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Synthesis of Oligosaccharide Mimetics with Glycoaminoxy Acids

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From readily available di-*O*-isopropylidene-D-glucose, a D-ribofuranoid glycoaminoxy acid and its *t*Bu ester have been efficiently prepared as a new family of sugar building blocks by introducing the phthalimido aminoxy group by a Mitsunobu reaction. We found that the *t*Bu ester can be selectively deprotected with 13.7% TFA in CH_2Cl_2 at 0 °C in the presence of the 1,2-*O*-isopropylidene acetal. This selective deprotection has made possible the synthesis of homo-oligomers of glycoaminoxy acids (up to six sugar units) as a novel type of oligosaccharide mimetics.

Introduction

Carbohydrates exist in all living systems and play key roles in a number of biological events, including various intracellular recognition processes.[1] The rapidly growing importance of carbohydrates in biological systems and their potential medical applications incite the synthesis of various carbohydrate mimetics.[2] During the last decade, sugar amino acids have been successfully used as building blocks in the synthesis of various glycoconjugates and in designing bioactive molecules for drug discovery.[3] Very recently, we synthesized pyranoid glycoaminoxy acids as a new class of sugar building blocks from α-*C*-allyl glycosides.[4] Due to the presence of both aminoxy and carboxylic acid functional groups on the sugar ring, these compounds can be easily used for the synthesis of oxyamide-linked disaccharides and glycosyl amino acid mimetics. Studies on aminoxy acids have shown that aminoxy peptides can easily form intramolecular hydrogen bonds to facilitate turns and helical structures, and a new family of foldamers has been developed from α-, β- and γ-aminoxy acids.[5] The synthesis and characterization of a dimer and trimer of D-xylofuranoid glycoaminoxy acids have also been recently reported.[6] These interesting results encouraged us to prepare new glycoaminoxy acids as sugar building blocks. In our continuing program on the development of carbohydrate mimetics,[7] we report herein the synthesis of D-ribofuranoid glycoaminoxy acids and their homo-oligomers.

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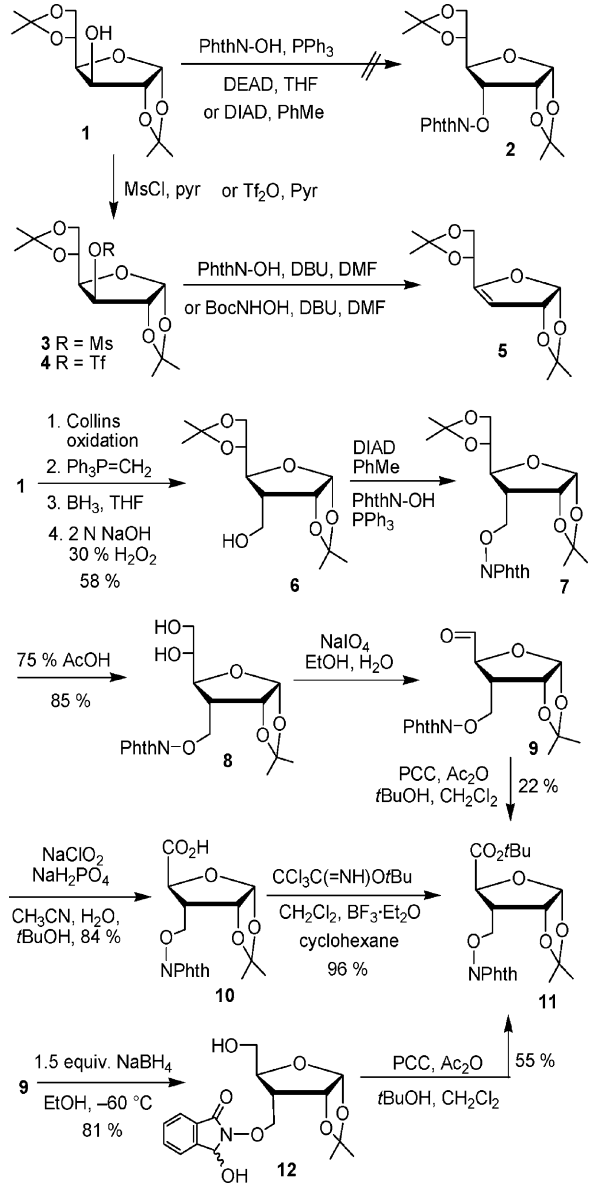
Results and Discussion

We chose di-*O*-isopropylidene-D-glucose **1** as the starting material (Scheme 1) because of its ready availability and low cost. We decided to introduce the aminoxy acid group onto the 3- and 5-position of the furanose ring, which could allow the further functionalization of the anomeric position. We attempted to introduce the phthalimidoxy group through a Mitsunobu reaction. However, **1** did not react with *N*-hydroxyphthalimide (PhthN-OH) in the presence of DEAD or DIAD. This might be due to the steric hindrance of the 3-OH group. Burke and co-workers reported the introduction of the phthalimidoxy group through the mesylate.[8] We then transformed **1** into the mesylate **3** or the triflate **4** under the usual conditions. We observed no reaction upon the treatment of **3** with PhthN-OH or BocNHOH in the presence of DBU. For the triflate **4**, we obtained only the elimination product **5**.[9] We tried a second approach by introducing a cyano group, which could be further modified. Once again, the reaction of **4** with KCN[10] in DMSO or tBu_4NCN[11] in CH_3CN led to the elimination product **5**.

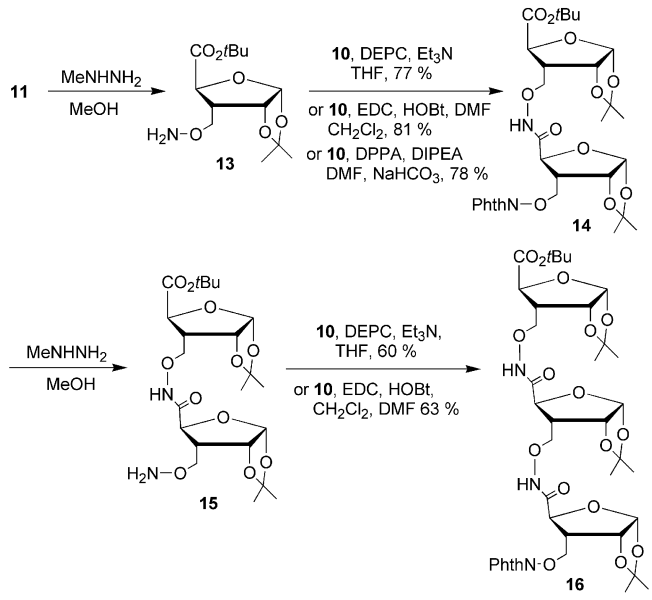
To avoid the steric hindrance of the 3-position, we converted **1** into the known **6**[12] through a Collins oxidation, Wittig reaction, hydroboration and hydroxylation in 58% total yield. The Mitsunobu reaction of **6** with PhthN-OH led successfully to the phthalimidoxy derivative **7**, which we selectively deprotected to **8** in 85% yield. The oxidative cleavage with $NaIO_4$ gave aldehyde **9**, which we oxidized to the acid **10** in 84% yield. Because hydrazinolysis is necessary to remove the phthalimido protecting group, we protected the carboxylic acid as the *t*Bu ester to avoid a transacylation reaction.[5] We obtained the *t*Bu ester **11** after esterification with *t*Bu trichloroacetimidate. The direct oxidation of **9** with PCC in the presence of *t*BuOH and Ac_2O led also to ester **11** in 22% yield. Interestingly, when we reduced the aldehyde group of **9** to the alcohol so as to



Scheme 1. Synthesis of a furanoid glycoaminoxy acid.

oxidize it directly to the *t*Bu ester,[7d] the phthalimido group was partially reduced to **12**, even at –60 °C. The $NaBH_4$ reduction at room temp. led to the deprotection of the phthalimidoxy group.[13] Fortunately, a subsequent PCC oxidation of **12** offered the desired ester **11** in 55% yield.

