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Carbohydrate-Based VEGF Inhibitors

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Cyclic peptide–carbohydrates (compounds **1a–c**, **2**, **33**, **34**) were designed and synthesized to act as mimetics of loop 2 of the proangiogenic molecule vascular endothelial growth factor D (VEGF-D). The mimetics were designed to inhibit dimerization of the receptors (VEGFR-2 and VEGFR-3) by VEGF-D, and thus have the potential to inhibit angiogenesis. To this end, in the previously described cyclic octapeptide CNEESLIC and the cyclic nonapeptide CGNEESLIC inhibitors derived from VEGF-D loop 2, the NEES tetrapeptide residue was replaced by a carbohydrate scaffold having the amino acid side chain mimics in positions proposed by modeling studies. Attachment of the additional amino acids using the Fmoc technology, then formation of the cyclic disulfides, and finally total deprotection afforded the target molecules of which **2** and **34** showed an ability to inhibit the biological activity of VEGF-D through VEGFR-2 in cell-based assays, albeit at high mimetic concentration.

Introduction

As far back as in 1971 it was proposed that angiogenesis plays an important role in tumour growth.[1] Since then, this proposal has been confirmed and widely accepted[2,3] and the mechanism of angiogenesis has been extensively studied.[4–6] Various factors stimulating or inhibiting angiogenesis have been found.[6,7] Important stimulators of angiogenesis and tumour angiogenesis are the vascular endothelial growth factors (VEGFs), a family consisting of VEGF-A, -B, -C, -D, and -E.[8] Their three-dimensional structure has been determined by X-ray analysis[10] A three-dimensional model of the VEGF-D dimer was deduced from the VEGF-A X-ray structure[10] by applying protein-homology modeling techniques.[9] The VEGF monomer consists essentially of a central four-stranded antiparallel β-sheet, three additional β-sheet segments, and two short α-helices. The stabilization of the tertiary structure of the monomer is based on a cystine knot consisting of three intramolecular disulfide bridges. There are three loops connecting the central β-sheets, which are located at the tips of the monomers. The amino acids of these loops are responsible for the interaction with the receptors.[8,10] The monomer forms as quaternary structure a side-by-side homodimer, in which the monomers are covalently linked through two disulfide bridges. The head-to-tail orientation of the monomers in the dimer provides two poles for binding to the VEGF receptors (VEGFRs) of which the most important are VEGFR-1, -2 and -3.[8,11] They are transmembrane proteins and, when dimerized by VEGF dimers, they undergo a conformational change leading to autophosphorylation of tyrosine side chains of the tyrosine kinase domain in the intracellular part. This way, a signalling cascade leading to angiogenesis is induced.

In the pathologic angiogenesis, VEGFR-1 and VEGFR-2 seem to play a particularly important role,[12,13] therefore the search for therapeutic pro- and particularly anti-angiogenic compounds has concentrated on these receptors.[8] Success in in vivo and in vitro studies strongly promoted this endeavour,[2,8,14–16] and various clinical studies have been performed.[17] Because of the complexity of angiogenesis various possibilities exist to fight tumour growth.[18] We concentrated on the inhibition of the VEGF homodimer binding to VEGFR.

It was previously found that monocyclic peptides possessing the sequence and the conformation, for instance of loops 1–3 of VEGF-D by constructing the loop sequence between two cysteine residues and cyclising this construct by a disulfide bridge, leads to excellent inhibitors of VEGF-D binding to VEGFR-2.[9] The therapeutic importance of such compounds is generally compromized by their lability towards proteases.[19] Therefore, mimicking peptides by different scaffolds has become an important goal. In this context, carbohydrate scaffolds have been shown to be useful:[20–25] they are rigid, stereochemically defined, polyfunctional, and generally the starting materials are readily available. This way, peptide mimetic molecules can be designed with the required functionalities in the required positions in space. In this paper carbohydrate-based mimetics of

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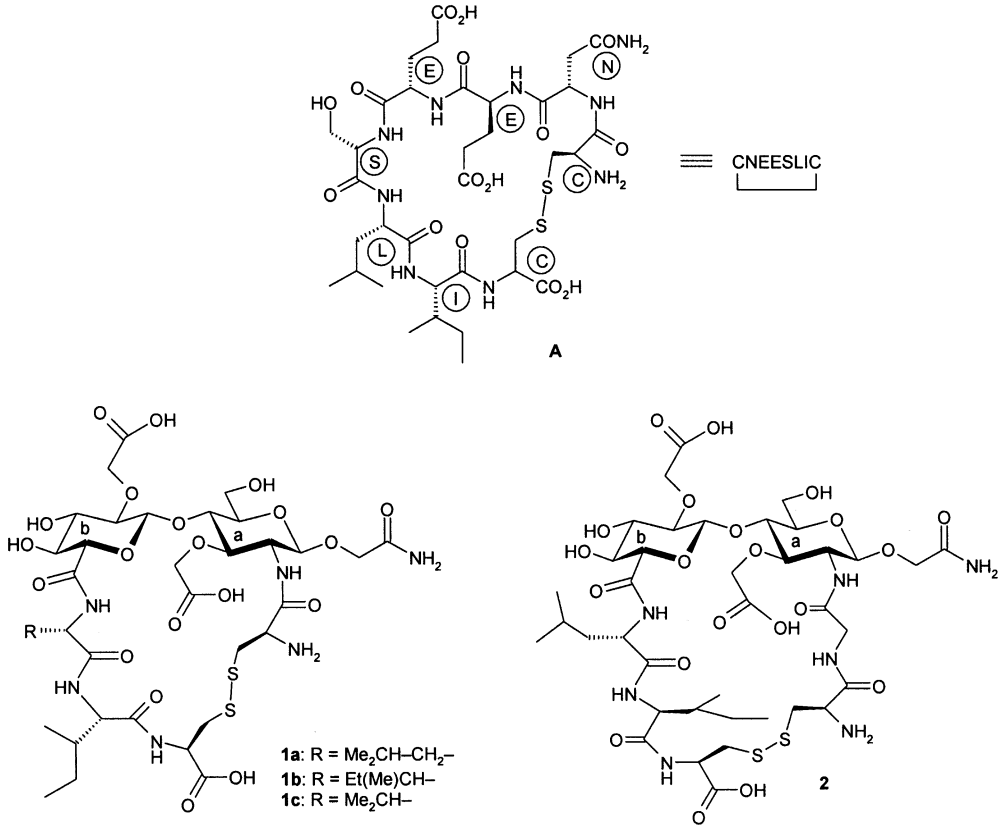


Figure 1. Structure of target molecules **1a**–**c** and **2**.

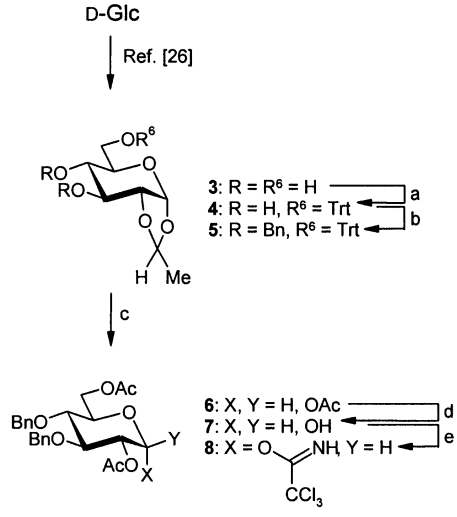
VEGF-D loop 2 mimetic CNEESLIC (**A** in Figure 1) are presented, which were designed based on molecular modeling studies.[9]

Results and Discussion

Synthesis of Target Molecules 1a–1c and 2

The modeling studies exhibited that the NEES tetrapeptide moiety of cyclic octapeptide **A** can be relatively well accommodated by an appropriately functionalized Glcβ(1–4)GlcNH$_2$ disaccharide residue. Hence, the mimetic **1a** was designed as target molecule (Figure 1). These studies also permitted replacement of the leucine residue by isoleucine or valine, therefore also the mimetics **1b** and **1c**, respectively, were target molecules. Additionally, ring expansion by one glycine residue between the first cysteine and the asparagine residues gave a good fit with **A**, therefore also compound **2** was considered as target molecule.

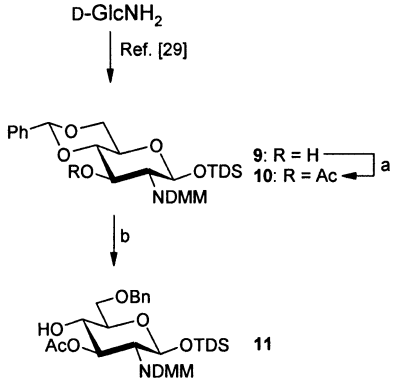
For the synthesis of the Glcβ(1–4)GlcNH$_2$ disaccharide moiety, the **b** residue (see Figure 1) requires temporary protection at 1-*O*, 2-*O* and 6-*O*. To this end, glucose was transformed, according to a known procedure,[26] into 1,2-*O*-ethylidene derivative **3** (Scheme 1). Regioselective 6-*O*-tritylation with trityl chloride in pyridine[27] afforded compound **4**, which on *O*-benzylation with benzyl bromide and sodium hydride in DMF furnished the fully protected glucose derivative **5**, which had at 3-*O* and 4-*O* the desired



Scheme 1. Synthesis of glycosyl donor **8**. Reagents and conditions: (a) Trt-Cl, Pyr (62%); (b) BnBr, NaH, DMF (78%); (c) HOAc, H_2O; Ac_2O, Pyr (90%); (d) N_2H_4·HOAc (90%); (e) CCl_3CN, DBU, CH_2Cl_2 (99%).

"permanent" protection. Acid-catalyzed cleavage of the trityl and the 1,2-*O*-ethylidene groups and then *O*-acetylation afforded compound **6**. Treatment with hydrazinium acetate led to regioselective 1-*O*-deacetylation (→ **7**); reaction with trichloroacetonitrile in the presence of 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU)[28] afforded the *O*-glucosyl trichloroacetimidate **8** in good overall yield.

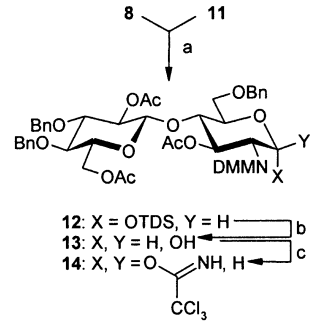
For the synthesis of the **a** residue (see Figure 1) requiring selective access to 1-*O*, 2-*N*, 3-*O* and 4-*O*, D-glucosamine was transformed into *N*-dimethylmaleoyl (*N*-DMM) protected thexyldimethylsilyl (TDS) 2-amino-4,6-*O*-benzylidene-2-deoxy-glucopyranoside **9** according to a known procedure (Scheme 2).[29] 3-*O*-Acetylation with acetic anhydride in pyridine afforded compound **10** which on treatment with sodium cyanoborohydride in the presence of hydrochloric acid in diethyl ether[30] furnished the 6-*O*-benzyl-protected derivative **11** which had the required protecting-group pattern for selectively accessing the functional groups in positions 1–4. Glycosylation of **11** with glycosyl donor **8** and trimethylsilyl trifluoromethanesulfonate (TMSOTf) as catalyst (0.1 equiv.) in dichloromethane at –5 °C afforded the desired β-linked disaccharide **12** ($J_{1b,2b}$ = 8.0 Hz) in high yield (Scheme 3). Treatment of **12** with tetrabutylammonium fluoride (TBAF) in THF led to the 1-*O*-desilylated compound **13** which gave with trichloroacetonitrile in the presence of DBU the trichloroacetimidate **14** as glycosyl donor.



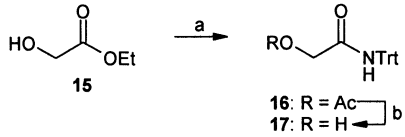
Scheme 2. Synthesis of acceptor **11**. Reagents and conditions: (a) Ac_2O, Pyr (98%); (b) $NaCHBH_3$, HCl, Et_2O (93%).

For the attachment of the asparagine side-chain mimic, ethyl glycolate (Scheme 4, **15**)[31] was treated with ammonia in methanol; *O*-acetylation with acetic anhydride in pyridine and following *N*-tritylation with triphenylcarbinol in acetic anhydride/sulfuric acid furnished the intermediate **16**. *O*-Deacetylation with sodium methoxide in methanol gave the desired acceptor **17**.

Glycosylation of **17** with the disaccharide donor **14** and TMSOTf as catalyst (0.08 equiv.) in dichloromethane at –15 °C furnished the β-linked glycoside **18** ($J_{1a,2a}$ = 8.5 Hz) in high yield (Scheme 5). For the regioselective introduction of the other amino acid side-chain mimics the *O*-acetyl groups of **18** were removed by treatment with sodium methoxide in methanol (→ **19**) and then the DMM group was

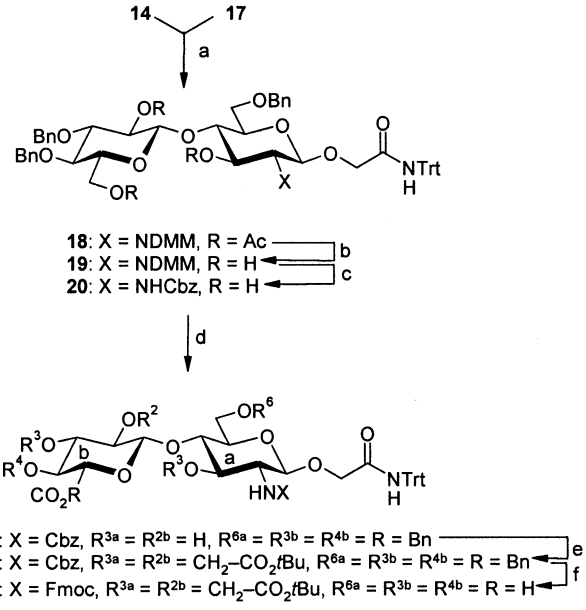


Scheme 3. Synthesis of disaccharide donor **14**. Reagents and conditions: (a) TMSOTf, –5 °C, CH_2Cl_2 (95%); (b) TBAF, HOAc, THF (95%); (c) CCl_3CN, DBU, CH_2Cl_2 (92%).



Scheme 4. Synthesis of acceptor **17**. Reagents and conditions: (a) (1) NH_3, MeOH; Ac_2O, Pyr; (2) Trt-OH, H_2SO_4, Ac_2O (42%); (b) NaOMe, MeOH (93%).

replaced by a Cbz group because the DMM group is not stable under the following oxidation conditions. To this end, **19** was first treated with sodium hydroxide, and thereafter the pH was adjusted to 4.5 with hydrochloric acid, this way liberating the amino group;[29,32] following treatment with benzyloxycarbonyl (Cbz) chloride in the presence of potassium carbonate furnished the Cbz-protected disaccharide **20**. Chemoselective oxidation of the primary hydroxymethyl

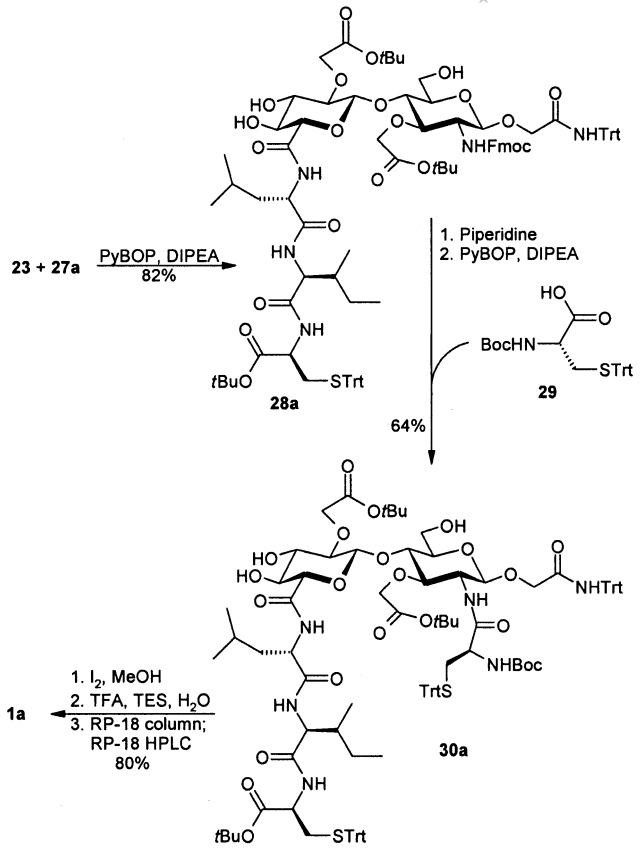


Scheme 5. Synthesis of disaccharide **23**. Reagents and conditions: (a) TMSOTf, CH_2Cl_2 (65%); (b) NaOMe, MeOH (95%); (c) NaOH; HCl; Cbz-Cl, K_2CO_3 (73%); (d) TEMPO, NaOCl; BnBr, CsF (93%); (e) $BrCH_2CO_2tBu$, Ag_2O (82%); (f) Pd/C, H_2; Fmoc-ONSu (68%).

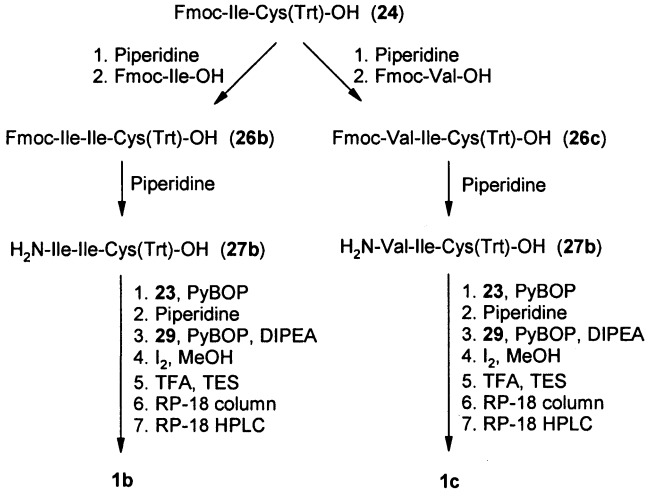
group with tetramethylpiperidine *N*-oxide (TEMPO) and NaOCl[33–36] and then benzylation with benzyl bromide and cesium fluoride[37] transformed the **b** residue into the desired glucuronic acid leading to compound **21**. The glutamate side-chain mimics were introduced with *tert*-butyl bromoacetate in the presence of silver oxide to afford compound **22**. Hydrogenolytic cleavage of the benzyl groups with Pd/C as catalyst led to an amino acid intermediate which on reaction with fluorenylmethoxycarbonyloxy–succinimide (Fmoc-ONSu)[38] led to *N*-Fmoc protection furnishing NEES tetrapeptide mimic **23**.

The required leucinyl–isoleucinyl–cysteine tripeptide **27a** (Scheme 6) was obtained according to standard Fmoc strategies. The commercially available cysteine building block **24** was treated with piperidine and then with Fmoc-protected isoleucine in the presence of (benzotriazol-1-yloxy)tripyrrolidinophosophonium hexafluorophosphate (PyBOP)[39] and Hünig's base (*N*-ethyldiisopropylamine, DIPEA) to afford the dipeptide **25**. Similarly, with Fmoc-protected leucine the tripeptide **26a** was obtained. Removal of the Fmoc group with piperidine furnished the derivative **27a** which was coupled to **23** under the same conditions to afford the protected heptapeptide mimic **28a** (Scheme 7). Attachment of the cysteine residue **29** to the 2a-amino group of this construct required again cleavage of the Fmoc group with piperidine and then PyBOP/DIPEA-supported condensation to furnish the ring-open octapeptide mimic **30a** in 64% yield. Treatment of **30a** with iodine in methanol led to loss of the *S*-trityl groups and to disulfide bond formation.[40] Following cleavage of the acid-labile protecting groups with trifluoroacetic acid (TFA) and addition of triethylsilane (TES) to scavenge carbenium ion intermediates[41] led to the crude target molecule **1a**. Purification by RP-18 flash chromatography led to the separation of salts and most of the byproducts. Final purification of **1a** was performed by RP-18 HPLC with acetonitrile/water/TFA as eluent to give the target molecule in 80% yield. Similarly, from **25** the additional leucine- or valine-containing tripeptides **26b** and **26c**, respectively, were obtained (Scheme 8); removal of the Fmoc protecting group with piperidine afforded **27b** and **27c**. Condensation with **23** and with **29** as described above and following ring closure under disulfide bond formation, protecting group cleavage and then purification afforded the target molecules **1b** and **1c**.

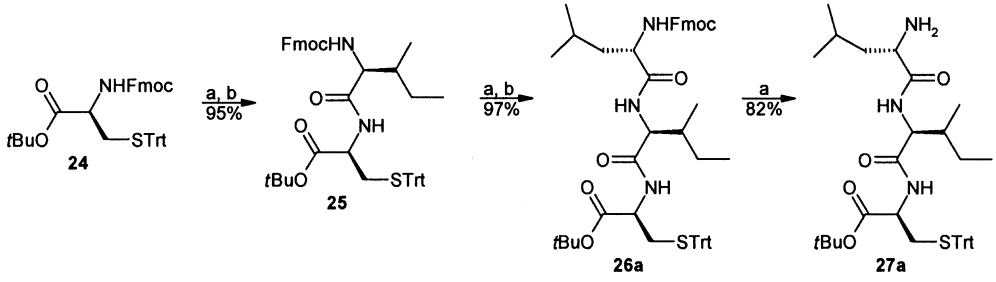
The target molecule **2** was obtained by the same procedure (Scheme 9). Reaction of **29** with glycine methyl ester and PyBOP/DIPEA as condensing agent afforded dipeptide



Scheme 7. Synthesis of target molecule **1a**.

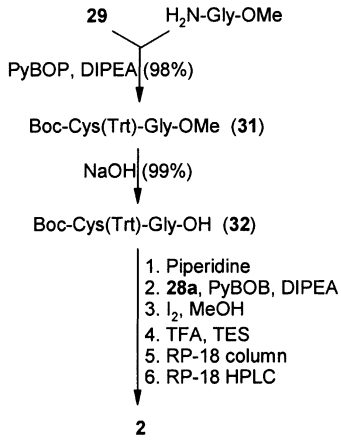


Scheme 8. Synthesis of target molecules **1b** and **1c**.



Scheme 6. Synthesis of LIC tripeptide **27a**.

ester **31** in practically quantitative yield. Ester hydrolysis with sodium hydroxide in aqueous methanol led to the desired dipeptide **32**. Attachment of **32** to **28a** required first cleavage of the Fmoc residue from **28a** with piperidine and then condensation with PyBOP/DIPEA. Treatment of this intermediate with iodine in methanol led as described above to ring closure under disulfide bond formation; acid-catalyzed deprotection and then purification gave the target molecule **2** in very good yield.



Scheme 9. Synthesis of target molecule **2**.

In a cell-based assay[9] compound **2** was found in preliminary studies to exhibit some inhibition (ca. 20%) of VEGF-D-mediated survival activity through VEGFR-2, albeit at high concentration of compound **2** (10^{-4} M).[42] The cyclic octapeptide mimics **1a**–**c** had only a marginal effect in this assay.

Synthesis of Target Molecules 33 and 34

The low inhibition of compounds **1a**–**c** and **2** was the reason to consider a configurational change for the attachment of one of the glutamate side-chain mimics because an even better fit with **A** (Figure 1) was proposed by the modeling studies for this structural modification. Hence, the cyclic octapeptide mimic **33** and the cyclic nonapeptide mimic **34** became the new target molecules (Figure 2).

