131. Synthesis of Pyrrolidine Analogues of *N*-Acetylneuraminic Acid as Potential Sialidase Inhibitors

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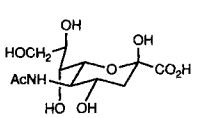
The pyrrolidine derivatives **3**, **4**, and **5** were prepared from the methyl ester **7** of Neu2en5Ac *via* the pyrrolidine-borane adduct **33**. They inhibit *Vibrio cholerae* sialidase competitively with K_i = 4.4 10^{-3} M, 5.3 10^{-5} M, and 4.0 10^{-2} M, respectively. Benzylation of **7** gave the fully *O*-benzylated **8** besides **9**, **10**, and **11**. Ozonolysis and reduction with $NaBH_4$ of **8** and **9** gave the 1,4-diols **12** and **15**, the hydroxy acetates **13** and **16**, and the furanoses **14** and **17** (*Scheme 1*), respectively. The diol **12** was selectively protected (→ **19** → **20** → **23**) and transformed into the azide **27** by a *Mitsunobu* reaction. Selective base-catalysed deprotection of the diacetate **22**, obtained from **12**, was hampered by an easy acetyl-group migration. The mesylate **28** proved unstable. The azide **27** was transformed *via* **29** into the ketone **30** (*Scheme 2*). Hydrogenation of **30** gave the dihydropyrrole **31** and, hence, the pyrrole **32.** The adduct **33** was obtained from **30** by a *Staudinger* reaction (→ **31**) and reduction with $LiBH_4/HBF_4$. It was transformed into the pyrrolidine **34**. The structure of **34** was established by X-ray analysis. Reductamination of the pyrrolidine-borane adduct with glyoxylic acid gave **40** and, hence, **3**. *N*-Alkylation afforded **44** and, hence, the phosphonate **4**. The acid **5** was obtained from **33** by acylation (→ **47**) and deprotection (*Scheme 4*).

Introduction. – The importance of conjugates of sialic acids, particularly of *N*-acetylneuraminic acid (Neu5Ac, **1**) is well documented [1]. Similarly, the importance of *N*-acetylneuraminidases is well known (see [2][5] and ref. cit. therein) and several *N*-acetylneuraminidase inhibitors have been isolated [3] and prepared [4]. Both piperidine [2] and pyrrolidine [6–8] analogues of hexoses are among the best inhibitors of glycosidases, and the piperidine analogue **2** of 2-deoxy-Neu5Ac, possessing an equatorial



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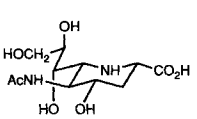

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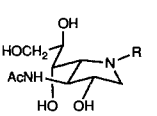

3 R = CH_2CO_2H **5** R = $COCO_2H$
4 R = $CH_2PO_3H_2$ **6** R = H

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COOH group[3]), is indeed a good inhibitor of *N*-acetylneuraminidases from *Vibrio cholerae* [9][10] and *Arthrobacter sialophilus* [11]. Among the simplest pyrrolidine analogues of Neu5Ac, possessing the trihydroxypropyl side chain and an acid function, are compounds **3–5** which are formally derived from the pyrrolidine **6** by *N*-alkylation or by *N*-acylation .

Plan. – We intended to prepare the protected pyrrolidine **34** and, hence, **3–5** from Neu5Ac **1**. This requires cleavage of the bond between C(2) and C(3) and replacing the O–C(3) and O–C(6) bond by N–C bonds, in the latter case with retention of configuration. We planned to cleave the C(2)–C(3) bond by ozonolysis of a protected derivative of methyl *N*-acetyl-2-deoxyneur-2-enaminate (**7**, see *Scheme 1*), such as benzyl ether **8**, and to introduce the N–C bonds either by reductive amination or by substitution.

Results and Discussion. – *Synthesis of the Pyrrolidine* **34**. Neu5Ac (**1**), obtained from edible birds nest [12], was converted into the methyl ester **7** of Neu2en5Ac according to known procedures [13–15]. Benzylation of **7** (*Scheme 1*), in the presence of BaO, as mentioned by *Ito* and *Ogawa* [16], or in DMF and in the presence of BaO and $Ba(OH)_2$, following a procedure of *Korytnyk* and coworkers [17] gave the desired product **8** in unsatisfactory yields. The use of NaH as base afforded a mixture of **8** and the *O*- and *N*-benzylated ester **9**.The highest yields of **8** (64%) were obtained by the use of 5 equiv. of benzyl bromide and by repeated benzylation of chromatographically isolated, partially benzylated material[4]). Small amounts of the benzyl ester **10** were also formed, and **10** was best transformed into **8** by base-catalyzed transesterification (NaOMe/MeOH). The ratio in which **8** and **9** were obtained depended upon the excess of benzyl bromide and the reagents, but **9** was formed even in the presence of sub-stoichiometric amounts of benzyl bromide. The ^{1}H-NMR spectra of **9** are complex and show the presence of two rotamers in a ratio of *ca.* 3:1 ($CHCl_3$), as proven by recording spectra of solutions in (D_6)DMSO (ratio 1.5:1) with a temperature gradient. The temperature of coalescence was 100°.

Ozonolysis of **8** and treatment of the crude ozonides with $NaBH_4$ in MeOH gave a mixture from which the desired, crystalline diol **12** (65%), the hydroxy-acetate **13** (6.4%), and the furanose **14** (2%) were obtained. Prolonged treatment of the ozonides with $NaBH_4$ converted **13** and **14** into **12**, raising its yield to 78%. Similarly, ozonolysis of **9** followed by reduction with $NaBH_4$ yielded the diol **15** (54%), the furanose **17** (9.6%), and the hydroxy-acetate **18** (2.8%; presumably formed from the hypothetical **16** by an N → O acetyl migration under the acidic workup conditions). Treatment of the ozonides with Me_2S gave the furanose **17** in 81% yield.

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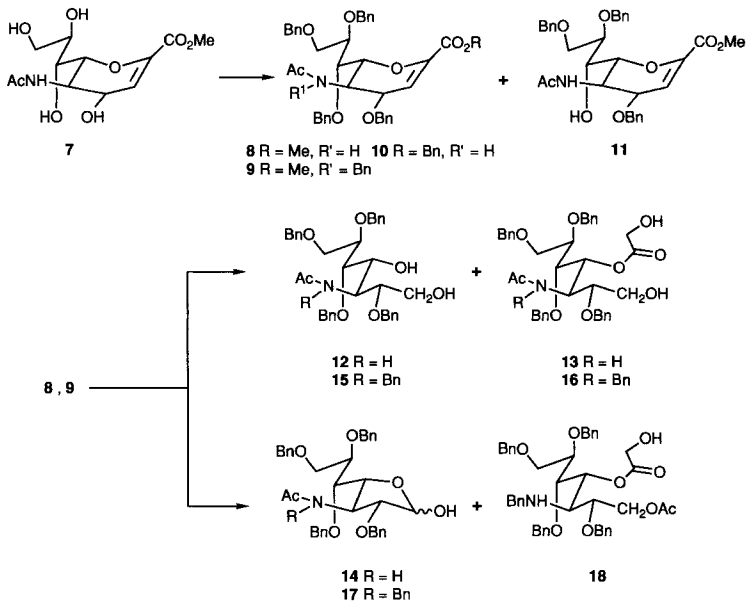
[3]) The fact that both Neu2en5Ac and **2** are quite good inhibitors of *N*-acetylneuraminidases, while the epimer of **2**, possessing an axial COOH group, is not, suggests a transition state with a flattened ring and a COOH group which is lying in the ring plane. The advantage of a (flattened) ring in the pyrrolidines **3–5** (as compared to **2**) may be offset by the conformational flexibility of the *N*-substituent in **3** and **4**, but then, **3** and **4** appear to be more easily available then the corresponding piperidino analogues, such as **2**.

[4]) From this material, the 4,8,9-tri-*O*-benzyl ester **11** was obtained crystalline. The assigment of its structure is based on a comparison of its ^{1}H-NMR spectrum with that of **8**, where the resonances of H–C(6) and H–C(7) (J(6,7) = 1.5, J(7,8) = 4, J(7,OH) = 9 Hz) are strongly shifted ($\Delta\delta$(H–C(6)) > 0.35 and $\Delta\delta$(H–C(7)) > 0.7 ppm).

Scheme 1



The structure of **12** and **15** are evident from their analytical data. The conformation of **12** appears to be largely as depicted in *Scheme 1*, as evidenced by the values of $J(1,2) = 10$, $J(2,3) = 9.5$, and $J(3,4) = 10$ Hz. The *N*-benzylated **15** is present as a mixture of rotamers (*ca.* 2:1, r.t., (D_6)DMSO), and its ^{1}H-NMR spectra are poorly resolved. The structure of **13** is deduced from the strong C=O band at 1745 cm^{-1} in its IR spectrum, the chemical shift of H–C(4) (5.53 ppm, $J = 9.6$ and 3.0 Hz), and from its conversion into **12**. The IR spectrum of **18** shows no amide band, but two C=O bands at 1760 and 1745 cm^{-1}. In the ^{1}H-NMR spectrum, the HN signal is detected at 3.41 ppm (*d*, $J = 6$ Hz), the H–C(1) signal between 4.78 and 4.5, and the Ac *s* at 1.66 ppm. The hemiacetal **14** is present ($CDCl_3$) as a 3:1 mixture of the α- and β-D-anomers, as determined by the integration of the AcN signals at 1.76 and 1.87 ppm. The configuration of the anomeric center was deduced from the chemical shift of the C(1) signals (100.6 and 95.0 ppm for the α- and β-D-anomer, resp.). The anomers of the *N*-benzylated furanose **17** are mixtures of rotamers. In solution in (D_6)DMSO at 140°, the α-D-anomer largely predominates, as evidenced by the H–C(1) signal at 5.25 ppm ($J(1,2) = 2.1$ Hz).

Several routes were explored for the transformation of **12** into the pyrrolidine **34**. Silylation and subsequent acetylation of **12**, best in pyridine solution and without isolation of **19**, yielded 92% of **20**[5]) (*Scheme 2*), while the imidazole-catalyzed silylation of **12** in DMF solution [18] gave **19** in 81% yield. Acetylation of **12** afforded the diacetate **22** in high yield. Acid-catalyzed desilylation [19] of **20** yielded the desired monoacetate **23** (94%), whereas base-catalyzed reactions gave rise to acetyl migration. Desilylation of **20**

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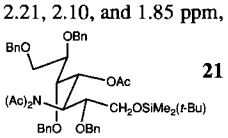
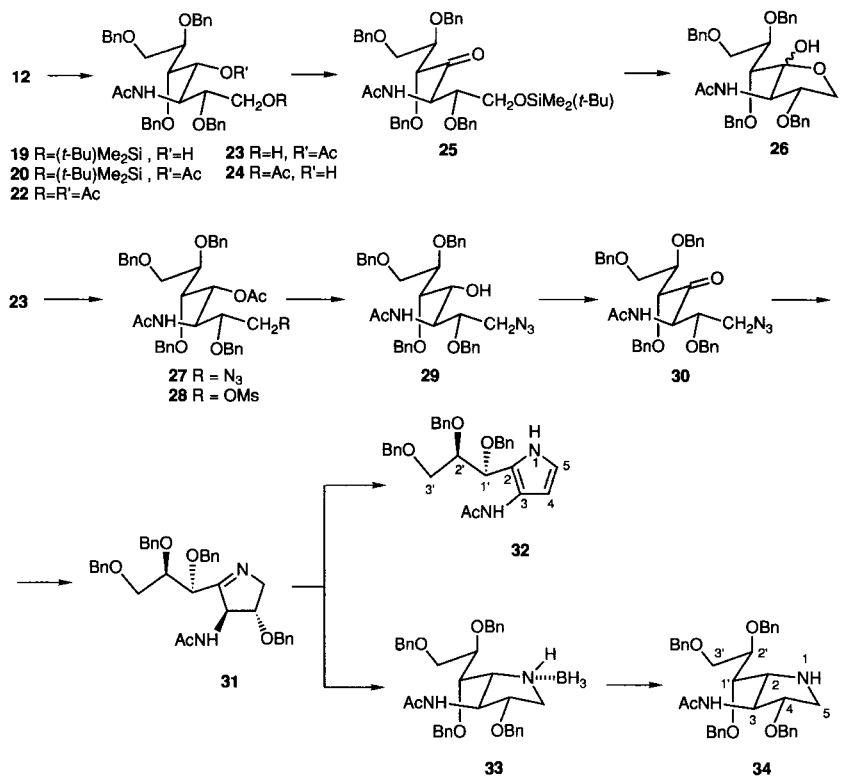
[5]) The diacetylamino derivative **21** was formed as a by-product (5%). It showed a H–C(4) signal at 6.13 ppm (*dd*, $J = 8.5$ and 1.7 Hz), Ac signals at 2.21, 2.10, and 1.85 ppm, and C=O bands at 1735 and 1690 cm^{-1}.



with Bu_4NF in THF afforded both **23** (22%) and **24** (67%). Mild transesterification of **22** (NaOMe/MeOH, 0°) gave mixtures containing the starting diol **12** and the monoacetates **23** and **24** from which the main product **23** was isolated in 53% yield[6]. The ^{1}H-NMR spectra of **20** and **22–24** are poorly resolved, but they show the characteristic signal of H–C(4) either at 3.8–3.9 ppm (**19** and **24**) or between 5.40 and 5.48 ppm (**20**: 5.40 ppm (*dd*, J = 9.6 and 2.0 Hz); **22**: 5.4 ppm (*dd*, J = 9.6 and 2.4 Hz); **23**: 5.48 ppm (*dd*, J = 9.7 and 3.0 Hz)).

Scheme 2



Attempts to introduce an azido group at C(1) *via* the mesylate **28** met with little success [20]. The mesylate was formed in high yields, but proved unstable, even in solution. Its reaction with tetrabutylammonium azide gave an intermediate which decomposed during workup. Isolation of the monoacetates **23** (57%) and **24** (7%), and of the azide **27** (3.4%) indicate a neighbouring-group participation of the AcO group, leading to a 1,3-dioxepinylium cation, which is hydrolyzed during workup. The azide **27**, was,

[6]) Treatment of **21** with 1M H_2SO_4 in MeOH gave **22** (78%).

however, obtained in good yield (86%) under conditions of the *Mitsunobu* reaction [21][22] and deacetylated to the hydroxy azide **29**. This hydroxy azide could not be obtained directly from **12**. According to *Swern* and coworkers [23][24], **29** yielded the 4-ketose **30** (96%), showing a C=O band of medium intensity at 1730 cm^{-1} and a relatively strong band at 3430 cm^{-1}. Similarly, oxidation of **19** gave the 4-ketose **25** which formed neither an oxime nor an *N*-benzylimine. It was desilylated to the furanose **26**, presumably the β-D-anomer, which was not examined further.

