if hyperacute rejection is minimized, such as acute vascular and cell-mediated phenomena, the notion of neutralizing anti-α-Gal natural antibodies with synthetic α-GalOR containing oligosaccharides prior to organ transplantation remains as an attractive protocol. It appears that once 'removed', the acquired acceptance (accommodation) can persist, even when the humoral antibodies are restored, as evidenced in allografts.[13] Once the new organ is in place and antibody activity is curtailed, immunotherapy using immunosuppressant drugs can be initiated to ensure the patient's well being and to maintain the new organ.

Extensive studies have shown that carbohydrate therapy in xenotransplantation with the aim of neutralizing anti-α-Gal antibodies is a viable experimental protocol. Although the clinical aspects of the procedure are not resolved, one extreme but successful protocol is the use of pretransplant extracorporal immunoadsorption with columns containing pertinent α-GalOR epitope motifs that can entrap anti-α-Gal antibodies from the 'patient's' blood that is perfused through the column.[2b,8c] Transplantation could then be done when a low titer of the anti-α-Gal antibodies is reached. Another approach relies on specific intravenous α-GalOR therapy as demonstrated in baboon allografts.[14]

These and other studies directed at exploiting xenoreactive antigen–human antibody interactions[15] has instigated a need to devise practical syntheses of the Galα1-3GalOR (B disaccharide) **1** and Galα1→3Galβ-1→4GlcNAcOR (linear B type 2 trisaccharide) **2**.

Although several syntheses are known,[16–22] we were particularly interested in devising synthetic protocols that avoided the use of thiol-based reagents, hydrolytically labile glycosyl donors, and potentially toxic reagents, with the prospects of adapting the protocol to potentially produce relatively large quantities of **1** and/or **2** in a process group environment. In order to explore practical methods to access the intended targets **1** and **2**, we chose a strategy that capitalizes on the ability of a common Gal unit to act as a donor and acceptor. We have previously shown that 2-pyridyl and 3-methoxy-2-pyridyl (MOP) glycosides are excellent anomeric activators under mild conditions.[23] Thus, unprotected MOP β-D-galactopyranoside **3** (Fig. 1) affords alkyl α-D-galactopyranosides (and oligosaccharides) upon treatment with a suitable alcohol or partially protected MOP glycoside.[24] Activation of the newly formed disaccharide, for example, and reaction with a suitably protected MOP glycoside allows for an iterative oligosaccharide synthesis. *O*-Protected MOP β-D-galactopyranosides can serve as glycosyl donors or acceptors depending on the nature of the *O*-protecting group.

Fig. 1 illustrates the common Gal donor/acceptor strategy in conjunction with the synthesis of **1** and **2**. It should be pointed out that MOP glycoside donors which contain participating groups at C-2 (ester) will lead to 1,2-*trans*-glycosides, while those with non-participating groups (ex. benzyl) will afford the 1,2-*cis*-glycosides as major products,[25] as in



Scheme 1. (a) i. HBr, Ac_2O, AcOH, 2 h rt. for **5** ii. silver 2-pyridoxide, toluene, reflux, 1 h, 71%; for **6** ii. silver 3-methoxy-2-pyridoxide, toluene, reflux, 1 h, 86%. (b) MeONa, MeOH, rt, 3-6 h, 94–95% (c) i. TBDPSCl, imidazole, DMF, 6 h, rt, 78–81% ii. $MeC(OEt)_3$, pyridinium triflate, DCM, 45–60 min, rt iii. BzCl, DMAP, DCM, 1 h 30 min, rt, (d) for R=H: i. 90% AcOH, 10 min, rt, 76%; for R=OMe: ii. AcOH, AcONa, H_2O pH=3–4, 1 h, 67%. (e) DCM, 1 h, rt, for **10a**: $HBF_4.Et_2O$, 80%; for **10b**: HBF_4.EtO, ~80%; for **11a**: $HBF_4.Et_2O$, 80% for TMStriflate, 78% or $Cu(OTf)_2$, 65%; for **11b**: $HBF_4.Et_2O$, 72%. (f) for **14a**: DCM, 2 h, rt, $Yb(OTf)_3$, 76% or toluene, 1 d, rt $Cu(OTf)_2$, 60%; for **14b**: toluene, 2d, 51%. (g) i. MeONa, MeOH, rt, 48 h. ii TBAF, THF, rt, 24 h. iii. 20% $Pd(OH)_2/C$, H_2, 60 psi, dioxane/water, 1 h, then HCl, H_2, 60 psi, rt, overnight.

well precedented examples using other anomeric activating groups.[26] Due to the much decreased reactivity of MOP glycosides that are only partially protected with ester groups,[27] they can also act as acceptors when allowed to react with other more reactive MOP glycosyl donors.

In order to test the feasibility of this strategy we considered the synthesis of the Galα1→3GalOR motif **1** in the form of its 6-aminohexyl β-D-glycoside as a representative hapten first (Scheme 1). Pyridyl[28] and MOP β-D-galactopyranosides were conveniently prepared from β-D-galactopyranose pentaacetate **4** in two steps to afford first the peracetates **5** and **6**, then the free glycosides **7** and **3**, respectively. Selective protection of the primary hydroxy group followed by treatment with trimethylorthoacetate led to the corresponding orthoesters, which where benzoylated to give **8** and **9**, respectively. Treatment with 90% acetic acid afforded the partially esterified MOP glycosides **10** and **11** in excellent yield. Previous work in our laboratory[29] had shown that compounds related to the corresponding orthoamide, easily prepared from **3** by selective protection then by treatment with *N*,*N*-dimethylacetamide dimethyl acetal, also afforded the diester **10**, but the cleavage was not as regioselective as in the case of the orthoesters **8** or **9**. As a parallel series, we also prepared the 2,6-dibenzoate analogs of **10** and **11**.

Perbenzylation of MOP β-D-galactopyranoside under standard conditions gave the perbenzylated ether **13** which would act as the α-orienting Gal donor.[25] Having access to pyridyl and MOP Gal acceptors **10** and **11**, with ether and ester C-6 substituents, we studied the coupling reaction with 6-*N*-benzyloxycarbonylamino 1-hexanol in the presence of a variety of activators. The Lewis acids TMS triflate, $Yb(TfO)_3$,[30] and $Cu(TfO)_2$,[25] and the protic acid $HBF_4{\cdot}Et_2O$[31] were effective activators, affording the alkyl β-D-galactopyranosides **12a** and **12b** in good yields. As expected, the glycosylation reaction was selective, favoring the acceptor alcohol (1.5 equiv.), with no trace of self-condensation products arising from **10a**,**b** or **11a**,**b**, acting as donor and acceptor to each other. It was important to use pre-dried $Yb(TfO)_3$ and $Cu(TfO)_2$ for efficient glycosylations. The reaction between the donor **13** and the acceptor **12a** was best achieved in the presence of dry $Yb(TfO)_3$ as activator, affording a 76% yield of the intended disaccharide **14a**. With $Cu(TfO)_2$, toluene was found to be better than dichloromethane as solvent, but conditions needed to be rigorously anhydrous. The yield of the glycosylation was found to be diminished when the dibenzoate **12b** was used as an acceptor. Sequential deprotection of **14a** afforded the intended disaccharide hapten **15**.

The above sequence demonstrated the successful utilization of a common Gal donor/acceptor to construct the Galα1→β GalOR disaccharide. For the synthesis of **2** we considered two approaches (Fig. 1). In the first, we envisaged the stepwise construction of the trisaccharide, utilizing a substituted MOP Galβ1→4 donor and an MOP GlcNAc(or NPht) acceptor, followed by coupling with MOP Galα1→3 donor

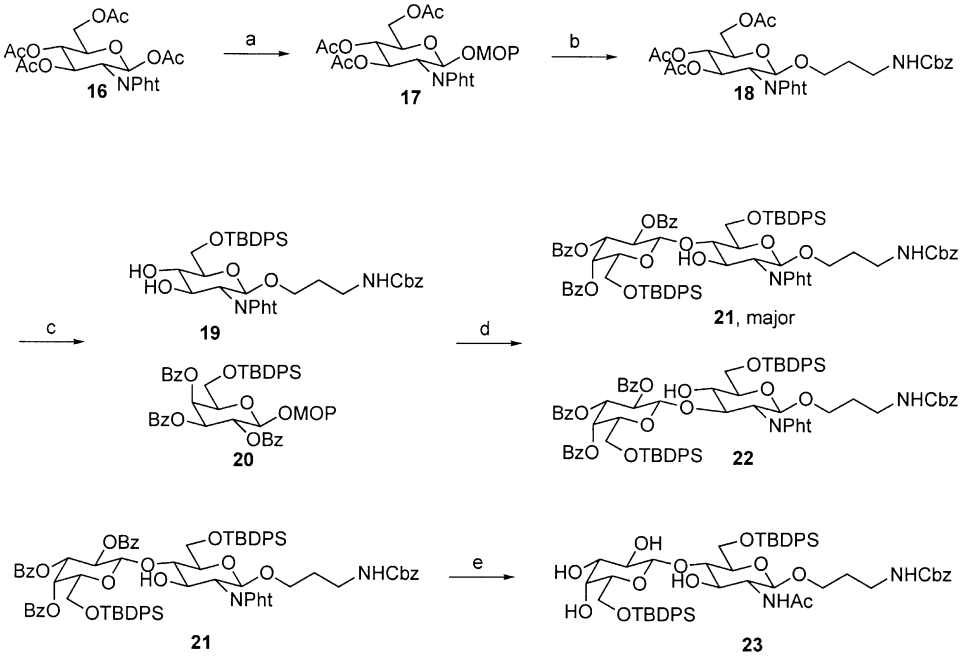
13. A more practical approach would capitalize on the ready availability of alkyl *N*-acetyl lactosaminides via chemoenzymatic routes as acceptor,[32] and using **13** as a Galα1→3 donor.

Scheme 2 illustrates the first approach in which 2-deoxy-2-phthalimido-β-D-glucopyranose pentaacetate **16** was converted to the corresponding MOP glycoside **17**. Treatment of **17** with 3-benzyloxycarbonylamino 1-propanol in the presence of $HBF_4{\cdot}Et_2O$ in dichloromethane led to the expected β-D-glycoside **18** in 65% yield. Deacetylation and selective protection of the primary hydroxy group afforded **19** in excellent yield. Glycosylation with 2,3,4,-tri-*O*-benzoyl 6-*O*-*tert*-butyldiphenylsilyl MOP β-galactopyranoside **20** in the presence of $Cu(TfO)_2$[25] as activator gave the intended Galβ1→4GlcNPht disaccharide **21** in 64% yield accompanied by the regioisomeric glycoside **22** as a minor product. Hydrolysis of the ester groups in the presence of sodium methoxide in methanol followed by hydrazinolysis and *N*-acetylation afforded **23**.

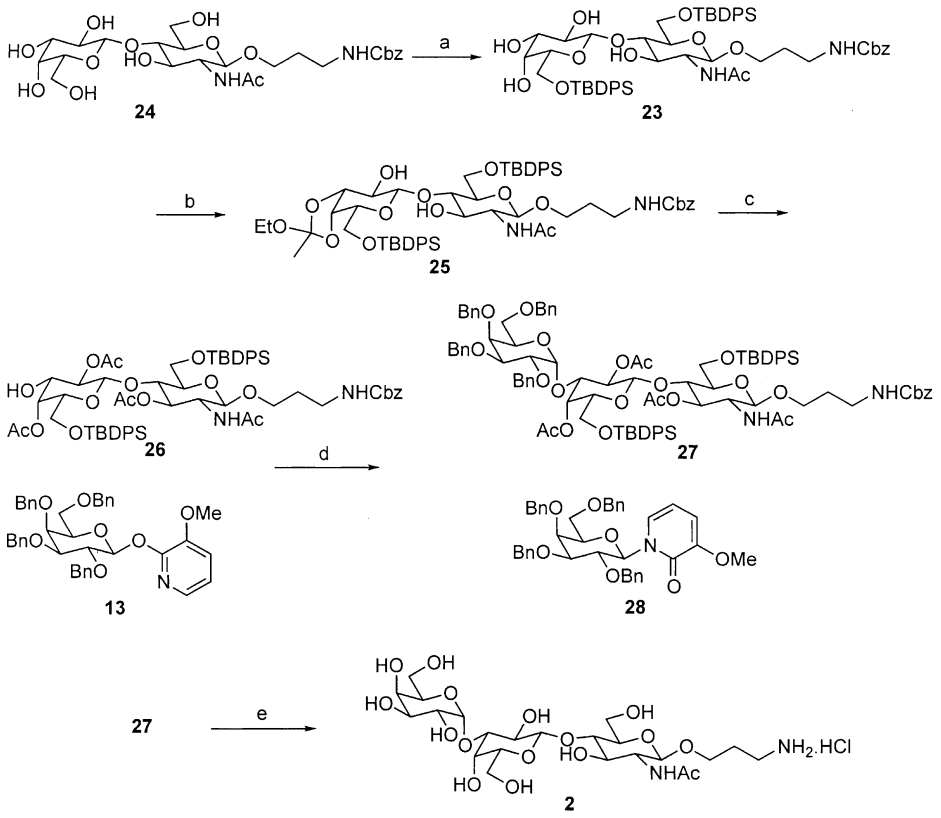
The alternative strategy utilizing a preformed 3-benzyloxylcarbonylamino β-*N*-acetyl lactosaminide **24**,[32] was next investigated (Scheme 3). Treatment with *tert*-butyldiphenylsilyl chloride afforded the selectively protected ether derivative **23** in excellent yield identical to the product obtained previously (Scheme 2). At this point we adapted the orthoester protocol to achieve selective esterification of the 3,4-diol in the terminal Gal unit, as was successfully implemented for the synthesis of **1** (Scheme 1). Thus, treatment of **23** with trimethyl orthoacetate in the presence of pyridinium triflate afforded the corresponding orthoester **25**, which was converted to the diacetate **26** upon treatment with acetic acid. We next studied the critical α1→3 galactosylation reaction with **13** as donor and **26** as acceptor in the presence of two activators. Using $Yb(TfO)_3$ in dichloromethane required 2 equiv. of donor **13**, affording 63% of the desired Galα1→3 trisaccharide **27**. Portionwise addition of 1 equiv. of **13** first and another equivalent after 4 h was found to give better results than addition in one portion. The reaction with **26** was slower in the presence of $Cu(TfO)_2$, but only 1 equiv. of donor **13** was required to give a 60% yield of **27**. Removal of traces of moisture by using previously dried activator was found to be highly beneficial. In both cases, a minor by-product was identified as the 2,3,4,6-tetra-*O*-benzyl β-D-galactopyranosyl *N*-3-methoxy-2-pyridone **28**. We have observed such *N*-glycosides in glycosylations of MOP donors with somewhat less reactive acceptors. They presumably result from the condensation of the 3-methoxy-2-pyridone formed in the reaction or cleaved due to adventitious moisture with the glycosyl cation.

