Synthesis of the C-Analog of 2-Acetylamino-2-deoxy-β-D-glucopyranosyl L- and D-Serine

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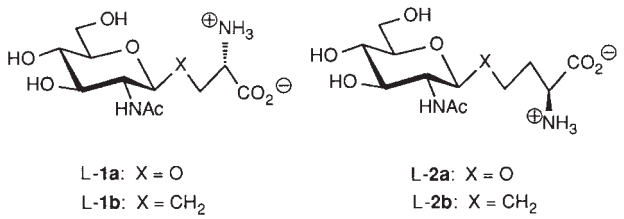
Received 9 October 1997

Abstract: Glucosamine was transformed into *N*-tetrachlorophthaloyl-protected fluoride **5** which gave with allyltrimethylsilane as *C*-nucleophile in the presence of BF_3•OEt_2 as catalyst β-*C*-allyl derivative **6** in good yield. Removal of the TCP group, introduction of the *N*-acetyl group, and then ozonolysis afforded *C*-glycosyl acetaldehyde derivative **8** which gave with a glycine derived phosphonate in a Wittig–Horner reaction α-acylaminoacrylate **10**. Hydrogenolysis and removal of the protective groups furnished target molecule L-**1b** and also the corresponding D-isomer (D-**1b**). The configuration of these compounds was assigned.

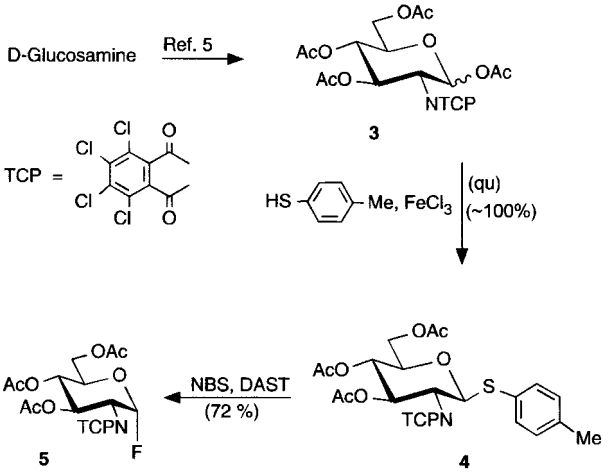
Key words: glucosamine, glycopeptides, synthesis, C-analog of glycosyl serine derivatives

Intracellular posttranslational protein glycosylation, through which *N*-acetylglucosamine (GlcNAc) residues are β-glycosidically linked to the hydroxy group of serine and/or threonine, has been observed for some time.[1] The specific functions of *O*-GlcNAc attachment to proteins have not yet been fully elucidated. Indirect evidence led to the hypothesis that the *O*-GlcNAc linkage may have a reciprocal relationship to the regulatory effect of protein phosphorylation and dephosphorylation.[2] Therefore, access to glycopeptides carrying hydrolytically stable GlcNAc residues is of great interest. Hydrolytic stability without largely affecting the glycopeptide structure can best be accommodated by the *C*-glycosyl analog[3] of *O*-(2-acetamido-2-deoxy-β-D-glucopyranosyl)serine (Scheme 1, **1a,b**) as glycopeptide building block. An efficient synthesis of L- and D-**1b** is reported in this paper. A synthesis of the corresponding homolog derived from homoserine (L-**2a,b**) (regarded in the literature as analog of *N*-glucoasparagine) based on demanding carbanion chemistry has been recently reported.[4]



Scheme 1

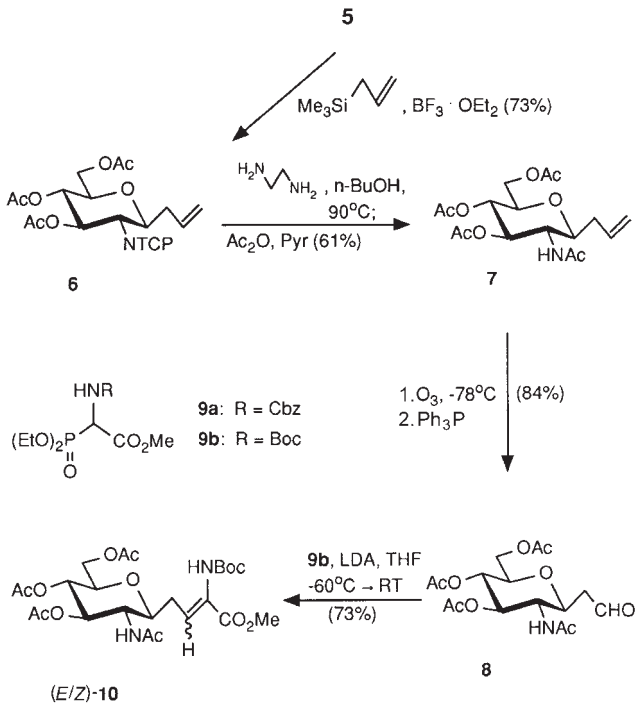
N-Tetrachlorophthaloyl (TCP) protection of glucosamine provides excellent glycosyl donors for β-selective glycoside bond formation; for example, *O*-, *S*-, *N*-, and *C*-nucleophiles have been already successfully employed in this reaction.[5, 6] To this aim, known TCP-protected glucosamine derivative **3**[5] (Scheme 2) was transformed with *p*-toluenethiol in the presence of $FeCl_3$ into thioglycoside **4** which gave with NBS/DAST the corresponding fluoride **5** as glycosyl donor. Reaction of **5** with allyltrimethylsilane in the presence of BF_3• OEt_2 as catalyst afforded C-allyl glycoside **6** in a β-selective reaction (Scheme 3). Removal of the TCP group with ethylenediamine in butanol at 90 °C and then acetylation with acetic anhydride in pyridine furnished known *N*-acetyl derivative **7**,[7] a useful intermediate for the synthesis of **1b** and various other *C*-glycosyl amino acids, such as, for example **2b**.



Scheme 2

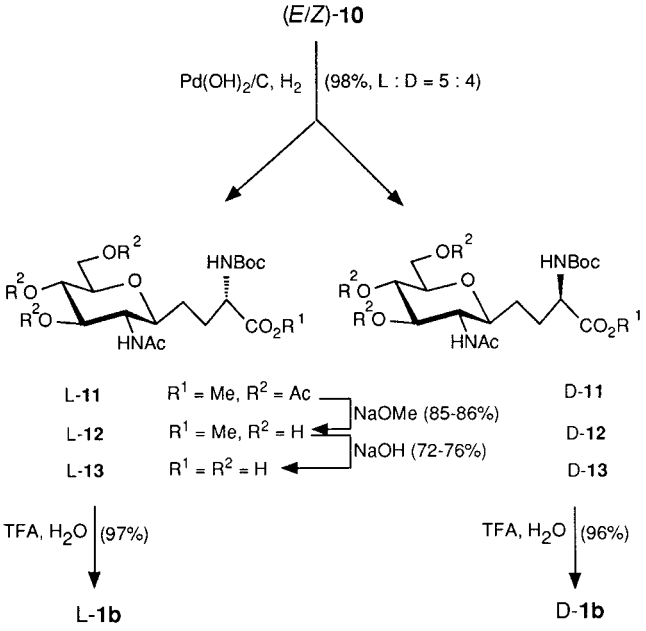
For the synthesis of the amino acid moiety, construction of an α-acylamino acrylate moiety using a Wittig–Horner reaction with glycine phosphonate derivative **9b** was envisaged. To this aim, *N*-Cbz-protected α-methoxyglycine methyl ester **8** was transformed under standard conditions into phosphonate **9a** (Scheme 3).[8, 9] For the replacement of the Cbz group by the Boc group hydrogenation with Pearlman's catalyst [$Pd(OH)_2$/C] in the presence of trifluoroacetic acid and then treatment with di-*tert*-butyl dicarbonate was performed leading to **9b**. Ozonolysis of **7** at –78 °C furnished aldehyde **8**, which gave with **9b** in the presence of lithium diisopropylamide as base α-acylaminoacrylate derivative (*E*/*Z*)-**10** in good yield (73%, E/Z 1:2).