Transfer hydrogenation of **30** (ammonium formate, Pd/C) gave an unstable compound, later identified as the dihydropyrrole **31** which was transformed into the pyrrole **32**, even under the reducing conditions of its formation. The pyrrole **32** slowly decomposed to red-brown products.

The structure of **32** was deduced from the spectroscopic data, showing the presence of the AcNH group (IR: 3470, 1670 cm^{-1}; ^{1}H-NMR: *s* (3 H) at 1.59 ppm) and of three benzyloxy groups (^{1}H-NMR: 15 arom H at 7.61–7.20 ppm; 6 H at 4.78–4.28 ppm). Two new signals for arom. H's at 6.62 (*t*, *J* = 2.9 Hz) and 6.58 ppm (*t*, *J* = 2.9 Hz), coupling with H–N(1) (8.14 ppm) were assigned to H–C(4) and H–C(5). In the ^{13}C-NMR spectrum, C(2) and C(5) possess similar chemical shifts (116.5 and 116.3 ppm [25]), while the signal of C(4) appeared at 104.3 ppm.

Attempts to reduce **30** under conditions which would also effect the reduction of **31** to **34**[7]) only gave **32**. The desired transformation **30**→**33** was realized in an overall yield of 70% by converting the azide into the imine **31** (Ph_3P,THF [35][36]), protonating **31** with HBF_4, and reducing the iminium salt with $LiBH_4$. The reduction was completely diastereoselective, and the configuration of the product, isolated as the borane adduct **33** of **34**, was deduced from the nuclear *Overhauser* effects between H–C(2), H–C(4), and AcN*H*, and established by X-ray analysis of the amine **34**, into which **33** was transformed by heating with EtOH. The crystal structure of **34** is illustrated in the *Figure*; crystal data and acquisition parameters are given in *Table 1*. Selected bond and torsion angles are listed in *Tables 2* and *3*, respectively.

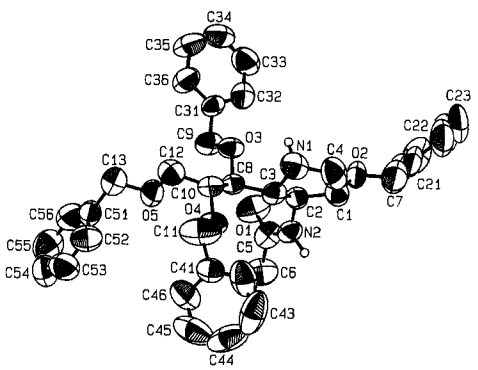


Figure. *View of* N-{*(2R,3S,4S)-4-(benzyloxy)-2-[(1'S,2'R)-1',2',3'-tris(benzyloxy)propyl]pyrrolidin-3-yl}-acetamid* (**34**)

[7]) Conditions tried were hydrogenation in the presence of Pd/C [26][27], *Adams* catalyst [28], PtO_2 [29], *Raney*-Ni [30] and reduction with $NaBH_4/ZnCl_2$ [31], $NaBH_4$/AcOH [32], $NaBH_4/CF_3CO_2H$, $NaBH_3CN$/AcOH [33], and $NaBH_3CN/ZnCl_2$ [34]. For a recently published one-step synthesis of a pyrrolidine from an azido alcohol, see [20].

Table. *Crystal Data and Experimental Conditions for the X-Ray Analysis of* **34**

Molecular formula	$C_{37}H_{42}N_2O_5$
Formula weight	594.75
Crystal system	orthorombic, non-centrosymmetric
Space group	$P2_12_12_1$
a [Å]	16.186(2)
b [Å]	16.513(2)
c [Å]	25.700(3)
V [Å^3]	6868(2)
Z	8 (2 molecules/asymmetric unit)
Calc. density [g/cm^3]	1.150
Temp. of data collection [°C]	22
Radiation	MoK_α
λ [Å] (graphite monochrom.)	0.70926
Diffractometer	*Nicolet-R3*
2 θ Range [°]	20-28
No. of reflections measured	13423
Observed reflections [$I > 2\sigma(I)$]	5022
Final R factor	0.0497
R_w	0.046
μ(MoK_α) [cm^{-1}]	0.710

Table 2. *Selected Bond Angles* [°] *with e.s.d.'s in Parentheses for* **34**

C(2)–C(1)–C(4)	104.9(5)	O(2)–C(7)–C(21)	112.3(6)
C(2)–C(1)–O(2)	108.5(4)	C(3)–C(8)–O(3)	107.3(3)
C(4)–C(1)–O(2)	114.3(5)	C(3)–C(8)–C(10)	111.2(4)
C(1)–C(2)–C(3)	103.3(4)	O(3)–C(8)–C(10)	108.6(3)
C(1)–C(2)–N(2)	114.4(4)	C(8)–O(3)–C(9)	113.9(3)
C(3)–C(2)–N(2)	113.1(4)	O(3)–C(9)–C(31)	107.6(4)
C(2)–C(3)–N(1)	104.3(4)	C(8)–C(10)–O(4)	103.2(4)
C(2)–C(3)–C(8)	113.5(4)	C(8)–C(10)–C(12)	113.8(4)
N(1)–C(3)–C(8)	113.7(4)	O(4)–C(10)–C(12)	113.0(4)
C(3)–N(1)–C(4)	104.5(4)	C(10)–O(4)–C(11)	113.8(4)
C(1)–C(4)–N(1)	108.3(5)	O(4)–C(11)–C(41)	107.3(5)
C(2)–N(2)–C(5)	124.6(4)	C(10)–C(12)–O(5)	108.7(4)
N(2)–C(5)–C(6)	116.7(5)	C(12)–O(5)–C(13)	112.9(4)
N(2)–C(5)–O(1)	121.2(5)	O(5)–C(13)–C(51)	109.7(5)
C(6)–C(5)–O(1)	122.1(5)	C(7)–C(21)–C(22)	121.0(8)
C(1)–O(2)–C(7)	115.8(5)	C(7)–C(21)–C(26)	120.5(8)

Table 3. *Selected Torsion Angles* [°] *with e.s.d.'s in Parentheses for* **34**

C(2)–C(1)–C(4)–N(1)	–2.1(6)	O(2)–C(7)–C(21)–C(22)	132.0(8)
C(4)–C(1)–C(2)–C(3)	–20.3(5)	O(2)–C(7)–C(21)–C(26)	–46.1(10)
C(4)–C(1)–C(2)–N(2)	–143.6(4)	C(3)–C(8)–O(3)–C(9)	129.5(3)
C(2)–C(1)–O(2)–C(7)	–162.3(4)	C(3)–C(8)–C(10)–O(4)	–65.9(4)
O(2)–C(1)–C(2)–C(3)	–142.8(3)	C(3)–C(8)–C(10)–C(12)	171.2(4)
O(2)–C(1)–C(2)–N(2)	93.9(4)	O(3)–C(8)–C(10)–O(4)	176.2(3)
C(4)–C(1)–O(2)–C(7)	81.1(5)	O(3)–C(8)–C(10)–C(12)	53.3(4)

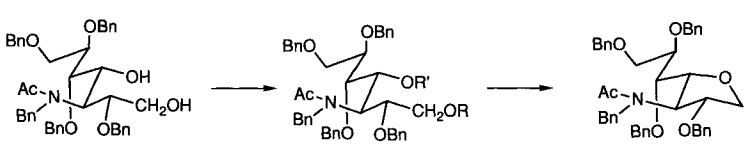
Table 3 (cont.)

O(2)–C(1)–C(4)–N(1)	16.6(4)	C(10)–C(8)–O(3)–C(9)	–110.2(3)
C(1)–C(2)–C(3)–N(1)	36.2(4)	C(8)–O(3)–C(9)–C(31)	–173.1(3)
C(1)–C(2)–C(3)–C(8)	160.5(4)	O(3)–C(9)–C(31)–C(32)	84.6(5)
C(1)–C(2)–N(2)–C(5)	–140.6(5)	O(3)–C(9)–C(31)–C(36)	–97.4(5)
C(3)–C(2)–N(2)–C(5)	101.4(5)	C(8)–C(10)–O(4)–C(11)	168.6(4)
N(2)–C(2)–C(3)–N(1)	160.4(3)	C(8)–C(10)–C(12)–O(5)	61.8(4)
N(2)–C(2)–C(3)–C(8)	–75.3(4)	O(4)–C(10)–C(12)–O(5)	–55.6(4)
C(2)–C(3)–N(1)–C(4)	–37.7(5)	C(12)–C(10)–O(4)–C(11)	–68.0(5)
C(2)–C(3)–C(8)–O(3)	–71.4(4)	C(10)–O(4)–C(11)–C(41)	–170.8(4)
C(2)–C(3)–C(8)–C(10)	170.0(3)	O(4)–C(11)–C(41)–C(42)	89.7(7)
N(1)–C(3)–C(8)–O(3)	47.6(4)	O(4)–C(11)–C(41)–C(46)	–92.9(7)
N(1)–C(3)–C(8)–C(10)	–71.0(4)	C(10)–C(12)–O(5)–C(13)	–179.4(4)
C(8)–C(3)–N(1)–C(4)	–161.8(4)	C(12)–O(5)–C(13)–C(51)	–145.1(4)
C(3)–N(1)–C(4)–C(1)	25.1(5)	O(5)–C(13)–C(51)–C(52)	63.5(7)
C(2)–N(2)–C(5)–C(6)	–174.0(4)	O(5)–C(13)–C(51)–C(56)	–117.8(6)
C(2)–N(2)–C(5)–O(1)	5.4(7)	C(7)–C(21)–C(22)–C(23)	–179.6(8)
C(1)–O(2)–C(7)–C(21)	171.2(5)	C(7) –C(21)–C(26)–C(25)	–179.3(8)

The IR spectrum of **33** shows the amide band at 1680 cm^{-1} and bands of medium intensity at 2370–2280 (B–H stretching [37]) and 1170 cm^{-1} (B–H deformation [37]), which are absent in the IR spectrum of **34** (amide band at 1670 cm^{-1}). The ^{1}H-NMR spectra ($CDCl_3$) of **33** and **34** are very similar to each other, but the spectrum of **33** shows an additional br. *s* at 5.64 ppm, which does not exchange within 48 h with D_2O, and which couples with the H–C(2) and CH_2(5) signals at 3.23 and 3.04 ppm, resp. Irradiation at the signal at –13.8 ppm (reference $BF_3 \cdot Et_2O$) [38] in the ^{11}B-NMR spectrum ((D_6)DMSO) shows a correlation in the ^{1}H-NMR spectrum ((D_6)DMSO) with the signal at 1.57 ppm. The CI-MS does not, however, give any indication as to the presence of a BH_3 group in **33**. Amine-borane complexes are well documented [39][40].

Attempts to introduce an N-substituent at C(1) or C(4) of the *N*-benzylated diol **15** were abandoned, when it appeared that HO–C(4) is quite hindered, and that Ac migrations from *O*–C(4) to *O*–C(1) occurred even more easily than in the analogous secondary amides. Thus, silylation of **15** (*Scheme 3*) gave **35** in good yields. Acetylation of **35** to **36** was slow, even at 100° and desilylation of **36** with Bu_4NF gave only **37** which was also obtained from **15** by acetylation at room temperature. The diacetate **38** was only formed under quite harsh conditions (Ac_2O, pyridine, 100°, 22 h).Tosylation (TsCl/pyridine) of **35** failed. In the presence of NaH, reductive desilylation [41], followed by tosylation of HO–C(1), gave the tetrahydrofuran **39** which was also formed, as expected, by mesylating **15**.

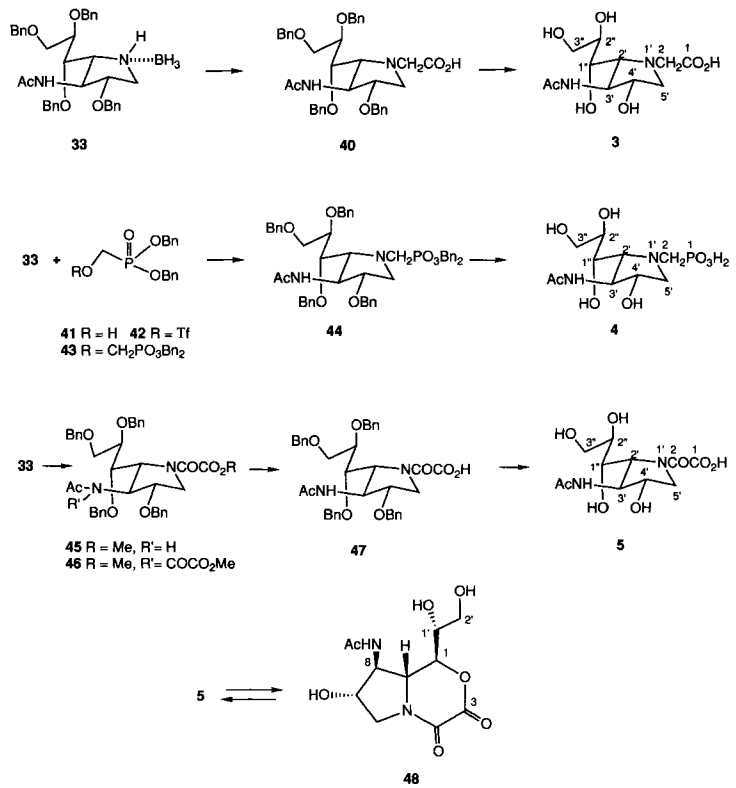
Scheme 3



15 **35** R = (*t*-Bu)Me_2Si, R' = H **37** R = Ac, R' = H **39**
36 R = (*t*-Bu)Me_2Si, R' = Ac **38** R = R'= Ac

Synthesis of the N*-Substituted Pyrrolidines* **3–5** *and their Evaluation as Inhibitors.* The pyrrolidine-acetic acid **40** was obtained in 77.5% yield by reductive amination of **33** with excess glyoxylic acid in THF (*Scheme 4*). Presumably, borane, liberated in the presence of the glyoxylic-acid hydrate, promotes imine formation and acts as *in situ* generated reducing agent. That indeed **40** is formed (and not an addition product) is evident from the ^{13}C- (new *t* at 59.0 ppm) and ^{1}H-NMR spectrum (signal of CH_2 group at 3.56–3.71 ppm). Hydrogenation of **40** in presence of $Pd(OH)_2/C$ gave the desired crystalline pyrrolidine-acetic acid **3** in high yields.