There remained to deprotect **27** en route to the intended target **2**. Removal of the TBDPS protecting groups with fluoride ion was slow and afforded mixtures of esters, possibly resulting from ester migration. On the other hand, deesterification with sodium methoxide in methanol proceeded smoothly, after which the silyl ethers could be easily removed. Hydrogenolysis of the *N*-benzyloxycarbonyl and benzyl ether groups proved problematic, resulting in mixtures. However, using 20% palladium hydroxide on charcoal (Pearlman's catalyst) in aqueous dioxane proved successful, affording the desired trisaccharide **2** as a colorless powder.

We have reported on synthetic protocols for the elaboration of hapten-like motifs based on B disaccharide **1** and linear B type 2 trisaccharide **2**. A noteworthy feature in these protocols is the utilization of a common Gal unit as donor and acceptor having the same leaving group but differing in the *O*-substituents. The syntheses have elements of practicality and the potential for scale-up since they avoid the use



Scheme 2. (a) i. HBr, AcOH, Ac_2O, rt, 20 h. ii. silver 3-methoxy-2-pyridoxide, toluene, reflux 1 h, 50% two steps. (b) $HBF_4{\cdot}Et_2O$, DCM, 12 h, rt, 65%. (c) i. MeONa, MeOH, overnight, rt, 91%. ii. TBDPSCl, imidazole, DMF, rt, overnight, 92%. (d) $Cu(OTf)_2$, DCM, rt, 6 h, 64%. (e) i. MeONa/MeOH, rt, overnight. ii. hydrazine hydrate, EtOH, reflux, 4 h. iii. Ac_2O, MeOH, 61%.



Scheme 3. (a) TBDPSCl, imidazole, DMF, 6 h, rt. (b) $MeC(OEt)_3$, pyridinium triflate, DCM, 45–60 min, rt. (c) i. Ac_2O, DMAP, DCM, 1 h. ii. 90% AcOH, 10 min, rt, 86%. (d) $Cu(OTf)_2$, toluene, 20 h, **27**, 60%; or 2 equiv. **13**, $Yb(OTf)_3$, DCM, 8 h, **27**, 63%, **28** also isolated. (e) i. MeONa, MeOH, rt, 48 h. ii. TBAF, THF, rt, 24 h. iii. 20% $Pd(OH)_2$/C, H_2, 60 psi, dioxane/water, 1 h, then HCl, H_2, 60 psi, rt, overnight, 65%.

of toxic heavy metal salts, thiol reagents, or unstable intermediates.

2. Experimental

2.1. General information

Solvents were distilled under positive pressure of dry nitrogen before use and dried by standard methods: THF and ether, from Na/benzophenone; and CH_2Cl_2, from CaH_2. All commercially available reagents were used without further purification. All reactions were performed under nitrogen atmosphere. NMR (^1H, ^{13}C) spectra were recorded on AMX-300 and ARX-400 spectrometers. The term [(−)] in ^{13}C data refers to the sign of the corresponding peak in the DEPT 135 NMR experiment. Low- and high-resolution mass spectra were recorded on VG Micromass, AeI-MS902 or Kratos MS-50 spectrometers using fast atom bombardment (FAB) or electrospray techniques. Optical rotations were recorded on a Perkin–Elmer 241 polarimeter in a 1 dm cell at ambient temperature. Analytical thin-layer chromatography was performed on Merck $60F_{254}$ pre-coated silica gel plates. Visualization was performed by ultraviolet light and/or by staining with ceric ammonium molybdate or ninhydrine. Flash column chromatography was performed using (40–60 μm) silica gel at increased pressure.

2.1.1. Silver 2-pyridoxide. 2-Hydroxypyridine (10 g, 105.14 mmol) was dissolved in a solution of sodium hydroxide (4.2 g, 1 equiv.) in H_2O (70 mL). This solution was poured under heavy stirring into a solution of silver nitrate (17.8 g, 1 equiv.) in H_2O (70 mL). The mixture was stirred for 15 min, the slurry was filtered, washed with water (500 mL), MeOH (100 mL) and dried under vacuum overnight. The crusty material thus obtained was pulverized and the powder further dried overnight under vacuum to give silver 2-pyridoxide (20.5 g, 101.5 mmol, 97%) as an amorphous white solid.

2.1.2. 3-Methoxy-2-(1*H*)-pyridone. To a 1.4 M aqueous solution of sodium hydroxide at 0°C was added 2,3-dihydroxypyridine (100 g, 0.9 mol). After 15 min dimethylsulfate (85.2 mL, 1 equiv.) was added carefully at 0°C and the mixture was stirred at room temperature for 3 h. Neutralization with acetic acid till pH 7, extraction of the crude product with chloroform (10×1 L) and concentration of the organic layer gave the title compound, which was recrystallized in chloroform to provide pure 3-methoxy-2-(1*H*)-pyridone as cream-colored needles (85.1 g, 75.5%): mp 118°C. ^1H NMR ($CDCl_3$, 400 MHz); δ: 7.04 (d, J_{ac}= 6.5 Hz, 1H, H–C), 6.76 (d, J_{ab}=7.4 Hz, 1H, H-B), 6.23 (dd, J_{ab}=7.4 Hz, J_{ac}=6.5 Hz, 1H, H–A), 3.84 (s, 3H,OMe). ^{13}C NMR (CD_3OD, 100 MHz); δ: 160.3 (CO-pyridyl), 149.6 (CO-pyridyl), 125.3 (CH-pyridyl), 114.7 (CH-pyridyl), 106.5 (CH-pyridyl), 55.7 (OMe). HR-FABMS calcd for $C_6H_7O_2N$ *m/z* 125.0477; found 125.0479.

2.1.3. Silver 3-methoxy-2-pyridoxide. 3-Methoxy-2-(1*H*)-pyridone (6 g, 48 mmol) was dissolved in a solution of sodium hydroxide (1.92 g, 1 equiv.) in water (140 mL). This solution was poured under heavy stirring into a

solution of silver nitrate (8.15 g, 1 equiv.) in water (70 mL), the mixture was stirred for 30 min, the slurry was filtered, washed with water (500 mL), methanol (100 mL) and dried under vacuum overnight. The crusty material thus obtained was pulverized and the powder further dried overnight under vacuum to give silver 3-methoxy-2-pyridoxide as a purple powder (10.5 g, 45 mmol, 94%).

2.1.4. 2-Pyridyl 2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranoside (5). To a suspension of 1,2,3,4,6-penta-*O*-acetyl-β-D-galactopyranose **4** (10 g, 25.63 mmol) in Ac_2O (1.25 mL) and AcOH (25 mL) was added HBr (30% in AcOH, 12.5 mL) dropwise. The reaction mixture was stirred for 2 h at room temperature, diluted with toluene (250 mL), washed with ice water (2×150 mL), cold saturated $NaHCO_3$ (100 mL), ice water (100 mL) and concentrated. The residue was redissolved in toluene, concentrated and the residue dried by codistillation with dry toluene (2×75 mL). The residue was redissolved in dry toluene (80 mL) and silver 2-pyridoxide (5.95 g, 15% excess) was added in one portion. The mixture was refluxed under vigorous stirring for 1 h, allowed to cool down to room temperature, filtered through Celite®, and the bed was washed with toluene (150 mL). The filtrate was washed with saturated $NaHCO_3$ (100 mL); the heterogeneous mixture was filtered through a Celite® pad, rinsed with toluene and both phases separated. The organic phase was washed with water (100 mL), dried (Na_2SO_4), concentrated and purified by flash chromatography (EtOAc/hexanes 1:1) giving **5** (7.73 g, 18.17 mmol, 71% yield) as a white foam: $[\alpha]_D=+27$ (*c* 1.0, $CHCl_3$). ^1H NMR ($CDCl_3$, 400 MHz); δ ppm: 8.13 (1H), 7.61 (1H), 6.97 (1H) and 6.80 (1H) (4m, PyH), 6.17 (d, 1H, H-1, $J_{1,2}=8.3$ Hz), 5.49 (dd, 1H, H-2, $J_{2,3}=10.4$ Hz), 5.45 (dd, 1H, H-4, $J_{4,3}=3.4$ Hz, $J_{4,5}=0.0$ Hz), 5.15 (dd, 1H, H-3), 4.13 (m, 3H, H-5, H-6 and H-6A), 2.15 (s, 3H), 1.99 (s, 6H) and 1.95 (s, 3H), ($COCH_3$). ^{13}C NMR ($CDCl_3$, 100 MHz); δ ppm: 170.2, 170.1, 169.9 and 169.4 (CO), 161.1 (PyC), 146.6, 139.2, 118.7, and 111.6 (4PyCH), 93.7 (C-1), 70.9, 70.9, 68.3, and 66.8 (C-2 to C-5), 60.8 [(−), C-6], 20.5, (2C), 20.4 and 20.4 ($4COCH_3$). HR-FABMS calcd for $C_{19}H_{24}O_{10}N$ *m/z* 426.1400; found 426.1417.

2.1.5. 3-Methoxy-2-pyridyl 2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranoside (6). Using the same procedure as above, a solution of **4** (4 g, 10.25 mmol), Ac_2O (0.5 mL) and AcOH (10 mL), and HBr (30% in AcOH, 5 mL) afforded the corresponding bromide which was dissolved in dry toluene (36 mL). Silver 3-methoxy-2-pyridoxide (2.8 g, 20% excess) was added in one portion, and the system was refluxed under vigorous stirring for 1 h. Work-up and purification (flash chromatography, EtOAc/hexanes 1:1) gave **6** (4.03 g, 8.85 mmol, 86% yield) as a white foam: $[\alpha]_D=+35.18$ (*c* 1.1, $CHCl_3$). ^1H NMR ($CDCl_3$, 400 MHz); δ ppm: 7.70 (dd, 1H, *J*=1.3, 4.9 Hz, PyCH), 7.10 (dd, 1H, *J*=1.3, 7.9 Hz, PyCH), 6.94 (dd, 1H, *J*=4.9, 7.8 Hz, PyCH), 6.21 (d, 1H, H-1, $J_{1,2}=8.3$ Hz), 5.57 (dd, 1H, H-2, $J_{2,3}=10.4$ Hz), 5.45 (dd, 1H, H-4, $J_{4,3}=3.3$ Hz, $J_{4,5}=0.0$ Hz), 5.16 (dd, 1H, H-3), 4.13 (m, 3H, H-5, H-6 and H-6A), 3.82 (s, 3H, OCH_3), 2.15 (s, 3H), 1.99 (s, 6H), and 1.95 (s, 3H) (CH_3CO). ^{13}C NMR ($CDCl_3$, 100 MHz); δ ppm: 170.3, 170.2, 170.1 and 169.3 (CO), 151.5, and 144.1 (PyC), 136.6, 119.1, and 118.9 (PyCH), 93.8 (C-1), 71.1, 71.0, 68.3, and 66.9 (C-2 to C-5), 61.0 [(−), C-6], 55.8 (OCH_3), 20.6, and 20.5 ($COCH_3$). HR-FABMS calcd for $C_{20}H_{26}O_{11}N$ *m/z* 456.1505; found 456.1496.