Hydrogenation of (*E*/*Z*)-**10** was performed with Pearlman's catalyst in order to obtain both potential diastereomers L-**11** and D-**11** (Scheme 4); the yield was practically quantitative and after separation the L/D ratio was 5:4. Later it was found that none of the common chiral hydrogenation catalysts for the selective synthesis of either L-**11** or D-**11** worked well in this case; this is presumably due to the presence of the additional acetylamino group in the sugar residue.[10] In order to obtain the target molecules the



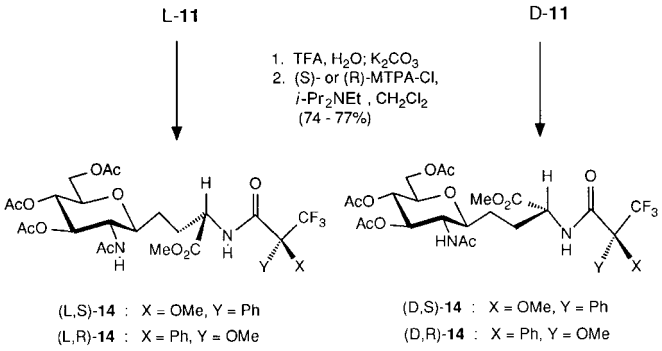
Scheme 3

O-acetyl groups in L- and D-**11** were removed with NaOMe/MeOH (L- and D-**12**), then the ester moiety was hydrolyzed with NaOH (L- and D-**13**) and finally the Boc group was cleaved by treatment with TFA in water, thus furnishing L-**1b** and D-**1b**, respectively, in good overall yield.



Scheme 4

The structural assignment of L- and D-**1b** was based on the method of Dale and Mosher.[11] To this aim, the Boc group in L- and D-**12** was removed with TFA/H_2O and the reaction with (R)- and (S)-α-methoxy-α-phenyl-α-(trifluoromethyl)acetyl chloride (MTPA-Cl)[12] in the presence of Hünig's base (i-Pr_2NEt) was carried out affording diastereoisomers (L,*S*)-, (L,*R*)-**14** and (D,*S*)-, (D,*R*)-**14**, respectively. The ^{1}H NMR downfield shift of 0.20 ppm of the *O*-methyl group in the MTPA moiety of (L,*S*)-**14** compared with (L,*R*)-**14** due to interaction with the ester moiety indicates L-configuration for the amino acid residue.[10] In accordance with this assignment (D,*R*)-**14** exhibits a 0.17 ppm downfield shift of the corresponding *O*-methyl group in comparison with (D,*S*)-**14**, thus confirming D-configuration for the amino acid residue (Scheme 5).



Scheme 5

In conclusion, an efficient synthesis of target molecule L-**1b** and the corresponding D-isomer can be based on readily available allyl *C*-glycosides **6** and **7**, respectively.

Reagents and solvents were obtained from commercial suppliers. Solvents were purified by distillation and dried as usual, except for distilled CH_2Cl_2 and toluene which were passed through columns of commercially available neutral alumina (ICN Alumina N, activity grade super I) as an alternative drying procedure. All nonhydrolytic reactions were conducted in oven-dried glassware and under dry argon. Analytical TLC was performed on silica gel Merck Kieselgel 60 F_{254} plates (0.2 mm). The plates were visualized by immersion in mostain [200 mL 10% H_2SO_4, 10 g $(NH_4)_6Mo_7O_{24}$•$4H_2O$, 200 mg $Ce(SO_4)_2$] or ninhydrin solution (1% in EtOH) followed by heating (165 °C). Flash chromatography was carried out on Mallinckrodt–Baker 7024-02 silica gel 40 μ. MPLC was performed by using columns of silica gel LiChrep 60 with approx. 4600 plates and solvent pressures of 0.7 to 0.8 MPa. FAB-MS were recorded on a modified Finnigan MAT 312/AMD 5000. ^{1}H NMR and ^{13}C NMR spectra were recorded on a Bruker AC 250 Cryospec and a Bruker DRX 600 instrument. Proton chemical shifts are reported in ppm relative to the corresponding solvent peak, as are carbon chemical shifts. Assignments of proton and carbons were carried out with the aid of 600 MHz spectra: COSY, HMBC, HMQC, DEPT, ROESY [strength of observed interactions (ROE): classification into strong (s), medium (m), and weak (w)]. Measurements of optical rotations were performed on a Perkin–Elmer polarimeter 241 MC (1 dm cell).

4-Methylphenyl 3,4,6-Tri-*O*-acetyl-2-deoxy-2-(tetrachlorophthalimido)-1-thio-β-D-glucopyranoside (4):

Compound **3**[5] (15.2 g, 24.71 mmol) was dissolved in anhyd CH_2Cl_2 (213 mL) under dry Ar. Subsequently, *p*-thiocresol (6.44 g, 51.88 mmol) was added and the solution was stirred for 15 min at r.t. Anhyd $FeCl_3$ (4.81 g, 29.65 mmol) was added and the mixture was stirred for 2.5 h. For workup it was diluted with CH_2Cl_2 (220 mL) and the brown mixture filtered through a Celite pad which was washed

with the solvent. The filtrate was extracted with sat. $NaHCO_3$ to give a light yellow organic layer which was dried ($MgSO_4$) and concentrated to dryness. The residue was purified by flash chromatography (toluene/EtOAc, gradient: 10:1 → 2:1) to afford **4** as a yellow oil (16.78 g, quantitative); TLC (toluene/EtOAc 8:1): R_f 0.27; $[\alpha]_D$ –8 (c = 1.0, CH_2Cl_2).
^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.84, 1.99, 2.08 (3 s, 9 H, 3 OAc), 2.28 (s, 3 H, Me), 3.82 (ddd, $^3J_{4,5}$ = 10.1, $^3J_{5,6}$ = 4.8, $^3J_{5,6'}$ = 2.5 Hz, l H, 5-H), 4.16 (dd, $^2J_{gem}$ = 12.4, $^3J_{5,6'}$ = 2.5 Hz, 1 H, 6′-H), 4.26 (dd, $^2J_{gem}$ = 12.4, $^3J_{5,6}$ = 4.8 Hz, 1 H, 6-H), 4.28 (dd, $^3J_{1,2}$ = $^3J_{2,3}$ = 10.1 Hz, 1 H, 2-H), 5.10 (dd, $^3J_{3,4}$ = $^3J_{4,5}$ = 10.1 Hz, 1 H, 4-H), 5.58 (d, $^3J_{1,2}$ = 10.1 Hz, 1 H, l-H), 5.67 (dd, $^3J_{2,3}$ = $^3J_{3,4}$ = 10.1 Hz, 1 H, 3-H), 7.02–7.06, 7.23–7.27 (2 m, 4 H, phenyl).
^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 20.4, 20.5, 20.7, 21.1 [4 C, OC(O) *C*H$_3$, SPh*C*H$_3$], 54.6, 62.0, 68.4, 71.6, 76.0 (5 C, 2-, 3-, 4-, 5-, 6-C), 82.3 (1 C, 1-C), 126.5–140.5 (12 C, Ph), 162.1, 163.2 {2 C, N[C(O)]$_2$}, 169.3, 170.4, 170.5 [3 C, O*C*(O)CH$_3$].
Anal. calcd for $C_{27}H_{23}Cl_4NO_9S$ (679.36): C 47.74, H 3.41, N 2.06; found: C 47.64, H 3.46, N 2.01.

3,4,6-Tri-*O*-acetyl-2-deoxy-2-(tetrachlorophthalimido)-α-D-glucopyranosyl Fluoride (5):
Compound **4** (1.0 g, 1.47 mmol) was dissolved in anhyd CH_2Cl_2 (14 mL) under dry Ar and was cooled to –15 °C. Then DAST (292 μL, 2.21 mmol) was added and, after stirring for 5 min, NBS (341 mg, 1.91 mmol) was added and stirring was continued for 10 min. Thereafter, the red mixture was allowed to warm up to r.t. TLC (toluene/EtOAc 8:1) indicated complete fluorination after 5 h. The solution was diluted with CH_2Cl_2 and extracted with sat. $NaHCO_3$ and NaS_2O_3. The organic layer was dried ($MgSO_4$) and concentrated in vacuo. The residue was purified by flash chromatography (toluene/EtOAc 10:1) to yield **5** (610 mg, 72%) as a yellow foam; TLC (toluene/EtOAc 8:1): R_f 0.25; $[\alpha]_D$ +55 (c = 1.0, CH_2Cl_2).
^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.89, 2.02, 2.11 (3 s, 9 H, 3 OAc), 3.95 (ddd, $^3J_{5,6}$ = 4.8, $^3J_{5,6'}$ = 2.0, $^3J_{4,5}$ = 9.2 Hz, 1 H, 5-H), 4.18 (dd, $^3J_{5,6'}$ = 2.0, $^2J_{gem}$ = 12.5 Hz, 1 H, 6′-H), 4.28–4.45 (m, 2 H, 2-, 6-H), 5.19 (dd, $^3J_{3,4}$ = 10.0, $^3J_{4,5}$ = 9.5 Hz, 1 H, 4-H), 5.71 (dd, $^3J_{2,3}$ = 9.5, $^3J_{3,4}$ = 10.0 Hz, 1 H, 3-H), 6.02 (dd, $^3J_{1,2}$ = 7.7, $^2J_{1,F}$ = 52.2 Hz, 1 H, 1-H).
FAB-MS (positive mode, matrix: CH_2Cl_2/3-nitrobenzyl alcohol 1:1, NA1): *m/z* (%) = 748 (4) [(M + NA1)Na]$^+$, 598 (37) [MNa]$^+$.
Anal. calcd for $C_{20}H_{16}Cl_4FNO_9$ (575.16): C 41.77, H 2.80, N 2.44; found C 41.64, H 2.91, N 2.32.

