D-Glucose as a Pentavalent Chiral Scaffold

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Keywords: Combinatorial chemistry / Solid-phase synthesis / Carbohydrates / Peptidomimetics

A novel carbohydrate-based scaffold for combinatorial chemistry has been developed. This scaffold allows the selective attachment of five different side chains, giving rise to products of enormous structural diversity. As a demonstration of its usefulness, a series of model compounds has been prepared in high purity and yield by multistep parallel synthesis on a solid phase.

Introduction

One way of generating molecular diversity is the attachment of various functional side chains to a multivalent scaffold.[1] Carbohydrates have several advantages over the synthetic tri- or tetravalent scaffolds described in the literature: they are readily available in a variety of diastereomeric forms, they are inherently polyfunctional and, in the case of a monosaccharide, allow the attachment of up to five substituents. In addition, some of them are among the cheapest enantiopure organic compounds available.

In 1993, Hirschmann et al. described the use of D-glucose for the construction of mimetics of a biologically active peptide.[2] Based on this work, a number of carbohydrate-based peptidomimetics have been developed.[3] Surprisingly, a combinatorial approach involving selective manipulations at all five positions of the monosaccharide core is still missing.[4–7] In order to achieve this goal, a suitable set of selectively removable protecting groups in combination with a cleavable anchor is required, especially if the reaction sequences are to be performed on a solid phase. Herein, the preparation and use of a novel pentavalent glucose scaffold for combinatorial chemistry on a solid support are described. The choice of suitable protecting groups for the hydroxy functions is not only restricted by the usual limitations for solid-phase syntheses but also by the fact that Williamson etherifications should be included in the set of derivatization reactions of the deprotected hydroxy groups. Therefore, the desired fully protected scaffold can carry only one base-labile protecting group, which has to be removed prior to the first Williamson reaction.[5]

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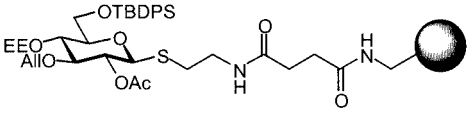

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Figure 1. A selectively deprotectable monosaccharide template

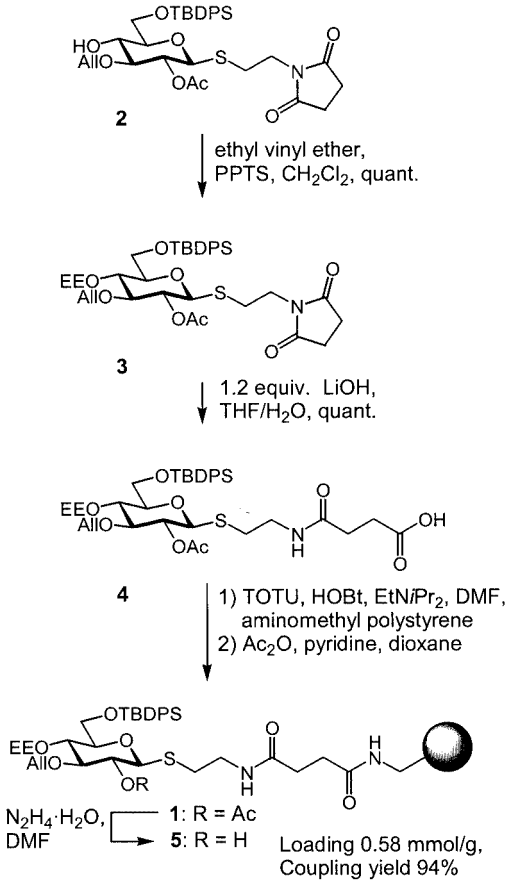
Template **1** (see Figure 1) was synthesized as a candidate. It carries the TBDPS-ether for protection of O-6, a 1-ethoxyethyl (EE) group on O-4, and an allyl ether on O-3. The hydroxy group in the 2-position is protected by an acetyl group, which, for convenience, is removed first.

The anomeric center is linked to the polymeric support via a thioglycoside anchor.[8] Like a conventional thioglycoside, this anchor can be activated by addition of an electrophile, yielding a reactive intermediate, which, in turn, can be converted into an *O*-, *N*- or *S*-glycoside by reaction with a suitable nucleophile.[5–7]

Results and Discussion

The polymer-bound glucose template **1** was synthesized in three steps from succinimide **2** (see Scheme 1), the preparation of which has been described recently:[7] The hydroxy function in the 4-position was protected as its 1-ethoxyethyl acetal by treatment with ethyl vinyl ether in the presence of a catalytic amount of pyridinium *p*-toluenesulfonate. Opening of the succinimide ring of the resulting compound **3** with lithium hydroxide yields carboxylic acid **4**, which was linked to aminomethyl polystyrene with the active coupling reagent *O*-[(ethoxycarbonyl)cyanomethylenamino]-*N*,*N*,*N*′,*N*′-tetramethyluronium tetrafluoroborate (TOTU)[9] and 1-hydroxybenzotriazole as the additive.

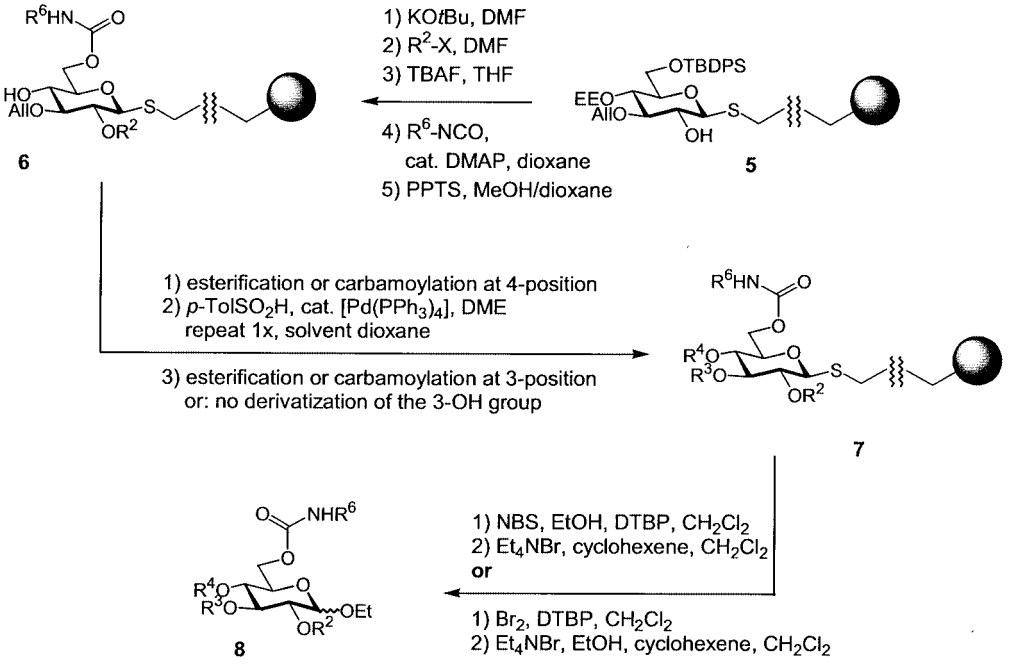
A capping acetylation was performed in order to prevent problems originating from the remaining amino functions



Scheme 1. Preparation of templates **1** and **5**

on the polymer. Experiments revealed that side reactions occur at the allyl moiety during cleavage of the anchor so that hydrogenated analogs of **1** and **5** were used for the optimization of deprotection and derivatization reactions.[5,7] The construction of a pentavalent galactose scaffold has already been reported.[6]

Removal of the acid- and base-stable allyl ether, which is preferably performed as the last deprotection, turned out to be a puzzling problem, since suitable reagents must not attack either the sulfur at C-1 or any functionality introduced in previous steps. The use of Baudry's catalyst[10] for isomerization of the allyl- to the 2-propenyl ether (which in turn can be cleaved by acidolysis) failed in a number of cases. Therefore, a reliable method for clean removal of the allyl ether on the solid phase had to be developed.[11] With protocols for all necessary deprotections and for the introduction of a variety of alkyl, acyl and carbamoyl substituents at hand, the fivefold derivatization of template **1** was attempted: Cleavage of the acetyl group by hydrazine hydrate, deprotonation of the free 2-hydroxy group with potassium *tert*-butoxide and addition of an alkyl halide furnished 2-*O*-alkyl glucosides. Deprotection of O-6 with tetrabutylammonium fluoride was followed by carbamoylation with an isocyanate and subsequent removal of the ethoxyethyl group by acid catalyzed transacetalization, yielding resins **6**. The hydroxy group at the 4-position was derivatized either by carbamoylation or by a modified Steglich esterification.[12] The resulting polymers were then subjected to a Pd^0-catalyzed deallylation with *p*-toluenesulfinic acid, acting as the proton source as well as the allyl acceptor.[11,13] The deprotected hydroxy group at C-3 was carbamoylated, esterified or left underivatized, furnishing the resin-bound glucosides **7**.



Scheme 2. Preparation of compounds **8**

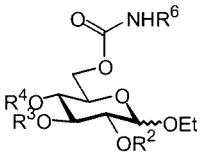


Figure 2. General structure of compounds **8** listed in Table 1

Addition of bromine or *N*-bromosuccinimide (NBS) and the sterically hindered base 2,6-di-*tert*-butylpyridine (DTBP) in dichloromethane resulted in the cleavage of the thioglycoside anchor and led to formation of reactive 1-bromosugars, which were converted into the corresponding 1-*O*-ethyl glycosides **8** (Scheme 2, Figure 2) by Lemieux activation with tetraethylammonium bromide and reaction with ethanol.[14] Excess bromine or NBS was trapped with cyclohexene. The desired products were purified by a simple solid-phase extraction step using silica as the adsorbent. They could be obtained in high purity and moderate to good yield (see Table 1).

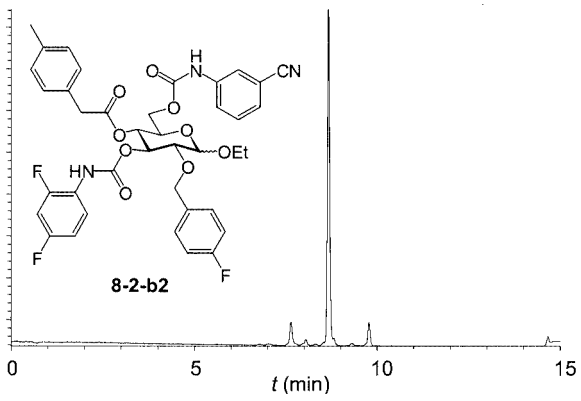


Figure 3. RP-HPLC of compound **8-2-b2** (ELS detection)

The analytical HPLC of compound **8-2-b2** (Figure 3) as well as the ^{1}H NMR spectrum (Figure 4) obtained after purification of the crude material by semipreparative HPLC illustrate the usefulness of the presented technique.