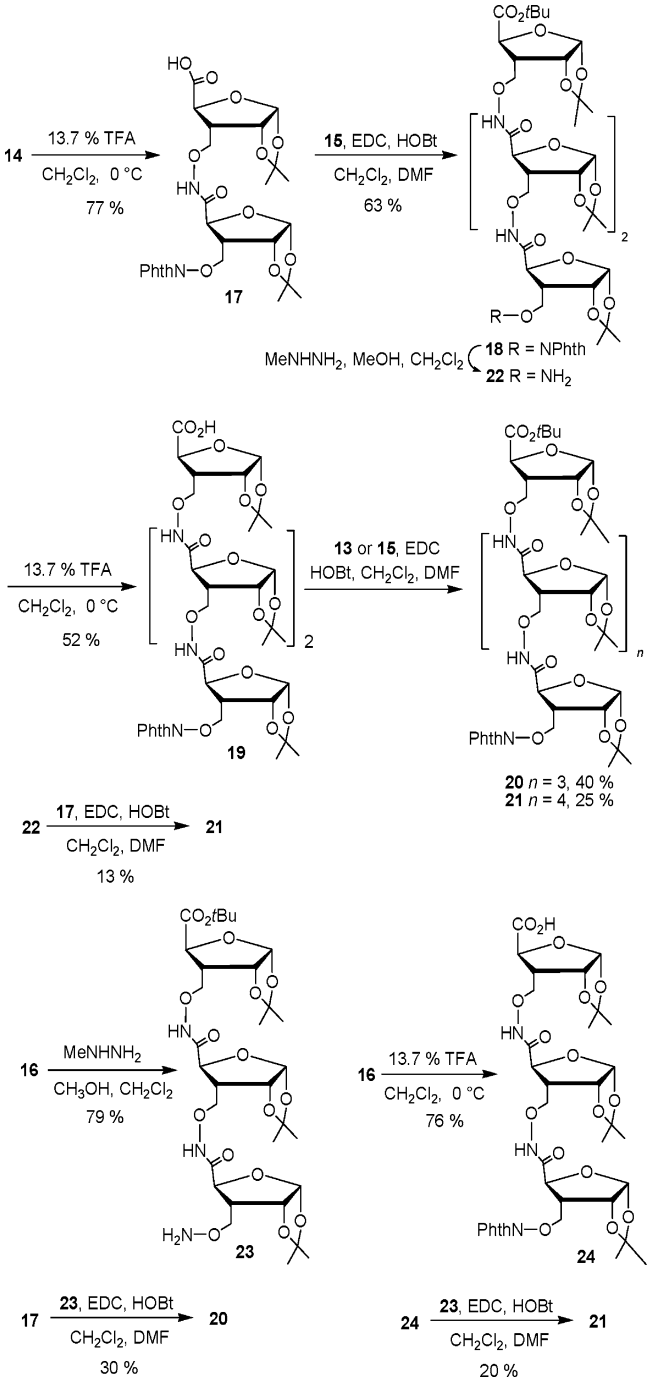
In order to obtain oligomers of furanoid glycoaminoxy acids, we deprotected the aminoxy group of **11** with methylhydrazine (Scheme 2). The tentative chromatographic purification of **13** led to its partial decomposition. After isolation, we treated **13** with the acid **10**. The dimer **14** was isolated in 77–81% yield under three different coupling conditions: EDC/HOBt, DPPA (diphenylphosphoryl azide)/DIPEA/$NaHCO_3$ and DEPC (diethyl cyanophosphonate)/Et_3N; DPPA and DEPC are organophosphorous reagents that have been successfully used in the oligomerization of sugar amino acids.[7d,7e] Hydrazinolysis of **14** followed by coupling with **10** led successfully to trimer **16** in 63% yield. We could clearly identify the aminoxy peptide NH proton at δ = 9–10.5 ppm in ^{1}H NMR spectra.



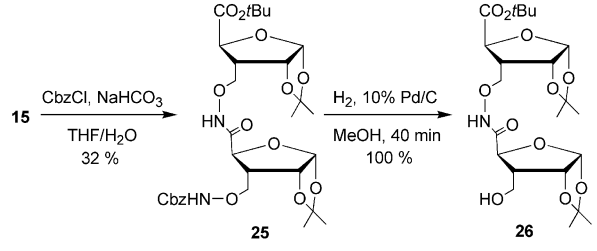
Scheme 2. Synthesis of a homo-oligodimer and -trimer of a furanoid glycoaminoxy acid.

For the synthesis of oligomers with more than three sugar units, it is necessary to selectively deprotect the *t*Bu ester without cleaving the 1,2-*O*-isopropylidene group. After careful examination of the reaction conditions, we found that treatment of **14** with 13.7% TFA in CH_2Cl_2 at 0 °C led to the desired free acid **17** in 77% yield (Scheme 3). The reaction with TFA/CH_2Cl_2 (1:1 or 1:2) led mostly to the fully deprotected product. With less than 10% TFA, the deprotection rate was relatively slow. The coupling of acid **17** with aminoxy ester **15** in the presence of EDC/HOBt gave the tetramer **18** in 63% yield. DEPC failed to promote the formation of **18**. The acidic hydrolysis of **18** offered the acid **19**, which was coupled with aminoxy ester **13** or **15**, leading to the corresponding pentamer **20** (40%) or hexamer **21** (25%). The reaction of aminoxy ester **22** with acid **17** led to a lower yield of **21** (13%). Similarly, the trimer **16** can be deprotected to the corresponding aminoxy ester **23** and free acid **24**. The EDC-promoted coupling of **23** with **17** or **24** led to the corresponding pentamer **20** or hexamer **21** in 30% or 20% yield, respectively. However, the EDC- or DPPA-promoted coupling of tetramer **19** with **22** failed to give the desired octamer.

We also tried to protect the aminoxy group with the Cbz group, so as to replace the acid-sensitive *t*Bu ester with a base-sensitive methyl or ethyl ester. The treatment of aminoxy ester **15** with CbzCl led to **25** in only 32% yield (Scheme 4). We note that after hydrogenolysis, the N–O bond of the Cbz-aminoxy group was cleaved, leading to the alcohol **26**. This result is in contrast to that observed by Hu et al.[14] Nevertheless, the aminoxy peptide bond remained stable under these conditions.



Scheme 3. Synthesis of tetramers to hexamers of a furanoid glycoaminoxy acid.



Scheme 4. Dimer protection-group modification.

Conclusions

From the readily available di-*O*-isopropylidene-D-glucose, D-ribofuranoid glycoaminoxy acid derivatives have been successfully prepared as a novel family of sugar building blocks. Homo-oligomers (dimer to hexamer) have also been generated as oligosaccharide mimetics. The easy derivatization of glycoaminoxy acids should allow the design and synthesis of various carbohydrate-based molecules and find wide applications like sugar amino acids.

