O-Glycosyl Amino Acids by 2-Nitrogalactal Concatenation − Synthesis of a Mucin-Type *O*-Glycan

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Base-promoted Michael-type addition of *N*-Boc- and *N*-Fmoc-protected serine and threonine esters to 2-nitrogalactal derivatives **2** and **26** led highly selectively to α-glycosides **4a**–**d** and **27a**,**c**, respectively. Ensuing transformation of threonine derivative **4d** and serine derivatives **4a**,**b** resulted in compounds useful as lysine and dipeptide mimetics. 6-*O*-Desilylation of **27a**,**c**, then 6-*O*-sialylation, and transformation of the nitro group of the galactose moiety into a 2-acetamido functionality, afforded *N*-Boc-protected serine and threonine *tert*-butyl esters **31a**,**c** carrying the *O*-protected ST_N-antigen at the hydroxy group. The threonine derivative **31c** was then transformed into the *N*-Fmoc-protected amino acid building block **33**, which was employed for the synthesis of mucin repeating unit partial structure Ac-GS(ST_N)-TAP-PAHG-NH_2 (**1**).

Introduction

The mucin class of glycopeptides has attracted much attention, because it consists of numerous structures of fundamental importance in biological processes like cell−cell adhesion, cell growth, fertilization, parasitic infection, and inflammation.[1−3] The interest of biologists and chemists has been sparked especially by the occurrence of aberrant glycoforms of the mucin family in tumours of epithelial tissues.[1,2]

Chemical synthesis of the characteristic α-glycosidic linkage between 2-acetamido-2-deoxy-D-galactopyranose and the side chain hydroxy groups of L-serine and L-threonine, however, has proven to be difficult. Despite the endeavours and achievements of synthetic chemists, most syntheses of α-*O*-linked glycopeptides have relied essentially on the methodology introduced by Paulsen in 1978.[4−6] The non-participating azido group as a latent amino function at position 2 is combined with a good leaving group at the anomeric position in the glycosylation reaction. Proceeding from this concept, many syntheses of mucin structures have been reported that use different anomeric leaving groups for the glycosidation step.[7−18] *N*-Acetyl-protected galactosamine donors also have been transformed directly into *O*-linked α-glycosyl amino acid derivatives,[19] and enzymatic syntheses have been investigated successfully in this endeavour.[20,21] Recently, we have shown that for the synthesis of the simplest mucin structure, the T_N-antigen, Michael addition to 2-nitrogalactal serves as an efficient alternative approach[22−25] to practically all mucin core structures.

Mucins, a family of highly glycosylated glycoproteins that are found in mucus and on cell surfaces of epithelial cells, all have a characteristic unit consisting of a variable number of tandem repeat units. The repeating units are rich in serine and threonine residues that allow for heavy *O*-glycosyl-

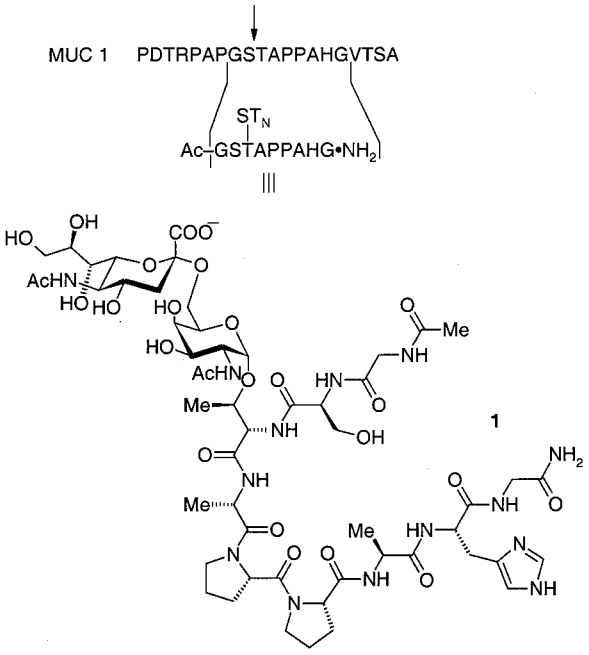

Figure 1. *O*-Glycosylated MUC 1 nonapeptide **1** as part of the MUC 1 tandem repeat unit; the arrow indicates the glycosylation site

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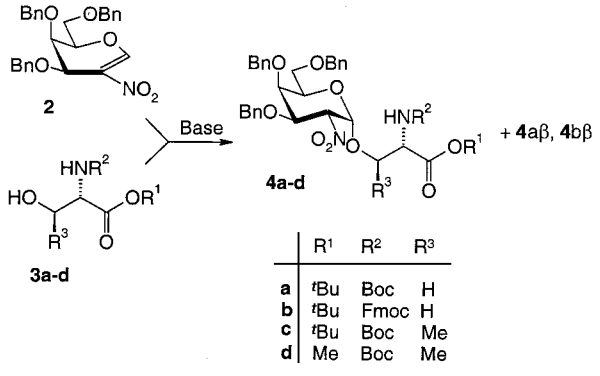
ation.[3,40,41] Malignantly transformed cells show increased expression of mucins and, because of incomplete glycosylation, are covered with shorter carbohydrate chains.[26,27] One of the prominent, incomplete glycan structures is the ST_N-antigen. It is an end product in the biosynthetic pathway and cannot be converted further into complex structures.[28] Antibody titres against ST_N have been reported to correlate with improved prognosis in breast cancer patients. The preparation of immunogenic structures eliciting the formation of antibodies, or more importantly cytotoxic T-lymphocytes, directed against the ST_N-antigen, therefore, seems an attractive synthetic and biological challenge.[29,30] Syntheses of an ST_N glycopeptide fragment of HIV gp 120 and of ST_N peptides of the MUC 1 repeating unit, with the help of differently prepared ST_N building blocks, have been reported.[31–38]

In this paper, we extend our studies to the synthesis of useful GalNAcα(1-*O*)Ser and GalNAcα(1-*O*)Thr conjugates — i.e., T_N antigen building blocks — and to the synthesis of their 6-*O*-sialylated derivative, the ST_N antigen.[39] This building block is employed for the construction of the MUC 1 mucin type glycopeptide **1** that is derived from the tandem repeat eicosapeptide as shown in Figure 1.[40,41]

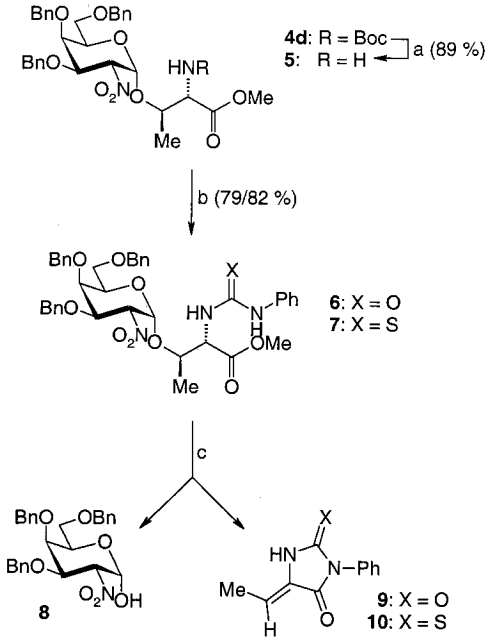
Results and Discussion

3,4,6-Tri-*O*-benzyl-2-nitro-D-galactal (**2**), which is readily available from the corresponding galactal derivative,[42] furnished upon reaction with *N*-Boc-protected serine derivative **3a** the α-galactoside derivative **4a** (80%) together with some β-anomer (13%)[22,43] (Scheme 1). Even direct potassium *tert*-butoxide-promoted addition of *N*-Fmoc-protected serine derivative **3b** to **2** was possible, affording α-galactoside derivative **4b** in 83% yield practically without loss of the base-sensitive Fmoc group; in addition, 14% of the corresponding β-anomer was obtained, which could be separated readily from **4b**.[22] It was confirmed also that no racemisation had occurred under the reaction conditions. Addition of threonine derivatives **3c** and **3d** led to stereoselective formation of **4c**[22] and **4d**, respectively; β-anomer formation was not observed, and thus two new stereogenic centres were generated stereoselectively in this reaction. The structural assignment could be derived readily from the ^1H NMR spectra (**4a**–**d**; $J_{1,2} \approx 4.2$, $J_{2,3} \approx 10.7$ Hz).



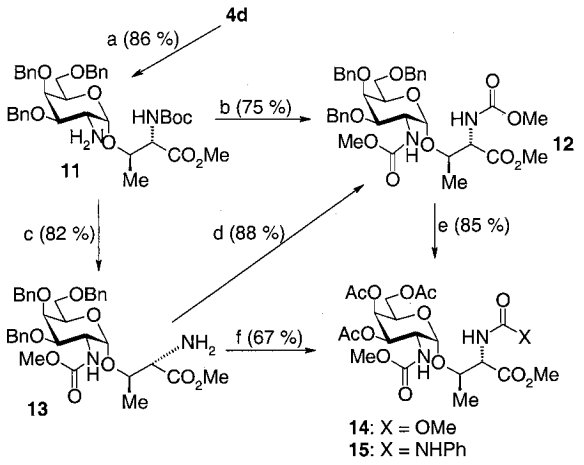
Scheme 1. Addition of serine and threonine derivatives to 2-nitrogalactal **2**

Transformation of, for instance, **4d** into *N*-deprotected threonine derivative **5** (Scheme 2) was accomplished by treatment with trifluoroacetic acid (TFA) under standard conditions. Reaction of **5** with phenyl isocyanate or phenyl isothiocyanate as electrophiles afforded *N*-carbamoyl derivatives **6** and **7**, respectively, in high yields. Investigation of the base-promoted ring closure to the corresponding hydantoin derivatives led — as shown, for example, upon treatment with ammonia — to elimination of 2-deoxy-2-nitro-α-D-galactose **8** and formation of 5-(ethylidene)hydantoin **9** and formation of 5-(ethylidene)thiohydantoin **10**, respectively. The (*Z*) configuration of **9** and **10** was determined by comparison with previous studies based on ^{13}C NMR spectroscopic data.[44,45]



Scheme 2. Reaction of adduct **4d** with heterocumulenes; a) TFA; b) PhNCX, EtOH, reflux; c) NH_3, MeOH

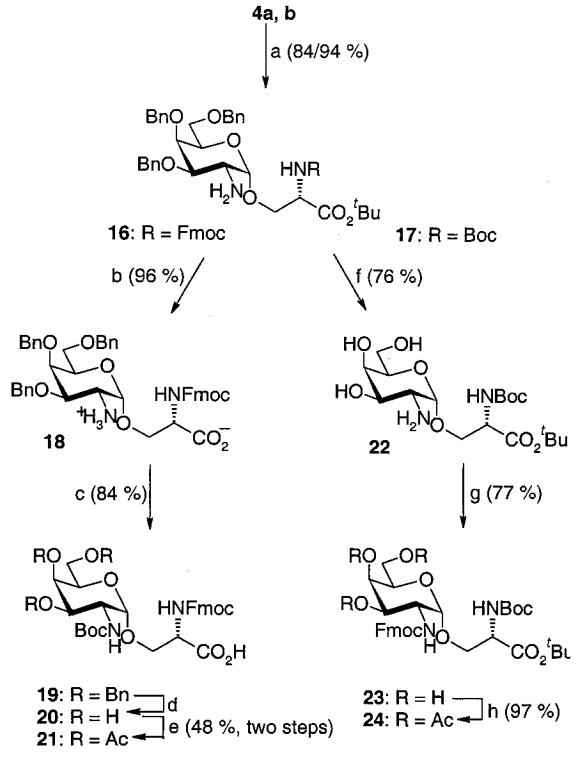
Reduction of the 2-nitro group in **4d** with hydrogen and platinized Raney-Ni T4[46] as catalyst afforded amino derivative **11**, which also can be regarded as a dipeptide mimetic (Scheme 3). Acid-catalysed removal of the *N*-Boc protecting group and subsequent treatment with diphosgene in dichloromethane/pyridine, and then with methanol, furnished N^{α},N^{ε}-bis(methoxycarbonyl) derivative **12**. An alternative reaction sequence led from **11** to N^{ε}-(methoxycarbonyl) derivative **13**, which also serves as a starting material for the synthesis of **12**. Hydrogenolytic *O*-debenzylation of **12** with palladium on carbon in methanol/acetic acid and then *O*-acetylation afforded *O*-acetyl derivative **14**. Similarly, N^{α}-(phenylcarbamoyl) derivative **15** was obtained from **13** after carbamoylation of the unprotected amino group with phenyl isocyanate, *O*-debenzylation, and then *O*-acetylation.



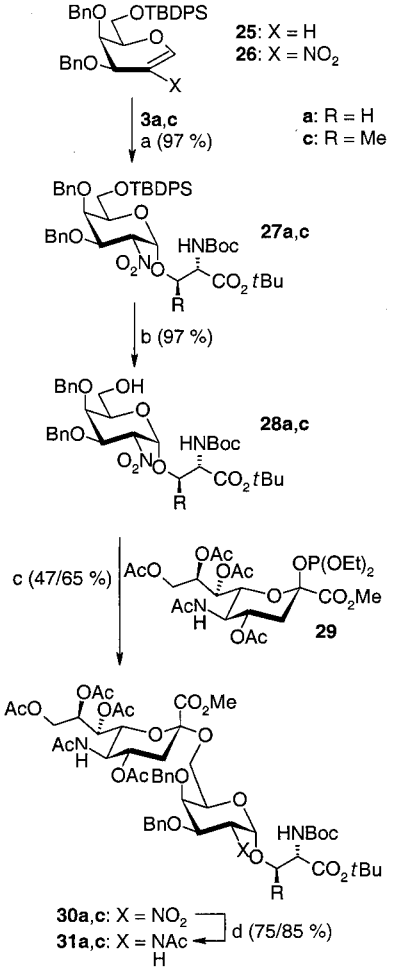
Scheme 3. Liberation of amino groups in **4d** and reaction with electrophiles; a) Raney-Ni T4/Pt, H_2, EtOH; b) 1. HCl, Et_2O; 2. diphosgene, CH_2Cl_2, Pyr; 3. MeOH; c) 1. diphosgene, CH_2Cl_2, Pyr; 2. MeOH; 3. HCl, Et_2O; d) diphosgene, Pyr; MeOH; e) 1. Pd/C, H_2, MeOH/AcOH; 2. Ac_2O, Pyr; f) 1. PhNCO; 2. Pd/C, H_2; 3. Ac_2O, Pyr

In order to generate useful peptidomimetics, the nitro groups in compounds **4a**,**b** were transformed into amino groups, as described above, thus furnishing **16** and **17** after N^{α}-Fmoc and N^{α}-Boc protection, respectively (Scheme 4). Acid-catalysed cleavage of the *tert*-butyl group in the ester **16** furnished the acid **18**, which on treatment with 2-(*tert*-butoxycarbonyloximino)-2-phenylacetonitrile (BocON) in the presence of triethylamine as base furnished N^{α}-Fmoc-N^{ε}-Boc-protected dipeptide mimetic **19**. Hydrogenolysis of **19** removed both the *O*-benzyl and *N*-Fmoc groups; subsequent treatment with Fmoc chloride, in the presence of triethylamine, furnished the useful *O*-unprotected derivative **20**, which on *O*-acetylation led to **21**. Hydrogenolytic *O*-debenzylation of **17** gave *O*-unprotected *tert*-butyl ester **22**, which on reaction with Fmoc chloride in the presence of triethylamine led to N^{α}-Boc-N^{ε}-Fmoc-protected dipeptide mimetic **23**; *O*-acetylation furnished per-*O*-acetyl derivative **24**.