Table 1. Library of compounds **8**

	R^2	R^3	R^4	R^6	Crude yield	HPLC-purity[a]
8-1-a1	Me	H	4-CH_3-$C_6H_4CH_2CO$	4-F-C_6H_4	72%	80.6% (α)
8-1-a2	Me	4-Cl-C_6H_4NHCO	4-CH_3-$C_6H_4CH_2CO$	4-F-C_6H_4	58%	83.6% (α+β)
8-1-a3	Me	Ac	4-CH_3-$C_6H_4CH_2CO$	4-F-C_6H_4	56%	63.9% (α)
8-1-a4	Me	Boc-Gly	4-CH_3-$C_6H_4CH_2CO$	4-F-C_6H_4	56%	81.7% (α)
8-1-b1	Me	H	Bz	4-F-C_6H_4	86%	80.4% (α), 13.8% (β)
8-1-b2	Me	4-Cl-C_6H_4NHCO	Bz	4-F-C_6H_4	60%	84.5% (α)
8-1-b3	Me	Ac	Bz	4-F-C_6H_4	48%	56.2% (α)
8-1-b4	Me	Boc-Gly	Bz	4-F-C_6H_4	45%	47.4% (α)
8-1-c1	Me	H	4-CF_3-C_6H_4NHCO	4-F-C_6H_4	74%	74.6% (α), 12.9% (β)
8-1-c2	Me	4-Cl-C_6H_4NHCO	4-CF_3-C_6H_4NHCO	4-F-C_6H_4	45%	63.7% (α), 5.5% (β)
8-1-c3	Me	Ac	4-CF_3-C_6H_4NHCO	4-F-C_6H_4	47%	68.7% (α)
8-1-c4	Me	Boc-Gly	4-CF_3-C_6H_4NHCO	4-F-C_6H_4	27%	55.9% (α)
8-2-a1	4-F-$C_6H_4CH_2$	H	4-F-C_6H_4NHCO	3-CN-C_6H_4	75%	86.3% (α), 8.4% (β)
8-2-a2	4-F-$C_6H_4CH_2$	2,4-F_2-C_6H_3NHCO	4-F-C_6H_4NHCO	3-CN-C_6H_4	41%	77.4% (α)
8-2-a3	4-F-$C_6H_4CH_2$	4-EtO_2C-C_6H_4NHCO	4-F-C_6H_4NHCO	3-CN-C_6H_4	52%	83.4% (α), 11.0% (β)
8-2-a4	4-F-$C_6H_4CH_2$	4-CF_3-C_6H_4NHCO	4-F-C_6H_4NHCO	3-CN-C_6H_4	50%	86.0% (α), 8.6% (β)
8-2-b1	4-F-$C_6H_4CH_2$	H	4-CH_3-$C_6H_4CH_2CO$	3-CN-C_6H_4	72%	82.0% (α), 9.8% (β)
8-2-b2	4-F-$C_6H_4CH_2$	2,4-F_2-C_6H_3NHCO	4-CH_3-$C_6H_4CH_2CO$	3-CN-C_6H_4	40%	81.4% (α)
8-2-b3	4-F-$C_6H_4CH_2$	4-EtO_2C-C_6H_4NHCO	4-CH_3-$C_6H_4CH_2CO$	3-CN-C_6H_4	35%	71.2% (α)
8-2-b4	4-F-$C_6H_4CH_2$	4-CF_3-C_6H_4NHCO	4-CH_3-$C_6H_4CH_2CO$	3-CN-C_6H_4	55%	69.1% (α)
8-2-c1	4-F-$C_6H_4CH_2$	H	4-Cl-C_6H_4NHCO	3-CN-C_6H_4	64%	81.7% (α), 13.0% (β)
8-2-c2	4-F-$C_6H_4CH_2$	2,4-F_2-C_6H_3NHCO	4-Cl-C_6H_4NHCO	3-CN-C_6H_4	34%	81.7% (α), 9.2% (β)
8-2-c3	4-F-$C_6H_4CH_2$	4-EtO_2C-C_6H_4NHCO	4-Cl-C_6H_4NHCO	3-CN-C_6H_4	52%	78.9% (α), 13.9% (β)
8-2-c4	4-F-$C_6H_4CH_2$	4-CF_3-C_6H_4NHCO	4-Cl-C_6H_4NHCO	3-CN-C_6H_4	52%	81.4% (α), 13.5% (β)
8-3-a1	4-Me-$C_6H_4CH_2$	H	4-F-C_6H_4NHCO	4-Cl-C_6H_4	81%	69.8% (α), 14.4% (β)
8-3-a2	4-Me-$C_6H_4CH_2$	2,4-F_2-C_6H_3NHCO	4-F-C_6H_4NHCO	4-Cl-C_6H_4	43%	66.6% (α)
8-3-a3	4-Me-$C_6H_4CH_2$	4-EtO_2C-C_6H_4NHCO	4-F-C_6H_4NHCO	4-Cl-C_6H_4	56%	87.4% (α), 6.7% (β)
8-3-a4	4-Me-$C_6H_4CH_2$	4-CF_3-C_6H_4NHCO	4-F-C_6H_4NHCO	4-Cl-C_6H_4	60%	87.4% (α), 7.7% (β)
8-3-b1	4-Me-$C_6H_4CH_2$	H	4-CH_3-$C_6H_4CH_2CO$	4-Cl-C_6H_4	79%	80.8% (α), 9.7% (β)
8-3-b2	4-Me-$C_6H_4CH_2$	2,4-F_2-C_6H_3NHCO	4-CH_3-$C_6H_4CH_2CO$	4-Cl-C_6H_4	42%	84.5% (α)
8-3-b3	4-Me-$C_6H_4CH_2$	4-EtO_2C-C_6H_4NHCO	4-CH_3-$C_6H_4CH_2CO$	4-Cl-C_6H_4	61%	80.2% (α), 16.2% (β)
8-3-b4	4-Me-$C_6H_4CH_2$	4-CF_3-C_6H_4NHCO	4-CH_3-$C_6H_4CH_2CO$	4-Cl-C_6H_4	56%	81.1% (α), 15.3% (β)
8-3-c1	4-Me-$C_6H_4CH_2$	H	3-CN-C_6H_4NHCO	4-Cl-C_6H_4	78%	83.8% (α), 8.5% (β)
8-3-c2	4-Me-$C_6H_4CH_2$	2,4-F_2-C_6H_3NHCO	3-CN-C_6H_4NHCO	4-Cl-C_6H_4	38%	63.0% (α)
8-3-c3	4-Me-$C_6H_4CH_2$	4-EtO_2C-C_6H_4NHCO	3-CN-C_6H_4NHCO	4-Cl-C_6H_4	52%	85.2% (α), 6.1% (β)
8-3-c4	4-Me-$C_6H_4CH_2$	4-CF_3-C_6H_4NHCO	3-CN-C_6H_4NHCO	4-Cl-C_6H_4	52%	82.4% (α), 6.0% (β)

[a] ELS detection.

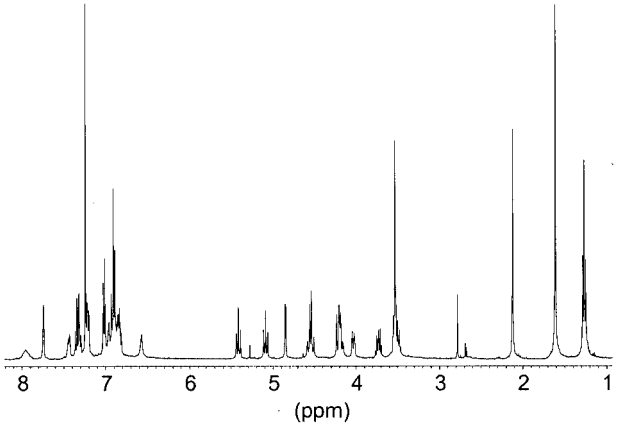


Figure 4. ^{1}H NMR spectrum of compound **8-2-b2** (pure α-anomer)

Conclusion

In conclusion, a versatile pentavalent glucose scaffold has been synthesized and its use for the combinatorial preparation of structurally diverse glucose derivatives has been demonstrated. None of the transformations requires heating or cooling and only the cleavage of the allyl ether has to be performed under oxygen-free conditions. Therefore, the presented synthetic transformations can be run in an automatic fashion.

Experimental Section

Materials and Methods: Analytical TLC was performed on aluminium-backed TLC-plates coated with silica 60 F_{254} (E. Merck). Column chromatography was performed on silica (63−200 μm, Baker or 40−63 μm, E. Merck). Aminomethylated polystyrene was purchased from Rapp Polymere. Solid-phase extraction cartridges and 13 mm polyethylene frits for standard 5-mL polyethylene syringes were purchased from Isolute. Melting points were measured on a Dr. Tottoli apparatus and are uncorrected. Optical rotations were measured on a Perkin−Elmer 241 polarimeter. NMR spectra were recorded on a Bruker ARX-400 spectrometer; chemical shifts are expressed in ppm downfield from tetramethylsilane. ESI-MS spectra were measured on a Navigator (ThermoQuest) between 200 and 1300 amu at a cone voltage of 70 V using a flow rate of 0.75 mL/min acetonitrile/water (70:30, v/v) and a nitrogen flow of 300 L/h. A Basic-Marathon autosampler was employed for sample injection (20 μL at 0.1 g/L in acetonitrile). ESI-HMRS analyses were performed on a Micromass Q-TOF Ultima spectrometer. HPLC analyses were performed on a Knauer system with a Luna C18−2 column (Phenomenex, 75 × 4.6 mm, 3 μm particle size) using the following gradient: (*t*, % MeCN): 0 min, 50%; 0.75 min, 50%; 10 min, 99%; 12.5 min, 99%; 13.5 min, 50%; 15 min, 50%. The HPLC system was equipped with an autosampler, an online-degasser, a column oven (25 °C) and an ELS (evaporative light scattering) detector, model PL-ELS 1000 (Polymer Laboratories). The detector was operated at a nebulizer temperature of 85 °C and an evaporator temperature of 95 °C with a nitrogen flow of 1 L/min. For analytical HPLC, the flow rate was 1 mL/ min, the sample concentration 1 g/L and the injection volume was 20 μL. HPLC-MS analyses were performed on the Navigator instrument by using the HPLC system described above in combination with a flow splitter (ratio 10:1) and a sample concentration of 0.1 g/L. The notation of the ions of side products detected in mass spectra uses the numbering of the glucose skeleton. All substituents denoted are attached to the oxygen atoms at the mentioned positions with the exception of substituents at the anomeric center. All signals showed isotope patterns consistent with the composition of the indicated ion species and the corresponding charge state. Preparative HPLC separations were performed on a Knauer system equipped with a Eurospher C18 column (250 × 20 mm, 10 μm particle size) and a diode array UV detector at a flow rate of 10 mL/min.

Preparation of Polymer-Bound Building Block 5: Ethyl vinyl ether (5.42 mL, 56.7 mmol) and pyridinium *p*-toluenesulfonate (1.43 g, 5.7 mmol) were added to a solution of the succinimide **2**[7] (7.28 g, 11.3 mmol) in dry dichloromethane (100 mL) and the solution was stirred at room temperature for 3 h . The solution was washed several times with a saturated $NaHCO_3$ solution, dried over Na_2SO_4 and concentrated in vacuo to yield the crude EE-protected succinimide **3** (8.10 g, quantitative) as a viscous colorless oil. Lithium hydroxide (351 mg, 14.7 mmol) was added to a solution of crude **3** (8.05 g, 11.3 mmol) in a mixture of THF (75 mL) and water (25 mL), and the solution was stirred at room temperature until TLC indicated complete hydrolysis of the starting material (ca. 1.5 h). The reaction mixture was neutralized by addition of phosphate buffer (pH = 7) and, after addition of brine (100 mL), was extracted twice with ethyl acetate (250 mL). The combined organic layers were dried over Na_2SO_4 and the solvent was removed in vacuo at temperatures below 40 °C to prevent decomposition of the material. Carboxylic acid **4** (8.32 g, quantitative) was obtained as a colorless oil which proved to decompose slowly. Therefore, the crude material was directly coupled to the polymer: In a solid-phase reaction vessel, the solution of the crude acid **4** (8.32 g, 11.3 mmol) in dry DMF (60 mL) was added to aminomethyl polystyrene (11.2 g, 12.2 mmol, loading 1.1 mmol/g, particle size 100−200 mesh, crosslinked with 1% divinylbenzene). After addition of 1-hydroxybenzotriazole (1.88 g, 11.8 mmol, water content 15%), *N*-ethyldiisopropylamine (4.1 mL, 23.6 mmol) and *O*-[(ethoxycarbonyl)cyanomethylenamino]-*N*,*N*,*N*′,*N*′-tetramethyluronium tetrafluoroborate (TOTU, 3.88 g, 11.8 mmol), the mixture was shaken for 20 h at room temperature. Small amounts of dry DMF were added to prevent solidification of the mixture. The polymer was washed with DMF, water, methanol, dioxane and toluene (50 mL each). A mixture of acetic anhydride (10 mL), pyridine (30 mL) and dioxane (30 mL) was added and the mixture was shaken for 1 h. The resin was washed with DMF, dioxane and DMF (50 mL each) and after addition of hydrazine monohydrate (35 mL) and DMF (70 mL), the mixture was shaken for 16 h at room temperature. The resin was washed with DMF, water, methanol, dioxane, toluene and twice with diethyl ether (50 mL each) and dried thoroughly in vacuo. Yield: 18.4 g of the polymer **5** with a loading of 0.58 mmol/g (determined by gravimetry), corresponding to a coupling yield of 94%.