2.1.6. 2-Pyridyl β-D-galactopyranoside (7). To a solution of **5** (10.99 g, 25.84 mmol) in MeOH (85 mL) was added sodium methoxide (0.5N in MeOH, 0.2 mL) and the reaction mixture was stirred for 6 h at room temperature. The solution was neutralized with Amberlite® IRC-50S (H^+) ion-exchange resin, the resin filtered off, and washed with MeOH. The resulting solution was concentrated under vacuum giving 2-pyridyl β-D-galactopyranoside **7** (6.3 g, 24.5 mmol, 95%) as a white foam: $[\alpha]_D=-14$ (*c* 1.0, CH_3OH). ^1H NMR (CD_3OD, 400 MHz); δ ppm: 8.16 (m, 1H, PyCH), 7.76 (m, 1H, PyCH), 7.06 (m, 1H, PyCH), 6.96 (m, 1H, PyCH), 5.63 (d, 1H, H-1, $J_{1,2}=8.0$ Hz), 3.94 (dd, 1H, H-4, $J_{4,3}=3.3$ Hz, $J_{4,5}=0.0$ Hz), 3.84 (dd, 1H, H-2, $J_{2,3}=9.8$ Hz), 3.73–3.76 (m, 3H, H-5, H-6 and H-6A) and 3.62 (dd, 1H, H-3). ^{13}C NMR (CD_3OD, 100 MHz); δ ppm: 164.0 (PyC), 147.8, 141.1, 119.7, and 112.5 (PyCH), 98.9 (C-1), 77.0, 74.9, 71.9, 70.1 (C-2 to C-5), 62.3 [(−), C-6]. HR-FABMS calcd for $C_{11}H_{16}O_6N$ *m/z* 258.0977; found 258.0967.

2.1.7. 3-Methoxy-2-pyridyl β-D-galactopyranoside (3). Using the same procedure **7** (4.01 g, 8.8 mmol) was dissolved in MeOH (30 mL) and sodium methoxide (0.5N in MeOH, 0.2 mL). Neutralization and concentration gave **3** (2.37 g, 8.25 mmol, 94%) as a white foam: $[\alpha]_D=+0.7$ (*c* 0.7, CH_3OH). ^1H NMR (CD_3OD, 400 MHz); δ ppm: 7.68 (dd, 1H, *J*=1.3, 4.9 Hz), 7.10 (dd, 1H, *J*=1.3, 7.9 Hz), and 6.94 (dd, 1H, *J*=4.9, 7.8 Hz) (PyCH), 5.86 (d, 1H, H-1, $J_{1,2}=8.1$ Hz), 3.93 (dd, 1H, H-4, $J_{4,3}=3.2$ Hz, $J_{4,5}=0.0$ Hz), 3.90 (dd, 1H, H-2, $J_{2,3}=9.5$ Hz), 3.86 (m, 3H, H-5, H-6 and H-6A), 3.72 (s, 3H, OCH_3), 3.62 (dd, 1H, H-3). ^{13}C NMR (CD_3OD, 100 MHz); δ ppm: 153.7 and 145.8 (PyC), 137.7, 120.5, and 119.7 (PyCH), 97.8 (C-1), 76.9, 75.0, 71.7, and 70.1 (C-2 to C-5), 62.2 [(−), C-6], 56.3 (OCH_3). HR-FABMS calcd for $C_{12}H_{18}O_7N$ *m/z* 288.1083; found 288.1078.

2.1.8. 2-Pyridyl 4-*O*-acetyl-2-*O*-benzoyl-6-*O*-*tert*-butyldiphenylsilyl-β-D-galactopyranoside (10a). (a) *Orthoester approach*. To a solution of **7** (1.42 g, 5.52 mmol) in dry DMF (20 mL) was added TBDPSCl (1.58 mL, 1.1 equiv.) dropwise and the reaction mixture stirred for 5 h at room temperature. The solution was diluted with EtOAc (150 mL), extracted with H_2O (2×100 mL), dried (Na_2SO_4) and concentrated. The residue was purified by flash chromatography (EtOAc/hexanes 1:2 then EtOAc) affording 2-pyridyl 6-*O*-*tert*-butyldiphenylsilyl-β-D-galactopyranoside (2.21 g, 4.46 mmol, 81%) as a white foam: HR-FABMS calcd for $C_{27}H_{34}O_6NSi$ *m/z* 496.2155; found 496.2126. A solution of the preceding compound (1.95 g, 3.93 mmol), triethyl orthoacetate (1.00 mL, 2 equiv.) and pyridinium triflate (2 mg) in CH_2Cl_2 (35 mL) was stirred at room temperature for 45 min. The reaction mixture was quenched with DMAP (0.96 g, 7.88 mmol), the solvent removed under vacuum, and the solid residue dried under high vacuum (20 min at 40°C bath temperature). The residue was redissolved in CH_2Cl_2 (17.5 mL), BzCl (0.55 mL, 20% excess) was added and the solution stirred for 1 h 30 min at room temperature. The excess BzCl was quenched

by stirring the reaction mixture for 15 min after addition of MeOH (0.5 mL). The solution was concentrated under vacuum and the residue consisting of **8** was redissolved in AcOH (90%, 20 mL). The solution was stirred for 15 min at room temperature, diluted with CH_2Cl_2 (150 mL), washed with ice water (100 mL), cold saturated $NaHCO_3$ solution (100 mL), ice H_2O (100 mL), dried (Na_2SO_4), filtered and concentrated. The crude product was purified by flash chromatography (EtOAc/hexanes 1:3) giving **10a** (1.92 g, 2.99 mmol, 76%) as white foam: $[\alpha]_D=-14.4$ (*c* 1.1, $CHCl_3$). ^1H NMR ($CDCl_3$, 300 MHz); δ ppm: 8.15 (1H), 6.92 (1H) and 6.74 (1H) (m, 3PyH), 7.98 (2H), 7.62–7.58 (4H), 7.58–7.48 (2H), 7.42–7.30 (8H), (m, 15PhCH and 1PyH), 6.36 (d, 1H, H-1, $J_{1,2}=8.3$ Hz), 5.64 (dd, 1H, H-4, $J_{4,3}=3.5$ Hz, $J_{4,5}=0.7$ Hz), 5.54 (dd, 1H, H-2, $J_{2,3}=10.0$ Hz), 4.20 (dd, 1H, H-3), 4.05 (ddd, 1H, H-5, $J_{5,6}=6.0$ Hz, $J_{5,6A}=7.6$ Hz), 3.78 (dd, 1H, H-6, $J_{6,6A}=10.0$ Hz), 3.73 (dd, 1H, H-6A), 2.10 (s, 3H, $COCH_3$), 1.03 (s, 9H, $SiC(CH_3)_3$). ^{13}C NMR ($CDCl_3$, 100 MHz); δ ppm: 171.1 and 166.7 (CO), 161.5 (PyC), 133.0, 132.9, and 129.4 (PhC), 135.6, 133.3, 129.9, 129.8, 129.7, 128.3, 127.7, and 127.7 (PhCH), 146.6, 139.3, 118.6, and 111.9 (PyCH), 93.7 (C-1), 74.1, 73.0, 72.0, and 69.8 (C-2 to C-5), 61.5 [(−), C-6], 20.8 ($COCH_3$), 26.7 and 19.1 (q) ($SiC(CH_3)_3$). FABMS (rel. intensity) 642.4 (29), $[M+H]^+$. HR-FABMS calcd for $C_{36}H_{40}O_8NSi$ *m/z* 642.2523; found 642.2513.

(b) *Orthoamide approach*. To a solution of **7** (317 mg, 0.632 mmol) in dry CH_2Cl_2 (9 mL) was added *N*,*N*-dimethylacetamide dimethyl acetal (0.11 mL, 20% excess) under nitrogen and the reaction mixture was stirred for 15 min at room temperature. The solvent was removed under vacuum and the residue concentrated under high vacuum (20 min, 40°C bath temperature). To a solution of the crude product in dry CH_2Cl_2 (6 mL) was added a solution of dry DMAP (154.4 mg, 2 equiv.) in CH_2Cl_2 (3 mL) via cannula followed by benzoyl chloride (0.077 mL, 5% excess). The reaction mixture was stirred under nitrogen for 2 h at room temperature, diluted with CH_2Cl_2 (30 mL), washed with water (20 mL), dried (Na_2SO_4), and concentrated. The crude product was dissolved in AcOH (90% aq., 5 mL) and stirred for 15 min at room temperature. The solution was diluted with CH_2Cl_2 (50 mL), washed with ice water (30 mL), cold saturated $NaHCO_3$ (30 mL), ice water (30 mL), dried (Na_2SO_4) and concentrated. The crude product was purified by flash chromatography (EtOAc/hexanes 1:3, two columns were necessary) affording pure **10a** (228 mg, 0.35 mmol, 55%) and the corresponding 3-acetate (68 mg, 0.11 mmol, 17%), both as white foams.

2.1.9. 3-Methoxy-2-pyridyl 4-*O*-acetyl-2-*O*-benzoyl-6-*O*-*tert*-butyldiphenylsilyl-β-D-galactopyranoside (11a). A solution of **3** (2 g, 6.69 mmol) and TBDPSCl (1.9 mL, 1.1 equiv.) in DMF (24 mL) was stirred at room temperature for 5 h to afford after work-up and purification 3-methoxy-2-pyridyl 6-*O*-*tert*-butyldiphenylsilyl-β-D-galactopyranoside (2.75 g, 5.23 mmol, 78%) as a white foam: HR-FABMS calcd for $C_{28}H_{36}O_7NSi$ *m/z* 526.2261; found 526.2286. The preceding compound (142.5 mg, 0.271 mmol), triethyl orthoacetate (99 μmL) and pyridinium triflate (1 mg), in CH_2Cl_2 (2.5 mL), was stirred at room temperature for 1 h 15 min, and DMAP (66 mg, 2 equiv.) was added; the solid residue obtained after evaporation was dissolved in CH_2Cl_2 (1.3 mL) and the solution stirred for 1 h at room temperature after addition of BzCl (38 μL). The excess BzCl was quenched by addition of methanol and the crude product obtained after work-up consisting of **9** was treated with a solution of AcOH, AcONa and water (90% aq. AcOH+AcONa until pH ~4, 2 mL). The solution was stirred at room temperature until no more starting material was detected by TLC (~2 h). Work-up and purification (flash chromatography with pure EtOAc) afforded **11a** (122.9 mg, 0.183 mmol, 67%) as white foam: $[\alpha]_D=-7.9$ (*c* 1.1, $CHCl_3$). ^1H NMR ($CDCl_3$, 300 MHz); δ ppm: 7.98 (2H), 7.65 (4H), 7.52 (1H), and 7.46–7.32 (8H) (4m, 15H, 15PhCH), 7.72 (1H), 7.02 (1H), and 6.90 (1H) (3m, 3H, PyCH), 6.44 (d, 1H, H-1, $J_{1,2}=8.2$ Hz), 5.66 (dd, 1H, H-4, $J_{4,3}=3.4$ Hz, $J_{4,5}=0.0$ Hz), 5.59 (dd, 1H, H-2, $J_{2,3}=9.9$ Hz), 4.20 (ddd, 1H, $J_{3,OH}=3.0$ Hz, H-3), 4.04 (ddd, 1H, H-5, $J_{5,6}=4.1$ Hz, $J_{5,6A}=6.4$ Hz), 3.88–3.72 (m, 2H, H-6, and H-6A), 3.70 (s, 3H, OCH_3), 3.06 (d, 1H, OH), 2.10 (s, 3H, $COCH_3$), 1.03 (s, 9H, $SiC(CH_3)_3$). ^{13}C NMR ($CDCl_3$, 100 MHz); δ ppm: 171.0 and 166.6 (CO), 151.8 and 144.1 (PyC), 132.9, 129.4, and 128.4 (PhC), 136.5, 119.0, and 118.7 (PyCH), 135.5, 133.1, 129.8, 129.7, 129.6, 128.1, 127.6, and 127.5 (PhCH), 93.7 (C-1), 74.0, 73.3, 72.0, and 69.5 (C-2 to C-5), 61.2 [(−), C-6], 55.6 (OCH_3), 20.7 ($COCH_3$), 26.6 and 18.9 (q) ($SiC(CH_3)_3$). HR-FABMS calcd for $C_{37}H_{42}O_9NSi$ *m/z* 672. 2628; found 672.2623.