For the synthesis of *allo*-configured fragment **a**, compound **9** was transformed into the 3-*O*-levulinoyl (Lev) derivative **35** by treatment with levulinic acid and dicyclohexyl carbodimide (DCC) and Steglich's reagent (DMAP)[43] as condensing agents (Scheme 10). Reductive opening of the 4,6-*O*-benzylidene group with triethylsilane (TES) in the presence of trifluoroacetic anhydride and TFA at 0 °C[44] furnished the 4-*O*-unprotected 6-*O*-benzyl-protected glucose derivative **36**. Glycosylation with **8** as glycosyl donor and TMSOTf as catalyst (0.08 equiv.) gave the β-linked disaccharide **37** ($J_{1b,2b}$ = 8.0 Hz) in 68% yield. The levulinoyl group was selectively cleaved by treatment with hydrazinium acetate in pyridine[45] to furnish 3a-*O*-unprotected derivative **38**. The inversion of the 3a-hydroxy group was performed by oxidation with Dess–Martin periodinane to the ketone, which upon reduction with sodium borohydride[46,47] gave mainly the *allo*-configured compound **39**. Reaction with acetic anhydride in pyridine afforded compound **40** which was selectively deprotected at 1-*O* by treatment with TBAF in THF to afford compound **41**. Reaction of **41** with trichloroacetonitrile in the presence of DBU as base led to trichloroacetimidate **42** as disaccharide donor. Glycosylation of acceptor **17** with **42** as donor and tin(II) triflate as catalyst[48] (0.005 equiv.) in dichloromethane at room temperature gave the desired β-linked glycoside **43** ($J_{1a,2a}$ = 8.7 Hz) in 64% yield. *O*-Deacetylation with sodium methoxide in methanol (→ **44**), cleavage of the DMM group by treatment with sodium hydroxide, adjustment of the pH to 4.5 with hydrochloric acid and finally introduction of the Cbz group to the liberated amino group with Cbz-Cl in the presence of potassium carbonate led to the desired 2a-*O*-, 2b-*O*- and 6b-*O*-unprotected intermediate **45**.

Oxidation of the primary hydroxymethyl group of **45** with TEMPO/NaOCl to a carboxy group and then treatment with benzyl bromide in the presence of cesium fluoride as base in DMF afforded the disaccharide **46** containing the desired benzyl ester at the glucuronic acid moiety

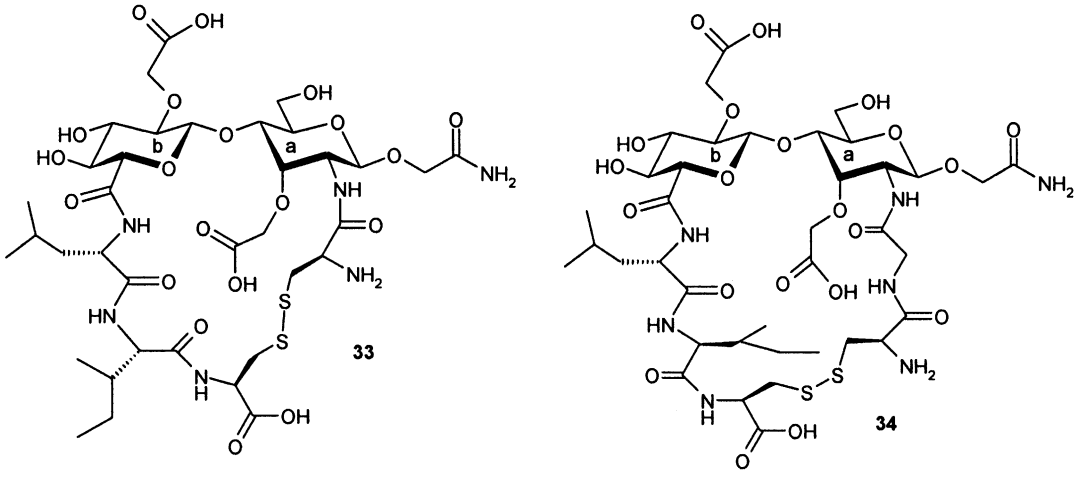
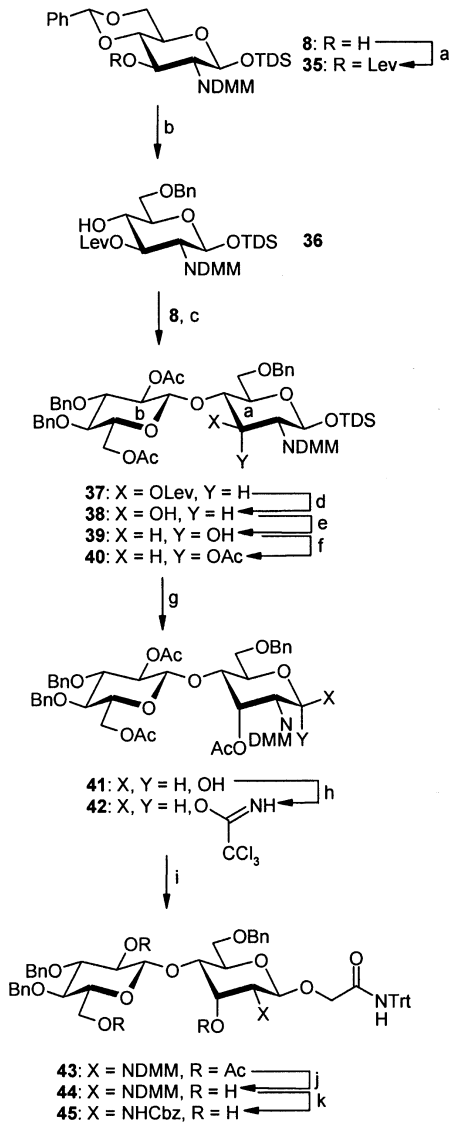
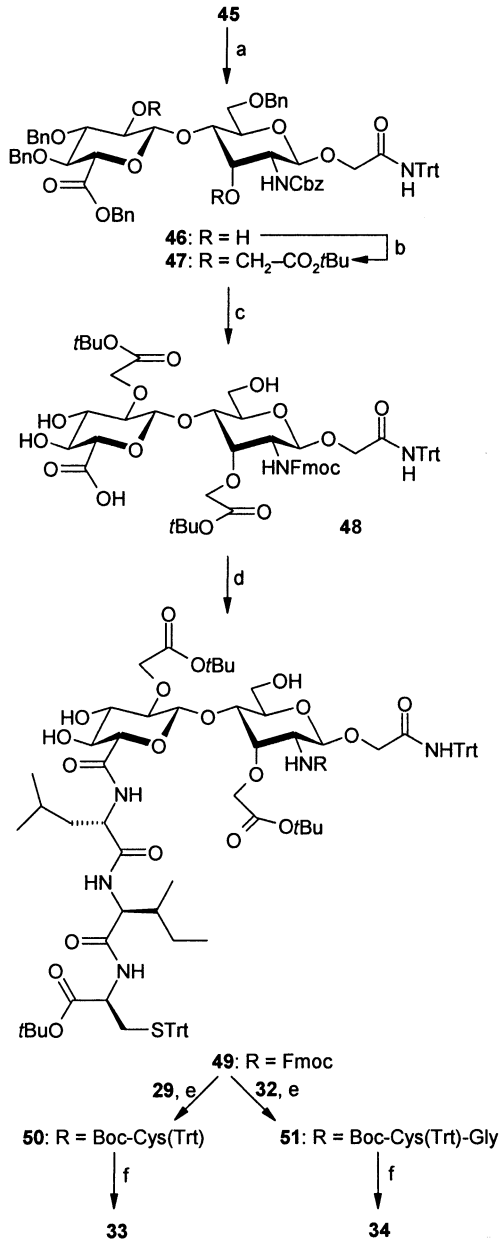


Figure 2. Structure of target molecules **33** and **34**.



Scheme 10. Synthesis of disaccharide **45**. Reagents and conditions: (a) Lev-OH, DCC, DMAP (89%); (b) TES, TFA (78%); (c) TMSOTf, CH_2Cl_2 (68%); (d) N_2H_4·HOAc, Pyr (98%); (e) periodinane; $NaBH_4$ (68%); (f) Ac_2O, Pyr (97%); (g) TBAF, THF (93%); (h) CCl_3CN, DBU, CH_2Cl_2 (98%); (i) **17**, $Sn(OTf)_2$, CH_2Cl_2 (64%); (j) NaOMe, MeOH (98%); (k) NaOH; HCl; Cbz-Cl, K_2CO_3 (80%).

(Scheme 11). The glutamate side-chain mimics were again introduced with *tert*-butyl bromoacetate and silver oxide to afford compound **47**. Palladium/carbon-catalyzed hydrogenolysis of all *O*-benzyl groups led to an amino acid intermediate which on reaction with Fmoc-ONSu led to *N*-Fmoc protection and furnished the new NEES tetrapeptide mimetic **48**. Coupling of LIC-tripeptide **27a** to **48** with PyBOP/DIPEA as condensing agent afforded heptapeptide mimetic **49** in 64% yield. Attachment of the cysteine residue **29** required first cleavage of the Fmoc group of **49** with piperidine and then PyBOP/DIPEA-supported condensation to give the octapeptide mimetic **50** in 91% yield. Similarly, from **49** and CG-dipeptide **32** the nonapeptide mimetic **51** was obtained in the same yield. Compounds **50** and **51** were deprotected and ring-closed to compounds **33** and **34**, respectively, as described for **1a**, thus providing these target molecules in high yields.



Scheme 11. Scheme 7. Synthesis of target molecules **33** and **34**. Reagents and conditions: a) TEMPO, NaOCl; BnBr, CsF (78%); b) Br-CH_2–CO_2tBu, Ag_2O (70%); c) Pd/C, H_2; Fmoc-ONSu (50%); d) PyBOP, DIPEA (64%); e) Piperidine; PyBOP, DIPEA (**50**: 91%, **51**: 91%); f) I_2, MeOH; TES, TFA, H_2O; RP-18 column; RP-18 HPLC (**33**: 78%, **34**: 75%).

Conclusion

In preliminary cell-based assays for VEGF-D-mediated survival activity through VEGFR-2, compound **34** showed better inhibition values (inhibition ca. 35% at 10^{-4} M of **34**) than for compound **2**,[42] although it should be noted that

neither **2** nor **34** were as effective as the parent cyclic octapeptide **A** as previously reported.[9] Therefore, further structural optimization of these VEGF-D loop mimetics is in progress. Detailed studies on the in vivo stability, potential unspecific interactions, and toxicities of **1a**–**c**, **2**, **33** and **34** will be reported in due course.

Experimental Section

General: Solvents were purified by standard procedures. NMR spectra were recorded at 22 °C with a Bruker AC 250 Cryospec or a Bruker DRX 600 spectrometer. Tetramethylsilane (TMS) or the resonance of residual undeuterated solvent was used as internal standard: $CDCl_3$ (δ = 7.24 ppm), D_2O (δ = 4.63 ppm), [D_6]DMSO (δ = 2.49 ppm). MALDI mass spectra were recorded with a Kratos Kompact Maldi 2 spectrometer, and 2,5-dihydroxybenzoic acid (DHB) or 6-aza-2-thiothymine (ATT) was used as matrix. FAB mass spectra were obtained with a Finnigan MAT 312/AMD 5000 instrument; +6 kV for positive ions, –4 kV for negative ions. Thin-layer chromatography was performed on Merck 60 F_{254} silica gel plastic plates or Merck RP-18 F_{254} glass plates; compounds were visualized by treatment with a solution of [$(NH_4)_6Mo_7O_{24}\cdot 4H_2O$] (20 g) and $Ce(SO_4)_2$ (0.4 g) in 10% sulfuric acid (400 mL) and then heating to 120 °C. Flash chromatography was performed on J. T. Baker silica gel 60 (40–63 μm) at a pressure of 0.3 bar. Preparative RP-18 HPLC was carried out with a Eurospher 100 C18 column (Fa. Knauer) with a Shimadzu LC-8A pump and a Rainin Dynamax UV-1 detector at a flow rate of 10 mL/min. Optical rotations were measured at 20 °C with a Polar-Monitor, Fa. Büchi, at the sodium D line.

1,2-*O*-Ethylidene-6-*O*-(triphenylmethyl)-α-D-glucopyranose (4): Compound **3**[26] (6.0 g, 29.1 mmol) was dissolved in dry pyridine (50 mL), and TrtCl (6.74 g, 26.2 mmol) was added. After stirring overnight, the reaction mixture was diluted with ethyl acetate and washed three times with saturated NaCl solution. The organic phase was dried with $MgSO_4$, filtered, purified and coevaporated twice with toluene. Purification of the residue by flash chromatography (silica gel, toluene/acetone, 3:1) furnished **4** (8.0 g, 17.8 mmol, 62%) as slightly yellow foam. TLC: R_f = 0.48 (toluene/acetone, 2:1). $[\alpha]_D^{20}$ = +9.6 (c = 1, $CHCl_3$). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.31 (d, ^3J = 4.9 Hz, 1.5 H, CH_3), 1.41 (d, ^3J = 4.9 Hz, 1.5 H, CH_3), 2.5 (br. s, 2 H, OH), 3.26–3.41 (m, 2 H, 6-H), 3.61–3.89 (m, 3 H, 3-H, 4-H, 5-H), 4.02 (dd, $^3J_{1,2}$ = $^3J_{2,3}$ = 4.9 Hz, 0.5 H, 2-H), 4.10 (dd, $^3J_{1,2}$ = 4.9, $^3J_{2,3}$ = 6.4 Hz, 0.5 H, 2-H), 5.06 [q, ^3J = 4.9 Hz, 0.5 H, $CH(CH_3)_2$], 5.40 [q, ^3J = 4.9 Hz, 0.5 H, $CH(CH_3)_2$], 5.54 (d, $^3J_{1,2}$ = 4.6 Hz, 0.5 H, 1-H), 5.55 (d, $^3J_{1,2}$ = 5.1 Hz, 0.5 H, 1-H), 7.11–7.39 (m, 15 H, phenyl) ppm. MALDI-MS (pos. mode, matrix DHB, THF): m/z = 471 $[M + Na]^+$, 487 $[M + K]^+$.

3,4-Di-*O*-benzyl-1,2-*O*-ethylidene-6-*O*-(triphenylmethyl)-α-D-glucopyranose (5): Compound **4** (6.5 g, 14.5 mmol) was dissolved in dry DMF (120 mL), and NaH (1.4 g, 58.3 mmol) was added at 0 °C under cooling in an ice bath. After 10 min, benzyl bromide (10.3 g, 60 mmol) was added, and the solution was then stirred at room temperature for 4 h. The reaction mixture was then diluted with MeOH (10 mL), concentrated under reduced pressure, dissolved in ethyl acetate and washed twice with saturated NaCl solution. The organic phase was dried with $MgSO_4$ and concentrated. Purification by flash chromatography (silica gel, petroleum ether/ethyl acetate, 10:1 → 5:1) furnished the two epimers (**h**: 4.45 g, 7.08 mmol; **t**: 2.62 g, 4.17 mmol, 78%) as slightly yellowish foam. TLC: R_f = 0.85 (**h**), 0.75 (**t**) (toluene/ethyl acetate, 4:1). $[\alpha]_D^{20}$ = –46.2 (c = 0.5, $CHCl_3$) (**h**), $[\alpha]_D^{20}$ = –30.2 (c = 0.5, $CHCl_3$) (**t**).

5h: ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.37 (d, ^3J = 4.9 Hz, 1 H, CH_3), 3.22 (dd, $^2J_{gem}$ = 10.1, $^3J_{vic}$ = 2.9 Hz, 1 H, 6-H), 3.50 (dd, $^2J_{gem}$ = 10.0, $^3J_{vic}$ = 1.4 Hz, 1 H, 6′-H), 3.78 (m, 3 H, 3-H, 4-H, 5-H), 4.31 (d, ^3J = 10.7 Hz, 1 H, CHHPh), 4.36 (dd, $^3J_{1,2}$ = $^3J_{2,3}$ = 5 Hz, 1 H, 2-H), 4.64 (m, 2 H, CH_2Ph), 4.82 (d, ^3J = 11.5 Hz, 1 H, CHHPh), 4.52 (q, ^3J = 4.9 Hz, 1 H, CH_3), 5.74 (d, $^3J_{1,2}$ = 4.9 Hz, 1 H, 1-H), 7.13–7.45 (m, 25 H, phenyl) ppm.

5t: ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.44 (d, ^3J = 4.9 Hz, 1 H, CH_3), 3.18 (dd, $^2J_{gem}$ = 10.1, $^3J_{vic}$ = 3.5 Hz, 1 H, 6-H), 3.50 (dd, $^2J_{gem}$ = 10.0, $^3J_{vic}$ = 1.7 Hz, 1 H, 6′-H), 3.85–3.92 (m, 3 H, 3-H, 4-H, 5-H), 4.14 (dd, 1 H, 2-H), 4.23 (d, ^3J = 11.2 Hz, 1 H, CHHPh), 4.43 (d, ^3J = 10.8 Hz, 1 H, CHHPh), 4.62 (2d, 2 H, CH_2Ph), 5.11 (q, ^3J = 4.9 Hz, 1 H, CH_3), 5.68 (d, $^3J_{1,2}$ = 4.9 Hz, 1 H, 1-H), 7.12–7.46 (m, 25 H, phenyl) ppm. $C_{41}H_{40}O_6$ (628.7): calcd. C 78.32, H 6.41; found C 78.27, H 6.81.

Acetyl 2,6-Di-*O*-acetyl-3,4-di-*O*-benzyl-α,β-D-glucopyranoside (6): Compound **5** (7.4 g, 11.76 mmol) was dissolved in acetic acid (200 mL), H_2O (40 mL) and the mixture stirred in an oil bath at 125 °C for 8 h; the reaction mixture was concentrated in vacuo and coevaporated four times with toluene. The residue was diluted in pyridine (200 mL), and acetic acid anhydride (100 mL) was slowly added while cooling in an ice bath. After 16 h, the reaction mixture was concentrated in vacuo and coevaporated twice with toluene. Purification of the residue by flash chromatography (silica gel, toluene/ethyl acetate, 7:1 → 5:1) furnished the anomeric mixture of compound **6** (5.2 g, 10.6 mmol, 90%) as colorless oil. TLC: R_f = 0.65 (toluene/ethyl acetate, 3:1). $[\alpha]_D^{20}$ = +47.2 (c = 1, $CHCl_3$). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.92, 1.94, 1.95, 2.01, 2.02, 2.06 (6 s, 9 H, acetyl), 3.62–3.73 (m, 2 H, 3-H, 4-H), 3.98–4.02 (m, 1 H, 5-H), 4.21–4.32 (m, 1 H, 2-H), 4.52–4.60 (m, 2 H, CH_2Ph), 4.69 (d, 1 H, CH_2Ph), 4.78–4.89 (m, 3 H, 6-H, CH_2Ph), 5.02–5.10 (m, 1 H, 6′-H), 5.60 (d, $^3J_{1,2}$ = 8.2 Hz, 0.5 H, 1-H), 6.22 (d, $^3J_{1,2}$ = 3.6 Hz, 0.5 H, 1-H), 7.21–7.35 (m, 10 H, phenyl) ppm. $C_{26}H_{30}O_9$ (486.5): calcd. C 64.19, H 6.22; found C 64.28, H 6.36.

2,6-Di-*O*-acetyl-3,4-di-*O*-benzyl-α,β-D-glucopyranose (7): Compound **6** (5.0 g, 10.3 mmol) was dissolved in dry DMF (25 mL), and $N_2H_4\cdot$HOAc (1.13 g, 1.2 equiv.) was added at room temperature. After 1 h, the reaction mixture was diluted with ethyl acetate and washed three times with cold saturated NaCl solution. The organic phase was dried with $MgSO_4$ and concentrated in vacuo. The residue was purified by column chromatography (silica gel, toluene/ethyl acetate, 5:1) which furnished the anomeric mixture of compound **7** (4.1 g, 9.2 mmol, 90%) as colorless oil. TLC: R_f = 0.25 (toluene/ethyl acetate, 3:1). $[\alpha]_D^{20}$ = +70.0 (c = 1, $CHCl_3$). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.99, 2.01 (2 s, 6 H, acetyl), 3.14 (br. s, 1 H, OH), 3.54–3.62 (m, 2 H, 3-H, 4-H), 4.20–4.35 (m, 3 H, 5-H, CH_2Ph), 4.61 (d, 1 H, CH_2Ph), 4.72–4.82 (m, 4 H, 2-H, 6-H, CH_2Ph), 5.41 (br. s, 1 H, 1-H), 7.21–7.39 (m, 10 H, phenyl) ppm. $C_{24}H_{28}O_8$ (444.5): calcd. C 64.85, H 6.35; found C 64.67, H 6.70.

***O*-2,6-Di-*O*-acetyl-3,4-di-*O*-benzyl-α-D-glucopyranosyl Trichloroacetimidate (8):** Compound **7** (4.5 g, 10.1 mmol) was dissolved in dry CH_2Cl_2 (40 mL), and trichloroacetonitrile (5.81 mL, 57.9 mmol) was added. After the addition of 5 drops of DBU, the reaction mixture was stirred for 1 h. The dark reaction mixture was concentrated to 3/4 of its volume, and the residue was purified by column chromatography (silica gel, petroleum ether/ethyl acetate, 2.5:1 + 1% NEt_3). This furnished imidate **8** (5.8 g, 9.8 mmol, 97%) which was immediately used for the next step. TLC: R_f = 0.45 (petroleum ether/ethyl acetate, 1:1). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.93 (s, 3 H, acetyl), 2.02 (s, 3 H, acetyl), 3.69 (dd, $^3J_{2,3} \approx {}^3J_{3,4} \approx$

9.6 Hz, 1 H, 3-H), 4.01–4.07 (m, 1 H, 5-H), 4.12 (dd, $^3J_{3,4} \approx {}^3J_{4,5} \approx 9.2$ Hz, 1 H, 4-H), 4.20–4.33 (m, 2 H, 6-H), 4.59 (d, $^3J = 10.7$ Hz, 1 H, CH_2Ph), 4.75–4.89 (m, 3 H, CH_2Ph), 5.06 (dd, $^3J_{1,2} = 3.6$, $^3J_{2,3} = 10.1$ Hz, 1 H, 2-H), 6.45 (d, $^3J_{1,2} = 3.4$ Hz, 1 H, 1-H), 7.24–7.31 (m, 10 H, phenyl), 8.58 (s, 1 H, NH). $C_{26}H_{28}Cl_3NO_8$ (588.9) ppm.

Dimethyl(thexyl)silyl 3-*O*-Acetyl-4,6-*O*-benzylidene-2-deoxy-2-(dimethylmaleimido)-β-D-glucopyranoside (10): To a solution of **9**[29] (25.5 g, 49.2 mmol) in pyridine (200 mL) acetic acid anhydride (100 mL) was slowly added dropwise at 0 °C. After 3 h, the reaction mixture was concentrated in vacuo and coevaporated four times with toluene. The residue was purified by flash chromatography (silica gel, petroleum ether/ethyl acetate, 8:1 → 5:1) which furnished acetylated compound **10** (27.1 g, 48.4 mmol, 98%) as colorless foam. TLC: $R_f = 0.25$ (toluene/ethyl acetate, 3:1). $[\alpha]_D^{20} = -34.8$ ($c = 1$, $CHCl_3$). ^{1}H NMR (250 MHz, $CDCl_3$): $\delta = 0.01$, 0.05 (2 s, 6 H, 2× $SiCH_3$), 0.72 (m, 12 H, 4× CH_3), 1.48 [m, 1 H, $CH(CH_3)_2$], 1.92 (s, 9 H, acetyl, DMM-H), 3.63–3.72 (m, 2 H, 4-H, 5-H), 3.79 (dd, $^3J_{1,2} = {}^3J_{3,4} = 9.5$ Hz, 1 H, 2-H), 3.98 (dd, $^2J_{gem} = 10.4$, $^3J_{vic} = 8.0$ Hz, 1 H, 6-H), 4.30 (dd, $^2J_{gem} = 10.4$, $^3J_{vic} = 4.3$ Hz, 1 H, 6′-H), 5.46 (d, $^3J_{1,2} = 9.4$ Hz, 1 H, 1-H), 5.48 (s, 1 H, CHphenyl), 5.70 (dd, $^3J_{2,3} = 9.0$, $^3J_{3,4} = 10.2$ Hz, 1 H, 3-H), 7.31–7.44 (m, 5 H, phenyl) ppm. $C_{29}H_{41}NO_8Si$ (559.7): calcd. C 62.23, H 7.38, N 2.50; found C 62.23, H 7.13, N 2.67.