3: Colorless oil; R_f = 0.59 (hexanes/ethyl acetate, 1:1). $[\alpha]_D^{22}$ = −25 (*c* = 1.0, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.92 (t, *J* = 7.0 Hz, 1.5 H, CH_3CH_2), 1.03, 1.04 (2 s, 2 × 4.5 H, *t*Bu), 1.15 (t, *J* = 7.0 Hz, 1.5 H, CH_3CH_2), 1.22, 1.23 (2 d, *J* = 5.1 Hz, 2 × 1.5 H, CH_3CH), 2.09 (s, 3 H, Ac), 2.63, 2.64 (2 s, 2 × 2 H, CH_2CO Suc), 2.66−2.91 (m, 2 H, SCH_2), 3.18 (dq, J_d = 9.0, J_q = 7.0 Hz, 0.5 H, CH_3CH_2), 3.28 (br. d, 0.5 H), 3.38−3.98 (m, 7.5 H), 4.07−4.21 (m, 2 H), 4.37 (br. dd, J_{gem} = 12.5, J_{vic} = 5.5 Hz, 0.5 H, allyl-OCH_2), 4.44, 4.47 (2d, *J* = 9.8 Hz, 2 × 0.5 H, 1-H), 4.83 [q, *J* = 5.1 Hz, 0.5 H, $(RO)_2CHCH_3$], 4.87−4.98 [m, 1.5 H, 2-H, $(RO)_2CHCH_3$], 5.12 (br. d, J_{cis} = 10.6 Hz, 1 H, $=CH_2$), 5.22 (mc, 1 H, $=CH_2$), 5.85 (mc, 1 H, =CH−), 7.32−7.45 (m, 6 H, $SiPh_2$),

7.65−7.74 (m, 4 H, $SiPh_2$) ppm. ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 15.15, 15.44 (CH_3CH_2), 19.20 (C_q *t*Bu), 20.62 (CH_3CH), 21.02 (CH_3CO), 21.40 (CH_3CH), 26.77 [$(CH_3)_3$], 27.19, 27.24 (SCH_2), 28.03 (CH_2 Suc), 37.93 (CH_2N), 62.03, 62.35, 63.15, 63.56 (C-6, CH_3CH_2), 71.81, 72.02, 73.84, 73.89, 74.09, 80.32, 80.52, 82.71, 82.90, 83.14, 84.01 (C-1 − C-5, allyl OCH_2), 101.48, 101.83 (CH_3CH), 116.40, 116.76 (CH_2=), 127.49, 127.54, 127.65 (*o*-Ph_2Si), 129.50, 129.61, 129.66 (C_p Ph_2Si), 132.74, 133.36, 133.43, 133.61 (C_i Ph_2Si), 134.43, 134.87 (=CH−), 135.51, 135.57, 135.71, 135.87 (C_m Ph_2Si), 169.56, 169.59 (CH_3CO), 176.64, 176.67 (CO Suc) ppm. $C_{37}H_{51}NO_9SSi$ (714.0): calcd. C 62.25, H 7.20, N 1.96, found C 61.61, H 6.86, N 2.00 (crude product).

Note that many NMR signals are split due to the formation of a 1:1 mixture of diastereomers.

Preparation of Compounds 8-1: In a solid-phase reaction vessel, a solution of potassium *tert*-butoxide (2.81 g, 23 mmol) in dry DMF (15 mL) was added to the polymer **5** (5 g, loading 0.58 mmol/g, 2.9 mmol). The mixture was shaken under argon for 15 min and the supernatant solution was filtered off. A solution of methyl iodide (3.1 mL, 50 mmol) in 20 mL dry DMF was added and the mixture was shaken for 1 h under argon. The polymer was washed with DMF, methanol, DMF, dioxane and three times with diethyl ether (40 mL each). Drying in vacuo gave 5.48 g of the 2-*O*-methylated product. A portion of this polymer (4.48 g, 2.37 mmol, loading determined gravimetrically based on the initial amount of **5**) was shaken with a solution of tetrabutylammonium fluoride trihydrate (7.07 g, 22.4 mmol) in 23 mL THF under argon for 16 h. The polymer was washed (THF, DMF, dioxane, toluene, 2 × diethyl ether, 30 mL each) and dried in vacuo, yielding 3.92 g of the 6-*O*-desilylated product. The loading was determined by combustion analysis to be 0.60 mmol/g (S content); gravimetric determination gave the same result. A solution of 4-fluorophenyl isocyanate (2.19 mL, 19.3 mmol) in dioxane (20 mL), together with a catalytic amount of DMAP, was added to a portion of this polymer (2.57 g, 1.54 mmol), and the mixture was shaken for 16 h. The resin was washed with dioxane, DMF, dioxane, diethyl ether and toluene (15 mL each) and shaken with a solution of pyridinium *p*-toluenesulfonate (250 mg, 0.99 mmol) in a mixture of methanol (2.5 mL) and dioxane (20 mL) for 10 min. The solution was filtered off, replaced by the same volume of fresh solution (identical composition) and the mixture was shaken for 16 h. After washing (dioxane, DMF, dioxane, diethyl ether, dioxane and 2 × diethyl ether; 15 mL each), the resin was dried in vacuo to yield 2.56 g of the polymer **6-1** with a loading of 0.6 mmol/g. Three portions of this resin (400 mg, 240 μmol each) were filled in 5 mL syringes equipped with 20 μm polyethylene frits.

To the first syringe, a solution of *p*-tolylacetic acid (210 mg, 1.4 mmol), *N*,*N*′-diisopropylcarbodiimide (219 μL, 1.4 mmol) and DMAP (17 mg, 140 μmol) in dry DMF (4 mL) was added. To the second syringe, a mixture of benzoyl chloride (460 μL, 4.0 mmol), pyridine (1 mL) and dioxane (2 mL) was added. The polymer in the third syringe was swollen with a 2% solution of DMAP in dioxane and, after removal of the liquid phase, a solution of 4-(trifluoromethyl)phenyl isocyanate (0.43 mL, 3 mmol) in dioxane (3.5 mL) was added. All three syringes were shaken for 16 h. The polymers were washed (dioxane, methanol, DMF, dioxane, 2 × diethyl ether, dioxane, 3 × diethyl ether; 4 mL each) and dried in vacuo. For cleavage of the allyl ether, a solution of *p*-toluenesulfinic acid (156 mg, 1 mmol) in 1,2-dimethoxyethane (DME, 6 mL) was added to each of the three resin samples and the mixtures were degassed by ultrasonication under an argon atmosphere. Tetrakis(triphenylphosphane)palladium (58 mg, 50 μmol) was added and the mixtures were shaken under argon in the dark for 18 h. The resins were filtered off, washed repeatedly with dioxane and DME and the cleavage procedure was repeated with dioxane as the solvent. The polymers were filtered off, washed with dioxane, DMF, dioxane, a 0.1% solution of ammonium diethyldithiocarbamate in DMF, dioxane, DMF dioxane, methanol, dioxane, diethyl ether, toluene, dioxane and twice with diethyl ether. This procedure was necessary to remove traces of palladium complexes and triphenylphosphane. The resin samples were dried in vacuo and each of them was divided into four equal portions which were filled in 5 mL syringes with polyethylene frits. Each of the 12 syringes contained about 100 mg of resin, carrying 60 μmol of the corresponding thioglucoside. Three of the syringes were set aside without further derivatization of O-3. The polymers in three other syringes were swollen with a 1% solution of DMAP in dioxane and, after removal of excess liquid, 2 mL (each) of a 10% solution of 4-chlorophenyl isocyanate in dioxane was added. To three syringes, a mixture of acetic anhydride (0.4 mL), pyridine (0.8 mL) and dioxane (1 mL) was added. To the remaining three syringes, solutions of Boc-glycine (88 mg, 0.5 μmol), *N*,*N*′-diisopropylcarbodiimide (78 μL, 0.5 μmol) and DMAP (6.1 mg, 50 μmol) in dry DMF (2 mL) were added. The nine syringes were shaken for 15 h and the resins **7-1** were washed (DMF, dioxane, DMF, dioxane, diethyl ether, dioxane, diethyl ether and toluene; 3 mL each). Cleavage of the thioglycoside anchor was achieved by addition of a solution of *N*-bromosuccinimide (26.6 mg, 150 μmol), 2,6-di-*tert*-butylpyridine (40 μL, 180 μmol) and ethanol (100 μL, 1.7 mmol) in dry dichloromethane (2.5 mL) to all 12 syringes. After 20 min shaking, the solutions were removed from the syringes. Each of the solutions was filled in a vessel containing a solution of tetraethylammonium bromide (38 mg, 180 μmol) and cyclohexene (30 μL, 0.3 mmol) in dry dichloromethane (2.5 mL). Each resin sample was washed once with the resulting mixture in order to extract remaining glycosyl bromide and the vessels were closed. After 3 h, the caps were removed from the vessels and the volatile components were allowed to evaporate in a fume hood for 16 h. Twelve solid-phase extraction cartridges (3 mL, with 20 μm polyethylene frit) were filled with silica (2 mL each) and the adsorbent was wetted with hexanes (2−3 mL). The remaining compound mixtures were dissolved in dichloromethane (400 μL each) and applied on top of the silica layers. All nonpolar components were washed out with hexanes (10 mL) and the desired products were eluted with a mixture of toluene and ethanol (4:1, 7.5 mL). After removal of the solvents in vacuo, the obtained products **8−1** were weighed and analyzed by TLC, RP-HPLC and ESI-MS.

Ethyl 6-*O*-[(4-Fluorophenyl)carbamoyl]-2-*O*-methyl-4-*O*-(4-tolylacetyl)-α/β-D-glucopyranoside (8-1-a1): 20.3 mg (72%), colorless crystals; R_f (α) = 0.26 (Tol/EtOH, 9:1). HPLC: t_R = 2.55 min (5.5%), 4.65 min (80.6%, α). ESI-MS: *m*/*z* (%) = 555.2 (8) [M + MeCN + Na]$^+$, 514.2 (100), [M + Na]$^+$ {calcd. for [$C_{25}H_{30}FNO_8$ + Na] 514.2}, 391.2 (22) [2,6-Me_2 + Na]$^+$.

Ethyl 3-*O*-[(4-Chlorophenyl)carbamoyl]-6-*O*-[(4-fluorophenyl)-carbamoyl]-2-*O*-methyl-4-*O*-(4-tolylacetyl)-α/β-D-glucopyranoside (8-1-a2): 21.3 mg (58%), colorless crystals; R_f (α) = 0.39 (Tol/EtOH, 9:1). HPLC: t_R = 7.27 min (6.9%), 7.53 min (9.5%), 8.43 min (83.6%, α+β). ESI-MS: *m*/*z* (%) = 720.1 (20) [1-NSu + Na]$^+$, 708.1 (18) [M + MeCN + Na]$^+$, 667.1 (85) [M + Na]$^+$ {calcd. for $C_{32}H_{34}ClFN_2O_9$ + Na: 667.2}, 664.7 (17) [2M + Ca]$^{2+}$, 609.1 (18), 585.1 (42) [2,6-Me_2 + MeCN + Na]$^+$, 556.2 (27, contains Cl), 544.2 (100) [2,6-Me_2 + Na]$^+$, 517.1 (16), 433.2 (15, contains 2Cl), 394.2 (14), 393.2 (14), 373.1 (14), 278.1 (28), 222.0 (20).

Ethyl 3-*O*-Acetyl-6-*O*-[(4-fluorophenyl)carbamoyl]-2-*O*-methyl-4-*O*-(4-tolylacetyl)-α/β-D-glucopyranoside (8-1-a3): 16.9 mg (56%), colorless crystals; R_f (α) = 0.42 (Tol/EtOH, 9:1). HPLC-MS: t_R = 3.68 min, {4.1%; *m/z* = 438.2 [4,6-(4-F-$C_6H_4NHCO)_2$ + Na]$^+$, 479.1 [4,6-(4-F-$C_6H_4NHCO)_2$ + MeCN + Na]$^+$, 486.1}, 4.47 min {3.5%; *m/z* = 528.2), 4.88 min {8.4%; *m/z* = 433.2 [2,6-Me_2(α) + Na]$^+$, 474.1 [2,6-Me_2(α) + MeCN + Na]$^+$}, 5.53 min {20.1%; *m/z* = 609.1 [1-NSu(α) + Na]$^+$}, 6.57 min {63.9%; *m/z* = 556.2 [M(α) + Na]$^+$, 571.1 [M(α) + MeCN + Na]$^+$}. ESI-MS: *m/z* (%) = 655.2 (12), 609.1 (48) [1-NSu + Na]$^+$, 597.2 (15), 556.2 (100) [M + Na]$^+$ {calcd. for $C_{27}H_{32}FNO_9$ + Na: 556.3}, 528.2 (11), 486.1 (30) [2,6-Me_2-1-NSu + Na]$^+$, 474.1 (35) [2,6-Me_2 + MeCN + Na]$^+$, 447.2 (14), 438.2 (10) [4,6-(4-F-$C_6H_4NHCO)_2$ + Na]$^+$, 433.2 (83) [2,6-Me_2 + Na]$^+$, 406.2 (23), 324.1 (10), 283.2 (15), 278.1 (27), 222.0 (19).