As previously shown, 6-*O*-*tert*-butyldiphenylsilyl-(TBDPS-)protected 2-nitrogalactal **26**, which is readily available from the corresponding galactal **25**, afforded exclusively the α-galactopyranosides **27c** and **27a**, respectively, not only with threonine derivative **3c** but also with serine derivative **3a** (Scheme 5).[22] Obviously, these T_N antigen intermediates are versatile building blocks for the construction, for instance, of mucin-type *O*-glycopeptides. In order to demonstrate this versatility in the synthesis of target molecule **1**, the TBDPS groups of **27a**,**c** were removed upon treatment

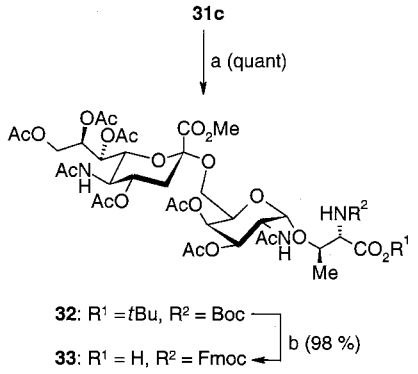


Scheme 4. Transformation of **4a**,**b** into lysine and peptido mimetics; a) Raney-Ni T4/Pt, H_2, EtOH, b) TFA; c) BocON, NEt_3, d) Pd/C, H_2; FmocCl, NEt_3; e) Ac_2O, Pyr; f) Pd/C, H_2, AcOH, MeOH; g) FmocCl, NEt_3; h) Ac_2O, Pyr



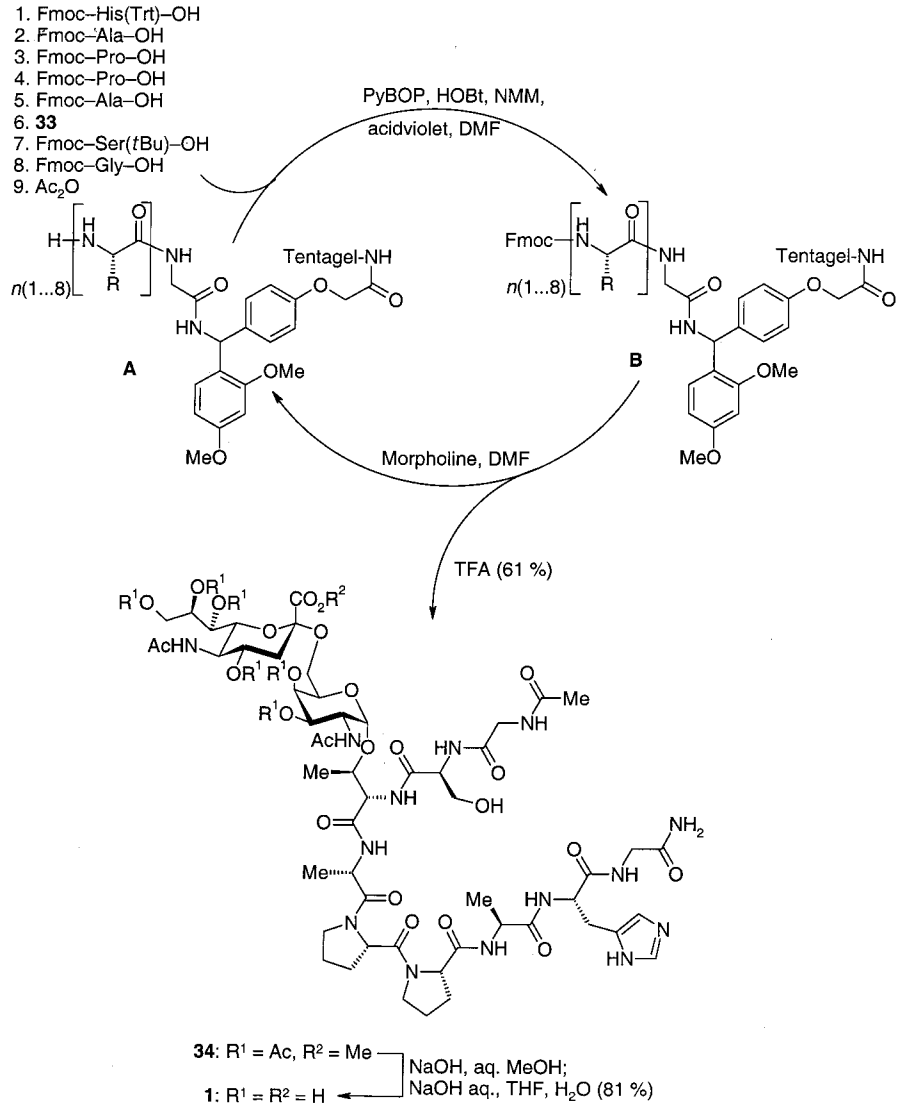
Scheme 5. Synthesis of ST_N structures by Michael addition and sialylation; a) KO*t*Bu, Tol; b) TBAF, THF; c) TMSOTf (0.1 equiv.), EtCN, −60 to −40 °C; d) 1. Raney-Ni T4/Pt, H_2, EtOH; 2. Ac_2O, Pyr

with tetrabutylammonium fluoride (TBAF) in THF/acetic acid affording 6-*O*-unprotected derivatives **28a**,**c**. Sialylation with the known[47,48] sialyl donor **29** — at low temperatures in propionitrile as solvent and with trimethylsilyl trifluoromethanesulfonate (TMSOTf) as catalyst — furnished ST_N antigen derivatives **30a** and **30c**. Reduction of the nitro groups under the conditions described above led, despite the powerful reducing properties of the catalyst, to clean formation of the amines that, on *N*-acetylation, furnished the desired building blocks **31a** and **31c**, respectively. The α-linkage of the sialyl groups in **30a**,**c** and **31a**,**c** was confirmed by comparison of the ^{1}H NMR chemical shifts of 3b-H_e and 4b-H, the coupling constants of 7b-H and 8b-H, and the differences of the chemical shift of 9b-H and 9b′-H, with averages of values reported in the literature.[49]



Scheme 6. Preparation of an ST_N building block for glycopeptide synthesis; a) 1. Pd/C, H_2, AcOH, MeOH; 2. Ac_2O, Pyr; b) 1. TFA, CH_2Cl_2; 2. FmocONSu, $NaHCO_3$

For the synthesis of target molecule **1**, hydrogenolytic *O*-debenzylation of **31c** in the presence of Pd/C as catalyst was performed; subsequent treatment with acetic anhydride in pyridine afforded *O*-acetylated *O*-glycosyl threonine derivative **32** (Scheme 6). Acid-catalysed removal of the *N*-Boc and the *tert*-butyl ester groups, and then treatment with *N*-(fluorenylmethoxycarbonyloxy)succinimide (FmocONSu)



Scheme 7. Solid-phase glycopeptide synthesis of **34** and deprotection to glycopeptide **1**: Ac-GS(ST_N)-TAPPAHG-NH_2

in acetonitrile/water in the presence of sodium bicarbonate, afforded ST_N building block **33**, which is suitable for Fmoc-based glycopeptide synthesis.

We chose PyBOP/HOBT activation[50−52] for glycopeptide coupling in the synthesis of target molecule **1** (Scheme 7), using TentaGel S RAM Gly Fmoc (Rapp Polymere) as the prefunctionalised resin. Previously, we have used this system — a Rink amide linker together with the Tentagel S resin — for the synthesis of a *C*-linked glycopeptide,[53] but with the amino acids used directly as their Dhbt or Pfp activated esters. In the present study, the free carboxylic acid is converted into the active ester in situ, thus shortening the synthesis of the glycopeptide building block.

Protected glycopeptide **34** was assembled via intermediates **A** and **B**, using standard procedures. *N*,*N*-Dimethylformamide was used as solvent in all coupling steps in the peptide synthesis, and for washing. Fmoc cleavage was performed with morpholine and monitored at λ = 360 nm. Functionalised Fmoc amino acids were added successively to the peptide chain in the specified sequence. Glycosylated threonine building block **33** was used in twofold excess and activated in the same manner as the simple amino acids.

After the peptide had been assembled completely, the resin-bound peptide was cleaved from the solid phase and partially deprotected using trifluoroacetic acid/triisopropylsilane/water. The crude glycopeptide, still fully protected on the glycan moiety, was then purified on a column of Sephadex LH-20 to give the desired product **34** as a colourless lyophilisate in 61% yield. This material was characterised by NMR spectroscopic and mass spectrometric analysis. The acetyl groups protecting the carbohydrate hydroxy functions were still intact, as was the neuraminic acid methyl ester. Basic hydrolysis of the acyl groups is a delicate procedure because the *O*-glycan **34** can undergo β-elimination of the carbohydrate moiety. It is important, therefore, to find hydrolytic conditions that are strong enough to cleave a tertiary methyl ester, but that do not affect the threonine glycoside.

As a basis for the deprotection of **34**, we examined the protocol that Kunz et al. had used for the deprotection of a similar structure.[34] In the first step, the *O*-acetyl groups were cleaved within 3 h by treatment with aqueous sodium hydroxide in methanol at a controlled pH of 10−11. Methyl ester hydrolysis was performed in THF/water with aqueous sodium hydroxide (pH = 11−11.5). After 4 h, this procedure led to complete methyl ester cleavage with no considerable loss of material resulting from β-elimination. After purification on a column of Sephadex LH-20, the deprotected glycopeptide **1** was isolated as a lyophilisate in 81% yield for these last two steps. Deprotected glycopeptide **1** was characterised fully by NMR spectroscopic and mass spectrometric analyses.

In conclusion, coupling of *N*-protected serine and threonine esters to *O*-protected 2-nitrogalactal gives ready access to *N*-acetylgalactosamine-derived α-glycosyl amino acids. These versatile building blocks can be transformed into dipeptide and lysine mimetics, as well as being employed in *O*-glycopeptide synthesis.

Experimental Section

General Remarks: Solvents were evaporated under reduced pressure while maintaining the water bath temperature below 40 °C. Chromatography was performed on silica gel for flash chromatography 40 μm (J. T. Baker) at 3 bar pressure. For thin-layer chromatography (TLC) plastic sheets of silica gel 60 F_{254} were used and the compounds visualized by illumination under UV light at 253 nm and by treatment with a solution of 5% $(NH_4)_2MoO_4$ and 0.1% $Ce(SO_4)_2$ in 10% H_2SO_4 followed by heating to 160 °C. Optical rotations were measured at 25 °C with a Perkin−Elmer polarimeter 241/MS using the sodium D line. NMR spectra: Bruker AC 250 Cryospec, Bruker DR 600; TMS or the solvent residual peak were used as internal standard. Coupling constants ($^3J_{C,H}$) were observed in gradient-selected heteronuclear multi-bond correlations (HMBC). MALDI-MS: Kratos Kompact Maldi 1; 2.5-dihydroxybenzoic acid was used as matrix. FAB-MS: Finnigan MAT 312/AMD 5000, 790 eV, 70 °C. Where its recovery is stated, yields are calculated based on reagents consumed.

***N*-(*tert*-Butoxycarbonyl)-*O*-(3,4,6-tri-*O*-benzyl-2-deoxy-2-nitro-α-DL-threonine Methyl Ester (4d):** Compounds **3d**[54] (1.16 g, 5.00 mmol) and **2** (2.10 g, 5.00 mmol) were dried under high vacuum and dissolved in dry toluene (60 mL) under argon. Freshly activated molecular sieves (3 Å, 3 g) were introduced and the mixture stirred for 1 h. Then a solution of 1 M potassium *tert*-butoxide in THF (0.50 mL, 0.50 mmol) was added and stirring continued for 2 h. Acetic acid (0.50 mL) was used to acidify the reaction mixture, the molecular sieves were filtered off, and all the solvents were evaporated. The residue was purified by column chromatography (petroleum ether/ethyl acetate, 9:1) to furnish **4d** (3.34 g, 96%). No corresponding β-glycoside was detected. TLC (petroleum ether/ethyl acetate, 4:1): R_f = 0.58. $[\alpha]_D$ = +75.5 (*c* = 1.5; $CHCl_3$). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.22 (d, $^3J_{\gamma,\beta}$ = 6.3 Hz, 3 H, γ-CH_3), 1.49 (s, 9 H, C_4H_9), 3.26 (m, 2 H, 6-H, 6′-H), 3.68 (s, 3 H, OCH_3), 3.95 (m, 2 H, 4-H, 5-H), 4.20−4.48 (m, 6 H, 3-H, O*C*H_2Ph, β-CH, α-CH), 4.64 (s, 2 H, O*C*H_2Ph), 4.75 (d, ^2J = 11.1 Hz, 1 H, O*C*H_2Ph), 4.86 (dd, $^3J_{2,1}$ = 4.2, $^3J_{2,3}$ = 10.8 Hz, 1 H, 2-H), 5.00 (d, $^3J_{NH,\alpha}$ = 8.2 Hz, 1 H, NH), 5.26 (d, $^3J_{1,2}$ = 4.3 Hz, 1 H, 1-H), 7.11−7.32 (m, 15 H, Ar-H) ppm. ^{13}C NMR (150.8 MHz, $CDCl_3$): δ = 18.8 (γ-CH_3), 29.01 (C*Me*$_3$), 53.5 (OCH_3), 58.8 (α-C), 69.0 (C-6), 70.7 (C-5, β-C), 73.7 (C-4, 2 × O*C*H_2Ph), 75.8 (O*C*H_2Ph, C-3), 80.9 (*C*Me$_3$), 85.0 (C-2), 98.3 (C-1), 128.4, 128.5, 128.8, 129.0, 129.2 138.0, 138.4, 138.6 (C-Ar), 156.2 (CO_2Me), 171.1 (Boc-CO) ppm. MS (MALDI): *m*/*z* = 717 $[M + Na]^+$. $C_{37}H_{46}N_2O_{11}$ (694.8): calcd. C 63.96, H 6.67, N 4.03; found C 63.87, H 6.60, N 4.17.

***O*-(3,4,6-Tri-*O*-benzyl-2-deoxy-2-nitro-α-D-galactopyranosyl)-L-threonine Methyl Ester (5): 3d** (1.00 g, 1.44 mmol) was dissolved in a mixture of trifluoroacetic acid and CH_2Cl_2 (20 mL, 1:1), the solution was stirred at room temp. for 12 h, and then the solvents were evaporated. The residue was dissolved in CH_2Cl_2, then saturated aqueous $NaHCO_3$ was added with vigorous stirring. The layers were separated and the aqueous layer was extracted with CH_2Cl_2. The combined organic layers were dried ($MgSO_4$), filtered, concentrated under reduced pressure, and purified by column chromatography (CH_2Cl_2/MeOH, 98:2) to furnish **5** (0.76 g, 89%). TLC (CH_2Cl_2/MeOH, 98:2): R_f = 0.20. $[\alpha]_D$ = +62.0 (*c* = 1.0; $CHCl_3$). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.35 (d, $^3J_{\gamma,\beta}$ = 6.4 Hz, 3 H, γ-

CH_3), 3.27 (d, $^3J_{\alpha,\beta}$ = 3.0 Hz, 1 H, α-CH), 3.52 (m, 2 H, 6-H, 6′-H), 3.78 (s, 3 H, OCH_3), 3.81 (d, $^3J_{5,6}$ = 2.7 Hz, 1 H, 5-H), 4.04 (m, 2 H, 3-H, 4-H), 4.20 (dq, $^3J_{\beta,\alpha}$ = 3.3, $^3J_{\beta,\gamma}$ = 6.5 Hz, 1 H, β-CH), 4.39−4.52 (m, 5 H, OCH_2Ph, NH_2), 4.71 (s, 2 H, OCH_2Ph), 4.84 (d, ^2J = 11.1 Hz, 1 H, OCH_2Ph), 4.95 (dd, $^3J_{2,1}$ = 4.2, $^3J_{2,3}$ = 10.7 Hz, 1 H, 2-H), 5.38 (d, $^3J_{1,2}$ = 4.2 Hz, 1 H, 1-H), 7.19−7.35 (m, 15 H, Ar-H) ppm. MS (MALDI): *m*/*z* = 595 $[M + H]^+$. $C_{32}H_{38}N_2O_9$ (594.7): calcd. C 64.63, H 6.44, N 4.71; found C 64.23, H 6.41, N 4.30.