1,3,4-Tri-*O*-acetyl-2,6-anhydro-5,7,8,9-tetradeoxy-5-(tetrachlorophthalimido)-L-*glycero*-L-*gulo*-non-8-enitol (6):
Compound **5** (2.5 g, 4.38 mmol) was dissolved in anhyd CH_2Cl_2 (42 mL) and allyltrimethylsilane (6.94 mL, 43.47 mmol) was added under dry Ar. The solution was cooled to –10 °C. A catalytic amount of BF_3•Et_2O (273 μL, 2.17 mmol) was added dropwise and stirring was continued at –5 °C for 14 h. During this time a cloudy precipitate was formed. Thereafter, the mixture was diluted with CH_2Cl_2, extracted with sat. $NaHCO_3$, dried ($MgSO_4$) and concentrated to dryness. The remaining residue was purified by flash chromatography (toluene/EtOAc, 6:1) to afford **6** (1.89 g, 73%) as a yellow foam; TLC (toluene/EtOAc 6:1): R_f 0.37.
The reported analytic and spectroscopic data[7] are in accordance to our results.

5-Acetamido-1,3,4-tri-*O*-acetyl-2,6-anhydro-5,7,8,9-tetradeoxy-L-glycero-L-*gulo*-non-8-enito1 (7):
Compound **6** (1.16 g, 1.94 mmol) was dissolved in BuOH (10 mL) under dry Ar. Ethane-1,2-diamine (1.94 mL 28.89 mmol) was added and the solution heated to 90 °C for 22 h. The resulting reddish solution was concentrated in vacuo and coevaporated with toluene. The red oil was dissolved in anhyd pyridine (40 mL) and Ac_2O (30 mL) after removal of all volatile residues (high vacuum). A catalytic amount of DMAP was added and stirring was continued at r.t. for 14 h. The solution was concentrated in vacuo and again coevaporated with toluene to remove pyridine. The residue was purified by flash chromatography (toluene/EtOAc, gradient: 1:1 → 1:2; amount of silica gel: 10 fold excess of the crude product is sufficient) to afford 7 (440 mg, 6l%) as a white solid; TLC (toluene/EtOAc 1:3): R_f 0.20.
The reported analytic and spectroscopic data[7] are in accordance with our results.

4-Acetamido-5,6,8-tri-*O*-acetyl-3,7-anhydro-2,3,4-trideoxy-D-*glycero*-D-*gulo*-octose (8):
A solution of 7 (100 mg, 270 μmol) in anhyd MeOH (10 mL) was cooled to –78°C. Ozone was then passed through the solution under vigorous stirring. The maximum time for the ozone treatment was 5 min (flow: approx. 60 L O_2/h generating 3 L O_3/h). This resulted in the formation of a bluish solution. Dry Ar was passed through the cold solution in order to remove excess ozone. Ph_3P (70.6 mg, 270 μmol) and CH_2Cl_2 (4 mL) were added and the solution was allowed to warm up to r.t. while stirring was continued for 1.5 h. The clear solution was concentrated to dryness and purified by flash chromatography (CH_2Cl_2/MeOH 30:1) to yield **8** (84.4 mg, 84%) as a colorless oil; TLC (CH_2Cl_2/MeOH 10:1): R_f 0.38; $[\alpha]_D$ –26 (c = 1.0, CH_2Cl_2).
^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.89 (s, 3 H, NH*Ac*), 2.01 (s, 6 H, 2 OAc), 2.05 (s, 3 H, OAc), 2.71 (ddd, $^3J_{1,2'}$ < 1.0, $^2J_{gem}$ = 18.0, $^3J_{2',3}$ = 7.4 Hz, 1 H, 2′-H), 2.81 (ddd, $^3J_{1,2}$ <1.0, $^2J_{gem}$ = 18.0, $^3J_{2,3}$ = 4.5 Hz, 1 H, 2-H), 3.61 (ddd, $^3J_{6,7}$ = 9.8, $^3J_{7,8'}$ = 2.2, $^3J_{7,8}$ = 4.8 Hz, 1 H, 7-H), 3.89 (ddd, $^3J_{3,4}$ = 9.8, $^3J_{2,3}$ = 4.5, $^3J_{2',3}$ = 7.4 Hz, 1 H, 3-H), 4.03 (dd, $^3J_{7,8'}$ = 2.2, $^3J_{gem}$ = 12.4 Hz, 1 H, 8′-H), 4.08 (dd, $^3J_{3,4}$ = $^3J_{4,5}$ = 9.8 Hz, 1 H, 4-H), 4.99 (dd, $^3J_{4,5}$ = $^3J_{5,6}$ = 9.8 Hz, 1 H, 5-H), 5.06 (dd, $^3J_{5,6}$ = $^3J_{6,7}$ = 9.8 Hz, 1 H, 6-H), 5.59 (d, $^3J_{NH,4}$ = 9.1 Hz, 1 H, N*H*Ac), 9.72 (dd, $^3J_{1,2}$ = $^3J_{1,2'}$ < 1 Hz, 1 H, 1-H).
$^{1\,3}$C NMR (62.9 MHz, $CDCl_3$): δ = 20.5, 20.6, 20.7 [3 C, OC(O)*C*H$_3$], 23.0 [1 C, NHC(O)*C*H$_3$], 37.2, 46.0, 53.4, 62.2, 68.3, 74.0, 75.7 (7 C, 2-, 3-, 4-, 5-, 6-, 7-, 8-C), 169.3–173.2 [4 C, 3 O*C*(O)CH$_3$, NH*C*(O)CH$_3$], 199.5 (1 C, 1-C).
FAB-MS (positive mode, matrix: 3-nitrobenzyl alcohol): *m/z* (%) = 747 (5) [$(M_2H)^+$, 374 (89) $[MH]^+$.
Anal. calcd for $C_{16}H_{23}NO_9$ (373.36): C 51.47, H 6.21, N 3.75; found C 51.36, H 6.34, N 3.60.

Methyl 2-(Benzyloxycarbonylamino)-2-(diethoxyphosphoryl)acetate (9a):
2-(Benzyloxycarbonylamino)-2-methoxyacetic acid[9] (**8**) (12 g, 47.38 mmol) was dissolved in anhyd toluene (72 mL) at 50 °C under dry Ar. The solution was cooled to r.t. and PCl_3 (5.17 mL, 59.22 mmol) was added. The solution was stirred for 18 h at 70 °C, then it was cooled again to r.t., $(EtO)_3P$ (8.53 mL, 49.75 mmol) was added and then it was heated to 70 °C for 3 h. For workup the mixture was concentrated in vacuo and the residue was partitioned between Et_2O and sat. $NaHCO_3$. The organic layer was dried ($MgSO_4$) and concentrated to dryness. Flash silica gel chromatography eluting with a gradient of toluene/EtOAc (2:1 → 1:1) afforded **9a** (10.83 g, 64%) as a white, waxy solid; TLC (toluene/EtOAc 1:1): R_f 0.18.
^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.23–1.30 (m, 6 H, 2 OCH$_2$C*H*$_3$), 3.77 (s, 3 H, CO_2Me), 4.05–4.16 (m, 4 H, 2 OC*H*$_2$CH$_3$), 4.85 (dd, $^2J_{2,P}$ = 22.3, $^3J_{2,NH}$ = 9.2 Hz, 1 H, 2-H), 5.09 [m, 2 H, CH_2 (Cbz)], 5.63 (br. d, $^3J_{2,NH}$ ~9.2 Hz, 1 H, NH), 7.24–7.30 (m, 5 H, phenyl).
$^{1\,3}$C NMR (62.9 MHz, $CDCl_3$): δ = 16.1, 16.2 (2 C, 2 OCH$_2$*C*H$_3$), 52.5 (d, $^1J_{2,P}$ = 146.9 Hz, 1 C, 2-C), 53.1 (1 C, CO_2*Me*), 63.6–63.8 (2 C, 2 OCH$_2$CH$_3$), 67.4 [1 C, CH_2 (Cbz)], 128.0–128.4, 135.8 (6 C, phenyl), 155.5–155.6 [1 C, NH*C*(O)O], 167.3–167.4 (1 C, *C*O$_2$Me).
Anal. calcd for $C_{15}H_{22}NO_7P$ (359.31): C 50.14, H 6.17, N 3.90; found C 50.11, H 6.19, N 3.97.