Experimental Section

General: ^1H and ^{13}C NMR and DEPT-135 spectra were recorded with a Jeol 400 spectrometer in $CDCl_3$ solutions. Column chromatography was performed with Silica 60 (40–63 μM). Analytical thin-layer chromatography was performed with aluminum precoated plates of Silica Gel 60F-254 with detection by UV light or by spraying with 6 N H_2SO_4 and heating at 300 °C for about 2 min for sugar derivatives. IR spectra were recorded with a Shimadzu FTIR-8400S spectrometer. Optical rotations were measured by using a Jasco P-2000 polarimeter. High-resolution mass spectra (HRMS) were measured by the Service de Spectrométrie de Masse de l'Université Pierre et Marie Curie-Paris 6.

General Procedure for Hydrazinolysis: To a solution of phthalimidoxy compound (1 mmol) in MeOH/CH_2Cl_2 (1:4, 12 mL), was added $MeNHNH_2$ (3 mmol). After the mixture was stirred at room temp. for 6 h, it was concentrated to dryness and directly used for the next step without further purification.

General Procedure for the Selective Deprotection of the *t*Bu Ester: To a solution of the *t*Bu ester (1 mmol) in dry CH_2Cl_2 (19 mL), was added dropwise TFA/CH_2Cl_2 (1:1, 7.2 mL) at 0 °C, and the reaction mixture was stirred for 7 h. EtOAc (10 mL) was added to the mixture, most of the solvent was evaporated at room temp., and the residue was dried under high vacuum (oil pump) until no acidic smell could be detected. The residue was purified by chromatography to afford the corresponding free acid as a colorless syrup.

General Procedure for the Coupling Reaction: To a solution of free acid (1 mmol) in anhydrous DMF/CH_2Cl_2 (1:1, 20 mL), was added HOBt (1.8 equiv.) and EDC (1.8 equiv.) under nitrogen at 0 °C. After the mixture had been stirred for 20 min, the aminoxy derivative (0.5–2 equiv.) in anhydrous CH_2Cl_2 (10 mL) was added. The reaction mixture was stirred at room temp. overnight. The solution was diluted with EtOAc (25 mL), washed with aq. HCl (1 N, 2 × 10 mL), saturated aq. $NaHCO_3$ (2 × 10 mL) and brine (10 mL), dried, filtered, concentrated to dryness and then purified by column chromatography.

3-Deoxy-3-(hydroxymethyl)-1,2:5,6-di-*O*-isopropylidene-α-D-allofuranose (6): To a solution of pyridine (11.3 mL, 140.5 mmol) in CH_2Cl_2 (70 mL), was added CrO_3 (6.96 g, 69.6 mmol) in one portion.[15] The mixture was stirred at room temp. for 30 min and then cooled to 0 °C. A solution of di-*O*-isopropylidene-D-glucose **1** (4.6 g, 17.6 mmol) in CH_2Cl_2 (10 mL) was added, followed by Ac_2O (6.87 mL, 72.6 mmol). After the mixture had benn stirred at room temp. for 1 h, most of the solvent was evaporated. The addition of toluene/EtOAc (1:1, 100 mL) to the mixture precipitated most of the chromium compounds. The decanted solution was filtered through a 70–200 mesh silica gel column (9 g) and concentrated under reduced pressure. The obtained ketone was dissolved in anhydrous THF (20 mL) and directly used for the Wittig reac-

tion without further purification. To a mixture of methyltriphenylphosphonium bromide (16.5 g, 46.1 mmol) in anhydrous THF (70 mL), was added *t*BuOK (5.07 g, 45.2 mmol) in anhydrous THF (20 mL) under nitrogen at 0 °C. The yellow mixture was warmed to room temp., stirred for 30 min and then heated to reflux for 2 h. After the mixture was cooled to 0 °C, the solution of ketone in anhydrous THF was added and the mixture stirred at room temp. for 2 h. The reaction mixture was poured into water and extracted with EtOAc (2 × 50 mL). The combined organic layers were washed with brine (2 × 50 mL), dried ($MgSO_4$), filtered and concentrated to give a yellow crude product, which was purified by chromatography (petroleum ether/EtOAc, 15:1, 10:1, then 8:1) to afford the corresponding alkene as a colorless syrup (3.15 g, 70%). R_f = 0.82 (petroleum ether/EtOAc, 2:1). To the borane/THF complex (1 M, 1.37 mL, 1.37 mmol) at 0 °C under nitrogen, was added the alkene (150 mg, 0.585 mmol) in THF (1.24 mL). The solution was stirred at room temp. for 2 h. After the mixture was cooled to 0 °C, THF/H_2O (1:1, 0.92 mL), aq. NaOH (2 N, 1.1 mL) and aq. H_2O_2 (30%, 0.92 mL) were added. The mixture was stirred at room temp. for 2 h and then diluted with H_2O (10 mL) and brine (10 mL) and extracted with EtOAc (2 × 20 mL). The combined organic layers were washed with brine (2 × 20 mL), dried ($MgSO_4$), filtered and concentrated under reduced pressure to yield 158 mg of crude product, which was purified by column chromatography (CH_2Cl_2/EtOAc, 20:1) to afford **6** as a colorless syrup (131.9 mg, 82.2%). R_f = 0.35 (petroleum ether/EtOAc, 2:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.32 (s, 3 H, Me), 1.37 (s, 3 H, Me), 1.46 (s, 3 H, Me), 1.52 (s, 3 H, Me), 2.09–2.17 (m, 1 H, 3-H), 3.27 (dd, J = 3.2, 10.1 Hz, 1 H, OH), 3.82–3.95 (m, 3 H, 4-H and 3-CH_2), 3.95–4.05 (m, 2 H, 5-H and 6-H_a), 4.13–4.20 (m, 1 H, 6-H_b), 4.75 (t, J = 4.4 Hz, 1 H, 2-H), 5.77 (d, J = 3.7 Hz, 1 H, 1-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 25.2, 26.3, 26.6, 26.8 (CH_3), 51.5 (CH), 59.7, 68.1 (CH_2), 77.2, 81.8, 82.6, 104.9 (CH), 110.0, 112.4 (C) ppm.

3-Deoxy-1,2-*O*-isopropylidene-3-(phthalimidoxymethyl)-α-D-allofuranose (8): To a solution of **6** (8.4 g, 30.6 mmol), PhthN-OH (6.15 g, 37.7 mmol) and PPh_3 (13.1 g, 49.9 mmol) in toluene (286 mL) at 0 °C, was added dropwise DIAD (95%, 9.9 g, 46.5 mmol). The resultant red mixture was stirred at room temp. for 5 h. The mixture was then washed with H_2O (3 × 100 mL) and brine (2 × 100 mL), dried ($MgSO_4$), filtered, concentrated and purified by column chromatography (CH_2Cl_2/EtOAc, 60:1) to afford **7** (18.1 g) as a yellow syrup, containing impurities from DIAD, which would be separated completely after the next step. A solution of **7** (18.1 g, crude product) in 75% AcOH (266 mL) was stirred at 40 °C for 3 h and then concentrated and purified by column chromatography (CH_2Cl_2/MeOH, 80:1 to 55:1) to afford the title product (9.87 g, 85% over two steps) as a colorless syrup. R_f = 0.3 (CH_2Cl_2/MeOH, 20:1). $[\alpha]_D^{23}$ = +82.1 (c = 0.95, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.30 (s, 3 H, Me), 1.49 (s, 3 H, Me), 2.35–2.55 (m, 2 H, 3-H and OH), 3.23–3.33 (m, 1 H, OH), 3.68–3.78 (m, 1 H, 6-H_a), 3.80–3.90 (m, 2 H, 5-H and 6-H_b), 3.98–4.05 (m, 1 H, 4-H), 4.41 (dd, J = 6.4, 10.6 Hz, 1 H, 3-CH_a), 4.71 (m, 1 H, 3-CH_b), 4.90 (t, J = 4.4 Hz, 1 H, 2-H), 5.82 (d, J = 4.1 Hz, 1 H, 1-H), 7.75–7.90 (m, 4 H, Phth) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 26.4, 26.7 (CH_3); 46.6 (CH), 63.9 (CH_2), 73.0 (CH), 75.5 (CH_2), 81.3, 81.5, 104.8 (CH), 112.4 (C), 123.8 (CH), 128.8 (C), 134.9 (CH), 163.8 (C) ppm. IR (neat): $\tilde{\nu}$ = 2987, 2896, 1788, 1725 cm^{-1}. HRMS (ESI): calcd. for $C_{18}H_{21}NO_8$ [M + Na]$^+$ 402.1165; found 402.1159.