Dimethyl(thexyl)silyl 3-*O*-Acetyl-6-*O*-benzyl-2-deoxy-2-(dimethylmaleimido)-β-D-glucopyranoside (11): Compound **10** (6.0 g, 10.7 mmol) was dissolved in dry THF (100 mL), cooled down to 0 °C, $NaCNBH_3$ (6.72 g, 100 mmol) was added, and then a saturated solution of HCl in diethyl ether (20 mL) was slowly added in the presence of freshly heated molecular sieves (4 Å). After gas development had ceased, the reaction mixture was immediately neutralized with solid $NaHCO_3$, diluted with diethyl ether and washed three times with saturated $NaHCO_3$ solution. The organic phase was dried with $MgSO_4$, filtered, concentrated and the residue purified by column chromatography (silica gel, toluene/ethyl acetate, 6:1) to furnish compound **11** (5.6 g, 10.0 mmol, 93%) as amorphous solid. TLC: $R_f = 0.25$ (toluene/ethyl acetate, 3:1). $[\alpha]_D^{20} = -16.6$ ($c = 1$, $CHCl_3$). ^{1}H NMR (250 MHz, $CDCl_3$): $\delta = 0.01$, 0.10 (2 s, 6 H, 2× $SiCH_3$), 0.72–0.75 (m, 12 H, 4× CH_3), 1.47 [sept, $^3J = 6.8$ Hz, 1 H, $CH(CH_3)_2$], 1.91 (s, 6 H, DMM-H), 1.97 (s, 3 H, acetyl), 2.96 (br. s, 1 H, OH), 3.61–3.78 (m, 4 H, 2-H, 4-H, 5-H, 6-H), 3.93 (dd, $^2J_{gem} = 10.8$, $^3J_{vic} = 8.0$ Hz, 1 H, 6′-H), 4.59 (s, 2 H, CH_2Ph), 5.36 (d, $^3J = 8.1$ Hz, 1 H, 1-H), 5.50 (dd, $^3J_{2,3} = 8.3$, $^3J_{3,4} = 10.8$ Hz, 1 H), 7.13–7.33 (m, 5 H, phenyl) ppm. $C_{29}H_{43}NO_8Si$ (561.7): calcd. C 62.01, H 7.72, N 2.49; found C 62.00, H 7.89, N 2.42.

Dimethyl(thexyl)silyl (2,6-Di-*O*-acetyl-3,4-di-*O*-benzyl-β-D-glucopyranosyl)(1→4)-3-*O*-acetyl-6-*O*-benzyl-2-deoxy-2-(dimethylmaleimido)-β-D-glucopyranoside (12): TMSOTf (0.1 M in dry CH_2Cl_2, 8 mL, 0.1 equiv.) was added to a solution of **8** (5.06 g, 8.6 mmol) and **11** (5.4 g, 9.62 mmol) in dry CH_2Cl_2 at –5 °C; the reaction mixture was stirred at this temperature for 1 h and then neutralized with NEt_3. The reaction mixture was concentrated in vacuo and the residue purified by flash chromatography (silica gel, petroleum ether/ethyl acetate, 5:1) to furnish compound **12** (8.11 g, 8.2 mmol, 95%) as colorless foam. TLC: $R_f = 0.48$ (petroleum ether/ethyl acetate, 2:1). $[\alpha]_D^{20} = +3.6$ ($c = 1$, $CHCl_3$). ^{1}H NMR (600 MHz, $CDCl_3$): $\delta = 0.02$, 0.13 (2 s, 6 H, 2× $SiCH_3$), 0.70–0.76 (m, 12 H, 4× CH_3), 1.49 [sept, $^3J = 6.8$ Hz, 1 H $CH(CH_3)_2$], 1.86 (d, 1 H, DMM-H), 1.88, 1.90, 2.01 (3 s, 12 H, acetyl), 3.41 (m, 1 H, 5b-H), 3.54 (m, 2 H, 3b-H, 4b-H), 3.64 (dd, $^2J_{gem} = 10.8$ Hz, 1 H, 6a-H), 3.77 (dd, $2J_{gem} = 10.9$, $^3J_{vic} = 2.9$ Hz, 1 H, 6a′-H), 3.90 (dd, $^3J_{3,4} = {}^3J_{4,5} = 9.4$ Hz, 1 H, 4a-H), 3.93 (dd, $^3J_{1,2} = 8.1$, $^3J_{2,3} = 10.9$ Hz, 2a-H), 4.21 (m, 2 H, 6b-H), 4.45 (d, $^3J_{1,2} = 8.0$ Hz, 1 H, 1b-H), 4.50, 4.53, 4.63, 4.72, 4.74, 4.77 (6 d, 6 H, 3× CH_2Ph), 4.88 (m, 1 H, 2b-H), 5.35 (d, $^3J_{1,2} = 8.1$ Hz, 1 H, 1a-H), 5.52 (dd, $^3J_{2,3} = 10.5$, $^3J_{3,4} = 9.2$ Hz, 1 H, 3a-H), 7.23–7.37 (m, 15 H, phenyl) ppm. ^{13}C NMR (150.8 MHz, $CDCl_3$, selected data): $\delta = 56.9$ (1 C, 2a-C), 63.0 (1 C, 6b-C), 67.7 (1 C, 6a-C), 70.9 (1 C, 3a-C), 72.8 (1 C, 5b-C), 73.0 (1 C, 2b-C), 74.7 (1 C, 5a-C), 75.9 (1 C, 4a-C), 77.2 (1 C, 3b-C), 83.2 (1 C, 4b-C), 93.1 (1 C, 1a-C), 100.4 (1 C, 1b-C) ppm. MALDI-MS (pos. mode, matrix DHB, THF): $m/z = 1010$ [M + Na]$^+$, 1026 [M + K]$^+$. $C_{53}H_{69}NO_{15}Si$ (988.2): calcd. C 64.42, H 7.04, N 1.42; found C 64.32, H 7.39, N 1.41.

(2,6-Di-*O*-acetyl-3,4-di-*O*-benzyl-β-D-glucopyranosyl)(1→4)-3-*O*-acetyl-6-*O*-benzyl-2-deoxy-2-(dimethylmaleimido)-α,β-D-glucopyranose (13): Acetic acid (0.48 mL, 1 equiv.) was added to a solution of **12** (7.8 g, 7.83 mmol) in THF (130 mL), and the mixture was cooled to 0 °C. After addition of TBAF (1 M in THF, 9.3 mL, 9.3 mmol), the reaction mixture was stirred at 0 °C for 2 h, then diluted with diethyl ether and washed twice with saturated NaCl solution. The aqueous phase was reextracted with diethyl ether, and the combined organic phases were dried with $MgSO_4$, filtered, and concentrated in vacuo. Purification by flash chromatography furnished the anomeric mixture of compound **13** (6.45 g, 7.62 mmol, 95%) as colorless foam. TLC: $R_f = 0.35$ (toluene/ethyl acetate, 6:4). $[\alpha]_D^{20} = +18.7$ ($c = 1$, $CHCl_3$). ^{1}H NMR (600 MHz, $CDCl_3$): $\delta =$ 1.86–2.04 (8 s, 15 H, 3× acetyl, DMM-H), 3.39 (m, 1 H, 5b-H), 3.50 (m, 1 H, 3b-H), 3.57 (m, 1 H, 4b-H), 3.64 [m, 0.5 H, 5a-H(β)], 4.68 [m, 0.5 H, 6a-H(α)], 3.74 [m, 0.5 H, 6a-H(β)], 3.79 [m, 0.5 H, 6a′-H(β)], 3.86 [m, 0.5 H, 6a′-H(α)], 3.94–3.96 [m, 1 H, 2a-H(β), 4a-H(β)], 4.00 [m, 0.5 H, 4a-H(α)], 4.17 [m, 0.5 H, 5a-H(α)], 4.24 (m, 2 H, 6b-H), 4.38 [m, 0.5 H, 2a-H(α)], 4.41 (m, 1 H, 1b-H), 4.47–4.54 (m, 2 H, CH_2Ph), 4.64 (m, 1 H, CHHPh), 4.75–4.80 (m, 3 H, CH_2Ph, CHHPh), 4.88 (m, 1 H, 2b-H), 5.30 [d, $^3J_{1,2} = 3.5$ Hz, 0.5 H, 1a-H(α)], 5.44 [d, $^3J_{1,2} = 8.5$ Hz, 0.5 H, 1a-H(β)], 5.56 [dd, $^3J_{2,3} = 9.1$, $^3J_{3,4} = 10.6$ Hz, 0.5 H, 3a-H(β)], 5.71 [dd, $^3J_{2,3} = 8.9$, $^3J_{3,4} = 11.3$ Hz, 0.5 H, 3a-H(α)], 7.26–7.40 (m, 15 H, phenyl) ppm. ^{13}C NMR (150.8 MHz, $CDCl_3$, selected data): $\delta = 54.7$ [0.5 C, 2a-C(α)], 56.3 [0.5 C, 2a-C(β)], 62.8 (1 C, 6b-C), 67.1 [0.5 C, 6a-C(α)], 67.4 [0.5 C, 6a-C(β)], 68.5 [0.5 C, 3a-C(α)], 69.4 [0.5 C, 5a-C(α)], 70.7 [0.5 C, 3a-C(β)], 72.8 (1 C, 5b-C), 72.9 (1 C, 2b-C), 75.4 [0.5 C, 4a-C(β)], 75.5 [0.5 C, 4a-C(α)], 77.1 (1 C, 4b-C), 83.2 (1 C, 3b-C), 92.6 (1 C, 1a-C), 100.4 (1 C, 1b-C) ppm. $C_{45}H_{51}NO_{15}$ (845.9): calcd. C 63.90, H 6.08, N 1.66; found C 63.55, H 6.24, N 2.38.

***O*-[(2,6-Di-*O*-acetyl-3,4-di-*O*-benzyl-β-D-glucopyranosyl)(1→4)-3-*O*-acetyl-6-*O*-benzyl-2-deoxy-2-(dimethylmaleimido)-β-D-glucopyranosyl] Trichloroacetimidate (14):** Trichloroacetonitrile (4.25 mL, 6.12 g, 42.4 mmol) was added to a solution of **13** (6.25 g, 7.38 mmol) in dry CH_2Cl_2 (35 mL), then DBU (5 drops), and the solution was stirred at room temperature for 1 h. The dark reaction mixture was concentrated in vacuo to 3/4 of its volume and the residue purified by column chromatography (silica gel, petroleum ether/ethyl acetate, 3:2 + 1% NEt_3) to furnish **14** (7.43 g, 6.80 mmol, 92%) as slightly brownish foam which was immediately used in the next step. TLC: $R_f = 0.69$ (petroleum ether/ethyl acetate, 1:1). $[\alpha]_D^{20} = +20.1$ ($c = 1$, $CHCl_3$). ^{1}H NMR (250 MHz, $CDCl_3$): $\delta =$ 1.87, 1.89, 2.01 (3 s, 15 H, 3× acetyl, DMM-H), 3.34–3.40 (m, 1 H, 5b-H), 3.41–3.52 (m, 2 H, 3b-H, 4b-H), 3.42–3.53 (m, 3 H, 5a-H, 6a-H), 4.02 (dd, $^3J_{3,4} \approx {}^3J_{4,5} \approx 9.4$ Hz, 1 H, 4a-H), 4.07–4.20 (m, 2 H, 6b-H), 4.27 (dd, $^3J_{1,2} = 9.1$, $^3J_{2,3} = 10.5$ Hz, 1 H, 2a-H), 4.39 (d, $^3J_{1,2} = 8.0$ Hz, 1 H, 1b-H), 4.44, 4.47 (2 d, 2 H, CH_2Ph), 4.59 (d, 1 H, CHHPh), 4.72–4.78 (m, 3 H, CH_2Ph, CHHPh), 4.84 (dd, $^3J_{1,2} \approx {}^3J_{2,3} \approx 8.4$ Hz, 1 H, 2b-H), 4.84 (dd, $^3J_{2,3} \approx {}^3J_{3,4} \approx$

9.8 Hz, 1 H, 3a-H), 6.40 (d, $^3J_{1,2}$ = 8.9 Hz, 1 H, 1a-H), 7.22–7.34 (m, 15 H, phenyl), 8.62 (s, 1 H, NH). $C_{47}H_{51}Cl_3N_2O_{15}$ (990.3) ppm.

***N*-(Triphenylmethyl)methoxyacetamide (16):** A solution of **15** (5.2 g, 50 mmol, 4.82 mL) was combined with a 2 M methanolic NH_3 solution (15 mL) and the mixture stirred at room temperature overnight. The solvents were removed under reduced pressure to furnish a white, amorphous solid (3.75 g, 49.9 mmol, quant.). The intermediate was dissolved in pyridine (50 mL), and acetic anhydride (25 mL) was added under ice-bath cooling. After stirring overnight, the reaction mixture was concentrated and coevaporated four times with toluene. The acetylated amide (5.0 g, 42.1 mmol) was suspended with triphenylmethanol (22 g, 84.2 mmol) in acetic acid (120 mL) and acetic anhydride (8 mL) and after addition of sulfuric acid (2.56 mL, concentrated) stirred at 55 °C for 4 h. The dark red solution was then slowly poured into ice-cold water (400 mL) while stirring to furnish a white amorphous solid. Filtration and drying in vacuo furnished **16** (7.54 g, 21 mmol, 42% from **33**) as colorless powder. TLC: R_f = 0.60 (toluene/ethyl acetate, 6:4). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 2.14 (s, 3 H, acetyl), 4.57 (s, 2 H, CH_2C=O), 7.16–7.31 (m, 15 H, Trityl) ppm. $C_{23}H_{21}NO_3$ (359.4): calcd. C 76.86, H 5.89, N 3.90; found C 76.27, H 6.02, N 3.91.

2-Hydroxy-*N*-(triphenylmethyl)acetamide (17): Sodium methoxide (0.1 M in dry MeOH, 5 mL) was added to a solution of **16** (7.37 g, 20.5 mmol) in dry MeOH (60 mL). The solution was then stirred at room temperature for 2 h and neutralized with ion exchange resin IR 120 (H^+), filtered, and concentrated in vacuo. The residue was dissolved in ethyl acetate and heated to reflux; then *n*-hexane was added until the mixture became slightly turbid. After cooling, the residue was filtered and dried under reduced pressure which furnished **17** (6.1 g, 19 mmol, 93%) as colorless powder. TLC: R_f = 0.25 (toluene/ethyl acetate, 6:4). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 3.99 (s, 2 H, CH_2–CO), 7.16–7.26 (m, 15 H, Trityl), 7.53 (br. s, 1 H, NH) ppm. $C_{21}H_{19}NO_2$ (317.4): calcd. C 79.47, H 6.03, N 4.41; found C 78.89, H 6.13, N 4.38.

[*N*-(Triphenylmethyl)carbamoyl]methyl (2,6-Di-*O*-acetyl-3,4-di-*O*-benzyl-β-D-glucopyranosyl)(1→4)-3-*O*-acetyl-6-*O*-benzyl-2-deoxy-2-(dimethylmaleimido)-β-D-glucopyranoside (18): A solution of **14** (5.84 g, 5.90 mmol) and **17** (2.15 g, 6.77 mmol, 1.15 equiv.) in dry CH_2Cl_2 (30 mL) was cooled to –5 °C; a TMSOTf solution (0.1 M in dry CH_2Cl_2, 5.0 mL, 0.08 equiv.) was added and the mixture stirred at –5 °C for 1 h. After neutralising the reaction mixture with NEt_3, it was concentrated in vacuo and the residue purified twice by column chromatography (silica gel, toluene/ethyl acetate, 4:1 → 3:1) to furnish **18** (4.2 g, 3.67 mmol, 65%) as colorless foam. TLC: R_f = 0.30 (toluene/ethyl acetate, 6:4). $[\alpha]_D^{20}$ = –4.9 (c = 1, $CHCl_3$). ^{1}H NMR (600 MHz, $CDCl_3$): δ = 1.83 (br. d, 6 H, DMM-H), 1.85, 1.86, 2.00 (3 s, 12 H, 4× acetyl), 3.34 (m, 1 H, 5b-H), 3.41 (dd, $^3J_{2,3}$ = $^3J_{3,4}$ = 9.1 Hz, 1 H, 3b-H), 3.52 (dd, $^3J_{3,4}$ = $^3J_{4,5}$ = 9.2 Hz, 1 H, 4b-H), 3.56 (m, 2 H, 5a-H, 6a-H), 3.68 (dd, $^2J_{gem}$ = 10.8, $^3J_{vic}$ = 2.4 Hz, 6a′-H), 3.96 (dd, $^3J_{3,4}$ = $^3J_{4,5}$ = 9.1 Hz, 1 H, 4a-H), 4.03 (dd, 1 H, 2a-H), 4.04, 4.08, 4.21 (3 d, 3 H, CH_2Ph, CHHPh), 4.22 (m, 2 H, 6b-H), 4.34 (d, $^3J_{1,2}$ = 8.0 Hz, 1 H, 1b-H), 4.42, 4.49, 4.58 (3 d, 3 H, CH_2Ph, CHHPh), 4.71, 4.76 (2 d, CH_2C=O), 5.27 (d, $^3J_{1,2}$ = 8.5 Hz, 1 H, 1a-H), 5.46 (dd, $^3J_{2,3}$ ≈ $^3J_{3,4}$ ≈ 9.8 Hz, 1 H, 3a-H), 7.14–7.33 (m, 30 H, phenyl), 7.73 (s, 1 H, NH) ppm. ^{13}C NMR (150.8 MHz, $CDCl_3$, selected data): δ = 54.7 (1 C, 2a-C), 62.8 (1 C, 6b-C), 66.7 (1 C, 6a-C), 70.7 (1 C, 3a-C), 72.7 (2 C, 2b-C, 5b-C), 74.6 (1 C, 5a-C), 74.7 (1 C, 4a-C), 76.9 (1 C, 4b-C), 83.0 (1 C, 3b-C), 99.0 (1 C, 1a-C), 100.1 (1 C, 1b-C) ppm. MALDI-MS (pos. mode, matrix DHB, THF): m/z = 1069 [M + Na]$^+$. $C_{66}H_{68}N_2O_{16}$ (1145.3): calcd. C 69.22, H 5.98, N 2.45; found C 69.18, H 6.25, N 2.51.

[*N*-(Triphenylmethyl)carbamoyl]methyl (3,4-Di-*O*-benzyl-β-D-glucopyranosyl)(1→4)-6-*O*-benzyl-2-deoxy-2-(dimethylmaleimido)-β-D-glucopyranoside (19): Sodium methoxide (20 mg, 0.37 mmol) was added to a solution of **18** (5.0 g, 4.4 mmol) in dry MeOH and the mixture stirred at room temperature overnight. The reaction mixture was neutralized with ion exchange resin IR 120 (H^+), filtered, and concentrated in vacuo to furnish **19** (4.3 g, 4.2 mmol, 95%) as slightly yellowish foam. TLC: R_f = 0.35 (toluene/ethyl acetate, 1:1). $[\alpha]_D^{20}$ = –14.9 (c = 1, $CHCl_3$). ^{1}H NMR (600 MHz, [D$_6$]DMSO): δ = 1.80 (s, 6 H, DMM-H), 3.26 (dd, $^3J_{1,2}$ ≈ $^3J_{2,3}$ ≈ 8.0 Hz, 1 H, 2b-H), 3.31 (m, 1 H, 5b-H), 3.34 (dd, $^3J_{3,4}$ ≈ $^3J_{4,5}$ ≈ 9.0 Hz, 1 H, 4b-H), 3.44 (m, 2 H, 3b-H, 6b-H), 3.52 (dd, $^3J_{3,4}$ = $^3J_{4,5}$ = 8.8 Hz, 1 H, 4a-H), 3.65 (m, 3 H, 2a-H, 5a-H, 6b′-H), 3.77 (m, $^2J_{gem}$ = 10.4, $^3J_{vic}$ = 4.4 Hz, 1 H, 6a-H), 3.82 (dd, $^2J_{gem}$ = 10.4 Hz, 1 H, 6a′-H), 4.05–4.15 (m, 3 H, 3a-H, CH_2Ph), 4.31 (d, $^3J_{1,2}$ = 7.8 Hz, 1 H, 1b-H), 4.38 (2 d, 2 H, OCH_2C=O), 4.54, 4.67, 4.73 (3 d, 3 H, CH_2Ph, CHHPh), 4.74 (m, 1 H, 6b-OH), 4.82 (m, 1 H, 3a-OH), 4.90 (d, 1 H, CHHPh), 5.03 (d, 1 H, $^3J_{1,2}$ = 8.6 Hz, 1a-H), 5.69 (d, 1 H, ^3J = 5.7 Hz, 2b-OH), 7.08–7.35 (m, 30 H, phenyl), 7.99 (s, 1 H, NH) ppm. ^{13}C NMR (150.8 MHz, [D$_6$]DMSO, selected data): δ = 55.7 (1 C, 2a-C), 60.1 (1 C, 6b-C), 68.2 (1 C, 6a-C), 68.5 (1 C, 3a-C), 72.3 (1 C, OCH_2C=O), 73.5 (1 C, 2b-C), 74.0 (1 C, 5a-C), 75.1 (1 C, 5b-C), 77.1 (1 C, 4b-C), 80.4 (1 C, 4a-C), 84.3 (1 C, 3b-C), 98.2 (1 C, 1a-C), 103.0 (1 C, 1b-C) ppm. $C_{66}H_{62}N_2O_{13}$ (1019.1): calcd. C 70.71, H 6.13, N 2.75; found C 70.43, H 6.14, N 3.00.

[*N*-(Triphenylmethyl)carbamoyl]methyl (3,4-Di-*O*-benzyl-β-D-glucopyranosyl)(1→4)-6-*O*-benzyl-2-[(benzyloxycarbonyl)amino]-2-deoxy-β-D-glucopyranoside (20): NaOH (790 mg, 19.8 mmol) was added to a solution of **19** (1.4 g, 1.37 mmol) in dioxane (80 mL) and water (20 mL) at room temperature, and the reaction mixture was stirred at room temperature overnight. Then the pH was adjusted to 4.5 with 1 M HCl, monitored every 30 min for the next 4 h and if necessary adjusted to 4.5 with 1 M HCl. After stirring overnight at pH = 4.5, the reaction mixture was neutralized with ethanolamine (110 μL) and NaOH. Thereafter K_2CO_3 (600 mg, 4.4 mmol) was added; after addition of benzyl chloroformate (0.56 mL, 669 mg, 3.92 mmol), the mixture was stirred at room temperature for 1.5 h. The reaction mixture was concentrated to 1/2 of its volume and extracted three times with CH_2Cl_2. The combined organic phases were dried with $MgSO_4$, filtered and concentrated. Purification by flash chromatography (silica gel, toluene/acetone, 4:1) furnished Z-protected **20** (1.05 g, 1.0 mmol, 73%) as colorless, hygroscopic foam. TLC: R_f = 0.57 (toluene/acetone, 1:1). $[\alpha]_D^{20}$ = –16.3 (c = 1, $CHCl_3$). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 2.32 (m, 1 H, OH), 3.32–3.52 (m, 5 H, 2b-H, 3b-H, 4b-H, 5b-H, 6b-H), 3.53–3.69 (m, 3 H, 2a-H, 6a-H, 6b′-H), 3.81 (dd, $^2J_{gem}$ = 12.5, $^3J_{vic}$ = 3.5 Hz, 6a′-H), 4.12 (d, 1 H, CHHPh), 4.26 (dd, $^3J_{2,3}$ ≈ $^3J_{3,4}$ ≈ 7.8 Hz, 3a-H), 4.29 (s, 2 H, CH_2Ph), 4.51 (m, 2 H, CH_2–CO), 4.59 (d, $^3J_{1,2}$ = 8.9 Hz, 1 H, 1b-H), 4.81–4.90 (m, 4 H, 2× CH_2Ph), 5.03 (d, $^3J_{1,2}$ = 9.5 Hz, 1 H, 1a-H), 7.13–7.35 (m, 35 H, phenyl), 7.91 (s, 1 H, NH) ppm. MALDI-MS (pos. mode, matrix DHB, THF): m/z = 1068 [M + Na]$^+$, 1084 [M + K]$^+$.