Scheme 4



As **34** had not reacted with ethyl bromoacetate under a variety of conditions, we attempted to obtain the phosphonate **44** directly from **33**. *N*-Alkylation of **33** with the triflate **42** (Tf = trifluoromethanesulfonyl) in Et_2O at room temperature gave **44** in 55% yield. The triflate **42** was obtained from the dibenzyl ester **41**, which was prepared from dibenzyl phosphite and formaldehyde, similarly as described for the diethyl ester [42]. The reaction of **41** with TfCl had to be performed between –20 and –15°. The resulting triflate **42** (43%) and ether **43** (25%) were separated by chromatography[8]). Only **43** was produced

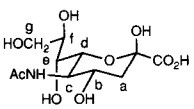
[8]) Both structures were proven by ^{31}P-NMR, as the shifts of the P-atoms differed significantly (13.8 ppm for **42** and 18.5 ppm for **43**).

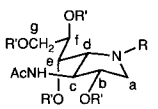
at room temperature. Hydrogenation of **44** gave the desired, analytically pure phosphonic acid **4** (^{1}H-NMR: new resonances at 3.79–3.64 ppm (*AB*, J = 11.8 Hz, $H_2C(2)$); ^{13}C-NMR: 2 new signals at 54.3 and 51.6 ppm (J(P,C(2)) = 135.3 Hz, C(2)); ^{31}P-NMR: 1 signal (8.5 ppm downfield from 85% phosphoric acid)).

The amide **45** was best prepared by treating a CH_2Cl_2 soln. of the hydrochloride of **33** with methoxalyl chloride and then with Et_3N. Some diacylamido derivative **46** was also formed. It was hydrolyzed during aqueous workup, and **45** was obtained in 78% yield. The acid **47** was obtained by basic hydrolysis of **45** and acidification (75%); IR: 1650 cm^{-1} (C=O); ^{1}H-NMR: new signal at 3.48 ppm (COOMe) and (as compared to **33**) disappearance of the signal at 5.64 ppm (H–N(1)). Hydrogenation of **47** gave the desired **5** in good yield. Recrystallization of **5** in AcOH afforded the lactone **48** which proved unstable in aqueous solution, quickly reverting to the hydroxy acid **5**. The structure of **48** was deduced from its ^{1}H-NMR and IR spectra (^{1}H-NMR: H-C(1) at 4.71 ppm (*dd*, J = 2.7, 10.7 Hz)) as compared to H–C(1") of **5** at 3.68 ppm (*dd*, J = 1.4, 9.2 Hz); IR: 1770, 1705, and 1650 cm^{-1})

The main ^{1}H-NMR data of **3–5** and of *N*-acetylneuraminic acid [43] are summarized in *Table 4*.

Table 4. *Selected ^{1}H-NMR Chemical Shifts* [ppm] *and Coupling Constants* [Hz] *for the Compounds* **3–5, 34**, *and for Neu5Ac* **1**





1 **3** R = CH_2CO_2H, R' = H **4** R = $CH_2PO_3H_2$, R' = H
5 R = $COCO_2H$, R' = H **34** R = H, R' = Bn

H-Atom or J	**1**[a])	**3**[a])	**4**[a])	**4**[b])	**5**[a])	**34**[c])
H_a	2.25	3.75	3.64	3.24	3.90	3.05
$H_{a'}$	1.86	3.63	3.50	3.08	3.36	2.93
H_b	4.06	4.50	3.83	3.75–3.95	4.11–4.28	3.86
H_c	3.95	4.43	4.07	3.73–3.95	4.48	4.23
H_d	4.02	3.97	4.02	3.73–3.95	4.11–4.28	3.05
H_e	3.55	4.08	4.37	4.30	3.68	3.86
H_f	3.80	3.83	4.45	4.30	3.54	3.69
H_g	3.88	3.80	3.77	3.73–3.95	3.82	3.80
$H_{g'}$	3.65	3.69	3.77	3.73–3.95	3.59	3.80
J(a,a')	13.0	12.3	[d])	13.1	11.3	12.3
J(a,b)	4.9	4.8	3.4	[d])	9.3	[d])
J(a',b)	11.6	4.1	3.4	[d])	7.0	5.4
J(b,c)	10.2	*ca.* 4.8	3.4	[d])	6.8	2.3
J(c,d)	10.1	4.9	3.4	[d])	6.8	7.1
J(d,e)	0.9	5.1	*ca.* 6.0	[d])	1.4	4.0
J(e,f)	9.3	*ca.* 7.0	5.6	[d])	9.2	5.2
J(f,g)	6.5	5.3	9.3	[d])	6.3	2.7
J(f,g')	2.8	*ca.* 3.5	3.7	[d])	2.0	5.2
J(g,g')	11.8	12.5	11.6	[d])	11.5	[d])

[a]) In D_2O. [b]) In $CDCl_3$. [c]) In D_2O at pH 8. [d]) Not defined.

The oxalamide **5** and Neu5Ac (**1**) possess similar coupling constants for the trihydroxypropyl side chain, while the amino acids **3** and **4** show quite different values. According to the chemical shift of H_a and $H_{a'}$, **3** and **4** exist largely as zwitterions of unknown (1,2-*trans* ?), but uniform configuration at the tetra-ligated N(1).The side-chain conformation of **3** and **4** most certainly depends upon H-bonds with N(1) and/or H–N(1) as discussed in [44] and, for 1,2-*cis*-configurated zwitterions, also upon H-bonds between the AcNH group and H–N(1) (*cf.* [45] and ref. cit. therein). That **3** and **4** exist (largely) as zwitterions is supported by the shift to higher fields observed for the H_a and $H_{a'}$ resonances in the poorly resolved spectrum at pH 8 ($\Delta\delta = 0.4$ and 0.42, or 0.56 and 0.25 ppm).

Compounds **3–5** are competitive inhibitors of *Vibrio cholerae* sialidase with inhibition constants of $4.4 \cdot 10^{-3}$, $5.3 \cdot 10^{-5}$, and $4.0 \cdot 10^{-2}$ M, respectively. While both the oxalamide **5** and the acetate **3** are poor inhibitors, the phosphonate **4** is about equipotent with Neu2en5Ac and with the piperidine **2**, in spite of a presumably unfavourable preferred conformation of the trihydroxypropyl side chain. This effect of the phosphono group is remarkable and, if generally valid, may be an important clue to the design of stronger inhibitors.

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Experimental Part

General. Solvents were distilled before use. TLC: *Merck* precoated silica gel *60 F-254* plates; detection by spraying with a 5% vanillin/conc. H_2SO_4 soln followed by heating to *ca.* 200°. Flash chromatography (FC): silica gel *Merck 60* (40–63 μm). Workup in the usual way means quenching of the reaction with H_2O, partitioning of the mixture between aq. phase (0°) and the indicated org. phase (3 ×), washing of the org. phase with H_2O or brine, drying ($MgSO_4$), filtration, and evaporation at 40° (water pump), followed by drying of the residue under high vacuum for 30 min. M. p.: uncorrected . Optical rotations: 1-dm cell at 25° and at 365, 436, 546, 578, and 589 nm; $[\alpha]_{589}$ was determined with the help of a regression curve. IR spectra: $CHCl_3$ solns. NMR spectra: at 400, 300, and 200 MHz for ^1H, at 50 MHz for ^{13}C, and at 81 MHz for ^{31}P; $CDCl_3$ as solvent, unless stated otherwise. MS: by chemical ionisation (CI).

Determination of the Inhibition Constants K_i. The sialidase (*Vibrio cholerae*) was purchased from *Calbiochem.* Prior to use, a 100-mU soln. of the enzyme was prepared in 10 ml of 0.1M acetate buffer of pH 5.5 containing 0.5 mM of $CaCl_2$ and 0.1 mg/ml of bovine serum albumine (*Merck*) [46]. The substrate (MU-Neu5Ac) was prepared and purified according to known procedures [47]. The incubations were carried out at 37° in a total volume of 100 ml containing 0.2 mU of enzyme (20 μl of the above soln.), 0.5 mM of $CaCl_2$, $2.0 \cdot 10^{-4}$ M of MU-Neu5Ac, and a final acetate buffer concentration of 0.1M of pH 5.5. After 15 min, the reaction was stopped by the addition of 900 μl of glycine buffer of pH 10 (0.042M Na_2CO_3, 0.06M NaCl, and 0.133M glycine). The amounts of liberated methylumbelliferone was determined fluorimetrically at 365 nm for excitation and 450 nm for emission on a *Shimadzu* spectrofluorophotometer *RF-510*. Blank values (from experiments without enzyme) were substracted from the enzyme values before calculation of the nmoles of Neu5Ac released.

For the calculation of the K_i values of the inhibitors, various concentrations of MU-Neu5Ac (ranging from 0.5 to $4.0 \cdot 10^{-4}$ M) were incubated in the presence of various inhibitor concentrations. The reciprocal reaction rates were plotted against the reciprocal MU-Neu5Ac (substrate) concentrations (*Linweaever-Burk* plot). In a second plot, the slopes of the first plot were reported against the inhibitor concentration. Extrapolation of the linear regression curve obtained gives the K_i value (intercept on the horizontal axis).

Methyl 5-Acetamido-4,7,8,9-tetra-O-*benzyl-3,5-dideoxy*-D-glycero-D-galacto-*non-2-enonate* (**8**), *Methyl 5-(*N-*acetyl*-N-*benzylamino)-4,7,8,9-tetra*-O-*benzyl-3,5-dideoxy*-D-glycero-D-galacto-*non-2-enonate* (**9**), *Benzyl 5-Acetamido-4,7,8,9-tetra*-O-*benzyl-7-hydroxy-3,5-dideoxy*-D-glycero-D-galacto-*non-2-enoate* (**10**), *and Methyl 5-Acetamido-4,8,9-tri*-O-*benzyl-3,5-dideoxy*-D-glycero-D-galacto-*non-2-enonate* (**11**). NaH (50%, 185 mmol, 5 equiv.) was added to a stirred soln. of **7** [13–15] (11.30 g, 37 mmol) in dry DMF (200 ml), and the slurry was stirred at r.t. for 1 h. The mixture was cooled in an ice bath to 15°, and benzyl bromide (37.8 g, 26 ml, 6 equiv.) was added gradually, while keeping the temp. at 25–30°. When the intensive development of H_2 ceased, the clear soln. was kept for 1 h at r.t. and then poured into ice/H_2O (600 ml), 1M H_2SO_4 (10 ml), and $CHCl_3$ (400 ml). The aq. soln. was processed as usual ($CHCl_3$). FC (AcOEt/hexane 1:3, then 1:1, and finally AcOEt) of the resulting oil gave **9** (4.46 g, 16.2%), **10** (1.40 g, 5.1%), **8** (10.5 g, 42.6%), **11** (0.32 g, 1.2%), and a mixture of partially benzylated products (8.6 g), which, on repeated benzylation in DMF (100 ml) with NaH (50%, 1 g) and benzyl bromide (4 ml), afforded a further amount of **8** (5.3 g, 21.5%).

Data of **8**: R_f(AcOEt/hexane 1:1) 0.45. $[\alpha]_D$ = –1 (*c* = 4). IR: 3440*w*, 3095*w*, 3070*w*, 3040*w*, 3005*w*, 2980*w*, 2880*w*, 1735*s*, 1680*s*, 1655*s*, 1500*s*, 1455*m*, 1440*m*, 1370*m*, 1305*s*, 1270*s*, 1245–1200*s*, 1130*s*, 1100*s*, 1080*s*, 1030*s*, 910*m*, 695*w*, 660*w*. ^{1}H-NMR (400 MHz): 7.37–7.20 (*m*, 20 arom. H); 6.14 (*d* , *J* = 3.6, H–C(3)); 5.23 (*d*, *J* = 7.5, AcN*H*); 4.70–4.45 (*m*, 4 PhCH_2, H–C(6)); 4.24 (*ddd* app. as *q*, *J* ≈ 7.0, H–C(5)); 4.21–4.15 (*m*, H–C(4), H–C(7)); 4.00 (*ddd* app. as *q*, *J* ≈ 5, H–C(8)); 3.93 (*dd*, *J* = 5.5, 10.0, H_a–C(9)); 3.78 (*s*, COOMe); 3.72 (*dd*, *J* = 4.5, 10.0, H_b–C(9)); 1.74 (*s*, Ac). ^{13}C-NMR: 169.5 (*s*); 162.5 (*s*); 143.5 (*s*); 138.6 (*s*); 138.5(*s*); 138.1 (*s*); 137.8 (*s*); 128.5–127.3 (*d*); 109.0 (*d*); 78.1 (*d*); 77.6 (*d*); 74.8 (*d*); 74.3 (*t*); 73.4 (*t*); 72.1(*t*); 70.9 (*d*); 70.8 (*t*); 68.8 (*t*); 52.3 (*q*); 48.2 (*d*); 23.2 (*q*). Anal. calc. for $C_{40}H_{43}NO_8$ (665.75): C 72.16, H 6.46, N 2.10; found: C 71.99, H 6.92, N 2.21.

Data of **9**: R_f(AcOEt/hexane 1:2) 0.60. M.p. 99–100° (from Et_2O/hexane). $[\alpha]_D$ = +37.4 (*c* = 2.6). IR: 3090*w*, 3070*w*, 3040*w*, 3000*w*, 2960*w*, 2870*w*, 1735*s*, 1645*s*, 1495*w*, 1455*m*, 1440*m*, 1355*m*, 1310*w*, 1290*m*, 1270*s*, 1128*s*, 1095*s*, 1030*m*, 985*w*, 695*w*. ^{1}H-NMR (400 MHz): 7.38–7.14 (*m*, 25 arom. H); 6.07 (*d*, *J* = 2.8, H–C(3), minor); 6.04 (*d*, *J* = 2.3, H–C(3), major); 5.18 (*d*, *J* = 15.6, 1 H); 4.80–4.34 (*m*, 10 H); 4.12–3.62 (*m*, 6 H); 3.78 (*s*, MeO); 2.11 (*s*, Ac, major); 2.00 (*s*, Ac, minor): ^{1}H-NMR (200 MHz, (D_6)DMSO), major isomer: 6.16 (*d*, *J* = 1.4, H–C(3)); 3.70 (*s*, MeO); 1.97 (*s*, Ac); minor isomer: 6.10 (*d*, *J* = 2.7, H–C(3)); 3.66 (*s*, MeO); 1.94 (*s*, Ac); coalesc. temp. 100°. ^{13}C-NMR: major isomer: 173.5 (*s*); 162.2 (*s*); 144.6 (*s*); 138.9 (*s*); 138.5 (*s*); 138.0 (*s*); 137.9 (*s*); 137.4 (*s*); 128.7–126.2 (*d*); 108.5 (*d*); 77.5 (*d*); 76.9 (*d*); 75.5 (*d*); 73.4 (*t*); 73.0 (*t*); 72.8 (*d* +*t*); 70.5 (*t*); 69.0 (*t*); 56.5 (*t*); 52.3 (*d*); 45.1 (*t*); 22.4 (*q*); minor isomer: 172.3 (*s*); 162.4 (*s*); 144.8 (*s*); 138.6 (*s*); 138.4 (*s*); 138.3 (*s*); 137.3 (*s*); 109.7 (*d*); 78.2 (*d*); 76.8 (*d*); 75.8 (*d*); 73.3 (*t*); 72.9 (*d* + *t*); 71.6 (*t*); 69.4 (*t*); 52.1 (*d*); 23.0 (*q*). CI-MS: 756.5 ([*M* + 1]). Anal. calc. for $C_{47}H_{49}NO_8$ (755.87): C 74.68, H 6.53, N 1.85; found: C 74.69, H 6.67, N 2.06.