***N*-(Phenylaminocarbonyl)-*O*-(3,4,6-tri-*O*-benzyl-2-deoxy-2-nitro-α-D-galactopyranosyl)-L-threonine Methyl Ester (6):** A mixture of **5** (450 mg, 0.71 mmol) and phenyl isocyanate (169 mg, 1.42 mmol) in anhydrous ethanol (3 mL) was heated under reflux for 12 h. The solvent was evaporated under reduced pressure and the residue was purified by column chromatography (petroleum ether/ethyl acetate, 4:1) to furnish **6** (0.40 g, 79%). TLC (petroleum ether/ethyl acetate, 4:1): R_f = 0.3. $[\alpha]_D$ = +84.8 (*c* = 0.75; $CHCl_3$). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.32 (d, $^3J_{\gamma,\beta}$ = 6.4 Hz, 3 H, γ-CH_3), 3.52 (m, 2 H, 6-H, 6′-H), 3.74 (s, 3 H, OCH_3), 4.00 (m, 2 H, 4-H, 5-H), 4.26 (dd, $^3J_{3,4}$ = 2.8, $^3J_{3,2}$ = 10.7 Hz, 1 H, 3-H), 4.37 (dq, $^3J_{\beta,\alpha}$ = 2.6, $^3J_{\beta,\gamma}$ = 5.8 Hz, 1 H, β-CH), 4.42−4.47 (m, 4 H, OCH_2Ph, α-CH), 4.64 (d, ^2J = 12.6 Hz, 2 H, OCH_2Ph), 4.75 (d, ^2J = 11.2 Hz, 1 H, OCH_2Ph), 4.93 (dd, $^3J_{2,1}$ = 4.2, $^3J_{2,3}$ = 10.7 Hz, 1 H, 2-H), 5.35 (d, $^3J_{1,2}$ = 4.3 Hz, 1 H, 1-H), 5.50 (br. s, 1 H, NH), 7.06 (br. s, 1 H, NHPh), 7.18−7.40 (m, 20 H, Ar-H) ppm. MS (MALDI): *m*/*z* = 736 $[M + Na]^+$. $C_{39}H_{43}N_3O_{10}$ (713.8): calcd. C 65.63, H 6.07, N 5.89; found C 65.52, H 6.17, N 5.86.

***N*-(Phenylaminothiocarbonyl)-*O*-(3,4,6-tri-*O*-benzyl-2-deoxy-2-nitro-α-D-galactopyranosyl)-L-threonine Methyl Ester (7):** A mixture of **5** (300 mg, 0.50 mmol) and phenyl isothiocyanate (135 mg, 1.00 mmol) in anhydrous ethanol (3 mL) was heated under reflux for 12 h. The solvent was evaporated under reduced pressure and the residue was purified by column chromatography (petroleum ether/ethyl acetate, 9:1) to furnish **7** (0.30 g, 82%). TLC (petroleum ether/ethyl acetate, 2:1): R_f = 0.4. $[\alpha]_D$ = +64.1 (*c* = 0.56; $CHCl_3$). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.26 (d, $^3J_{\gamma,\beta}$ = 6.4 Hz, 3 H, γ-CH_3), 3.48 (m, 2 H, 6-H, 6′-H), 3.77 (s, 3 H, OCH_3), 3.82 (dd, $^3J_{5,6}$ = 6.6, $^3J_{5,6'}$ = 6.6 Hz, 1 H, 5-H), 3.89 (d, $^3J_{4,3}$ = 1.8 Hz, 1 H, 4-H), 4.00 (dd, $^3J_{3,4}$ = 2.3, $^3J_{3,2}$ = 10.7 Hz, 1 H, 3-H), 4.37−4.47 (m, β-CH, 4 H, OCH_2Ph), 4.53 (d, ^2J = 10.6 Hz, 1 H, OCH_2Ph), 4.58 (d, ^2J = 10.6 Hz, 1 H, OCH_2Ph), 4.78 (d, ^2J = 11.2 Hz, 1 H, OCH_2Ph), 4.86 (dd, $^3J_{2,1}$ = 4.1, $^3J_{2,3}$ = 10.7 Hz, 1 H, 2-H), 5.31 (d, $^3J_{1,2}$ = 4.1 Hz, 1 H, 1-H), 5.42 (d, $^3J_{\alpha,NH}$ = 9.5 Hz, 1 H, α-CH), 6.62 (d, $^3J_{NH,\alpha}$ = 9.4 Hz, 1 H, NH), 7.17−7.50 (m, 20 H, Ar-H), 8.05 (s, 1 H, NHPh) ppm. ^{13}C NMR (150.8 MHz, $CDCl_3$): δ = 18.6 (γ-CH_3), 53.0 (OCH_3), 62.3 (α-C), 68.1 (C-6), 70.0 (C-5), 72.9 (β-C, C-4), 73.7 (OCH_2Ph), 73.6 (OCH_2Ph), 75.0 (C-3), 75.2 (OCH_2Ph), 84.1 (C-2), 97.3 (C-1), 125.0, 127.2, 127.8, 127.9, 127.9, 128.0, 128.1, 128.2, 128.3, 128.5, 128.6, 130.3 135.9, 137.1, 137.5, 137.7 (C-Ar), 170.0 (CO_2Me) 181.6 (C=S) ppm. MS (MALDI): *m*/*z* = 730 $[M + H]^+$. $C_{39}H_{43}N_3O_9S$ (729.9): calcd. C 64.18, H 5.94, N 5.76; found C 64.11, H 5.80, N 5.55.

***O*-3,4,6-Tri-*O*-benzyl-2-deoxy-2-nitro-α-D-galactopyranose (8) and (5*Z*)-5-Ethylidene-3-phenylhydantoin (9):** A saturated solution of NH_3 in anhydrous CH_3OH (5 mL) was added to a stirred suspension of **6** (100 mg, 0.14 mmol) in anhydrous CH_3OH (10 mL) at room temp. and stirring was continued 2 h. The solvent was evaporated under reduced pressure and the residue was chromatographed on silica gel using petroleum ether/ethyl acetate (4:1) as eluent to give **8** (60 mg, 63%) as a colourless oil and **9** (25 mg, 26%) as a white solid.

Compound 8: TLC (petroleum ether/ethyl acetate, 2:1): R_f = 0.56. $[\alpha]_D$ = −70.0 (*c* = 0.1; $CHCl_3$). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 2.50 (br. s, 1 H, OH), 3.42 (dd, $^3J_{6,5}$ = 5.7, $^2J_{6,6'}$ = 9.4 Hz, 1 H, 6-H), 3.54 (dd, $^3J_{6',5}$ = 5.7, $^2J_{6',6}$ = 9.5 Hz, 1 H, 6′-H), 3.82 (m, 2 H, 5-H, 4-H), 4.35−4.78 (m, 9 H, 3-H, 2-H, 1-H, OCH_2Ph), 7.20−7.40 (m, 15 H, Ar-H) ppm. ^{13}C NMR (62.8 MHz, $CDCl_3$): δ = 65.3 (C-6), 69.8 (C-5, OCH_2Ph), 70.8 (C-4), 73.3 (OCH_2Ph), 73.5 (OCH_2Ph), 74.6 (C-3), 77.9 (C-1), 126.9, 127.6, 127.9, 128.0, 128.2, 128.4, 128.5 137.0, 137.2, 137.5 (C-Ar), 148.8 (C-2) ppm. EI-MS (positive mode): *m*/*z* = 449 $[M^+ - NO]$. $C_{27}H_{29}NO_7$ (479.5): calcd. C 67.63, H 6.10, N 2.92; found C 67.92, H 6.51, N 3.23.

Compound 9: M.p. 228−230 °C. TLC (petroleum ether/ethyl acetate, 2:1): R_f = 0.30. ^{1}H NMR (600 MHz, [D$_6$]DMSO): δ = 1.83 (d, *J* = 7.6 Hz, 3 H, CH_3), 5.78 (q, *J* = 7.6 Hz, 1 H, =CH), 7.37−7.48 (m, 5 H, Ar-H), 10.72 (s, 1 H, N^1-H) ppm. ^{13}C NMR (150.8 MHz, [D$_6$]DMSO): δ = 12.7 (CH_3), 108.9 (=CH), 126.9, 127.8, 128.7, 129.6, 131.8 (C-Ar), 153.2 (C-2), 161.8 (C-4) ppm. MS (MALDI): *m*/*z* = 203 $[M + H]^+$. $C_{11}H_{10}N_2O_2$ (202.2): calcd. C 65.34, H 4.98, N 13.85; found C 64.93, H 5.14, N 13.69.

***O*-3,4,6-Tri-*O*-benzyl-2-deoxy-2-nitro-α-D-galactopyranose (8) and (5*Z*)-5-Ethylidene-3-phenyl-2-thiohydantoin (10):** A saturated solution of NH_3 in anhydrous CH_3OH (5 mL) was added to a stirred suspension of **7** (102 mg, 0.14 mmol) in anhydrous CH_3OH (10 mL) at room temp. and stirring was continued 2 h. The solvent was evaporated under reduced pressure and the residue was chromatographed on silica gel using petroleum ether/ethyl acetate (4:1) as eluent to give **8** (58 mg, 59%) as a colourless oil and of **10** (26.5 mg, 27%) as a white solid.

Compound 10: M.p. 232−234 °C (ref.[4] 238−240 °C). TLC (petroleum ether/ethyl acetate, 2:1): R_f = 0.40. ^{1}H NMR (250 MHz, [D$_6$]DMSO): δ = 1.95 (d, *J* = 7.7 Hz, 3 H, CH_3), 5.93 (q, *J* = 7.7 Hz, 1 H, =CH), 7.31−7.53 (m, 5 H, Ar-H), 12.42 (s, 1 H, N_1-H) ppm. ^{13}C NMR (62.8 MHz, [D$_6$]DMSO): δ = 11.66 (CH_3), 112.29 (=CH), 127.73, 129.22, 132.21 (C-Ar), 161.20 (C-4), 176.56 (C-2) ppm.

***O*-(2-Amino-3,4,6-tri-*O*-benzyl-2-deoxy-α-D-galactopyranosyl)-*N*-(*tert*-butoxycarbonyl)-L-threonine Methyl Ester (11): 4d** (1.00 g, 1.44 mmol) was dissolved in ethanol (15 mL) and transferred to a hydrogenolysis vessel. Platinized Raney-Ni T4 catalyst was freshly prepared as described previously[46] and the material obtained from Raney nickel/aluminium alloy (2 g) was suspended in ethanol (15 mL). A homogeneous suspension of this catalyst (15 mL) was added to the reaction vessel and the suspension shaken under H_2 for 48 h at ambient temp. and pressure. The catalyst was filtered off and the solvent evaporated. The residue was purified by column chromatography (CH_2Cl_2/MeOH, 98:2) to furnish **11** (0.82 g, 86%) as a colourless oil. TLC (CH_2Cl_2/MeOH, 9:1): R_f = 0.30. $[\alpha]_D$ = +30.0 (*c* = 2.0; $CHCl_3$); ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.28 (d, $^3J_{\gamma,\beta}$ = 6.2 Hz, 3 H, γ-CH_3), 1.45 (s, 9 H, C_4H_9), 3.22 (d, $^2J_{6,6'}$ = 10.5 Hz, 1 H, 6-H), 3.40 (d, $^2J_{6',6}$ = 10.5 Hz, 1 H, 6′-H), 3.50−3.64 (m, 2 H, 5-H, 4-H), 3.72 (s, 3 H, OCH_3), 3.95 (m, 3 H, 3-H, NH_2), 4.22 (dq, $^3J_{\beta,\alpha}$ = 3.0, $^3J_{\beta,\gamma}$ = 5.6 Hz, 1 H, β-CH), 4.30 (d, $^3J_{\alpha,NH}$ = 10.3 Hz, 1 H, α-CH), 4.42−4.58 (m, 5 H, OCH_2Ph), 4.72 (d, ^2J = 11.3 Hz, 1 H, OCH_2Ph), 4.83 (m, 2 H, 2-H, 1-H), 5.20 (d, $^3J_{NH,\alpha}$ = 10.0 Hz, 1 H, NH), 7.16−7.33 (m, 15 H, Ar-H) ppm. MS (MALDI): 687 $[M + Na]^+$. $C_{37}H_{48}N_2O_9$ (664.8): calcd. C 66.85, H 7.28, N 4.21; found C 67.00, H 7.50, N 3.95.

***N*-(Methoxycarbonylamino)-*O*-(3,4,6-tri-*O*-benzyl-2-deoxy-2-methoxycarbonylamino-2-nitro-α-D-galactopyranosyl)-L-threonine Methyl Ester (12). − From 11:** Compound **11** (664 mg, 1 mmol)

was dissolved in dry Et_2O (20 mL) and HCl/Et_2O (10 mL) was added and the mixture stirred at room temp. for 15 min (TLC: CH_2Cl_2/MeOH, 10%). Concentration under reduced pressure and then re-evaporation with toluene (3 × 10 mL) gave the hydrochloride salt of the diamino derivative, which was subjected immediately for further reaction. A solution of diamino derivative (664 mg, 1 mmol) and DMAP (cat.) in dry CH_2Cl_2/pyridine (25 mL, 4:1) was cooled to 0 °C, then diphosgene (69 μL) was added by syringe and the mixture warmed up to room temp. After stirring for 30 min, methanol (25 mL) was added and the mixture was stirred further for 5 min. The solvents were then removed in vacuo, the residue was dissolved in Et_2O, then water was added with vigorous stirring. The layers were separated and the aqueous phase was extracted with Et_2O. The combined organic phases were dried ($MgSO_4$), filtered, concentrated in vacuo, and purified by flash chromatography (CH_2Cl_2/MeOH, 98:2) to furnish **12** (0.51 g, 75%) as a yellow foam. TLC (CH_2Cl_2/MeOH, 9:1): R_f = 0.28. $[\alpha]_D$ = +49.2 (c = 0.65; $CHCl_3$). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.27 (d, $^3J_{\gamma,\beta}$ = 6.4 Hz, 3 H, γ-CH_3), 3.50−3.60 (m, 2 H, 6-H, 6′-H), 3.68 and 3.72 (2s, 9 H, 3 OCH_3), 3.90 (dd, $^3J_{5,6}$ = 6.5, $^3J_{5,6'}$ = 6.7 Hz, 1 H, 5-H), 3.98 (m, 1 H, 4-H), 4.18 (m, 1 H, β-CH), 4.33−4.56 (m, 8 H, α-CH, OCH_2Ph, 3-H, 2-H), 4.72 (d, ^2J = 12.1 Hz, 1 H, OCH_2Ph), 4.86 (d, $^3J_{1,2}$ = 3.7 Hz, 1 H, 1-H), 4.94 (d, $^3J_{NH,\alpha}$ = 11.4 Hz, 1 H, NH), 5.30 (d, $^3J_{NH,2}$ = 10.5 Hz, 1 H, NH), 7.26−7.40 (m, 15 H, Ar-H) ppm. MS (MALDI): m/z = 703 $[M + Na]^+$. $C_{36}H_{44}N_2O_{11}$ (680.7): calcd. C 63.52, H 6.51, N 4.12; found C 63.87, H 6.66, N 3.95.

From 13: A solution of **13** (311 mg, 0.50 mmol) in dry CH_2Cl_2/pyridine (12.5 mL, 4:1) was cooled to 0 °C, diphosgene (34.50 μL) was added via syringe, and the mixture was warmed to room temp. After stirring for 30 min, methanol (12.50 mL) was added and the mixture was stirred further for 5 min. The solvents were evaporated in vacuo, the residue was dissolved in diethyl ether, and then water was added with stirring. The layers were separated and the aqueous layer was extracted with diethyl ether. The combined organic layers were dried ($MgSO_4$), filtered, concentrated in vacuo, and then re-evaporated with toluene. The residue was purified by flash chromatography (CH_2Cl_2/MeOH, 95:5) to furnish **12** (0.30 g, 88%) as a yellow foam.