[*N*-(Triphenylmethyl)carbamoyl]methyl (Benzyl 3,4-di-*O*-benzyl-β-D-glucopyranosyluronate)(1→4)-6-*O*-benzyl-2-[(benzyloxycarbonyl)amino]-2-deoxy-β-D-glucopyranoside (21): A mixture of an NaOCl solution (10%, 1.2 mL), H_2O (1 mL) and an $NaHCO_3$ solution (saturated, 1.7 mL) was added dropwise to a solution of **20** (300 mg, 0.29 mmol), NaBr (5 mg), TBAB (5 mg), and TEMPO (4 mg, 0.025 mmol) in CH_2Cl_2 (5.2 mL) and H_2O (0.85mL) at 0 °C; then the mixture was stirred at 0 °C for 20 min, then methanol (1 mL) was added. The reaction mixture was diluted with H_2O and extracted with CH_2Cl_2. The aqueous phase was acidified with a $KHSO_4$ solution (5%) and extracted three times with CH_2Cl_2. The

combined organic phases were dried with $MgSO_4$, filtered, and concentrated in vacuo to furnish the free acid (290 mg, 95%) as intermediate which was dissolved in dry DMF (5 mL); CsF (90 mg, 0.59 mmol) and benzyl bromide (75 μL, 107.9 mg, 0.63 mmol) were added, and the mixture was stirred at room temperature overnight. The reaction mixture was then diluted with ethyl acetate and washed 3× with saturated NaCl solution. The organic phase was dried with $MgSO_4$, filtered, and the solvents were evaporated. After coevaporating twice with toluene, the residue was purified by column chromatography (silica gel, toluene/acetone, 4.5:1) to furnish **21** as colorless foam (305 mg, 0.27 mmol, 93%). TLC: R_f = 0.57 (toluene/acetone, 1:1). $[\alpha]_D^{20}$ = –11.4 (*c* = 1, $CHCl_3$). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 2.66 (s, 1 H, OH), 3.39–3.51 (m, 3 H, 5a-H, 3b-H, 2b-H), 3.53–3.68 (m, 5 H, 2a-H, 3a-H, 6a-H, 5b-H), 3.88 (d, 1 H, CHHPh), 4.02 (dd, 1 H, 4b-H), 4.14 (dd, 1 H, 4a-H), 4.23 (d, 2 H, CH_2Ph), 4.42 (d, 2 H, CH_2Ph), 4.60 (bd, $^3J_{1,2} \approx 8.0$ Hz, 1 H, 1a-H), 4.64 (d, 1 H, CHHPh), 4.72 (s, 1 H, OH), 4.86 (d, $^3J_{1,2}$ = 8.4 Hz, 1 H, 1b-H), 4.89 (d, 2 H, CH_2Ph), 5.12 (s, 1 H, OH), 7.13–7.35 (m, 40 H, phenyl) ppm. MALDI-MS (pos. mode, matrix DHB, THF): *m*/*z* = 1183 $[M + Na]^+$, 1199 $[M + K]^+$. $C_{69}H_{68}N_2O_{14}$ (1149.3): calcd. C 72.11, H 5.96, N 2.44; found C 71.87, H 6.01, N 2.46.

[*N*-(Triphenylmethyl)carbamoyl]methyl [Benzyl 3,4-di-*O*-benzyl-2-*O*-(*tert*-butyloxycarbonylmethyl)-β-D-glucopyranosyluronate](1→4)-6-*O*-benzyl-2-[(benzyloxycarbonyl)amino]-3-*O*-[(*tert*-butyloxycarbonyl)methyl]-2-deoxy-β-D-glucopyranoside (22): *tert*-Butyl bromoacetate (880 μL, 1.16 g, 5.96 mmol) and molecular sieves (4 Å) were added to a solution of **21** (960 mg, 0.82 mmol) in CH_2Cl_2 (25 mL). After stirring at room temperature for 10 min, silver(I) oxide (2.85 g, 12.3 mmol) and TBAI (700 mg, 1.89 mmol) were added to the reaction mixture which was then stirred in the dark overnight. The reaction mixture was filtered through Celite and purified by flash chromatography (silica gel, petroleum ether/ethyl acetate, 3:1 → 2.5:1 → 2:2) to furnish **22** (936 mg, 0.68 mmol, 82%) as colorless foam. TLC: R_f = 0.30 (toluene/ethyl acetate, 4:1). $[\alpha]_D^{20}$ = –20.0 (*c* = 1, $CHCl_3$). ^{1}H NMR (600 MHz, $CDCl_3$): δ = 1.46, 1.47 (2 s, 18 H, 2× *tert*-butyl), 3.23 (dd, $^3J_{1,2} = {}^3J_{2,3}$ = 8.4 Hz, 1 H, 2b-H), 3.39 (m, 1 H, 5a-H), 3.49 (dd, $^3J_{2,3}$ = 8.4 Hz, 1 H, 3b-H), 3.57 (m, 1 H, 3a-H), 3.58 (m, 1 H, 2a-H), 3.64 (dd, $^2J_{gem}$ = 10.8 Hz, 1 H, 6a-H), 3.69 (d, ^3J = 9.8 Hz, 1 H, 5b-H), 3.73 (dd, 1 H, $^3J_{3,4} \approx {}^3J_{4,5} \approx$ 4b-H), 3.85 (dd, 1 H, $^2J_{gem}$ = 11.0 Hz, $^3J_{vic}$ = 2.7 Hz, 6a′-H), 4.02 (m, 1 H, 4a-H), 4.03–4.08 (m, 2 H, CH_2–CO), 4.12–4.20 (m, 2 H, CH_2–CO), 4.27–4.34 (m, 3 H, CH_2–CO, CHHPh), 4.40 (d, 1 H, $^3J_{1,2}$ = 7.5 Hz, 1a-H), 4.41–4.46 (m, 3 H, CH_2Ph, 1b-H), 4.68–4.76 (m, 3 H, CH_2Ph, CHHPh), 4.92 (d, 1 H, CHHPh), 4.95 (s, 1 H, CHHPh), 5.13, 5.16 (2 d, 2 H, CH_2Ph), 5.30 (s, 1 H, CHHPh), 6.74 (s, 1 H, 2a-NH), 7.13–7.31 (m, 40 H, phenyl), 8.13 (s, 1 H, NH) ppm. ^{13}C NMR (150.8 MHz, $CDCl_3$, selected data): δ = 28.0 (3 C, *tert*-butyl), 28.1 (3 C, *tert*-butyl), 56.1 (1 C, 2a-C), 67.2 (1 C, 6a-C), 73.9 (1 C, 5b-C), 74.8 (1 C, 5a-C), 77.6 (1 C, 4a-C), 78.6 (1 C, 3a-C), 79.2 (1 C, 4b-C), 82.8 (1 C, 2b-C), 83.2 (1 C, 3b-C), 102.2 (1 C, 1b-C), 103.5 (1 C, 1a-C), 168.2 (1 C, 6b-C) ppm. MALDI-MS (pos. mode, matrix DHB, THF): *m*/*z* = 1400 $[M + Na]^+$, 1416 $[M + K]^+$.

[*N*-(Triphenylmethyl)carbamoyl]methyl {2-*O*-[(*tert*-Butyloxycarbonyl)methyl]-β-D-glucopyranosyluronate}-(1→4)-3-*O*-[(*tert*-butyloxycarbonyl)methyl]-2-deoxy-2-{[(9-fluorenyl)methoxycarbonyl]-amino}-β-D-glucopyranoside (23): Pd/C (100 mg) was added to a solution of **22** (150 mg, 0.11 mmol) in THF/H_2O (5:1, 20 mL). After stirring under hydrogen for 48 h, the catalyst was filtered off through Celite, the filtrate concentrated to 1/2 of its volume, diluted with CH_3CN/H_2O (2:1, 20 mL), and then Fmoc-ONSu (90 mg, 0.27 mmol) and $NaHCO_3$ (225 mg, 2.67 mmol) were added, and the mixture was stirred at room temperature overnight. Then the reaction mixture was concentrated in vacuo until it became turbid, then diluted with H_2O and extracted four times with $CHCl_3$. The combined organic phases were dried with $MgSO_4$, concentrated, and the residue was purified by column chromatography (silica gel, ethyl acetate/MeOH, 10:3 → 3:1). Not all byproducts could be separated. Compound **23** (82 mg, 0.074 mmol, 68%) was used in the next step without further purification. MALDI-MS (pos. mode, matrix DHB, THF): *m*/*z* = 1128 $[M + Na]^+$, 1144 $[M + K]^+$.

***N*-[(9-Fluorenyl)methoxycarbonyl]-*S*-(triphenylmethyl)-L-cysteine *tert*-Butyl Ester (24):** TBTA (874 mg, 4 mmol) in dry cyclohexane (4 mL) was added to a solution of Fmoc-Cys(Trt)-OH (1.17 g, 2.0 mmol) in CH_2Cl_2 (2 mL). After addition of $BF_3{\cdot}Et_2O$ (40 μL), the reaction mixture was stirred at room temperature for 3 h and neutralized with NEt_3. The reaction mixture was then concentrated and the residue purified by column chromatography (silica gel, petroleum ether/ethyl acetate, 8:1) to furnish **24** (1.12 g, 1.75 mmol, 87%) as colorless foam. TLC: R_f = 0.70 (petroleum ether/ethyl acetate, 2:1). $[\alpha]_D^{20}$ = +10.0 (*c* = 1, $CHCl_3$). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.41 (s, 9 H, *tert*-butyl), 2.54 (m, 2 H, Cys-β-H), 4.25 (m, 1 H, Cys-α-H), 5.31 (d, ^3J = 7.8 Hz, 1 H, NH), 7.16–7.29 (m, 17 H, phenyl, Fmoc), 7.36–7.43 (m, 4 H, Fmoc) ppm. $C_{41}H_{39}NO_4S$ (641.8): calcd. C 76.73, H 6.12, N 2.18; found C 76.41, H 6.54, N 2.10.

***N*-[(9-Fluorenyl)methoxycarbonyl]-L-isoleucyl-*S*-(triphenylmethyl)-L-cysteine *tert*-Butyl Ester (25):** Piperidine (4 mL) was added to a solution of **24** (3.0 g, 4.67 mmol) in CH_2Cl_2 (25 mL) and the mixture stirred at room temperature for 3 h. The reaction mixture was concentrated in vacuo and coevaporated with toluene. After purification of the residue by column chromatography (silica gel, toluene/ethyl acetate, 20:1 → 4:1 → 2.5:1) the resulting unprotected amino acid (1.8 g, 4.29 mmol, 92%) was dissolved in dry CH_2Cl_2 (25 mL), and Fmoc-Ile-OH (1.8 g, 5.15 mmol, 1.2 equiv.) and PyBOP (2.6 g, 4.99 mmol) were added. The pH was adjusted to ca. 8 with DIPEA (ca. 1.1 g, 2 equiv., 1.46 mL). After stirring at room temperature for 1 h, the reaction mixture was diluted with ethyl acetate and washed with $KHSO_4$ and $NaHCO_3$ solution. The organic phase was dried with $MgSO_4$, filtered, concentrated and the residue purified by flash chromatography (silica gel, toluene/ethyl acetate, 15:1) to furnish dipeptide **25** (3.1 g, 4.11 mmol, 96%) as colorless foam. TLC: R_f = 0.65 (toluene/ethyl acetate, 5:1). $[\alpha]_D^{20}$ = +2.5 (*c* = 1, $CHCl_3$). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.92 (m, 6 H, 2× Ile-CH_3), 1.20 (m, 1 H, Ile-CHH), 1.42 (s, 9 H, *tert*-butyl), 1.44 (m, 1 H, Ile-CHH), 1.84 (m, 1 H, Ile-β-H), 2.49–2.62 (m, 2 H, Cys-β-H), 4.04 (m, 1 H, Cys-α-H), 4.21 (m, 1 H, Ile-α-H), 4.35–4.51 (m, 1 H, Fmoc-CH_2), 5.38 (d, ^3J = 8.5 Hz, 1 H, NH), 6.18 (d, ^3J = 7.6 Hz, 1 H, NH), 7.11–7.39 (m, 19 H, phenyl, Fmoc), 7.85, 7.75 (2 m, 4 H, Fmoc) ppm. $C_{47}H_{50}N_2O_5S$ (754.98): calcd. C 74.77, H 6.68, N 3.71; found C 74.98, H 6.95, N 3.90.

***N*-[(9-Fluorenyl)methoxycarbonyl]-L-leucyl-L-isoleucyl-*S*-(triphenylmethyl)-L-cysteine *tert*-Butyl Ester (26a):** Piperidine (3 mL) was added dropwise to a solution of **25** (1.88 g, 2.5 mmol) in CH_2Cl_2 (20 mL). After stirring at room temperature for 1 h, the reaction mixture was concentrated, coevaporated with toluene and the residue purified by column chromatography (silica gel, toluene/ethyl acetate, 10:1 → 5:1 → 2:1). The resulting unprotected dipeptide (1.1 g, 2.0 mmol, 80%) was dissolved in dry CH_2Cl_2 (15 mL), and Fmoc-Leu-OH (0.85 g, 2.4 mmol) and PyBOP (1.25 g, 2.4 mmol) were added. The pH was adjusted to 8 with DIPEA (ca. 0.68 mL) and the reaction mixture stirred at room temperature. After 1 h, it was diluted with $CHCl_3$ and washed with $KHSO_4$, $NaHCO_3$ and NaCl solution. The organic phase was dried with $MgSO_4$, filtered

and concentrated. Purification by column chromatography (silica gel, toluene/ethyl acetate, 10:1) furnished tripeptide **26a** (1.68 g, 1.93 mmol, 97%) as colorless foam. TLC: R_f = 0.59 (toluene/ethyl acetate, 1:1). $[\alpha]_D^{20}$ = +3.6 (c = 0.5, $CHCl_3$). ^1H NMR (600 MHz, [D$_6$]DMSO): δ = 0.75 (m, 3 H, Ile-CH_3), 0.79 (m, 3 H, Ile-CH_3), 0.83 (m, 6 H, Leu-CH_3), 1.03 (m, 1 H, Ile-CHH), 1.27 (s, 9 H, *tert*-butyl), 1.39 (m, 1 H, Ile-CHH), 1.45 (m, 2 H, Leu-β-H), 1.57 [m, 1 H, Leu-CH(CH_3)$_2$], 1.67 (m, 1 H, Ile-β-H), 2.30, 2.34 (2 m, Cys-β-H), 3.92 (m, 1 H, Cys-α-H), 4.09 (m, 1 H, Leu-α-H), 4.19–4.29 (m, 3 H, Fmoc-CH_2, Ile-α-H), 7.21–7.32 (m, 19 H, phenyl, Fmoc), 7.39, 7.67 (2 m, 4 H, Fmoc), 7.54 (m, 1 H, Leu-NH), 7.70 (m, 1 H, Ile-NH), 8.37 (m, 1 H, Cys-NH) ppm. ^{13}C NMR (150.8 MHz, $CDCl_3$, selected data): δ = 10.8 (1 C, Ile-CH_3), 14.9 (1 C, Ile-CH_3), 21.1 (1 C, Leu-CH_3), 22.8 (1 C, Leu-CH_3), 23.8 (1 C, Ile-CH_2), 23.9 [1 C, Leu-CH(CH_3)$_2$], 32.5 (1 C, Cys-β-C), 36.9 (1 C, Ile-β-C), 40.5 (1 C, Leu-β-C), 46.5 (1 C, Fmoc), 52.0 (1 C, Cys-α-C), 52.9 (1 C, Leu-α-C), 55.9 (1 C, Ile-α-C) ppm. $C_{53}H_{61}N_3O_6S$ (868.1): calcd. C 73.33, H 7.08, N 4.84; found C 73.26, H 7.37, N 4.80.

L-Leucyl-L-isoleucyl-*S*-(triphenylmethyl)-L-cysteine *tert*-Butyl Ester (27a): The protected tripeptide **26a** (867 mg, 1.0 mmol) was dissolved in CH_2Cl_2 (15 mL), and piperidine (3 mL) was added. After 3 h of stirring at room temperature, the reaction mixture was concentrated and coevaporated twice with toluene. The residue was purified by flash chromatography (silica gel, toluene/ethyl acetate, 10:1 → 5:1) to furnish deprotected tripeptide **27a** (640 mg, 0.99 mmol, 99%) which was immediately used in the next step.

[*N*-(Triphenylmethyl)carbamoyl]methyl {2-*O*-[(*tert*-Butyloxycarbonyl)methyl]-β-D-glucopyranosyluronyl[L-leucyl-L-isoleucyl-*S*-(triphenylmethyl)-L-cysteine *tert*-butyl ester]}-(1→4)-3-*O*-[(*tert*-butyloxycarbonyl)methyl]-2-deoxy-2-{[(9-fluorenyl)methoxycarbonyl]amino}-β-D-glucopyranoside (28a): A solution of **23** (55 mg, 0.049 mmol), **27a** (38 mg, 0.058 mmol) and PyBOP (34 mg, 0.065 mmol) in DMF (3 mL) was treated with DIPEA (ca. 20 μL) to adjust the pH to ca. 8. After stirring at room temperature for 2 h, the reaction mixture was diluted with ethyl acetate and washed with $KHSO_4$ solution (5%), $NaHCO_3$ solution and saturated NaCl solution. The organic phase was dried with $MgSO_4$, filtered, and concentrated in vacuo. Purification by column chromatography (silica gel, toluene/acetone, 4:1 → 3.5:1) furnished **28a** (70 mg, 0.040 mmol, 82%) as colorless lyophilisate from dioxane. TLC: R_f = 0.75 (toluene/acetone, 1:1). $[\alpha]_D^{20}$ = –16.7 (c = 0.3, $CHCl_3$). ^1H NMR (600 MHz, $CDCl_3$): δ = 0.84–0.88 (m, 12 H, CH_3), 1.09 (m, 1 H, Ile-CHH), 1.38 (s, 9 H, *tert*-butyl), 1.42 (m, 1 H, Ile-CHH), 1.45 (s, 9 H, *tert*-butyl), 1.50 (s, 9 H, *tert*-butyl), 1.52, 1.68 (2 m, 2 H, Leu-β-H), 1.58 [m, 1 H, Leu-CH(CH_3)$_2$], 1.78 (m, 1 H, Ile-β-H), 2.46, 2.64 (2 m, 2 H, Cys-β-H), 3.09 (m, 1 H, 2b-H), 3.35 (m, 1 H, 4a-H), 3.61 (m, 1 H, 2a-H), 3.63–3.70 (m, 3 H, 3b-H, 4b-H, 5b-H), 3.72–3.76 (m, 4 H, 5-H, 6-H, 6′-H, Fmoc), 3.97 (m, 1 H, 3a-H), 4.04–4.10 (m, 3 H, OCH_2C=O, Fmoc), 4.10–4.18 (m, 3 H, Fmoc, OCH_2C=O), 4.19–4.22 (m, 3 H, Ile-α-H, OCH_2C=O), 4.23–4.41 (m, 5 H, Cys-α-H, Leu-α-H, 1b-H, OCH_2C=O), 4.61 (m, 1 H, 1a-H), 6.01 (br. s, 1 H, Leu-NH), 6.68 (d, 1 H, Ile-NH), 6.83 (br. s, 1 H, Cys-NH), 7.12–7.73 (m, 39 H, Fmoc, phenyl, 2a-NH), 8.10 (br. s, 1 H, NHTrt) ppm. ^{13}C NMR (150.8 MHz, $CDCl_3$, selected data): δ = 11.5, 15.1, 21.6, 22.8 (4 C, 4× CH_3), 24.7 [2 C, Leu-CH(CH_3)$_2$, Ile-CH_2], 27.8, 28.1, 28.2 (9 C, 3× *tert*-butyl), 33.7 (1 C, Cys-β-C), 37.8 (1 C, Ile-β-C), 40.9 (1 C, Leu-β-C), 46.4 (1 C, Fmoc), 51.8 (1 C, Leu-α-C), 52.0 (1 C, Cys-α-C), 57.4 (1 C, Ile-α-C), 60.0 (1 C, 6a-C), 66.8 (1 C, Fmoc), 69.2 (2 C, OCH_2C=O), 70.1 (1 C, OCH_2C=O), 72.3 (1 C, 4b-C), 72.7 (1 C, 5a-C), 74.8 (1 C, 3b-C), 75.2 (1 C, 4a-C), 77.7 (1 C, 3a-C), 78.6 (1 C, 2a-C), 83.4 (1 C, 2b-C), 102.1 (1 C, 1a-C), 103.6 (1 C, 1b-C) ppm. MALDI-MS (pos. mode, matrix DHB, THF): m/z = 1756 [M + Na]$^+$, 1772 [M + K]$^+$.

[*N*-(Triphenylmethyl)carbamoyl]methyl {2-*O*-[(*tert*-Butyloxycarbonyl)methyl]-β-D-glucopyranosyluronyl[L-leucyl-L-isoleucyl-*S*-(triphenylmethyl)-L-cysteine *tert*-butyl ester]}-(1→4)-3-*O*-[(*tert*-butyloxycarbonyl)methyl]-2-{[*N*-(*tert*-butyloxycarbonyl)-*S*-(triphenylmethyl)-L-cysteinyl]amido}-2-deoxy-β-D-glucopyranoside (30a): Piperidine (1 mL) was added to a solution of **28a** (50 mg, 0.029 mmol) in CH_2Cl_2 (5 mL). After 3 h, the reaction mixture was concentrated in vacuo, coevaporated twice with toluene and the residue purified by column chromatography (silica gel, $CHCl_3$/MeOH, 200:1 → 50:1 → 25:1). The NH-unprotected compound (30 mg, 0.020 mmol, 70%) was dissolved with **29** (11 mg, 0.023 mmol) and PyBOP (14 mg, 0.027 mmol) in dry DMF (1 mL). The pH was adjusted to 8 with DIPEA (ca 8 μL), and the reaction mixture stirred at room temperature for 1 h. After dilution with ethyl acetate, the mixture was washed with NH_4Cl solution and NaCl solution. The organic phase was dried with $MgSO_4$, filtered and concentrated. Purification by flash chromatography (silica gel toluene/acetone, 4.5:1 → 3.25:1) furnished **30a** (36 mg, 0.018 mmol, 93%, 64% over 2 steps) as colorless lyophilisate from dioxane. TLC: R_f = 0.62 (toluene/acetone, 1:1). ^1H NMR (600 MHz, [D$_6$]-DMSO): δ = 0.78 (m, 13 H, 2× Leu-CH_3, 2× Ile-CH_3, Ile-β-H), 1.02 (m, 1 H, Ile-CHH), 1.28–1.40 (m, 37 H, 3× *tert*-butyl, Boc, Ile-CHH), 1.44 (m, 2 H, Leu-β-H), 1.63 [m, 2 H, Ile-β-H, Leu CH(CH_3)$_2$], 2.34 (m, 2 H, Cys-β-H), 2.44 (m, 2 H, Cys-β-H), 2.99 (m, 1 H, 2b-H), 3.30–3.34 (m, 3 H, 5a-H, 3b-H, 4b-H), 3.48 (dd, 1 H, 2a-H), 3.54 (m, 1 H, 6a-H), 3.65–3.71 (m, 4 H, 3a-H, 4a-H, 6a′-H, 5b-H), 3.88–3.90 (m, 3 H, CHHC=ONHTrt, Cys-α-H, Cys-α-H), 4.02 (d, $^2J_{gem}$ = 15 Hz, 1 H, CHHC=ONHTrt), 4.14 (m, 2 H, CH_2C=O), 4.19 (m, 2 H, CH_2C=O), 4.26 (dd, ^3J = 8.2 Hz, 1 H, Ile-α-H), 4.36 (m, 1 H, Leu-α-H), 4.53 (d, $^3J_{1,2} \approx$ 7.3 Hz, 2 H, 1a-H, 1b-H), 4.63 (m, 1 H, OH), 5.24 (m, 1 H, OH), 5.40 (m, 1 H, OH), 6.49 (d, ^3J = 8.1 Hz, 1 H, Cys-NH), 7.15–7.33 (m, 45 H, Trt), 7.72 (d, ^3J = 7.4 Hz, 1 H, 2a-NH), 7.91 (d, ^3J = 9.0 Hz, 1 H, Ile-NH), 8.03 (s, 1 H, C=ONHTrt), 8.05 (d, ^3J = 7.3 Hz, 1 H, Leu-NH), 8.47 (d, ^3J = 7.2 Hz, 1 H, Cys-NH) ppm. ^{13}C NMR (150.8 MHz, [D$_6$]DMSO, selected data): δ = 50.9 (1 C, Leu-α-C), 52.0 (1 C, Cys-α-C), 53.2 (1 C, Cys-α-C), 53.9 (1 C, 2a-C), 55.9 (1 C, Ile-α-C), 58.9 (1 C, 6a-C), 68.2 (1 C, CH_2C=O), 68.5 (1 C, CH_2C=O), 69.0 (1 C, CH_2C=O), 74.6 (1 C, 5b-C), 76.5 (1 C, 4a-C), 78.9 (1 C, 3a-C), 81.7 (1 C, 2b-C), 101.1 (1 C, 1b-C), 101.4 (1 C, 1a-C) ppm. MALDI-MS (pos. mode, matrix DHB, THF): m/z = 1978 [M + Na]$^+$, 1994 [M + K]$^+$.