Data of **10**: R_f(AcOEt/hexane 1:1) 0.55. $[\alpha]_D$ = –17.2 (*c* = 4.7). IR: 3438*w*, 3095*w*, 3070*w*, 3040*w*, 3005*w*, 2960*w*, 2930*w*, 2875*w*, 1730*m*, 1680*s*, 1655*m*, 1515*w*, 1500*m*, 1455*m*, 1370*m*, 1303*m*, 1265*s*, 1250–1200*m*, 1100*s*, 1070*s*, 1030*m*, 910*w*, 695*w*, 660*w*. ^{1}H-NMR (400 MHz): 7.37–7.18 (*m*, 25 arom. H); 6.15 (*d*, *J* = 3.9, H–C(3)); 5.22 (br. *s*, AcNH); 4.71–4.39 (*m*, 5 PhCH_2, H–C(6)); 4.25 (*dt*, *J* = 7.5, 6.4, H–C(5)); 4.16 (*m*, H–C(4), H–C(7)); 3.97 (*ddd* app. as *q*, *J* ≈ 5.0, H–C(8)); 3.89 (*dd*, *J* = 4.5, 10.0, H_a–C(9)); 3.70 (*dd*, *J* = 5.5, 10.0, H_b–C(9)); 1.74 (*s*, Ac). ^{13}C-NMR: 169.4 (*s*); 161.9 (*s*); 143.5 (*s*); 138.6 (*s*); 138.5 (*s*); 138.1 (*s*); 137.8 (*s*); 135.2 (*s*); 128.6–127.3 (*d*); 109.3 (*d*); 78.2 (*d*); 77.9 (*d*); 75.0 (*d*); 74 .4 (*t*); 73.4 (*t*); 72.1 (*t*); 71.0 (*d*); 70.9 (*t*); 68.8 (*t*); 67.1 (*t*); 48.1 (*d*); 23.3 (*q*). Anal. calc. for $C_{46}H_{47}NO_8$ (741.84): C 74.47, H 6.39, N 1.89; found: C 74.27, H 6.26, N 1.87.

Data of **11**: R_f(AcOEt/hexane 1:1) 0.40. M.p. 175–176° (from AcOEt), $[\alpha]_D$ = +72 (*c* = 1.8). IR: 3415*m*, 3090*w*, 3070*w*, 3040*w*, 3000*w*, 2955*w*, 2920*w*, 2865*w*, 1760*s*, 1660*s*, 1500*m*, 1450*w*, 1440*m*, 1370*m*, 1305*m*, 1260*s*, 1270–1200*s*, 1140*m*, 1120*s*, 1070*s*, 1045*m*, 1025*m*, 980*m*, 910*w*. ^{1}H-NMR (400 MHz): 7.40–7.23 (*m*, 15 arom. H); 6.10 (*d*, *J* = 2.5, H–C(3)); 5.36 (*d*, *J* = 7.3, AcN*H*); 4.70 (*d*, *J* = 12, 1 H, PhCH_2); 4.69(*d*, *J* = 12, 1 H, PhCH_2); 4.68 (br. *s*, OH, exchanged with D_2O); 4.58–4.47 (*m*, 2 PhCH_2); 4.28 (*ddd*, *J* = 9.7, 8, 7.3, H–C(5)); 4.22 (*dd*, *J* = 8, 2.5, H–C(4)); 4.10 (*dd*, *J* = 9.7, 1.5, H–C(6)); 3.94 (*m*, H–C(8)); 3.83 (*dd*, *J* = 2.4, 10.0, H_a–C(9)); 3.79 (*s*, COOMe); 3.76 (*ddd*, *J* = 9.0, 4.0, 1.5, H–C(7)); 3.72 (*dd*, *J* = 4.4, 10.0, H_b–C(9)); 1.94 (*s*, Ac). ^{13}C-NMR: 172.6 (*s*); 162.2 (*s*); 145.7 (*s*); 138.3 (*s*); 138.1 (*s*); 137.6 (*s*); 128.5–127.5 (*d*); 108.2 (*d*); 77.3 (*d*); 76.6 (*d*); 73.3 (*t*); 73.0 (d); 72.9 (*t*); 69.4 (*t*); 69.1 (*t*); 67.6 (*d*); 52.3 (*q*); 47.7 (*d*); 23.0 (*q*). CI-MS: 576.3 ([*M* + 1]$^+$). Anal. calc. for $C_{33}H_{37}NO_8$ (575.63): C 68.85, H 6.48, N 2.43; found: C 68.77, H 6.64, N 2.36.

3-Acetamido-2,5,6,7-tetra-O-*benzyl-3-deoxy*-D-glycero-D-galacto-*heptitol* (**12**), *3-Acetamido-2,5,6,7-tetra*-O-*benzyl-3-deoxy-4*-O-*(hydroxyacetyl)*-D-glycero-D-galacto-*heptitol* (**13**), *and 3-Acetamido-2,5,6,7-tetra*-O-*benzyl-3-deoxy*-D-glycero-D-galacto-*heptofuranose* (**14**). A stream of O_3/O_2 was passed into a cooled (–70°) soln. of **8** (6.65 g, 10 mmol) in CH_2Cl_2 (330 ml) until the color turned blue (15 min). The soln. was purged with N_2 (10 min) and evaporated to give a foam. An ice-cold and stirred soln. of this foam in MeOH (330 ml) was

treated with $NaBH_4$ (0.8 g). After 1.5 h at 0°, further $NaBH_4$ (0.4 g) was added and stirring was continued for 2 h. The pH of the soln. was then adjusted to *ca.* 6 by addition of *Amberlite IR-120* (H^+). The filtered soln. was evaporated and the semicrystalline residue diluted with MeOH and filtered to give **12** (3.66 g, 59.7%). The filtrate was evaporated. FC of the residue (AcOEt/hexane 1:1) gave **14** (121 mg, 1.98%), **12** (330 mg, 5.9%), and **13** (430 mg, 6.4%). When the reduction with $NaBH_4$ was continued for further 12 h at r.t., the yield of **12** was 78%.

Data of **12**: R_f (AcOEt/hexane 3:1) 0.60. M.p. 123–124° (from MeOH/H_2O). $[\alpha]_D$ = –31.0 (*c* = 1.9). IR: 3620*w*, 3575*w*, 3500*w*, 3440*m*, 3100*w*, 3080*w*, 3050*w*, 3010*m*, 2950*m*, 2890*m*, 1730*w*, 1660*s*, 1610*w*, 1520*m*, 1505*m*, 1460*m*, 1400*w*, 1375*m*, 1310*w*, 1270–1200*w*, 1100*s*, 1080*s*, 1060*s*, 1030*m*, 920*w*. ^{1}H-NMR (400 MHz): 7.34–7.24 (*m*, 20 arom. H); 5.80 (*d*, *J* = 10.0, AcN*H*); 4.71–4.50 (*m*, 8 H); 4.35 (*dt*, *J* = 10, 1.2, H–C(3)); 4.12 (*ddd*, *J* = 10, 9.5, 1.2, H–C(2)); 4.04 (*t*, *J* = 10, H–C(4)); 3.81–3.75 (*m*, 3 H); 3.67 (*dd*, *J* = 10, 3.2, H_a–C(1)); 3.44 (br. *s*, HO–C(1)); 3.32 (*t*, *J* =10, H_b–C(1)); 2.67 (*d*, *J* = 10, HO–C(4)); 1.97 (*s*, Ac). ^{13}C-NMR: 171.8 (*s*); 138.2 (*s*); 137.8 (*s*); 137.7(*s*); 137.6 (*s*); 128.4–127.5 (*d*); 77.8 (*d*); 77.0 (*d*); 76.5 (*d*); 74.5 (*t*); 73.5 (*t*); 73.4 (*t*); 72.9 (*t*); 68.2 (*d*); 60.4 (*t*); 51.1 (*d*); 23.1 (*q*). Anal. calc. for $C_{37}H_{43}NO_7$ (613.7): C 72.40, H 7.06, N 2.28; found: C 72.36, H 6.92, N 2.24.

Data of **13**: R_f(AcOEt/hexane 3:1) 0.5. Solid foam. $[\alpha]_D$ = +13.4 (*c* =3.2). IR: 3550*w*, 3425*m*, 3395*m*, 3360*m*, 3340*w*, 3305*w*, 3090*w*, 3060w, 3025*w*, 3000*w*, 2940*w*, 2910*w*, 2870*m*, 1745*s*, 1655*s*, 1510*m*, 1495*m*, 1450*m*, 1365*w*, 1300–1200*m*, 1090*s*, 1055*m*, 1035*m*, 1005*m*, 990*m*, 915*w*, 890*w*. ^{1}H-NMR (400 MHz): 7.36–7.16 (*m*, 20 arom. H); 6.27 (*d*, *J* = *9.3*, AcN*H*); 5.53 (*dd*, *J* = 9.6, 3, H–C(4)); 4.72–4.36 (*m*, 9 H, 4 PhCH_2, H–C((3)); 4.00 (*dd*, *J* = 7.3, 3.9, H_a–C(9)); 3.93 (*dd*, *J* = 7.3, 3.0, H_b–C(9)); 3.86–3.75 (*m*, H–C(5), H_a–C(7), HO–C(1)); 3.71–3.61 (*m*, H_a–C(1), H–C(2), H–C(6), H_b–C(7)); 3.27 (*t*, *J* = 9.1, H_b–C(1)); 2.33 (br. *s*, HO–C(9)); 1.72 (*s*, Ac). ^{13}C-NMR: 172.6 (*s*); 172.1 (*s*); 137.9 (*s*); 137.6 (*s*); 137.5 (*s*); 137.4 (*s*); 128.6–127.7 (*d*); 78.5 (*d*); 76.2 (*d*); 75.7 (*d*); 74.3 (*t*); 73.3 (*t*); 72.5 (*t*); 70.5 (*d*); 67.7 (*t*); 60.4 (*t*); 59.3 (*t*); 50.6 (*d*); 22.6 (*q*). Anal. calc. for $C_{39}H_{45}NO_9$ (671.70): C 69.73, H 6.75, N 2.08; found: C 69.46, H 6.53, N 2.00.

Data of **14**: R_f(AcOEt/hexane 3:1) 0.75. $[\alpha]_D$ = –3.7 (*c* = 1.9). IR: 3440*m*, 3090*w*, 3070*w*, 3040*w*, 3000*m*, 2915*w*, 2870*m*, 1640*s*, 1510*m*, 1495*m*, 1450*m*, 1365*w*, 1090*s*, 1075*s*, 1030*s*, 990*w*, 910*w*. ^{1}H-NMR (200 MHz): 7.34–7.22 (*m*, 20 arom. H); 5.42–5.40 (*m*, 2 H); 5.22–5.18 (*m*, 1 H); 4.74–4.37 (*m*, 8 H); 4.08–3.66 (*m*, 7 H); 1.87, 1.76 (2 *s*, 1:3, Ac). ^{13}C-NMR: major isomer (α-D): 170.3 (*s*); 138.2 (*s*); 138.1 (*s*); 137.6 (*s*); 137.2 (*s*); 128.8–127.3 (*d*); 100.6 (*d*); 88.6 (*d*); 79.8 (*d*); 78.2 (*d*); 76.1 (*d*); 74.0 (*t*); 73.3 (*t*); 72.6 (*t*); 71.1 (*t*); 68.5 (*t*); 56.5 (*d*); 23.1 (*q*); minor isomer: (β-D): 170.3 (*s*); 138.1 (*s*); 138.0 (*s*); 137.5 (*s*); 137.2 (*s*); 95.0 (*d*); 82.5 (*d*); 81.0 (*d*); 77.9 (*d*); 77.0 (*d*); 75.3 (*t*); 73.3 (*t*); 72.5 (*t*); 71.7 (*t*); 68.1 (*t*); 53.4 (*d*); 23.1 (*q*). Anal. calc. for $C_{37}H_{41}NO_7$ (611.70): C 72.64, H 6.76, N 2.29; found: C 72.84, H 6.72, N 2.27.

*3-(*N*-Acetyl-*N*-benzylamino)-2,5,6,7-tetra-*O*-benzyl-3-deoxy-*D-glycero-D-galacto-*heptitol* (**15**), *3-(*N*-acetyl-*N*-benzylamino)-2,5,6,7-tetra-*O*-benzyl-3-deoxy-*D-glycero-D-galacto-*heptafuranose* (**17**), *and 1-*O*-Acetyl-3-(benzylamino)-3-deoxy-4-*O*-(hydroxyacetyl)-*D-glycero-D-galacto-*heptitol* (**18**). As described for **8**, a soln. of **9** (3.9 g, 5.15 mmol) in CH_2Cl_2 (200 ml) was first treated with O_3 and then with $NaBH_4$. FC of the residue (AcOEt/hexane 1:2) gave **15** (1.95 g, 54%), **17** (348 mg, 9.6%), and **18** (100 mg, 2.8%), all three as oils. Treatment of the CH_2Cl_2 soln. of the ozonide with Me_2S (4 ml) and usual workup yielded 81% of **17.**

Data of **15**: R_f(AcOEt/hexane 1:1) 0.50. $[\alpha]_D$ = –23.7 (*c* = 6.5). IR: 3440*w*, 3090*w*, 3070*w*, 3040*w*, 3000*m*, 2940*w*, 2875*m*, 1740*w*, 1640*s*, 1495*w*, 1455*s*, 1410*m*, 1365*m*, 1330*m*, 1250–1200*m*, 1100*s*, 1070*s*, 1055*s*, 1030*s*, 940*w*, 910*w*, 690*w*, 660*w*. ^{1}H-NMR (200 MHz, (D_6)DMSO, 140°): 7.33–7.12 (*m*, 25 arom. H); 4.68–4.45 (*m*, 11 H); 4.22–3.95 (*m*, 4 H); 3.85–3.50 (*m*, 6 H); 1.95 (*s*, Ac); at 20°: 2.03, 1.93 (2*s*, ratio 2:1, Ac). ^{13}C-NMR: 175.5 (*s*, major); 173.5 (*s*, minor); 138.7 (*s*); 138.0 (2*s*); 137.5 (*s*); 137.4 (*s*); 128.9–126.4 (*d*); 78.9 (*d*); 78.3 (*d*); 76.6 (*d*); 74.4 (*t*); 73.2 (*t*); 72.7 (*t*); 68.7 (*t*); 67.1 (*t*); 60.3 (*t*); 55.2 (*d*); 50.2 (*t*, major); 46.7 (*t*, minor); 22.6 (*q*, major); 22.1 (*q*, minor). Anal. calc. for $C_{44}H_{49}NO_7$ (703.84): C 75.08, H 7.02, N 1.99; found: C 74.92, H 7.15, N 1.80.