2.1.10. 2-Pyridyl 4-*O*-acetyl-2,6-di-*O*-benzoyl-6-*O*-*tert*-butyldiphenylsilyl-β-D-galacto-pyranoside (10b). A solution of **8** (1.50 g, 3.03 mmol), triethyl orthoacetate (0.73 mL, 1.3 equiv.) and pyridinium triflate (1 mg) in CH_2Cl_2 (30.3 mL) was stirred at room temperature for 45 min. After the addition of one drop of Et_3N and stirring the solution for 5 min at room temperature, the reaction mixture was concentrated to dryness under vacuum. The residue was dissolved in THF (3 mL), TBAF (3.3 mL, 1.1 equiv.) was added and the solution stirred for 2 h at room temperature. The reaction mixture was diluted with CH_2Cl_2 (100 mL), extracted with water, dried (Na_2SO_4) and concentrated. To the solution of the crude product in CH_2Cl_2 (15.2 mL), DMAP (3.3 g, 1.2 equiv.) and benzoyl chloride (0.772 mL, 1.1 equiv.) were added and the mixture was stirred for 1 h 30 min at room temperature. Excess BzCl was quenched by addition of MeOH (0.5 mL) and stirring for 15 min. The solution was concentrated under vacuum, the residue dissolved in AcOH (90%, 20 mL), and stirred for 15 min at room temperature. The reaction mixture was diluted with CH_2Cl_2 (150 mL), washed with ice water (100 mL), cold saturated $NaHCO_3$ (100 mL), ice water (100 mL), dried (Na_2SO_4), filtered and concentrated. The crude was purified by flash chromatography (EtOAc/hexanes 1:2) to give **10b** (0.84 g, 1.66 mmol, 55%) as a white foam: $[\alpha]_D=+18.6$ (*c* 1.1, $CHCl_3$). ^1H NMR ($CDCl_3$, 300 MHz); δ ppm: 8.10 (1H), 6.92 (1H), and 6.78 (1H) (3m, 3PyCH), 8.01 (4H), 7.55 (3H), and 7.44 (4H) (3m, 10PhCH and 1PyCH), 6.39 (d, 1H, H-1, $J_{1,2}=8.3$ Hz), 5.64 (dd, 1H, H-2, $J_{2,3}=10.0$ Hz), 5.61 (dd, 1H, H-4, $J_{4,3}=3.4$ Hz, $J_{4,5}=0.0$ Hz), 4.50 (dd, 1H, H-6, $J_{6,5}=7.1$ Hz, $J_{6,6A}=11.1$ Hz), 4.40 (dd, 1H, H-6A, $J_{6A,5}=6.3$ Hz), 4.30 (dd, 1H, H-5), 4.21 (dd, 1H, H-3), 3.44 (br, 1H, OH), 2.24 (s, 3H, $COCH_3$). ^{13}C NMR

($CDCl_3$, 100 MHz); δ ppm: 170.8, 166.7 and 165.9 (CO), 161.3 (PyC), 129.4 and 129.1 (2PhC), 146.5, 139.1, 118.5, and 111.7 (4PyCH), 133.3, 133.0, 129.8, 129.6, 128.2 (2C) (PhCH), 93.6 (C-1), 72.8, 71.6, 71.4, and 69.7 (C-2 to C-5), 61.8 [(−), C-6], 20.7 ($3COCH_3$). HR-FABMS calcd for $C_{27}H_{26}O_9N$ *m/z* 508.1607; found 508.1619.

2.1.11. 3-Methoxy-2-pyridyl 4-*O*-acetyl-2,6-di-*O*-benzoyl-6-*O*-*tert*-butyldiphenylsilyl-β-D-galactopyranoside (11b). A solution of **9** (1.90 g, 3.03 mmol), triethyl orthoacetate (0.73 mL, 1.3 equiv.) and pyridinium triflate (1 mg) in CH_2Cl_2 (30.3 mL) was stirred for 45 min. The mixture was treated with Et_3N (1 drop) and worked-up as described above. The solid residue was redissolved in THF (2.1 mL), TBAF (2.09 mL, 1.1 equiv.) was added and the mixture was stirred for 2 h at room temperature and worked-up as usual. The crude product was treated with DMAP (0.557 g, 1.2 equiv.) and BzCl (485 mL, 1.1 equiv) in CH_2Cl_2 (9.5 mL) for 3 h at room temperature and the reaction mixture worked-up as before. The crude product was dissolved in 15 mL of buffered AcOH (90% AcOH+AcONa, pH ~4, 10 mL) and stirred at room temperature until TLC indicated the completeness of the reaction, ~1 h. After the same work-up described for **10b**, the crude was purified by flash chromatography (EtOAc/hexanes 2:3) giving **11b** (0.61 g, 1.66 mmol, 60%) as white foam: $[\alpha]_D$=+16.1 (*c* 1.0, $CHCl_3$). ^1H NMR ($CDCl_3$, 300 MHz); δ ppm: 8.00 (4H), 7.55 (2H), and 7.41 (4H) (3m, 10H, PhCH), 7.70 (1H), 7.04 (1H), and 6.92 (1H) (3m, 3H, PyCH), 6.47 (d, 1H, H-1, $J_{1,2}$=8.2 Hz), 5.65 (dd, 1H, H-2, $J_{2,3}$=9.8 Hz), 5.60 (dd, 1H, H-4, $J_{4,3}$=3.2 Hz, $J_{4,5}$=0.0 Hz), 4.51 (dd, 1H, H-6, $J_{6,5}$=6.9 Hz, $J_{6,6A}$=11.2 Hz), 4.39 (dd, 1H, H-6A, $J_{6A,5}$=6.5 Hz), 4.29 (dd, 1H, 3H), 4.20 (ddd, 1H, H-3, $J_{3,OH}$=6.2 Hz), 3.71 (s, 3H, OCH_3), 3.25 (d, 1H, OH), 2.25 (s, 3H, $COCH_3$). ^{13}C NMR ($CDCl_3$, 100 MHz); δ ppm: 170.9, 166.9 and 166.0 (CO), 151.7 and 144.2 (PyC), 129.5 and 129.3 (PhC), 136.6, 119.1, and 118.9 (PyCH), 133.3, 133.1, 129.9, 129.7, 128.3, and 128.3 (PhCH), 93.7 (C-1), 73.2, 72.0, 71.6, and 69.7 (C-2 to C-5), 62.0 [(−), C-6], 55.7 (OCH_3), 20.8 ($COCH_3$). HR-FABMS calcd for $C_{28}H_{28}O_{10}N$ *m/z* 538.1713; found 538.1724.

2.1.12. 6-Benzyloxycarbonylamino-1-hexanyl 4-*O*-acetyl-2-*O*-benzoyl-6-*O*-*tert*-butyldiphenylsilyl-β-D-galactopyranoside (12a). A. *From **10a** using $HBF_4{\cdot}Et_2O$ as activator*. To a solution of **10a** (0.96 g, 1.5 mmol) and 6-benzyloxycarbonylamino-1-hexanol (0.45 g, 1.2 equiv.) in CH_2Cl_2 (21.4 mL) was added $HBF_4{\cdot}Et_2O$ (58% in Et_2O, 184 μL, 1.1 equiv.) in one portion and the mixture was stirred for 1 h at room temperature. The reaction mixture was diluted with CH_2Cl_2 (150 mL), washed with water (75 mL), 1N HCl (75 mL), water (75 mL), dried (Na_2SO_4) and concentrated. The crude product was purified by flash chromatography (EtOAc/hexanes 1:2) giving **12a** (0.96 g, 1.2 mmol, 80%) as a white foam.

B. *From **11a***. a. Using $HBF_4{\cdot}Et_2O$ as activator: To a solution of **11a** (2.0 g, 2.98 mmol) and 6-benzyloxycarbonylamino-1-hexanol (1.12 g, 1.2 equiv.) in CH_2Cl_2 (60 mL) was added $HBF_4{\cdot}Et_2O$ (58% in Et_2O, 365 μL, 1.1 equiv.) in one portion and the mixture stirred for 1 h at room temperature. The reaction mixture was diluted with CH_2Cl_2 (150 mL), washed with water (75 mL), 1N HCl (75 mL), water (75 mL), dried (Na_2SO_4) and concentrated. The crude was purified by flash chromatography (EtOAc/hexanes 1:2) giving **12a** (1.95 g, 2.44 mmol, 82%) as a white foam.

b. Using TMS triflate as activator: To a solution of **11a** (1 g, 1.49 mmol) and 6-benzyloxycarbonylamino-1-hexanol (411 mg, 1.1 equiv.) in CH_2Cl_2 (29.8 mL) was added TMSTf (285 μL mg, 1.1 equiv.) in one portion and the mixture stirred for 1 h at room temperature. The reaction mixture was diluted with CH_2Cl_2 (150 mL), washed with water (50 mL), 1N HCl (50 mL), water (50 mL), dried (Na_2SO_4) and concentrated. The crude was purified by flash chromatography (EtOAc/hexanes 1:2) giving **12a** (0.94 mg, 1.17 mmol, 78%) as a white foam.

c. Using $Cu(TfO)_2$ as activator: To a solution of **11a** (55.0 mg, 0.082 mmol) and 6-benzyloxycarbonylamino-1-hexanol (30.5 mg, 1.5 equiv.) in CH_2Cl_2 (2 mL) containing molecular sieves (20 mg) was added $Cu(TfO)_2$ (43.9 mg, 1.5 equiv.) in one portion and the mixture stirred for 6 h at room temperature. The reaction mixture was quenched with a drop of pyridine, diluted with CH_2Cl_2 (20 mL) and filtered through a Celite® pad. The solution was washed with water (15 mL), 1N HCl (15 mL), water (15 mL), dried (Na_2SO_4) and concentrated. The crude product was purified by flash chromatography (EtOAc/hexanes 1:2) giving **12a** (43 mg, 0.053 mmol, 65%) as a white foam: $[\alpha]_D$=−28.5 (*c* 1.1, $CHCl_3$). ^1H NMR ($CDCl_3$, 300 MHz); δ ppm: 8.06 (2H), 7.66 (4H), 7.56 (1H), 7.48–7.31 (13H), (4m, 20H, PhCH), 5.56 (dd, 1H, H-4, $J_{4,3}$=3.5 Hz, $J_{4,5}$=0.0 Hz), 5.24 (dd, 1H, H-2, $J_{2,1}$=7.9 Hz, $J_{2,3}$= 10.0 Hz), 5.09 (s, 2H, CH_2Ph), 4.62 (m, 1H, NHCbz), 4.56 (d, 1H, H-1), 4.03 (dd, 1H, H-3), 3.87 (1H) and 3.43 (1H) (2 m, OCH_2R), 3.78 (m, 3H, H-5, H-6 and H-6A), 3.01 (m, 3H, $2NCH_2R$), 2.78 (br, 1H, OH), 2.08 (s, 3H, $COCH_3$), 1.48 (2H) and 1.16 (6H) (2 m, $-CH_2-$), 1.08 (s, 9H, $SiC(CH_3)_3$). ^{13}C NMR ($CDCl_3$, 100 MHz); δ ppm: 171.1 and 166.5 (CO), 133.1, 132.9, 128.0 and 129.7 (PhC), 135.6, 135.5, 133.2, 129.8, 129.8, 128.4, 128.3, 127.7, and 127.7 (PhCH), 101.1 (C-1), 73.6 (2C), 71.8 and 69.7 (C-2 to C-5), 69.8, 66.5, and 61.6 [(−), OCH_2R, CH_2Ph, and C-6], 40.8 [(−), $NHCH_2R$], 29.6, 29.2, 26.2, and 25.5 [(−), $-CH_2-$], 20.7 ($COCH_3$), 26.7 and 19.1 (q) ($SiC(CH_3)_3$). HR-FABMS calcd for $C_{45}H_{56}O_{10}NSi$ *m/z* 798.3673; found 798.3689.

2.1.13. 6-Benzyloxycarbonylamino-1-hexanyl 4-*O*-acetyl-2,6-di-*O*-benzoyl-β-D-galactopyranoside (12b) from 11b using $HBF_4{\cdot}Et_2O$ as activator. Adopting the same procedure as described for **11a** but using **11b** (0.301 g, 0.56 mmol) and 6-benzyloxycarbonylamino-hexanol (0.189 g, 1.2 equiv.) in CH_2Cl_2 (8 mL) and $HBF_4{\cdot}Et_2O$ (58% in Et_2O, 54.4 μL, 1.1 equiv.) afforded after flash chromatography (EtOAc/hexanes 1:1) **12b** (0.267 g, 0.40 mmol, 72%) as syrup: $[\alpha]_D$=−12.0 (*c* 1.1, $CHCl_3$). ^1H NMR ($CDCl_3$, 300 MHz); δ ppm: 8.04 (4H), 7.58 (2H), 7.46 (4H), 7.35 (5H), (4m, 15H, PhCH), 5.53 (dd, 1H, H-4, $J_{3,4}$=3.0 Hz, $J_{4,5}$=0.6 Hz), 5.31 (dd, 1H, H-2, $J_{2,1}$=7.9 Hz, $J_{2,3}$=10.0 Hz), 5.08 (s, 2H, CH_2Ph), 4.70 (m, 1H, NHCbz), 4.61 (d, 1H, H-1), 4.55 (dd, 1H, H-6, $J_{6,5}$=6.9 Hz, $J_{6,6A}$=11.3 Hz), 4.36 (dd, 1H, H-6A, $J_{6A,5}$=6.6 Hz), 4.01 (m, 2H, H-3, H-5), 3.90 (1H) and 3.47 (1H) (2m, 2H, $2OCH_2R$), 3.18 (br, 1H, OH), 2.18 (m, 2H, $NHCH_2R$),

2.00 (s, 3H, $COCH_3$), 1.50 (1H) and 1.18 (1H) (m, 2H, 8 –CH_2–). ^{13}C NMR ($CDCl_3$, 100 MHz); δ ppm: 171.0, 166.5, 166.1, and 156.3 (CO), 136.0 and 128.6 (2C) (3PhC), 133.3, 133.3, 129.8, 129.7, 129.5, 128.4, 128.4 and 128.0 (PhCH), 101.3 (C-1), 73.4, 71.3, 71.0 and 69.9 (C-2 to C-5), 70.1, 66.5 and 62.1 [(−), C-6, OCH_2R and CH_2Ph], 40.8 [(−), $NHCH_2R$], 29.6, 29.2, 26.2, and 25.4 [(−), 4 –CH_2–], 20.8 ($COCH_3$). HR-FABMS calcd for $C_{36}H_{42}O_{11}N$ *m/z* 664.2757; found 664.2770.