Methyl 2-(*tert*-Butoxycarbonylamino)-2-(diethoxyphosphoryl)acetate (9b):
Compound **9a** (200 mg, 557 μmol) was dissolved in EtOAc (23 mL). To this solution was subsequently added TFA (52 μL, 670 μmol), wa-

ter (0.2 mL) and Pearlman' s catalyst $Pd(OH)_2$/C (60 mg). The mixture was treated with hydrogen for 2 h at normal pressure and r.t. Thereafter, the black suspension was filtered through a Celite pad which was washed with MeOH. The clear filtrate was concentrated in vacuo to a volume of approx. 6 mL to remove MeOH. Then it was again diluted with EtOAc (4 mL) and $NaHCO_3$ (47 mg) was added followed by vigorous stirring in order to neutralize TFA. After 10 min Boc_2O (244 mg, 1.12 mmol) was added. When this was completely dissolved, Et_3N (39 μL) was added and stirring was continued for l4 h at r.t. For workup the mixture was concentrated to dryness and the remaining residue was purified by flash chromatography (toluene/EtOAc 1:2) to afford **9b** (151 mg, 83%) as an amorphous, white solid; TLC (toluene/EtOAc 1:3): R_f 0.37 (ninhydrin).

^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.27–1.33 (m, 6 H, 2 OCH_2CH_3), 1.41 [br. s, 9 H, CMe_3 (Boc)], 3.78 (s, 3 H, CO_2Me), 4.08–4.20 (m, 4 H, 2 OCH_2CH_3), 4.80 (dd, $^2J_{2,P}$ = 22.5, $^3J_{2,NH}$ = 9.3 Hz, 1 H, 2-H), 5.30 (br. d, $^3J_{2,NH}$ ~9.3 Hz, 1 H, NH).

^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 16.2–16.3 (2 C, 2 OCH_2CH_3), 28.2 (3 C, CMe_3), 52.1 (d, $^1J_{2,P}$ = 147.0 Hz, 1 C, 2-C), 53.0 (1 C, CO_2Me), 63.6–63.7 (2 C, 2 OCH_2CH_3), 80.7 (1 C, CMe_3), 154.8–154.9 [1 C, $NHC(O)O$], 167.6–167.7 (1 C, CO_2Me).

Anal. calcd for $CM_2H_{24}NO_7P$ (325.30): C 44.31, H 7.44, N 4.31; found C 44.10, H 7.46, N 4.31.

Methyl (*E* and *Z*)-6-Acetamido-7,8,10-tri-*O*-acetyl-5,9-anhydro-2-(*tert*-butoxycarbonylamino)-2,3,4,6-tetradeoxy-D-*glycero*-D-*gulo*-dec-2-enonate (*E*/*Z*-10):

i-Pr_2NH (58 μL, 411 μmol) was added under dry Ar to a two-necked 50-mL flask charged with anhyd THF (2 mL). The solution was cooled to –30 °C, BuLi (257 μL, 411 μmol) was added and stirring was continued for 20 min. **9b** (134 mg, 411 μmol) was dissolved in anhyd THF (5 mL) and was added to the mixture at –40 °C. Over the course of 20 min, the solution was allowed to warm up to –10 °C. Then the solution was cooled to –60 °C and **8** (128 mg, 343 μmol, dissolved in 5 mL of anhyd THF) was added dropwise. The cooling was stopped after 10 min and the solution warmed up to r.t. while stirring was continued for an additional 3 h. The appearance of a light yellow color after addition of **8** indicates that the reaction is proceeding. For workup the mixture was diluted with Et_2O and extracted with sat. NH_4Cl. The aqueous layer was washed with additional Et_2O. The combined organic layers were dried ($MgSO_4$), filtered, concentrated to dryness and the remaining residue was purified by flash chromatography (CH_2Cl_2/MeOH 40:1) to afford (*E*/*Z*)-**10** (135 mg, 73%) as a white foam comprising an inseparable mixture (MPLC) of the *E*- and *Z*-isomers (*E*/*Z* 1:2 as determined by peak integration of ^{1}H NMR); TLC (CH_2Cl_2/MeOH 10:1): R_f 0.61–0.63.

^{1}H NMR (250 MHz, $CDCl_3$): (*E*)-**10** and (*Z*)-**10** (unassigned signals): δ = 1.42 (br. s, 9 H, CMe_3), 1.89 (s, 3 H, NH*Ac*), 1.99 (br. s, 6 H, 2 OAc), 2.07 (s, 3 H, OAc). (*E*)-**10**: δ = 2.68 (ddd, $^2J_{gem}$ = 16.1, $^3J_{3,4'}$ = $^3J_{4',5}$ = 7.6 Hz, 1 H, 4′-H), 2.92 (ddd, $^2J_{gem}$ = 16.1, $^3J_{3,4}$ = 7.8, $^3J_{4,5}$ = 3.7 Hz, 1 H, 4-H), 3.40 (ddd, $^3J_{4,5}$ = 3.7, $^3J_{4',5}$ = 7.6, $^3J_{5,6}$ = 10.0 Hz, 1 H, 5-H), 3.60 (m, 1 H, 9-H), 3.76 (s, 3 H, CO_2Me), 4.00 (dd, $^3J_{5,6}$ = $^3J_{6,7}$ = 10.0 Hz, 1 H, 6-H), 4.04 (dd, $^2J_{gem}$ = 12.2, $^3J_{9,10'}$ = 2.3 Hz, 1 H, 10′-H), 4.19 (dd, $^2J_{gem}$ – 12.2, $^3J_{9,10}$ = 5.6 Hz, 1 H, 10-H), 5.01 (dd, $^3J_{6,7}$ = 10.0, $^3J_{7,8}$ = 9.5 Hz, 1 H, 7-H), 5.02 (dd, $^3J_{7,8}$ = $^3J_{8,9}$ = 9.5 Hz, 1 H, 8-H), 5.62 (d, $^3J_{6,NH}$ = 9.3 Hz, 1 H, N*H*Ac), 6.59 (br. s, 1 H, N*H*-Boc), 6.68 (br. dd, $^3J_{3,4}$ = $^3J_{3,4'}$ ~7.7 Hz, 1 H, 3-H). (*Z*)-**10**: δ = 2.36 (ddd, $^2J_{gem}$ = 16.1, $^3J_{3,4'}$ = $^3J_{4',5}$ = 7.6 Hz, 1 H, 4′-H), 2.54 (ddd, $^2J_{gem}$ = 16.1, $^3J_{3,4}$ = 7.8, $^3J_{4,5}$ = 3.7 Hz, 1 H, 4-H), 3.53 (m, 1 H, 5-H), 3.60 (m, 1 H, 9-H), 3.74 (s, 3 H, CO_2Me), 3.96 (dd, $^3J_{5,6}$ = $^3J_{6,7}$ = 10.0 Hz, 1 H, 6-H), 4.08 (dd, $^2J_{gem}$ = 12.2, $^3J_{9,10'}$ = 2.3 Hz, 1 H, 10′-H), 4.17 (dd, $^2J_{gem}$ = 12.2, $^3J_{9,10}$ = 5.5 Hz, 1 H, 10-H), 5.02 (dd, $^3J_{7,8}$ = $^3J_{8,9}$ = 9.5 Hz, 1 H, 8-H), 5.04 (dd, $^3J_{6,7}$ = 10.0, $^3J_{7,8}$ = 9.5 Hz, 1 H, 7-H), 5.67 (d, $^3J_{NH,6}$ = 9.3 Hz, 1 H, N*H*Ac), 6.39 (br. s, 1 H, N*H*Boc), 6.49 (br. dd, $^3J_{3,4}$ = $^3J_{3,4'}$ ~7.7 Hz, 1 H, 3-H).