3-Deoxy-1,2-*O*-isopropylidene-3-(phthalimidoxymethyl)-α-D-ribofuranuronic Acid (10): To a solution of **8** (4.48 g, 11.8 mmol) in EtOH (169 mL) at 0 °C, was added $NaIO_4$ (5.63 g, 26.3 mmol) in H_2O (45 mL). After the mixture had been stirred at 0 °C for 30 min, it was diluted with CH_2Cl_2 (150 mL), washed with H_2O (100 mL), dried ($MgSO_4$), filtered and concentrated to give aldehyde **9** as a pure colorless syrup (4.1 g, 100%), which was directly used for NMR determination and the next step without further purification. To a solution of **9** (4.1 g, 11.8 mmol) in *t*BuOH/CH_3CN/H_2O (2:2:1, 61.9 mL), was added $NaClO_2$ (6.1 g, 67.4 mmol) and NaH_2PO_4 (4.05 g, 33.8 mmol) at 0 °C, and the mixture was warmed to room temp. and stirred overnight. H_2O (200 mL) was then added, and the mixture was extracted with Et_2O (2 × 100 mL). The aq. layer was acidified to pH = 1–2 with aq. HCl (4 M, 11 mL) and then extracted with EtOAc (2 × 200 mL). The combined organic layers were washed with brine (2 × 200 mL), dried ($MgSO_4$), filtered and concentrated to give **10** (3.6 g, 84%) as a colorless syrup, pure enough for the next step. An analytical sample was purified by column chromatography (CH_2Cl_2/MeOH/AcOH, 60:1:0.1). R_f = 0.61 (CH_2Cl_2/MeOH/AcOH, 6:0.3:0.15). $[\alpha]_D^{23}$ = +100.6 (c = 0.36, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.33 (s, 3 H, Me), 1.51 (s, 3 H, Me), 2.73–2.80 (m, 1 H, 3-H), 4.35 (d, J = 11.0 Hz, 1 H, 4-H), 4.45 (dd, J = 4.6, 11.0 Hz, 1 H, 3-CH_a), 4.67 (t, J = 10.1 Hz, 1 H, 3-CH_b), 5.07 (t, J = 3.6 Hz, 1 H, 2-H), 6.01 (d, J = 3.2 Hz, 1 H, 1-H), 7.76–7.84 (m, 4 H, Phth) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 26.4, 26.9 (CH_3), 47.2 (CH), 74.0 (CH_2), 76.2, 80.3, 106.1 (CH), 113.2 (C), 123.8 (CH), 128.9 (C), 134.8 (CH), 163.7 (C), 173.2 (C) ppm. IR (neat): $\tilde{\nu}$ = 2987, 2900, 1721 cm^{-1}. HRMS (ESI): calcd. for $C_{17}H_{17}NO_8$ [M + Na]$^+$ 386.0852; found 386.0846.

Compound 12: To a solution of aldehyde **9** (113 mg, 0.327 mmol) in EtOH (4.67 mL) and H_2O (1.23 mL), was added $NaBH_4$ (13.6 mg, 0.359 mmol) at –60 °C. After the mixture had been stirred for 40 min, H_2O (10 mL) was added, and the mixture was extracted with CH_2Cl_2 (3 × 10 mL). The combined organic layers were dried ($MgSO_4$), filtered, concentrated under reduced pressure to dryness and purified by column chromatography (CH_2Cl_2/MeOH, 60:1) to yield the title product (92.6 mg, 81%) as a colorless syrup. The ^{1}H NMR spectrum showed a 2:1 mixture of two diastereoisomers. R_f = 0.3 (CH_2Cl_2/MeOH, 20:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.25–1.33 (m, 3 H, Me), 1.45–1.55 (m, 3 H, Me), 2.60–2.70 (m, 0.34 H), 3.70–3.81 (m, 0.68 H), 3.75–4.12 (m, 3 H, 4-H and 5-CH_2), 4.22–4.65 (m, 2 H, 3-CH_2), 4.73–4.83 (m, 1 H, 2-H), 5.80–5.85 (m, 1 H, 1-H), 5.89 (s, 0.68 H), 5.82 (s, 0.34 H), 7.50–7.80 (m, 4 H, Phth) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 26.3, 26.6 (CH_3), 42.7, 43.6 (CH), 61.8, 74.3, 74.6 (CH_2), 81.1, 81.5, 81.6, 81.6, 82.9, 83.0, 104.9, 105.0 (CH), 112.1, 112.4 (C), 123.5, 123.7, 123.8 (CH), 128.9, 129.1 (C), 130.1, 130.3, 133.6 (CH), 141.1 (C) ppm. IR (neat): $\tilde{\nu}$ = 3343, 2987, 2922, 1704 cm^{-1}. HRMS (ESI): calcd. for $C_{17}H_{21}NO_7$ [M + Na]$^+$ 374.1216; found 374.1208.

***tert*-Butyl 3-Deoxy-1,2-*O*-isopropylidene-3-(phthalimidoxymethyl)-α-D-ribofuranuronate (11). Method A:** To a solution of **10** (800 mg, 2.2 mmol) in anhydrous CH_2Cl_2 (8 mL) and cyclohexane (16 mL), was added *tert*-butyl 2,2,2-trichloroacetimidate[16] (0.8 mL, 4.47 mmol). After the mixture had been stirred at room temp. overnight, catalytic $BF_3{\cdot}Et_2O$ (31.2 μL, 0.247 mmol) was added, and the mixture was stirred for 1 h. Solid $NaHCO_3$ (64 mg, 0.79 mmol) was then added in one portion, and the mixture was stirred for another 1 h. After the mixture was filtered, saturated aq. $NaHCO_3$ (20 mL) was added, and the mixture was extracted with EtOAc (50 mL). The organic layer was washed with saturated aq. $NaHCO_3$ (20 mL) and brine (20 mL), dried ($MgSO_4$), filtered and concentrated under reduced pressure to dryness. The crude material was purified by chromatography (petroleum ether/EtOAc, 9:1, 6:1 then 4:1) to yield the title compound (890.4 mg, 96%) as a colorless syrup. R_f = 0.55 (petroleum ether/EtOAc, 2:1). $[\alpha]_D^{23}$ = +87.1 (c = 0.19, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.30 (s, 3 H, Me), 1.46 (s, 9 H, *t*Bu), 1.52 (s, 3 H, Me), 2.62–2.71 (m, 1