Data of **17**: R_f(AcOEt/hexane) 0.70. $[\alpha]_D$ = +17.7 (*c* = 5.7). IR: 3340*w*, 3090*w*, 3070*w*, 3040*w*, 3005*m*, 2940*w*, 2870*m*, 1780*w*, 1740*w*, 1630*s*, 1495*w*, 1455*s*, 1430*m*, 1400*w*, 1360*m*, 1310*w*, 1250–1200*m*, 1095*s*, 1075*s*, 1050*s*, 1030*s*, 990*m*, 960*m*, 910*w*, 690*w*. ^{1}H-NMR (200 MHz, (D_6)DMSO, 140°): 7.37–7.18 (*m*, 25 arom. H); 6.25 (*d*, *J* = 6.3, OH); 5.25 (*dd*, *J* = 6.3, 2.1, H–C(1)); 4.89–4.85 (*m*, 1 H); 4.72–4.37 (*m*, 11 H); 4.01 (*dd*, *J* = 4.7, 2.1, 1 H); 3.90–3.63 (*m*, 4 H); 1.99 (*s*, Ac). ^{1}H-NMR ($CDCl_3$, 25°): 2.08, 2.05 (2*s*, ratio 10:1, Ac). ^{13}C-NMR: 171.8 (*s*); 138.3 (*s*); 138.1 (*s*); 137.8 (*s*); 137.6 (*s*); 136.1 (*s*); 128.9–125.7 (*d*); 100.8 (*s*); 89.5 (*d*); 78.6 (*d*); 77.0 (*d*); 76.4 (*d*); 73.3 (*t*); 73.2 (*t*); 73.1 (*t*); 71.8 (*t*); 69.2 (*t*); 67.4 (*d*); 55.8 (*t*, major); 49.9 (*t*, minor); 22.7 (*q*, major); 22.4 (*q*, minor). Anal. calc. for $C_{44}H_{47}NO_7$ (701.82): C 75.29, H 6.75, N 1.99; found: C 75.34, H 6.77, N 1.94.

Data of **18**: R_f(AcOEt/hexane 1:1) 0.60. $[\alpha]_D$ = –13.8 (*c* = 6.5). IR: 3540*w*, 3090*w*, 3070*w* , 3040*w*, 3005*w*, 2920*w* , 2870*w*, 1760*s*, 1745*s*, 1495*w*, 1455*m*, 1365*m*, 1280*m*, 1240–1200*m*, 1190*m*, 1090*s*, 1030*s*, 1000*m*, 910*w*, 690*w*. ^{1}H-NMR (400 MHz): 7.36–7.20 (*m*, 25 arom. H); 4.78–4.49 (*m*, 4 PhC*H*$_2$, CH$_2$(1)); 4.39–4.36 (*m*, H–C(2), H–C(5)); 4.26 (*dd*, *J* = 9.4, 6.0, H–C(3)); 4.21, 4.15 (*d*, *J* = 14.2, PhC*H*$_2$); 4.05 (*d*, *J* = 5.1, 2 H, CH$_2$(9)); 4.00 (*ddd*, *J* = 9.4, 5.2, 4.1, H–C(6)); 3.83 (*dd*, *J* = 10.4, 4.1, H$_a$–C(7)); 3.73 (*dd*, *J* = 10.4, 5.2, H$_b$–C(7)); 3.46 (*dd*, *J* = 9.4, 2.8, H–C(4)); 3.41 (*d*, *J* = 6, BnN*H*); 2.36 (br. *s*, OH); 1.66 (*s*, Ac). ^{13}C-NMR: 172.6 (*s*); 168.5 (*s*); 138.0 (*s*); 137.9 (*s*); 137.8 (*s*); 137.7 (*s*); 136.6 (*s*); 128.5–126.9 (*d*); 78.6 (*d*); 77.0 (*d*); 76.8 (*d*); 73.5 (*t*); 73.0 (*t*); 72.7 (*t*); 72.5 (*t*); 69.2 (*t*); 67.9 (*d*); 66.6 (*t*); 65.4 (*d*); 60.1 (*t*); 58.9 (*t*); 18.7 (*q*). Anal. calc. for $C_{46}H_{51}NO_9$ (761.87): C 72.51, H 6.75, N 1.84; found: C 72.33, H 6.75, N 1.75.

3-Acetamido-2,5,6,7-tetra-O-*benzyl-1*-O-*[(*tert-*butyl)dimethylsilyl]-3-deoxy*-D-glycero-D-galacto-*heptitol* (**19**). (*t*-Bu)Me$_2$SiCl (160 mg, 1.07 mmol) and imidazole (200 mg, 2.94 mmol) were added to a soln. of **12** (610 mg, 1 mmol) in DMF (6 ml). After 3 h at r.t., the mixture was evaporated under high vacuum, soln. of the residue in CH_2Cl_2 was washed with H_2O and dried. The solvent was evaporated and the residue purified by FC (AcOEt/hexane 1:5): **19** (660 mg, 81.4%) as an oil. R_f(AcOEt/hexane 1:3) 0.50. $[\alpha]_D$ = –14.3 (*c* =5.6). IR: 3540*w*, 3430*w*, 3090*w*, 3070*w*, 3030*w*, 3000*w*, 2950*m*, 2930*m*, 2860*m*, 1955*w*, 1682*s*, 1600*w*, 1510*m*, 1495*m*, 1455*m*, 1365*w*, 1305*w*, 1250*s*, 1200*s*, 1120*s*, 1095*s*, 1070*s*, 1050*s*, 1030*m*, 1005*w*, 925*w*, 835*s*, 695*w*. ^{1}H-NMR (400 MHz): 7.35–7.26 (*m*, 20 arom. H); 5.73 (*d*, *J* = 10.0, AcN*H*); 4.84–4.54 (*m*, 4 PhC*H*$_2$); 4.31 (*dt*, *J* = 10.0, 0.7, H–C(3)); 4.17 (*dt*, *J* = 6.8, 1.2, H–C(2)); 3.88–3.81 (*m*, H–C(4), H–C(6)); 3.74 (*dd*, *J* = 10.3, 3.3, H$_a$–C(7)); 3.72–3.64 (*m*, H$_a$–C(1), H$_b$–C(1), H–C(5)); 3.61 (*dd*, *J* = 10.3, 6.0, H$_b$–C(7)); 2.80 (*d*, *J* = 9.0, HO–C(4)); 1.93 (*s*, Ac); 0.90 (*s*, *t*-Bu); 0.06, 0.05 (2*s*, Me$_2$Si). ^{13}C-NMR: 169.7 (*s*); 138.6 (*s*); 138.3 (*s*); 138.1 (*s*); 137.9 (*s*); 128.3–127.6 (*d*); 78.3 (*d*); 78.0 (*d*); 76.2 (*d*); 74.2 (*t*); 74.1 (*t*); 73.4 (*t*); 72.9 (*t*); 69.1 (*d*); 68.9 (*t*); 63.8 (*t*); 51.0 (*d*); 25.9 (*q*); 23.4 (*q*); 18.1 (*s*); 5.5 (*q*). Anal. calc. for $C_{43}H_{57}NO_7Si$ (727.98): C 70.94, H 7.89, N 1.92; found: C 70.78, H 7.70, N 2.02.

3-Acetamido-4-O-*acetyl-2,5,6,7-tetra*-O-*benzyl-1*-O-*[(*tert-*butyl)dimethylsilyl]-3-deoxy*-D-glycero-D-galacto-*heptitol* (**20**) *and* 4-O-*Acetyl-2,5,6,7-tetra*-O-*benzyl-1*-O-*[(*tert-*butyl)dimethylsilyl]-3-deoxy-(*N,N-*diacetylamino)*-D-glycero-D-galacto-*heptitol* (**21**). A mixture of (*t*-Bu)Me$_2$SiCl (1.25 g, 8.4 mmol, 1.1 equiv.), **12** (4.70 g, 7.66 mmol) and pyridine (40 ml) was stirred at r.t. for 20 h. Additional (*t*-Bu)Me$_2$SiCl (110 mg, 0.73 mmol) was added and the mixture was heated to 80°. After 30 min, Ac_2O (8 ml) was added and the temp. raised to 95°. After 2 h, the soln. was cooled to r.t., and MeOH (8 ml) was added. The residue obtained after evaporation was processed in the usual way to give, after FC (AcOEt/hexane 1:5), **21** (310 mg, 5%) and **20** (5.40 g, 92%), both as oils.

Data of **20**: R_f(AcOEt/hexane 1:3) 0.30. $[\alpha]_D$ = +4.4 (*c* = 3.0). IR: 3430*w*, 3090*w*, 3070*w*, 3040*w*, 3000*w*, 2957*m*, 2930*m*, 2860*m*, 1765*s*, 1675*s*, 1500*w*, 1455*w*, 1370*m*, 1240–1200*s*, 1100*s*, 1075*s*, 1030*m*, 840*s*, 695*w*, 660*w*. ^{1}H-NMR (200 MHz): 7.41–7.22 (*m*, 20 arom. H); 5.80 (*d*, *J* = 9.1, AcN*H*); 5.40 (*dd*, *J* = 9.6, 2.0, H–C(4)); 4.82–4.44 (*m*, 10 H); 3.81–3.60 (*m*, 6 H); 1.99 (*s*, Ac); 1.76 (*s*, Ac); 0.90 (*s*, *t*-Bu); 0.07, 0.06 (2*s*, Me$_2$Si). ^{13}C-NMR: 170.4 (*s*); 170.0 (*s*); 138.4 (*s*); 138.3 (*s*); 138.2 (2*s*); 128.4–127.5 (*d*); 78.6 (*d*); 78.1 (*d*); 76.1 (*d*); 74.0 (*t*); 73.8 (*t*); 73.3 (*t*); 72.7 (*t*); 70.6 (*d*); 68.7 (*t*); 64.2 (*t*); 50.2 (*d*); 25.9 (*q*); 23.2 (*q*) 21.1 (*q*); 18.2 (*s*); –5.5 (*q*); –5.6 (*q*). Anal. calc. for $C_{45}H_{59}NO_8Si$ (770.01): C 70.18; H 7.72, N 1.82; found: C 70.38, H 7.86, N 1.93.

Data of **21**: R_f(AcOEt/hexane 1:3) 0.55. $[\alpha]_D$ = –11.5 (*c* = 3.3). IR: 3090*w*, 3070*w*, 3040*w*, 3005*w*, 2955*s*, 2930*s*, 2860*s*, 1735*s*, 1690*s*, 1495*w*, 1455*m*, 1370*s*, 1240–1200*s*, 1100*s*, 1028*s*, 985*m*, 940*w*, 910*w*, 838*s*, 695*w*, 660*w*. ^{1}H-NMR (200 MHz): 7.37–7.20 (*m*, 20 arom. H); 6.13 (*dd* , *J* = 8.5, 1.7, H–C(4)); 4.78–4.54 (*m*, 7 H); 4.44–4.25 (*m*, 3 H); 4.03–3.99 (*m*, 1 H); 3.86–3.75 (*m*, 6 H); 3.55–3.49 (*m*, 1 H); 2.21 (*s*, Ac); 2.10 (*s*, Ac); 1.85 (*s*, Ac); 0.90 (*s*, *t*-Bu); 0.02 (*s*, Me$_2$Si). ^{13}C-NMR: 176.0 (*s*); 175.3(*s*); 170.5(*s*); 138.5(*s*); 138.2 (2*s*); 138.0 (*s*); 128.5–127.3 (*d*); 78.3 (*d*); 77.9 (2*d*); 73.34 (*t*); 73.27 (*t*); 72.9 (*d*); 72.2 (*t*); 71.7 (*t*); 70.5 (*t*); 62.8 (*t*); 57.4 (*d*); 25.7 (*q*); 21.2 (*q*); 18.2 (*s*); –5.4 (*q*); –5.5 (*q*). Anal. calc. for $C_{47}H_{61}NO_9$ Si (812.05): C 69.51, H 7.57, N 1.72; found: C 69.55, H 7.58, N 1.71.

3-Acetamido-1,4-di-O-*acetyl-2,5,6,7-tetra*-O-*benzyl-3-deoxy*-D-glycero-D-galacto-*heptitol* (**22**), *3-Acetamido-4*-O-*acetyl-2,5,6,7-tetra*-O-*benzyl-3-deoxy*-D-glycero-D-galacto-*heptitol* (**23**), *and 3-Acetamido-1*-O-*acetyl-2,5,6,7-tetra*-O-*benzyl-3-deoxy*-D-glycero-D-galacto-*heptitol* (**24**). *Conversion of* **12** *into* **22**. A soln. of **12** (1228 mg, 2 mmol) in pyridine (20 ml) and Ac_2O (15 ml) was stirred at 100° for 6 h. MeOH (10 ml) was added to the cooled soln. to give, after evaporation, co-evaporation with toluene, and FC (AcOEt/hexane 1:2), **22** (1380 mg, 99%) as an oil.

Conversion of **21** *into* **22**. To a soln. of **21** (130 mg, 0.16 mmol) in MeOH (5 ml), 1M H_2SO_4 (0.2 ml) was added. After 1 h at r.t., the soln. was neutralized with $NaHCO_3$, filtered, and evaporated. FC (AcOEt/hexane 1:1) of the residue gave **22** (87 mg, 78%).