^{13}C NMR (62.9 MHz, $CDCl_3$): (*E*)-**10** and (*Z*)-**10** (not assigned signals): δ = 20.620.7 [3 C, 3 $OC(O)CH_3$], 23.1–23.2 [1 C, $NHC(O)CH_3$], 28.1–28.2 (3 C, CMe_3), 68.6 (1 C, 169.3–171.4 [4 C, 3 $OC(O)CH_3$, $NHC(O)CH_3$]. (*E*)-**10**: δ = 31.1 (1 C, 4-C), 52.2 (1 C, CO_2Me), 53.9 (1 C, 6-C), 62.4 (1 C, 10-C), 68.5 (1 C, 8-C), 74.4 (1 C, 7-C), 75.6 (1 C, 9-C), 79.3 (1 C, 5-C), 124.5 (1 C, 3-C), 128.8 (1 C, 2-C), 153.0 [1 C, $NHC(O)O$], 164.3 (1 C, 1-C). (*Z*)-**10**: δ = 30.5 (1 C, 4-C), 52.3 (1 C, CO_2Me), 53.7 (1 C, 6-C), 62.3 (1 C, 10-C), 68.5 (1 C, 8-C), 74.1 (1 C, 7-C), 75.5 (1 C, 9-C), 78.1 (1 C, 5-C), 125.5 (1 C, 3-C), 129.3 (1 C, 2-C), 153.5 [1 C, $NHC(O)O$], 165.1 (1 C, 1-C).

ROESY (600 MHz, $CDCl_3$, characteristic ROE): (*E*)-**10**: δ = 2.92, 3.76 (4-H, CO_2Me; m). (*Z*)-**10**: δ = 3.74, 6.49 (3-H, CO_2Me; m).

FAB-MS (positive mode, matrix: 3-nitrobenzyl alcohol, NaI): *m/z* (%) = 717 (6) $[(M + NaI)Na]^+$, 567 (100) $[MNa]^+$, 467 (9) $[(M - C_4H_8 - CO_2)Na]^+$.

Anal. calcd for $C_{24}H_{36}N_2O_{12}$ (544.55): C 52.94, H 6.66, N 5.14; found C 52.95, H 6.65, N 5.26.

Methyl (2*S*)-6-Acetamido-7,8,10-tri-*O*-acetyl-5,9-anhydro-2-(*tert*-butoxycarbonylamino)-2,3,4,6-tetradeoxy-D-*glycero*-D-*gulo*-deconate (L-11), Methyl (2*R*)-6-Acetamido-7,8,10-tri-*O*-acetyl-5,9-anhydro-2-(*tert*-butoxycarbonylamino)-2,3,4,6-tetradeoxy-D-*glycero*-D-*gulo*-deconate (D-11):

Compound (*E*/*Z*)-**10** (100 mg, 184 μmol) was dissolved in EtOAc (7.4 mL). To this solution was subsequently added MeOH (0.4 mL), water (0.1 mL), HOAc (10 μL, 89 μmol) and Pearlman's catalyst $Pd(OH)_2$/C (30 mg). The mixture was treated with hydrogen for 24 h under normal conditions. Thereafter, the black suspension was filtered through a Celite pad which was washed with MeOH. The clear filtrate was concentrated to dryness to afford a mixture of the pure compounds L-**11** and D-**11** (98.4 mg, 98%). Separation of the compound mixture was performed by MPLC eluting with toluene/acetone (3:2) to yield L-**11** (54.2 mg, 54%) as a colorless, waxy solid and D-**11** (44.2 mg, 44%) as an amorphous, white solid; TLC (toluene/acetone 2:1): R_f L-**11** 0.25; R_f D-**11** 0.19; $[\alpha]_D$ L-**11** –27 (*c* = 1.0, CH_2Cl_2); $[\alpha]_D$ D-**11** –32 (*c* = 1.0, CH_2Cl_2).

^{1}H NMR (250 MHz, $CDCl_3$): L-**11**: δ = 1.39 (br. s, 9 H, CMe_3), 1.42–1.79 (m, 4 H, 3-, 3′-, 4-, 4′-H), 1.89 (s, 3 H, NH*Ac*), 1.98 (br. s, 6 H, 2 OAc), 2.05 (s, 3 H, OAc), 3.36 (m, 1 H, 5-H), 3.55 (m, 1 H, 9-H), 3.69 (s, 3 H, CO_2Me), 3.99 (ddd, $^3J_{5,6}$ = $^3J_{6,7}$ = $^3J_{NH,6}$ = 9.6 Hz, 1 H, 6-H), 4.05 (dd, $^2J_{gem}$ = 12.3, $^3J_{9,10'}$ = 2.6 Hz, 1 H, 10′-H), 4.17 (dd, $^2J_{gem}$ = 12.3, $^3J_{9,10}$ = 5.5 Hz, 1 H, 10-H), 4.14 (br. m, 1 H, 2-H), 4.96 (dd, $^3J_{6,7}$ = $^3J_{7,8}$ = 9.5 Hz, 1 H, 7-H), 5.01 (dd, $^3J_{7,8}$ = $^3J_{8,9}$ = 9.5 Hz, 1 H, 8-H), 5.17 (d, $^3J_{NH,6}$ = 9.6 Hz, 1 H, N*H*Ac), 5.60 (br. d, $^3J_{NH,2}$ ~9.0 Hz, 1 H, N*H*Boc).

^{1}H NMR (250 MHz, $CDCl_3$): D-**11**: δ = 1.41 (br. s, 9 H, CMe_3), 1.54–1.73, 1.81–2.04 (2 m, 4 H, 3-, 3′-, 4-, 4′-H), 1.91 (s, 3 H, NH*Ac*), 2.00 (br. s, 6 H, 2 OAc), 2.07 (s, 3 H, OAc), 3.29 (m, 1 H, 5-H), 3.52 (ddd, $^3J_{8,9}$ = 9.7, $^3J_{9,10}$ = 5.2, $^3J_{9,10'}$ = 2.4 Hz, 1 H, 9-H), 3.70 (s, 3 H, CO_2Me), 3.97 (ddd, $^3J_{5,6}$ = $^3J_{6,7}$ = $^3J_{NH,6}$ = 9.8 Hz, 1 H, 6-H), 4.06 (dd, $^2J_{gem}$ = 12.4, $^3J_{9,10'}$ = 2.4 Hz, 1 H, 10′-H), 4.16 (dd, $^2J_{gem}$ = 12.4, $^3J_{9,10}$ = 5.2 Hz, 1 H, 10-H), 4.18 (br. m, 1 H, 2-H), 4.92 (dd, $^3J_{6,7}$ = $^3J_{7,8}$ = 9.8 Hz, 1 H, 7-H), 5.02 (dd, $^3J_{7,8}$ = $^3J_{8,9}$ = 9.8 Hz, 1 H, 8-H), 5.16 (br. d, $^3J_{NH,2}$ ~9.5 Hz, 1 H, N*H*Ac), 5.47 (d, $^3J_{NH,2}$ = 9.5 Hz, 1 H, N*H*Boc).

^{13}C NMR (62.9 MHz, $CDCl_3$): L-**11**: δ = 20.5–20.6 [3 C, 3 $OC(O)CH_3$], 27.0, 27.7 (2 C, 3-, 4-C), 28.3 (3 C, CMe_3), 52.2, 52.6 (2 C, 2-, 6-C), 53.2 (1 C, CO_2Me), 68.6 (1 C, CMe_3), 62.5, 74.5, 75.7, 77.7, 79.8 (5 C, 5-, 7-, 8-, 9-, 10-C), 155.8 [1 C, $NC(O)O$], 169.3, 170.2, 170.7, 171.5, 173.1 [5 C, $NHC(O)CH_3$, CO_2Me, 3 $OC(O)CH_3$].

Anal. calcd for $C_{24}H_{38}N_2O_{12}$ (546.58): C 52.74, H 7.01, N 5.13; found C 52.94, H 7.10, N 5.14.