H, 3-H), 4.21 (d, J = 10.5 Hz, 1 H, 4-H), 4.45 (dd, J = 4.6, 10.5 Hz, 1 H, 3-CH_a), 4.63 (t, J = 10.5 Hz, 1 H, 3-CH_b), 4.98 (t, J = 4.1 Hz, 1 H, 2-H), 5.98 (d, J = 3.7 Hz, 1 H, 1-H), 7.75–7.85 (m, 4 H, Phth) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 26.4, 26.9, 28.0 (CH_3), 47.1 (CH), 73.9 (CH_2), 77.1, 80.1 (CH), 82.8 (C), 106.0 (CH), 112.6 (C), 123.7 (CH), 128.9 (C), 134.7 (CH), 163.8, 169.0 (C) ppm. IR (neat): $\tilde{\nu}$ = 3660, 2991, 2930, 1730 cm^{-1}. HRMS (ESI): calcd. for $C_{21}H_{25}NO_8$ [M + Na]$^+$ 442.1478; found 442.1472. **Method B:** To a solution of **12** (77.6 mg, 0.222 mmol) in CH_2Cl_2 (3 mL) was added PCC (98%, 98 mg, 0.444 mmol), Ac_2O (0.21 mL, 2.22 mmol) and *t*BuOH (0.422 mL, 4.44 mmol). After the mixture had been stirred overnight, CH_2Cl_2 was removed under reduced pressure, and the residue was purified by column chromatography to yield **11** (51 mg, 55%). The oxidation of **9** under similar conditions afforded **11** in 22% yield.

***tert*-Butyl 3-Aminoxy-3-deoxy-1,2-*O*-isopropylidene-α-D-ribofuranuronate (13):** Prepared from **11** (950.4 mg, 2.265 mmol) according to the general procedure of hydrazinolysis. To obtain an analytically pure sample, the residue was treated with saturated aq. Na_2CO_3 after the evaporation and extracted with EtOAc. The combined organic layers were washed with brine, dried ($MgSO_4$), filtered and concentrated to dryness to afford the pure product as a colorless oil (100%). $[\alpha]_D^{23}$ = +46.4 (c = 0.47, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.31 (s, 3 H, Me), 1.47 (s, 9 H, *t*Bu), 1.50 (s, 3 H, Me), 2.57–2.65 (m, 1 H, 3-H), 3.83 (dd, J = 6.4, 10.5 Hz, 1 H, 3-CH_a), 3.98 (dd, J = 7.8, 10.5 Hz, 1 H, 3-CH_b), 4.18 (d, J = 10.6 Hz, 1 H, 4-H), 4.69 (t, J = 4.1 Hz, 1 H, 2-H), 5.45 (br. s, 2 H, ONH_2), 5.93 (d, J = 3.2 Hz, 1 H, 1-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 26.5, 26.9, 28.0 (CH_3), 47.0 (CH), 71.5 (CH_2), 78.6 (CH), 80.6 (CH), 82.2 (C), 106.1 (CH), 112.5, 169.6 (C) ppm. IR (neat): $\tilde{\nu}$ = 2986, 2900, 1743 cm^{-1}. HRMS (ESI): calcd. for $C_{13}H_{23}NO_6$ [M + Na]$^+$ 312.1423; found 312.1418.

Dimer 14: Prepared by the coupling of **10** (822.8 mg, 2.265 mmol) and **13** (655.3 mg, 2.265 mmol); 81% yield, R_f = 0.47 (CH_2Cl_2/MeOH, 20:1). $[\alpha]_D^{23}$ = +57.3 (c = 0.66, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.30 (s, 3 H, Me), 1.32 (s, 3 H, Me), 1.43 (s, 9 H, *t*Bu), 1.47 (s, 3 H, Me), 1.50 (s, 3 H, Me), 2.50–2.68 (m, 2 H, 2 × 3-H), 4.05–4.28 (m, 4 H, CH_2-ON and 2 × 4-H), 4.52 (dd, J = 5.0, 11.0 Hz, 1 H, CH-ON), 4.70 (t, J = 11.0 Hz, 1 H, CH-ON), 4.74 (t, J = 4.1 Hz, 1 H, 2-H), 5.09 (t, J = 3.6 Hz, 1 H, 2-H), 5.91 (d, J = 3.2 Hz, 1 H, 1-H), 5.92 (d, J = 3.2 Hz, 1 H, 1-H), 7.73–7.84 (m, 4 H, Phth), 9.25 (s, 1 H, O-NH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 26.4, 26.5, 26.9, 28.0 (CH_3), 46.5, 48.0 (CH), 72.8, 74.7 (CH_2), 76.7, 77.9, 80.2, 80.3 (CH), 82.8 (C), 105.9, 106.0 (CH), 112.7, 113.2 (C), 123.7 (CH), 128.9 (C), 134.8 (CH), 163.8, 167.3, 169.2 (C) ppm. IR (neat): $\tilde{\nu}$ = 2987, 2900, 1730 cm^{-1}. HRMS (ESI): calcd. for $C_{30}H_{38}N_2O_{13}$ [M + Na]$^+$ 657.2272; found 657.2266.

Aminoxy Dimer 15: Prepared from dimer **14** (367.9 mg, 0.58 mmol) according to the general procedure of hydrazinolysis. An analytical sample was obtained as for **13**: 95% yield, colorless oil. $[\alpha]_D^{23}$ = +18.4 (c = 0.76, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.32 (s, 3 H, Me), 1.33 (s, 3 H, Me), 1.46 (s, 12 H, *t*Bu and Me), 1.49 (s, 3 H, Me), 2.50–2.65 (m, 2 H, 2 × 3-H), 4.00–4.30 (m, 6 H, 2 × CH_2O-N and 2 × 4-H), 4.72 (t, J = 4.1 Hz, 1 H, 2-H), 4.76 (t, J = 4.1 Hz, 1 H, 2-H), 5.46 (br. s, 2 H, ONH_2), 5.85 (d, J = 3.7 Hz, 1 H, 1-H), 5.93 (d, J = 3.2 Hz, 1 H, 1-H), 9.18 (s, 1 H, O-NH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 26.5, 26.9, 27.0, 28.0 (CH_3), 46.5, 47.5 (CH), 71.1, 72.9 (CH_2), 77.7, 78.1, 80.3, 80.5 (CH), 82.8 (C), 105.7 (CH), 106.0 (CH), 112.7, 113.1, 167.6, 169.3 (C) ppm. IR (neat): $\tilde{\nu}$ = 2982, 2900, 1743, 1696 cm^{-1}. HRMS (ESI): calcd. for $C_{22}H_{36}N_2O_{11}$ [M + Na]$^+$ 527.2217; found 527.2211.