2.1.14. 3-Methoxy-2-pyridyl 2,3,4,6-tetra-*O*-benzyl-β-D-galactopyranoside (13). To a solution of **3** (2 g, 6.97 mmol) in dry DMF (69.7 mL) was added NaH (1.4, 60% in mineral oil, washed with hexanes) at 0°C; the mixture was stirred until no more gas evolved, ~1 h. At the same temperature was added dropwise BnBr (4.01 mL, 1.25 equiv.) and the mixture stirred for 1 h. The reaction mixture was allowed to warm up to room temperature then stirred overnight. The excess BnBr was quenched by adding MeOH then diluted with EtOAc (250 mL), extracted with water (2×150 mL) and brine (50 mL), dried (Na_2SO_4), concentrated, and purified by flash chromatography (EtOAc/hexanes 1:3) giving **13** as a syrup: $[\alpha]_D$=+29.9 (*c* 1.0, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 300 MHz); δ ppm: 7.78 (1H), 7.12 (1H), and 6.96 (1H) (3m, PyH), 7.48–7.22 (m, 20PhCH), 6.13 (d, 1H, H-1, $J_{1,2}$=8.0 Hz), 5.05 and 4.83 (AB, 2H, *J*=11.6 Hz), 5.01 and 4.68 (AB, 2H, *J*=11.4 Hz), 4.83 (narrow AB, 2H), 4.52 and 4.45 (AB, 2H, *J*=11.7 Hz) (8CH_2Ph), 4.27 (dd, 1H, H-2, $J_{2,3}$=9.7 Hz), 4.07 (dd, 1H, H-4, $J_{4,3}$=2.9 Hz, $J_{4,5}$=0.0 Hz), 3.90 (ddd, 1H, H-5, $J_{5,6}$=5.8 Hz, $J_{5,6A}$=6.8 Hz), 3.85 (s, 3H, OCH_3), 3.79–3.66 (m, 3H, H-3, H-6 and H-6′). ^{13}C NMR ($CDCl_3$, 100 MHz); δ ppm: 149.93 and 141.70 (PyC), 136.3, 136.2, 136.0, and 135.4 (PhC), 134.4, 115.4, and 115.7 (PyCH), 125.8, 125.6, 125.5, 125.5, 125.4, 125.2, 125.0, 124.9, 124.8, and 124.4 (PhCH), 94.1 (C-1), 79.7, 76.4, 71.3, and 71.1 (C-2 to C-5), 72.6, 72.1, 70.9 and 70.4 [(−), 4CH_2Ph], 62.7 [(−), C-6], 53.1 (OCH_3). HR-FABMS calcd for $C_{40}H_{42}O_7N$ *m/z* 648.2961; found 648.2976.

2.1.15. 6-Benzyloxycarbonylamino-1-hexanyl *O*-(2,3,4,6-tetra-*O*-benzyl-α-D-galactopyranosyl)-(1→3)-4-*O*-acetyl-2-*O*-benzoyl-6-*O*-*tert*-butyldiphenylsilyl-β-D-galactopyranoside (14a). (a) *Using Yb(TFO)$_3$ as activator*. A 10 mL round bottom flask containing a mixture of **12a** (150 mg, 0.188 mmol) and **13** (121 mg, 1.0 equiv.), and a magnetic stirrer were dried overnight under vacuum over P_2O_5. The mixture was dissolved in dry CH_2Cl_2 (2.7 mL) and $Yb(TfO)_3$ (117 mg, 1.0 equiv. dried at 200°C 2 h under vacuum just before use) was added quickly and the mixture stirred for 2 h at room temperature under argon. A second portion of **13** (24.3 mg, 0.2 equiv.) was added and the mixture stirred at room temperature for 2 h. The reaction mixture was diluted with CH_2Cl_2 (50 mL), washed with water (20 mL), 1N HCl (20 mL), water (20 mL), dried (Na_2SO_4) and concentrated. Purification (flash chromatography, EtOAc/hexanes 1:3) afforded pure **14a** (189 mg, 0.143 mmol, 76%) as a white foam.

(b) *Using Cu(TFO)$_2$ as activator*. A 10 mL round bottom flask containing a mixture of **12a** (423.9 mg, 0.531 mmol) and **13** (344 mg, 1.0 equiv.), and a magnetic stirrer was dried overnight under vacuum over P_2O_5. The mixture was dissolved in dry toluene (7.6 mL) and $Cu(TfO)_2$ (192 mg, 1.0 equiv. dried at 200°C for 2 h under vacuum just before use) was added quickly and the mixture stirred for one day at room temperature under argon. The same work-up as described above afforded **14a** (424.3 g, 0.321 mmol, 60%) as a white foam: $[\alpha]_D$=+34.5 (*c* 1.1, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 300 MHz, assigned by COSY45); δ ppm: 8.03 (2H), 7.66 (4H), 7.5–7.20 (32H), and 7.15 (2H) (4m, 40H, PhH), 5.67 (dd, 1H, H-4, $J_{4,3}$=3.1 Hz, $J_{4,5}$=0.0 Hz), 5.48 (dd, 1H, H-2, $J_{2,1}$=8.0 Hz, $J_{2,3}$=10.2 Hz), 5.31 (d, 1H, H-1′, $J_{1',2'}$=4.0 Hz), 4.43 (d, 1H, H-2), 5.1 (s, 2H), 4.79–4.54 (m, 6H) and 4.42–4.30 (m, 3H) (5 CH_2Ph and NHCbz), 4.12 (dd, 1H, H-3), 3.95 (2H), 3.80–3.62 (3H), 3.62–3.48 (2H) and 3.28–3.20 (2H) (4m, 9H, H-5, H-6, H-6A, H-2′, H-3′, H-4′, H-5′, H-6′ and H-6A′), 3.84 (1H) and 3.39 (1H) (2 m, OCH_2R), 2.98 (m, 2H, NCH_2R), 1.78 (s, 3H, $COCH_3$), 1.48 (2H) and 1.16 (6H) (2 m, –CH_2–), 1.08 (s, 9H, $SiC(CH_3)_3$). ^{13}C NMR ($CDCl_3$, 100 MHz); δ ppm: 170.11, 164.8 and 156.3 (CO), 138.8 (3C), 138.4 (2C), 136.7, 133.2 and 133.1 (8PhC), 135.6, 135.6, 133.1, 129.8, 129.7, 128.5, 128.4, 128.3, 128.2, 128.0, 127.9, 127.7, 127.7, 127.9, 127.4, 127.3, and 127.2 (PhCH), 101.6 (C-1), 93.2 (C-1′), 78.8, 77.3, 75.8, 75.0, 71.6, 71.0, 73.9 and 64.7 (C-2 to C-5 and C-2′ to C-5′) 74.5, 73.4, 73.3, 73.1, 69.8 (2C), 66.5 and 61.8 [all (−), C-6, C-6′, OCH_2R and 5CH_2Ph], 40.8 [(−), $NHCH_2R$], 29.6, 29.2, 26.2, and 25.5 [all (−), 4-CH_2–], 20.52 ($COCH_3$), 26.8 and 19.1 (q) ($SiC(CH_3)_3$). FABMS (rel. intensity) 1320.3 (2), $[M]^+$. Anal. Calcd for $C_{79}H_{89}NO_{15}Si$: C, 71.85; H, 6.79; N, 1.06. Found: C, 71.82; H, 6.67; N, 1.1.

2.1.16. 6-Benzyloxycarbonylamino-1-hexanyl *O*-(2,3,4,6-tetra-*O*-benzyl-α-D-galactopyranosyl)-(1→3)-4-*O*-acetyl-2,6-di-*O*-benzoyl-β-D-galactopyranoside (14b). Using $Cu(TfO)_2$ as activator applying the same procedure as described for **14a** but using: **12b** (150 mg, 0.226 mmol) and **13** (146 mg, 1.0 equiv.), and $Cu(TfO)_2$ (81.0 mg, 1.0 equiv.) in toluene (5.3 mL) and stirring the reaction mixture for two days at room temperature gave after flash chromatography (EtOAc/hexanes 1:2, two columns were necessary) **14b** (178 mg, 0.116 mmol, 51%) as a white foam: $[\alpha]_D$=+36.2 (*c* 1.1, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 300 MHz); δ ppm: 8.05 (4H), 7.60 (1H), 7.48 (3H), 7.40–7.18 (25H), and 7.15 (2H) (m, 35H, PhH), 5.66 (d, 1H, H-4, $J_{4,3}$=3.0 Hz, $J_{4,5}$=0.0 Hz), 5.54 (dd, 1H, H-2, $J_{2,1}$=8.0 Hz, $J_{2,3}$=10.2 Hz), 5.23 (d, 1H, H-1′, $J_{1',2'}$=3.4 Hz), 5.1 (s, 2H), 4.77 (d, 1H, *J*=11.5 Hz), and 4.69–4.28 (m, 11H) (5CH_2Ph, H-1A, NHCbz, H-6, and H-6A), 4.14 (dd, 1H, H-3), 3.97–3.85 (m, 4H), 3.61 (dd, 1H, *J*=2.7, 10.1 Hz), 3.50–3.43 (m, 2H), and 3.27–3.19 (m, 2H) (4m, 9H, H-5, H-2′, H-3′, H-4′, H-5′, H-6′, H-6A′, and 2OCH_2R), 3.01–2.98 (m, 2H, NCH_2R), 1.90 (s, 3H, $COCH_3$), 1.48 (2H) and 1.16 (6H) (2 m, –CH_2–). ^{13}C NMR ($CDCl_3$, 100 MHz); δ ppm: 170.4, 166.0, 164.7 and 156.3 (4CO), 138.6, 138.3, 133.2, 133.1, 129.7, 128.4, 128.3, 128.2, 128.1, 127.8, 127.5, 127.5, and 127.4 (PhC and PhCH), 101. 7 (C-1), 98.5 (C-1′), 78.7, 75.6, 74.9, 71.5, 71.0, 70.7, 69.8, and 64.8, (C-2 to C-5 and C-2′ to C-5′), 74.4, 73.3, 73.2, 70.0, 69.6, 66.5, and 62.1 [all (−), C-6, C-6′, 2 OCH_2R and 5 CH_2Ph], 40.8 [(−), $NHCH_2R$], 29.6, 29.2, 26.2, and 25.4 [all (−), 4 –CH_2–], 20.50 ($COCH_3$). FABMS (rel intensity) 1186.7 (5), $[M]^+$. Anal. Calcd for $C_{70}H_{75}O_{16}N$: C, 70.87; H, 6.37; N, 1.18. Found: C, 69.61; H, 6.46; N, 1.21.

2.1.17. 6-Amino-1-hexanyl *O*-(α-D-galactopyranosyl)-β-D-galactopyranoside hydrochloride (15). To a solution of **14a** (72.5 mg, 0.0549 mmol) in dry MeOH (2 mL) was added sodium methoxide (0.5 M in MeOH, 100 μL) and the reaction mixture stirred for 48 h at room temperature. The solution was concentrated under vacuum, the residue dissolved in CH_2Cl_2 (30 mL), washed with water, dried and concentrated. To a solution of the crude product in THF (0.6 mL) was added in one portion TBAF (60 μL, 1.1 equiv.). The solution was stirred for 6 h at room temperature, concentrated and purified by flash chromatography (CH_2Cl_2/MeOH 15:1) affording 6-benzyloxycarbonylamino-1-hexanyl 3-*O*-(2,3,4,6-tetra-*O*-benzyl-α-D-galactopyranosyl)-β-D-galactopyranoside (33 mg, 0.035 mmol, 65%) as a syrup: FABMS (rel intensity) 936.4 (1.0), $[M]^+$. To a solution of the preceeding compound in dioxane/water (2:1, 5 mL) was added 20% palladium-on-carbon (Pearlman's catalyst, ~20 mg). The mixture was stirred for 2 h under hydrogen (60 psi) at room temperature, the hydrogen pressure was relieved, HCl (1N in dioxane, ~1 equiv.) was added and the mixture stirred under hydrogen (60 psi) overnight. The suspension was filtered through a Celite® pad, and the pad rinsed with water (20 mL). The filtrate was concentrated under vacuum to about 5 mL, the solution was passed through an ion exchange resin column (Dowex® 1×8–50 in the chloride form), the column was rinsed with water and lyophilized to give pure **15** (17.3 mg, 0.039 mmol, 95%; overall yield from **14a**, 62%) as a white powder: $[\alpha]_D$=+76.2 (*c* 0.5, DMSO). ^{1}H NMR (D_2O, CH_3OD internal standard at δ=3.35 ppm, 300 MHz); δ ppm: 5.15 (d, 1H, H-1′, $J_{1',2'}$=3.7 Hz), 4.46 (d, 1H, H-1, $J_{1,2}$=7.9 Hz), 4.02–3.60 (m, 12H, H-2 to H-6 and H-6A, H-1′ to H-6′ and H-6A′, and 2OCH_2R), 3.00 (m, 2H, NCH_2R), 1.64 (4H) and 1.40 (4H) (2 m, 8H, $-CH_2-$). ^{13}C NMR (D_2O, CH_3OD internal standard at δ=49.6 ppm, 100 MHz); δ ppm: 103.2 (C-1′), 95.9 (C-1), 78.0, 75.5, 71.5, 69.9 (2C), 69.8, 68.9, 65.5 (C-2 to C-5 and C-2′ to C-5′), 71.0 and 61.6 (2C) [(−), C-6, C-6′, and OCH_2R], 40.1 [(−), $NHCH_2R$], 29.1, 27.3, 26.0, and 25.2 [(−), 4 $-CH_2-$]. FABMS (rel. intensity) 442.2 (11), $[M-Cl]^+$. HR-FABMS calcd for $C_{18}H_{36}O_{11}N$ *m/z* 442.2288; found 442.2275.