***O*-(3,4,6-Tri-*O*-benzyl-2-deoxy-2-methoxycarbonylamino-α-D-galactopyranosyl)-L-threonine Methyl Ester (13):** A solution of **11** (664 mg, 1.00 mmol) in dry CH_2Cl_2/pyridine (25 mL, 4:1) was cooled to 0 °C, diphosgene (69 μL) was added via syringe, and the mixture warmed to room temp. After stirring for 30 min, methanol (25 mL) was added and the mixture stirred for 5 min. The solvents were removed in vacuo, the residue was dissolved in diethyl ether, and then water was added with stirring. The layers were separated and the aqueous phase was extracted with diethyl ether. The combined organic phases were dried (MgSO4), filtered, concentrated in vacuo. The residue was dissolved in dry diethyl ether (20 mL), HCl/Et_2O (10 mL) was added, and the mixture stirred at room temp. for 2 h. The solvents were evaporated under reduced pressure, followed by re-evaporation with toluene. The residue was dissolved in CH_2Cl_2 followed by addition of saturated aqueous $NaHCO_3$ with vigorous stirring. The layers were separated and the aqueous phase was extracted with CH_2Cl_2. The combined organic phases were dried ($MgSO_4$), filtered, concentrated under reduced pressure, and purified by flash chromatography (CH_2Cl_2/MeOH, 95:5) to furnish **13** (0.51 g, 82%) as a yellow oil. TLC (CH_2Cl_2/MeOH, 9:1): R_f = 0.28. $[\alpha]_D$ = +62.0 (c = 0.3, $CHCl_3$). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.32 (d, $^3J_{\gamma,\beta}$ = 6.4 Hz, 3 H, γ-CH_3), 1.93 (br. s, 2 H, NH_2), 3.38 (m, 1 H, 6-H), 3.55 (m, 3 H, 6′-H, 4-H, 5-H), 3.69 and 3.70 (2s, 6 H, 2 OCH_3), 3.98 (m, 2 H, 3-H, α-CH), 4.06 (dq, $^3J_{\beta,\alpha}$ = 3.2, $^3J_{\beta,\gamma}$ = 6.4 Hz, 1 H, β-CH), 4.30−4.60 (m, 6 H, OCH_2Ph, 2-H), 4.88 (d, $^3J_{1,2}$ = 3.6 Hz, 1 H, 1-H), 4.70 (d, ^2J = 12.1 Hz, 1 H, OCH_2Ph), 4.98 (d, $^3J_{NH,2}$ = 11.5 Hz, 1 H, NH), 7.25−7.34 (m, 15 H, Ar-H) ppm. ^{13}C NMR (150.8 MHz, [D$_6$]DMSO): δ = 18.4 (γ-CH_3), 51.6, 52.4 (2 OCH_3), 59.3 (α-C), 69.3 (C-6), 70.5 (C-5), 72.1 (β-C, C-4), 73.2 (2 OCH_2Ph), 74.7 (C-3), 77.8 (OCH_2Ph, C-2), 100.4 (C-1), 127.7, 127.8, 127.9, 128.0, 128.4, 128.5, 128.7 138.3, 138.4, 138.9 (C-Ar), 157.1 (CO_2Me), 175.0 (HNCOOMe) ppm. MS (MALDI): m/z = 645 $[M + Na]^+$. $C_{34}H_{42}N_2O_9$ (622.7): calcd. C 65.58, H 6.80, N 4.50; found C 65.74, H 6.72, N 4.44.

***N*-(Methoxycarbonylamino)-*O*-(3,4,6-tri-*O*-acetyl-2-deoxy-2-methoxycarbonylamino-α-D-galactopyranosyl)-L-threonine Methyl Ester (14):** Compound **12** (200 mg, 0.29 mmol) was dissolved in methanol/acetic acid (1:1, 8 mL) and Pd/C (0.1 g, 10% Pd) was suspended in the solution. This mixture was stirred for 12 h under H_2 at room temp. After complete disappearance of the starting material (TLC: CH_2Cl_2/MeOH, 9:1), the catalyst was filtered off and all the solvents were evaporated. The residue of *O*-unprotected material was treated with pyridine/acetic anhydride (3:2, 10 mL) and stirred at room temp. for 12 h. All volatiles were evaporated and the product purified by flash chromatography (petroleum ether/ethyl acetate, 1:1) to give **14** (132 mg, 85%) as a colourless oil. TLC (CH_2Cl_2/MeOH, 95:5): R_f = 0.3. $[\alpha]_D$ = +55.9 (c = 0.22; $CHCl_3$); ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.28 (d, $^3J_{\gamma,\beta}$ = 6.1 Hz, 3 H, γ-CH_3), 1.93, 1.98, 2.09 (3s, 9 H, 3 Ac), 3.62, 3.66, 3.69 (3s, 9 H, 3 OCH_3), 4.03 (m, 2 H, 6-H, 6′-H), 4.11−4.21 (m, 3 H, 5-H, 4-H, β-CH), 4.34 (dd, $^3J_{\alpha,\beta}$ = 1.7, $^3J_{\alpha,NH}$ = 9.7 Hz, 1 H, α-CH), 4.88 (dd, $^3J_{3,4}$ = 3.0, $^3J_{3,2}$ = 11.5 Hz, 1 H, 3-H), 5.01 (dd, $^3J_{2,1}$ = 2.8, $^3J_{2,3}$ = 11.5, $^3J_{2,N,H}$ = 9.4 Hz, 1 H, 2-H), 5.06 (d, 1 H, $^3J_{NH,\alpha}$ = 10.1 Hz, NH), 5.32 (d, $^3J_{1,2}$ = 2.7 Hz, 1 H, 1-H), 5.69 (d, 1 H, $^3J_{NH,2}$ = 9.4 Hz, NH) ppm. MS (MALDI): m/z = 559 $[M + Na]^+$. $C_{21}H_{32}N_2O_{14}$ (536.5): calcd. C 47.01, H 6.01, N 5.22; found C 47.03, H 6.17, N 4.91.

***N*-(Phenylaminocarbonyl)-*O*-(3,4,6-tri-*O*-acetyl-2-deoxy-2-methoxycarbonylamino-α-D-galactopyranosyl)-L-threonine Methyl Ester (15):** A mixture of **13** (500 mg, 0.80 mmol) and phenyl isocyanate (119 mg, 1.00 mmol) in dioxane (15 mL) was heated under reflux for 2 h. The solvent was evaporated under reduced pressure and the residue was dissolved in methanol/acetic acid (1:1, 10 mL) and Pd/C (0.10 g, 10% Pd) was suspended in the solution. This mixture was stirred for 12 h under H_2 at room temp. After complete disappearance of the starting material (TLC: CH_2Cl_2/MeOH, 95:5), the catalyst was filtered off and all the solvents were evaporated. The residue was treated with pyridine/acetic anhydride (3:2, 10 mL) and stirred at room temp. for 12 h. All volatiles were evaporated and the product purified by flash chromatography (petroleum ether/ethyl acetate, 1:1) to give **15** (320 mg, 67%) as a yellow foam. TLC (CH_2Cl_2/MeOH, 95:5): R_f = 0.3. $[\alpha]_D$ = +30.8 (c = 0.26; $CHCl_3$). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.33 (d, $^3J_{\gamma,\beta}$ = 6.3 Hz, 3 H, γ-CH_3), 1.95, 1.98, 2.10 (3s, 9 H, 3 Ac), 3.60, 3.66 (2s, 6 H, 2 OCH_3), 4.00 (m, 2 H, 6-H, 6′-H), 4.12−4.29 (m, 3 H, 5-H, 4-H, β-CH), 4.68 (d, $^3J_{\alpha,NH}$ = 8.7 Hz, 1 H, α-CH), 4.90 (d, $^3J_{3,1}$ = 3.4, $^3J_{3,2}$ = 11.3 Hz, 1 H, 3-H), 4.95 (ddd, $^3J_{2,1}$ = 2.9, $^3J_{2,3}$ = 11.4, $^3J_{2,NH}$ = 9.3 Hz, 1 H, 2-H), 5.09 (d, $^3J_{NH,\alpha}$ = 9.6 Hz, 1 H, NH), 5.29 (br. d, $^3J_{1,2}$ = 3.7 Hz, 1 H, 1-H), 6.18 (d, $^3J_{NH,2}$ = 9.3 Hz, 1 H, NH), 7.00 (t, J = 7.3 Hz, 1 H, Ar-H), 7.25 (t, J = 7.7 Hz, 2 H, Ar-H), 7.38 (d, J = 7.9 Hz, 2 H, Ar-H), 7.65 (s, 1 H, NHPh) ppm. MS (MALDI): m/z = 620 $[M + Na]^+$. $C_{26}H_{35}N_3O_{13}$ (597.6): calcd. C 52.26, H 5.90, N 7.03; found C 52.21, H 6.23, N 6.87.

***O*-(2-Amino-3,4,6-tri-*O*-benzyl-2-deoxy-α-D-galactopyranosyl)-*N*-(fluorenyl-9-methoxycarbonyl)-L-serine *tert*-Butyl Ester (16): 4b**

(1.66 g, 2.00 mmol) was dissolved in ethanol (15 mL) and transferred to a hydrogenolysis vessel. Platinized Raney-Ni T4 catalyst was freshly prepared as described previously[7] and the material obtained from Raney nickel/aluminium alloy (2 g) was suspended in ethanol (15 mL). A homogeneous suspension of this catalyst (15 mL) was added to the reaction vessel and the suspension shaken under H_2 for 48 h at ambient temp. and pressure. The catalyst was filtered off and the solvent evaporated. The residue was purified by column chromatography (CH_2Cl_2/MeOH, 95:5) to furnish **16** (1.50 g, 94%) as a colourless oil, which was immediately used in the next step. TLC (petroleum ether/ethyl acetate, 1:1): R_f = 0.30. $[\alpha]_D$ = +12.0 (c = 1.0; $CHCl_3$). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.58 (s, 9 H, C_4H_9), 3.44 (dd, $^3J_{6,5}$ = 3.5, $^2J_{6,6'}$ = 10.5 Hz, 1 H, 6-H), 3.52 (dd, $^3J_{6',5}$ = 2.3, $^2J_{6',6}$ = 10.5 Hz, 1 H, 6′-H), 3.70 (m, 2 H, 4-H, 5-H), 4.06−4.33 (m, 5 H, β-CH_2, 3-H, NH_2), 4.44−5.00 (m, 11 H, Fmoc-CH, Fmoc-CH_2, OCH_2Ph, α-CH, 2-H, 1-H), 6.12 (d, $^3J_{NH,\alpha}$ = 8.5 Hz, 1 H, NH), 7.28−7.88 (m, 23 H, Ar-H) ppm. MS (MALDI): m/z = 837 $[M + Na]^+$.

***O*-(2-Amino-3,4,6-tri-*O*-benzyl-2-deoxy-α-D-galactopyranosyl)-*N*-(*tert*-butoxycarbonyl)-L-serine *tert*-Butyl Ester (17): 4a** (1.45 g, 2.00 mmol) was dissolved in ethanol (15 mL) and transferred to a hydrogenolysis vessel. Platinized Raney-Ni T4 catalyst was freshly prepared as described previously[46] and the material obtained from Raney nickel/aluminium alloy (2 g) was suspended in ethanol (15 mL). A homogeneous suspension of this catalyst (15 mL) was added to the reaction vessel and the suspension shaken under H_2 for 48 h at ambient temp. and pressure. The catalyst was filtered off and the solvent evaporated. The residue was purified by column chromatography (CH_2Cl_2/MeOH, 98:2) to furnish **17** (1.16 g, 84%) as a colourless oil, which was immediately used in the next step. TLC (CH_2Cl_2/MeOH, 9:1): R_f = 0.50. $[\alpha]_D$ = +60.7 (c = 0.3; $CHCl_3$). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.43 (s, 18 H, 2 C_4H_9), 3.26 (dd, $^3J_{6,5}$ = 3.5, $^2J_{6,6'}$ = 10.5 Hz, 1 H, 6-H), 3.42 (dd, $^3J_{6',5}$ = 2.3, $^2J_{6',6}$ = 10.5 Hz, 1 H, 6′-H), 3.56−3.62 (m, 2 H, 4-H, 5-H), 3.85−4.00 (m, 5 H, β-CH_2, 3-H, NH_2), 4.34−4.55 (m, 6 H, OCH_2Ph, α-CH, 2-H), 4.70 (d, ^2J = 11.5 Hz, 1 H, OCH_2Ph), 4.81 (d, ^2J = 11.1 Hz, 1 H, OCH_2Ph), 4.85 (d, $^3J_{1,2}$ = 2.8 Hz, 1 H, 1-H), 5.48 (d, $^3J_{NH,\alpha}$ = 8.5 Hz, 1 H, NH), 7.22−7.40 (m, 15 H, Ar-H) ppm. ^{13}C NMR (150.8 MHz, $CDCl_3$): δ = 28.0 (CMe_3), 28.3 (CMe_3), 51.2 (α-C), 54.6 (β-C), 68.7 (C-6), 69.8 (C-5), 70.1 (1C, OCH_2Ph), 71.8 (OCH_2Ph), 72.4 (C-4), 73.5 (C-OCH_2Ph) 74.5 (C-3), 79.8 (C-2), 80.9 (CMe_3), 82.2 (CMe_3), 101.0 (C-1), 127.5, 127.7, 127.8, 128.0, 128.2, 128.4, 128.5 138.0, 138.6 (C-Ar), 155.5 (ester-CO), 169.4 (Boc-CO) ppm. MS (MALDI): m/z = 715 $[M + Na]^+$. $C_{39}H_{52}N_2O_9$ (692.84): calcd. C 67.61, H 7.56, N 4.04; found C 67.67, H 7.23, N 4.01.

***O*-(2-Amino-3,4,6-tri-*O*-benzyl-2-deoxy-α-D-galactopyranosyl)-*N*-(fluorenyl-9-methoxycarbonyl)-L-serine (18): 16** (1.78 g, 2.22 mmol) was dissolved in a mixture of trifluoroacetic acid and dichloromethane (50 mL, 1:1), the solution was stirred at room temp. for 6 h, then the solvents were evaporated and re-evaporated with toluene several times. The residue was dissolved in CH_2Cl_2 followed by addition of saturated aqueous $NaHCO_3$ with vigorous stirring. The layers were separated and the aqueous phase was extracted with CH_2Cl_2. The combined organic phases were dried ($MgSO_4$), filtered, concentrated under reduced pressure, and purified by column chromatography (CH_2Cl_2/MeOH, 95:5) to furnish **18** (1.62 g, 96%) as a white foam, which was used immediately in the next step. TLC (CH_2Cl_2/MeOH, 9:1): R_f = 0.4. $[\alpha]_D$ = +76.2 (c = 0.32; $CHCl_3$). ^{1}H NMR (250 MHz, [D$_6$]DMSO): δ = 3.38 (dd, $^3J_{6,5}$ = 3.5, $^2J_{6,6'}$ = 10.5 Hz, 1 H, 6-H), 3.54 (m, 2 H, 6′-H, 5-H), 3.70 (m, 1 H, 4-H), 3.74−4.15 (m, 3 H, β-CH_2, 3-H), 4.00 (br. t, J = 7.1 Hz, 2 H, NH_2) 4.18−4.80 (m, 11 H, Fmoc-CH, Fmoc-CH_2, OCH_2Ph, α-CH, 2-H), 5.08 (d, $^3J_{1,2}$ = 2.9 Hz, 1 H, 1-H), 6.98 (br. d, $^3J_{NH,\alpha}$ = 10.7 Hz, 1 H, NH), 7.18−7.90 (m, 24 H, Ar-H, COOH) ppm. MS (MALDI): m/z = 781 $[M + Na]^+$. $C_{45}H_{46}N_2O_9$ (758.8): calcd. C 71.22, H 6.11, N 3.69; found C 71.42, H 5.86, N 3.47.

***N*-(Fluorenyl-9-methoxycarbonyl)-*O*-(3,4,6-tri-*O*-benzyl-2-*tert*-butoxycarbonylamino-2-deoxy-α-D-galactopyranosyl)-L-serine (19):** BocON (0.30 g, 1.17 mmol) was added to a mixture of **18** (1.04 g, 1.40 mmol) and triethylamine (0.80 mL, 5.70 mmol) in water (10 mL) and dioxane (10 mL). The mixture was stirred at room temp. for 3 h, diluted with water (100 mL), and then extracted with diethyl ether (2 × 20 mL) and ethyl acetate (2 × 20 mL). The aqueous phase was acidified with 1 M HCl and extracted with dichloromethane (3 × 20 mL). All the organic extracts were combined, dried ($MgSO_4$), and concentrated. The residue was purified by column chromatography (CH_2Cl_2/MeOH, 95:5) to furnish **19** (0.84 g, 84%) as a white foam. TLC (CH_2Cl_2/MeOH, 9:1): R_f = 0.5. $[\alpha]_D$ = +68.2 (c = 2.0; $CHCl_3$). ^{1}H NMR (250 MHz, [D$_6$]DMSO): δ = 1.38 (s, 9 H, C_4H_9), 3.54−3.71 (m, 4 H, 6-H, 6′-H, 5-H, 4-H), 3.92 (m, 4 H, β-CH_2, 3-H, Fmoc-CH), 4.14 (m, 3 H, Fmoc-CH_2, α-CH), 4.37−4.61 (m, 7 H, OCH_2Ph, 2-H), 4.89 (m, 2 H, 1-H, Boc-NH), 6.00 (br. s, 1 H, Fmoc-NH), 6.80 (br. s, 1 H, COOH), 7.26−7.72 (m, 23 H, Ar-H) ppm. ^{13}C NMR (62.8 MHz, $CDCl_3$): δ = 28.3, 28.4 (CMe_3), 47.3 (Fmoc-CH_2), 52.0 (α-C), 54.5 (β-C), 67.1 (C-6), 68.6 (Fmoc-CH), 70.1 (C-5, OCH_2Ph), 72.5 (C-4), 73.3 (C-3) 73.5 (OCH_2Ph), 74.7 (OCH_2Ph), 78.7 (OCH_2Ph), 79.4 (CMe_3), 81.7 (C-2), 98.9 (C-1), 120.0, 125.9, 127.1, 127.5, 127.62, 127.7, 127.8, 128.1, 128.2, 128.3, 128.4, 137.9, 138.7, 141.2, 144.0 (C-Ar), 156.0 (CO_2H), 158.5 (Fmoc-CO), 170.3 (Boc-CO) ppm. MS (MALDI): m/z = 881 $[M + Na]^+$. $C_{50}H_{54}N_2O_{11}$ (858.97): calcd. C 69.91, H 6.34, N 3.26; found C 69.68, H 6.45, N 3.12.