Ethyl 3-*O*-[(*N*-*tert*-Butoxycarbonyl)glycyl]-6-*O*-[(4-fluorophenyl)-carbamoyl]-2-*O*-methyl-4-*O*-(4-tolylacetyl)-α/β-D-glucopyranoside (8-1-a4): 20.5 mg (56%), yellowish crystals; R_f (α) = 0.38 (Tol/EtOH, 9:1). HPLC: t_R = 5.90 min (4.1%), 6.43 min (5.9%), 6.77 min (8.3%), 7.73 min (81.7%, α). ESI-MS: *m/z* (%) = 671.2 (100) [M + Na]$^+$ {calcd. for $C_{32}H_{41}FN_2O_{11}$ + Na: 671.3}, 615.1 (75) [M − C_4H_8 + Na]$^+$, 724.1 (8), 571.2 (22) [M − Boc + Na]$^+$, 568.6 (11) [2 × (M − Boc) + Ca]$^{2+}$, 548.3 (42) [2,6-Me_2 + Na]$^+$, 496.2 (12), 492.1 (52) [2,6-Me_2 − C_4H_8 + Na]$^+$, 448.2 (30) [2,6-Me_2 − Boc + Na]$^+$, 373.2 (7), 278.1 (16). ESI-HRMS: calcd. for $C_{32}H_{41}FN_2O_{11}$ + Na: 671.2592, found 671.2589. The crude product was purified by semi-preparative RP-HPLC: 11.0 mg (28%), colorless crystals, m.p. 118 °C. $[\alpha]_D^{25}$ = +66 (*c* = 0.92, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.28 (t, *J* = 7.0 Hz, 3 H, OCH_2CH_3), 1.45 (s, 9 H, *t*Bu), 2.32 (s, 3 H, $ArCH_3$), 3.36−3.49 [m, 5 H, 2-H, CH_2 (Gly, 1 H), OCH_3], contained in this multiplet: 3.40 (s, 3 H, OCH_3), 3.54−3.64 [m, 3 H, OCH_2CH_3 (1 H), $ArCH_2CO$], contained in this multiplet: 3.56 (s, 2 H, $ArCH_2CO$), 3.73−3.81 [m, 2 H, OCH_2CH_3 (1 H), CH_2 (Gly, 1 H)], 4.04 (ddd, $J_{4,5}$ = 10.1, $J_{5,6b}$ = 4.0, $J_{5,6a}$ = 2.4 Hz, 1 H, 5-H), 4.18 (dd, J_{gem} = 12.2, $J_{5,6b}$ = 4.0 Hz, 1 H, 6b-H), 4.24 (dd, J_{gem} = 12.2, $J_{5,6a}$ = 2.4 Hz, 1 H, 6a-H), 4.69 (br. t, *J* ≈ 5 Hz, 1 H, Boc-N*H*), 5.01−5.10 (m, 2 H, 1-H, 4-H), contained in this multiplet: 5.04 (d, $J_{1,2}$ = 3.5 Hz, 1 H, 1-H), 5.46 (pseudo-t, *J* ≈ 9.7 Hz, 1 H, 3-H), 6.63 (br. s, 1 H, Ar-N*H*CO), 7.00 [mc, 2 H, *m*-H_2 (4-F-C_6H_4)], 7.13 (mc, 4 H, 4-CH_3-$C_6H_4CH_2$), 7.30 [br. dd, $^3J_{H,H}$ = 8.7, $^4J_{H,F}$ = 4.5 Hz, 2 H, *o*-H_2 (4-F-C_6H_4)] ppm. ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 14.94 (C-2, Et), 21.02 ($ArCH_3$), 28.35 (CH_3, Boc), 40.69 (CH_2, $ArCH_2CO$), 42.25 (CH_2, Gly), 58.84 (OMe), 62.93 (C-6), 64.10 (C-1, Et), 67.48 (C-5), 68.67 (C-4), 72.91 (C-3), 79.02 (C-2), 79.89 (C_q, Boc), 96.11 (C-1), 115.68 [d, $^2J_{C,F}$ = 23.2 Hz, C_m (4-F-C_6H_4)], 120.85 [br. d, $^3J_{C,F}$ ≈ 6 Hz, C_o (4-F-C_6H_4)], 129.20, 129.37 [$C_{o,m}$ (4-Tol)], 130.38 [C_i, (4-Tol)], 137.01, 135.56 [C_p (4-Tol), C_i (4-F-C_6H_4)], 152.99 (CO, ArNHCO), 160.44 (CO, Boc), 169.48 (CO, Gly), 170.85 (CO, $ArCH_2CO$) ppm. The signals were assigned with the aid of an HMQC-spectrum.

Ethyl 4-*O*-Benzoyl-6-*O*-[(4-fluorophenyl)carbamoyl]-2-*O*-methyl-α/β-D-glucopyranoside (8-1-b1): 22.7 mg (86%), colorless crystals; R_f (α) = 0.28 (Tol/EtOH, 9:1). HPLC-MS: t_R = 1.95 min {5.8%; *m/z* = 363.1 [2,6-Me_2(α) + Na]$^+$, 404.3 [2,6-Me_2(α) + MeCN + Na]$^+$}, 3.83 min {80.4%; *m/z* = 486.1 [M(α) + Na]$^+$, 527.2 [M(α) + MeCN + Na]$^+$}, 4.13 min {13.8%; *m/z* = 486.1 [M(β) + Na]$^+$, 527.2 [M(β) + MeCN + Na]$^+$}. ESI-MS: *m/z* (%) = 527.2 (64) [M + MeCN + Na]$^+$, 486.1 (100) [M + Na]$^+$ {calcd. for $C_{23}H_{26}FNO_8$ + Na: 486.2}, 483.6 (5) [2M + Ca]$^{2+}$, 404.2 (15) [2,6-Me_2 + MeCN + Na]$^+$, 363.1 (20) [2,6-Me_2 + Na]$^+$.

Ethyl 4-*O*-Benzoyl-3-*O*-[(4-chlorophenyl)carbamoyl]-6-*O*-[(4-fluorophenyl)carbamoyl]-2-*O*-methyl-α/β-D-glucopyranoside (8-1-b2): 21.2 mg (60%), colorless crystals; R_f (α) = 0.40 (Tol/EtOH, 9:1). HPLC: t_R = 6.27 min (5.3%), 7.53 min (84.5%, α). ESI-MS: *m/z* (%) = 680.2 (23) [M + MeCN + Na]$^+$, 639.1 (100) [M + Na]$^+$ {calcd. for $C_{30}H_{30}ClFN_2O_9$ + Na: 639.2}, 637.2 (25) [2M + Ca]$^{2+}$, 569.2 (7) [2,6-Me_2 − 1-NSu + Na]$^+$, 557.2 (40) [2,6-Me_2 + MeCN + Na]$^+$, 528.1 (17), 516.1 (50) [2,6-Me_2 + Na]$^+$, 446.2 (10, contains Cl), 406.2 (14), 365.1 (17), 345.0 (8), 283.1 (13), 278.1 (24).

Ethyl 3-*O*-Acetyl-4-*O*-benzoyl-6-*O*-[(4-fluorophenyl)carbamoyl]-2-*O*-methyl-α/β-D-glucopyranoside (8-1-b3): 13.7 mg (48%), colorless oil; R_f (α) = 0.43 (Tol/EtOH, 9:1). HPLC: t_R = 2.93 min (6.4%), 3.68 min (7.5%), 4.00 min (7.6%), 4.70 min (20.1%), 5.73 min (56.2%, α). ESI-MS: *m/z* (%) = 627.1 (9), 581.1 (64) [1-NSu + Na]$^+$, 578.1 (12), 569.2 (23) [M + MeCN + Na]$^+$, 551.8 (10), 528.2 (100) [M + Na]$^+$ {calcd. for $C_{25}H_{28}FNO_9$ + Na: 528.2}, 500.1 (16), 479.1 (7), 458.2 (23) [2,6-Me_2-1-NSu + Na]$^+$, 446.1 (38) [2,6-Me_2 + MeCN + Na]$^+$, 438.1 (14), 405.2 (42) [2,6-Me_2 + Na]$^+$, 283.1 (10), 278.1 (33), 245.0 (8), 222.0 (38). ESI-HRMS: calcd. for $C_{25}H_{28}FNO_9$ + Na: 528.1646, found 528.1645. The crude product was purified by semi-preparative RP-HPLC: 6.3 mg (21%) of a colorless oil. $[\alpha]_D^{25}$ = +52 (*c* = 0.53, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.32 (t, *J* = 7.0 Hz, 3 H, OCH_2CH_3), 1.95 (s, 3 H, Ac), 3.45−3.51 (m, 4 H, 2-H, OCH_3), contained in this multiplet: 3.47 (s, 3 H, OCH_3), 3.64 (br. dq, J_d = 9.5, J_q = 7.0 Hz, 1 H, OCH_2CH_3), 3.82 (br. dq, J_d = 9.5, J_q = 7.0 Hz, 1 H, OCH_2CH_3), 4.17 (ddd, $J_{4,5}$ = 10.2, $J_{5,6b}$ = 4.6, $J_{5,6a}$ = 3.0 Hz, 1 H, 5-H), 4.26 (dd, J_{gem} = 12.0, $J_{5,6b}$ = 4.6 Hz, 1 H, 6b-H), 4.34 (dd, J_{gem} = 12.0, $J_{5,6a}$ = 3.0 Hz, 1 H, 6a-H), 5.10 (d, $J_{1,2}$ = 3.5 Hz, 1 H, 1-H), 5.31 (br. pseudo-t, *J* ≈ 10 Hz, 1 H, 4-H), 5.63 (pseudo-t, *J* = 9.7 Hz, 1 H, 3-H), 6.60 (br. s, 1 H, NH), 6.98 [mc, 2 H, *m*-H_2 (4-F-C_6H_4)], 7.24−7.29 [m, *o*-H_2 (4-F-C_6H_4)], 7.44 [br. pseudo-t, *J* ≈8 Hz, 2 H, *m*-H_2 (Ph)], 7.58 [tt, ^3J = 7.5, ^4J = 1.2 Hz, 1 H, *p*-H (Ph)], 8.01 [dd, ^3J = 8.2, ^4J = 1.2 Hz, 2 H, *o*-H_2 (Ph)] ppm.

Ethyl 4-*O*-Benzoyl-3-*O*-[(*N*-*tert*-butoxycarbonyl)glycyl]-6-*O*-[4-fluorophenyl)carbamoyl]-2-*O*-methyl-α/β-D-glucopyranoside (8-1-b4): 15.8 mg (45%), colorless crystals; R_f (α) = 0.36 (Tol/EtOH, 9:1). HPLC: t_R = 2.83 min (3.1%), 4.10 min (4.7%), 4.75 min (3.1%), 5.22 min (14.8%), 5.63 min (17.9%), 6.65 min (47.4%, α). ESI-MS: *m/z* (%) = 696.2 (18) [1-NSu + Na]$^+$, 643.1 (85) [M + Na]$^+$ {calcd. for $C_{30}H_{37}FN_2O_{11}$ + Na: 643.2}, 640.2 (14) [2M + Ca]$^{2+}$, 587.1 (100) [M − C_4H_8 + Na]$^+$, 573.2 (14) [2,6-Me_2-1-NSu + Na]$^+$, 543.2 (33) [M − Boc + Na]$^+$, 520.2 (52) [2,6-Me_2 + Na]$^+$, 517.1 (15) [2 × (2,6-Me_2) + Ca]$^{2+}$?, 505.6 (13), 464.1 (92) [2,6-Me_2−C_4H_8 + Na]$^+$, 461.2 (20), 420.2 (48) [2,6-Me_2 − Boc + Na]$^+$, 278.1 (22), 222.0 (27).