Conversion of **20** *into* **23**. At r.t., 1M H_2SO_4 (0.2 ml) was added to a soln. of **20** (175 mg, 0.227 mmol) in MeOH (5 ml). After 1 h, the mixture was neutralized with solid $NaHCO_3$. The filtered soln. was evaporated. FC of the residue gave **23** (140 mg, 94%). When crude **20** (13 g, containing *ca.* 5% of **21**) was used, the yield of **23** was 9.5 g (85.8%). Diol **12** (0.85 g, 8.2%) was recovered from the combined fractions of the by-products, after deacetylation with NaOMe/MeOH.

Conversion of **20** *into* **23/24**. $Bu_4NF \cdot 3\ H_2O$ (430 mg, 1.2 equiv.) was added at r.t. to a soln. of **20** (875 mg, 1.136 mmol) in THF (20 ml). When, according to TLC, **20** was consumed (1 h), the mixture was evaporated. FC of the residue (AcOEt/hexane 1:3) yielded **24** (501 mg, 67%) and **23** (159 mg, 22%) as oils.

Conversion of **22** *into* **12/23/24**. At 0°, 2.5M NaOMe/MeOH (0.05 ml) was added to a stirred soln. of **23** (1.40 g, 2 mmol) in MeOH (20 ml) in the presence of phenolphthaleine. The soln. was kept at 20° for 3 h, when according to TLC (AcOEt/hexane 3:2), **22** (R_f0.65), **24** (R_f0.55), **23** (R_f0.45), and **12** (R_f 0.3) were present in a ratio of *ca.* 1:1:4:1. Solid CO_2 was added, and the syrup, obtained after evaporation, was dissolved in CH_2Cl_2, washed with H_2O, dried, and evaporated. FC (AcOEt/hexane 1:1) of the residue gave **24/22** (35 mg), **23** (690 mg, 53%), and **12** (237 mg, 19%).

Data of **22**: R_f (AcOEt/hexane 1:1) 0.45. $[\alpha]_D$ = +4.8 (*c* = 2.4). IR: 3430*w*, 3090*w*, 3070*w*, 3030*w*, 3000*w*, 2870*w*, 1735*s*, 1675*s*, 1510*w*, 1500*m*, 1450*w*, 1330*m*, 1310*w*, 1240–1200*s*, 1095*s*, 1075*s*, 1045*m*, 1025*m*, 980*w*. ^{1}H-NMR (200 MHz): 7.39–7.18 (*m*, 20 arom. H); 5.80 (*d*, *J* = 10.0, AcN*H*); 5.40 (*dd*, *J* = 9.6, 2.4, H–C(4)); 4.67–4.41 (*m*, 10 H); 4.23–4.00 (*m*, 2 H); 3.83–3.59 (*m*, 4 H); 2.03 (*s*, Ac); 2.00 (*s*, Ac); 1.74 (*s*, Ac). ^{13}C-NMR: 170.6 (*s*); 170.3 (*s*); 170.1 (*s*); 138.1 (2*s*); 138.0 (*s*); 137.5 (*s*); 128.9–127.5 (*d*); 78.6 (*d*); 76.0 (*d*); 74.7 (*d*); 74.1 (*t*); 73.3 (2*t*); 72.6 (*t*); 70.1 (*d*); 68.4 (*t*); 63.5 (*t*); 50.4 (*t*); 23.0 (*q*); 21.0 (*q*); 20.8 (*q*). CI-MS: 698.6 (100, [*M* + 1]). Anal. calc. for $C_{41}H_{47}NO_9$ (697.79): C 70.57, H 6.79, N 2.01; found: C 70.38, H 7.86, N 1.93.

Data of **23**: R_f(AcOEt/hexane 1:1) 0.30. $[\alpha]_D$ = +7.6 (*c* = 2.7). IR: 3420*w*, 3380*m*, 3090*w*, 3065*w*, 3030*m*, 2930*m*, 2870*m*, 1730*s*, 1650*s*, 1510*m*, 1497*m*, 1450*w*, 1365*m*, 1235*s*, 1080*s*, 1050*s*, 1025*s*, 690*w*. ^{1}H-NMR (400 MHz): 7.34–7.22 (*m*, 20 arom. H); 6.36 (*d*, *J* = 8.9, AcN*H*); 5.48 (*dd*, *J* = 9.7, 3.0, H–C(4)); 4.65–4.39 (*m*, 9 H); 3.97 (*ca. d*, *J* = 10, HO–C(1)); 3.82–3.61 (*m*, 6 H); 3.27 (*dd*, *J* = 9.4, 11.2, 1 H); 1.98 (*s*, Ac); 1.72 (*s*, Ac). ^{13}C-NMR: 172.2 (*s*); 170.3 (*s*); 138.1 (*s*); 137.7 (3*s*); 128.5–127.7 (*d*); 79.0 (*d*); 76.6 (*d*); 75.9 (*d*); 74.4 (*t*); 73.3 (2*t*); 72.8 (*t*); 72.7 (*t*); 69.5 (*d*); 68.0 (*t*); 59.6 (*t*); 51.0 (*d*); 22.6 (*q*); 20.9 (*q*). Anal. calc. for $C_{39}H_{45}NO_6$ (655.76): C 71.43, H 6.92, N 2.08; found: C 71.29, H 6.80, N 2.21.

Data of **24**: R_f(AcOEt/hexane 1:1) 0.40. $[\alpha]_D$ = –30.0 (*c* = 1.7). IR: 3540*w*, 3435*w*, 3090*w*, 3070*w*, 3040*w*, 3000*w*, 2960*w*, 2870*w*, 1740*s*, 1675*s*, 1500*m*, 1450*m*, 1370*m*, 1310*w*, 1240–1200*s*, 1090*s*, 1070*s*, 1050*s*, 1028*m*, 980*w*, 910*w*. ^{1}H-NMR (400 MHz): 7.52–7.26 (*m*, 20 arom. H); 5.69 (*d* , *J* = 10.1, AcN*H*); 4.78–4.54 (*m*, 4 PhCH_2); 4.35–4.30 (*m*, H–C(2), H–C(3)); 4.14 (*dd*, *J* = 11.4, 6.4, H_a–C(1)); 4.05 (*dd*, *J* = 11.4, 6.4, H_b–C(1)); 3.89–3.82 (*m*, H–C(4), H–C(6)); 3.74 (*dd*, *J* = 10.4, 3.5, H_a–C(7)); 3.70 (*d*, *J* = 7.2, H–C(5)); 3.66 (*dd*, *J* = 10.4, 4.3, H_b–C(7)); 2.86 (*d*, *J* = 8.8, HO–C(4)); 2.02 (*s*, Ac); 1.94 (*s*, Ac). ^{13}C-NMR: 170.6 (*s*); 170.0 (*s*); 138.3 (*s*); 138.2 (*s*); 138.1 (*s*); 138.0 (*s*); 128.4–127.5 (*d*); 78.4 (*d*); 76.3 (*d*); 74.9 (*d*); 74.2 (*t*); 74.0 (*t*); 73.5 (*t*); 73.0 (*t*); 69.0 (*d*); 68.9 (*t*); 63.9 (*t*); 51.5 (*d*); 23.3 (*q*); 20.8 (*q*). Anal. calc. for $C_{39}H_{45}NO_6$ (655.76): C 71.43, H 6.92, N 2.08; found: C 71.37, H 6.94, N 1.90.

3-Acetamido-2,5,6,7-tetra-O-*benzyl-1*-O-*[(*tert*-butyl)dimethylsilyl]-3-deoxy*-D-gluco-*4-heptulose* (**25**). A soln. of **19** (600 mg, 0.825 mmol) in CH_2Cl_2 (6 ml) was added at –70° to a stirred soln. of DMSO (0.5 ml, 0.55 g, 8.7 equiv.) and oxalyl chloride (0.32 ml, 0.47 g, 4.4 equiv.) in CH_2Cl_2 (10 ml), prepared at –70°. The mixture was warmed to –30°, kept at –30° for 1 h, cooled to –70°, and treated with Et_3N (4 ml). After warming the mixture to 0°, it was diluted with H_2O (20 ml). Workup as usual (CH_2Cl_2) gave, after FC (AcOEt/hexane 1:3), **25** (455 mg, 76%). R_f(AcOEt/hexane 1:3) 0.35. $[\alpha]_D$ = –12.2 (*c* = 3.9). IR: 3435*w*, 3095*w*, 3070*w*, 3040*w*, 3000*m*, 2960*m*, 2935*m*, 2863*m*, 1730*m*, 1675*s*, 1495*m*, 1455*m*, 1370*w*, 1250*m*, 1100*s*, 1030*m*, 1005*w*, 910*w*, 840*s*, 695*w*. ^{1}H-NMR (200 MHz): 7.33–7.14 (*m*, 20 arom. H); 6.38 (*d*, *J* = 8.4, AcN*H*); 5.08 (*dd*, *J* = 8.4, 2.2, H–C(3)); 4.77–4.39 (*m*, 4 PhCH_2, H–C(5)); 4.16 (*dt*, *J* = 6.1, 2.2, H–C(2)); 3.98 (*ddd* app. as *q*, *J* = 4.9, H–C(6)); 3.71–3.54 (*m*, H_a–C(1), H_b–C(1), H_a–C(7), H_b–C(7)); 1.85 (*s*, Ac); 0.87 (*s*, *t*-Bu); 0.0 (*s*, Me_2Si). ^{13}C-NMR: 207.1 (*s*); 169.9 (*s*); 138.2 (*s*); 138.0 (*s*); 137.9 (*s*); 137.4 (*s*); 128.3–127.5 (*d*); 81.8 (*d*); 79.1 (*d*); 77.7 (*d*); 73.4 (*t*); 73.2 (*t*); 73.1 (*t*); 72.5 (*t*); 68.9 (*t*); 63.6 (*t*); 57.8 (*d*); 25.8 (*q*); 22.9 (*q*); 18.2 (*s*); –5.5 (*q*). Anal. calc. for $C_{43}H_{55}NO_7Si \cdot H_2O$ (743.98): C 69.41, H 7.72, N 1.88; found: C 69.40, H 7.92, N 1.98.

3-Acetamido-2,5,6,7-tetra-O-*benzyl*-D-gluco-*4-heptulofuranose* (**26**). A soln. of **25** (130 mg, 0.18 mmol) and $Bu_4NF \cdot 3\ H_2O$ (70 mg, 0.22 mmol) in THF (15 ml) was stirred at r.t. for 5 h and then evaporated. FC (AcOEt/hexane 1:2) of the residue gave **26** (37 mg, 33.6%). R_f(AcOEt/hexane 1:1) 0.60. $[\alpha]_D$ = –11.6 (*c* = 3.5). IR: 3440*m*, 3095*w*, 3070*w*, 3040*w*, 3005*m*, 2940*w*, 2880*w*, 1675*s*, 1500*m*, 1455*m*, 1370*m*, 1330*w*, 1090*s*, 1030*m*, 990*m*, 950*w*, 695*w*. ^{1}H-NMR (200 MHz): 7.39–7.20 (*m*, 20 arom. H); 6.07 (*d*, *J* = 8.4, AcN*H*); 5.59 (*d*,

J = 1.3, OH); 4.87 (*ddd*, J = 7.9, 5.3, 1.4, 1 H); 4.77–4.42 (*m*, 9 H); 4.20–4.01 (*m*, 3 H); 3.87–3.62 (*m*, 4 H); 2.02 (*s*, Ac). ^{13}C-NMR: 169.2 (*s*); 138.2 (*s*); 137.7 (*s*); 137.4 (*s*); 136.8 (*s*); 128.8–127.5 (*d*); 105.1 (*s*); 83.4 (*d*); 79.9 (*d*); 75.1 (*t*); 74.7 (*d*); 73.4 (*t*); 72.4 (*t*); 71.2 (*t*); 69.7 (*t*); 67.2 (*t*); 57.0 (*d*); 23.6 (*q*).

*3-Acetamido-4-*O*-acetyl-1-azido-2,5,6,7-tetra-*O*-benzyl-1,3-dideoxy-*D*-glycero-*D*-galacto-heptitol* (**27**). a) Mesyl chloride (0.16 ml, 2 equiv.) and Et_3N (0.44 ml, 3 equiv.) were added at 0° to a stirred soln. of **23** (690 mg, 1.05 mmol) in CH_2Cl_2 (10 ml). According to TLC (AcOEt/hexane 1:1), **23** (R_f 0.30) was consumed after 5 min, and a new spot appeared corresponding to **28** (R_f 0.40) (blue on development with 4-(4-nitrobenzyl)pyridine). After 30 min, MeOH (1 ml) was added, the mixture was warmed to r.t., diluted with CH_2Cl_2, and worked up as usual to give crude **28** (750 mg, 97%). Bu_4NN_3 (560 mg, 2 mmol) was added to the stirred soln. of the crude **28** in MeCN (20 ml) at r.t. According to TLC, no reaction took place within 20 h. The mixture was boiled for 5 h, when, according to TLC, **28** was almost completely converted to a new compound (R_f 0.90). Azide **27** (R_f 0.80) was present only as a by-product. The mixture was evaporated. A soln. of the residue in CH_2Cl_2 was washed with H_2O, dried and evaporated. FC (AcOEt/hexane 1.3) gave **24** (50 mg, 7%), **23** (372 mg, 57%), and **27** (23 mg, 3.4%).

b) Ph_3P (5.0 g, 1.3 equiv.), diethyl diazodicarboxylate (3.3 g, 3.0 ml, 1.3 equiv.) and a 2M soln. of HN_3 in benzene (11 ml, 1.5 equiv.) were added at r.t. to a stirred soln of **23** (9.5 g, 14.5 mmol) in benzene (200 ml) . The mixture was evaporated after 14 h. The residue was treated with AcOEt/hexane 1:1 and filtered. The filtrate was evaporated. FC (AcOEt/hexane 1:3) of the residue gave **27** (8.5 g, 86%) as an oil. R_f(AcOEt/hexane 1:2) 0.50. $[\alpha]_D$ = –3.6 (*c* = 6.2). IR: 3430*w*, 3090*w*, 3070*w*, 3040*w*, 3000*m*, 2940*w*, 2870*m*, 2103*s*, 1740*s*, 1680*s*, 1500*m*, 1455*m*, 1380*s*, 1240–1200*s*, 1090*s*, 1045*s*, 1030*s*, 915*w*, 690*w*. ^{1}H-NMR (200 MHz): 7.42–7.18 (*m*, 20 arom. H); 5.88 (*d*, J = 10.2, AcN*H*); 5.37 (*dd*, J = 9.8, 2.0, H–C(4)); 4.71–4.39 (*m*, 9 H); 3.81–3.58 (*m*, 5 H); 3.37 (*d*, J = 6.0, CH_2(1)); 1.98 (*s*, Ac); 1.72 (*s*, Ac). ^{13}C-NMR: 170.4 (*s*); 138.1 (*s*); 138.0 (2*s*); 137.3 (*s*); 128.6–127.6 (*d*); 78.7 (*d*); 76.2 (*d*); 75.7 (*d*); 74.2 (*t*); 73.9 (*t*); 73.3 (*t*); 72.6 (*t*); 70.2 (*d*); 68.2 (*t*); 52.8 (*t*); 51.3 (*d*); 23.0 (*q*); 21.0 (*q*). Anal. calc. for $C_{39}H_{44}N_4O_7$ (680.77): C 68.80, H 6.51, N 8.23; found: C 68.62, H 6.43, N 8.17.