Methyl (2*S*)-6-Acetamido-5,9-anhydro-2-(*tert*-butoxycarbonylamino)-2,3,4,6-tetradeoxy-D-*glycero*-D-*gulo*-deconate (L-12):

Compound L-**11** (108 mg, 197.6 μmol) was dissolved in anhyd MeOH (2.4 mL). 0.173 M NaOMe in MeOH (36 μL, 5.93 μmol) was added and the reaction solution (8.0 < pH ≤ 8.5) was stirred at r.t. for 2 h. Subsequently, the solution was diluted with MeOH, and Amber-

lite IR-120 [H^+] (8.0 mg) was added and stirring was continued for 15 min (pH neutral). The mixture was filtered and concentrated to dryness to afford L-**12** (70.6 mg, 85%) as a colorless solid; TLC (CH_2Cl_2/MeOH 3:1): R_f 0.67; $[\alpha]_D$ –19 (*c* = 1.0, MeOH).
^{1}H NMR (250 MHz, MeOH-d_4): δ = 1.48 (br. s, 9 H, CMe_3), 1.54–1.77 (m, 2 H, 4-, 4′-H), 1.87–1.98 (m, 2 H, 3-, 3′-H), 2.03 (s, 3 H, NH*Ac*), 3.21–3.31 (m, 2 H, 5-, 9-H), 3.32 (dd, $^3J_{7,8} = {}^3J_{8,9}$ = 8.6 Hz, 1 H, 8-H), 3.41 (dd, $^3J_{6,7} = {}^3J_{7,8}$ = 8.6 Hz, 1 H, 7-H), 3.66 (dd, $^3J_{5,6} = {}^3J_{6,7}$ = 8.6 Hz, 1 H, 6-H), 3.69 (dd, $^2J_{gem}$ = 12.0, $^3J_{9,10'}$ = 5.8 Hz, 1 H, 10′-H), 3.75 (s, 3 H, CO_2Me), 3.89 (dd, $^2J_{gem}$ = 12.0, $^3J_{9,10}$ = 2.3 Hz, 1 H, 10-H), 4.11 (dd, $^3J_{2,3}$ = 4.3, $^3J_{2,3'}$ = 8.7 Hz, 1 H, 2-H), 4.93 (s, 5 H, 3 OH, 2 NH).
FAB-MS (positive mode, matrix: MeOH/3-nitrobenzyl alcohol 1:1): *m/z* (%) = 421 (17) $[MH]^+$, 365 (34) $[(M - C_4H_8)H]^+$, 321 (100) $[(M - C_4H_8 - CO_2)H]^+$.

(2*S*)-6-Acetamido-5,9-anhydro-2-(*tert*-butoxycarbonylamino)-2,3,4,6-tetradeoxy-D-*glycero*-D-*gulo*-deconic Acid (L-13):
To a solution of L-**12** (70 mg, 166.4 μmoL) in MeOH (6 mL) and water (4 mL) was added 1.0 M NaOH (0.5 mL, 500 μmoL). The solution was stirred for 14 h at r.t. Subsequently, Amberlite IR-120 [H^+] (ca. 450 mg) was added and after stirring for 30 min, the pH dropped to 7. The mixture was filtered and concentrated to dryness to give L-**13** (51.4 mg, 76%) as a colorless oil; TLC (CH_2Cl_2/MeOH 1:1): R_f 0.32; $[\alpha]_D$ –16 (*c* = 1.0, MeOH).
^{1}H NMR (250 MHz, MeOH-d_4): δ = 1.41–1.95 (m, 4 H, 3-, 3′-, 4-, 4′-H), 1.48 (br. s, 9 H, CMe_3), 2.03 (s, 3 H, NHAc), 3.21–3.34 (m, 3 H, 5-, 8-, 9-H), 3.41 (dd, $^3J_{6,7} = {}^3J_{7,8}$ = 9.0 Hz, 1 H, 7-H), 3.67 (dd, $^3J_{5,6} = {}^3J_{6,7}$ = 9.0 Hz, 1 H, 6-H), 3.69 (dd, $^2J_{gem}$ = 12.0, $^3J_{9,10'}$ = 5.7 Hz, 1 H, 10′-H), 3.90 (dd, $^2J_{gem}$ = 12.0, $^3J_{9,10'}$ = 2.4 Hz, 1 H, 10-H), 4.08 (dd, $^3J_{2,3}$ = 4.9, $^3J_{2,3'}$ = 9.0 Hz, 1 H, 2-H), 4.93 (br. s, 6 H, 4 OH, 2 NH).
Anal. calcd for: $C_{17}H_{30}N_2O_9 \bullet 1.3\ H_2O$ (429.86): C 47.50, H 7.64, N 6.52; found C 47.61, H 7.79, N 6.33.

(2*S*)-6-Acetamido-2-amino-5,9-anhydro-2,3,4,6-tetradeoxy-D-*glycero*-D-*gulo*-deconic Acid (L-1b):
Compound L-**13** (46 mg, 113.2 μmol) was dissolved in TFA (2 mL). Water (0.2 mL) was added and the solution was stirred for 2.5 h at r.t. Then the solution was concentrated in vacuo and coevaporated with water. After drying under high vacuum pure L-**1b** (33.6 mg, 97%) could be obtained as a colorless solid; TLC ($CHCl_3$/MeOH/H_2O 60:35:8): R_f 0.1; $[\alpha]_D$ –5 (*c* = 0.66, MeOH).
^{1}H NMR (250 MHz, D_2O): δ = 1.31–1.45 (m, 1 H, 4′-H), 1.60–1.74 (m, 1 H, 4-H), 1.89 (s, 3 H, NH*Ac*), 1.90–1.98 (m, 2 H, 3-, 3′-H), 3.21–3.29 (m, 3 H, 5-, 8-, 9-H), 3.32 (dd, $^3J_{6,7} = {}^3J_{7,8}$ = 9.3 Hz, 1 H, 7-H), 3.48 (dd, $^3J_{5,6} = {}^3J_{6,7}$ = 9.3 Hz, 1 H, 6-H), 3.54 (dd, $^2J_{gem}$ = 12.2, $^3J_{9,10'}$ = 5.4 Hz, 1 H, 10′-H), 3.74 (dd, $^2J_{gem}$ = 12.2, $^3J_{9,10}$ = 2.0 Hz, 1 H, 10-H), 3.86 (dd, $^3J_{2,3} = {}^3J_{2,3'}$ = 6.3 Hz, 1 H, 2-H), 4.63 (br. s, 7 H, 3 OH, 4 NH).
Anal. calcd for: $C_{12}H_{22}N_2O_7 \bullet 0.75\ H_2O$ (319.83): C 45.06, H 7.41, N 8.76; found C 45.17, H 7.39, N 8.80.

Methyl (2*R*)-6-Acetamido-5,9-anhydro-2-(*tert*-butoxycarbonylamino)-2,3,4,6-tetradeoxy-D-*glycero*-D-*gulo*-deconate (D-12):
For the preparation see L-**12**. Compound D-**11** (103 mg, 188.4 μmol) was dissolved in anhyd MeOH (2.3 mL). 0.173 M NaOMe in MeOH (34 μL, 5.66 μmol) was added. D-**12** (68.1 mg, 86%) was obtained as a colorless solid; TLC (CH_2Cl_2/MeOH 3:1): R_f 0.67; $[\alpha]_D$ –25 (*c* = 1.0, MeOH).
^{1}H NMR (250 MHz, MeOH-d_4): δ = 1.37 (br. s, 9 H, CMe_3), 1.42–1.69 (m, 4 H, 3-, 3′-, 4-, 4′-H), 1.92 (s, 3 H, NH*Ac*), 3.13–3.24 (m, 3 H, 5-, 8-, 9-H), 3.29 (dd, $^3J_{6,7} = {}^3J_{7,8}$ = 9.0 Hz, 1 H, 7-H), 3.51 (dd, $^3J_{5,6} = {}^3J_{6,7}$ = 9.0 Hz, 1 H, 6-H), 3.60 (m, 1 H, 10′-H), 3.64 (s, 3 H, CO_2Me), 3.79 (dd, $^2J_{gem}$ = 12.0, $^3J_{9,10}$ ~2.5 Hz, 1 H, 10-H), 4.09 (br. m, 1 H, 2-H), 4.93 (s, 5 H, 3 OH, 2 NH).
FAB-MS (positive mode, matrix: MeOH/3-nitrobenzyl alcohol 1:1): *m/z* (%) = 421 (12) $[MH]^+$, 365 (22) $[(M - C_4H_8)H]^+$, 321 (100) $[(M - C_4H_8 - CO_2)H]^+$.