***N*-(Fluorenyl-9-methoxycarbonyl)-*O*-(3,4,6-tri-*O*-acetyl-2-*tert*-butoxycarbonylamino-2-deoxy-α-D-galactopyranosyl)-L-serine (21): 19** (0.10 g, 0.115 mmol) was dissolved in methanol/acetic acid (1:1, 5 mL) and Pd/C (0.04 g, 10% Pd) was suspended in the solution. This mixture was stirred for 3 h under H_2. After complete disappearance of the starting material (TLC: CH_2Cl_2/MeOH, 8:2), the catalyst was filtered off and the solvents were evaporated. The residue was suspended in dry CH_2Cl_2 (25 mL) and cooled to 0 °C. Et_3N (0.06 mL) and FmocCl (0.035 g, 0.115 mmol) were added dropwise simultaneously. The stirring was continued for 14 h at room temp., then the reaction mixture was diluted with CH_2Cl_2 (25 mL), washed with 0.5 M HCl (3 × 10 mL) and H_2O, dried ($MgSO_4$), filtered, and the solvents evaporated to dryness. The residue consisting of crude **20** was treated with pyridine/acetic anhydride (2:1, 6 mL) and stirred at room temp. for 12 h. The solvents were evaporated and the product purified by column chromatography (CH_2Cl_2/MeOH, 19:1) to furnish **21** (0.043 g, 48%) as a white foam. TLC (CH_2Cl_2/MeOH, 19:1): R_f = 0.5. $[\alpha]_D$ = +6.5 (c = 0.2; $CHCl_3$). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.39, 1.41 (2s, 9 H, C_4H_9), 1.90, 2.01, 2.10 (3s, 9 H, 3 Ac), 3.62 (m, 1 H, 6-H), 3.90 (m, 2 H, 6′-H, 5-H), 4.00−4.50 (m, 7 H, β-CH_2, 4-H, α-CH, Fmoc-CH, Fmoc-CH_2), 4.75 (m, 1 H, 3-H), 4.88 (m, 1 H, 2-H), 5.10 (br. d, $^3J_{NH,\alpha}$ = 8.0 Hz, 1 H, NH), 5.36 (m, 2 H, 1-H, NH), 6.50 (br. s, 1 H, COOH), 7.23−7.72 (m, 8 H, Ar-H) ppm. MS (MALDI): m/z = 737 $[M + Na]^+$.

***O*-(2-Amino-2-deoxy-α-D-galactopyranosyl)-*N*-(*tert*-butoxycarbonyl)-L-serine *tert*-Butyl Ester (22): 17** (0.69 g, 1.00 mmol) was dissolved in methanol/acetic acid (1:1, 20 mL) and Pd/C (0.36 g, 10% Pd) was suspended in the solution. This mixture was stirred for 3 h under H_2. After complete disappearance of the starting material (TLC: CH_2Cl_2/MeOH, 4:1), the catalyst was filtered off, and the

solvents were evaporated. The residue was purified by column chromatography (CH_2Cl_2/MeOH, 9:1) to furnish **22** (0.32 g, 76%) as a white foam, which was used immediately in the next step. TLC (CH_2Cl_2/MeOH, 4:1): R_f = 0.25. $[\alpha]_D$ = +91.7 (*c* = 0.3; $CHCl_3$). ^{1}H NMR (250 MHz, CD_3OD): δ = 1.41, 1.43 (2s, 18 H, 2 C_4H_9), 2.72 (br. s, 3 H, NH_2, 6-OH), 3.06 (m, 3 H, 6-H, 6′-H, 5-H), 3.58−3.88 (m, 6 H, β-CH_2, 3-H, 4-H, 3-OH, 4-OH), 4.06 (br. s, 1 H, α-CH), 4.32 (br. m, 1 H, 2-H), 4.84 (d, $^3J_{1,2}$ = 3.0 Hz, 1 H, 1-H), 5.60 (d, 1 H, $3J_{NH,\alpha}$ = 7.9 Hz, NH) ppm. ^{13}C NMR (62.8 MHz, $CDCl_3$): δ = 28.6, 28.9 (2 C*Me*$_3$), 52.1 (α-C), 56.0 (β-C), 62.50 (C-6), 69.9 (C-5), 71.2 (C-3, C-4), 80.6 (*C*Me$_3$), 83.0 (C-2, *C*Me$_3$), 101.1 (C-1), 156.2 ($CO_2C_4H_9$), 170.4 (Boc-CO) ppm. MS (MALDI): *m*/*z* = 445 [M + Na]$^+$. $C_{18}H_{34}N_2O_9$ (422.5): calcd. C 51.17, H 8.11, N 6.63; found C 51.30, H 8.32, N 6.59.

***N*-(*tert*-Butoxycarbonyl)-*O*-[2-deoxy-2-(fluorenyl-9-methoxycarbonylamino)-α-D-galactopyranosyl]-L-serine *tert*-Butyl Ester (23):** **22** (0.25 g, 0.5 mmol) was suspended in dry CH_2Cl_2 (25 mL) and cooled to 0 °C. Et_3N (0.25 mL) and FmocCl (0.15 g, 0.5 mmol) were added dropwise simultaneously. Stirring was continued for 14 h at room temp., then the reaction mixture was diluted with CH_2Cl_2 (25 mL), washed with 0.5 M HCl (3 × 10 mL) and H_2O, dried ($MgSO_4$), and filtered. The residue was purified by column chromatography (CH_2Cl_2/MeOH, 9:1) to furnish **23** (0.25 g, 77%) as a white foam, which was used immediately in the next step. TLC (CH_2Cl_2/MeOH, 4:1): R_f = 0.35. $[\alpha]_D$ = +68.7 (*c* = 0.3; $CHCl_3$). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.40, 1.42 (2s, 18 H, 2 C_4H_9), 2.52 (br. s, 1 H, 6-OH), 3.42 (m, 1 H, 6-H), 3.87 (m, 6 H, 6′-H, 3-H, 5-H, β-CH_2, 4-H), 4.03−4.18 (m, 5 H, 2-H, α-CH, Fmoc-CH, Fmoc-CH_2), 4.36 (m, 2 H, 3-OH, 4-OH), 4.85 (d, $3J_{1,2}$ = 2.9 Hz, 1 H, 1-H), 5.22 (br. d, $^3J_{NH,\alpha}$ = 8.2 Hz, 1 H, NH), 5.45 (br. d, $^3J_{NH,2}$ = 8.0 Hz, 1 H, NH), 7.24−7.75 (m, 8 H, Ar-H) ppm. ^{13}C NMR (62.8 MHz, $CDCl_3$): δ = 27.9, 28.2 (2 C*Me*$_3$), 47.0 (Fmoc-CH_2), 51.7 (α-C), 54.4 (β-C), 62.6 (C-6), 67.3 (C-5), 68.9 (Fmoc-CH), 69.8 (C-3, C-4), 80.1 (*C*Me$_3$), 82.6 (C-2, *C*Me$_3$), 98.7 (C-1), 119.8, 125.1, 127.0, 127.6, 141.2 (C-Ar), 155.4 ($CO_2C_4H_9$), 157.5 (Fmoc-CO), 169.6 (Boc-CO) ppm. MS (MALDI): *m*/*z* = 667 [M + Na]$^+$. $C_{33}H_{44}N_2O_{11}$ (644.7): calcd. C 61.48, H 6.88, N 4.35; found C 61.35, H 6.47, N 4.06.

***O*-[3,4,6-Tri-*O*-acetyl-2-deoxy-2-(fluorenyl-9-methoxy-carbonyl amino)-α-D-galactopyranosyl]-*N*-(*tert*-butoxycarbonyl)-L-serine *tert*-Butyl Ester (24):** **23** (0.10 g, 0.16 mmol) was treated with pyridine/acetic anhydride (2:1, 6 mL) and stirred at room temp. for 12 h. All volatiles were evaporated and the product purified by column chromatography (CH_2Cl_2/MeOH, 19:1) to furnish **24** (0.12 g, 97%) as a white foam. TLC (CH_2Cl_2/MeOH, 19:1): R_f = 0.45. $[\alpha]_D$ = +62.7 (*c* = 0.3; $CHCl_3$). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.43, 1.45 (2s, 18 H, 2 C_4H_9), 1.92, 2.04, 2.13 (3 s, 9 H, 3 Ac), 3.86 (m, 2 H, 6-H, 6′-H), 4.00−4.50 (m, 9 H, β-CH_2, 5-H, 2-H, 4-H, α-CH, Fmoc-CH, Fmoc-CH_2), 4.86 (d, $^3J_{1,2}$ = 3.6 Hz, 1 H, 1-H), 4.96 (d, $^3J_{NH,\alpha}$ = 8.2 Hz, 1 H, NH), 5.10 (dd, $^3J_{2,1}$ = 3.3, $^3J_{2,3}$ = 11.3 Hz, 1 H, 2-H), 5.38 (br. d, $^3J_{NH,2}$ = 8.0 Hz, 1 H, NH), 7.24−7.76 (m, 8 H, Ar-H) ppm. ^{13}C NMR (62.8 MHz, $CDCl_3$): δ = 20.6 (3 Ac), 27.9, 28.3 (2 C*Me*$_3$), 47.1 (Fmoc-CH), 49.6 (α-C), 54.4 (β-C), 61.7 (C-6), 67.2 (C-5), 68.6 (Fmoc-CH_2), 69.6 (C-3, C-4), 80.2 (*C*Me$_3$), 82.8 (C-2, *C*Me$_3$), 98.9 (C-1), 120.0, 125.0, 125.1, 127.1, 127.7, 141.3, 143.7, 143.9 (C-Ar), 155.2 ($CO_2C_4H_9$), 156.0 (Fmoc-CO), 169.1, 170.2, 170.3, 170.6 (Boc-CO, 3 Ac) ppm. MS (MALDI): *m*/*z* = 793 [M + Na]$^+$. $C_{39}H_{50}N_2O_{14}$ (770.8): calcd. C 60.77, H 6.54, N 3.63; found C 60.35, H 6.79, N 3.64.

1,5-Anhydro-3,4-di-*O*-benzyl-6-*O*-*tert*-butyldiphenylsilyl-2-deoxy-2-nitro-D-*lyxo*-hex-1-enitol (26): Concentrated nitric acid (24 mL, 0.38 mol) was added dropwise to acetic anhydride (240 mL) with constant stirring. The external temperature of −10 °C was used to maintain the internal temperature in the range of 10−20 °C during the addition. Once the addition was complete, the solution was cooled to −50 °C at which point a precipitate was formed. A solution of galactal[23] **25** (30 g, 0.053 mol) in acetic anhydride (120 mL) was added over a period of 10−15 min, and the mixture was stirred at this temperature for 0.5 h. The temperature was then raised to −22 °C, at which point the reaction medium became clear. The reaction mixture was poured into iced water (500 mL), brine (250 mL) was added, and the aqueous layer was extracted with diethyl ether (3 × 300 mL). The combined organic extracts were dried with sodium sulfate and the solvents removed by co-evaporation with toluene. The crude intermediate 2-nitrogalactopyranose was dissolved in dichloromethane (50 mL) and was added slowly to an ice-cold, stirred solution of triethylamine (22 mL, 0.159 mol) in dichloromethane (50 mL). The cooling bath was removed and stirring continued for 20 min. The organic phase was washed with 2 N HCl solution and dried with sodium sulfate. Evaporation of the solvents and column chromatographic purification (toluene/ethyl acetate, 98:2) of the residue furnished **26** as a light-yellow oil (27 g, 84%). TLC (toluene): R_f = 0.46. $[\alpha]_D$ = −7.5 (*c* = 1.2; $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$): δ = 1.05 (s, 9 H, C_4H_9), 3.81 (t, $^3J_{4,3}$ = 4.6, $^3J_{4,5}$ = 4.6 Hz, 1 H, 4-H), 4.14−4.22 (m, 2 H, 6-H, 6′-H), 4.51 (d, ^2J = 12.0 Hz, 1 H, OCH_2Ph), 4.57−4.59 (m, 2 H, 5-H, OCH_2Ph), 4.68 (d, ^2J = 10.9 Hz, 1 H, OCH_2Ph), 4.75 (d, ^2J = 10.9 Hz, 1 H, OCH_2Ph), 4.78 (d, $^3J_{3,4}$ = 4.5 Hz, 1 H, 3-H), 7.14−7.34 (m, 15 H, Ar-H), 7.40−7.41 (m, 2 H, Ar-H), 7.60−7.61 (m, 3 H, Ar-H), 7.77 (s, 1 H, 1-H) ppm. ^{13}C NMR (150.8 MHz, $CDCl_3$): δ = 26.9 (C*Me*$_3$), 61.5 (C-6), 67.4, 71.9 (C-3), 73.1, 74.6 (C-4), 80.1 (C-5), 95.7 (C-2), 127.4−128.6 129.7, 129.8, 131.3, 133.3, 133.5, 135.6 136.9, 138.1 (C-Ar), 154.6 (C-1) ppm. FAB-MS: (positive mode, NBOH/NaI matrix): *m*/*z* = 610 [M + H]$^+$, 632 [M + Na]$^+$.

***N*-(*tert*-Butoxycarbonyl)-*O*-(3,4-di-*O*-benzyl-6-*O*-*tert*-butyldiphenylsilyl-2-deoxy-2-nitro-α-D-galactopyranosyl)-L-serine *tert*-Butyl Ester (27a):** Nitrogalactal **26** (0.120 g, 0.20 mmol) and serine derivative **3a** (0.077 g, 0.30 mmol) were dried under high vacuum and dissolved in dry toluene (2 mL) under argon. Freshly activated molecular sieves (3 Å, 0.2 g) were introduced and the mixture stirred for 1 h, then potassium *tert*-butoxide solution (1 M in THF, 20 μL) was added, and stirring was continued for 10 min. Acetic acid (20 μL) was used to acidify the reaction mixture, the molecular sieves was filtered off and all solvents were evaporated. The residue was purified by column chromatography (toluene/ethyl acetate, 20:1) to furnish **27a** as colourless oil (0.166 g, 97%). TLC (toluene/ethyl acetate, 10:1): R_f = 0.50. $[\alpha]_D$ = +55.2 (*c* = 5.0; $CHCl_3$). ^{1}H NMR (600 MHz, $CDCl_3$): δ = 1.05 (s, 9 H, C_4H_9), 1.43, 1.46 (2s, 18 H, 2 C_4H_9), 3.73−3.84 (m, 5 H, 5-H, 6-H, 6′-H, β-CH, β′-CH), 3.99 (d, $^3J_{4,3}$ = 2.7 Hz, 1 H, 4-H), 4.29−4.30 (m, 1 H, α-CH), 4.41 (dd, $^3J_{3,2}$ = 10.7, $^3J_{3,4}$ = 2.9 Hz, 1 H, 3-H), 4.46 (d, ^2J = 11.0 Hz, 1 H, OCH_2Ph), 4.73−4.83 (m, 3 H, OCH_2Ph), 4.94 (dd, $^3J_{2,1}$ = 4.2, $^3J_{2,3}$ = 10.7 Hz, 1 H, 2-H), 5.21−5.23 (m, $^3J_{2,1}$ = 4.2 Hz, 2 H, 1-H, NH), 7.15−7.43 (m, 16 H, Ar-H), 7.60−7.63 (m, 4 H, Ar-H) ppm. ^{13}C NMR (150.8 MHz, $CDCl_3$): δ = 26.9 (C*Me*$_3$), 27.9 (C*Me*$_3$), 28.3 (C*Me*$_3$), 54.1 (α-C), 61.8 (C-6), 69.3 (β-C), 71.5 (C-5), 73.1, 73.2 (C-4), 75.0, 75.1, 79.9, 82.7 (C-3), 84.1 (C-2), 96.8 (C-1), 127.7−137.9 (C-Ar), 155.20 ($CO_2C_4H_9$), 168.8 (Boc-CO) ppm. FAB-MS: (positive mode, NBOH/NaI matrix): *m*/*z* = 893 [M + Na]$^+$. $C_{48}H_{62}N_2O_{11}Si\cdot(H_2O)_{0.5}$ (880.1): calcd. C 65.51, H 7.21, N 3.18; found C 65.51, H 7.11, N 3.06.