*3-Acetamido-1-azido-2,5,6,7-tetra-*O*-benzyl-1,3-dideoxy-*D*-glycero-*D*-galacto-heptitol* (**29**). At r.t., 2.5M NaOMe/MeOH (1 ml) was added to a soln. of **27** (8.5 g, 12.5 mmol) in MeOH (50 ml). After 14 h, the mixture was evaporated. A soln. of the residue in CH_2Cl_2 was washed with H_2O, dried, and evaporated to give **29** (8.0 g, 100%), pure enough for the next step. The anal. sample was obtained after FC (AcOEt/hexane 1:2). R_f(AcOEt/hexane 1:1) 0.70. $[\alpha]_D$ = –32.0 (*c* = 4.8). IR: 3540*w*, 3430*m*, 3090*w*, 3070*w*, 3040*w*, 3000*m*, 2930*w*, 2870*m*, 2103*s*, 1675*s*, 1497*m*, 1455*m*, 1370*m*, 1350*w*, 1250–1200*m*, 1090*s*, 1075*s*, 1028*m*, 910*w*, 690*w*. ^{1}H-NMR (200 MHz): 7.40–7.23 (*m*, 20 arom. H); 5.68 (*d*, J = 9.7, AcN*H*); 4.79–4.50 (*m*, 8 H); 4.27–4.17 (*m*, 2 H); 3.90–3.74 (*m*, 2 H); 3.70–3.59 (*m*, 3 H); 3.40–3.22 (*m*, 2 H); 2.88 (*d*, J = 8.7, HO–C(4)); 1.93 (*s*, Ac). ^{13}C-NMR: 170.1 (*s*); 138.0 (*s*); 137.9 (*s*); 137.8 (2*s*); 128.4–127.7 (*d*); 78.1 (*d*); 76.3 (*d*); 76.1 (*d*); 74.5 (*t*); 74.2 (*t*); 73.4 (*t*); 72.9 (*t*); 68.9 (*d*); 68.6 (*t*); 53.3 (*t*); 52.2 (*d*); 23.4 (*q*). CI-MS: 639.5 (100 [M + 1]). Anal. calc. for $C_{37}H_{42}N_4O_6$ (638.73): C 69.57, H 6.63, N 8.77; found: C 69.53, H 6.73, N 8.91.

*3-Acetamido-1-azido-2,5,6,7-tetra-*O*-benzyl-1,3-dideoxy-*D*-gluco-4-heptulose* (**30**). A soln. of **29** (8.0 g, 12.5 mmol) in CH_2Cl_2 (100 ml) was oxidized with DMSO/oxalyl chloride/Et_3N (9.75 g, 7.5 g, and 15 ml, resp.) at –30°, as described for **25** to give, after FC (AcOEt/hexane 1:2), **30** (7.644 g, 96%). Oil. R_f(AcOEt/hexane 1:1) 0.70. $[\alpha]_D$ = –24.0 (*c* = 5.7). IR: 3430*m*, 3090*w*, 3070*w*, 3040*w*, 3000*m*, 2920*w*, 2870*m*, 2103*s*, 1730*m*, 1675*s*, 1495*m*, 1455*m*, 1370*m*, 1350*w*, 1280*m*, 1250–1200*m*, 1095*s*, 1028*s*, 915*w*, 690*w*. ^{1}H-NMR (200 MHz): 7.37–7.14 (*m*, 20 arom. H); 6.40 (*d*, J = 8.2, AcNH); 4.97 (*dd*, J = 8.2, 2.4, H–C(3)); 4.64–4.34 (*m*, 9 H); 4.21–4.14 (*m*, H–C(2)); 3.97 (*dd*, J = 5.0, 5.5, H–C(6)); 3.73 (*dd*, J = 10.2, 5.0, H_a–C(7)); 3.64 (*dd*, J = 10.2, 4.7, H_b–C(7)); 3.17 (*dd*, J = 12.7, 6.9, H_a–C(1)); 3.08 (*dd*, J = 12.7, 5.2, H_b–C(1)); 1.81 (*s*, Ac). ^{13}C-NMR: 206.4 (*s*); 170.2 (*s*); 137.9 (*s*); 137.5 (*s*); 137.4 (*s*); 137.1 (*s*); 128.4–127.7 (*d*); 81.6 (*d*); 79.2 (*d*); 76.0 (*d*); 73.4 (*t*); 73.3 (*t*); 73.2 (*t*); 72.6 (*t*); 68.5 (*t*); 57.9 (*d*); 52.0 (*t*); 22.8 (*q*). Anal. calc. for $C_{37}H_{40}N_4O_6$ (636.72): C 69.79, H 6.33, N 8.80; found: C 69.80, H 6.31, N 8.70.

*3-Acetamido-2-[(1'*S*,2'*R*)-1',2',3'-tris(benzyloxy)propyl]-1*H*-pyrrole* (**32**). A stirred soln. of **30** (64 mg, 0.1 mmol) in MeOH (5 ml) was treated with $HCOONH_4$ (32 mg, 0.5 mmol) and 10% Pd/C (20 mg). According to TLC (AcOEt/hexane 1:1), **30** (R_f 0.70) was converted completely into **31** (R_f 0.20) within 3 h at r.t., and hence gradually into **32** (R_f 0.30). The mixture was filtered through *Celite* and evaporated. FC (AcOEt/hexane 1:1) of the residue gave **32** (16 mg, 33%) and **31/32** (20 mg). Pure **31** could not be obtained by rechromatography of **31/32** as it was continuously transformed into **32**, a pale yellow oil, which slowly turned red-brown, even in soln. and when protected from O_2.

Data of **32**: IR: 3470*m*, 3440*w*, 3390*w*, 3090*w*, 3070*w*, 3000*m*, 2920*w*, 2870*w*, 1670*s*, 1610*m*, 1490*m*, 1455*w*, 1410*w*, 1365*w*, 1330*w*, 1305*w*, 1250–1200*w*, 1090*s*, 1025*s*, 690*w*. ^{1}H-NMR (400 MHz): 8.14 (br., H–N(1)); 7.61–7.20 (*m*, 15 arom. H); 6.62, 6.58 (2*t*, J = 2.9, H–C(4), H–C(5)); 4.78–4.28 (*m*, 3 PhC*H*$_2$); 4.60 (*d*,

J = 4.7, H–C(1')); 4.04 (*ddd*, J = 6.7, 5.3, 4.7, H–C(2')); 3.58 (*dd*, J = 10.0, 5.3, H_a–C(3')); 3.37 (*dd*, J = 10.0, 6.7, H_b–C(3')); 1.59 (*s*, Ac). ^{13}C-NMR: 167.9 (*s*); 138.0 (*s*); 137.9 (*s*); 137.8 (*s*); 128.4–127.4 (arom.); 122.0 (*s*); 116.5 (*s*); 116.3 (*d*); 104.3 (*d*); 80.3 (*d*); 73.9 (*t*); 73.3 (*t*); 72.6 (*t*); 70.3 (*t*); 69.5 (*t*); 23.0 (*q*).

N-{(2R,3S,4S)-4-(Benzyloxy)-2-[(1'S,2'R)-1',2',3'-tris(benzyloxy)propyl]pyrrolidin-3-yl}acetamid–Borane (1/1) (**33**). Ph_3P (263 mg, 1 mmol) was added to a stirred soln. of **30** (128 mg, 0.2 mmol) in THF (5 ml). When according to TLC (AcOEt/hexane 1:1), the transformation of **30** to **31** (R_f 0.70→0.20) was complete (*ca.* 5 h), the mixture was cooled in an ice-bath. A soln. of HBF_4 (40 mg) in Et_2O (4 ml) and subsequently a soln. of $LiBH_4$ (40 mg) in Et_2O (2 ml) were added. The mixture was diluted with Et_2O (20 ml), washed with 0.1M NaOH and brine, and processed as usual. FC (AcOEt/hexane 1:2) of the residue gave **33** (83 mg, 70.3%). Oil. R_f (AcOEt/hexane 1:1) 0.50. $[\alpha]_D$ = –24.3 (c = 1.5). IR: 3440*w*, 3235*w*, 3095*w*, 3075*w*, 3040*m*, 2875*m*, 2370*m*, 2320*m*, 2280*w*, 1680*s*, 1510*s*, 1500*s*, 1455*s*, 1370*m*, 1310*w*, 1260*w*, 1210*m*, 1170*m* 1095*s*, 1030*s*, 820*w*. ^{1}H-NMR ($CDCl_3$, 400 MHz): 7.38–7.24 (*m*, 20 arom. H); 5.76 (*d*, J = 8.8, AcN*H*); 5.64 (br. H–N(1); no exchange with D_2O); 4.71–4.48 (*m*, 4 PhCH_2, H–C(3)); 4.13 (*t*, J = 4.5, H–C(1')); 4.07 (*ddd* app. as *q*, J = 5.6, H–C(4)); 4.03 (*ddd* app. as *q*, $J \approx$ 4.5, H–C(2')); 3.72 (*d*, J = 4.5, CH_2(3')); 3.23 (*ddd* app. as *q*, $J \approx$ 4.5, H–C(2)); 3.04 (*t*, J = 5.6, CH_2(5)); 1.89 (*s*, Ac). ^{1}H-NMR (400 MHz, (D_6)DMSO): 8.36 (*d*, J = 8.18, AcNH); 7.35–7.22 (*m*, 20 arom. H); 5.90 (br., H–N(1); no exchange with D_2O); 4.70–4.39 (*m*, 9 H); 4.02 (*dd*, J = 2.6, 8.5, 1 H); 3.97 (*m*, 2 H); 3.80 (*dd*, J = 1.8, 11.0, 1 H); 3.60 (*dd*, J = 3.6, 11.0, 1 H); 3.27 (*dd*, J = 1.6, 2.4, 7.5, 1 H); 3.05 (*ddd*, J = 4.8, 5.2, 12.1, 1 H); 2.90 (*ddd*, J = 5.5, 7.7, 13.2, 1 H); 1.80 (*s*, 3 H); 1.57 (br. *s*, 3 H). ^{13}C-NMR: 169.7 (*s*); 137.8 (*s*); 137.7 (*s*); 137.3 (*s*); 137.2 (*s*); 128.3–127.3 (*d*); 81.9 (*d*); 78.5 (*d*); 75.3 (*d*); 73.2 (*t*); 73.1 (*t*); 72.1 (*t*); 71.6 (*d*); 71.4 (*t*); 68.3 (*t*); 58.0 (*t*); 57.2 (*d*); 22.9 (*q*). ^{11}B-NMR ((D_6)DMSO, 128.4 MHz): –13.8 ppm. Anal. calc. for $C_{37}H_{45}BN_2O_5 \cdot H_2O$ (626.5): C 70.92, H 7.56, N 4.47; found: C 70.78, H 7.27, N 4.39.

On a larger scale (3.2 g), the conversion of **30** into **31** was complete within 2 h. Longer reaction time led to the formation of **32** as a by-product, diminishing the yields of **33**.

N-{(2R,3S,4S)-4-(Benzyloxy)-2-[(1'S,2'R)-1',2',3'-tris(benzyloxy)propyl]pyrrolidin-3-yl}acetamid (**34**). A soln. of **33** (50.0 mg, 0.078.mmol) in EtOH (5ml) was heated at 70° for 15 h and then evaporated. FC ($CHCl_3$/MeOH 100:1) of the residue gave **34** (45 mg, 96.%) as colorless crystals. Recrystallization from AcOEt and hexane gave an anal. sample. R_f($CHCl_3$/MeOH 100:1) 0.20. M.p. 85–87° (from AcOEt/hexane). $[\alpha]_D$ = –23.4 (c = 2.25). IR: 3440*w*, 3340*w*, 3090*w*, 3070*w*, 3000*m*, 2920*m*, 2870*m*, 1670*s*, 1510*m*, 1495*m*, 1455*m*, 1370*m*, 1200*w*, 1190*s*, 1070*s*, 1030*m*, 910*w*, 690*w*, 660*w*. ^{1}H-NMR: 7.34–7.25 (*m*, 20 arom. H); 5.48 (*d*, J = 8.2, AcNH); 4.72–4.59 (*m*, 4 PhCH_2); 4.23 (*ddd*, J = 2.3, 7.5, 7.5, H–C(3)); 3.86 (*m*, H–C(4), H–C(1')); 3.80 (*m*, CH_2(3')); 3.69 (*ddd*, J = 2.7, 5.3, 5.3, H–C(2')); 3.05 (*m*, H–C(2), H_a–C(5)); 2.93 (*dd*, J = 5.5, 12.3, H_b–C(5)); 1.88 (*s*, Ac). ^{13}C-NMR: 169.5 (*s*); 138.3 (*s*); 138.2 (*s*); 138.1 (*s*); 137.8 (*s*); 128.2–127.3 (*d*); 85.5 (*d*); 78.9 (*d*); 77.0 (*d*); 74.5 (*t*); 73.3 (*t*); 72.5 (*t*); 70.6 (*t*); 68.7 (*t*); 65.5 (*d*); 57.9 (*d*); 52.0 (*t*); 23.2 (*q*). CI-MS: 595.7 ([M + 1]). Anal. calc. for $C_{37}H_{42}N_2O_5$ (594.7): C 74.72, H 7.12, N 4.71; found: C 74.74, H 7.33, N 4.55.