Trimer 16: Prepared by the coupling of **10** (83.1 mg, 0.229 mmol) and **15** (115.4 mg, 0.229 mmol), 63% yield, R_f = 0.36 (CH_2Cl_2/MeOH, 20:1). $[\alpha]_D^{23}$ = +40.7 (c = 0.86, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.29 (s, 3 H, Me), 1.31 (s, 6 H, 2 × Me), 1.44 (s, 9 H, *t*Bu), 1.46 (s, 3 H, Me), 1.48 (s, 6 H, 2 × Me), 2.40–2.70 (m, 3 H, 3 × 3-H), 4.07 (dd, J = 6.0, 10.1 Hz, 1 H, CH-ON), 4.12–4.32 (m, 6 H, 3 × CH-ON and 3 × 4-H), 4.51 (dd, J = 5.0, 11.0 Hz, 1 H, CH-ON), 4.67 (t, J = 11 Hz, 1 H, CH-ON), 4.76 (t, J = 4.1 Hz, 1 H, 2-H), 4.84 (t, J = 4.2 Hz, 1 H, 2-H), 5.05 (t, J = 4.1 Hz, 1 H, 2-H), 5.85 (d, J = 3.6 Hz, 1 H, 1-H), 5.91 (d, J = 3.7 Hz, 1 H, 1-H), 5.92 (d, J = 3.2 Hz, 1 H, 1-H), 7.73–7.84 (m, 4 H, Phth), 9.37 (s, 1 H, O-NH), 9.42 (s, 1 H, O-NH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 26.4, 26.5, 27.0, 28.0 (CH_3), 46.6, 47.1, 47.8 (CH), 72.8, 73.3, 74.7 (CH_2), 76.8, 77.6, 78.0, 80.2, 80.3, 80.6 (CH), 82.7 (C), 105.9, 106.0 (CH), 112.6, 113.2, 113.2 (C), 123.7 (CH), 128.9 (C), 134.7 (CH), 163.7, 167.6, 169.3 (C) ppm. IR (neat): $\tilde{\nu}$ = 2987, 2904, 1735 cm^{-1}. HRMS (ESI): calcd. for $C_{39}H_{51}N_3O_{18}$ [M + Na]$^+$ 872.3065; found 872.3060.

Acid Dimer 17: Prepared from dimer **14** (287.9 mg, 0.454 mmol) according to the general procedure of the selective deprotection of the *t*Bu group. Column chromatography (CH_2Cl_2/MeOH/AcOH, 100:2:0.25 then 100:2.5:0.25) afforded **17** (77%) as a colorless syrup. R_f = 0.45 (CH_2Cl_2/MeOH/AcOH, 6:0.3:0.15). $[\alpha]_D^{23}$ = +66.7 (c = 0.50, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.30 (s, 3 H, Me), 1.31 (s, 3 H, Me), 1.47 (s, 3 H, Me), 1.49 (s, 3 H, Me), 2.50–2.70 (m, 2 H, 2 × 3-H), 4.11 (dd, J = 6.0, 10.1 Hz, 1 H, CH-ON), 4.20–4.30 (m, 3 H, CH-ON and 2 × 4-H), 4.47 (dd, J = 5.0, 10.5 Hz, 1 H, CH-ONPhth), 4.69 (t, J = 10.5 Hz, 1 H, CH-ONPhth), 4.81 (t, J = 10.5 Hz, 1 H, 2-H), 5.05 (t, J = 3.6 Hz, 1 H, 2-H), 5.92 (d, J = 3.7 Hz, 1 H, 1-H), 5.94 (d, J = 3.6 Hz, 1 H, 1-H), 7.73–7.84 (m, 4 H, Phth), 9.46 (s, 1 H, O-NH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 26.4, 26.5, 26.9 (CH_3), 46.5, 47.7 (CH), 73.0, 74.7 (CH_2), 76.8, 77.2, 80.3, 80.5, 106.0, 106.1 (CH), 113.1, 113.3 (C), 123.8 (CH), 128.9 (C), 134.8 (CH), 163.9, 168.0, 171.6 (C) ppm. IR (neat): $\tilde{\nu}$ = 2987, 2904, 1726 cm^{-1}. HRMS (ESI): calcd. for $C_{26}H_{30}N_2O_{13}$ [M + Na]$^+$ 601.1646; found 601.1640.

Tetramer 18: Prepared by the coupling of **17** (195 mg, 0.337 mmol) and **15** (170 mg, 0.337 mmol), 63% yield, R_f = 0.29 (CH_2Cl_2/MeOH, 20:1). $[\alpha]_D^{23}$ = +20.5 (c = 0.38, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.30 (s, 3 H, Me), 1.33 (s, 3 H, Me), 1.34 (s, 6 H, 2 × Me), 1.48 (s, 3 H, Me), 1.48 (s, 9 H, *t*Bu), 1.49 (s, 3 H, Me), 1.51 (s, 3 H, Me), 1.52 (s, 3 H, Me), 2.40–2.95 (m, 4 H, 4 × 3-H), 3.95 (dd, J = 6.0, 11.4 Hz, 1 H, CH-ON), 3.90–4.40 (m, 9 H, 5 × CH-ON and 4 × 4-H), 4.55 (dd, J = 4.6, 10.6 Hz, 1 H, CH-ON), 4.65–4.80 (m, 3 H, CH-ON and 2 × 2-H), 4.97 (t, J = 4.1 Hz, 1 H, 2-H), 5.10 (t, J = 4.1 Hz, 1 H, 2-H), 5.85 (d, J = 3.7 Hz, 1 H, 1-H), 5.93 (d, J = 3.7 Hz, 1 H, 1-H), 5.96 (d, J = 3.2 Hz, 1 H, 1-H), 5.97 (d, J = 2.7 Hz, 1 H, 1-H), 7.73–7.84 (m, 4 H, Phth), 9.47 (s, 1 H, O-NH), 9.62 (s, 1 H, O-NH), 9.87 (s, 1 H, O-NH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 26.6, 27.0, 28.0 (CH_3), 46.3, 46.7, 47.1, 47.3 (CH), 72.7, 72.9, 74.0, 74.5 (CH_2), 76.7, 77.3, 78.2, 78.3, 80.3, 80.6, 80.7 (CH), 82.8 (C), 105.7, 106.1, 106.2 (CH), 112.8, 113.0, 113.2, 113.3 (C), 123.7 (CH), 129.0 (C), 134.7 (CH), 163.7, 167.6, 168.0, 168.3, 169.4 (C) ppm. IR (neat): $\tilde{\nu}$ = 3674, 2987, 2900, 1726, 1691 cm^{-1}. HRMS (ESI): calcd. for $C_{48}H_{64}N_4O_{23}$ [M + Na]$^+$ 1087.3859; found 1087.3854.

Acid Tetramer 19: Prepared from tetramer **18** (69.5 mg, 0.065 mmol) according to the general procedure of the selective deprotection of the *t*Bu group. Column chromatography (CH_2Cl_2/MeOH/HOAc, 100:2.5:0.25 to 100:3.5:0.25) afforded the title compound in 52% yield. R_f = 0.28 (CH_2Cl_2/MeOH/AcOH, 6:0.3:0.15). $[\alpha]_D^{23}$ = +40.4 (c = 0.16, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ =

1.28 (s, 3 H, Me), 1.30 (s, 3 H, Me), 1.32 (s, 6 H, 2×Me), 1.46 (s, 3 H, Me), 1.47 (s, 3 H, Me), 1.49 (s, 6 H, 2×Me), 1.51 (s, 3 H, Me), 2.40–2.90 (m, 4 H, 4×3-H), 3.90–4.40 (m, 10 H, 3×CH_2-ON and 4×4-H), 4.48 (dd, J = 5.0, 11 Hz, 1 H, CH-ON), 4.68 (t, J = 10.6 Hz, 1 H, CH-ON), 4.75 (t, J = 4.1 Hz, 1 H, 2-H), 4.82 (s, 2 H, 2×2-H), 5.05 (t, J = 4.1 Hz, 1 H, 2-H), 5.80 (d, J = 3.7 Hz, 1 H, 1-H), 5.91 (d, J = 3.9 Hz, 1 H, 1-H), 5.94 (d, J = 2.3 Hz, 1 H, 1-H), 5.95 (d, J = 3.2 Hz, 1 H, 1-H), 7.73–7.84 (m, 4 H, Phth), 9.74 (s, 1 H, O-NH), 9.88 (s, 1 H, O-NH), 10.02 (s, 1 H, O-NH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 26.5, 27.0 (CH_3), 46.6, 46.5, 46.9, 47.5 (CH), 72.5, 73.2, 73.7, 74.6 (CH_2), 76.8, 77.4, 77.9, 78.0, 80.2, 80.4, 80.6, 106.0 (CH), 113.1, 113.3 (C), 123.7 (CH), 129.0 (C), 134.8 (CH), 163.8, 168.2, 168.3, 168.3, 169.4 (C) ppm. IR (neat): $\tilde{\nu}$ = 2987, 2904, 1734, 1682 cm^{-1}. HRMS (ESI): calcd. for $C_{44}H_{56}N_4O_{23}$ $[M + Na]^+$ 1031.3233; found 1031.3228.

Pentamer 20: Prepared by the coupling of **19** (10 mg, 0.01 mmol) and **13** (5.73 mg, 0.02 mmol) in 40% yield and by the coupling of **17** (12 mg, 0.021 mmol) and **23** (10 mg, 0.014 mmol) in 30% yield. R_f = 0.24 (CH_2Cl_2/MeOH, 20:1). $[\alpha]_D^{23}$ = +11.7 (c = 0.21, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.31 (s, 3 H, Me), 1.32 (s, 3 H, Me), 1.34 (s, 6 H, 2×Me), 1.35 (s, 3 H, Me), 1.48 (s, 15 H, tBu and 2×Me), 1.51 (s, 3 H, Me), 1.52 (s, 3 H, Me), 2.50–2.90 (m, 5 H, 5×3-H), 3.95 (dd, J = 6.9, 10.6 Hz, 1 H, CH-ON), 4.05–4.40 (m, 12 H, 7×CH-ON and 5×4-H), 4.55 (dd, J = 4.6, 11.0 Hz, 1 H, CH-ON), 4.70 (t, J = 11.0 Hz, 1 H, CH-ON), 4.78 (dd, J = 5.0, 10.5 Hz, 2 H, 2×2-H), 4.88 (m, 2 H, 2×2-H), 5.09 (t, J = 3.7 Hz, 1 H, 2-H), 5.90 (d, J = 3.2 Hz, 2 H, 2×1-H), 5.95 (d, J = 3.6 Hz, 1 H, 1-H), 5.96 (d, J = 3.7 Hz, 2 H, 2×1-H), 7.73–7.84 (m, 4 H, Phth), 9.57 (s, 1 H, O-NH), 9.76 (s, 1 H, O-NH), 9.80 (s, 1 H, O-NH), 9.91 (s, 1 H, O-NH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 26.5, 26.6, 27.0, 27.06, 27.11, 28.1 (CH_3), 46.4, 46.6, 46.8, 46.9, 47.5 (CH), 72.8, 72.9, 73.2, 73.9, 74.6 (CH_2), 76.8, 77.6, 77.8, 78.1, 78.3, 80.3, 80.6, 80.7, 80.8 (CH), 82.9 (C), 105.9, 106.0, 106.08, 106.2 (CH), 112.8, 113.0,113.2 (C), 123.7 (CH), 129.0 (C), 134.7 (CH), 163.8, 167.9, 168.0, 168.5, 169.4 (C) ppm. IR (neat): $\tilde{\nu}$ = 2978, 2900, 1743, 1683 cm^{-1}. HRMS (ESI): calcd. for $C_{57}H_{77}N_5O_{28}$ $[M + Na]^+$ 1302.4653; found 1302.4647.

Hexamer 21: Prepared by the coupling of **19** (10 mg, 0.01 mmol) and **15** (10 mg, 0.02 mmol) in 25% yield, by the coupling of **17** (10.9 mg, 0.018 mmol) and **22** (8.8 mg, 0.009 mmol) in 13% yield and by the coupling of **24** (18.6 mg, 0.023 mmol) and **23** (16.9 mg, 0.023 mmol) in 20% yield. R_f = 0.21 (CH_2Cl_2/MeOH, 20:1). $[\alpha]_D^{23}$ = +11.2 (c = 0.17, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.28–1.38 (m, 18 H, 6×Me), 1.48 (s, 15 H, tBu and 2×Me), 1.49–1.51 (s, 12 H, 4×Me), 2.50–2.90 (m, 6 H, 6×3-H), 3.90–4.40 (m, 16 H, 5×CH_2-ON and 6×4-H), 4.55 (dd, J = 5.0, 11.0 Hz, 1 H, CH-ON), 4.70 (t, J = 10.6 Hz, 1 H, CH-ON), 4.74–4.87 (m, 4 H, 4×2-H), 4.90 (t, J = 3.1 Hz, 1 H, 2-H), 5.07 (t, J = 3.6 Hz, 1 H, 2-H), 5.89–5.97 (m, 6 H, 6×1-H), 7.73–7.84 (m, 4 H, Phth), 9.80 (s, 1 H, O-NH), 9.82 (s, 1 H, O-NH), 9.84 (s, 1 H, O-NH), 10.05 (s, 1 H, O-NH), 10.16 (s, 1 H, O-NH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 26.5, 27.1, 28.1 (CH_3), 46.4, 46.6, 46.7, 46.9, 47.5 (CH), 72.7, 72.9, 73.3, 73.4, 73.8, 74.6 (CH_2), 76.9, 77.7, 77.9, 78.0, 78.2, 78.3, 80.3, 80.4, 80.7, 80.79, 80.83, 81.0 (CH), 82.9 (C), 105.96, 106.0, 106.1, 106.3 (CH), 112.7, 113.1, 113.2 (C), 123.7 (CH), 129.0 (C), 134.7 (CH), 163.8, 168.1, 168.2, 168.3, 168.5, 169.4 (C) ppm. IR (neat): $\tilde{\nu}$ = 2987, 2913, 1734, 1687 cm^{-1}. HRMS (ESI): calcd. for $C_{66}H_{90}N_6O_{33}$ $[M + Na]^+$ 1517.5446; found 1517.5441.

Aminoxy Trimer 23: Prepared from the trimer (**16**, 195.5 mg, 0.23 mmol) according to the general procedure of hydrazinolysis. An analytical sample was obtained as for **13**: 79% yield, $[\alpha]_D^{23}$ = +12.1 (c = 0.42, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.30–1.36 (m, 9 H, 3×Me), 1.46 (s, 9 H, 3×Me), 1.49 (s, 9 H, tBu), 2.55–2.70 (m, 3 H, 3×3-H), 4.00–4.40 (m, 9 H, 3×CH_2-ON and 3×4-H), 4.71 (t, J = 3.6 Hz, 1 H, 2-H), 4.77 (t, J = 4.1 Hz, 1 H, 2-H), 4.84 (t, J = 4.1 Hz, 1 H, 2-H), 5.49 (br. s, 2 H, ONH_2), 5.85 (d, J = 3.7 Hz, 1 H, 1-H), 5.88 (d, J = 3.2 Hz, 1 H, 1-H), 5.93 (t, J = 3.7 Hz, 1 H, 1-H), 9.41 (s, 1 H, O-NH), 9.54 (s, 1 H, O-NH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 26.5, 26.9, 27.0, 28.0 (CH_3), 46.6, 47.1, 47.3 (CH), 71.2, 72.8, 73.6 (CH_2), 77.7, 77.9, 78.0, 80.3, 80.6, 80.7 (CH), 82.8 (C), 105.7, 105.9, 106.0 (CH), 112.7, 113.1, 113.2, 167.9, 169.4 (C) ppm. IR (neat): $\tilde{\nu}$ = 2978, 2896, 1691 cm^{-1}. HRMS (ESI): calcd. for $C_{31}H_{49}N_3O_{16}$ $[M + Na]^+$ 742.3011; found 742.3005.