2.1.18. 3-Methoxy-2-pyridyl 3,4,6-tri-*O*-acetyl-2-deoxy-2-phthalimido-β-D-glucopyranoside (17). A solution of tetra-*O*-acetyl-2-deoxy-2-phthalimido-β-D-glucopyranose **16** (2.77 g, 5.81 mmol) and Ac_2O (1.38 mL) in HBr (30% in AcOH, 90 mL) was stirred for 2 h at room temperature. The reaction mixture was diluted with toluene (250 mL), washed with ice water (2×150 mL), cold saturated $NaHCO_3$ (100 mL), ice water (100 mL) and concentrated. The residue was redissolved in toluene, concentrated and codistilled twice with dry toluene (2×75 mL). The residue was redissolved in dry toluene (110 mL) and silver 3-methoxy-2-pyridoxide (1.66 g, 1.3 equiv.) was added in one portion. The system was refluxed under vigorous stirring for 1 h, and allowed to cool down to room temperature. The mixture was filtered through Celite®, and the bed was washed with toluene (150 mL). The filtrate was treated with saturated $NaHCO_3$ (100 mL), the biphasic mixture was filtered through a Celite® pad, the pad rinsed with toluene and both phases separated. The organic phase was washed with water (100 mL), dried (Na_2SO_4), concentrated and purified by flash chromatography (EtOAc/hexanes 1:1) giving **17** (1.58 g, 2.9 mmol) as a white foam: $[\alpha]_D$=+73 (*c* 1.0, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 400 MHz, assigned by COSY45); δ ppm: 7.78 (2H) and 7.67 (2H) (2m, ArCH), 7.55 (dd, 1H, *J*=1.5, 4.9 Hz), 6.95 (dd, 1H, *J*=1.5, 7.9 Hz), and 6.79 (dd, 1H, *J*=4.9, 7.8 Hz) (PyCH), 6.91 (d, 1H, H-1, $J_{1,2}$=8.8 Hz), 5.96 (dd, 1H, H-3, $J_{3,2}$=10.6 Hz, $J_{3,4}$=9.1 Hz), 5.24 (dd, 1H, H-4, $J_{4,5}$=10.0 Hz), 4.68 (dd, 1H, H-2), 4.31 (dd, 1H, H-6, $J_{6,5}$=4.4 Hz, $J_{6,6A}$=12.4 Hz), 4.13 (dd, 1H, H-6A, $J_{6A,5}$=2.2 Hz), 4.08 (ddd, 1H, H-5), 3.62 (s, 3H, OCH_3), 2.08, 2.06, and 1.85 (s, 9H, $COCH_3$). ^{13}C NMR ($CDCl_3$, 100 MHz); δ ppm: 170.7, 170.1, 169.5, and 167.5 (CO), 151.4 and 144.0 (PyC), 131.4 (ArC), 136.9, 119.1, and 119.0 (PyCH), 134.4, 134.1, 123.7, and 123.5 (ArCH), 91.8 (C-1), 72.1, 70.8, 78.74, 55.6, and 54.1 (C-2 to C-5, OCH_3), 61.8 [(−), C-6], 20.7, 20.6, and 20.4 ($COCH_3$). HR-FABMS calcd for $C_{26}H_{27}O_{11}N_2$ *m/z* 543.1615; found 543.1666.

2.1.19. 3-Benzyloxycarbonylamino-1-propyl 3,4,6-tri-*O*-acetyl-2-deoxy-2-phthalimido-β-D-glucopyranoside (18). To a solution of **17** (0.5 g, 0.92 mmol) and 3-benzyloxycarbonylamino-1-propanol (0.289 g, 1.5 equiv.) in CH_2Cl_2 (13.1 mL) was added $HBF_4{\cdot}Et_2O$ (58% in Et_2O, 90 μL, 1.1 equiv.) in one portion and the mixture was stirred for 12 h at room temperature. The reaction mixture was diluted with CH_2Cl_2 (150 mL), washed with water (75 mL), 1N HCl (75 mL), water (75 mL), dried (Na_2SO_4) and concentrated. The crude product was purified by flash chromatography (EtOAc/hexanes 1:1) giving **18** (375.4 mg, 0.6 mmol, 65%) as a white foam: $[\alpha]_D$=+18.1 (*c* 1.1, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 400 MHz, assigned by COSY45); δ ppm: 7.82 (2H) and 7.72 (2H) (m, ArCH), 7.34 (m, 5H, PhCH), 5.76 (dd, 1H, H-3, $J_{3,2}$=10.6 Hz, $J_{3,4}$=9.2 Hz), 5.38 (d, 1H, H-1, $J_{1,2}$=8.5 Hz), 5.16 (d, 1H, H-4, $J_{4,5}$=9.9 Hz), 4.99 (m, 3H, CH_2Ph and NHCbz), 4.29 (dd, 1H, H-6, $J_{6,5}$=4.4 Hz, $J_{6,6A}$=12.3 Hz), 4.31 (dd, 1H, H-2), 4.19 (dd, 1H, H-6A, $J_{6A,5}$=1.9 Hz), 3.85 (m, 2H, H-5, OCH_2R), 3.56 (m, 1H, OCH_2R), 3.10 (m, 2H, NCH_2R), 2.06, 2.02, and 1.86 (s, 9H, $COCH_3$), 1.68 (m, 2H, $-CH_2-$). ^{13}C NMR ($CDCl_3$, 100 MHz); δ ppm: 170.7, 170.1, 169.4, and 156.2 (CO), 136.5 and 131.2 (PhC), 134.3, 128.4, 127.9, and 123.5 (PhCH), 98.0 (C-1), 71.8, 70.6, 68.8, and 54.4 (C-2 to C-5), 67.2, 66.3, and 61.8 [all (−), C-6, OCH_2R and CH_2Ph], 37.6 and 37.5 [(−), $NHCH_2R$], 29.2 [(−), $-CH_2-$], 20.6, 20.5, and 20.3 (3$COCH_3$). HR-FABMS calcd for $C_{31}H_{35}O_{12}N_2$ *m/z* 627.2189; found 627.2183.

2.1.20. 3-Benzyloxycarbonylamino-1-propyl 6-*O*-*tert*-butyldiphenylsilyl-2-deoxy-2-phthalimido-β-D-glucopyranoside (19). To a solution of **18** (303.6 mg, 0.485 mmol) in MeOH (9.7 mL) was added sodium methoxide (0.5N in MeOH, 0.1 mL) and the reaction mixture stirred for 6 h at room temperature. The solution was neutralized with Amberlite® IRC-50S (H^+) ion-exchange resin, the resin filtered off, and washed with MeOH. The resulting solution was concentrated under vacuum giving 3-benzyloxycarbonylamino-1-propyl 2-deoxy-2-phthalimido-β-D-glucopyranoside (0.22 g, 0.41 mmol, 91%) as white foam: FABMS (rel. intensity) 501.1 (7), $[M+H]^+$. HR-FABMS calcd for $C_{25}H_{29}O_{10}N_2$ *m/z* 501.18732; found 501.1859. To a solution of the preceding product (219.4 mg, 0.438 mmol) and imidazole (59.6 mg, 2 equiv.) in dry DMF (2.2 mL) was added TBDPSCl (180 μL,

1.5 equiv.) dropwise and the reaction mixture stirred for 5 h at room temperature. The solution was diluted with EtOAc (50 mL), extracted with H_2O (2×25 mL), dried (Na_2SO_4) and concentrated. The residue was purified by flash chromatography (CH_2Cl_2/MeOH 20:1) affording **19** (300 mg, 0.406 mmol, 92%) as a white foam: $[\alpha]_D$=+20.2 (*c* 1.0, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 400 MHz, assigned by COSY45); δ ppm: 7.80–7.55 (m, 8H), 7.50–7.39 (m, 6H), and 7.30 (m, 5H) (PhCH), 5.20 (d, 1H, H-1, $J_{1,2}$=8.4 Hz), 5.00–4.92 (m, 3H, $2CH_2Ph$ and NHCbz), 4.33 (dd, 1H, H-3, $J_{3,2}$=10.8 Hz, $J_{3,4}$=8.6 Hz), 4.11 (dd, 1H, H-2B), 3.97 (m, 2H, H-6 and H-6A), 3.81 (m, 1H, OCH_2R), 3.66 (dd, 1H, H-4, $J_{4,5}$=9.3 Hz), 3.58 (ddd, 1H, H-5, $J_{5,6}$=$J_{5,6A}$=4.8 Hz), 3.47 (m, 1H, OCH_2R), 3.06 (m, 2H, NCH_2R), 1.62 (m, 2H, $-CH_2-$), 1.05 (s, 9H, $SiC(CH_3)_3$). ^{13}C NMR ($CDCl_3$, 100 MHz); δ ppm: 168.3 and 156.2 (CO), 136.5, 132.8, 132.7, and 131.4 (PhC), 135.5, 135.4, 134.0, 129.8, 128.3, 127.8, 127.7, and 123.3 (PhCH), 98.0 (C-1), 74.8, 73.5, 71.6, and 56.2 (C-2 to C-5), 66.9, 66.2, and 64.5 [all (−), C-6, OCH_2R and CH_2Ph], 38.0 [(−), $NHCH_2R$], 29.2 [(−), $-CH_2-$], 26.6 and 19.2 (q) ($SiC(CH_3)_3$). HR-FABMS calcd for $C_{41}H_{47}O_9N_2Si$ *m/z* 739.3051; found 739.3085.

2.1.21. 3-Methoxy-2-pyridyl 2,3,4-tri-*O*-benzoyl-6-*O*-*tert*-butyldiphenylsilyl-β-D-galactopyranoside (20). To a solution of 3-methoxy-2-pyridyl 6-*O*-*tert*-butyldiphenylsilyl-β-D-galactopyranoside[24] (2.31 g, 4.30 mmol) in pyridine (43.9 mL) was added BzCl (2.1 mL, ~4 equiv.) dropwise and the solution stirred overnight at room temperature. The excess BzCl was quenched with MeOH and the mixture concentrated under vacuum. The crude product was redissolved in CH_2Cl_2 (50 mL) and washed with aqueous dilute HCl (1N, 25 mL) and water (25 mL), dried (Na_2SO_4), concentrated, and purified by flash chromatography (EtOAc/hexanes 1:3) affording **20** (2.95 g, 3.52 mmol, 82%) as a white foam: $[\alpha]_D$=+131 (*c* 1.0, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 300 MHz); δ ppm: 8.08 (2H), 7.86 (4H), 7.72 (1H), 7.60 (3H), 7.50–7.21 (14H), 7.04 (3H), and 6.90 (1H) (8m, 28H, 3PyCH and 25PhCH), 6.53 (d, 1H, H-1, $J_{1,2}$=8.3 Hz), 6.17 (dd, 1H, H-4, $J_{4,3}$=3.4 Hz, $J_{4,5}$=1.0 Hz), 6.09 (dd, 1H, H-2, $J_{2,3}$=10.4 Hz), 5.79 (dd, 1H, H-3), 4.36 (ddd, 1H, H-5, $J_{5,6}$=$J_{5,6A}$=6.5 Hz), 3.86 (m, 2H, H-6 and H-6A), 3.70 (s, 3H, OCH_3), 0.98 (s, 9H, $SiC(CH_3)_3$). ^{13}C NMR ($CDCl_3$, 100 MHz); δ ppm: 165.5, 165.4, and 165.0 (CO), 151.8 and 144.1 (2PyC), 132.6, 132.4, and 128.9 (PhC), 136.7, 119.1, and 118.8 (3PyCH), 135.5, 135.3, 133.1, 132.9, 132.8, 129.9, 129.7, 129.6, 129.4, 128.3, 128.1, 128.0, 127.5, and 127.3 (PhCH), 94.6 (C-1), 74.2, 72.2, 69.6, and 67.7 (C-2 to C-5), 61.0 [(−), C-6], 55.7 (OCH_3), 26.5 and 18.8 (q) ($SiC(CH_3)_3$). HR-FABMS calcd for $C_{49}H_{48}O_{10}NSi$ *m/z* 838.3047; found 838.3067.