Ethyl 6-*O*-[(4-Fluorophenyl)carbamoyl]-2-*O*-methyl-4-*O*-[(4-trifluoromethylphenyl)carbamoyl]-α/β-D-glucopyranoside (8-1-c1): 22.9 mg (74%), colorless crystals; R_f (α) = 0.19 (Tol/EtOH, 9:1). HPLC: t_R = 2.77 min (12.5%), 4.60 min (74.6%, α), 4.80 min (12.9%, β). ESI-MS: *m/z* (%) = 1115.2 (10) [2M + Na]$^+$, 839.3 (10) [3M + Ca]$^{2+}$, 610.0 (83) [M + MeCN + Na]$^+$, 569.1 (100) [M + Na]$^+$ {calcd. for $C_{24}H_{26}F_4N_2O_8$ + Na: 569.1}, 566.7 (23) [2M + Ca]$^{2+}$, 487.1 (17) [2,6-Me_2 + MeCN + Na]$^+$, 478.1 (12), 446.1 (15) [2,6-Me_2 + Na]$^+$, 263.1 (8).

Ethyl 3-*O*-[(4-Chlorophenyl)carbamoyl]-6-*O*-[(4-fluorophenyl)-carbamoyl]-2-*O*-methyl-4-*O*-[(4-trifluoromethylphenyl)carbamoyl]-α/β-D-glucopyranoside (8-1-c2): 18.1 mg (45%), yellowish crystals; R_f (α) = 0.35 (Tol/EtOH, 9:1). HPLC-MS: t_R = 6.15 min (4.4%), 6.58 min {10.4%; *m/z* = 599.1 [2,6-Me_2(α) + Na]$^+$, 640.1 [2,6-Me_2(α) + MeCN + Na]$^+$}, 6.95 min {16.0%; *m/z* = 775.0 [1-

NSu(α) + Na]$^+$}, 7.68 min {63.7%; *m/z* = 722.1 [M(α) + Na]$^+$, 763.0 [M(α) + MeCN + Na]$^+$}, 7.83 min {5.5%; *m/z* = 722.1 [M(β) + Na]$^+$, 763.0 [M(β) + MeCN + Na]$^+$}. ESI-MS: *m/z* (%) = 775.0 (41) [1-NSu + Na]$^+$, 745.4 (45), 722.0 (98) [M + Na]$^+$ {calcd. for $C_{31}H_{30}ClF_4N_3O_9$ + Na: 722.2}, 720.0 (49) [2M + Ca]$^{2+}$, 562.1 (47) [2,6-Me_2-1-NSu + Na]$^+$, 640.1 (55) [2,6-Me_2 + MeCN + Na]$^+$, 599.0 (53) [2,6-Me_2 + Na]$^+$, 549.2 (53, contains 2Cl), 311.3 (54), 283.1 (56), 278.1 (100), 222.0 (85).

Ethyl 3-*O*-Acetyl-6-*O*-[(4-fluorophenyl)carbamoyl]-2-*O*-methyl-4-*O*-{[4-(trifluoromethyl)phenyl]carbamoyl}-α/β-D-glucopyranoside (8-1-c3): 15.7 mg (47%), colorless crystals; R_f (α) = 0.38 (Tol/EtOH, 9:1). HPLC: t_R = 4.72 min (4.3%), 5.07 min (9.4%), 5.58 min (14.3%), 6.45 min (68.7%, α). ESI-MS: *m/z* (%) = 664.1 (47) [1-NSu + Na]$^+$, 652.1 (33) [M + MeCN + Na]$^+$, 634.6 (25), 611.0 (100) [M + Na]$^+$ (calcd. for $C_{26}H_{28}F_4N_2O_9$ + Na: 611.2}, 608.6 (23) [2M + Ca]$^{2+}$, 583.1 (16), 529.2 (31) [2,6-Me_2 + MeCN + Na]$^+$, 488.1 (33) [2,6-Me_2 + Na]$^+$, 479.1 (16), 438.2 (33), 278.1 (45), 222.0 (29). ESI-HRMS: calcd. for $C_{26}H_{28}F_4N_2O_9$ + Na: 611.1629, found 611.1668. The crude product was purified by flash chromatography on silica gel (eluent hexanes/ethyl acetate, 3:1): 7.6 mg (22%), colorless crystals; m.p. 213−216 °C (dec.). $[\alpha]_D^{25}$ = +64 (*c* = 0.63, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.29 (t, *J* = 7.0 Hz, 3 H, OCH_2CH_3), 2.04 (s, 3 H, OAc), 3.41−3.48 (m, 4 H, 2-H, OCH_3), contained in this multiplet: 3.46 (s, 3 H, OCH_3), 3.58−3.67 (m, 1 H, OCH_2CH_3), 3.75−3.84 (m, 1 H, OCH_2CH_3), 4.07 (pseudo-dt, $J_{4,5}$ = 10.3 Hz, $J_t \approx$ 3.5 Hz, 1 H, 5-H), 4.31−4.41 (m, 2 H, 6-H_2), 5.02 (br. pseudo-t, *J* ≈ 10 Hz, 1 H, 4-H), 5.07 (d, $J_{1,2}$ = 3.5 Hz, 1 H, 1-H), 5.47 (pseudo-t, 1 H, *J* ≈ 10 Hz, 3-H), 6.74 (br. s, 1 H, 4-F-C_6H_4-N*H*), 6.98 [mc, 2 H, *m*-H_2 (4-F-C_6H_4)], 7.03 (br. s, 1 H, 4-CF_3-C_6H_4-N*H*), 7.26−7.31 (m, *o*-H_2 (4-F-C_6H_4), $CHCl_3$), 7.46 [d, *J* = 8.5 Hz, 2 H, *o*-H_2 (4-CF_3-C_6H_4)], 7.54 [d, *J* = 8.5 Hz, 2 H, *m*-H_2 (4-CF_3-C_6H_4)] ppm.

Ethyl 3-*O*-(*N*-*tert*-Butoxycarbonylglycyl)-6-*O*-[(4-fluorophenyl)-carbamoyl]-2-*O*-methyl-4-*O*-{[4-(trifluoromethyl)phenyl]carbamoyl}-α/β-D-glucopyranoside (8-1-c4): 10.7 mg (27%), colorless crystals; R_f (α) = 0.34 (Tol/EtOH, 9:1), HPLC-MS: t_R = 4.15 min (4.1%), 5.00 min {3.4%; *m/z* = 553.1, 497.1, 453.2}, 5.25 min {17.2%; *m/z* = 656.2 [2,6-Me_2-1-NSu(α) + Na]$^+$, 600.0 [2,6-Me_2 − 1-NSu(α) − C_4H_8 + Na]$^+$, 556.1 [2,6-Me_2-1-NSu(α) − Boc + Na]$^+$}, 6.47 min {15.2%; *m/z* = 779.1 [1-NSu(α) + Na]$^+$, 723.1 [1-NSu(α) − C_4H_8 + Na]$^+$}, 7.27 min {55.9%; *m/z* = 726.1 [M(α) + Na]$^+$, 670.2 [M(α) − C_4H_8 + Na]$^+$, 626.1 [M(α) − Boc + Na]$^+$}. ESI-MS: *m/z* (%) = 779.1 (22) [1-NSu + Na]$^+$, 726.1 (100) [M + Na]$^+$ {calcd. for $C_{31}H_{37}F_4N_3O_{11}$ + Na: 726.2}, 670.2 (100) [M − C_4H_8 + Na]$^+$, 626.1 (40) [M − Boc + Na]$^+$, 603.1 (69) [2,6-Me_2 + Na]$^+$, 553.2 (28), 547.2 (94) [2,6-Me_2 − C_4H_8 + Na]$^+$, 503.1 (73) [2,6-Me_2 − Boc + Na]$^+$, 497.2 (31), 453.1 (24), 278.1 (37).

Preparation of Compounds 8−2: The synthesis was carried out according to the protocol for preparation of compounds **8-1**, starting from 2 g of the polymer **5** with a loading of 0.58 mmol/g. 4-Fluorobenzyl bromide was used for alkylation of O-2, O-6 was carbamoylated with 3-cyanophenyl isocyanate (8.6 equiv. as a 10% solution in dioxane, 11 mol% DMAP as catalyst). Variation of O-4 was achieved by carbamoylation with 4-fluorophenyl isocyanate or 4-chlorophenyl isocyanate or by Steglich esterification with 4-tolylacetic acid. After cleavage of the allyl ether, O-3 was carbamoylated with 2,4-difluorophenyl isocyanate, ethyl 4-isocyanatobenzoate or 4-(trifluoromethyl)phenyl isocyanate. Alternatively, O-3 was left underivatized.

For cleavage of the 3-*O*-[4-(trifluoromethyl)phenyl]- and the 3-*O*-[(4-ethoxycarbonyl)phenyl] carbamates from the resin, an alternative cleavage procedure was used as a test: A solution of bromine (7.7 μL, 150 μmol) and 2,6-di-*tert*-butylpyridine (56 μL, 250 μmol) in dry dichloromethane (2 mL) was added to all 12 syringes. After 15 min shaking, the solutions were removed from the syringes. Each of the solutions was filled in a vessel containing a solution of tetraethylammonium bromide (52.5 mg, 250 μmol), ethanol (200 μL, 3.4 mmol) and cyclohexene (30 μL, 0.3 mmol) in dry dichloromethane (1.5 mL). Each resin sample was washed once with the resulting mixture in order to extract remaining glycosyl bromide and the vessels were closed.

The rest of the workup procedure (same for all 12 substances) was identical to the one described for isolation of the products **8−1**, except that the compounds **8−2** were eluted from the solid-phase extraction cartridges with hexanes/ethyl acetate (2:3).

Ethyl 6-*O*-[(3-Cyanophenyl)carbamoyl]-2-*O*-(4-fluorobenzyl)-4-*O*-[(4-fluorophenyl)carbamoyl]-α/β-D-glucopyranoside (8-2-a1): 21.3 mg (75), colorless crystals; R_f (α) = 0.28 (Tol/EtOH, 9:1). HPLC-MS: t_R = 5.40 min {86.3%; *m/z* = 617.2 [2M(α) + Ca]$^{2+}$, 620.1 [M(α) + Na]$^+$, 637.7 [2M(α) + MeCN + Ca]$^{2+}$, 661.2 [M(α) + MeCN + Na]$^+$, 916.1 [3M(α) + Ca]$^{2+}$, 1217.3 [2M(α) + Na]$^+$}, 5.67 min {8.4%; *m/z* = 617.2 [2M(β) + Ca]$^{2+}$, 620.1 [M(β) + Na]$^+$, 637.7 [2M(β) + MeCN + Ca]$^{2+}$, 661.2 [M(β) + MeCN + Na]$^+$, 916.1 [3M(β) + Ca]$^{2+}$, 1217.3 [2M(β) + Na]$^+$}, 6.63 min {3.6%; *m/z* = 584.1 [2,6-(4-F-$C_6H_4CH_2$)$_2$(α) + Na]$^+$, 625.1 [2,6-(4-F-$C_6H_4CH_2$)$_2$(α) + MeCN + Na]$^+$}. ESI-MS: *m/z* (%) = 1217.4 (14) [2M + Na]$^+$, 916.2 (18) [3M + Ca]$^{2+}$, 661.2 (35) [M + MeCN + Na]$^+$, 637.9 (23) [2M + MeCN + Ca]$^{2+}$, 625.1 (30) [2,6-(4-F-$C_6H_4CH_2$)$_2$ + MeCN + Na]$^+$, 620.1 (100) [M + Na]$^+$ {calcd. for $C_{30}H_{29}F_2N_3O_8$ + Na: 620.2}, 617.4 (39) [2M + Ca]$^{2+}$, 609.2 (8) [2M + Mg]$^{2+}$, 584.2 (8) [2,6-(4-F-$C_6H_4CH_2$)$_2$ + Na]$^+$.