Carbamoylmethyl [2-*O*-(Carboxymethyl)-β-D-glucopyranosyluronyl(L-leucyl-L-isoleucyl-L-hemicystine)]-(1→4)-3-*O*-(carboxymethyl)-2-deoxy-2-[(L-hemicystinyl)amido]-β-D-glucopyranoside (1a): A solution of **30a** (35 mg, 0.018 mmol) in CH_2Cl_2/MeOH (7:1, 18 mL) was slowly added dropwise to a solution of iodine (23 mg, 0.091 mmol) in CH_2Cl_2/MeOH (7:1, 18 mL) at 0 °C . After stirring at 0 °C for 30 min, 0.01 M sodium thiosulfate solution was added until decolorization and the reaction mixture extracted three times with $CHCl_3$. The combined organic phases were dried with $MgSO_4$, filtered, and concentrated in vacuo. The intermediate was then dissolved in TFA (8 mL), Et_3SiH (0.4 mL) and H_2O (0.2 mL) and the mixture stirred at 0 °C for 4 h. After removal of TFA in vacuo, the reaction mixture was dried in vacuo and prepurified by chromatography (RP-18 silica gel, CH_3CN/H_2O, 1:2.5). RP-18 HPLC furnished **1a** (14 mg, 0.015 mmol, 80%) as colorless lyophilisate. HPLC (prep. RP-18: 0–5 min isocratic 5% CH_3CN + 0.1% TFA, 5–60 min linear gradient 5–50% CH_3CN + 0.1% TFA, flow 10 mL/min): t_R = 30.0 min. ^1H NMR (600 MHz, [D$_6$]DMSO): δ = 0.82–0.85 (m, 12 H, 4× CH_3), 1.08 (m, 1 H, Ile-CHH), 1.43–1.56 (m, 2

H, Ile-CHH, Leu-β-H), 1.52 (m, 1 H, Leu-β-H), 1.60 (m, 1 H, Ile-β-H), 1.68 [m, 1 H, Leu-CH(CH_3)$_2$], 2.92 (m, 1 H, Cys-β-H), 3.07 (m, 2 H, Cys-β-H, 2b-H), 3.17 (m, 1 H, Cys-β-H), 3.35–3.42 (m, 3 H, 3b-H, 4b-H, Cys-β-H), 3.48 (m, 1 H, 5a-H), 3.63–3.67 (m, 5 H, 2a-H, 3a-H, 6a-H, 5b-H), 3.73 (dd, $^3J_{3,4} = {}^3J_{4,5}$ = 7.4 Hz, 1 H, 4a-H), 3.89 (d, $^2J_{gem}$ = 15 Hz, 1 H, CHHC=ONHTrt), 4.06–4.09 (m, 3 H, CHHC=ONHTrt, Cys-α-H, Ile-α-H), 4.23–4.42 (m, 6 H, Leu-α-H, 2b-H, 2× CH_2–CO), 4.47 (d, $^3J_{1,2}$ = 7.2 Hz, 1 H, 1a-H), 4.58 (m, 1 H, Cys-α-H), 4.63 (d, $^3J_{1,2}$ = 7.7 Hz, 1 H, 1b-H), 4.77, 5.20, 5.66 (3 br.s, 3 H, OH), 7.68 (s, 1 H, Ile-NH), 7.90 (s, 1 H, Leu-NH), 8.36 (s, 1 H, Cys-NH), 8.45 (s, 1 H, Cys-NH), 8.58 (s, 1 H, 2a-NH) ppm. ^{13}C NMR (150.8 MHz, [D$_6$]-DMSO, selected data): δ = 10.8, 15.1, 21.3, 23.1 (4 C, 4× CH_3), 24.0 (1 C, Ile-β-C), 24.1 (1 C, Ile-CH_2), 36.4 [1 C, Leu-CH(CH_3)$_2$], 41.3 (1 C, Leu-β-C), 51.3 (1 C, Leu-α-C), 51.6 (1 C, Cys-α-C), 52.8 (1 C, Ile-α-C), 54.3 (1 C, 2a-C), 56.8 (1 C, Cys-α-C), 59.7 (1 C, 6a-C), 67.1, 67.9 (2 C, 2× CH_2C=O), 68.7 (1 C, 2b-C), 72.4 (1 C, 3b-C), 74.9 (2 C, 5b-C, 4b-C), 76.3 (1 C, 5a-C), 77.0 (1 C, 4a-C), 78.9 (1 C, 3a-C), 81.9 (1 C, 2b-C), 100.0 (1 C, 1a-C), 102.0 (1 C, 1b-C) ppm. MALDI-MS (pos. mode, matrix DHB, THF): *m*/*z* = 982 [M + Na]$^+$, 998 [M + K]$^+$.

***N*-[(9-Fluorenyl)methoxycarbonyl]-L-isoleucyl-L-isoleucyl-*S*-(triphenylmethyl)-L-cysteine *tert*-Butyl Ester (26b):** Compound **25** (317 mg, 0.42 mmol) was deprotected with piperidine (1.5 mL) in DMF (7 mL), the mixture concentrated in vacuo and purified by column chromatography (silica gel, toluene/ethyl acetate, 10:1 → 5:1). To the reaction mixture were added Fmoc-Ile-OH (171 mg, 0.49 mmol), PyBOP (240 mg, 0.46 mmol) and DIPEA (ca. 150 μL) in CH_2Cl_2 (3 mL) at pH = 8. After stirring at room temperature for 2 h, the mixture was diluted with ethyl acetate and washed with saturated NaCl solution. The organic phase was dried with $MgSO_4$, filtered, concentrated and purified by flash chromatography to furnish tripeptide **26b** (326 mg, 0.37 mmol, 89%) as fine colorless foam. TLC: R_f = 0.60 (toluene/ethyl acetate, 3:1). $[\alpha]_D^{20}$ = –16.8 (*c* = 0.5, $CHCl_3$). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.85–0.90 (m, 12 H, 4× CH_3), 1.10, 1.15 (2 m, 2 H, Ile-CH_2), 1.41 (s, 9 H, *tert*-butyl), 1.45 (m, 2 H, Ile-CH_2), 1.60 (m, 1 H, Ile-β-H), 1.83 (m, 1 H, Ile-β-H), 2.54, 2.60 (2 dd, 2 H, Cys-β-H), 4.04 (m, 1 H, Cys-α-H), 4.18–4.46 (m, 5 H, Ile-α-H, Ile-α-H, Fmoc), 5.38 (d, ^3J = 8.1 Hz, 1 H, NH), 6.07 (d, ^3J = 7.3 Hz, 1 H, NH), 6.40 (d, ^3J = 7.9 Hz, 1 H, NH), 7.15–7.42 (m, 19 H, phenyl, Fmoc), 7.57, 7.75 (2 d, 4 H, Fmoc) ppm. $C_{53}H_{61}N_3O_6S$ (868.1): calcd. C 73.33, H 7.08, N 4.84; found C 73.00, H 6.99, N 5.17.

L-Isoleucyl-L-isoleucyl-*S*-(triphenylmethyl)-L-cysteine *tert*-Butyl Ester (27b): Piperidine (2 mL) was added to a solution of **26b** (300 mg, 0.34 mmol) in DMF (10 mL). After stirring at room temperature for 2 h, the reaction mixture was concentrated in vacuo and purified by column chromatography (silica gel, toluene/ethyl acetate, 5:1 → 2:1) to furnish deprotected tripeptide **27b** (212 mg, 0.33 mmol 95%) as colorless foam. TLC: R_f = 0.10 (toluene/ethyl acetate, 3:1). $[\alpha]_D^{20}$ = –15.6 (*c* = 1, $CHCl_3$). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.85–0.95 (m, 12 H, 4× Ile-CH_3), 1.02 (m, 2 H, Ile-CH_2), 1.36, 1.47 (2 m, 2 H, Ile-CH_2), 1.40 (s, 9 H, *tert*-butyl), 1.97 (m, 2 H, 2× Ile-β-H), 2.46 (m, 2 H, Cys-β-H), 3.26 (d, 1 H, Ile-α-H), 4.26 (dd, 1 H, Ile-α-H), 4.39 (m, 1 H, Cys-α-H), 6.35 (d, 1 H, NH), 7.17–7.38 (m, 15 H, phenyl), 7.87 (d, 1 H, NH) ppm. $C_{38}H_{51}N_3O_4S$ (645.9): calcd. C 70.66, H 7.96, N 6.51; found C 69.94, H 7.81, N 6.92.

***N*-[(9-Fluorenyl)methoxycarbonyl]-L-valyl-L-isoleucyl-*S*-(triphenylmethyl)-L-cysteine *tert*-Butyl Ester (26c):** Compound **25** (317 mg, 0.42 mmol) was deprotected with piperidine (1.5 mL) in DMF (7 mL), the solution concentrated in vacuo and purified by column chromatography (silica gel, toluene/ethyl acetate, 10:1 → 5:1). To the reaction mixture was added Fmoc-Val-OH (165 mg, 0.49 mmol), PyBOP (240 mg, 0.46 mmol) and DIPEA (ca. 150 μL) in CH_2Cl_2 (3 mL) at pH = 8. After stirring at room temperature for 2 h, it was diluted with ethyl acetate and washed with saturated NaCl solution. The organic phase was dried with $MgSO_4$, filtered, concentrated and purified by flash chromatography to furnish tripeptide **26c** (307 mg, 0.36 mmol, 85%) as colorless foam. TLC: R_f = 0.60 (toluene/ethyl acetate, 3:1). $[\alpha]_D^{20}$ = –12.6 (*c* = 1, $CHCl_3$). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.87–0.91 (m, 12 H, 2× Ile-CH_3, 2× Val-CH_3), 1.21 (m, 1 H, Ile-CHH), 1.41 (s, 9 H, *tert*-butyl), 1.42 (m, 1 H, Ile-CHH), 1.82 (m, 1 H, Ile-β-H), 2.09 (m, 1 H, Val-β-H), 2.49–2.63 (m, 2 H, Cys-β-H), 4.00 (m, 1 H, Cys-α-H), 4.12–4.53 (m, 5 H, Val-α-H, Ile-α-H, Fmoc), 5.39 (d, ^3J = 8.6 Hz, 1 H, NH), 6.07 (d, ^3J = 8.4 Hz, 1 H, NH), 6.39 (d, ^3J = 8.4 Hz, 1 H, NH), 7.15–7.45 (m, 19 H, phenyl, Fmoc), 7.68, 7.77 (2d, 4 H, Fmoc) ppm. $C_{52}H_{59}N_3O_6S$ (854.1): calcd. C 73.12, H 6.96, N 4.92; found C 72.74, H 7.12, N 5.54.

L-Valyl-L-isoleucyl-*S*-(triphenylmethyl)-L-cysteine *tert*-Butyl Ester (27c): Piperidine (2 mL) was added to a solution of **26c** (300 mg, 0.35 mmol) in DMF (10 mL). After stirring at room temperature for 2 h, the reaction mixture was concentrated in vacuo and purified by flash chromatography (silica gel, toluene/ethyl acetate, 5:1 → 2:1) to furnish deprotected tripeptide **27c** (202 mg, 0.32 mmol 91%) as colorless foam. TLC: R_f = 0.10 (toluene/ethyl acetate, 3:1). $[\alpha]_D^{20}$ = –15.1 (*c* = 1, $CHCl_3$). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.78–0.99 (m, 12 H, 2× Val-CH_3, 2× Ile-CH_3), 1.12 (m, 1 H, Ile-CHH), 1.41 (s, 9 H, *tert*-butyl), 1.43 (m, 1 H, Ile-CHH), 1.91 (m, 1 H, Ile-β-H), 2.32 (m, 1 H, Val-β-H), 2.56 (m, 2 H, Cys-β-H), 3.22 (d, 1 H, Val-α-H), 4.27 (dd, 1 H, Ile-α-H), 4.42 (m, 1 H, Cys-α-H), 6.32 (d, 1 H, NH), 7.14–7.39 (m, 15 H, phenyl), 7.86 (d, 1 H, NH) ppm. $C_{37}H_{49}N_3O_4S$ (631.9): calcd. C 70.33, H 7.82, N 6.65; found C 70.45, H 7.68, N 6.78.

Carbamoylmethyl [2-*O*-(Carboxymethyl)-β-D-glucopyranosyluronyl(L-isoleucyl-L-isoleucyl-L-hemicystine)]-(1→4)-3-*O*-(carboxymethyl)-2-deoxy-2-[(L-hemicystinyl)amido]-β-D-glucopyranoside (1b): As in the synthesis of **1a**, for the preparation of **1b** the heptapeptide mimetic was synthesized as intermediate from **27b** and **23**, which after Fmoc deprotection, a new peptide coupling, cyclization and final deprotection gave **1b**. HPLC (prep. RP-18: 0–5 min isocratic 5% CH_3CN + 0.1% TFA, 5–50 min linear gradient 5–50% CH_3CN + 0.1% TFA, flow 10 mL/min): t_R = 33.6 min. ^{1}H NMR (600 MHz, [D$_6$]DMSO): δ = 0.77 (m, 3 H, Ile-CH_3), 0.82 (m, 6 H, 2× Ile-CH_3), 0.87 (m, 3 H, Ile-CH_3), 0.99 (m, 1 H, Ile-CHH), 1.11 (m, 1 H, Ile-CHH), 1.38 (m, 1 H, Ile-CHH), 1.48 (m, 1 H, Ile-CHH), 1.70 (m, 1 H, Ile-β-H), 1.75 (m, 1 H, Ile-β-H), 3.03 (m, 2 H, Cys-β-H), 3.10 (dd, $^3J_{1,2} = {}^3J_{2,3}$ = 8.3 Hz, 1 H, 2b-H), 3.16 (dd, $^2J_{gem}$ = 14.1, $^3J_{vic}$ = 4.1 Hz, 1 H, Cys-β-H), 3.30 (m, $^2J_{gem}$ = 14.1 Hz, 1 H, Cys-β′-H), 3.33–3.40 (m, 2 H, 3b-H, 4b-H), 3.47 (m, 1 H, 3a-H), 3.64 (m, 3 H, 2a-H, 5a-H, 6a-H), 3.68 (d, $^3J_{4,5}$ = 9.4 Hz, 1 H, 5b-H), 3.72 (dd, 1 H, 4a-H), 3.88 (d, $^2J_{gem}$ = 15.1 Hz, 1 H, CHHC=ONH$_2$), 3.99–4.08 (m, 3 H, Cys-α-H, Ile-α-H, CHHC=ONH$_2$), 4.27 (m, 3 H, Ile-α-H, CH_2C=O), 4.45 (m, 2 H, CH_2C=O), 4.48 (br. d, $^3J_{1,2} \approx$ 7.1 Hz, 1 H, 1a-H), 4.54 (dd, 1 H, Cys-α-H), 4.62 (d, 1 H, $^3J_{1,2}$ = 7.7 Hz, 1b-H), 6.88, 7.35 (2 br. s, 2 H, OH), 7.58 (br. s, 1 H, Ile-NH), 7.83 (br. s, 1 H, Ile-NH), 8.26 (br. s, 1 H, Cys-NH), 8.37 (br. s, 1 H, Cys-NH), 8.58 (br. s, 2a-NH) ppm. ^{13}C NMR (150.8 MHz, [D$_6$]DMSO, selected data): δ = 10.9, 11.1, 15.2, 15.4 (4 C, 4× CH_3), 24.0, 24.4 (2 C, CH_2CH_3), 36.0, 37.3 (2 C, 2× Ile-β-C), 40.1 (1 C, Cys-β-C), 40.6 (1 C, Cys-β-C), 51.7 (1 C, Cys-α-C), 52.9 (1 C, Cys-α-C), 54.3 (1 C, 2a-C), 56.5 (1 C, Ile-α-C), 57.3 (1 C, Ile-α-C), 59.4 (1 C, 6a-C), 67.0 (1 C, CH_2C=O), 67.6 (1 C, CH_2C=O), 68.7 (1 C, CH_2C=O), 72.7 (1 C,

4b-C), 74.4 (1 C, 5b-C), 74.9 (1 C, 3b-C), 75.9 (1 C, 3a-C), 77.4 (1 C, 4a-C), 78.4 (1 C, 5a-C), 82.0 (1 C, 2b-C), 99.9 (1 C, 1a-C), 101.8 (1 C, 1b-C) ppm. MALDI-MS (pos. mode, matrix DHB, THF): m/z = 960 $[M + H]^+$, 982 $[M + Na]^+$, 998 $[M + K]^+$.

Carbamoylmethyl [2-*O*-(Carboxymethyl)-β-D-glucopyranosyluronyl(L-valyl-L-isoleucyl-L-hemicystine)]-(1→4)-3-*O*-(carboxymethyl)-2-deoxy-2-[(L-hemicystinyl)amido]-β-D-glucopyranoside (1c): As in the synthesis of **1a**, for the preparation of **1c** the heptapeptide mimetic was synthesized as intermediate from **27c** and **23**, which after Fmoc deprotection, a new peptide coupling, cyclization and final deprotection gave **1c**. HPLC (prep. RP-18: 0–5 min isocratic 6% CH_3CN + 0.1% TFA, 5–55 min linear gradient 6–50% CH_3CN + 0.1% TFA, flow 10 mL/min): t_R = 29.6 min. ^1H NMR (600 MHz, $[D_6]$DMSO): δ = 0.77 (m, 3 H, Val-CH_3), 0.81 (m, 3 H, Ile-CH_3), 0.86 (m, 6 H, Val-CH_3, Ile-CH_3), 1.12 (m, 1 H, Ile-CHH), 1.48 (m, 1 H, Ile-CHH), 1.70 (m, 1 H, Ile-β-H), 2.02 (m, 1 H, Val-β-H), 3.03 (m, 2 H, Cys-β-H), 3.10 (dd, $^3J_{1,2}$ = $^3J_{2,3}$ = 8.9 Hz, 1 H, 2b-H), 3.15 (dd, 1 H, Cys-β-H), 3.30 (dd, 1 H, Cys-β-H), 3.35–3.38 (m, 2 H, 3b-H, 4b-H), 3.47 (dd, 1 H, 3a-H), 3.65–3.83 (m, 6 H, 2a-H, 4a-H, 5a-H, 6a-H, 5b-H), 3.88 (d, ^3J = 15.4 Hz, 1 H, CHHC=ONH$_2$), 3.99–4.08 (m, 3 H, Ile-α-H, Cys-α-H, CHHC=ONH$_2$), 4.27 (m, 3 H, Val-α-H, CH_2C=O), 4.47–4.52 (m, 3 H, CH_2C=O, 1a-H), 4.55 (dd, 1 H, Cys-α-H), 4.62 (d, ^3J = 7.7 Hz, 1 H, 1b-H), 6.87, 7.36 (2 s, 2 H, OH), 7.55 (br. s, 1 H, Val-NH), 7.83 (br. s, 1 H, Ile-NH), 8.24 (br. s, 1 H, Cys-NH), 8.37 (br. s, 3 H, Cys-NH, C=ONH$_2$), 8.57 (br. s, 1 H, 2a-NH) ppm. ^{13}C NMR (150.8 MHz, $[D_6]$DMSO, selected data): δ = 10.9, 15.2 (2 C, 2× Ile-CH_3), 17.8, 19.2 (2 C, 2× Val-CH_3), 24.3 (1 C, CH_2CH_3), 31.2 (1 C, Val-β-C), 35.8 (1 C, Ile-β-C), 40.1 (1 C, Cys-β-C), 40.4 (1 C, Cys-β-C), 51.8 (1 C, Cys-α-C), 52.9 (1 C, Cys-α-C), 54.4 (1 C, 2a-C), 57.0 (1 C, Val-α-C), 57.3 (1 C, Ile-α-C), 59.4 (1 C, 6a-C), 67.6, 68.8, 70.1 (3 C, 3× CH_2C=O), 72.8 (1 C, 4b-C), 74.6 (1 C, 5b-C), 74.8 (1 C, 3b-C), 75.8 (1 C, 3a-C), 77.5 (1 C, 4a-C), 78.2 (1 C, 5a-C), 81.9 (1 C, 2b-C), 100.1 (1 C, 1a-C), 102.0 (1 C, 1b-C) ppm. MALDI-MS (pos. mode, matrix DHB, THF): m/z = 967 $[M + Na]^+$, 984 $[M + K]^+$.

***N*-(*tert*-Butyloxycarbonyl)-*S*-(triphenylmethyl)-L-cysteinylglycine Methyl Ester (31):** DIPEA (ca. 0.2 mL) was added to a solution of Boc-Cys(Trt)-OH (230 mg, 0.50 mmol), NH_2-Gly-OMe (69 mg, 0.55 mmol) and PyBOP (301 mg, 0.58 mmol) in dry CH_2Cl_2 until pH = 8 was reached. The reaction mixture was stirred at room temperature for 2 h, diluted with ethyl acetate and washed twice with saturated NaCl solution. The organic phase was dried with $MgSO_4$, filtered and concentrated. Purification by column chromatography (silica gel, toluene/ethyl acetate, 3.5:1) furnished **31** (265 mg, 49 mmol, 98%) as colorless powder. TLC: R_f = 0.25 (toluene/ethyl acetate, 3:1). $[\alpha]_D^{20}$ = –15.3 (c = 0.5, $CHCl_3$). ^1H NMR (250 MHz, $CDCl_3$): δ = 1.37 (s, 9 H, Boc), 2.50 (dd, $^2J_{gem}$ = 12.9, $^3J_{vic}$ = 5.1 Hz, 1 H, Cys-β-H), 2.67 (dd, 1 H, Cys-β′-H), 3.67 (s, 3 H, OCH_3), 3.83 (m, 1 H, Cys-α-H), 3.92 (m, 2 H, Gly-α-H), 4.72 (br. d, 1 H, NH), 6.49 (br. s, 1 H, NH), 7.13–7.40 (m, 15 H, phenyl) ppm. $C_{30}H_{34}N_2O_5S$ (534.7): calcd. C 67.39, H 6.41, N 5.24; found C 67.09, H 6.16, N 5.16.