2.1.22. 3-Benzyloxycarbonylamino-1-propyl *O*-(2,3,4-tri-*O*-benzoyl-6-*O*-*tert*-butyldiphenyl-silyl-β-D-galactopyranosyl)-(1→4)-6-*O*-*tert*-butyldiphenylsilyl-2-deoxy-2-phthalimido-β-D-glucopyranoside (21). A 10 mL round bottom flask containing a mixture of **19** (191.3 mg, 0.259 mmol) and **20** (217 mg, 1.0 equiv.), and a magnetic stirrer was dried overnight under vacuum over P_2O_5. The mixture was dissolved in dry CH_2Cl_2 (3.7 mL) and $Cu(TfO)_2$ (112.4 mg, 1.2 equiv. dried at 200°C for 2 h under vacuum just before use) was added quickly and the mixture was stirred under argon for 6 h at room temperature. The reaction mixture was quenched with a drop of pyridine, diluted with CH_2Cl_2 (50 mL) and filtered through a Celite® pad. The solution was washed with water (25 mL), 1N HCl (25 mL), water (25 mL), dried (Na_2SO_4) and concentrated. The crude product was purified by flash chromatography (gradient elution EtOAc/hexanes 1:3 to 1:2) affording **21** (240 mg, 0.165 mmol, 64%, white foam), **22** (39.1 mg, 0.027 mmol, 10%, syrup), and a by-product presumed to be the *N*-pyridone analog of **20** (38.7 mg, 0.046 mmol, syrup, 18%).

For **21**: $[\alpha]_D$=+30.3 (*c* 1.4, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 400 MHz, assigned by COSY45); δ ppm: 7.98 (m, 2H), 7.82–7.56 (m, 15H), and 7.50–7.05 (m, 26H) [3m, 44H, PhCH and ArCH], 5.98 (dd, 1H, H-4′, $J_{4',3'}$=3.3 Hz, $J_{4',5'}$=0.0 Hz), 5.74 (dd, 1H, H-2′, $J_{2',1'}$=8.0 Hz, $J_{2',3'}$=10.5 Hz), 5.58 (dd, 1H, H-3′), 5.14 (d, 1H, H-1, $J_{1,2}$=8.5 Hz), 5.05 (d, 1H, H-1′), 5.00 (m, 2H, CH_2Ph), 4.80 (t, 1H, *J*=6.3 Hz, NHCbz), 4.52 (dd, 1H, H-3 $J_{3,2}$=10.6 Hz, $J_{3,4}$=8.6 Hz), 4.18 (dd, 1H, H-2), 4.09–4.03 (m, 2H, H-4 and H-5′), 3.88–3.70 (m, 6H, H-6, H-6A, H-6′, H-6A′, OH, and 1OCH_2R), 3.46–3.04 (m, 2H, H-5 and 1 OCH_2R), 3.20 (m, 2$NHCH_2R$), 1.64 (2m, 2H, $-CH_2-$), 1.10 and 0.92 (2 s, 18H, $2C(CH_3)_3$). ^{13}C NMR ($CDCl_3$, 100 MHz); δ ppm: 168.5, 165.5, 165.2, 165.0, and 156.2 (CO), 136.7, 133.7, 132.8, 132.4, 132.1, 131.7, 129.8, and 128.8 (PhC), 135.9, 135.5, 135.4, 134.0, 133.4, 133.2, 130.0, 129.8, 129.6, 128.6, 128.4, 128.2, 127.9, 127.8, 127.7, 123.6, and 123.1 (PhCH), 101.0 and 97.9 (C-1 and C-1′), 66.8, 66.3, 61.8, and 61.0 [all (−), C-6, C-6′, OCH_2R and CH_2Ph], 79.6, 74.7, 74.2, 71.7, 69.9, 69.5, 67.6, and 56.1 (C-2 to C-5 and C-2′ to C-5′), 38.3 [(−), $NHCH_2R$], 29.4 [(−), $-CH_2-$], 26.9, 26.6, 19.5 (q), and 18.8 (q) ($SiC(CH_3)_3$). FABMS (rel. intensity) 1473.9 (3.5), $[M+Na]^+$. Anal. Calcd for $C_{84}H_{86}N_2O_{17}Si_2$: C, 69.50; H, 5.97; N, 1.93. Found: C, 70.09; H, 6.66; N, 1.83.

For **22**: $[\alpha]_D$=+74.2 (*c* 1.2, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 400 MHz, assigned by COSY45); δ ppm: 7.98 (m, 2H), 7.70–7.68 (m, 4H), 7.64–7.57 (m, 6H), 7.53–7.51 (m, 2H), 7.48–7.28 (m, 24H), 7.20–7.10 (m, 4H) and 7.05 (t, 2H, *J*=7.9 Hz) [7m, 44H, PhCH and ArCH], 5.82 (dd, 1H, H-4′, $J_{4',3'}$=3.4 Hz, $J_{4',5'}$=0.0 Hz), 5.62 (dd, 1H, H-2′, $J_{2',1'}$=8.0 Hz, $J_{2',3'}$=10.4 Hz), 5.45 (dd, 1H, H-3′), 5.00 (s, 2H, CH_2Ph), 4.97 (d, 1H, H-1, $J_{1,2}$=8.6 Hz), 4.78 (m, 2H, H-1′ and NHCbz, $J_{1',2'}$=8.0 Hz), 4.60 (dd, 1H, H-3 $J_{3,2}$=10.9 Hz, $J_{3,4}$=8.3 Hz), 4.29–4.24 (m, H-2 and OH), 4.11 (t, 1H, H-5′, $J_{5',6'}$=$J_{5',6A'}$=6.8 Hz), 4.06 (dd, 1H, H-6, $J_{6,6A}$=11.2 Hz, $J_{6,5}$=2 Hz), 3.90–3.77 (m, 3H, H-6A, H-6′ and 1OCH_2R), 3.73–3.69 (m, 2H, H-4 and H-6A′), 3.53 (m, H-5), 2.98 (m, 2$NHCH_2R$), 1.64 (2m, 2H, $-CH_2-$), 1.05 and 0.97 (2 s, 18H, $2C(CH_3)_3$). ^{13}C NMR ($CDCl_3$, 100 MHz); δ ppm: 165.2, 165.1, 164.5 and 156.0 (CO), 136.5, 133.4 (2C), 132.2, 132.0, 130.6 (2C), and 128.4 (PhC), 135.5, 135.4, 135.3, 133.5, 133.3, 133.0, 132.5, 129.7, 129.4, 129.2, 128.4, 128.2, 127.9, 127.7, 127.6, 127.4, 123.2, and 122.6 (PhCH), 101.3 and 97.9 (C-1 and C-1′), 66.5, 66.1, 63.4, and 61.2 [all (−), C-6, C-6′, OCH_2R and CH_2Ph], 82.3, 74.1, 71.4, 69.9 (2C), 69.7, 67.3, and 54.6 (C-2 to C-5 and C-2′ to C-5′), 37.97 [(−), $NHCH_2R$], 29.3 [(−), $-CH_2-$], 26.6, 26.4, 19.1 (q), and 18.7 (q) ($SiC(CH_3)_3$). FABMS (rel.

intensity) 1474.5 (3.5), $[M+Na]^+$. Anal. Calcd for $C_{84}H_{86}N_2O_{17}Si_2$: C, 69.50; H, 5.97; N, 1.93. Found: C, 70.37; H, 6.78; N, 1.83.

2.1.23. 3-Benzyloxycarbonylamino-1-propyl *O*-(6-*O*-*tert*-butyldiphenylsilyl-β-D-galactopyranosyl)-(1→4)-2-acetamido-6-*O*-*tert*-butyldiphenylsilyl-2-deoxy-β-D-glucopyranoside (23). From **24**: To a solution of **24** (2.0 g, 0.438 mmol) and imidazole (1.07 g, 3 equiv.) in dry DMF (34.8 mL) was added TBDPSCl (2.9 mL, 3.0 equiv.) dropwise and the reaction mixture stirred for 6 h at room temperature. The excess TBDPSCl was quenched adding MeOH (5 mL) and the solution stirred for 30 min. The reaction mixture was concentrated under vacuum and the residue purified by flash chromatography (CH_2Cl_2/MeOH 20:1) affording **23** (3.36 g, 2.95 mmol, 85%) as a white foam.

From **21**: To a solution of **21** (112.3 mg, 77.35 μmol) in MeOH (3.8 mL) was added sodium methoxide (~10 equiv.) and the reaction mixture was stirred overnight at room temperature. The solution was neutralized with Amberlite® IRC-50S (H^+) ion-exchange resin, the resin filtered off, and washed with MeOH, the filtrate concentrated, purified by flash chromatography (CH_3OH/CH_2Cl_2 1:20) and the product redissolved in EtOH (7.7 mL). To the refluxing mixture was added H_2NNH_2 hydrate portionwise (5 μL at a time, every 15–20 min) until the reaction was completed. The solution was concentrated, the residue pumped overnight, and redissolved in MeOH (7.7 mL). To the solution was added Ac_2O (146 μL, 20 equiv.) and the solution stirred at room temperature for 1 h. The mixture was concentrated and purified by flash chromatography (CH_2Cl_2/MeOH 20:1) affording **23** (49.8 mg, 47.4 μmol, 61%) as a white foam: $[\alpha]_D=-6.47$ (*c* 1.0, CH_3OH). ^1H NMR (CD_3OD, 400 MHz, assigned by COSY45); δ ppm: 7.80–7.77 (m, 4H), 7.70–7.66 (m, 4H), 7.44–7.25 (m, 17H) (PhCH), 5.05 (s, 2H, CH_2Ph), 4.57 (d, 1H, *J*=7.7 Hz) and (d, 1H, *J*=8.3 Hz) (H-1 and H-1′), 4.22 (dd, 1H, *J*=11.0, 3.3 Hz), 3.98 (d, 1H, *J*=11.0 Hz), 3.89–3.83 (m, 5H), 3.77 (dd, 1H, *J*=10.2, 8.6 Hz), 3.67–3.58 (m, 3H), 3.49–3.43 (m, 3H), 3.27–3.13 (m, 2H, $NHCH_2R$), 1.95 (s, 18H, $SiC(CH_3)_3$). ^{13}C NMR (CD_3OD, 100 MHz); δ ppm: 173.5 and 158.8 (2CO), 138.4, 134.9, 134.3 (2C) and 134.2 (5CPh), 137.0, 136.8, 136.7, 130.9, 130.8, 129.4, 128.8 and 128.6 (CHPh), 104.8 and 102.5 (C-1 and C-1′), 79.6, 76.8, 76.5, 75.0, 73.9, 72.4, 69.7 and 56.8 (C-2 to C-5 and C-2′ to C-5′), 67.6, 67.3, 63.6 and 63.4 [all (−), C-6, C-6′, OCH_2R and CH_2Ph], 38.91 [(−), $NHCH_2R$], 30.8 [(−), $-CH_2-$], 23.0 ($COCH_3$), 27.4, 20.2 (q) and 19.9 (q) ($SiC(CH_3)_3$). FABMS (rel. intensity) 1073.5 (16), $[M+Na]^+$. Anal. Calcd for $C_{57}H_{74}N_2O_{13}Si_2$: C, 65.12; H, 7.09; N, 2.66. Found: C, 64.17; H, 6.88; N, 2.52.

2.1.24. 3-Benzyloxycarbonylamino-1-propyl *O*-(2,4-di-*O*-acetyl-6-*O*-*tert*-butyldiphenylsilyl-β-D-galactopyranosyl)-(1→4)-3-*O*-acetyl-2-acetamido-6-*O*-*tert*-butyldiphenylsilyl-2-deoxy-β-D-glucopyranoside (26). A solution of **23** (2.90 g, 2.77 mmol), triethyl orthoacetate (0.66 mL, 1.3 equiv.) and pyridinium triflate (2 mg) in CH_2Cl_2 (27.7 mL) was stirred at room temperature for 1 h. The mixture was quenched with DMAP (1.1 g, 3 equiv.), the solvent removed under vacuum, and the solid residue dried under high vacuum (20 min at 40°C bath temperature) to give the orthoester derivative **25** which was used in the next step. The residue was redissolved in CH_2Cl_2 (14 mL), Ac_2O (0.79 mL, 3 equiv.) was added and the solution stirred for 1 h at room temperature. The excess Ac_2O was quenched stirring the reaction mixture for 15 min after addition of MeOH (0.5 mL). The solution was concentrated under vacuum and the residue redissolved in AcOH (90%, 20 mL). The solution was stirred for 15 min at room temperature, then diluted with CH_2Cl_2 (150 mL), washed with ice water (100 mL), cold saturated $NaHCO_3$ solution (100 mL), cold water (100 mL), dried (Na_2SO_4), filtered and concentrated. The crude product was purified by flash chromatography (EtOAc/hexanes 1:4) giving **26** (2.80 g, 2.38 mmol, 86%) as a white foam: $[\alpha]_D=-7.8$ (*c* 1.0, $CHCl_3$). ^1H NMR ($CDCl_3$, 300 MHz); δ ppm: 7.76–7.24 (m, 25 PhCH), 6.64 (d, 1H, NHAc, *J*=8.6 Hz), 5.44 (dd, 1H, H-4′, $J_{3',4'}$=3.3 Hz, $J_{4',5'}$=0.0 Hz), 5.15–5.02 (m, 2H), 4.92 (dd, 1H, *J*=9.5, 9.5 Hz), 4.86 (dd, 1H, *J*=9.6, 8.4 Hz), 4.18–4.01 (m, 3H), 3.98–3.87 (m, 2H), 3.80–3.74 (m, 2H), 3.64–3.49 (m, 3H), and 3.36–3.40 (m, 3H) all other protons; 2.05 (s, 3H), 1.92 (s, 3H), 1.88 (s, 3H), and 1.80 (s, 3H) ($4COCH_3$), 1.62 (1H) and 1.00 (s, 19H) (2 m, 2 $-CH_2-$, and $2SiC(CH_3)_3$). ^{13}C NMR ($CDCl_3$, 100 MHz); δ ppm: 171.1, 170.9, 170.7, 170.5, and 156.7 (5CO), 136.7, 133.5, 132.6 (2C), and 132.2 (5CPh), 135.9, 135.5, 135.4, 129.9, 128.5, 128.1, 128.0, 127.8, 127.7, and 127.6 (PhCH), 101.3 and 100.1 (C-1 and C-1′), 75.1, 74.1, 73.3, 73.0, 72.9, 71.7, 69.3, and 53.2 (C-2 to C-5 and C-2′ to C-5′), 66.7, 66.0, 61.3, and 60.8 [all (−), C-6, C-6′, OCH_2R and CH_2Ph], 37.4 [(−), $NHCH_2R$], 29.6 [(−), $-CH_2-$], 23.0, 20.8, and 20.7 (2C) (4 $COCH_3$), 26.7, 19.2 (q) and 19.0 (q) ($SiC(CH_3)_3$). FABMS (rel. intensity) 1177.81 (65, $[M+H]^+$). Anal. Calcd for $C_{63}H_{80}N_2O_{16}Si_2$: C, 64.26; H, 6.85; N, 2.38. Found: C, 64.11; H, 7.05; N, 2.34.