Ethyl 6-*O*-[(3-Cyanophenyl)carbamoyl]-3-*O*-[(2,4-difluorophenyl)-carbamoyl]-2-*O*-(4-fluorobenzyl)-4-*O*-[(4-fluorophenyl)carbamoyl]-α/β-D-glucopyranoside (8-2-a2): 14.5 mg (41%), colorless oil; R_f (α) = 0.35 (Tol/EtOH, 9:1). HPLC: t_R = 6.40 min (5.5%), 7.37 min (77.4%, α), 8.07 min (4.1%), 8.47 min (8.7%). ESI-MS: *m/z* (%) = 775.1 (100) [M + Na]$^+$ {calcd. for $C_{37}H_{32}F_4N_4O_9$ + Na: 775.2}, 772.3 (38) [2M + Ca]$^{2+}$, 746.1 (27), 739.1 (44) [2,6-(4-F-$C_6H_4CH_2$)$_2$ + Na]$^+$, 662.2 (16) [3-Pr + Na]$^+$.

Ethyl 6-*O*-[(3-Cyanophenyl)carbamoyl]-3-*O*-[(4-ethoxycarbonyl-phenyl)carbamoyl]-2-*O*-(4-fluorobenzyl)-4-*O*-[(4-fluorophenyl)-carbamoyl]-α/β-D-glucopyranoside (8-2-a3): 19.6 mg (52%), colorless crystals; R_f (α) = 0.32 (Tol/EtOH, 9:1); HPLC: t_R = 7.52 min (83.4%, α), 7.70 min (11.0%, β), 8.58 min (5.0%). ESI-MS: *m/z* (%) = 1202.6 (11) [3M + Ca]$^{2+}$, 811.3 (95) [M + Na]$^+$, calcd. for $C_{40}H_{38}F_2N_4O_{11}$ + Na: 811.3; 808.6 (100) [2M + Ca]$^{2+}$, 800.4 (17) [2M + Mg]$^{2+}$, 782.3 (11), 775.2 (17) [2,6-(4-F-$C_6H_4CH_2$)$_2$ + Na]$^+$, 662.2 (16) [3-Pr + Na]$^+$.

Ethyl 6-*O*-[(3-Cyanophenyl)carbamoyl]-2-*O*-(4-fluorobenzyl)-4-*O*-[(4-fluorophenyl)carbamoyl]-3-*O*-[(4-trifluoromethylphenyl)-carbamoyl]-α/β-D-glucopyranoside (8-2-a4): 18.5 mg (50%), colorless crystals; R_f (α) = 0.33 (Tol/EtOH, 9:1). HPLC: t_R = 8.07 min (86.0%, α), 8.23 min (8.6%, β), 9.05 min (5.4%). ESI-MS: *m/z* (%) = 1196.6 (11) [3M + Ca]$^{2+}$, 807.2 (51) [M + Na]$^+$ {calcd. for $C_{38}H_{33}F_5N_4O_9$ + Na: 807.2}, 804.7 (100) [2M + Ca]$^{2+}$, 796.5 (19) [2M + Mg]$^{2+}$, 779.2 (7), 662.2 (11) [3-Pr + Na]$^+$.

Ethyl 6-*O*-[(3-Cyanophenyl)carbamoyl]-2-*O*-(4-fluorobenzyl)-4-*O*-(4-tolylacetyl)-α/β-D-glucopyranoside (8-2-b1): 20.2 mg (72%), colorless oil; R_f (α) = 0.37 (Tol/EtOH, 9:1), HPLC: t_R = 6.72 min (82.0%, α), 6.97 min (9.8%, β), 8.08 min (4.1%). ESI-MS: *m/z* (%) = 1207.4 (8) [2M + Na]$^+$, 908.6 (8) [3M + Ca]$^{2+}$, 656.2 (24)

$[M + MeCN + Na]^+$, 631.1 (6), 620.1 (12), 615.1 (100) $[M + Na]^+$ {calcd. for $C_{32}H_{33}FN_2O_8$ + Na: 615.2}, 612.5 (41) $[2M + Ca]^{2+}$, 604.4 (13) $[2M + Mg]^{2+}$, 579.2 (32) [2,6-(4-F-$C_6H_4CH_2)_2$ + $Na]^+$.

Ethyl 6-*O*-[(3-Cyanophenyl)carbamoyl]-3-*O*-[(2,4-difluorophenyl)-carbamoyl]-2-*O*-(4-fluorobenzyl)-4-*O*-(4-tolylacetyl)-α/β-D-glucopyranoside (8-2-b2): 14.3 mg (40%), colorless oil; R_f (α) = 0.44 (Tol/EtOH, 9:1). HPLC-MS: t_R = 7.65 min {7.2%; *m/z* = 823.2 [1-NSu(α) + $Na]^+$}, 8.67 min {81.4%; *m/z* = 770.1 [M(α) + $Na]^+$}, 9.78 min {6.1%; *m/z* = 734.1 [2,6-(4-F-$C_6H_4CH_2)_2$ + $Na]^+$}. ESI-MS: *m/z* (%) = 823.3 (8) [1-NSu + $Na]^+$, 793.9 (14), 787.2 (14) [2,6-(4-F-$C_6H_4CH_2)_2$-1-NSu + $Na]^+$, 778.2 (10), 770.2 (100) [M + $Na]^+$ {calcd. for $C_{39}H_{36}F_3N_3O_9$ + Na: 770.2}, 767.3 (35) [2M + $Ca]^{2+}$, 759.3 (8) [2M + $Mg]^{2+}$, 746.1 (14), 734.2 (72) [2,6-(4-F-$C_6H_4CH_2)_2$ + $Na]^+$, 657.3 (9) [3-Pr + $Na]^+$, 312.1 (12%). ESI-HRMS: calcd. for $C_{39}H_{36}F_3N_3O_9$+Na: 770.2301, found 770.2386. The crude product was purified by flash chromatography on silica gel (eluent hexanes/ethyl acetate/chloroform, 3:1:1). 9.3 mg (25%) colorless crystals, m.p. 138−139 °C. $[\alpha]_D^{25}$ = +42 (*c* = 0.78, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.29 (t, *J* = 7.0 Hz, 3 H, OCH_2CH_3), 2.15 (s, 3 H, $ArCH_3$), 3.48−3.59 [m, 4 H, 2-H, OCH_2CH_3 (1 H), $ArCH_2CO$], contained in this multiplet: 3.56 (s, 2 H, $ArCH_2CO$), 3.75 (br. dq, J_d = 9.7, J_q = 7.1 Hz, 1 H, OCH_2CH_3), 4.06 (br. pseudo-dt, J_d = 10.0, $J_t \approx$ 2.7 Hz, 1 H, 5-H), 4.17−4.27 (m, 2 H, 6-H_2), 4.55 (d, J_{gem} = 12.3 Hz, 1 H, $ArCH_2O$), 4.60 (d, J_{gem} = 12.3 Hz, 1 H, $ArCH_2O$), 4.88 (d, $J_{1,2}$ = 3.5 Hz, 1 H, 1-H), 5.11 (br. pseudo-t, 1 H, *J* ≈ 10 Hz, 4-H), 5.44 (pseudo-t, *J* ≈ 10 Hz, 1 H, 3-H), 6.60 (br. s, 1 H, 3-CN-C_6H_4NHCO), 6.83−7.01 [m, 7 H, 3,5,6-H, (2,4-F_2-C_6H_3), *m*-H_2 (4-Tol), *m*-H_2 (4-F-$C_6H_4CH_2$)], 7.04 [d, *J* = 7.9 Hz, 2 H, *o*-H_2 (4-Tol)], 7.21−7.28 [m, *o*-H_2 (4-F-$C_6H_4CH_2$), $CHCl_3$], 7.32−7.39 [m, 2 H, 4-H + 5-H (3-CN-C_6H_4)], 7.46 [br. d, *J* ≈ 7.3 Hz, 1 H, 6-H (3-CN-C_6H_4)], 7.76 [s, 1 H, 2-H (3-CN-C_6H_4)], 7.98 (br. s, 1 H, 2,4-F_2-C_6H_3NHCO) ppm. The signals were assigned with the aid of a COSY spectrum. ^{13}C NMR + DEPT (100.6 MHz, $CDCl_3$): δ = 14.98 (C-2, Et), 20.89 ($ArCH_3$), 40.70 (CH_2, $ArCH_2CO$), 63.15 (C-6), 64.30 (C-1, Et), 67.44 (C-5), 68.64 (C-4), 72.05 ($ArCH_2O$), 73.10 (C-3), 77.19 (C-2), 96.63 (C-1), 103.55 [dd, $^2J_{C,F}$ = 23 Hz + 26 Hz, C-3 (2,4-F_2-C_6H_3)], 111.24 [dd, $^2J_{C,F}$ = 22, $^4J_{C,F} \approx$ 4 Hz, C-5 (2,4-F_2-C_6H_3)], 113.27 (C-3, 3-CN-C_6H_4), 115.30 [d, $^2J_{C,F}$ = 20 Hz, C_m (4-F-$C_6H_4CH_2$)], 118.38 (C-6, 3-CN-C_6H_4), 121.83 [br., C-6 (2,4-F_2-C_6H_3)], 122.77 (C-2, 3-CN-C_6H_4), 127.08 (C-4, 3-CN-C_6H_4), 128.88, 129.27 [$C_{o,m}$ (4-Tol)], 129.58 [br. d, $^3J_{C,F}$ = 7 Hz, C_o (4-F-$C_6H_4CH_2$)], 129.86 (C-5, 3-CN-C_6H_4), 130.07 (C_i, 4-Tol), 133.52 (C_p, 4-Tol), 136.88 (C_i, 4-F-$C_6H_4CH_2$), 138.59 (C_i, 3-CN-C_6H_4), 152.05, 152.44 (2 × $ArNHCO$), 171.01 (CO, $ArCH_2CO$) ppm.

Ethyl 6-*O*-[(3-Cyanophenyl)carbamoyl]-3-*O*-[(4-ethoxycarbonylphenyl)carbamoyl]-2-*O*-(4-fluorobenzyl)-4-*O*-(4-tolylacetyl)-α/β-D-glucopyranoside (8-2-b3): 13.0 mg (35%), colorless oil; R_f (α) = 0.38 (Tol/EtOH, 9:1). HPLC: t_R = 8.87 min (71.2%, α), 9.00 min (24.8%, β?), 9.97 min (4.1%). ESI-MS: *m/z* (%) = 1195.2 (9) [3M + $Ca]^{2+}$, 806.3 (80) $[M + Na]^+$ {calcd. for $C_{42}H_{42}FN_3O_{11}$ + Na: 806.3}, 803.7 (100) $[2M + Ca]^{2+}$, 795.5 (17) $[2M + Mg]^{2+}$, 785.4 (7), 770.2 (14) [2,6-(4-F-$C_6H_4CH_2)_2$ + $Na]^+$, 657.3 (8) [3-Pr + $Na]^+$, 312.1 (6).

Ethyl 6-*O*-[(3-Cyanophenyl)carbamoyl]-2-*O*-(4-fluorobenzyl)-4-*O*-(4-tolylacetyl)-3-*O*-{[4-(trifluoromethyl)phenyl]carbamoyl}-α/β-D-glucopyranoside (8-2-b4): 20.4 mg (55%), colorless oil; R_f (α) = 0.40 (Tol/EtOH, 9:1). HPLC: t_R = 9.43 min (69.1%, α), 9.55 min (26.6%, β?), 10.40 min (3.9%). ESI-MS: *m/z* (%) = 1189.2 (19) [3M + $Ca]^{2+}$, 807.3 (19), 802.2 (100) $[M + Na]^+$ {calcd. for $C_{40}H_{37}F_4N_3O_9$ + Na: 802.2}, 799.3 (89) $[2M + Ca]^{2+}$, 791.5 (30) $[2M + Mg]^{2+}$, 781.3 (14), 778.1 (7), 766.2 (24) [2,6-(4-F-$C_6H_4CH_2)_2$ + $Na]^+$, 760.1 (8), 657.3 (23) [3-Pr + $Na]^+$, 631.2 (7), 621.2 (14) [2,6-(4-F-$C_6H_4CH_2)_2$-3-Pr + $Na]^+$, 528.2 (9), 321.1 (15).