***N*-(*tert*-Butyloxycarbonyl)-*S*-(triphenylmethyl)-L-cysteinylglycine (32):** NaOH (100 mg, 2.5 mmol) was added to a solution of **31** (250 mg, 0.46 mmol), dioxane (20 mL), MeOH (7 mL) and H_2O (7 mL), stirred overnight and then neutralized with ion exchange resin IR 120 (H^+), filtered and concentrated to furnish **32** (235 mg, 0.45 mmol, 99%) which was immediately used in the next step without further purification. TLC: R_f = 0.04 (toluene/ethyl acetate, 3:1). $[\alpha]_D^{20}$ = +10.5 (c = 0.5, $CHCl_3$). ^1H NMR (250 MHz, $[D_6]$DMSO): δ = 1.37 (s, 9 H, Boc), 2.36 (dd, 1 H, Cys-β-H), 2.48 (m, 1 H, Cys-β′-H), 3.47 (d, 2 H, Gly-α-H), 3.89 (m, 1 H, Cys-α-H), 7.07 (d, 1 H, NH), 7.20 (m, 15 H, phenyl), 7.55 (br. s, 1 H, NH) ppm. $C_{29}H_{31}N_2NaO_5S\cdot H_2O$ (560.6): calcd. C 62.13, H 5.72, N 5.00; found C 62.29, H 5.72, N 5.04.

Carbamoylmethyl [2-*O*-(Carboxymethyl)-β-D-glucopyranosyluronyl(L-leucyl-L-isoleucyl-L-hemicysteine)]-(1→4)-3-*O*-(carboxymethyl)-2-deoxy-[(L-hemicystinylglycyl)amido]-β-D-glucopyranoside (2): As in the synthesis of **1a**, for the preparation of **2** the nonapeptide mimetic was synthesized as intermediate from **32** and **28a**, which after cyclization and final deprotection gave **2** (45%). HPLC (prep. RP-18: 0–5 min isocratic 6% CH_3CN + 0.1% TFA, 5–55 min linear gradient 6–50% CH_3CN + 0.1% TFA, flow 10 mL/min): t_R = 31.1 min. ^1H NMR (600 MHz, $[D_6]$DMSO): δ = 0.80 (m, 3 H, Ile-CH_3), 0.83–0.87 (m, 9 H, Ile-CH_3, 2× Leu-CH_3), 1.13 (m, 1 H, Ile-CHH), 1.31 (m, 1 H, Leu-β-H), 1.44 (m, 2 H, Leu-β′-H, Ile-CHH), 1.54 [m, 1 H, Leu-CH(CH_3)$_2$], 1.72 (m, 1 H, Ile-β-H), 3.00 (m, 2 H, Cys-β-H), 3.07 (dd, $^3J_{1,2}$ = $^3J_{2,3}$ = 8.2 Hz, 1 H, 2b-H), 3.14 (m, 1 H, Cys-β-H), 3.31–3.39 (m, 4 H, 5a-H, 3b-H, 4b-H, Cys-β-H), 3.65–3.77 (m, 7 H, 2a-H, 3a-H, 4a-H, 6a-H, 5b-H, Gly-α-H), 3.88 (d, 1 H, CHHC=O), 3.99–4.01 (m, 2 H, Cys-α-H, Gly-α-H), 4.04–4.07 (m, 2 H, Ile-α-H, CHHC=O), 4.12 (d, 1 H, CHHC=O), 4.24 (m, 2 H, CH_2C=O), 4.26 (d, 1 H, CHHC=O), 4.45 (m, 2 H, Cys-α-H, 1a-H), 4.55 (m, 1 H, Leu-α-H), 4.66 (d, $^3J_{1,2}$ = 7.7 Hz, 1 H, 1b-H), 7.25 (d, ^3J = 7.0 Hz, 1 H, Leu-NH), 7.83 (d, ^3J = 7.2 Hz, 1 H, 2a-NH), 8.15 (d, ^3J = 6.8 Hz, 1 H, Ile-NH), 8.39 (br. s, 1 H, Cys-NH), 8.57 (d, ^3J = 7.6 Hz, 1 H, Cys-NH), 8.72 (m, 1 H, Gly-NH) ppm. ^{13}C NMR (150.8 MHz, $[D_6]$DMSO, selected data): δ = 10.9, 15.2 (2 C, 2× Ile-CH_3), 21.8, 22.9 (2 C, 2× Leu-CH_3), 24.3 [2 C, CH_2CH_3, CH(CH_3)$_2$], 36.0 (1 C, Ile-β-C), 38.9 (1 C, Cys-β-C), 40.1 (1 C, Cys-β-C), 41.6 (1 C, Leu-β-C), 42.2 (1 C, Gly-α-C), 49.8 (1 C, Leu-α-C), 50.9 (1 C, Cys-α-C), 51.2 (1 C, Cys-α-C), 53.7 (1 C, 2a-C), 57.2 (1 C, Ile-α-C), 59.4 (1 C, 6a-C), 67.3, 68.1, 68.9 (3 C, 3× CH_2C=O), 72.3 (1 C, 4b-C), 73.1 (1 C, 5b-C), 74.9 (2 C, 5a-C, 3b-C), 76.5 (1 C, 4a-C), 80.2 (1 C, 3a-C), 82.3 (1 C, 2b-C), 100.4 (1 C, 1a-C), 101.2 (1 C, 1b-C) ppm. MALDI-MS (pos. mode, matrix DHB, THF): m/z = 1039 $[M + Na]^+$, 1055 $[M + K]^+$.

Dimethyl(thexyl)silyl 4,6-*O*-Benzylidene-2-deoxy-2-(dimethylmaleimido)-3-*O*-levulinoyl-β-D-glucopyranoside (35): Levulinic acid (3.0 g, 25.8 mmol) and dicyclohexylcarbodiimide (5.3 g, 25.8 mmol) were added to a solution of **9**[29] (6.0 g, 11.5 mmol) in dry CH_2Cl_2 (60 mL). After the addition of catalytic amounts of DMAP, the turbid solution was stirred at room temperature for 2 h. The precipitated urea was filtered off, and the filtrate washed with saturated $NaHCO_3$ solution. The organic phase was dried with $MgSO_4$, filtered and concentrated. Purification by flash chromatography (silica gel, petroleum ether/ethyl acetate, 4.5:1 → 3:1) furnished **35** (6.3 g, 10.2 mmol 89%) as colorless powder. TLC: R_f = 0.48 (petroleum ether/ethyl acetate, 2:1). $[\alpha]_D^{20}$ = –2.5 (c = 1, $CHCl_3$). ^1H NMR (250 MHz, $CDCl_3$): δ = 0.01 (s, 3 H, $SiCH_3$), 0.08 (s, 3 H, $SiCH_3$), 0.68–0.75 (m, 12 H, 4× CH_3), 1.47 [m, 1 H, CH(CH_3)$_2$], 1.93 (s, 6 H, DMM-H), 2.04 (s, 3 H, Lev-C=OCH_3), 2.39–2.65 (m, 4 H, 2× Lev-CH_2), 3.62–3.69 (m, 3 H, 3-H, 4-H, 5-H), 3.78 (dd, $^3J_{1,2} \approx {}^3J_{2,3} \approx$ 9.9 Hz, 1 H, 2-H), 3.98 (dd, $^2J_{gem}$ = 10.5, $^3J_{vic}$ = 8.0 Hz, 1 H, 6-H), 4.30 (dd, $^2J_{gem}$ = 10.4, $^3J_{vic}$ = 4.3 Hz, 1 H, 6′-H), 5.43 (d, $^3J_{1,2}$ = 8.0 Hz, 1 H, 1-H), 5.47 (s, 1 H, CHphenyl), 4.24 (dd, $^3J_{2,3}$ = 10.5, $^3J_{3,4}$ = 8.9 Hz, 1 H, 3-H), 7.32 (m, 3 H, phenyl), 7.41 (m, 2 H, phenyl) ppm. $C_{32}H_{45}NO_9Si$ (615.8): calcd. C 62.41, H 7.37, N 2.27; found C 62.36, H 7.43, N 2.47.

Dimethyl(thexyl)silyl 6-*O*-Benzyl-2-deoxy-2-(dimethylmaleimido)-3-*O*-levulinoyl-β-D-glucopyranoside (36): Triethylsilane (13 mL) was added to a solution of **35** (6.0 g, 9.74 mmol) in dry CH_2Cl_2 (50 mL). The reaction mixture was then cooled to 0 °C, trifluoro-

acetic anhydride (3.5 mL) and trifluoroacetic acid (3.2 mL) were added, and after stirring at 0 °C for 4 h, the mixture was poured into a cold saturated $NaHCO_3$ solution. The mixture was then diluted with ethyl acetate and washed twice with $NaHCO_3$ solution. The organic phase was dried with $MgSO_4$, filtered, and concentrated in vacuo. Purification by flash chromatography (silica gel, toluene/acetone, 8:1) furnished **36** (4.7 g, 7.61 mmol, 78%) as colorless oil. TLC: R_f = 0.39 (toluene/acetone, 8:1). $[\alpha]_D^{20}$ = –8.9 (c = 1, $CHCl_3$). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.01 (s, 3 H, $SiCH_3$), 0.11 (s, 3 H, $SiCH_3$), 0.67–0.74 (m, 12 H, 4× CH_3), 1.46 [m, 1 H, $CH(CH_3)_2$], 1.91 (s, 6 H, DMM-H), 2.09 (s, 3 H, Lev-CH_3), 2.44 (m, 2 H, Lev-CH_2), 2.68 (m, 2 H, Lev-CH_2), 3.12 (d, ^3J = 2.4 Hz, 1 H, OH), 3.61–3.69 (m, 2 H, 4-H, 5-H), 3.70–3.77 (m, 2 H, 6-H), 3.94 (dd, $^3J_{1,2}$ = 8.0, $^3J_{2,3}$ = 10.9 Hz, 1 H, 2-H), 4.59 (s, 2 H, CH_2Ph), 5.33 (d, $^3J_{1,2}$ = 8.0 Hz, 1 H, 1-H), 5.54 (dd, $^3J_{2,3}$ = 10.9, $^3J_{3,4}$ = 8.3 Hz, 1 H, 3-H), 7.26–7.33 (m, 5 H, phenyl) ppm. $C_{32}H_{41}NO_9Si$ (617.8): calcd. C 62.21, H 7.67, N 2.27; found C 61.78, H 7.49, N 2.51.

Dimethyl(thexyl)silyl 2,6-Di-*O*-acetyl-3,4-di-*O*-benzyl-β-D-glucopyranosyl-(1→4)-6-*O*-benzyl-2-deoxy-2-(dimethylmaleimido)-3-*O*-levulinoyl-β-D-glucopyranoside (37): TMSOTf (0.1 M in CH_2Cl_2, 4 mL) was added to a mixture of **8** (2.90 g, 4.94 mmol) and **36** (2.78 g, 4.5 mmol) in dry CH_2Cl_2 (30 mL) at room temperature. After 1.5 h, the reaction mixture was neutralized with NEt_3 and concentrated. Purification by column chromatography (silica gel, toluene/ethyl acetate, 7:1) furnished **37** (3.21 g, 3.07 mmol, 68%) as colorless foam. TLC: R_f = 0.45 (toluene/ethyl acetate, 3:1). $[\alpha]_D^{20}$ = +6.3 (c = 1, $CHCl_3$). ^{1}H NMR (600 MHz, $CDCl_3$): δ = 0.02 (s, 3 H, $SiCH_3$), 0.12 (s, 3 H, $SiCH_3$), 0.70–0.76 (m, 12 H, 4× CH_3), 1.49 [m, 1 H, $CH(CH_3)_2$], 1.89–1.95 (m, 9 H, DMM-H, acetyl), 2.05, 2.07 (2 s, 6 H, acetyl, Lev-C=OCH_3), 2.35, 2.40, 2.50, 2.60 (4 m, 4 H, Lev-CH_2), 3.43 (m, 1 H, 5b-H), 3.53–3.56 (m, 3 H, 5a-H, 3b-H, 4b-H), 3.65 (dd, $^2J_{gem}$ = 10.5 Hz, 1 H, 6a-H), 3.76 (dd, $^2J_{gem}$ = 11.1, $^3J_{vic}$ = 3 Hz, 1 H, 6a′-H), 3.89 (dd, 1 H, $^3J_{3,4} \approx {}^3J_{4,5} \approx$ 9.5 Hz, 4a-H), 3.93 (dd, 1 H, $^3J_{1,2}$ = 8.1, $^3J_{2,3}$ = 10.8 Hz, 2a-H), 4.19–4.22 (m, 2 H, 6b-H), 4.46 (d, 1 H, $^3J_{1,2}$ = 8.0 Hz, 1b-H), 4.50, 4.52, 4.62 (3 d, 3 H, CH_2Ph, CHHPh), 4.71–4.78 (m, 3 H, CH_2Ph, CHHPh), 4.87 (dd, $^3J_{1,2} \approx {}^3J_{2,3} \approx$ 8.5 Hz, 2b-H), 5.35 (d, 1 H, $^3J_{1,2}$ = 8.1 Hz, 1a-H), 5.57 (dd, 1 H, $^3J_{2,3}$ = 10.7, $^3J_{3,4}$ = 9.2 Hz, 3a-H), 7.23–7.37 (m, 15 H, phenyl) ppm. ^{13}C NMR (150.8 MHz, $CDCl_3$, selected data): δ = 56.5 (1 C, 2a-C), 63.0 (1 C, 6b-C), 67.6 (1 C, 6a-C), 70.5 (1 C, 3a-C), 72.8 (1 C, 5b-C), 72.9 (1 C, 2b-C), 74.6 (1 C, 5a-C), 75.7 (1 C, 4a-C), 77.2 (1 C, 3b-C), 83.2 (1 C, 4b-C), 93.1 (1 C, 1a-C), 100.3 (1 C, 1b-C) ppm. $C_{56}H_{79}NO_{16}Si$ (1044.3): calcd. C 64.41, H 7.05, N 1.34; found C 64.33, H 7.12, N 1.44.

Dimethyl(thexyl)silyl 2,6-Di-*O*-acetyl-3,4-di-*O*-benzyl-β-D-glucopyranosyl-(1→4)-6-*O*-benzyl-2-deoxy-2-(dimethylmaleimido)-β-D-glucopyranoside (38): Acetic acid (29 mL) was added to a solution of **37** (4.29 g, 4.11 mmol) in pyridine (45 mL), the mixture cooled to 0 °C and hydrazine hydrate (3.25 mL, 3.35 g, 66.9 mmol) added dropwise. After stirring at 0 °C for 9 min, the reaction mixture was diluted with CH_2Cl_2 and the organic phase washed with saturated $NaHCO_3$ solution and NaCl solution. The organic phase was dried with $MgSO_4$, filtered, concentrated and coevaporated twice with toluene. Purification by column chromatography (silica gel, toluene/acetone, 7:1) furnished **38** (3.83 g, 4.04 mmol, 98%) as colorless foam. TLC: R_f = 0.68 (petroleum ether/ethyl acetate, 1:1). $[\alpha]_D^{20}$ = +12.0 (c = 1, $CHCl_3$). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.01 (s, 3 H, $SiCH_3$), 0.11 (s, 3 H, $SiCH_3$), 0.69–0.75 (m, 12 H, 4× CH_3), 1.48 [m, 1 H, $CH(CH_3)_2$], 1.88 (s, 3 H, acetyl), 1.89 (s, 6 H, DMM-H), 1.96 (s, 3 H, acetyl), 3.50–3.64 (m, 7 H, 3a-H, 4a-H, 5a-H, 6a-H, 3b-H, 4b-H, 5b-H), 3.84 (dd, $^3J_{1,2}$ = 8.2, $^3J_{2,3}$ = 10.9 Hz, 1 H, 2a-H), 3.91 (d, ^3J = 1.2 Hz, 1 H, OH), 4.04 (dd, $^2J_{gem}$ = 11.9, $^3J_{vic}$ = 6.2 Hz, 1 H, 6a′-H), 4.25 (m, $^2J_{gem}$ = 11.9 Hz, 2 H, 6b-H), 4.39 (d, $^3J_{1,2}$ = 8.1 Hz, 1 H, 1b-H), 4.49–4.80 (m, 6 H, 3× CH_2Ph), 4.95 (dd, $^3J_{1,2} \approx {}^3J_{2,3} \approx$ 8.4 Hz, 1 H, 2b-H), 5.21 (d, $^3J_{1,2}$ = 8.1 Hz, 1 H, 1a-H), 7.20–7.25 (m, 15 H, phenyl) ppm. $C_{51}H_{67}NO_{14}Si$ (946.16): calcd. C 64.74, H 7.14, N 1.48; found C 64.66, H 7.17, N 1.47.

Dimethyl(thexyl)silyl 2,6-Di-*O*-acetyl-3,4-di-*O*-benzyl-β-D-glucopyranosyl-(1→4)-6-*O*-benzyl-2-deoxy-2-(dimethylmaleimido)-β-D-allopyranoside (39): Dess–Martin periodinane reagent (1.40 g, 3.30 mmol) was added to a solution of **38** (1.10 g, 1.16 mmol) in CH_2Cl_2 (10 mL), the reaction mixture stirred at room temperature for 3 h, then sodium sulfate solution (8 mL) and $NaHCO_3$ solution (8 mL) were added, and the mixture was stirred for 30 min. The phases were separated, the aqueous phase was extracted twice with $CHCl_3$, and the combined organic phases were dried with $MgSO_4$, filtered, and concentrated in vacuo. The residue (1.15 g, quant.), the oxidized intermediate, was diluted in CH_2Cl_2 (9 mL) and MeOH (9 mL) and the mixture cooled to –10 °C. Under vigorous stirring, $NaBH_4$ (37.4 mg, 0.99 mmol) was added in one portion and the reaction mixture stirred for 210 s. Then acetone (2 mL) and NH_4Cl solution were added, and the mixture was stirred for 10 min. After dilution with H_2O, the reaction mixture was extracted three times with CH_2Cl_2, and the combined organic phases were dried with $MgSO_4$, filtered and concentrated. Purification by column chromatography (silica gel, petroleum ether/ethyl acetate, 3.5:1) furnished, beside some reactant **38** (105 mg, 0.11 mmol, 9%), the epimerized allose building block **39** (750 mg, 0.79 mmol, 68%) as white amorphous solid. TLC: R_f = 0.41 (petroleum ether/ethyl acetate, 2:1). $[\alpha]_D^{20}$ = –6.1 (c = 1, $CHCl_3$). ^{1}H NMR (600 MHz, $CDCl_3$): δ = 0.08 (s, 3 H, $SiCH_3$), 0.16 (s, 3 H, $SiCH_3$), 0.71–0.78 (m, 12 H, 4× CH_3), 1.50 [m, 1 H, $CH(CH_3)_2$], 1.89 (s, 3 H, acetyl), 1.94 (s, 3 H, acetyl), 1.95 (s, 6 H, DMM-H), 3.52–3.55 (m, 2 H, 4b-H, 5b-H), 3.60–3.68 (m, 2 H, 3b-H, 6a-H), 3.67 (dd, $^2J_{gem}$ = 11.2, $^3J_{vic}$ = 4.9 Hz, 1 H, 6a′-H), 3.86 (dd, $^3J_{3,4}$ = 2.9, $^3J_{4,5}$ = 9.8 Hz, 1 H, 4a-H), 3.92 (dd, $^3J_{1,2}$ = 8.2, $^3J_{2,3}$ = 2.8 Hz, 1 H, 2a-H), 3.99 (m, 1 H, 5a-H), 4.05 (dd, $^2J_{gem}$ = 11.8, $^3J_{vic}$ = 5.2 Hz, 1 H, 6b-H), 4.21 (dd, $^3J_{2,3}$ = 2.8, $^3J_{3,4}$ = 2.9 Hz, 3a-H), 4.27 (dd, $^2J_{gem}$ = 11.8, $^3J_{vic}$ = 1.7 Hz, 1 H, 6b′-H), 4.48 (d, $^3J_{1,2}$ = 8.2 Hz, 1 H, 1b-H), 4.54. 4.55, 4.65, 4.66, 4.79, 4.81 (6 d, 6 H, 3× CH_2Ph), 4.99 (dd, $^3J_{1,2}$ = 7.9, $^3J_{2,3}$ = 9.7 Hz, 1 H, 2b-H), 5.86 (d, $^3J_{1,2}$ = 8.2 Hz, 1 H, 1a-H), 7.24–7.35 (m, 15 H, phenyl) ppm. ^{13}C NMR (150.8 MHz, $CDCl_3$, selected data): δ = 57.3 (1 C, 2a-C), 63.0 (1 C, 6b-C), 68.9 (1 C, 6a-C), 70.3 (1 C, 3a-C), 72.1 (1 C, 5a-C), 72.9 (1 C, 2b-C), 73.2 (1 C, 4b-C), 77.2 (1 C, 4a-C), 77.5 (1 C, 5b-C), 82.9 (1 C, 3b-C), 91.2 (1 C, 1a-C), 101.3 (1 C, 1b-C) ppm. MALDI-MS (pos. mode, matrix DHB, THF): m/z = 969 $[M + Na]^+$. $C_{51}H_{67}NO_{14}Si$ (946.2): calcd. C 64.74, H 7.14, N 1.48; found C 64.52, H 6.92, N 1.33.

Dimethyl(thexyl)silyl 2,6-Di-*O*-acetyl-3,4-di-*O*-benzyl-β-D-glucopyranosyl-(1→4)-3-*O*-acetyl-6-*O*-benzyl-2-deoxy-2-(dimethylmaleimido)-β-D-allopyranoside (40): Acetic acid anhydride (10 mL) was added to a solution of **39** (1.00 g, 1.06 mmol) in pyridine (20 mL) at 0 °C. After stirring at room temperature overnight, the reaction mixture was concentrated in vacuo and coevaporated three times with toluene. Purification by flash chromatography furnished acetylated compound **40** (1.01 g, 1.02 mmol, 97%) as colorless foam. TLC: R_f = 0.49 (petroleum ether/ethyl acetate, 2:1). $[\alpha]_D^{20}$ = +22.3 (c = 0.5, $CHCl_3$). ^{1}H NMR (600 MHz, $CDCl_3$): δ = 0.04 (s, 3 H, $SiCH_3$), 0.12 (s, 3 H, $SiCH_3$), 0.66–0.72 (m, 12 H, 4× CH_3), 1.45 [m, 1 H, $CH(CH_3)_2$], 1.82 (d, 6 H, DMM-H), 1.88, 1.94, 1.97 (3 s, 9 H, 3× acetyl), 3.42 (m, 1 H, 5b-H), 3.49 (dd, $^3J_{3,4}$ = $^3J_{4,5}$ = 9.3 Hz, 1 H, 4b-H), 3.58 (m, 2 H, 3b-H, 6a-H), 3.63 (dd, $^2J_{gem}$ = 11.2, $^3J_{vic}$ = 3.6 Hz, 1 H, 6a′-H), 3.87 (dd, $^3J_{3,4}$ = 3.0, $^3J_{4,5}$ = 9.8 Hz, 1 H, 4a-H), 3.93 (dd, $^3J_{2,3}$ = 2.2 Hz, 1 H, 2a-H), 3.94 (m,

1 H, 5a-H), 4.09 (dd, $^2J_{gem}$ = 11.7, $^3J_{vic}$ = 4.8 Hz, 1 H, 6b-H), 4.18 (dd, $^2J_{gem}$ = 11.7, $^3J_{vic}$ = 1.3 Hz, 1 H, 6b′-H), 4.39 (d, $^3J_{1,2}$ = 7.9 Hz, 1 H, 1b-H), 4.48, 4.52, 4.61, 4.63, 4.73, 4.74 (6 d, 6 H, 3× CH_2Ph), 4.89 (dd, $^3J_{1,2}$ = 8.2, $^3J_{2,3}$ = 9.2 Hz, 1 H, 2b-H), 5.47 (dd, 1 H, 3a-H), 5.24 (d, $^3J_{1,2}$ = 8.2 Hz, 1 H, 1a-H), 7.21–7.31 (m, 15 H, phenyl) ppm. ^{13}C NMR (150.8 MHz, $CDCl_3$, selected data): δ = 56.0 (1 C, 2a-C), 62.7 (1 C, 6b-C), 68.6 (1 C, 6a-C), 70.7 (1 C, 3a-C), 72.8 (1 C, 2b-C), 72.9 (1 C, 5b-C), 73.1 (1 C, 5a-C), 74.4 (1 C, 4a-C), 77.3 (1 C, 4b-C), 82.8 (1 C, 3b-C), 91.4 (1 C, 1a-C), 101.2 (1 C, 1b-C) ppm. $C_{53}H_{69}NO_{15}Si$ (988.2): calcd. C 64.42, H 7.04, N 1.42; found C 64.28, H 7.10, N 1.39.