2.1.25. 3-Benzyloxycarbonylamino-1-propyl *O*-(2,3,4,6-tetra-*O*-benzyl-α-D-galactopyranosyl)-*O*-(1→3)-(2,4-di-*O*-acetyl-6-*O*-*tert*-butyldiphenylsilyl-β-D-galactopyranosyl)-*O*-(1→4)-3-*O*-acetyl-2-acetamido-6-*O*-*tert*-butyldiphenylsilyl-2-deoxy-β-D-glucopyranoside (27). (a) *Using $Cu(TfO)_2$ as activator*. A 25 mL round bottom flask containing a mixture of **26** (1.0 g, 0.849 mmol) and **13** (0.66 g, 1.2 equiv.), and a magnetic stirrer was dried overnight under vacuum over P_2O_5. The mixture was dissolved in dry toluene (17.0 mL) and $Cu(TfO)_2$ (0.614 g, 2.0 equiv. dried at 200°C for 2 h under vacuum just before use) was added quickly and the mixture was stirred for 20 h at room temperature under argon. The reaction mixture was quenched with a few drops of pyridine, diluted with CH_2Cl_2 (100 mL) and filtered through a Celite® pad. The solution was washed with water (50 mL), 1N HCl (50 mL), water (50 mL), dried (Na_2SO_4) and concentrated. The crude was purified by flash chromatography (EtOAc/hexanes 1:1) giving **27** (67 mg, 0.039 mmol, 60%) as a white foam.

(b) *Using $Yb(TfO)_3$ as activator*. A 10 mL round bottom flask containing a mixture of **26** (90.6 mg, 0.077 mmol) and **13** (50 mg, 1.0 equiv.), and a magnetic stirrer was dried overnight under vacuum over Drierite®. The mixture was dissolved in dry CH_2Cl_2 (1.1 mL) and $Yb(TfO)_3$ (47.7 mg, 1.0 equiv. dried at 200°C for 2 h under vacuum just before use) was added quickly and the mixture stirred

for 4 h at room temperature under argon, a second portion of **13** (50 mg, 1.0 equiv.) was added and the system stirred for 4 h at room temperature. The reaction mixture was diluted with CH_2Cl_2 (50 mL), washed with water (20 mL), 1N HCl (20 mL), water (20 mL), dried (Na_2SO_4) and concentrated. After purification (flash chromatography, gradient elution CH_2Cl_2/MeOH 30:1 to 20:1) the reaction afforded **27** (81.9 mg, 0.048 mmol, 63%) as a white foam and **28** (18.9 mg, 0.029 mmol, syrup).

For **27**: $[\alpha]_D$=+18.2 (*c* 1.1, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 300 MHz); δ ppm: 7.78–7.18 (m 45H, PhCH), 6.43 (d, 1H, NHAc, *J*=7.9 Hz), 5.73 (dd, 1H, H-4′, $J_{4',3}$=3.1 Hz, $J_{4',5}$=0.0 Hz), 5.20 (d, 1H, H-1″, $J_{1'',2''}$ =3.1 Hz), 5.17 (d, 1H) and 5.06 (d, 1H) (AB, *J*=12.0 Hz), 4.97 (d, 1H) and 4.54 (d, 1H) (AB, *J*=11.3 Hz), 4.88 (d, 1H) and 4.75 (d, 1H) (AB, *J*=11.8 Hz), 4.78 (2, 2H) and 4.72 (d, 1H) (AB, *J*=11.9 Hz), 4.51 (d, 1H) and 4.39 (d, 1H) (AB, *J*=11.8 Hz) (5CH_2Ph), 5.1 (m, 2H, NHCbz and H-2′), 4.93 (dd, 1H, H-3, $J_{3,2}$=$J_{3,4}$=8.7 Hz), 4.63 (d, 1H, H-1′, $J_{1',2'}$=8.0 Hz), 4.15–3.98 (m, 4H), 3.98–3.82 (m, 6H), 3.80 (dd, 1H, *J*=3.3, 6.3 Hz), 3.73 (dd, 1H, *J*=3.6 Hz), 3.65 (dd, 1H, *J*=8.6, 8.3 Hz), and 3.58–3.45 (m, 18H) (H-1, H-2, H-4 to H-6A, H-3′, H-5′ to H-6A′ and H-2″ to H-6A″, and OCH_2R), 3.32–3.11 (m, 3H, OCH_2R and 2NHCH_2R), 1.94 (s, 3H), 1.82 (s, 6H), and 1.78 (s, 3H) (4$COCH_3$), 1.62 (m, 2H, –CH_2–), 1.00 (s 18H) (2 s, Si$C(CH_3)_3$). ^{13}C NMR ($CDCl_3$, 100 MHz); δ ppm: 171.0, 170.8, 169.6, 169.1, and 156.9 (5CO), 139.0, 138.1, 136.9, 133.7, 133.1, 132.9, 132.7, and 128.5 (PhC), 136.0, 135.9, 135.7, 135.6, 130.0, 128.8, 128.3, 128.1, 128.0, 127.9, 127.8, 127.6, and 127.5 (PhCH), 101.7 and 100.4 (C-1 and C-1′), 95.9 (C-1″), 75.0, 73.7, 73.2 (2C), 68.4, 66.9, 66.3, and 61.2 (2C) [all (−), C-6, C-6′, C-6″, OCH_2R and 5CH_2Ph], 78.7, 76.2, 75.6, 75.5, 74.4, 73.5, 73.2 (2C), 71.6, 70.0, 65.3, and 53.2 (C-2 to C-5, C-2′ to C-5′, and C-2″ to C-5″), 37.6 [(−), NHCH_2R], 29.8 (–CH_2–), 23.3, 20.9, and 20.7 (2C) (4$COCH_3$), 27.1, 26.9, 19.5 (q) and 19.30 (q) (2Si$C(CH_3)_3$). FABMS (rel. intensity) 1700.8 (62), $[M+H]^+$, 1722.8 (50), $[M+Na]^+$. Anal. Calcd for $C_{97}H_{114}N_2O_{21}Si_2$: C, 68.53; H, 6.76; N, 1.65. Found: C, 68.04; H, 6.91; N, 1.67.

For **28**: $[\alpha]_D$=+37.6 (*c* 1.0, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 300 MHz); δ ppm: 7.44–7.08 (m, 20PhCH), 6.98 (dd, 1H, *J*=1.5, 7.1 Hz), 6.50 (dd, 1H, *J*=1.5, 7.4 Hz), 6.01 (dd, 1H, *J*=7.1, 7.4 Hz) (3PyCH), 6.27 (d, 1H, H-1, $J_{1,2}$=9.0 Hz), 5.0 (d, 1H, *J*=11.4 Hz), 4.75 (s, 2H), 4.64 (d, 2H, *J*=11.4 Hz), 4.63 (d, 1H, *J*=11.3 Hz), 4.46 (AB, 2H, *J*=11.8 Hz), and 4.35 (d, 1H, *J*=11.3 Hz) (4CH_2Ph), 4.06 (m, 2H), and 3.84 (m, 2H) (H-2, H-3, H-4 and H-5), 3.81 (s, 3H, OCH_3), 3.63 (dd, 1H, H-6, $J_{6,5}$=7.8 Hz, $J_{6,6A}$=9.1 Hz), 3.56 (dd, 1H, H-6A, $J_{6A,5}$=5.6 Hz). ^{13}C NMR ($CDCl_3$, 100 MHz); δ ppm: 157.9 and 149.6 (PyC), 138.9, 138.2, 137.8, and 137.7 (4PhC), 128.4, 128.3, 128.2, 127.9, 127.8, 127.7, 127.6, and 127.4 (PhCH), 123.9 and 111.8 (2PyCH), 104.9 (C-1), 83.2, 81.3, 78.0, 75.7, and 73.8 (C-2, C-3, C-4, C-5, and CHPy), 74.7, 74.5, 73.5, and 74.8 [(−), 4CH_2Ph], 68.0 [(−), C-6], 53.3 (OCH_3). HR-FABMS calcd for $C_{40}H_{42}O_7N$ *m/z* 648.2961; found 648.2976.

2.1.26. 3-Amino-1-propyl *O*-α-D-galactopyranosyl-(1→3)-*O*-β-D-galactopyranosyl-(1→4)-*O*-2-acetamido-2-deoxy-β-D-glucopyranoside hydrochloride (2). To a solution of **27** (303.2 mg, 0.229 mmol) in dry MeOH (11 mL) was added sodium methoxide (~10 equiv.) and the reaction mixture stirred for 48 h at room temperature. The solution was concentrated under vacuum. To a solution of the crude product in THF (2.3 mL) was added in one portion TBAF (0.55 mL, 1.2 equiv.). The solution was stirred for 6 h at room temperature, concentrated and purified by flash chromatography (CH_2Cl_2/MeOH 15:1) affording 3-benzyloxycarbonylamino-1-propyl 2,3,4,6-tetra-*O*-benzyl-α-D-galactopyranosyl-(1→3)-*O*-β-D-galactopyranosyl-(1→4)-*O*-2-acetamido-2-deoxy-β-D-glucopyranoside (172 mg, 0.156 mmol, 68%) as a glass: FABMS (rel. intensity) 1097.6 (13), $[M]^+$, also 1119.5 (69), $[M+Na]^+$. A portion of this product (64 mg, 0.58 mmol) was dissolved in dioxane (3.6 mL); water was added (18 mL) followed by 20% palladium-on-carbon (Pearlman's catalyst, ~20 mg). The mixture was stirred for 2 h under hydrogen (60 psi) at room temperature, the hydrogen pressure was relieved, HCl (1N in dioxane, ~1 equiv.) was added and the mixture stirred under hydrogen (60 psi) overnight. The suspension was filtered through a Celite® pad, and the pad rinsed with water (20 mL). The filtrate was concentrated under vacuum to about 5 mL passed through an ion exchange resin column (Dowex® 1×8–50 in the chloride form); the solution afforded after rinsing the column with water and lyophilizing the eluate pure **2** as the hydrochloride (35.8 mg, 0.056 mmol, 96% for the hydrogenation, 65% overall yield from **27**) as a white powder: $[\alpha]_D$=+50 (*c* 1.0, DMSO). ^{1}H NMR (D_2O, CH_3OD internal standard at δ= 3.35 ppm, 300 MHz); δ ppm: 5.15 (d, 1H, H-1″, $J_{1'',2''}$=3.7 Hz), 4.51 (2 d, 2H, H-1 and H-1′, $J_{1,2}$=7.6 Hz, $J_{1',2'}$=7.6 Hz), 4.19–4.15 (m, 2H) and 4.00–3.50 (m, 18H) [H-2 to H-6 and H-6A, H-2′ to H-6′ and H-6A′, H-2″ to H-6″ and H-6A″ and 2 OCH_2R], 3.00 (t, 2H, NCH_2R, $J_{-NCH2-,-CH2-}$=7 Hz), 2.05 (s, 3H, $COCH_3$), 1.95 (m, 2H, –CH_2–). ^{13}C NMR (D_2O, CH_3OD internal standard at δ=49.6 ppm, 100 MHz); δ ppm: 175.6 (CO), 104.0 and 102.4 (C-1 and C-1′), 96.7 (C-1″), 80, 78.5, 76.2, 75.9, 73.4, 72, 70.7, 70.5, 70.3, 69.4 and 66.0 (C-3 to C-5, C-2′ to C-5′, and C-2″ to C-5″), 69.1, 62.1 (2C), 61.2 [all (−), C-6, C-6′, C-6″, OCH_2R], 56.1 (C-2), 38.9 [(−), NHCH_2R], 27.8 [(−),–CH_2–], 23.2 ($COCH_3$). HR-FABMS calcd for $C_{23}H_{43}O_{16}N_2$ *m/z* 603.2612; found 603.2603.

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