Ethyl 4-*O*-[(4-Chlorophenyl)carbamoyl]-6-*O*-[(3-cyanophenyl)-carbamoyl]-2-*O*-(4-fluorobenzyl)-α/β-D-glucopyranoside (8-2-c1): 18.7 mg (64%), colorless crystals; R_f (α) = 0.29 (Tol/EtOH, 9:1), HPLC: t_R = 6.02 min (81.7%, α), 6.23 min (13.0%, β), 7.37 min (5.3%). ESI-MS: *m/z* (%) = 1249.3 (11) $[2M + Na]^+$, 940.7 (12) $[3M + Ca]^{2+}$, 677.2 (33) $[M + MeCN + Na]^+$, 659.7 (10, contains Cl), 653.6 (19) $[2M + MeCN + Ca]^{2+}$, 641.1 (26, contains Cl), 636.1 (100) $[M + Na]^+$ {calcd. for $C_{30}H_{29}ClFN_3O_8$ + Na: 636.2}, 634.2 (46) $[2M + Ca]^{2+}$, 625.3 (11) $[2M + Mg]^{2+}$, 600.1 (8) [2,6-(4-F-$C_6H_4CH_2)_2$ + $Na]^+$, 540.2 (9), 437.2 (8).

Ethyl 4-*O*-[(4-Chlorophenyl)carbamoyl]-6-*O*-[(3-cyanophenyl)-carbamoyl]-3-*O*-[(2,4-difluorophenyl)carbamoyl]-2-*O*-(4-fluorobenzyl)-α/β-D-glucopyranoside (8-2-c2): 12.6 mg (34%), colorless crystals; R_f (α) = 0.38 (Tol/EtOH, 9:1). HPLC: t_R = 7.93 min (81.7%, α), 8.07 min (9.2%, β), 9.10 min (9.1%). ESI-MS: *m/z* (%) = 791.2 (100) $[M + Na]^+$ {calcd. for $C_{30}H_{29}ClFN_3O_8$ + Na: 791.2}, 788.3 (30) $[2M + Ca]^{2+}$, 755.1 (46) [2,6-(4-F-$C_6H_4CH_2)_2$ + $Na]^+$, 746.1 (55), 678.3 (20) $[3-Pr + Na]^+$, 460.1 (12), 419.2 (16, contains Cl), 235.0 (13).

Ethyl 4-*O*-[(4-Chlorophenyl)carbamoyl]-6-*O*-[(3-cyanophenyl)-carbamoyl]-3-*O*-[(4-ethoxycarbonylphenyl)carbamoyl]-2-*O*-(4-fluorobenzyl)-α/β-D-glucopyranoside (8-2-c3): 20.0 mg (52%), colorless crystals; R_f (α) = 0.32 (Tol/EtOH, 9:1). HPLC-MS: t_R = 8.03 min (78.9%; *m/z* = 827.2 [M(α) + $Na]^+$}, 8.18 min {13.9%; *m/z* = 827.2 [M(β) + $Na]^+$}, 9.20 min {5.8%; *m/z* = 791.1 [2,6-(4-F-$C_6H_4CH_2)_2$(α) + $Na]^+$, 832.2 [2,6-(4-F-$C_6H_4CH_2)_2$(α) + MeCN + $Na]^+$}. ESI-MS: *m/z* (%) = 827.2 (100) $[M + Na]^+$ {calcd. for $C_{40}H_{38}ClFN_4O_{11}$ + Na: 827.2}, 824.4 (53) $[2M + Ca]^{2+}$, 817.4 (14) $[2M + Mg]^{2+}$, 791.2 (18) [2,6-(4-F-$C_6H_4CH_2)_2$ + $Na]^+$, 782.2 (13), 678.3 (14) $[3-Pr + Na]^+$, 483.6 (9), 304.1 (11), 288.1 (7).

Ethyl 4-*O*-[(4-Chlorophenyl)carbamoyl]-6-*O*-[(3-cyanophenyl)-carbamoyl]-2-*O*-(4-fluorobenzyl)-3-*O*-{[4-(trifluoromethyl)-phenyl]carbamoyl}-α/β-D-glucopyranoside (8-2-c4): 19.8 mg (52%), colorless amorphous powder; R_f (α) = 0.35 (Tol/EtOH, 9:1). HPLC: t_R = 8.65 min (81.4%, α), 8.77 min (13.5%, β), 9.68 min (5.1%). ESI-MS: *m/z* (%) = 1221.7 (12) $[3M + Ca]^{2+}$, 823.2 (91) $[M + Na]^+$ {calcd. for $C_{38}H_{33}ClF_4N_4O_9$ + Na: 823.2}, 820.5 (100) $[2M + Ca]^{2+}$, 813.4 (25) $[2M + Mg]^{2+}$, 778.2 (13), 693.2 (11, contains Cl), 678.2 (20) $[3-Pr + Na]^+$, 545.3 (10, contains Cl), 437.2 (11), 419.2 (12), 334.0 (12), 330.0 (12), 235.0 (10). ESI-HRMS: calcd. for $C_{38}H_{33}ClF_4N_4O_9$+Na: 823.1770, found 823.1773.

Preparation of Compounds 8-3: The synthesis was carried out according to the protocol for preparation of compounds **8-2**. 4-Methylbenzyl bromide was used for alkylation of O-2, O-6 was carbamoylated with 4-chlorophenyl isocyanate. Variation of O-4 and O-3 was carried out as described for the preparation of compounds **8-2**. Again, bromine was used for cleavage of the 3-*O*-(4-trifluoromethylphenyl)- and the 3-*O*-[4-(ethoxycarbonyl)phenyl] carbamates from the resin (vide supra).

Ethyl 6-*O*-[(4-Chlorophenyl)carbamoyl]-4-*O*-[(4-fluorophenyl)-carbamoyl]-2-*O*-(4-methylbenzyl)-α/β-D-glucopyranoside (8-3-a1): 21.9 mg (81%), colorless crystals; R_f (α) = 0.30 (Tol/EtOH, 9:1). HPLC: t_R = 5.80 min (5.4%), 7.15 min (69.8%, α), 7.37 min (14.4%, β), 7.80 min (5.0%). ESI-MS: *m/z* (%) = 1227.4 (7) $[2M + Na]^+$, 1178.4 (7) [M + 2,6-(4-Me-$C_6H_4CH_2)_2$ + $Na]^+$, 924.3 (8) [3M + $Ca]^{2+}$, 678.2 (8) [1-NSu + $Na]^+$, 666.2 (43) [M + MeCN + $Na]^+$, 663.3 (8), 642.6 (7, contains Cl), 625.1 (68) $[M + Na]^+$ {calcd. for $C_{30}H_{32}ClFN_2O_8$ + Na: 625.2}, 617.2 (40) [2,6-(4-Me-$C_6H_4CH_2)_2$

+ MeCN + Na]$^+$, 592.2 (14) [2,4-(4-Me-$C_6H_4CH_2)_2$ + Na]$^+$, 576.3 (100) [2,6-(4-Me-$C_6H_4CH_2)_2$ + Na]$^+$, 433.2 (11).

Ethyl 6-*O*-[(4-Chlorophenyl)carbamoyl]-3-*O*-[(2,4-difluorophenyl)-carbamoyl]-4-*O*-[(4-fluorophenyl)carbamoyl]-2-*O*-(4-methylbenzyl)-α/β-D-glucopyranoside (8-3-a2): 14.6 mg (43%), colorless crystals; R_f (α) = 0.36 (Tol/EtOH, 9:1). HPLC: t_R = 7.68 min (11.7%), 8.83 min (66.6%, α), 9.50 min (14.7%). ESI-MS: *m*/*z* (%) = 780.1 (43) [M + Na]$^+$ {calcd. for $C_{37}H_{35}ClF_3N_3O_9$ + Na: 780.2}, 775.2 (7, contains 2Cl), 752.5 (7, contains Cl), 747.1 (37) [2,4-(4-Me-$C_6H_4CH_2)_2$ + Na]$^+$, 731.2 (100) [2,6-(4-Me-$C_6H_4CH_2)_2$ + Na]$^+$, 698.3 (9), 667.3 (9) [3-Pr + Na]$^+$, 618.2 (12) [2,6-(4-Me-$C_6H_4CH_2)_2$-3-Pr + Na]$^+$, 576.2 (7) [2,6-(4-Me-$C_6H_4CH_2)_2$-3-OH + Na]$^+$, 433.2 (9).

Ethyl 6-*O*-[(4-Chlorophenyl)carbamoyl]-3-*O*-[(4-ethoxycarbonylphenyl)carbamoyl]-4-*O*-[(4-fluorophenyl)carbamoyl]-2-*O*-(4-methylbenzyl)-α/β-D-glucopyranoside (8-3-a3): 19.9 mg (56%) colorless oil; R_f (α) = 0.32 (Tol/EtOH, 9:1). HPLC-MS: t_R = 8.98 min {87.4%; *m*/*z* = 816.2 [M(α) + Na]$^+$, 857.2 [M(α) + MeCN + Na]$^+$}, 9.18 min {6.7%; *m*/*z* = 816.2 [M(β) + Na]$^+$, 857.2 [M(β) + MeCN + Na]$^+$}, 9.60 min {6.0%; *m*/*z* (%) = 767.2 [2,6-(4-Me-$C_6H_4CH_2)_2$ + Na]$^+$}. ESI-MS: *m*/*z* = 857.2 (17) [M + MeCN + Na]$^+$, 816.3 (49) [M + Na]$^+$ {calcd. for $C_{40}H_{41}ClF\ N_3O_{11}$ + Na: 816.2}, 813.6 (44) [2M + Ca]$^{2+}$, 805.5 (15) [2M + Mg]$^{2+}$, 788.9 (16), 783.2 (23, contains Cl), 767.2 (100) [2,6-(4-Me-$C_6H_4CH_2)_2$ + Na]$^+$, 667.3 (29) [3-Pr + Na]$^+$, 663.3 (12, contains Cl), 618.2 (22) [2,6-(4-Me-$C_6H_4CH_2)_2$-3-Pr + Na]$^+$, 433.2 (11), 304.1 (11). ESI-HRMS: calcd. for $C_{40}H_{41}ClFN_3O_{11}$+Na: 816.2311, found 816.2280. The crude product was purified by flash chromatography on silica gel (eluent hexanes/ethyl acetate, 3:1): 13.7 mg (37%) colorless crystals, m.p. 222−224 °C. $[\alpha]_D^{25}$ = +61 (*c* = 1.14, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.30 (t, *J* = 7.0 Hz, 3 H, 1-OCH$_2$C*H*$_3$), 1.38 (t, *J* = 7.0 Hz, 3 H, ArCOOCH$_2$C*H*$_3$), 2.24 (s, 3 H, ArCH$_3$), 3.52 (br. dq, J_d = 9.7, J_q = 7.0 Hz 1 H, 1-OC*H*$_2$CH$_3$), 3.79 (br. dq, J_d = 9.7, J_q = 7.0 Hz, 1 H, 1-OC*H*$_2$CH$_3$), 3.87 (br. d, *J* ≈ 10 Hz, 1 H, 2-H), 4.11 (br. pseudo-dt, J_d ≈ 10.3 Hz, 1 H, 5-H), 4.24 (br. d, J_{gem} ≈ 12 Hz, 1 H, 6b-H), 4.59 (d, J_{gem} = 11.4 Hz, 1 H, ArC*H*$_2$O), 4.52−4.69 (m, 3 H, 6a-H, ArC*H*$_2$O), contained in this multiplet: 4.66 (d, J_{gem} = 11.4 Hz, 1 H, ArC*H*$_2$O), 5.02 (d, 1 H, $J_{1,2}$ ≈ 2.6 Hz, 1-H), 5.18 (br. pseudo-t, 1 H, 4-H), 5.53 (pseudo-t, *J* ≈ 10 Hz, 1 H, 3-H), 6.73−6.87 [m, 4 H, *m*-H$_2$ (4-F-C_6H_4), (4-F-C_6H_4N*H*CO), (4-Cl-C_6H_4N*H*CO)], 6.96−7.25 [m, *o*-H$_2$ (4-EtO$_2$C-C_6H_4), (4-Cl-C_6H_4NH), *o*-H$_2$ (4-F-C_6H_4), (4-Me-$C_6H_4CH_2$)], 7.49 (br. s, 1 H, 4-EtO$_2$C-C_6H_4N*H*CO), 7.76 [d, *J* = 8.5 Hz, 2 H, *m*-H$_2$ (4-EtO$_2$C-C_6H_4)] ppm. The NMR spectrum shows minor impurities.