(2*R*)-6-Acetamido-5,9-anhydro-2-(*tert*-butoxycarbonylamino)-2,3,4,6-tetradeoxy-D-*glycero*-D-*gulo*-deconic Acid (D-13):
For the preparation see L-**13**. To a solution of D-**12** (66.2 mg, 157.4 μmol) in MeOH (6 mL) and water (4 mL) was added a solution of 1.0 M NaOH in MeOH (0.47 mL, 470 μmol). The workup afforded D-**13** (46.1 mg, 72%) as a colorless oil; TLC (CH_2Cl_2/MeOH 1:1): R_f 0.32; $[\alpha]_D$ –20 (*c* = 1.0, MeOH).
^{1}H NMR (250 MHz, MeOH-d_4): δ = 1.40–2.09 (m, 4 H, 3-, 3′-, 4-, 4′-H), 1.48 (br. s, 9 H, CMe_3), 2.02 (s, 3 H, NH*Ac*), 3.21–3.36 (m, 3 H, 5-, 8-, 9-H), 3.40 (dd, $^3J_{6,7} = {}^3J_{7,8}$ = 9.3 Hz, 1 H, 7-H), 3.62 (dd, $^3J_{5,6} = {}^3J_{6,7}$ = 9.3 Hz, 1 H, 6-H), 3.66 (dd, $^2J_{gem}$ = 12.6, $^3J_{9,10'}$ = 5.6 Hz, 1 H, 10,-H), 3.89 (dd, $^2J_{gem}$ = 12.6, $^3J_{9,10'}$ = 2.0 Hz, 1 H, 10-H), 4.15 (m, 1 H, 2-H), 4.92 (br. s, 6 H, 4 OH, 2 NH).
FAB-MS (positive mode, matrix: MeOH/3-nitrobenzyl alcohol 1:1): *m/z* (%) = 429 (18) $[MNa]^+$, 407 (32) $[MH]^+$, 351 (52) $[(M - C_4H_8)H]^+$, 307 (100) $[(M - C_4H_8 - CO_2)H]^+$.

(2*R*)-6-Acetamido-2-amino-5,9-anhydro-2,3,4,6-tetradeoxy-D-*glycero*-D-*gulo*-deconic Acid (D-1b):
For the preparation see L-**1b**. Compound D-**13** (45.7 mg, 112.4 μmol) was dissolved in TFA (2 mL) and water (0.2 mL) was added. D-**1b** (33.1 mg, 96%) was obtained as a colorless solid; TLC ($CHCl_3$/MeOH/H_2O 60:35:8): R_f 0.1; $[\alpha]_D$ –9 (*c* = 0.66, MeOH).
^{1}H NMR (250 MHz, MeOH-d_4): δ = 1.55–1.67, 1.78–1.88 (2 m, 2 H, 4-, 4′-H), 2.02 (s, 3 H, NH*Ac*), 1.92–2.25 (m, 2 H, 3-, 3′-H), 3.28–3.48 (m, 4 H, 5-, 7-, 8-, 9-H), 3.64 (dd, $^3J_{5,6} = {}^3J_{6,7}$ = 9.2 Hz, 1 H, 6-H), 3.67 (m, 1 H, 10′-H), 3.92 (dd, $^2J_{gem}$ = 11.9, $^3J_{9,10}$ < 2 Hz, 1 H, 10-H), 4.06 (dd, $^3J_{2,3}$ = 4.6, $^3J_{2,3'}$ = 9.2 Hz, 1 H, 2-H), 4.97 (br. s, 7 H, 3 OH, 4 NH).
$^{1\,3}$C NMR (150.8 MHz, MeOH-d_4): δ = 22.9 [1 C, NHC(O)*C*H$_3$], 27.9 (1 C, 3-C), 28.0 (1 C, 4-C), 53.7 (1 C, 2-C), 56.4 (1 C, 6-C), 62.9 (1 C, 10-C), 72.3 (1 C, 8-C), 77.0 (1 C, 7-C), 79.4 (1 C, 5-C), 81.7 (1 C, 9-C), 171.8 (1 C, NH*C*(O)CH$_3$), 173.9 (1 C, 1-C).
FAB-MS (positive mode, matrix: MeOH/3-nitrobenzyl alcohol 1:1): *m/z* (%) = 329 (9) $[MNa]^+$, 307 (68) $[MH]^+$.
Anal. calcd for: $C_{12}H_{22}N_2O_7 \bullet 0.5\ H_2O$ (315.33): C 45.71, H 7.35, N 8.88; found C 45.79, H 7.41, N 8.90.

General Procedure for the Synthesis of the MTPA-Amides (L,*S*)-, (L,*R*)-14, (D,*S*)-, (D,*R*)-14:
The compounds L- and D-**11** were dissolved in TFA (2 mL) then water (0.1 mL) was added. After stirring for approx. 2.5 h at r.t. the solution was concentrated to dryness in vacuo. The remaining oily residue was dissolved in CH_2Cl_2 (30 mL) and then washed with 43.5 mM aq K_2CO_3 (10 mL). The organic layer was dried ($MgSO_4$), filtered and evaporated to dryness. The oily residue was dissolved either in anhyd MeCN (2 mL) and in CH_2Cl_2 (1.5 mL; starting from L-**11**) or in CH_2Cl_2 only (2.5 mL; starting from D-**11**). Subsequently, *i*-Pr_2NEt (1.1 equiv) and the appropriate α-methoxy-α-trifluoromethyl-α-phenylacetyl chloride[12] (MTPA-Cl, 1.3 equiv) were added and stirring was continued for 2 h. Thereafter, the mixture was diluted with CH_2Cl_2, extracted with sat. $NaHCO_3$ and dried ($MgSO_4$). The suspension was filtered and concentrated in vacuo. The residue was purified by flash chromatography (CH_2Cl_2/MeOH 40:1) to afford the corresponding MTPA-amides as colorless oils.

Methyl (2*S*)-6-Acetamido-7,8,10-tri-*O*-acetyl-5,9-anhydro-2-{[(*R*)-(α-trifluoromethyl-α-methoxy-α-phenyl)methylcarbonyl]amino}-2,3,4,6-tetradeoxy-D-*glycero*-D-*gulo*-deconate [(L,*R*)-14]:
For the preparation see General Procedure. Compound L-**11** (50 mg, 91.5 μmol), *i*-Pr_2NEt (9.5 μL, 104 μmol) and (*S*)-(+)-MTPA-Cl (22.5 μL, 119.2 μmol) were employed to afford (L,*R*)-**14** (45 mg, 74%); TLC (CH_2Cl_2/MeOH, 10:1): R_f 0.70; $[\alpha]_D$ –27 (*c* = 1, CH_2Cl_2).
^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.53–1.87 (m, 2 H, 4-, 4′-H), 2.14–2.23 (m, 2 H, 3-, 3′-H), 1.90 (s, 3 H, NH*Ac*), 1.99 (s, 6 H, 2 OAc), 2.05 (s, 3 H, OAc), 3.30 (s, 3 H, OMe), 3.45 (ddd, $^3J_{4,5}$ = 3.0,

$^3J_{4',5}$ = 9.0, $^3J_{5,6}$ = 9.4 Hz, 1 H, 5-H), 3.55 (ddd, $^3J_{9,10}$ = 6.0, $^3J_{9,10'}$ = 2.7, $^3J_{8,9}$ = 9.1 Hz, 1 H, 9-H), 3.74 (s, 3 H, CO_2Me), 3.98 (ddd, $^3J_{5,6}$ = $^3J_{6,7}$ = 9.1, $^3J_{NH,6}$ = 9.7 Hz, 1 H, 6-H), 4.07 (dd, $^2J_{gem}$ = 12.1, $^3J_{9,10'}$ = 2.7 Hz, 1 H, 10′-H), 4.19 (dd, $^2J_{gem}$ = 12.1, $^3J_{9,10}$ = 6.0 Hz, 1 H, 10-H), 4.56 (ddd, $^3J_{2,3}$ = 3.3, $^3J_{2,3'}$ = 7.6, $^3J_{NH,2}$ = 9.0 Hz, 1 H, 2-H), 4.93 (dd, $^3J_{7,8}$ = $^3J_{8,9}$ = 9.1 Hz, 1 H, 8-H), 5.01 (dd, $^3J_{6,7}$ = $^3J_{7,8}$ = 9.1 Hz, 1 H, 7-H), 5.51 (d, $^3J_{NH,6}$ = 9.7 Hz, 1 H, N*H*Ac), 7.38–7.41, 7.49–7.52 (2 m, 5 H, phenyl), 7.61 (d, $^3J_{NH,2}$ = 9.0 Hz, 1 H, N*H*-MTPA).
FAB-MS (positive mode, matrix: MeOH/3-nitrobenzyl alcohol 1:1): *m/z* (%) = 663 (100) $[MH]^+$, 321 (22) $[(M - C_2H_2O)H]^+$, 603 (25) $[(M - C_2H_4O_2)H]^+$.