2,6-Di-*O*-acetyl-3,4-di-*O*-benzyl-β-D-glucopyranosyl-(1→4)-3-*O*-acetyl-6-*O*-benzyl-2-deoxy-2-(dimethylmaleimido)-α,β-D-allopyranose (41): Acetic acid (135 μL, 141 mg, 2.36 mmol) was added to a solution of **40** (2.20 g, 2.22 mmol) in tetrahydrofuran (40 mL) and the reaction mixture cooled to 0 °C. After addition of a TBAF solution (1 M in THF, 2.64 mL, 2.64 mmol) and stirring at 0 °C for 3 h, the reaction mixture was diluted with diethyl ether and washed with NaCl solution. The organic phase was dried with $MgSO_4$, filtered and concentrated. Purification by flash chromatography (silica gel, petroleum ether/ethyl acetate, 3:2) furnished anomerically deprotected **41** (1.75 g, 2.07 mmol, 93%) with an anomer ratio of α/β > 10:1 as colorless foam. TLC: R_f = 0.25 (petroleum ether/ethyl acetate, 1:1). $[\alpha]_D^{20}$ = +21.6 (*c* = 1, $CHCl_3$). ^{1}H NMR (600 MHz, $CDCl_3$): δ = 1.77 (s, 3 H, acetyl), 1.85 (s, 6 H, DMM-H), 1.93 (s, 3 H, acetyl), 1.99 (s, 3 H, acetyl), 3.37 (d, ^3J = 6.0 Hz, 1 H, OH), 3.41 (m, 1 H, 5b-H), 3.49 (dd, $^3J_{3,4}$ = $^3J_{4,5}$ = 9.2 Hz, 1 H, 4b-H), 3.54 (dd, $^3J_{2,3}$ = $^3J_{3,4}$ = 9.1 Hz, 1 H, 3b-H), 3.60 (m, 2 H, 6a-H, 6a′-H), 3.83 (dd, $^3J_{3,4}$ = 3.0, $^3J_{4,5}$ = 9.8 Hz, 1 H, 4a-H), 3.93 (dd, $^3J_{1,2}$ = 8.6, $^3J_{2,3}$ = 2.2 Hz, 1 H, 2a-H), 4.02 (m, 1 H, 5a-H), 4.05 (dd, $^2J_{gem}$ = 11.8, $^3J_{vic}$ = 5.0 Hz, 1 H, 6b-H), 4.18 (dd, $^2J_{gem}$ = 11.8, $^3J_{vic}$ = 1.1 Hz, 1 H, 6a′-H), 4.35 (d, $^3J_{1,2}$ = 7.9 Hz, 1 H, 1b-H), 4.46, 4.48, 4.59, 4.61, 4.73, 4.74 (6d, 6 H, 3× CH_2Ph), 4.85 (dd, $^3J_{1,2}$ = 7.9, $^3J_{2,3}$ = 9.1 Hz, 1 H, 2b-H), 5.49 (dd, 1 H, 3a-H), 5.91 (dd, $^3J_{1,2}$ = 8.3, $^3J_{1,OH}$ = 6.1 Hz, 1 H 1a-H), 7.21–7.30 (m, 15 H, phenyl) ppm. ^{13}C NMR (150.8 MHz, $CDCl_3$, selected data): δ = 55.5 (1 C, 2a-C), 62.8 (1 C, 6b-C), 68.8 (1 C, 6a-C), 70.8 (1 C, 3a-C), 72.9 (1 C, 5b-C), 73.0 (1 C, 2b-C), 73.2 (1 C, 5a-C), 74.2 (1 C, 4a-C), 77.2 (1 C, 4b-C), 83.0 (1 C, 3b-C), 90.4 (1 C, 1a-C), 101.0 (1 C, 1b-C) ppm. $C_{45}H_{51}NO_{15}$ (845.88): calcd. C 63.90, H 6.08, N 1.66; found C 63.95, H 6.19, N 1.58.

Trichloro-*O*-[2,6-Di-*O*-acetyl-3,4-di-*O*-benzyl-β-D-glucopyranosyl-(1→4)-3-*O*-acetyl-6-*O*-benzyl-2-deoxy-2-(dimethylmaleimido)-β-D-allopyranosyl]acetimidate (42): Trichloroacetonitrile (1.35 mL, 1.94 g, 13.5 mmol) and then DBU (5 drops) were added to a solution of **41** (1.70 g, 2.01 mmol) in CH_2Cl_2 (15 mL). The reaction mixture was stirred at room temperature for 1 h, concentrated to 3/4 of its volume and purified by column chromatography (silica gel, petroleum ether/ethyl acetate, 3:2 + 1% NEt_3) to furnish **42** as slightly yellowish foam (1.95 g, 1.97 mmol, 98%) which was stored under argon at –20 °C. TLC: R_f = 0.65 (petroleum ether/ethyl acetate, 1:1). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.58 (s, 3 H, acetyl), 1.59 (br. s, 6 H, DMM-H), 1.98, 2.03 (2 s, 6 H, 2× acetyl), 3.47–3.62 (m, 3 H, 3b-H, 4b-H, 5b-H), 3.69–3.74 (m, 2 H, 6a-H), 4.04 (dd, $^3J_{3,4}$ = 2.9, $^3J_{4,5}$ = 9.8 Hz, 1 H, 4a-H), 4.14 (m, 2 H, 2a-H, 5a-H), 4.21 (dd, $^2J_{gem}$ = 9.1 Hz, 1 H, 6b-H), 4.29 (dd, $^2J_{gem}$ = 9.1, $^3J_{vic}$ = 2.4 Hz, 1 H, 6b′-H), 4.43 (d, $^3J_{1,2}$ = 7.9 Hz, 1 H, 1b-H), 4.51 (2 d, 2 H, CH_2Ph), 4.63, 4.67 (2 d, 2 H, CH_2Ph), 4.77 (d, 2 H, CH_2Ph), 4.89 (dd, $^3J_{1,2}$ ≈ $^3J_{2,3}$ ≈ 8.5 Hz, 1 H, 2b-H), 5.60 (dd, 1 H, $^3J_{2,3}$ ≈ $^3J_{3,4}$ ≈ 2.6 Hz, 3a-H), 6.89 (d, 1 H, $^3J_{1,2}$ = 9.1 Hz, 1a-H), 7.22–7.33 (m, 15 H, phenyl), 8.68 (s, 1 H, NH) ppm.

[*N*-(Triphenylmethyl)carbamoyl]methyl 2,6-Di-*O*-acetyl-3,4-di-*O*-benzyl-β-D-glucopyranosyl-(1→4)-3-*O*-acetyl-6-*O*-benzyl-2-deoxy-2-(dimethylmaleimido)-β-D-allopyranoside (43): A solution of **42** (2.00 g, 2.02 mmol) and **17** (0.80 g, 2.52 mmol) in CH_2Cl_2 (25 mL) was cooled to –5 °C, then tin triflate (5 mg, 0.01 mmol) was added and the mixture stirred at room temperature for 1 h. The reaction mixture was neutralized with NEt_3 and concentrated. Purification by column chromatography (toluene/ethyl acetate, 15:1 → 14:1) furnished, beside some elimination product **43′**, compound **43** (1.47 g, 1.28 mmol, 64%) as colorless foam. TLC: R_f = 0.68 (petroleum ether/ethyl acetate, 1:1). $[\alpha]_D^{20}$ = +21.5 (*c* = 0.5, $CHCl_3$). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.81 (s, 6 H, DMM-H), 1.96 (s, 3 H, acetyl), 2.03 (s, 3 H, acetyl), 3.35–3.56 (m, 6 H, 5a-H, 6a-H, 6a′-H, 3b-H, 4b-H, 5b-H), 3.98–4.12 (m, 3 H, 2a-H, CHHC=ONHTrt, CHHPh), 4.20–4.26 (m, 4 H, 4a-H, 6b-H, 6b′-H, CHHC=ONHTrt), 4.35 (d, 1 H, CHHPh), 4.42 (d, $^3J_{1,2}$ = 7.9 Hz, 1 H, 1b-H), 4.51 (d, 1 H, CHHPh), 4.62 (d, 1 H, CHHPh), 4.78 (m, 2 H, CH_2Ph), 4.84 (dd, $^3J_{1,2}$ ≈ $^3J_{2,3}$ ≈ 8.8 Hz, 2b-H), 5.53 (dd, 1 H, 3a-H), 5.73 (d, $^3J_{1,2}$ = 8.7 Hz, 1 H, 1a-H), 7.09–7.36 (m, 15 H, phenyl), 7.71 (s, 1 H, C=ONHTrt) ppm. MALDI-MS (pos. mode, matrix DHB, THF): *m*/*z* = 1168 $[M + Na]^+$, 1184 $[M + K]^+$. $C_{66}H_{68}N_2O_{16}$ (1145.3): calcd. C 69.22, H 5.98, N 2.45; found C 69.25, H 5.86, N 2.68.

2,6-Di-*O*-acetyl-3,4-di-*O*-benzyl-β-D-glucopyranosyl-(1→4)-3-*O*-acetyl-1,5-anhydro-6-*O*-benzyl-2-deoxy-2-(dimethylmaleimido)-D-*arabino*-hex-1-enitol (43′): Colourless foam. TLC: R_f = 0.56 (toluene/ethyl acetate, 3:2). $[\alpha]_D^{20}$ = +122.4 (*c* = 1, $CHCl_3$). ^{1}H NMR (600 MHz, $CDCl_3$): δ = 1.85 (s, 3 H, acetyl), 1.95 (s, 6 H, DMM-H), 2.02 (s, 3 H, acetyl), 3.49 (m, 1 H, 5b-H), 3.52 (dd, $^3J_{3,4}$ ≈ $^3J_{4,5}$ ≈ 9.1 Hz, 4b-H), 3.61 (dd, $^3J_{2,3}$ ≈ $^3J_{3,4}$ ≈ 9.0 Hz, 3b-H), 3.77 (m, 2 H, 6a-H), 4.11 (dd, $^2J_{gem}$ = 11.7, $^3J_{vic}$ = 4.7 Hz, 6b-H), 4.21 (dd, $^2J_{gem}$ = 11.7 Hz, 6b′-H), 4.25 (m, 2 H, 4a-H, 5a-H), 4.53 (m, 3 H, 1b-H, CH_2Ph), 4.64 (m, 2 H, CH_2Ph), 4.78 (m, 2 H, CH_2Ph), 4.96 (dd, $^3J_{1,2}$ ≈ $^3J_{2,3}$ ≈ 8.6 Hz, 2b-H), 5.25 (d, $^3J_{3,4}$ = 2.2 Hz, 1 H, 3a-H), 6.59 (s, 1 H, 1a-H), 7.25–7.36 (m, 15 H, phenyl) ppm. ^{13}C NMR (150.8 MHz, $CDCl_3$, selected data): δ = 62.9 (1 C, 6b-C), 65.5 (1 C, 3a-C), 68.0 (1 C, 6a-C), 72.9 (1 C, 5b-C), 73.0, 73.3 73.7 (3 C, 4a-C, 5a-C, 2b-C), 77.4 (1 C, 4b-C), 82.9 (1 C, 3b-C), 101.4 (1 C, 1b-C), 105.8 (1 C, 2a-C), 149.3 (1 C, 1a-C) ppm. MALDI-MS (pos. mode, matrix DHB, THF): *m*/*z* = 850 $[M + Na]^+$, 866 $[M + K]^+$. $C_{45}H_{49}NO_{14}\cdot 0.5H_2O$ (836.9): calcd. C 64.58, H 6.02, N 1.67; found C 64.47, H 6.12, N 1.71.

[*N*-(Triphenylmethyl)carbamoyl]methyl 3,4-Di-*O*-benzyl-β-D-glucopyranosyl-(1→4)-6-*O*-benzyl-2-deoxy-2-(dimethylmaleimido)-β-D-allopyranoside (44): Sodium methoxide (20 mg, 0.37 mmol) was added to a solution of **43** (1.40 g, 1.22 mmol) in dry MeOH (40 mL) and the mixture stirred overnight. The reaction mixture was neutralized with ion exchange resin IR 120 (H^+), filtered and the filtrate concentrated in vacuo. Purification by column chromatography (silica gel, toluene/acetone, 5:1) furnished **44** (1.22 g, 1.20 mmol, 98%) as colorless, amorphous solid. TLC: R_f = 0.25 (petroleum ether/ethyl acetate, 1:1). $[\alpha]_D^{20}$ = +3.2 (*c* = 1, $CHCl_3$). ^{1}H NMR (600 MHz, $[D_6]$DMSO): δ = 1.75 (br. s, 6 H, DMM-H), 3.22 (m, 1 H, 5b-H), 3.26 (m, 1 H, 2b-H), 3.38 (m, 2 H, 3b-H, 4b-H), 3.54 (m, 1 H, 6b-H), 3.61 (m, 1 H, 6b′-H), 3.71–3.73 (m, 3 H, 2a-H, 4a-H, 6a-H), 3.78 (dd, $^2J_{gem}$ = 10.4 Hz, 1 H, 6a′-H), 3.98 (d, $^2J_{gem}$ = 15.3 Hz, 1 H, CHHC=ONHTrt), 4.00 (m, 1 H, 5a-H), 4.13 (m, 1 H, 3a-H), 4.19 (d, $^2J_{gem}$ = 15.2 Hz, 1 H, CHHC=ONHTrt), 4.35 (d, 1 H, CHHPh), 4.36 (d, 1 H, 1b-H), 4.40 (d, 1 H, CHHPh), 4.57 (d, 1 H, CHHPh), 4.61 (m, 1 H, 6b-OH), 4.69 (d, 1 H, CHHPh), 4.73 (d, 1 H, CHHPh), 4.89 (d, 1 H, CHHPh), 5.08 (d, ^3J = 4.3 Hz, 1 H, 3a-OH), 5.62 (d, ^3J = 5.4 Hz, 1 H, 2b-OH), 5.75 (d, $^3J_{1,2}$ = 8.6 Hz, 1 H, 1a-H), 7.06–7.34 (m, 30 H, phenyl, Trt), 7.84 (s, 1 H, C=ONHTrt) ppm. ^{13}C NMR (150.8 MHz, $[D_6]$DMSO, selected data): δ = 56.5 (1 C, 2a-C), 60.1

(1 C, 6b-C), 68.8 (1 C, 6a-C), 68.9 (1 C, 3a-C), 69.8 (1 C, OCH_2-C=ONHTrt), 72.3 (1 C, 5a-C), 73.6 (1 C, 2b-C), 75.0 (1 C, 5b-C), 75.3 (1 C, 4a-C), 76.6 (1 C, 3b-C), 84.3 (1 C, 4b-C), 97.3 (1 C, 1a-C), 103.9 (1 C, 1b-C) ppm. $C_{60}H_{62}N_2O_{13}$ (1019.1): calcd. C 70.71, H 6.13, N 2.75; found C 70.30, H 6.22, N 2.88.

[*N*-(Triphenylmethyl)carbamoyl]methyl 3,4-Di-*O*-benzyl-β-D-glucopyranosyl-(1→4)-6-*O*-benzyl-2-[(benzyloxycarbonyl)amino]-2-deoxy-β-D-allopyranoside (45): Solid NaOH (600 mg, 15.0 mmol) was added to a solution of **44** (1.20 g, 1.17 mmol) in a mixture of dioxane (48 mL) and water (12 mL). The turbid two-phase solution was stirred at room temperature overnight. The pH was adjusted to 4.5 with 1 M HCl and monitored every 30 min for the next 5 h and if necessary adjusted to 4.5 with 1 M HCl. The reaction mixture was stirred at room temperature overnight, ethanolamine (80 μL, 80.9 mg, 1.325 mmol) was added and the solution neutralized with 1 M NaOH. K_2CO_3 (540 mg, 3.91 mmol) was immediately added and then benzyl chloroformate (480 μL, 0.57 g, 3.36 mmol). The reaction mixture was stirred at room temperature for 1 h, concentrated to 1/2 of its volume, diluted with NaCl solution and extracted three times with $CHCl_3$. The combined organic phases were dried with $MgSO_4$, filtered and concentrated. Purification by column chromatography (silica gel, toluene/acetone, 5:1) furnished **45** (0.98 g, 9.38 mmol, 80%) as colorless, hygroscopic foam. TLC: R_f = 0.45 (toluene/acetone, 2:1). $[\alpha]_D^{20}$ = –9.6 (c = 1, $CHCl_3$). ^{1}H NMR (600 MHz, $CDCl_3$): δ = 3.13 (br. s, 1 H, OH), 3.28 (m, 1 H, 5b-H), 3.43 (dd, $^3J_{1,2} \approx {}^3J_{2,3} \approx$ 8.2 Hz, 1 H, 2b-H), 3.48 (dd, $^3J_{2,3} \approx {}^3J_{3,4} \approx$ 8.9 Hz, 1 H, 3b-H), 3.54–3.58 (m, 2 H, 4b-H, 6a-H), 3.63 (dd, $^2J_{gem}$ = 9.6 Hz, 1 H, 6a′-H), 3.68 (dd, $^2J_{gem}$ = 13.2 Hz, 1 H, 6b-H), 3.77 (dd, $^2J_{gem}$ = 12.9 Hz, 1 H, 6b′-H), 3.80 (m, 1 H, 4a-H), 3.84–3.86 (m, 2 H, 2a-H, 5a-H), 4.07 (d, $^2J_{gem}$ = 15.1 Hz, 1 H, CHHC=ONHTrt), 4.22 (m, 1 H, 3a-H), 4.24 (d, 1 H, CHHC=ONHTrt), 4.27 (d, 1 H, CHHPh), 4.31 (d, $^3J_{1,2}$ = 7.4 Hz, 1 H, 1b-H), 4.36 (d, 1 H, CHHPh), 4.59 (d, $^3J_{1,2}$ = 8.2 Hz, 1 H, 1a-H), 4.64. 4.76 (2d, 2 H, CH_2Ph), 4.83 (m, 3 H, CH_2Ph, CHHPh), 4.93 (d, 1 H, CHHPh), 5.44 (d, 1 H, 2a-NH), 7.20–7.36 (m, 35 H, phenyl), 7.96 (s, 1 H, C=ONHTrt) ppm. ^{13}C NMR (150.8 MHz, $CDCl_3$, selected data): δ = 53.3 (1 C, 2a-C), 61.4 (1 C, 6b-C), 69.0 (1 C, 6a-C), 69.7 (1 C, 3a-C), 70.1 (1 C, OCH_2-C=ONHTrt), 71.4 (1 C, 5a-C), 74.3 (1 C, 2b-C), 75.5 (1 C, 5b-C), 76.3 (1 C, 4b-C), 77.0 (1 C, 4a-C), 83.9 (1 C, 3b-C), 100.9 (1 C, 1a-C), 103.7 (1 C, 1b-C) ppm. MALDI-MS (pos. mode, matrix DHB, THF): m/z = 1068 $[M + Na]^+$, 1084 $[M + K]^+$. $C_{62}H_{64}N_3O_{13}$ (1045.2): calcd. C 71.25, H 6.17, N 2.68; found C 71.13, H 6.25, N 2.47.

[*N*-(Triphenylmethyl)carbamoyl]methyl (Benzyl 3,4-di-*O*-benzyl-β-D-glucopyranosyluronate)-(1→4)-6-*O*-benzyl-2-[(benzyloxycarbonyl)-amino]-2-deoxy-β-D-allopyranoside (46): The pyranoside **45** (500 mg, 0.47 mmol), NaBr (8 mg, 0.077 mmol) and TBAB (8 mg, 0.024 mmol) were dissolved in a two-phase mixture of CH_2Cl_2/H_2O (6:1, 10 mL), and at 0 °C under ice-bath cooling TEMPO (5 mg, 0.032 mmol) was added. Then slowly a solution of NaOCl (5%, 3.6 mL) and a saturated $NaHCO_3$ solution (2.8 mL) were added dropwise, the reaction mixture was stirred at 0 °C for 30 min, diluted with H_2O and extracted with CH_2Cl_2. The aqueous phase was acidified with $KHSO_4$ solution (5%) and extracted three times with CH_2Cl_2. The combined organic phases were dried with $MgSO_4$, filtered, and concentrated in vacuo to furnish the free acid (480 mg, 95%) as intermediate which was dissolved in dry DMF (10 mL); CsF (140 mg, 0.59 mmol) and benzyl bromide (100 μL, 144 mg, 0.84 mmol) were added, and the mixture was stirred at room temperature overnight. The reaction mixture was diluted with ethyl acetate and washed three times with a saturated NaCl solution. The organic phase was dried with $MgSO_4$, filtered and concentrated. After two coevaporations with toluene, the residue was purified by column chromatography (silica gel, toluene/acetone, 6:1 → 5:1) to furnish **46** as colorless foam (420 mg, 0.37 mmol, 78%). TLC: R_f = 0.55 (toluene/acetone, 6:4). $[\alpha]_D^{20}$ = –15.7 (c = 1, $CHCl_3$). ^{1}H NMR (600 MHz, $CDCl_3$): δ = 3.46 (m, 2 H, 2b-H, 3b-H), 3.57 (dd, $^2J_{gem}$ = 9.9 Hz, 1 H, 6a-H), 3.60 (dd, $^2J_{gem}$ = 9.9 Hz, 1 H, 6a′-H), 3.75 (m, 1 H, 4b-H), 3.79 (m, 1 H, 4a-H), 3.84–3.87 (m, 2 H, 2a-H, 4a-H), 3.90 (d, $^3J_{4,5}$ = 9.3 Hz, 1 H, 5b-H), 4.07 (d, $^2J_{gem}$ = 15.2 Hz, 1 H, CHHC=ONHTrt), 4.20 (dd, 1 H, 3a-H), 4.25 (d, 1 H, CHHC=ONHTrt), 4.35 (m, 2 H, 1b-H, CHHPh), 4.48 (d, 1 H, CHHPh), 4.60 (d, ^3J = 8.3 Hz, 1 H, 1a-H), 4.70 (d, 1 H, CHHPh), 4.74–4.81 (m, 3 H, CH_2Ph, CHHPh), 4.94 (d, 1 H, CHHPh), 5.12 (d, 1 H, CHHPh), 5.15 (d, 1 H, CHHPh), 5.42 (d, ^3J = 9.5 Hz, 1 H, 2a-NH), 7.13–7.31 (m, 40 H, phenyl), 7.99 (s, 1 H, C=ONHTrt) ppm. ^{13}C NMR (150.8 MHz, $CDCl_3$, selected data): δ = 53.2 (1 C, 2a-C), 69.0 (1 C, 6a-C), 69.8 (1 C, 3a-C), 70.1 (1 C, OCH_2-C=ONHTrt), 71.2 (1 C, 5a-C), 73.7 (1 C, 2b-C), 74.4 (1 C, 5b-C), 77.4 (1 C, 4a-C), 78.6 (1 C, 4b-C), 82.9 (1 C, 3b-C), 101.1 (1 C, 1a-C), 103.8 (1 C, 1b-C) ppm. MALDI-MS (pos. mode, matrix DHB, THF): m/z = 1172 $[M + Na]^+$, 1188 $[M + K]^+$. $C_{69}H_{68}N_2O_{14}$ (1149.3): calcd. C 72.11, H 5.96, N 2.44; found C 71.71, H 5.96, N 2.51.