Acid Trimer 24: Prepared from trimer **16** (73 mg, 0.086 mmol) according to the general procedure of the selective deprotection of the tBu group. Column chromatography (CH_2Cl_2/MeOH/AcOH, 100:2.5:0.25 then 100:3:0.25) afforded the title compound (76%) as a colorless syrup. R_f = 0.32 (CH_2Cl_2/MeOH/AcOH, 6:0.3:0.15). $[\alpha]_D^{23}$ = +51.6 (c = 0.39, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.27 (s, 3 H, Me), 1.31 (s, 6 H, 2×Me), 1.45 (s, 3 H, Me), 1.48 (s, 6 H, 2×Me), 2.50–2.80 (m, 3 H, 3×3-H), 4.01–4.10 (m, 2 H, 2×CH-ON), 4.20–4.35 (m, 5 H, 2×CH-ON and 3×4-H), 4.49 (dd, J = 5.0, 11.0 Hz, 1 H, CH-ON), 4.68 (t, J = 10.1 Hz, 1 H, CH-ON), 4.74 (t, J = 3.7 Hz, 1 H, 2-H), 4.86 (s, 1 H, 2-H), 5.03 (t, J = 3.7 Hz, 1 H, 2-H), 5.92 (d, J = 2.8 Hz, 1 H, 1-H), 5.94 (d, J = 3.2 Hz, 2 H, 2×1-H), 7.70–7.85 (m, 4 H, Phth), 9.80 (s, 1 H, O-NH), 9.97 (s, 1 H, O-NH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 26.4, 26.5, 26.9 (CH_3), 46.6, 46.9, 47.4 (CH), 72.3, 73.6, 74.5 (CH_2), 76.8, 77.0, 78.1, 80.3, 80.4, 80.6, 106.0, 106.1 (CH), 112.9, 113.1, 113.3 (C), 123.8 (CH), 128.9 (C), 134.8 (CH), 163.8, 168.0 (C) ppm. IR (neat): $\tilde{\nu}$ = 2986, 2900, 1721, 1673 cm^{-1}. HRMS (ESI): calcd. for $C_{35}H_{43}N_3O_{18}$ $[M + Na]^+$ 816.2439; found 816.2444.

Cbz Dimer 25: To a mixture of **15** (60 mg, 0.119 mmol) and $NaHCO_3$ (60 mg, 0.713 mmol) in THF/H_2O (4:1, 2.5 mL), was added CBzCl (50 μL, 0.357 mmol) at room temp. After the mixture had been stirred overnight, the solvent was evaporated in vacuo, and the residue was dissolved in EtOAc (10 mL), washed with saturated aq. $NaHCO_3$ (3×5 mL) and brine (10 mL), dried, filtered, concentrated to dryness and purified by column chromatography (petroleum ether/EtOAc, 7:3 then 1:1) to afford 24 mg of **25** as a colorless syrup. Yield: 31.6%. R_f = 0.41 (CH_2Cl_2/MeOH, 20:1). $[\alpha]_D^{23}$ = +5.48 (c = 0.49, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.30 (s, 3 H, Me), 1.31 (s, 3 H, Me), 1.46 (s, 9 H, tBu), 1.48 (s, 3 H, Me), 1.49 (s, 3 H, Me), 2.50–2.65 (m, 2 H, 2×3-H), 4.10–4.32 (m, 6 H, 2×CH_2-ON and 2×4-H), 4.73–4.80 (m, 2 H, 2×2-H), 5.12 (d, J = 11.9 Hz, 1 H, PhCH-), 5.17 (d, J = 12.4 Hz, 1 H, PhCH-), 5.82 (d, J = 3.7 Hz, 1 H, 1-H), 5.92 (d, J = 3.2 Hz, 1 H, 1-H), 7.30–7.40 (m, 5 H, Ph), 7.86 (s, 1 H, NH), 9.30 (s, 1 H, O-NH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 26.5, 26.9, 28.0 (CH_3), 46.5, 47.1 (CH), 67.7, 72.8, 73.2 (CH_2), 77.8, 78.1, 80.3, 80.6 (CH), 82.8 (C), 105.7, 106.0 (CH), 112.7, 113.2 (C), 128.4, 128.6, 128.7 (CH), 135.5, 157.6, 167.7, 169.3 (C) ppm. IR (neat): $\tilde{\nu}$ = 3665, 3287, 2983, 2900, 1726 cm^{-1}. HRMS (ESI): calcd. for $C_{30}H_{42}N_2O_{13}$ $[M + Na]^+$ 661.2585; found 661.2579.

Alcohol Dimer 26: Compound **25** (12 mg, 0.0188 mmol) in MeOH (2 mL) was hydrogenated in the presence of 10% Pd/C (1.2 mg) at room temp. for 40 min. The mixture was then filtered, and the solvents were evaporated to dryness to afford the pure title compound (9.1 mg, 100%). R_f = 0.32 (CH_2Cl_2/MeOH, 20:1). $[\alpha]_D^{23}$ = –18.3 (c = 0.21, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.33 (s, 3 H, Me), 1.34 (s, 3 H, Me), 1.46 (s, 9 H, tBu), 1.51 (s, 3 H, Me), 1.52 (s, 3 H, Me), 2.26–2.35 (m, 1 H, 3′-H), 2.60–2.70 (m, 1 H, 3-H),

3.79 (t, J = 6 Hz, 1 H, OH), 3.99 (t, J = 6.0 Hz, 2 H, CH_2O-), 4.10–4.35 (m, 3 H, CH_2ON and 4-H), 4.50 (d, J = 10.1 Hz, 1 H, 4′-H), 4.74 (t, J = 4.1 Hz, 1 H, 2′-H), 4.76 (t, J = 4.1 Hz, 1 H, 2-H), 5.84 (d, J = 3.6 Hz, 1 H, 1′-H), 5.93 (d, J = 3.2 Hz, 1 H, 1-H), 9.34 (s, 1 H, O-NH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 26.3, 26.5, 26.9, 28.0 (CH_3), 46.5, 50.2 (CH), 59.8, 73.1 (CH_2), 78.1, 80.0, 80.3, 81.6 (CH), 82.9 (C), 105.4, 106.0 (CH), 112.7, 113.3, 168.6, 169.3 (C) ppm. IR (neat): $\tilde{\nu}$ = 2987, 2900, 2326, 1734, 1678 cm^{-1}. HRMS (ESI): calcd. for $C_{22}H_{35}NO_{11}$ $[M + Na]^+$ 512.2108; found 512.2102.

Supporting Information (see footnote on the first page of this article): Synthesis and characterization of **7**, **9** and **14** and copies of ^1H, ^{13}C and DEPT NMR spectra of all compounds.

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