***N*-(*tert*-Butoxycarbonyl)-*O*-(3,4-di-*O*-benzyl-6-*O*-*tert*-butyldiphenylsilyl-2-deoxy-2-nitro-α-D-galactopyranosyl)-L-threonine *tert*-**

Butyl Ester (27c): Nitrogalactal **26** (13 g, 21.3 mmol) and threonine derivative **3c** (7.1 g, 25.6 mmol) were dried under high vacuum and dissolved in dry toluene (250 mL) under argon. Potassium *tert*-butoxide solution (1 M in THF, 2.1 mL) was added and stirring continued for 2 h. Acetic acid (2 mL) was used to acidify the reaction mixture and then all solvents were evaporated. The residue was purified by column chromatography (toluene/ethyl acetate, 20:1) to furnish **27c** as colourless oil (18.3 g, 97%). TLC (toluene/ethyl acetate, 10:1): R_f = 0.57. $[\alpha]_D$ = +53.3 (*c* = 5.0; $CHCl_3$). ^{1}H NMR (600 MHz, $CDCl_3$): δ = 1.04 (s, 9 H, C_4H_9), 1.15 (s, 3 H, γ-CH_3), 1.45, 1.49 (2s, 18 H, 2 C_4H_9), 3.68 (dd, $^3J_{6',5}$ = 5.9, $^2J_{6',6}$ = 10.0 Hz, 1 H, 6′-H), 3.74 (dd, $^3J_{6,5}$ = 7.6, $^2J_{6,6'}$ = 10.3 Hz, 1 H, 6-H), 3.88 (br. t, $^3J_{5,6}$ = 6.8, $^3J_{5,6'}$ = 6.8 Hz, 1 H, 5-H), 4.05−4.06 (m, 2 H, α-CH, 4-H), 4.23−4.24 (br. d, 1 H, β-CH), 4.43 (dd, $^3J_{3,2}$ = 10.6, $^3J_{3,4}$ = 2.9 Hz, 1 H, 3-H), 4.50 (d, ^2J = 11.1 Hz, 1 H, OCH_2Ph), 4.73 (d, ^2J = 11.0 Hz, 1 H, OCH_2Ph), 4.77 (d, ^2J = 11.0 Hz, 1 H, OCH_2Ph), 4.83 (d, ^2J = 11.0 Hz, 2 H, OCH_2Ph), 4.93 (dd, $^3J_{2,1}$ = 4.1, $^3J_{2,3}$ = 10.6 Hz, 1 H, 2-H), 4.96 (d, $^3J_{NH,\alpha}$ = 9.7 Hz, 1 H, NH), 5.32 (d, $^3J_{1,2}$ = 4.4 Hz, 1 H, 1-H), 7.18−7.39 (m, 16 H, Ar-H), 7.60−7.61 (m, 4 H, Ar-H) ppm. ^{13}C NMR (150.8 MHz, $CDCl_3$): δ = 18.9 (γ-CH_3), 26.8 (CMe_3), 27.9 (CMe_3), 28.4 (CMe_3), 58.6 (α-C), 61.9 (C-6), 71.4 (C-5), 73.1, 73.3 (4-C), 75.2, 75.2 (C-3), 75.5, 79.9, 82.7 (β-C), 84.4 (C-2), 96.7 (C-1), 127.6−138.0 (Ar-C), 156.2 ($CO_2C_4H_9$), 169.2 (Boc-CO) ppm. FAB-MS: (positive mode, NBOH/NaI matrix): *m*/*z* = 907 $[M + Na]^+$. $C_{49}H_{64}N_2O_{11}Si\cdot(H_2O)_2$ (921.17): calcd. C 63.90, H 7.44, N 3.04; found C 63.74, H 7.35, N 3.26.

***N*-(*tert*-Butoxycarbonyl)-*O*-(3,4-di-*O*-benzyl-2-deoxy-2-nitro-α-D-galactopyranosyl)-L-serine *tert*-Butyl Ester (28a): 27a** (0.500 g, 0.570 mmol) was dissolved in dry THF (5 mL) and treated with tetrabutylammonium fluoride (1 M in THF, 1.10 mL) and acetic acid (0.031 mL, 0.550 mmol). The reaction was stirred for 2 h at room temp. and then diluted with ethyl acetate and water. The organic layer was separated, dried with sodium sulfate, and concentrated. The residue was purified on silica gel (30 g; toluene/ethyl acetate eluent, 3:1) to give **28a** as colourless foam (0.351 g, 97%). TLC (toluene/ethyl acetate, 2:1): R_f = 0.38. $[\alpha]_D$ = +77.5 (*c* = 1.0; $CHCl_3$). ^{1}H NMR (600 MHz, $CDCl_3$): δ = 1.45, 1.47 (2s, 18 H, 2 C_4H_9), 3.54 (d, $^3J_{6',5}$ = 5.3, $^2J_{6,6'}$ = 11.4 Hz, 1 H, 6′-H), 3.75 (d, $^3J_{6,5}$ = 6.8, $^2J_{6,6'}$ = 11.4 Hz, 1 H, 6-H), 3.87−3.89 (m, 2 H, β-H, 5-H), 3.93−3.95 (m, 2 H, β-H, 4-H), 4.29−4.30 (m, 1 H, α-CH), 4.37 (dd, $^3J_{3,2}$ = 10.6, $^3J_{3,4}$ = 2.9 Hz, 1 H, 3-H), 4.53 (d, ^2J = 11.4 Hz, 1 H, OCH_2Ph), 4.73−4.77 (m, 2 H, OCH_2Ph), 4.88 (d, ^2J = 11.4 Hz, 1 H, OCH_2Ph), 4.99 (dd, $^3J_{2,1}$ = 4.4, $^3J_{2,3}$ = 10.9 Hz, 1 H, 2-H), 5.31 (d, $^3J_{1,2}$ = 4.4 Hz, 1 H, 1-H), 5.56 (d, $^3J_{NH,\alpha}$ = 7.9 Hz, 1 H, NH), 7.25−7.38 (m, 10 H, Ar-H) ppm. ^{13}C NMR (150.8 MHz, $CDCl_3$): δ = 27.9 (CMe_3), 28.3 (CMe_3), 54.4 (α-C), 61.9 (C-6), 70.4 (β-C), 71.6 (C-5), 72.8 (OCH_2Ph), 73.3 (OCH_2Ph), 74.8 (C-4), 75.1 (*C*Me_3), 79.9 (*C*Me_3), 82.7 (C-3), 84.0 (C-2), 97.2 (C-1), 128.2−128.6, 137.1, 137.5 (C-Ar), 154.20 ($CO_2C_4H_9$), 168.8 (Boc-CO) ppm. FAB-MS: (positive mode, NBOH/NaI matrix): *m*/*z* = 655 $[M + Na]^+$, 805 $[M + 2\,Na + I]^+$.

***N*-(*tert*-Butoxycarbonyl)-*O*-(3,4-di-*O*-benzyl-2-deoxy-2-nitro-α-D-galactopyranosyl)-L-threonine *tert*-Butyl Ester (28c): 27c** (15.0 g, 16.9 mmol) was dissolved in dry THF (100 mL) and treated with tetrabutylammonium fluoride (1 M in THF, 51.0 mL) and acetic acid (1.4 mL, 25.4 mmol). The mixture was stirred for 2 h at room temp. and then diluted with ethyl acetate and water. The organic layer was separated, dried with sodium sulfate, and concentrated. The residue was purified on silica gel (600 g; toluene/ethyl acetate eluent, 3:1) to give **28c** as a colourless oil (8.9 g, 97%). TLC (toluene/ethyl acetate, 10:1): R_f = 0.60. $[\alpha]_D$ = +56.3 (*c* = 3.0; $CHCl_3$). ^{1}H NMR (600 MHz, $CDCl_3$): δ = 1.22−1.27 (m, $^3J_{\gamma,\beta}$ = 6.5 Hz, 3 H, γ-CH_3), 1.46, 1.47 (2s, 18 H, 2 C_4H_9), 3.53 (br. s, 1 H, 6′-H), 3.75 (dd, $^3J_{6,5}$ = 6.7, $^2J_{6,6'}$ = 11.3 Hz, 1 H, 6-H), 3.88 (t, $^3J_{5,6}$ = 6.0, $^3J_{5,6'}$ = 6.0 Hz, 1 H, 5-H), 3.95 (d, $^3J_{3,4}$ = 3.1 Hz, 1 H, 4-H), 4.14 (br. d, $^3J_{\alpha,NH}$ = 9.6 Hz, 1 H, α-CH), 4.31 (br. d, $^3J_{\beta,\gamma}$ = 6.5 Hz, 1 H, β-CH), 4.43 (dd, $^3J_{3,2}$ = 10.8, $^3J_{3,4}$ = 2.9 Hz, 1 H, 3-H), 4.51 (d, ^2J = 11.5 Hz, 1 H, OCH_2Ph), 4.73−4.78 (m, 2 H, OCH_2Ph), 4.86 (d, ^2J = 11.4 Hz, 1 H, OCH_2Ph), 5.00 (dd, $^3J_{2,1}$ = 4.1, $^3J_{2,3}$ = 10.8 Hz, 1 H, 2-H), 5.10 (d, $^3J_{NH,\alpha}$ = 9.6 Hz, 1 H, NH), 5.48 (d, $^3J_{1,2}$ = 4.1 Hz, 1 H, 1-H), 7.25−7.36 (m, 10 H, Ar-H) ppm. ^{13}C NMR (150.8 MHz, $CDCl_3$): δ = 18.2 (γ-CH_3), 28.0 (CMe_3), 28.3 (CMe_3), 58.0 (α-C), 61.8 (C-6), 71.5 (C-5), 72.7 (OCH_2Ph), 73.3 (OCH_2Ph), 74.8 (C-4), 75.2 (β-C), 75.3 (*C*Me_3), 80.0 (*C*Me_3), 82.8 (C-3), 84.3 (C-2), 95.6 (C-1), 128.1−137.5 (C-Ar), 156.1 ($CO_2C_4H_9$), 170.5 (Boc-CO) ppm. FAB-MS: (positive mode, NBOH/NaI matrix): *m*/*z* = 669 $[M + Na]^+$, 819 $[M + 2Na + I]^+$. $C_{33}H_{46}N_2O_{11}\cdot(H_2O)_{0.5}$ (664.7): calcd. C 60.44, H 7.22, N 4.27; found C 60.40, H 7.04, N 4.45.

***N*-(*tert*-Butoxycarbonyl)-*O*-{*O*-[methyl (5-acetamido-4,7,8,9-tetra-*O*-acetyl-3,5-dideoxy-D-*glycero*-α-D-*galacto*-non-2-ulopyranosyl)onate]-(2→6)-(3,4-di-*O*-benzyl-2-deoxy-2-nitro-α-D-galactopyranosyl)-L-serine *tert*-Butyl Ester (30a):** Sialyl donor[47,48] **29** (0.773 g, 1.26 mmol) and *O*-glycosylserine **28a** (0.400 g, 0.63 mmol) were carefully dried under high vacuum and dissolved in dry propionitrile (15 mL). The solution was cooled to −60 °C under nitrogen and the reaction activated by addition of TMSOTf (23 μL, 0.13 mmol). The reaction was warmed to −40 °C over a period of 1 h and then quenched by addition of solid sodium bicarbonate. The reaction mixture was filtered, concentrated, and the residue purified by flash chromatography on silica gel (100 g; toluene/ethanol eluent, 10:1) to give **30a** as a colourless foam (0.332 g, 47%). TLC (toluene/ethyl acetate, 5:1): R_f = 0.39. $[\alpha]_D$ = +33.0 (*c* = 1.0; $CHCl_3$). ^{1}H NMR (600 MHz, $CDCl_3$): δ = 1.47, 1.49 (2s, 18 H, 2 C_4H_9), 1.88−2.14 (m, 16 H, 4 Ac, NHAc, 3b′-H), 2.60 (dd, $^2J_{3,3'}$ = 13.0, $^3J_{3,4}$ = 4.8 Hz, 1 H, 3b-H), 3.49 (dd, $^3J_{6',5}$ = 6.2, $^2J_{6',6}$ = 9.5 Hz, 1 H, 6a′-H), 3.67 (s, 3 H, OCH_3), 3.79−3.83 (m, 2 H, 6a-H, β′-CH), 3.93−3.97 (m, 3 H, 4a-H, 5a-H, β-CH), 4.05−4.15 (m, 3 H, 5b-H, 6b-H, 9b′-H), 4.28−4.30 (m, 2 H, α-H, 9b-H), 4.42 (dd, $^3J_{3,2}$ = 11.0, $^3J_{3,4}$ = 2.6 Hz, 1 H, 3a-H), 4.59 (d, ^2J = 11.0 Hz, 1 H, OCH_2Ph), 4.73 (s, 2 H, OCH_2Ph), 4.83 (d, ^2J = 11.0 Hz, 1 H, OCH_2Ph), 4.88−4.90 (m, 1 H, 4b-H), 4.96 (dd, $^3J_{2,1}$ = 4.2, $^3J_{2,3}$ = 10.7 Hz, 1 H, 2a-H), 5.13−5.14 (m, $^3J_{NH,\alpha}$ = 9.8 Hz, 1 H, Ser-NH), 5.30−5.33 (m, $^3J_{1,2}$ = 4.2 Hz, 3 H, 1a-H, 7b-H, Neu5Ac-NH), 5.39−5.40 (m, 1 H, 8b-H), 7.25−7.34 (m, 10 H, Ar-H) ppm. ^{13}C NMR (150.8 MHz, $CDCl_3$): δ = 20.7−23.2 (5 Ac), 27.9 (CMe_3), 28.4 (CMe_3), 37.7 (C-3b), 49.4 (C-5b), 58.2 (OCH_3), 54.2 (α-C), 62.3 (C-9b), 63.1 (C-6a), 67.3 (C-7b), 68.5 (C-8b), 68.6 (C-4b), 68.7, 69.0 (β-C), 69.8, 72.5 (C-5a), 72.7, 72.9 (C-4a), 74.7 (OCH_2Ph), 74.9 (OCH_2Ph), 82.6 (C-3a), 83.7 (2 *C*Me_3), 83.9 (C-2a), 96.6 (C-1a), 98.6 (C-2b), 127.7−128.5, 137.3, 138.1, (C-Ar), 155.4, 167.8, 168.8, 170.2, 170.6, 170.9 (8 CO) ppm. FAB-MS: (positive mode, NBOH/NaI matrix): *m*/*z* = 1128 $[M + Na]^+$. $C_{52}H_{71}N_3O_{23}\cdot(H_2O)_2$ (1142.2): calcd. C 54.68, H 6.61, N 3.68; found C 54.80, H 6.65, N 3.53.