[*N*-(Triphenylmethyl)carbamoyl]methyl {Benzyl 3,4-di-*O*-benzyl-2-*O*-[(*tert*-butyloxycarbonyl)methyl]-β-D-glucopyranosyluronate}-(1→4)-6-*O*-benzyl-2-[(benzyloxycarbonyl)amino]-3-*O*-[(*tert*-butyloxycarbonyl)methyl]-2-deoxy-β-D-allopyranoside (47): Molecular sieves (4 Å) and *tert*-butyl bromoacetate (0.36 mL, 0.47 g, 2.43 mmol) were added to a solution of **46** (400 mg, 0.34 mmol) with TBAI (240 mg, 0.64 mmol) in dry CH_2Cl_2 (8 mL); the mixture was stirred at room temperature for 10 min, and then Ag_2O (800 mg, 3.43 mmol) was added. After stirring overnight, the reaction mixture was diluted with ethyl acetate and filtered through Celite. The filtrate was concentrated, coevaporated twice with toluene, and the residue purified by column chromatography (silica gel, petroleum ether/ethyl acetate, 3.25:1) to furnish **47** (330 mg, 0.24 mmol, 70%) as colorless foam. TLC: R_f = 0.40 (toluene/acetone, 6:4). $[\alpha]_D^{20}$ = –23.6 (c = 1, $CHCl_3$). ^{1}H NMR (600 MHz, $CDCl_3$): δ = 1.45, 1.46 (2 s, 18 H, 2× *tert*-butyl), 3.25 (dd, $^3J_{1,2}$ = $^3J_{2,3}$ = 8.4 Hz, 1 H, 2b-H), 3.54 (dd, $^3J_{2,3}$ = $^3J_{3,4}$ = 8.0 Hz, 1 H, 3b-H), 3.65 (m, 2 H, 6a-H), 3.72 (m, 2 H, 3a-H, 4b-H), 3.82 (m, 1 H, 2a-H), 3.84 (m, 1 H, 4a-H), 3.89 (m, 1 H, 5a-H), 3.92 (m, 1 H, 5b-H), 4.06, 4.07 (2 d, 2 H, CH_2C=O), 4.12, 4.17 (2 d, 2 H, CH_2C=O), 4.28 (m, 2 H, CH_2C=O), 4.23 ppm. 4.34 (2 d, 2 H, CH_2Ph), 4.43 (m, 3 H, 1b-H, CH_2Ph), 4.59 (d, $^3J_{1,2}$ = 8.2 Hz, 1 H, 1a-H), 4.72 (m, 4 H, 2× CH_2Ph), 4.98 (m, 2 H, CH_2Ph), 5.14 (m, 2 H, CH_2Ph), 7.11–7.33 (m, 40 H, CH_2Ph), 8.03 (s, 1 H, C=ONHTrt) ppm. ^{13}C NMR (150.8 MHz, $CDCl_3$, selected data): δ = 53.7 (1 C, 2a-C), 68.3 (1 C, 6a-C), 72.3 (1 C, 5a-C), 74.1 (1 C, 3a-C), 74.9 (1 C, 5b-C), 78.0 (1 C, 4b-C), 82.6 (1 C, 4a-C), 82.7 (1 C, 2b-C), 83.1 (1 C, 3b-C), 101.7 (1 C, 1a-C), 103.3 (1 C, 1b-C) ppm. MALDI-MS (pos. mode, matrix DHB, THF): m/z = 1400 $[M + Na]^+$, 1344 $[M + Na - tBu]^+$.$C_{81}H_{88}N_2O_{18}\cdot 0.5H_2O$ (1386.6) calcd. C 70.16, H 6.47, N 2.02; found C 69.95, H 6.51, N 1.88.

[*N*-(Triphenylmethyl)carbamoyl]methyl 2-*O*-[(*tert*-butyloxycarbonyl)methyl]-β-D-glucopyranosyluronate-(1→4)-3-*O*-[(*tert*-butyloxycarbonyl)methyl]-2-deoxy-2-{[(9-fluorenyl)methoxycarbonyl]amino}-β-D-allopyranoside (48): Pd/C (200 mg) was added to a solution of **47** (300 mg, 0.22 mmol) in MeOH/H_2O (5:1, 30 mL) and the mixture stirred under hydrogen for 48 h; the catalyst was filtered off through Celite, the filtrate concentrated to 1/2 of its volume, diluted with CH_3CN/H_2O (2:1, 40 mL), and Fmoc-ONSu (180 mg, 0.54 mmol) and $NaHCO_3$ (600 mg, 7.12 mmol) were added. The reaction mixture was stirred at room temperature overnight, concentrated until it became turbid, diluted with H_2O and then ex-

tracted four times with $CHCl_3$. The combined organic phases were dried with $MgSO_4$, concentrated, and the residue was purified by column chromatography (silica gel, ethyl acetate/MeOH, 9:1 → 4:1). This way not all byproducts could be separated. Therefore, compound **48** (120 mg, 0.108 mmol, 50%) was used in the next step without further purification. MALDI-MS (pos. mode, matrix DHB, THF): *m/z* = 1029 $[M + Na]^+$.

[*N*-(Triphenylmethyl)carbamoyl]methyl 2-*O*-[(*tert*-Butyloxycarbonyl)methyl]-β-D-glucopyranosyluronyl[L-leucyl-L-isoleucyl-*S*-(triphenylmethyl)-L-cystine *tert*-butyl ester]-(1→4)-3-*O*-[(*tert*-butyloxycarbonyl)methyl]-2-deoxy-2-{[(9-fluorenyl)methoxycarbonyl]amino}-β-D-allopyranoside (49): A solution of **48** (110 mg, 0.099 mmol), **27a** (80 mg, 0.124 mmol) and PyBOP (73 mg, 0.140 mmol) in dry DMF (5 mL) was treated with DIPEA (ca. 40 μL) to adjust the pH to ca. 8. After stirring at room temperature for 2 h, the reaction mixture was diluted with ethyl acetate and washed with a $KHSO_4$ solution (5%), a $NaHCO_3$ solution and a saturated NaCl solution. The organic phase was dried with $MgSO_4$, filtered and concentrated. Purification by column chromatography (silica gel, toluene/acetone, 3.75:1 → 3.5:1) furnished **49** (110 mg, 0.063 mmol, 64%) as colorless lyophilisate from dioxane. TLC: R_f = 0.68 (toluene/acetone, 1:1). $[\alpha]_D^{20}$ = –17.8 (*c* = 0.5, $CHCl_3$). ^1H NMR (600 MHz, $CDCl_3$): δ = 0.81 (m, 3 H, Ile-CH_3), 0.84 (m, 3 H, Ile-CH_3), 0.87 (m, 6 H, 2× Leu-CH_3), 1.05 (m, 1 H, Ile-CHH), 1.38 (m, 10 H, *tert*-butyl, Ile-CHH), 1.43 (s, 9 H, *tert*-butyl), 1.48 (s, 9 H, *tert*-butyl), 1.51 (m, 1 H, Leu-β-H), 1.65 [m, 1 H, Leu-CH(CH_3)$_2$], 1.66 (m, 1 H, Leu-β′-H), 1.70 (m, 1 H, Ile-β-H), 2.43, 2.66 (2 m, 2 H, Cys-β-H), 3.09 (dd, $^3J_{1,2}$ = $^3J_{2,3}$ = 8.1 Hz, 1 H, 2b-H), 3.60–3.67 (m, 3 H, 3b-H, 4b-H, 6a-H), 3.70–3.75 (m, 2 H, 5b-H, 6a′-H), 3.82 (m, 2 H, 2a-H, 5a-H), 3.86 (m, 2 H, 4a-H, Fmoc-CHH), 4.04 (m, 1 H, 3a-H), 4.07–4.09 (m, 3 H, Fmoc, CH_2C=O), 4.17 (m, 1 H, Fmoc), 4.18–4.23 (3 H, Ile-α-H, CH_2C=O), 4.27 (m, 1 H, CHHC=O), 4.29–4.35 (m, 3 H, Cys-α-H, CH_2C=O), 4.42 (m, 1 H, Leu-α-H), 4.56 (d, $^3J_{1,2}$ = 7.7 Hz, 1 H, 1b-H), 4.69 (d, $^3J_{1,2}$ = 8.4 Hz, 1 H, 1a-H), 5.91 (d, ^3J = 7.6 Hz, 1 H, Cys-NH), 6.43 (d, ^3J = 7.9 Hz, 1 H, Leu-NH), 6.85 (d, ^3J = 8.4 Hz, 1 H, Ile-NH), 7.11–7.35 (m, 38 H, phenyl, Fmoc), 7.52 (d, ^3J = 8.5 Hz, 1 H, 2a-NH), 8.00 (s, 1 H, C=ONHTrt) ppm. ^{13}C NMR (150.8 MHz, $CDCl_3$, selected data): δ = 11.4, 15.1, 23.0, 24.6 (4 C, 4× CH_3), 24.6 (1 C, Ile-CH_2), 33.9 (1 C, Cys-β-C), 38.5 (1 C, Ile-β-C), 41.3 (1 C, Leu-β-C), 51.9 (1 C, Cys-α-C), 52.6 (1 C, Leu-α-C), 54.0 (1 C, 2a-C), 57.5 (1 C, Ile-α-C), 61.0 (1 C, 6a-C), 72.3 (1 C, 4b-C), 73.1 (1 C, 5a-C), 74.4 (1 C, 5b-C), 74.9 (1 C, 3b-C), 75.3 (1 C, 4a-C), 82.7 (1 C, 3a-C), 83.2 (1 C, 2b-C), 101.9 (1 C, 1a-C), 103.4 (1 C, 1b-C) ppm. MALDI-MS (pos. mode, matrix DHB, THF): *m/z* = 1755 $[M + Na]^+$, 1771 $[M + K]^+$. $C_{98}H_{117}N_5O_{21}S{\cdot}H_2O$ (1751.1): calcd. C 67.22, H 6.85, N 4.00; found C 66.68, H 6.81, N 4.00.

[*N*-(Triphenylmethyl)carbamoyl]methyl 2-*O*-[(*tert*-Butyloxycarbonyl)methyl]-β-D-glucopyranosyluronyl[L-leucyl-L-isoleucyl-*S*-(triphenylmethyl)-L-cysteine *tert*-butyl ester]-(1→4)-3-*O*-[(*tert*-butyloxycarbonyl)methyl]-2-{[*N*-(*tert*-butyloxycarbonyl)-*S*-(triphenylmethyl)-L-cysteinyl]amido}-2-deoxy-β-D-allopyranoside (50): Piperidine (1.3 mL) was added to a solution of **49** (50 mg, 0.029 mmol) in DMF (5 mL) and the mixture stirred for 4 h, The reaction mixture was concentrated in vacuo, coevaporated twice with toluene and the residue purified by column chromatography (silica gel, $CHCl_3$/MeOH, 100:1 → 75:1 → 25:1). The resulting NH-unprotected compound (42 mg, 0.027 mmol, 99%) was dissolved with Boc-Cys(Trt)-OH (16 mg, 0.033 mmol) and PyBOP (19 mg, 0.036 mmol) in dry DMF (1.5 mL). The pH was adjusted to 8 with DIPEA (ca. 15 μL) and the reaction mixture stirred at room temperature for 1.5 h. It was then diluted with ethyl acetate and washed with $KHSO_4$, $NaHCO_3$ and NaCl solutions. The organic phase was dried with $MgSO_4$, filtered and concentrated. Purification by flash chromatography (silica gel toluene/acetone, 4.5:1 → 3.5:1) furnished **50** (50 mg, 0.026 mmol, 91%) as colorless lyophilisate from dioxane. TLC: R_f = 0.62 (toluene/acetone, 1:1). ^1H NMR (600 MHz, [D_6]-DMSO): δ = 0.77–0.79 (m, 13 H, 2× Leu-CH_3, 2× Ile-CH_3, Ile-β-H), 1.03 (m, 1 H, Ile-CHH), 1.27–1.41 (m, 37 H, 3× *tert*-butyl, Boc, Ile-CHH), 1.43 (m, 2 H, Leu-β-H), 1.62 [m, 2 H, Ile-β-H, Leu CH(CH_3)$_2$], 2.35 (m, 2 H, Cys-β-H), 2.44 (m, 2 H, Cys-β-H), 2.98 (m, 1 H, 2b-H), 3.29–3.35 (m, 3 H, 5a-H, 3b-H, 4b-H), 3.49 (dd, 1 H, 2a-H), 3.55 (m, 1 H, 6a-H), 3.64–3.72 (m, 4 H, 3a-H, 4a-H, 6a′-H, 5b-H), 3.87–3.91 (m, 3 H, CHH=ONHTrt, Cys-α-H, Cys-α-H), 4.02 (d, $^2J_{gem}$ = 15 Hz, 1 H, CHHC=ONHTrt), 4.15 (m, 2 H, CH_2–CO), 4.18 (m, 2 H, CH_2–CO), 4.27 (dd, Ile-α-H), 4.36 (m, 1 H, Leu-α-H), 4.55 (d, $^3J_{1,2}$ ≈ 7.3 Hz, 2 H, 1a-H, 1b-H), 4.64 (m, 1 H, OH), 5.25 (m, 1 H, OH), 5.41 (m, 1 H, OH), 6.49 (d, ^3J = 8.1 Hz, 1 H, Cys-NH), 7.15–7.33 (m, 45 H, Trt), 7.72 (d, ^3J = 7.4 Hz, 1 H, 2a-NH), 7.91 (d, ^3J = 9.0 Hz, 1 H, Ile-NH), 8.03 (s, 1 H, C=ONHTrt), 8.05 (d, ^3J = 7.3 Hz, 1 H, Leu-NH), 8.47 (d, ^3J = 7.2 Hz, 1 H, Cys-NH) ppm. ^{13}C NMR (150.8 MHz, [D_6]DMSO, selected data): δ = 51.0 (1 C, Leu-α-C), 52.1 (1 C, Cys-α-C), 53.4 (1 C, Cys-α-C), 54.1 (1 C, 2a-C), 56.0 (1 C, Ile-α-C), 58.9 (1 C, 6a-C), 68.3 (1 C, CH_2–CO), 68.5 (1 C, CH_2–CO), 69.1 (1 C, CH_2–CO), 74.7 (1 C, 5b-C), 76.7 (1 C, 4a-C), 79.0 (1 C, 3a-C), 81.8 (1 C, 2b-C), 101.2 (1 C, 1b-C), 101.5 (1 C, 1a-C) ppm. MALDI-MS (pos. mode, matrix DHB, THF): *m/z* = 1979 $[M + Na]^+$, 1995 $[M + K]^+$.

Carbamoylmethyl 2-*O*-(Carboxymethyl)-β-D-glucopyranosyluronyl(L-leucyl-L-isoleucyl-L-hemicystine)-(1→4)-3-*O*-(carboxymethyl)-2-[(L-hemicystinyl)amido]-2-deoxy-β-D-allopyranoside (33): A solution of **50** (40 mg, 0.020 mmol) in CH_2Cl_2/MeOH (7:1, 20 mL) was added dropwise to a solution of iodine (26 mg, 0.102 mmol) in CH_2Cl_2/MeOH (7:1, 20 mL) at 0 °C. After stirring at 0 °C for 30 min, a 0.01 M sodium thiosulfate solution was added until decoloration occurred, and the reaction mixture was extracted three times with $CHCl_3$. The combined organic phases were dried with $MgSO_4$, filtered and concentrated under reduced pressure. The cyclized intermediate was then dissolved in a mixture of TFA (9.5 mL), Et_3SiH (0.3 mL) and H_2O (0.2 mL) and the mixture stirred at 0 °C for 3.5 h. After removal of the TFA in vacuo, the residue was dried in vacuo and purified with flash chromatography (RP-18 silica gel, CH_3CN/H_2O, 1:2.5). RP-18 HPLC yielded **33** (15 mg, 0.016 mmol, 78%) as colorless lyophilisate. HPLC (prep. RP-18: 0–5 min isocratic 7% CH_3CN + 0.1% TFA, 5–60 min linear gradient 7–50% CH_3CN + 0.1% TFA, flow 10 mL/min): t_R = 32.4 min. ^1H NMR (600 MHz, [D_6]DMSO): δ = 0.80–0.87 (m, 12 H, 4× CH_3), 1.07 (m, 1 H, Ile-CHH), 1.46 (m, 2 H, Leu-β-H, Ile-CHH), 1.54 [m, 1 H, Leu-CH(CH_3)$_2$], 1.78 (m, 1 H, Ile-β-H), 2.99 (m, 2 H, 2b-H, Cys-β-H), 3.07 (m, 1 H, Cys-β-H), 3.24 (m, 1 H, Cys-β′-H), 3.32 (m, 1 H, Cys-β′-H), 3.35–3.41 (m, 2 H, 3b-H, 4b-H), 3.52 (m, 1 H, 6a-H), 3.65 (m, 1 H, 6a′-H), 3.68 (m, 1 H, 5b-H), 3.80 (m, 2 H, 4a-H, 5a-H), 3.88 (m, 1 H, 2a-H), 3.95–4.04 (m, 4 H, 3a-H, Cys-α-H, CH_2C=O), 4.15–4.27 (m, 4 H, Ile-α-H, CH_2C=O, CHHC=O), 4.34–4.36 (m, 2 H, Leu-α-H, CHHC=O), 4.54 (d, $^3J_{1,2}$ = 7.7 Hz, 1 H, 1b-H), 4.57 (d, $^3J_{1,2}$ = 8.5 Hz, 1 H, 1a-H), 4.61 (m, 1 H, Cys-α-H), 7.47 (d, ^3J = 7.8 Hz, 1 H, Leu-NH), 7.90 (d, ^3J = 8.7 Hz, 1 H, Ile-NH), 8.32 (d, ^3J = 8.2 Hz, 1 H, Cys-NH), 8.35 (d, 1 H, Cys-NH), 8.36 (s, 2 H, C=ONH_2), 8.59 (d, ^3J = 8.8 Hz, 1 H, 2a-NH) ppm. ^{13}C NMR (150.8 MHz, [D_6]DMSO, selected data): δ = 11.0, 15.2, 21.0, 22.9 (4 C, 4× CH_3), 23.9, 24.0 [2 C, Ile-CH_2, Leu-CH(CH_3)$_2$], 36.3 (1 C, Ile-β-C), 40.9 (1 C, Cys-β-C), 41.2 (1 C, Leu-β-C), 43.1 (1 C, Cys-β-C), 50.7 (1 C, Leu-α-C), 51.0 (1 C, Cys-α-C), 51.7 (1 C, 2a-C), 53.3 (1 C, Cys-α-C), 56.5 (1 C, Ile-α-C), 60.0 (1 C, 6a-C), 71.5 (1 C, 4b-C), 73.3 (1 C, 5a-C), 74.2 (1 C, 5b-C), 74.5 (1 C, 3b-C), 76.2 (1 C, 4a-C), 80.4 (1 C, 3a-

C), 81.7 (1 C, 2b-C), 98.5 (1 C, 1a-C), 102.9 (1 C, 1b-C) ppm. MALDI-MS (pos. mode, matrix DHB, THF): m/z = 983 $[M + Na]^+$, 999 $[M + K]^+$.

Carbamoylmethyl 2-*O*-(Carboxymethyl)-β-D-glucopyranosyluronyl(L-leucyl-L-isoleucyl-L-hemicystine)-(1→4)-3-*O*-(carboxymethyl)-2-deoxy-[(L-hemicystinylglycyl)amido]-β-D-allopyranoside (34): As in the synthesis of **33**, for the preparation of **34** the nonapeptide mimetic was synthesized as intermediate from **32** and **49**, which after cyclization and final deprotection gave **34**. HPLC (prep. RP-18: 0–5 min isocratic 8% CH_3CN + 0.1% TFA, 5–50 min linear gradient 8–55% CH_3CN + 0.1% TFA, flow 10 mL/min): t_R = 26.9 min. ^1H NMR (600 MHz, [D$_6$]DMSO): δ = 0.80–0.87 (m, 12 H, 2× Ile-CH_3, 2× Leu-CH_3), 1.13 (m, 1 H, Ile-CHH), 1.37 (m, 1 H, Leu-β-H), 1.45 (m, 1 H, Ile-CHH), 1.51 [m, 1 H, Leu-$CH(CH_3)_2$], 1.81 (m, 1 H, Ile-β-H), 2.86 (dd, $^2J_{gem}$ = 12.9, $^3J_{vic}$ = 9.6 Hz, 1 H, Cys-β-H), 2.97 (m, 2 H, 2b-H, Cys-β-H), 3.15 (dd, $^2J_{gem}$ = 13.2, $^3J_{vic}$ = 5.3 Hz, 1 H, Cys-β-H), 3.18 (dd, $^2J_{gem}$ = 14.1, $^3J_{vic}$ = 5.4 Hz, 1 H, Cys-β-H), 3.35 (dd, $^3J_{2,3}$ = $^3J_{3,4}$ = 8.9 Hz, 1 H, 3b-H), 3.46 (dd, $^3J_{3,4}$ = $^3J_{3,4}$ = 9.2 Hz, 1 H, 4b-H), 3.51 (dd, $^2J_{gem}$ = 11.7, $^3J_{vic}$ = 4.3 Hz, 1 H, 6a-H), 3.63 (m, 2 H, 6a′-H, 5b-H), 3.75 (m, 1 H, 5a-H), 3.83–3.91 (m, 5 H, 2a-H, 3a-H, 4a-H, Gly-α-H), 2.92 (d, 1 H, CHHC=O), 4.05 (d, 1 H, CHHC=O), 4.06 (m, 1 H, Cys-α-H), 4.12 (m, 1 H, Ile-α-H), 4.12–4.30 (m, 4 H, 2× CH_2C=O), 4.45 (d, $^3J_{1,2}$ = 7.8 Hz, 1 H, 1b-H), 4.50 (m, 1 H, Cys-α-H), 4.56 (d, $^3J_{1,2}$ = 8.4 Hz, 1 H, 1a-H), 4.60 (m, 1 H, Leu-α-H), 7.71 (d, ^3J = 8.4 Hz, 1 H, Cys-NH), 8.11 (d, ^3J = 8.0 Hz, 1 H, 2a-NH), 8.20 (m, 2 H, Gly-NH, Ile-NH), 8.27 (br. s, 1 H, Cys-NH), 8.47 (d, ^3J = 7.8 Hz, 1 H, Cys-NH) ppm. ^{13}C NMR (150.8 MHz, [D$_6$]DMSO, selected data): δ = 10.8, 15.2 (2 C, 2× Ile-CH_3), 22.1, 23.9 (2 C, 2× Leu-CH_3), 23.9, 24.0 [2 C, CH_2CH_3, $CH(CH_3)_2$], 35.6 (1 C, Ile-β-C), 38.7 (1 C, Cys-β-C), 38.8 (1 C, Cys-β-C), 41.8 (1 C, Leu-β-C), 42.4 (1 C, Gly-α-C), 50.0 (1 C, Leu-α-C), 50.6 (1 C, Cys-α-C), 51.0 (1 C, Cys-α-C), 51.9 (1 C, 2a-C), 57.1 (1 C, Ile-α-C), 60.1 (1 C, 6a-C), 71.1 (1 C, 4b-C), 73.5 (1 C, 5a-C), 74.8 (2 C, 5b-C, 3b-C), 77.0 (1 C, 4a-C), 81.1 (1 C, 3a-C), 81.8 (1 C, 2b-C), 98.9 (1 C, 1a-C), 104.0 (1 C, 1b-C) ppm. MALDI-MS (pos. mode, matrix DHB, THF): m/z = 1039 $[M + Na]^+$, 1055 $[M + K]^+$.

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