Ethyl 6-*O*-[(4-Chlorophenyl)carbamoyl]-4-*O*-[(4-fluorophenyl)-carbamoyl]-2-*O*-(4-methylbenzyl)-3-*O*-{[4-(trifluoromethyl)phenyl]-carbamoyl}-α/β-D-glucopyranoside (8-3-a4): 21.0 mg (60%), colorless crystals; R_f (α) = 0.34 (Tol/EtOH, 9:1), HPLC: t_R = 9.45 min (87.4%, α), 9.67 min (7.7%, β), 10.03 min (4.9%). ESI-MS: *m*/*z* (%) = 853.2 (26) [M + MeCN + Na]$^+$, 812.2 (43) [M + Na]$^+$ {calcd. for $C_{38}H_{36}ClF_4N_3O_9$ + Na: 812.2}, 810.4 (55) [2M + Ca]$^{2+}$, 805.4 (12, contains Cl), 802.6 (12), 784.7 (12), 779.2 (29, contains Cl), 763.2 (100) [2,6-(4-Me-$C_6H_4CH_2)_2$ + Na]$^+$, 730.2 (11), 667.3 (27) [3-Pr + Na]$^+$, 618.2 (21) [2,6-(4-Me-$C_6H_4CH_2)_2$ − 3-Pr + Na]$^+$, 433.2 (25), 415.2 (12), 392.2 (12), 311.1 (14).

Ethyl 6-*O*-[(4-Chlorophenyl)carbamoyl]-2-*O*-(4-methylbenzyl)-4-*O*-(4-tolylacetyl)-α/β-D-glucopyranoside (8-3-b1): 21.0 mg (79%), colorless oil; R_f (α) = 0.36 (Tol/EtOH, 9:1). HPLC-MS: t_R = 7.00 min {4.8%; *m*/*z* (%) = 673.2 [1-NSu(α) + Na]$^+$}, 8.52 min {80.8%; *m*/*z* (%) = 620.1 [M(α) + Na]$^+$, 661.2 [M(α) + MeCN + Na]$^+$}, 8.75 min {9.7%; *m*/*z* (%) = 620.1 [M(α) + Na]$^+$, 661.2 [M(α) + MeCN + Na]$^+$}, 9.33 min {3.7%; *m*/*z* (%) = 571.3 [2,6-(4-Me-$C_6H_4CH_2)_2$(α) + Na]$^+$, 612.2 [2,6-(4-Me-$C_6H_4CH_2)_2$(α) + MeCN + Na]$^+$}. ESI-MS: *m*/*z* (%) = 1217.5 (6) [2M + Na]$^+$, 1168.4 (7) [M + 2,6-(4-Me-$C_6H_4CH_2)_2$ + Na]$^+$, 673.3 (8) [1-NSu + Na]$^+$, 620.1 (96) [M + Na]$^+$ {calcd. for $C_{32}H_{36}ClNO_8$ + Na: 620.2}, 613.2 (10), 599.2 (17), 571.3 (100) [2,6-(4-Me-$C_6H_4CH_2)_2$ + Na]$^+$.

Ethyl 6-*O*-[(4-Chlorophenyl)carbamoyl]-3-*O*-[(2,4-difluorophenyl)-carbamoyl]-2-*O*-(4-methylbenzyl)-4-*O*-(4-tolylacetyl)-α/β-D-glucopyranoside (8-3-b2): 14.2 mg (42%), colorless amorphous solid; R_f (α) = 0.47 (Tol/EtOH, 9:1), HPLC: t_R = 9.02 min (5.1%), 10.07 min (84.5%, α), 10.75 min (6.7%). ESI-MS: *m*/*z* (%) = 779.2 (17%), 775.2 (44) [M + Na]$^+$ {calcd. for $C_{39}H_{39}ClF_2N_2O_9$ + Na: 775.2}, 770.2 (9, contains Cl), 747.2 (15) [1-OH + Na]$^+$, 726.2 (100) [2,6-(4-Me-$C_6H_4CH_2)_2$ + Na]$^+$, 698.3 (8) [2,6-(4-Me-$C_6H_4CH_2)_2$-1-OH + Na]$^+$, 613.2 (8) [2,6-(4-Me-$C_6H_4CH_2)_2$-3-Pr + Na]$^+$.

Ethyl 6-*O*-[(4-Chlorophenyl)carbamoyl]-3-*O*-[(4-ethoxycarbonylphenyl)carbamoyl]-2-*O*-(4-methylbenzyl)-4-*O*-(4-tolylacetyl)-α/β-D-glucopyranoside (8-3-b3): 21.6 mg (61%), colorless crystals; R_f (α) = 0.42 (Tol/EtOH, 9:1). HPLC: t_R = 10.22 min (80.2%, α), 10.40 min (16.2%, β), 10.92 min (3.6%). ESI-MS: *m*/*z* (%) = 811.3 (60) [M + Na]$^+$ {calcd. for $C_{42}H_{45}ClN_2O_{11}$ + Na: 811.3}, 809.6 (43) [2M + Ca]$^{2+}$, 801.4 (10) [2M + Mg]$^{2+}$, 790.3 (13), 784.3 (16, contains Cl), 762.3 (100) [2,6-(4-Me-$C_6H_4CH_2)_2$ + Na]$^+$, 662.3 (22) [3-Pr + Na]$^+$, 613.2 (31) [2,6-(4-Me-$C_6H_4CH_2)_2$ − 3-Pr + Na]$^+$, 312.1 (10).

Ethyl 6-*O*-[(4-Chlorophenyl)carbamoyl]-2-*O*-(4-methylbenzyl)-4-*O*-(4-tolylacetyl)-3-*O*-[[4-(trifluoromethyl)phenyl]carbamoyl}-α/β-D-glucopyranoside (8-3-b4): 19.8 mg (56%), colorless crystals; R_f (α) = 0.46 (Tol/EtOH, 9:1). HPLC: t_R = 10.70 min (81.1%, α), 10.87 min (15.3%, β), 11.30 min (3.6%). ESI-MS: *m*/*z* (%) = 848.3 (11) [M + MeCN + Na]$^+$, 807.3 (27) [M + Na]$^+$ {calcd. for $C_{40}H_{40}ClF_3N_2O_9$ + Na: 807.2}, 805.5 (26) [2M + Ca]$^{2+}$, 786.3 (13), 780.2 (15), 758.2 (100) [2,6-(4-Me-$C_6H_4CH_2)_2$ + Na]$^+$, 730.2 (8) [2,6-(4-Me-$C_6H_4CH_2)_2$-1-OH + Na]$^+$, 662.3 (21) [3-Pr + Na]$^+$, 613.2 (27) [2,6-(4-Me-$C_6H_4CH_2)_2$-3-Pr + Na]$^+$, 312.1 (10).

Ethyl 6-*O*-[(4-Chlorophenyl)carbamoyl]-4-*O*-[(3-cyanophenyl)-carbamoyl]-2-*O*-(4-methylbenzyl)-α/β-D-glucopyranoside (8-3-c1): 21.3 mg (78%), colorless amorphous solid; R_f (α) = 0.23 (Tol/EtOH, 9:1). HPLC: t_R = 6.75 min (83.8%, α), 6.98 min (8.5%, β), 7.40 min (4.0%). ESI-MS: *m*/*z* (%) = 1241.4 (12) [2M + Na]$^+$, 1192.4 (13) [M + 2,6-(4-Me-$C_6H_4CH_2)_2$ + Na]$^+$, 935.0 (12) [3M + Ca]$^{2+}$, 910.5 (8) [2M + 2,6-(4-Me-$C_6H_4CH_2)_2$ + Ca]$^{2+}$, 673.3 (22) [M + MeCN + Na]$^+$, 664.3 (10), 632.1 (100) [M + Na]$^+$ {calcd. for $C_{31}H_{32}ClN_3O_8$ + Na: 632.2}, 629.3 (15) [2M + Ca]$^{2+}$, 592.2 (33, contains Cl), 583.2 (79) [2,6-(4-Me-$C_6H_4CH_2)_2$ + MeCN + Na]$^+$, 543.3 (17), 433.2 (21), 421.3 (9), 392.2 (11).

Ethyl 6-*O*-[(4-Chlorophenyl)carbamoyl]-4-*O*-[(3-cyanophenyl)-carbamoyl]-3-*O*-[(2,4-difluorophenyl)carbamoyl]-2-*O*-(4-methylbenzyl)-α/β-D-glucopyranoside (8-3-c2): 13.1 mg (38%), colorless crystals; R_f (α) = 0.32 (Tol/EtOH, 9:1). HPLC: t_R = 7.22 min (5.6%), 7.47 min (3.3%), 8.45 min (63.0%, α), 9.07 min (20.4%). ESI-MS: *m*/*z* (%) = 828.3 (17) [M + MeCN + Na]$^+$, 791.2 (26%), 787.2 (44) [M + Na]$^+$ {calcd. for $C_{38}H_{35}ClF_2N_4O_9$ + Na: 787.2}, 747.1 (88, contains Cl), 738.2 (100) [2,6-(4-Me-$C_6H_4CH_2)_2$ + Na]$^+$, 698.3 (21), 674.3 (19) [3-Pr + Na]$^+$, 625.2 (19) [2,6-(4-Me-$C_6H_4CH_2)_2$-3-Pr + Na]$^+$, 433.2 (13), 415.2 (15), 311.1 (15), 261.1 (16), 209.0 (13).

Ethyl 6-*O*-[(4-Chlorophenyl)carbamoyl]-4-*O*-[(3-cyanophenyl)-carbamoyl]-3-*O*-[(4-ethoxycarbonylphenyl)carbamoyl]-2-*O*-(4-

methylbenzyl)-α/β-D-glucopyranoside (8-3-c3): 18.5 mg (52%), colorless crystals; R_f (α) = 0.27 (Tol/EtOH, 9:1). HPLC: t_R = 8.62 min (85.2%, α), 8.82 min (6.1%, β), 9.22 min (8.7%). ESI-MS: *m/z* (%) = 864.3 (18) [M + MeCN + Na]$^+$, 823.3 (82) [M + Na]$^+$ {calcd. for $C_{41}H_{41}ClN_4O_{11}$ + Na: 823.2}, 820.5 (41) [2M + Ca]$^{2+}$, 815.4 (34) [2,6-(4-Me-$C_6H_4CH_2$)$_2$ + MeCN + Na]$^+$, 783.3 (24), 774.3 (100) [2,6-(4-Me-$C_6H_4CH_2$)$_2$ + Na]$^+$, 674.3 (31) [3-Pr + Na]$^+$, 625.2 (22) [2,6-(4-Me-$C_6H_4CH_2$)$_2$ − 3-Pr + Na]$^+$, 536.2 (12), 311.1 (13).

Ethyl 6-*O*-[(4-Chlorophenyl)carbamoyl]-4-*O*-[(3-cyanophenyl)-carbamoyl]-2-*O*-(4-methylbenzyl)-3-*O*-{[4-(trifluoromethyl)-phenyl]carbamoyl}-α/β-D-glucopyranoside (8-3-c4): 15.4 mg (43%), colorless amorphous solid; R_f (α) = 0.28 (Tol/EtOH, 9:1). HPLC-MS: t_R = 9.10 min {82.4%; *m/z* = 819.2 [M(α) + Na]$^+$, 860.1 [M(α) + MeCN + Na]$^+$}, 9.30 min {6.0%; *m/z* = 819.2 [M(β) + Na]$^+$, 860.1 [M(β) + MeCN + Na]$^+$}, 9.65 min {10.1%; *m/z* = 770.2 [2,6-(4-Me-$C_6H_4CH_2$)$_2$(α) + Na]$^+$, 811.3 [2,6-(4-Me-$C_6H_4CH_2$)$_2$(α) + MeCN + Na]$^+$}. ESI-MS: *m/z* (%) = 860.2 (54) [M + MeCN + Na]$^+$, 819.3 (49) [M + Na]$^+$ {calcd. for $C_{39}H_{36}ClF_3N_4O_9$ + Na: 819.2}, 816.4 (55) [2M + Ca]$^{2+}$, 811.3 (59) [2,6-(4-Me-$C_6H_4CH_2$)$_2$ + MeCN + Na]$^+$, 779.2 (54, contains Cl), 770.2 (100) [2,6-(4-Me-$C_6H_4CH_2$)$_2$ + Na]$^+$, 674.3 (53) [3-Pr + Na]$^+$, 666.3 (23), 625.2 (31) [2,6-(4-Me-$C_6H_4CH_2$)$_2$-3-Pr + Na]$^+$, 433.2 (25).

Acknowledgments

T. O. is grateful to the Fonds der Chemischen Industrie for a Kekulé fellowship.

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Received October 26, 2002
[O02485]