***N*-(*tert*-Butoxycarbonyl)-*O*-{*O*-[methyl (5-acetamido-4,7,8,9-tetra-*O*-acetyl-3,5-dideoxy-D-*glycero*-α-D-*galacto*-non-2-ulopyranosyl)onate]-(2→6)-(3,4-di-*O*-benzyl-2-deoxy-2-nitro-α-D-galactopyranosyl)-L-threonine *tert*-Butyl Ester (30c):** Sialyl donor[47,48] **29** (7.565 g, 12.37 mmol) and *O*-glycosylserine **28c** (4.000 g, 6.19 mmol) were dried carefully under high vacuum and dissolved in dry propionitrile (60 mL) together with freshly activated 3-Å molecular sieves (7 g). The solution was cooled to −60 °C under nitro-

gen and the reaction activated by the addition of TMSOTf (0.224 mL, 1.24 mmol). The reaction was stirred for 1.5 h at this temperature and then quenched by the addition of triethylamine. The reaction mixture was filtered, concentrated, and the residue passed through a short column of silica gel (toluene/ethanol, 5:1). This procedure gave a crude product that was separated on BioBeads SX-3 (toluene) to give a disaccharide-containing fraction, which was purified finally on silica gel (100 g; toluene/ethanol eluent, 10:1) to give **30c** as a colourless foam (4.5 g, 65%). TLC (toluene/ethyl acetate, 5:1): R_f = 0.50. $[\alpha]_D$ = +34.8 (*c* = 1.0; $CHCl_3$). ^{1}H NMR (600 MHz, $CDCl_3$): δ = 1.32−1.33 (m, 3 H, γ-CH_3), 1.47, 1.48 (2s, 18 H, 2 C_4H_9), 1.89−2.14 (m, 16 H, 4 Ac, NHAc, 3b′-H), 2.56 (dd, $^2J_{3,3'}$ = 12.9, $^3J_{3,4}$ = 4.6 Hz, 1 H, 3b-H), 3.44 (dd, $^3J_{6',5}$ = 5.3, $^2J_{6',6}$ = 9.1 Hz, 1 H, 6a′-H), 3.68 (s, 3 H, OCH_3), 3.94−4.00 (m, 3 H, 4a-H, 5a-H, 6a-H), 4.03−4.10 (m, 4 H, 5b-H, 6b-H, 9b′-H, α-CH), 4.26 (dd, $^3J_{9,8}$ = 2.6, $^2J_{9,9'}$ = 12.4 Hz, 1 H, 9b-H), 4.34 (br. d, $^3J_{\beta,\gamma}$ = 6.7 Hz, 1 H, β-CH), 4.43 (dd, $^3J_{3,2}$ = 10.8, $^3J_{3,4}$ = 2.8 Hz, 1 H, 3a-H), 4.58 (d, ^2J = 11.1 Hz, 1 H, OCH_2Ph), 4.72 (s, 2 H, OCH_2Ph), 4.83 (d, ^2J = 11.1 Hz, 1 H, OCH_2Ph), 4.87−4.91 (m, 1 H, 4b-H), 4.95 (dd, $^3J_{2,1}$ = 4.2, $^3J_{2,3}$ = 10.8 Hz, 1 H, 2a-H), 4.99 (d, $^3J_{NH,\alpha}$ = 9.8 Hz, Thr-NH), 5.13 (br. d, $^3J_{NH,5}$ = 9.5 Hz, 1 H, Neu5Ac-NH), 5.31 (br. d, $^3J_{7,8}$ = 8.3 Hz, 1 H, 7b-H), 5.36−5.39 (m, 1 H, 8b-H), 5.39 (d, $^3J_{1,2}$ = 4.3 Hz, 1 H, 1a-H), 7.26−7.35 (m, 10 H, Ar-H) ppm. ^{13}C NMR (150.8 MHz, $CDCl_3$): δ = 18.8 (γ-CH_3), 20.7, 20.8, 21.1, 23.2 (5 Ac), 28.0 (CMe_3), 28.4 (CMe_3) 37.6 (C-3b), 49.4 (C-5b), 52.8 (OCH_3), 58.7 (α-C), 62.3 (C-9b), 63.1 (C-6a), 67.3 (C-7b), 68.5 (C8b), 68.9 (C-4b), 69.9 (C-5a), 72.6 (C-6b), 72.9 (C-4a), 73.1 (2 OCH_2Ph), 74.8 (2 CMe_3), 75.1 (C-3a), 76.1 (β-C), 82.6, 84.1 (C-2a) 84.2, 96.8 (C-1a), 98.6 (C-2b), 127.7−128.5, 137.3, 138.1 (C-Ar), 155.6, 167.9, 169.8, 170.1, 170.2, 170.9 (8 CO) ppm. MS (FAB): *m*/*z* = 1142 [M + Na]$^+$. $C_{53}H_{73}N_3O_{23}\cdot(H_2O)$ (1138.2) calcd.: C 55.93, H 6.64, N 3.69; found C 55.76, H 6.32, N 3.45.

***N*-(*tert*-Butoxycarbonyl)-*O*-{*O*-[methyl (5-acetamido-4,7,8,9-tetra-*O*-acetyl-3,5-dideoxy-D-*glycero*-α-D-*galacto*-non-2-ulopyranosyl)onate]-(2→6)-(2-acetamido-3,4-di-*O*-benzyl-2-deoxy-α-D-galacto pyranosyl)-L-serine *tert*-Butyl Ester (31a):** Nitroglycoside **30a** (0.250 g, 0.23 mmol) was dissolved in ethanol (5 mL) and then transferred to a hydrogenation vessel. Platinized Raney-Ni T4 catalyst was freshly prepared as described previously[46] and the material obtained from Raney nickel/aluminium alloy (2 g) was suspended in ethanol (15 mL). A homogeneous suspension of this catalyst (10 mL) was added to the reaction vessel and the suspension shaken under hydrogen for 48 h at ambient temp. and pressure. The catalyst was filtered off and the solvent evaporated. The residue was dissolved in pyridine/acetic anhydride (2:1, 10 mL) and stirred for 3 h. Removal of the volatiles and column chromatographic purification (toluene/ethanol, 10:1) gave **31a** as a colourless foam (0.189 g, 75%). TLC (chloroform/methanol, 9:1): R_f = 0.78. $[\alpha]_D$ = +34.8 (*c* = 1.0; $CHCl_3$). ^{1}H NMR (600 MHz, $CDCl_3$): δ = 1.44, 1.47 (2s, 18 H, 2 C_4H_9), 1.88−2.14 (m, 19 H, 4 Ac, NHAc, 3b′-H), 2.61 (dd, $^2J_{3,3'}$ = 12.9, $^3J_{3,4}$ = 4.6 Hz, 1 H, 3b-H), 3.48 (dd, $^3J_{6',5}$ = 7.3, $^2J_{6',6}$ = 7.3 Hz, 1 H, 6a′-H), 3.58−3.77 (m, 5 H, OCH_3, 3a-H, β-CH), 3.80 (t, $^3J_{5,6}$ = 6.6, $^3J_{5,6'}$ = 6.6 Hz, 1 H, 5a-H), 3.88−3.98 (m, 2 H, β-CH, 6a-H), 3.96 (br. s, 1 H, 4a-H), 4.07−4.12 (m, 3 H, 5b-H, 6b-H, 9b′-H), 4.30−4.31 (m, 2 H, α-H, 9b-H), 4.47 (d, ^2J =12.1 Hz, 1 H, OCH_2Ph), 4.61 (d, ^2J = 11.3 Hz, 1 H, OCH_2Ph), 4.70−4.72 (m, 2 H, 2a-H, OCH_2Ph), 4.79 (d, $^3J_{1,2}$ = 3.2 Hz, 1 H, 1a-H), 4.85−4.87 (m, 1 H, 4b-H), 4.95 (d, ^2J = 11.3 Hz, 1 H, OCH_2Ph), 5.24 (d, $^3J_{NH,5}$ = 8.9 Hz, 1 H, Neu5Ac-NH), 5.29 (br. d, 1 H, Ser-NH), 5.33 (br. d, $^3J_{7,6}$ = 7.8 Hz, 1 H, 7b-H), 5.39−5.43 (m, 2 H, GalNHAc-NH, 8b-H), 7.27−7.37 (m, 10 H, Ar-H) ppm. ^{13}C NMR (150.8 MHz, $CDCl_3$): δ = 20.7, 20.8, 21.1, 23.2, 23.4 (6 Ac), 28.0 (CMe_3), 28.3 (CMe_3) 37.8 (C-3b), 48.7 (C-2a), 49.4 (C-5b), 52.8 (OCH_3), 54.4 (α-C), 62.3 (C-9b), 63.1 (C-6a), 67.4 (C-7b), 68.5 (β-C), 68.8 (C-8b), 69.1 (C-4b), 69.8 (C-5a), 71.5, 72.4 (C-4a), 72.7 (C-6b), 74.1 (OCH_2Ph), 76.8 (OCH_2Ph), 77.1 (3a-C), 80.3 (CMe_3), 82.3 (CMe_3), 98.7 (C-2b), 99.0 (C-1a), 127.3−128.4, 138.1, 138.7 (C-Ar), 155.3, 167.8, 169.8, 169.9, 170.1, 170.2, 170.6, 170.9 (9 CO) ppm. FAB-MS: (positive mode, NBOH/NaI matrix): *m*/*z* = 1140 [M + Na]$^+$.

***N*-(*tert*-Butoxycarbonyl)-*O*-{*O*-[methyl (5-acetamido-4,7,8,9-tetra-*O*-acetyl-3,5-dideoxy-D-*glycero*-α-D-*galacto*-non-2-ulopyranosyl)onate]-(2→6)-(2-acetamido-3,4-di-*O*-benzyl-2-deoxy-α-D-galacto pyranosyl)-L-threonine *tert*-Butyl Ester (31c):** Nitroglycoside **30c** (2.000 g, 1.79 mmol) was dissolved in ethanol (40 mL) and then transferred to a hydrogenation vessel. Platinized Raney-Ni T4 catalyst was freshly prepared as described previously[46] and the material obtained from Raney nickel/aluminium alloy (6 g) was suspended in ethanol (45 mL). A homogeneous suspension of this catalyst (40 mL) was added to the reaction vessel and the suspension shaken under hydrogen for 12 h at ambient temp. and pressure. The catalyst was filtered off and the solvent evaporated. The residue was dissolved in pyridine/acetic anhydride (2:1, 45 mL) and stirred for 3 h. Removal of the volatiles and column chromatographic purification (toluene/ethanol, 10:1) gave **31c** as a colourless foam (1.710 g, 85%). TLC (chloroform/methanol, 9:1): R_f = 0.59. $[\alpha]_D$ = +38.6 (*c* = 2.0; $CHCl_3$). ^{1}H NMR (600 MHz, $CDCl_3$): δ = 1.30−1.32 (m, 3 H, γ-CH_3), 1.47, 1.49 (2s, 18 H, 2 C_4H_9), 1.88−2.14 (m, 19 H, 4 Ac, 2 NHAc, 3b′-H), 2.56 (dd, $^2J_{3,3'}$ = 12.9, $^3J_{3,4}$ = 4.8 Hz, 1 H, 3b-H), 3.45−4.42 (m, 1 H, 6a′-H), 3.57 (dd, $^3J_{3,2}$ = 10.9, $^3J_{3,4}$ = 2.4 Hz, 1 H, 3a-H), 3.65 (m, 3 H, OCH_3), 3.88−3.94 (m, 3 H, 4a-H, 5a-H, 6a-H), 4.05−4.13 (m, 5 H, 5b-H, 6b-H, 9b′-H, α-CH, β-CH), 4.27 (dd, $^3J_{9,8}$ = 2.3, $^2J_{9,9'}$ = 12.4 Hz, 1 H, 9b-H), 4.50 (d, ^2J =12.1 Hz, 1 H, OCH_2Ph), 4.63 (d, ^2J = 11.3 Hz, 1 H, OCH_2Ph), 4.71−4.78 (m, 3 H, 1a-H, 2a-H, OCH_2Ph), 4.85−4.87 (m, 1 H, 4b-H), 4.96 (d, ^2J = 11.3 Hz, 1 H, OCH_2Ph), 5.03 (d, $^3J_{NH,\alpha}$ = 9.0 Hz, 1 H, Thr-NH), 5.18 (d, $^3J_{NH,5}$ = 9.3 Hz, 1 H, Neu5Ac-NH), 5.31−5.36 (m, 2 H, 7b-H, 8b-H), 5.64 (d, $^3J_{NH,2}$ = 9.8 Hz, 1 H, GalNHAc-NH), 7.24−7.38 (m, 10 H, Ar-H) ppm. ^{13}C NMR (150.8 MHz, $CDCl_3$): δ = 18.6 (γ-CH_3), 20.7, 20.8, 20.8, 21.0, 21.4, 23.2, 23.5 (6 Ac), 28.1 (CMe_3), 28.3 (CMe_3) 37.6 (C-3b), 48.6 (C-2a), 49.4 (C-5b), 52.7 (OCH_3), 58.7 (α-C), 62.2 (C-9b), 63.4 (C-6a), 67.4 (C-7b), 68.6 (C-8b), 69.0 (C-4b), 70.1 (C-5a), 71.5 (OCH_2Ph), 72.6 (C-6b), 72.7 (C-4a), 74.1 (OCH_2Ph), 76.7 (β-C), 77.4 (C-3a), 80.1 (CMe_3), 82.6 (CMe_3), 98.6 (C-2b), 100.6 (C-1a), 125.3−129.0 138.2, 138.7 (C-Ar), 155.7, 167.9, 169.9, 170.0, 170.2, 170.5, 170.7, 170.9 (9 CO) ppm. FAB-MS: (positive mode, NBOH/NaI matrix): *m*/*z* = 1154 [M + Na]$^+$.

***N*-(*tert*-Butoxycarbonyl)-*O*-{*O*-[methyl (5-acetamido-4,7,8,9-tetra-*O*-acetyl-3,5-dideoxy-D-*glycero*-α-D-*galacto*-non-2-ulopyranosyl)onate]-(2→6)-(2-acetamido-3,4-di-*O*-acetyl-2-deoxy-α-D-galactopyranosyl)-L-threonine *tert*-Butyl Ester (32):** **31c** (1.60 g, 1.41 mmol) was dissolved in methanol/acetic acid (21 mL, 20:1), 10% Pd/C (0.4 g) was added, and the mixture stirred under hydrogen for 12 h. The catalyst was filtered off and the volatiles removed. The residue was dissolved in pyridine/acetic anhydride (15 mL, 2:1) and stirred for 12 h at room temp. The reaction mixture was concentrated and the crude residue purified by flash chromatography (toluene/ethanol, 8:1) to afford **32** as colourless foam (1.46 g, quantitative). TLC (chloroform/methanol, 9:1): R_f = 0.58. $[\alpha]_D$ = +33.8 (*c* = 2.0; $CHCl_3$). ^{1}H NMR (600 MHz, $CDCl_3$): δ = 1.36 (d, $^3J_{\gamma,\beta}$ = 6.1 Hz, 3 H, γ-CH_3), 1.46, 1.49 (2s, 18 H, 2 C_4H_9), 1.87−2.16 (m, 25 H, 2 NHAc, 6 Ac, 3b′-H), 2.51 (dd, $^2J_{3,3'}$ = 12.9, $^3J_{3,4}$ = 4.7 Hz, 1 H, 3b-H), 3.26 (dd, $^2J_{6',5}$ = 5.3, $^3J_{6',6}$ = 10.2 Hz,

1 H, 6′a-H), 3.78 (s, 3 H, OCH_3), 3.85 (dd, $^3J_{6,5}$ = 3.3, $^3J_{6,6'}$ = 10.2 Hz, 1 H, 6a-H), 4.01−4.08 (m, 3 H, 5b-H, 6b-H, 9b′-H), 4.14−4.19 (m, 3 H, α-H, β-H, 5a-H), 4.26 (dd, $^3J_{9,8}$ = 2.3, $^2J_{9,9'}$ = 12.4 Hz, 1 H, 9b-H), 4.59 (ddd, $^3J_{2,1}$ = 3.7, $^3J_{2,3}$ = 10.6, $^3J_{2,NH}$ = 10.3 Hz, 1 H, 2a-H), 4.83−4.87 (m, 2 H, 1a-H, 4b-H), 5.04 (dd, $^3J_{3,2}$ = 11.3, $^3J_{3,4}$ = 3.0 Hz, 1 H, 3a-H), 5.11 (d, $^3J_{NH,5}$ = 9.6 Hz, 1 H, Neu5Ac-NH), 5.22 (d, $^3J_{NH,\alpha}$ = 9.4 Hz, 1 H, Thr-NH), 5.31−5.36 (m, 3 H, 4a-H, 7b-H, 8b-H), 5.93 (d, $^3J_{NH,2}$ = 9.6 Hz, 1 H, GalNHAc-NH) ppm. ^{13}C NMR (150.8 MHz, $CDCl_3$): δ = 18.5 (γ-CH_3), 20.3, 20.8, 21.0, 23.2, 23.3 (8 Ac), 28.1 (C*Me*$_3$), 28.3 (C*Me*$_3$), 37.7 (C-3b), 47.2 (C-2a), 49.4 (C-5b), 52.9 (OCH_3), 58.6 (α-C), 62.3 (C-9b), 63.5 (C-6a), 67.2 (C-7b), 67.7 (C-4a), 68.1 (C-8b), 68.4 (C-5a), 68.9 (C-4b), 69.2 (C-3a), 72.6 (C-6b), 77.3 (*C*Me$_3$), 80.2 (*C*Me$_3$), 82.8 (β-C), 98.5 (C-2b), 100.1 (C-1a), 155.2, 167.9−170.9 (11 CO) ppm. FAB-MS: (positive mode, NBOH/NaI matrix): *m*/*z* = 1058 [M + Na]$^+$. $C_{45}H_{69}N_3O_{24}\cdot H_2O$ (1054.1): calcd. C 51.28, H 6.79, N 3.99; found C 51.33, H 6.60, N 3.81.