Methyl (2*S*)-6-Acetamido-7,8,10-tri-*O*-acetyl-5,9-anhydro-2-{[(*S*)-(α-trifluoromethyl-α-methoxy-α-phenyl)methylcarbonyl]amino}-2,3,4,6-tetradeoxy-D-*glycero*-D-*gulo*-deconate [(L,*S*)-14]:
For the preparation see General Procedure. Compound L-**11** (52 mg, 95.2 μmol), *i*-Pr_2NEt (9.8 μL, 108.1 μmol) and (*R*)-(–)-MTPA-Cl (23.4 μL, 124 μmol) were used to yield (L,*S*)-**14** (48.7 mg, 77%); TLC (CH_2Cl_2/MeOH, 10:1): R_f 0.69; $[\alpha]_D$ –42 (*c* = 1, CH_2Cl_2).
^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.32–1.49, 1.56–1.83, 1.90–2.15 (3 m, 4 H, 3-, 3′-, 4-, 4′-H), 1.53 (s, 3 H, NH*Ac*), 1.96, 1.99, 2.05 (3 s, 9 H, 3 OAc), 3.34 (ddd, $^3J_{4,5}$ = 3.0, $^3J_{4',5}$ = $^3J_{5,6}$ = 9.5 Hz, 1 H, 5-H), 3.50 (s, 3 H, OMe), 3.54 (m, 1 H, 9-H), 3.75 (s, 3 H, CO_2Me), 3.87 (ddd, $^3J_{5,6}$ = $^3J_{6,7}$ = $^3J_{NH,6}$ = 9.5 Hz, 1 H, 6-H), 4.64 (dd, $^2J_{gem}$ = 12.7, $^3J_{9,10'}$ = 2.4 Hz, 1 H, 10′-H), 4.17 (dd, $^2J_{gem}$ = 12.7, $^3J_{9,10}$ = 5.7 Hz, 1 H, 10-H), 4.55 (ddd, $^3J_{2,3}$ = 3.5, $^3J_{2,3'}$ = 7.8, $^3J_{NH,2}$ = 9.7 Hz, 1 H, 2-H), 4.89 (dd, $^3J_{7,8}$ = $^3J_{8,9}$ = 9.5 Hz, 1 H, 8-H), 4.97 (dd, $^3J_{6,7}$ = $^3J_{7,8}$ = 9.5 Hz, 1 H, 7-H), 5.46 (d, $^3J_{NH,6}$ = 9.2 Hz, 1 H, N*H*Ac), 7.24–7.52 (m, 6 H, N*H*-MTPA, phenyl).
FAB-MS (positive mode, matrix: MeOH/3-nitrobenzyl alcohol 1:1): *m/z* (%) = 663 (100) $[MH]^+$, 321 (31) $[(M^- C_2H_2O)H]^+$, 603 (12) $[(M - C_2H_4O_2)H]^+$.

Methyl (2*R*)-6-Acetamido-7,8,10-tri-*O*-acetyl-5,9-anhydro-2-{[(*R*)-(α-trifluoromethyl-α-methoxy-α-phenyl)methylcarbonyl]amino}-2,3,4,6-tetradeoxy-D-*glycero*-D-*gulo*-deconate [(D,*R*)-14]:
For the preparation see General Procedure. Compound D-**11** (51 mg, 93.3 μmol), *i*-Pr_2NEt (9.7 μL, 106.1 μmol) and (*S*)-(+)-MTPA-Cl (23 μL, 121.6 μmol) were employed to afford (D,*R*)-**14** (45.1 mg, 73%); TLC (CH_2Cl_2/MeOH 10:1): R_f 0.71; $[\alpha]_D$ –32 (*c* = 1, CH_2Cl_2).
^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.49–1.65 (m, 2 H, 4-, 4′-H), 1.72–1.91 (m, 2 H, 3-, 3′-H), 1.87 (s, 3 H, NH*Ac*), 1.99 (s, 6 H, 2 OAc), 2.01 (s, 3 H, OAc), 3.12 (ddd, $^3J_{4,5}$ = 2.9, $^3J_{4',5}$ = 7.4, $^3J_{5,6}$ = 9.7 Hz, 1 H, 5-H), 3.31 (m, 1 H, 9-H), 3.50 (s, 3 H, OMe), 3.72 (s, 3 H, CO_2Me), 3.87 (ddd, $^3J_{5,6}$ = $^3J_{6,7}$ = $^3J_{NH,6}$ = 9.5 Hz, 1 H, 6-H), 4.03 (dd, $^2J_{gem}$ = 12.7, $^3J_{9,10'}$ = 2.8 Hz, 1 H, 10′-H), 4.11 (dd, $^2J_{gem}$ = 12.7, $^3J_{9,10}$ = 5.2 Hz, 1 H, 10-H), 4.49 (ddd, $^3J_{2,3}$ = 4.6, $^3J_{2,3'}$ = 8.4, $^3J_{NH,2}$ = 9.4 Hz, 1 H, 2-H), 4.84 (dd, $^3J_{6,7}$ = $^3J_{7,8}$ = 9.5 Hz, 1 H, 7-H), 4.96 (dd, $^3J_{7,8}$ = $^3J_{8,9}$ = 9.5 Hz, 1 H, 8-H), 5.44 (d, $^3J_{NH,6}$ = 9.5 Hz, 1 H, N*H*Ac), 7.16 (d, $^3J_{NH,2}$ = 8.0 Hz, 1 H, N*H*-MTPA, 7.36–7.42, 7.52–7.56 (2 m, 5 H, phenyl).
FAB-MS (positive mode, matrix: MeOH/3-nitrobenzyl alcohol, 1:1): *m/z* (%) = 663 (100) $[MH]^+$, 321 (31) $[(M - C_2H_2O)H]^+$.

Methyl (2*R*)-6-Acetamido-7,8,10-tri-*O*-acetyl-5,9-anhydro-2-{[(*S*)-(α-trifluoromethyl-α-methoxy-α-phenyl)methylcarbonyl]amino}-2,3,4,6-tetradeoxy-D-*glycero*-D-*gulo*-deconate [(D,*S*)-14]:
For the preparation see General Procedure. Compound D-**11** (61 mg, 111.6 μmol), *i*-Pr_2NEt (11.6 μL, 126.9 μmol) and (*R*)-(–)-MTPA-Cl (28 μL, 148.3 μmol) were used to afford (D,*S*)-**14** (56.2 mg, 76%); TLC (CH_2Cl_2/MeOH 10:1): R_f 0.69; $[\alpha]_D$ –46 (*c* = 1, CH_2Cl_2).
^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.54–2.15 (m, 4 H, 3-, 3′-, 4-, 4′-H), 1.88 (s, 3 H, NH*Ac*), 2.00 (s, 6 H, 2 OAc), 2.06 (s, 3 H, OAc), 3.32 (m, 1 H, 5-H), 3.33 (s, 3 H, OMe), 3.54 (m, 1 H, 9-H), 3.71 (s, 3 H, CO_2Me), 3.92 (ddd, $^3J_{5,6}$ = $^3J_{6,7}$ = $^3J_{NH,6}$ = 9.5 Hz, 1 H, 6-H), 4.06 (dd, $^2J_{gem}$ = 11.8, $^3J_{9,10'}$ = 2.4 Hz, 1 H, 10′-H), 4.20 (dd, $^2J_{gem}$ = 11.8, $^3J_{9,10}$ = 5.6 Hz, 1 H, 10-H), 4.52 (ddd, $^3J_{2,3}$ = 5.6, $^3J_{2,3'}$ = 9.3, $^3J_{NH,2}$ = 9.3 Hz, 1 H, 2-H), 4.98 (dd, $^3J_{6,7}$ = $^3J_{7,8}$ = 9.5 Hz, 1 H, 7-H), 5.13 (dd, $^3J_{7,8}$ = $^3J_{8,9}$ = 9.5 Hz, 1 H, 8-H), 5.49 (d, $^3J_{NH,6}$ = 9.5 Hz, 1 H, N*H*Ac), 7.24–7.54 (m, 6 H, N*H*-MTPA, phenyl).
FAB-MS (positive mode, matrix: MeOH/3-nitrobenzyl alcohol, 1:1): *m/z* (%) = 663 (100) $[MH]^+$, 321 (17) $[(M - C_2H_2O)H]^+$, 603 (29) $[(M - C_2H_4O_2)H]^+$.

This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie.

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