***N*-(Fluoren-9-ylmethoxycarbonyl)-*O*-{*O*-[methyl (5-acetamido-4,7,8,9-tetra-*O*-acetyl-3,5-dideoxy-D-*glycero*-α-D-*galacto*-non-2-ulopyranosyl)onate]-(2→6)-(2-acetamido-3,4-di-*O*-acetyl-2-deoxy-α-D-galactopyranosyl)-L-threonine (33): 32** (0.400 g, 0.386 mmol) was dissolved in a mixture of trifluoroacetic acid and dichloromethane (10 mL, 1:1), and the solution stirred at room temp. for 12 h. The solvents were evaporated, the residue was dissolved together with FmocONSu (0.260 g, 0.772 mmol) and sodium bicarbonate (0.649 g. 7.720 mmol) in acetonitrile/water (20 mL, 1:1), and the mixture stirred for 12 h. The solution was acidified with 2 N HCl solution (150 mL) and the aqueous layer extracted with dichloromethane (3 × 100 mL). The combined organic extracts were dried with sodium sulfate and the volatiles evaporated. Column chromatographic purification (toluene/ethanol/acetic acid, 14:1:1) of the residue afforded **33** as colourless foam (0.415 g, 98%). TLC (chloroform/methanol, 4:1): R_f = 0.44. $[\alpha]_D$ = +35.5 (*c* = 2.5; $CHCl_3$). ^{1}H NMR (600 MHz, $CDCl_3$): δ = 1.31 (d, $^3J_{\gamma,\beta}$ = 5.3 Hz, 3 H, γ-CH_3), 1.87−2.16 (m, 25 H, 2 NHAc, 6 Ac, 3b′-H), 2.53 (dd, $^2J_{3,3'}$ = 12.6, $^3J_{3,4}$ = 4.3 Hz, 1 H, 3b-H), 3.30−3.32 (m, 1 H, 6′a-H), 3.77 (s, 3 H, OCH_3), 3.83 (br. t, 1 H, 6a-H), 4.00−4.10 (m, 4 H, 5a-H, 5b-H, 6b-H, 9b′-H), 4.13−4.53 (m, 7 H, 2a-H, β-H, 9b-H, α-H, Fmoc-CH_2, Fmoc-CH), 4.86 (br. s, 1 H, 4b-H), 5.02 (br. s, 1 H, 1a-H), 5.09 (d, $^3J_{3,2}$ = 11.4 Hz, 1 H, 3a-H), 5.17−5.24 (m, 1 H, NH), 5.30−5.32 (m, 1 H, 7b-H), 5.38 (br. s, 2 H, 4a-H, 8b-H), 5.88 (br. s, 1 H, NH), 6.16 (br. s, 1 H, NH), 7.29−7.40 (m, 4 H, Ar-H), 7.61 (d, *J* = 7.1 Hz, 2 H, Ar-H), 7.75 (d, *J* = 7.1 Hz, 2 H, Ar-H) ppm. ^{13}C NMR (150.8 MHz, $CDCl_3$): δ = 18.1 (γ-CH_3), 20.7, 20.8, 21.0, 23.2 (8 Ac), 37.7 (C-3b), 47.3 (C-2a), 49.4 (C-5b), 52.9 (OCH_3), 59.0 (α-C), 62.4 (C-9b), 64.0 (C-6a), 67.1 (C-7b), 67.6 (C-4a), 68.2 (C-8b), 68.6 (C-5a), 68.8 (C-3a), 69.2 (C-4b), 72.6 (C-6b), 77.6 (β-C), 98.7 (C-1a), 99.8 (C-2b), 120.0−127.8, 141.3 (C-Ar), 167.8−170.9 (11 CO). ^{1}H NMR (600 MHz, [D$_6$]DMSO): δ = 1.16 (d, $^3J_{\gamma,\beta}$ = 6.4 Hz, 3 H, γ-CH_3), 1.84−2.09 (m, 25 H, 6 Ac, 2 NHAc, 3b′-H), 2.47 (dd, $^2J_{3,3'}$ = 12.4, $^3J_{3,4}$ = 4.6 Hz, 1 H, 3b-H), 3.19 (dd, $^3J_{6,5}$ = 5.3, $^2J_{6,6'}$ = 9.9 Hz, 1 H, 6′a-H), 3.72−3.76 (m, 5 H, α-H, OCH_3, 6a-H), 3.92 (dd, $^3J_{5,4}$ = 10.3, $^3J_{5,6}$ = 10.0 Hz, 1 H, 5b-H), 3.96−4.00 (m, 2 H, 9b′-H, 6b-H), 4.08−4.09 (m, 1 H, 5a-H), 4.16−4.18 (m, 2 H, 9b-H, 2a-H), 4.26−4.28 (m, 2 H, Fmoc-CH, β-CH), 4.40 (dd, ^2J = 10.7, ^3J = 6.8 Hz, 1 H, Fmoc-CH_2), 4.46 (dd, ^2J = 10.8, ^3J = 6.8 Hz, 1 H, Fmoc-CH_2), 4.68 (ddd, $^3J_{4,3}$ = 4.7, $^3J_{4,3'}$ = 11.0, $^3J_{4,5}$ = 10.9 Hz, aH, 4b-H), 4.79 (d, $^3J_{1,2}$ = 3.8 Hz, 1 H, 1a-H), 4.98 (dd, $^3J_{3,2}$ = 11.6, $^3J_{3,4}$ = 3.3 Hz, 1 H, 3a-H), 5.15 (dd, $^3J_{7,6}$ = 8.7, $^3J_{7,8}$ = 1.7 Hz, 1 H, 7b-H), 5.24 (br. s, 2 H, 8b-H, 4a-H), 7.32 (t, *J* = 7.4 Hz, 2 H, Ar-H), 7.41 (t, *J* = 7.4 Hz, 2 H, Ar-H), 7.72 (d, *J* = 6.6 Hz, 2 H, Ar-H), 7.89 (d, *J* = 7.4 Hz, 2 H, Ar-H), 11.80−13.00 (br. m, 1 H, COOH) ppm. FAB-MS: (positive mode, NBOH/NaI matrix): *m*/*z* = 1124 [M + Na]$^+$, 1146 [M + 2 Na − H]$^+$. $C_{51}H_{63}N_3O_{24}\cdot(H_2O)_{2.5}$ (1147.1) calcd.: C 53.40, H 5.98, N 3.66; found C 53.45, H 5.68, N 3.71.

***N*-Acetyl-L-glycyl-L-seryl-*O*-{*O*-[methyl (5-acetamido-4,7,8,9-tetra-*O*-acetyl-3,5-dideoxy-D-*glycero*-α-D-*galacto*-non-2-ulopyranosyl)-onate]-(2→6)-(2-acetamido-3,4-di-*O*-acetyl-2-deoxy-α-D-galactopyranosyl)-L-threonyl-L-alanyl-L-prolyl-L-alanyl-L-histidyl-L-glycinamide (34):** Protected glycopeptide **34** (25 mg, 1.57 mmol) was assembled on a semiautomatic peptide synthesiser (NovaSyn Gem, Novabiochem) using a prefunctional resin (Tentagel S Ram Gly Fmoc, 310 mg, loading: 0.22 mmol/g, Rapp Polymere) as the solid phase. *N*,*N*-Dimethylformamide for peptide synthesis (Riedel-de Haën) was used as the solvent in all coupling steps, as well as for washing. Fmoc cleavage was performed with a 1:1 mixture of DMF/morpholine (pump speed 3.0 mL/min) and monitored at λ = 360 nm. Functionalised Fmoc amino acids (Novabiochem) were used in fivefold excess and activated with PyBOP (5 equiv.), HOBt (5 equiv.), and NMM (10 equiv.). Couplings were monitored using Coomassie Violett at λ = 600 nm. The standard building blocks were coupled in automatic mode. Glycosylated threonine building block **33** was used in twofold excess and activated as described above. Couplings were performed for 24 h. After the peptide had been assembled, the resin was washed with DMF, acetic acid/dichloromethane (1:1), and dichloromethane, and then dried under high vacuum for 15 h. The peptide was cleaved from the solid phase and partially deprotected using trifluoracetic acid/triisopropylsilane/water (38:1:1, 8 mL, 3 h). The solution of the peptide was collected and the resin washed with more TFA and dichloromethane. The combined solutions were concentrated and the residue dried by co-evaporation with toluene. The crude residue was purified on a column of Sephadex LH-20 with dichloromethane/methanol (1:1) as eluent, and the collected material lyophilized from 1,4-dioxane. This procedure gave **34** (66 mg, 61%) as a colourless lyophilisate. TLC (butanol/pyridine/acetic acid/water, 4:1:1:2): R_f = 0.33. $[\alpha]_D$ = −28.8 (*c* = 1.0; CH_3OH). ^{1}H NMR (600 MHz, CD_3OD): δ = 1.28−1.32 (m, 9 H, 3 Thrγ-H, 6 Alaβ-H), 1.76 (t, $^2J_{3',3}$ = 12.4 Hz, 1 H, 3b′-H), 1.80−2.15 (m, 33 H, 4 Proγ-H, 2 Proβ-H, 3 NHAc, 6 Ac), 2.21−2.30 (m, 2 H, 2 Proβ-H), 2.57 (dd, $^2J_{3,3'}$ = 12.9, $^3J_{3,4}$ = 4.3 Hz, 1 H, 3b-H), 3.03−3.09 (m, 1 H, Hisβ-H), 3.18 (br. s, 1 H, Hisβ-H), 3.25−3.30 (m, 1 H, 6′a-H), 3.52−3.83 (m, 8 H, Serβ-H, OCH_3, 3 Proδ-H, Glyα-H), 3.85−3.96 (m, 7 H, 5b-H, Proβ-H, 3 Glyα-H, Serβ-H, 6a-H), 4.05 (dd, $^3J_{9',8}$ = 5.1, $^2J_{9',9}$ = 12.3 Hz, 1 H, 9b′-H), 4.10 (d, $^3J_{6,5}$ = 10.5 Hz, 1 H, 6b-H), 4.18−4.20 (m, 2 H, 2a-H, 5a-H), 4.27 (br. d, $^2J_{9,9'}$ = 12.4 Hz, 1 H, 9b-H), 4.35−4.37 (m, 3 H, Thrβ-H, Serα-H, Alaα-H), 4.50−4.55 (m, 4 H, Thrα-H, Proα-H, Proα-H, Alaα-H), 4.67 (br. t, $^3J_{\alpha,NH}$ = 7.5 Hz, 1 H, Hisα-H), 4.80−4.81 (m, 1 H, 4b-H), 5.10−5.12 (m, 2 H, 1a-H, 4b-H), 5.31−5.35 (m, 3 H, 3a-H, 7b-H, 8b-H), 7.16 (br. s, 1 H, Hisδ-H), 7.57 (s, 1 H, Hisε-H) ppm. FAB-MS: (positive mode, NBOH/NaI matrix): *m*/*z* = 1596 [M + H]$^+$.

***N*-Acetyl-L-glycyl-L-seryl-*O*-{*O*-[(5-acetamido-3,5-dideoxy-D-*glycero*-α-D-*galacto*-non-2-ulopyranosyl)onic acid]-(2→6)-(2-acetamido-2-deoxy-α-D-galactopyranosyl)-L-threonyl-L-alanyl-L-prolyl-L-prolyl-L-alanyl-L-histidyl-L-glycinamide (1):** Protected glycopeptide **34** was dissolved in methanol (10 mL) and treated with aqueous sodium hydroxide solution (0.100 mL, 1 M). This solution was stirred at room temperature for 3 h and then brought to pH 6 by the addition of acetic acid. All solvents were evaporated, the residue was redissolved in a mixture of water/THF (4 mL, 1:1), aqueous sodium hydroxide (4 mL, 5 mM) was added, and the reaction mixture stirred at room temperature for 4 h. The solution was acidified to pH = 6 by the addition of acetic acid and the solvents were

lyophilised. The residue was purified on a column of Sephadex LH-20 with dichloromethane/methanol (1:1) as eluent and the collected material lyophilized from water/1,4-dioxane. This procedure gave **1** (17 mg, 81%) as a colourless lyophilisate. TLC (butanol/pyridine/acetic acid/water, 4:1:1:2): R_f = 0.09. $[\alpha]_D$ = −40.8 (*c* = 1.0; H_2O). ^{1}H NMR (600 MHz, D_2O): δ = 1.18−1.27 (m, 9 H, 6 Alaβ-H, 3 Thrγ-H), 1.59 (t, $^2J_{3',3}$ = 12.3, $^3J_{3',4}$ = 12.3 Hz, 1 H, 3b′-H), 1.71−1.74 (m, 1 H, Proβ-H), 1.81−1.83 (m, 1 H, Proβ-H), 1.92−2.04 (m, 11 H, 4 Proγ-H, 3 NHAc), 2.17−2.22 (m, 1 H, Proβ-H), 2.26−2.29 (m, 1 H, Proβ-H), 2.63 (dd, $^2J_{3,3'}$ = 12.2, $^3J_{3,4}$ = 4.1 Hz, 1 H, 3b-H), 3.03−3.08 (m, 2 H, 2 Hisβ-H), 3.42−3.69 (m, 7 H, 7b-H [3.43], 6a′-H [3.53], Proδ-H [3.53], Proδ-H [3.55], 9b′-H [3.56], 4b-H [3.58], 6b-H [3.62]), 3.70−3.86 (m, 10 H, Proδ-H [3.70], Proδ-H [3.73], 5b-H [3.74], Glyα-H [3.76], 3a-H [3.76], 9b-H [3.79], 8b-H [3.79], Serβ-H [3.81], 6a-H [3.83], Glyα-H [3.84]), 3.88−3.98 (m, 3 H, 2 Glyα-H [3.88, 3.88], 4a-H [3.90]), 4.00−4.01 (m, 2 H, 2a-H [4.00], 5a-H [4.01]), 4.15−4.17 (m, 1 H, Alaα-H), 4.24−4.25 (m, 1 H, Thrβ-H), 4.29 (t, $^3J_{\alpha,\beta}$ = 7.0, $^3J_{\alpha,\beta'}$ = 7.0 Hz, 1 H, Proα-H), 4.48−4.60 (m, 5 H, Thrα-H [4.48], Alaα-H [4.48], Hisα-H [4.52], Proα-H [4.56], Serα-H [4.58]), 4.85 (br. d, 1 H, 1a-H), 6.98 (s, 1 H, Hisδ-H), 7.86 (br. d, 1 H, Hisε-H) ppm. ^{13}C NMR (150.8 MHz, D_2O) (excerpt): δ = 15.5 (C-Alaβ), 16.5 (C-Alaβ), 18.7 (C-Thrγ), 24.9 (2 C-Proγ), 28.0 (C-Hisβ), 28.2 (C-Proβ), 29.4 (C-Proβ), 40.4 (C-3b), 42.3 (C-Glyα), 42.6 (C-Glyα), 47.7 (C-Alaα), 47.7 (C-Proδ), 47.9 (C-Proδ), 49.7 (C-2a), 50.0 (C- Alaα), 52.0 (C-5b), 53.6 (C-Hisα), 55.4 (C-Serα), 57.4 (C-Thrα), 58.6 (C-Proα), 60.3 (C-Proα), 61.4 (C-Serβ), 62.8 (C-9b), 64.1 (C-6a), 68.3 (C-3a), 68.5 (C-4b) 68.5 (C-7b), 68.8 (C-4a), 69.8 (C-6b), 70.2 (C-5a), 72.0 (C-8b), 76.5 (C- Thrβ), 99.1 (C-1a) ppm. FAB-MS: (positive mode, NBOH/NaI matrix): *m*/*z* = 1351.9 $[M + Na - H]^+$, 1373.6 $[M + 2\ Na - H]^+$.

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