*3-(N-Acetyl-N-benzylamino)-2,5,6,7-tetra-O-benzyl-1-O-[(tert-butyl)dimethylsilyl]-3-deoxy-*D-glycero-D-galacto-*heptitol* (**35**). (*t*-Bu)Me_2SiCl (140 mg, 1.1 equiv.) and imidazole (170 mg, 3 equiv.) were added at r.t. to a stirred soln. of **15** (600 mg, 0.83 mmol), in DMF (7 ml). After 15 min, further (*t*-Bu)Me_2SiCl (38 mg, 0.3 equiv.) was added, and after 20 h the solvent was evaporated. FC of the residue gave **35** (587 mg, 81.4%). Oil. R_f(AcOEt/hexane 1:5) 0.30. $[\alpha]_D$ = –27.7 (c = 5.5). IR: 3480*w*, 3090*w*, 3070*w*, 3000*m*, 2960*s*, 2930*s*, 2890*m*, 2860*s*, 1640*s*, 1495*w*, 1455*m*, 1410*m*, 1360*m*, 1320*w*, 1250*m*, 1240–1200*m*, 1095*s*, 1030*w*, 940*w*, 835*m*, 810*m*, 780–720*m*. ^{1}H-NMR (200 MHz, (D_6)DMSO, 140°): 7.35–7.13 (*m*, 25 arom. H); 4.73–4.46 (*m*, 11 H); 4.23–4.13 (*m*, 2 H); 3.86–3.56 (*m*, 7 H); 1.97 (*s*, Ac); 0.88 (*s*, *t*-Bu); 0.034, 0.028 (2*s*, Me_2Si). ^{13}C-NMR: 173.6 (*s*); 140.3 (*s*); 138.8 (*s*); 138.1 (*s*); 137.9 (*s*); 137.8 (*s*); 128.9–126.6 (*d*); 79.6 (*d*); 79.1 (*d*); 76.5 (*d*); 74.2 (*t*); 73.4 (*t*). 73.2 (*t*); 71.2 (*t*); 70.1 (*t*); 69.3 (*d*); 62.0 (*t*); 60.0 (*d*); 47.0 (*t*); 25.0 (*q*); 22.1 (*q*); 18.2 (*s*); –5.5 (*q*); –5.4 (*q*); minor component: 65.4 (*d*); 22.2 (*q*); major/minor 10:1. Anal. calc. for $C_{50}H_{63}NO_7Si$ (818.10): C 73.40, H 7.76, N 1.71; found: C 73.31, H 7.50, N 1.74.

Tosylation of **35**. NaH (55%, 5 mg, 3 equiv.) and subsequently a soln. of TsCl (17 mg, 1.2 equiv.) in DMF (1 ml) were added at r.t. to a soln. of **35** (60 mg, 0.073 mmol) in DMF (2 ml). After 2 h, more TsCl (17 mg, 1.2 equiv.) was added. After 24 h, the mixture was evaporated under high vacuum. The residue was worked up in the usual way. FC gave **39** (34 mg, 68%), identical with the product obtained from the reaction of **15** with methanesulfonyl chloride (MsCl; see below).

*4-O-Acetyl-3-(N-acetyl-N-benzylamino)-2,5,6,7-tetra-O-benzyl-1-O-[(tert-butyl)dimethylsilyl]-3-deoxy-*D-glycero-D-galacto-*heptitol* (**36**). A soln. of **35** (180 mg, 0.22 mmol) in pyridine (2 ml) and Ac_2O (1 ml) was heated at 100° for 20 h and then evaporated. The residue was co-evaporated twice with toluene, dissolved in CH_2Cl_2, washed with H_2O, and dried. FC (AcOEt/hexane 1:7) of the residue gave **36** (157 mg, 83%). R_f(AcOEt/hexane 1:5) 0.50. $[\alpha]_D$ = +10.2 (c = 3.0). IR: 3095*w*, 3070*w*, 3040*w*, 2960*m*, 2950*s*, 2890*m*, 2860*s*, 2250*w*, 1740*s*, 1645*s*, 1497*w*, 1455*m*, 1420*m*, 1330*m*, 1235*s*, 1100*s*, 1075*s*, 1030*s*, 840*s*, 780–690*w*. ^{1}H-NMR (200

MHz, (D_6)DMSO, 140°): 7.35–7.08 (*m*, 25 arom. H); 5.65 (*dd*, *J* = 8.7, 1.7, H–C(4)); 4.70–4.35 (*m*, 11 H); 3.80–3.63 (*m*, 7 H); 1.92, 1.90 (2*s*, 2 Ac); 0.87 (*s*, *t*-Bu); 0.026, 0.021 (2 *s*, Me_2Si). ^{13}C-NMR: 173.7 (*s*); 170.2 (*s*); 170.0 (*s*); 139.2 (*s*); 138.6 (*s*); 138.5 (*s*); 138.4 (*s*); 138.3 (*s*); 138.2 (*s*); 138.1 (*s*); 138.0 (*s*); 137.9 (*s*); 137.8 (*s*); 128.8–126.1 (*d*); 79.7 (*d*); 78.9 (*d*); 78.5 (*d*); 78.4 (*d*); 77.5 (*t*); 77.2 (*d*); 73.2 (*t*); 72.8 (*t*); 72.5 (*t*); 71.6 (*t*); 70.2 (*d*); 69.7 (*d*); 68.8 (*d*); 65.9 (*t*); 60.8 (*t*); 57.8 (*d*); 53.7 (*d*); 50.0 (*t*); 47.6 (*t*); 25.7 (*q*); 22.5 (*q*); 22.2 (*q*); 21.0 (*q*); 18.0 (*s*); –5.5 (*s*); ratio of the two rotamers *ca.* 1:1. Anal. calc. for $C_{52}H_{65}NO_8Si$ (860.10): C 72.60, H 7.62, N 1.63; found: C 72.82, H, 7.68, N 1.60.

*1-*O*-Acetyl-3-(*N*-acetyl-*N*-benzylamino)-2,5,6,7-tetra-*O*-benzyl-3-deoxy-*D*-glycero-*D*-galacto-heptitol* (**37**). *a*) Ac_2O (140 mg, 7 equiv.) was added at r.t. to a soln. of **15** (130 mg, 0.186 mmol) in CH_2Cl_2 (5 ml) and pyridine (1 ml). When **15** was consumed (40 h), MeOH (1 ml) was added, the mixture was evaporated, and co-evaporated with toluene. FC (AcOEt/hexane 1:2) of the residue gave **37** (113 mg, 81.7%).

b) $Bu_4NF \cdot 3\ H_2O$ (50 mg, 1.2 equiv.) was added at r.t. to a soln of **36** (110 mg, 0.128 mmol) in THF (10 ml). When, according to TLC, **36** was consumed (0.5 h), the soln. was evaporated. FC (AcOEt/hexane 1:2) yielded **37** (72 mg, 84%). Oil. R_f(AcOEt/hexane 1:1) 0.80. $[\alpha]_D = -21.0$ (*c* = 2.9). IR: 3460*w*, 3095*w*, 3070*w*, 3040*w*, 3005*m*, 2920*m*, 2870*m*, 1740*s*, 1645*s*, 1495*w*, 1453*m*, 1410*m*, 1365*m*, *1325m*, 1240–1200*s*, 1095*s*, 1075*s*, 1045*m*, 1030*m*, 985*w*, 695*w*. ^{1}H-NMR (200 MHz, (D_6)DMSO, 140°): 7.37–7.14 (*m*, 25 arom. H); 4.69–4.48 (*m*, 10 H); 4.35–4.04 (*m*, 5 H); 3.82–3.71(*m*, 2 H); 3.64–3.56 (*m*, 2 H); 1.95 (*s*, Ac); 1.94 (*s*, Ac). ^{13}C-NMR: 173.4 (*s*); 173.0 (*s*); 170.5 (*s*); 170.2 (*s*); 139.8 (*s*); 138.5 (*s*); 138.2 (*s*); 138.1 (*s*); 138.0 (*s*);137.8 (*s*); 137.6 (2*s*); 137.5 (*s*); 128.7–126.4 (*d*); 78.9 (*d*); 78.8 (*d*); 77.1 (*d*); 76.6 (*d*); 76.4 (*d*); 76.3 (*d*); 74.1 (*t*); 74.0 (*t*); 73.8 (*t*); 73.4 (*t*); 73.1 (*t*); 72.7 (*t*); 71.1 (*t*); 69.8 (*t*); 69.4 (*d*); 69.0 (*t*); 67.4 (*d*); 64.3 (*t*); 63.0 (*t*); 60.5 (*d*); 55.3 (*d*); 50.0 (*t*); 46.9 (*t*); 22.5 (*q*); 21.9 (*q*); 20.8 (*q*); 20.7 (*q*); ratio of the two rotamers *ca.* 1:1. Anal. calc. for $C_{46}H_{51}NO_8$ (745.87): C 74.07, H 6.89, N 1.88; found: C 74.00, H 7.03, N 1.91.

*1,4-Di-*O*-acetyl-3-(*N*-acetyl-*N*-benzylamino)-2,5,6,7-tetra-*O*-benzyl-3-deoxy-*D*-glycero-*D*-galacto-heptitol* (**38**). A soln. of **15** (210 mg, 0.3 mmol) in pyridine (2 ml) and Ac_2O (1 ml) was kept at 100° for 20 h and then evaporated. The residue, obtained after co-evaporation with toluene, was purified by FC (AcOEt/hexane 1:3): **38** (180 mg, 76%) as an oil. R_f(AcOEt/hexane 1:2) 0.45. $[\alpha]_D = +12.0$ (*c* = 4.06). IR: 3090*w*, 3070*w*, 3040*w*, 3000*w*, 2900*w*, 2870*w*, 1740*s*, 1645*s*, 1500*w*, 1455*m*, 1410*m*, 1370*s*, 1240–1200*s*, 1095*s*, 1045*s*, 1030*s*, 985*w*, 900*w*, 695*w*. ^{1}H-NMR (200 MHz, (D_6)DMSO, 140°): 7.37–7.11 (*m*, 25 arom. H); 5.66 (*dd*, *J* = 8.7, 2.4, H–C(4)); 4.90 (*d*, *J* = 5.3, 1 H); 4.69–4.29 (*m*, 11 H); 4.13–3.97 (*m*, 2 H); 3.77–3.64 (*m*, 4 H); 1.94 (*s*, Ac); 1.91 (*s*, 2 Ac). ^{13}C-NMR: major isomer: 173.8 (*s*); 170.5 (*s*); 170.1 (*s*); 138.9 (*s*); 138.5 (*s*); 138.2 (*s*); 138.1 (*s*); 137.8 (*s*); 128.7–126.4 (*d*); 78.5 (2*d*); 76.6 (2*d*); 74.8 (*t*); 73.2 (*t*); 73.0 (*t*); 72.9 (*t*); 68.8 (*t*); 64.0 (*t*); 58.8 (*d*); 47.5 (*t*); 22.6 (*t*); 21.0 (*q*); 20.7 (*q*); minor isomer: 173.3 (*s*); 170.1 (*s*); 170.0 (*s*); 138.4 (*s*); 137.9 (*s*); 137.8 (*s*); 137.7 (*s*); 137.3 (*s*); 77.2 (*d*); 76.8 (*d*); 75.5 (*d*); 72.8 (*t*); 72.5 (*t*); 71.9 (*t*); 70.2 (*t*); 69.7 (*d*); 62.2 (*t*); 53.7 (*d*); 50.4 (*t*); 22.1 (*q*); 21.0 (*q*); 20.7 (*q*); major/minor *ca.* 3:1. Anal. calc. for $C_{48}H_{53}NO_9$ (787.91): C 73.16, H 6.78; N 1.78; found: C 72.98, H 6.80, N 1.75.

*3-(*N*-Acetyl-*N*-benzylamino)-1,4-anhydro-2,5,6,7-tetra-*O*-benzyl-3-deoxy-*D*-glycero-*D*-galacto-heptitol* (**39**). MsCl (44 mg, 30 µl, 4 equiv.) was added at 0° to a soln. of **15** (120 mg) in pyridine (5 ml). After 20 h at r.t. additional MsCl (44 mg) was added. The mixture was processed in the usual way after 3 h to give, after FC (AcOEt/hexane 1:2), besides unchanged **15** (40 mg, 30%) and **39** (60 mg, 51.7%) as oils. R_f(AcOEt/hexane 1:1) 0.6. $[\alpha]_D = +6.8$ (*c* = 3.4). IR: 3090*w*, 3070*w*, 3000*m*, 2930*w*, 2870*w*, 1645*s*, 1495*w*, 1455*m*, 1440*w*, 1400*w*, 1365*w*, 1250–1200*m*, 1095*s*, 1030*s*, 990*w*, 680*w*. ^{1}H-NMR (400 MHz): 7.37–7.13 (*m*, 25 arom. H); 4.78–4.20 (*m*, 5 PhCH_2, H–C(2), H–C(3), H–C(4)); 4.03 (*dd*, *J* = 9.4, 5.4, H_a–C(1)); 3.91 (*dd J* = 9.4, 3.8, H_b–C(1)); 8.85 (*ddd*, *J* = 7.2, 4.3, 2.6, H–C(6)); 3.80 (*dd*, *J* =10.6, 2.6, H_a–C(7)); 3.74 (*dd*, *J* = 7.2, 2.3, H–C(5)); 3.69 (*dd*, *J* = 10.6, 4.3, H_b–C(7)); 2.02 (*s*, Ac). Anal. calc for $C_{44}H_{47}NO_6$ (685.8): C 77.05, H 6.91, N 2.04; found: C 76.99, H 6.95, N 2.13.

{(2'R,3'S,4'S)-3'-Acetamido-4'-(benzyloxy)-2'-[(1"S,2"R)-1",2",3"-tris(benzyloxy)propyl]pyrrolidin-1'-yl}-acetic Acid (**40**). A mixture of glyoxylic-acid monohydrate (40 mg, 0.43 mmol); **33** (100 mg, 0.168 mmol) and THF (10 ml) was stirred at r.t. for 3 h and then evaporated. FC ($CHCl_3$/MeOH 10:1) of the residue gave **52** (85 mg, 77.5%). Oil. R_f($CHCl_3$/MeOH 10:2) 0.5. $[\alpha]_D = -13.0$ (*c* = 1.5). IR: 3095*w*, 3070*w*, 3000*m*, 2920*w*, 2870*w*, 1730*s*, 1680*s*, 1550*m*, 1520*m*, 1500*m*, 1455*m*, 1400*m*, 1370*m*, 1310*m*, 1260*m*, 1100*s*, 1130*m*, 910*m*, 840*m*, 690*m*, 660*m*. ^{1}H-NMR (400 MHz, acetone/MeOH): 7.30–7.16 (*m*, 20 arom. H); 4.64–4.37 (*m*, 4 PhCH_2, H–C(3')); 4.03 (*dd*, *J* = 3.1, 7.4, H–C(1"); 3.99 (*dd*, *J* = 1.9, 4.1, H–C(4')); 3.83 (*dd*, *J* = 4.9, 7.9. H–C(2")); 3.71–3.56 (*m*, H–C(2'), CH_2(3"), CH_2(2)); 3.36 (*dd*, *J* = 2.3, 11.0, H_a–C(5')); 3.28 (*dd*, *J* = 4.5, 11.0, H_b–C(5')); 1.82 (*s*, Ac). ^{13}C-NMR: 174.6 (*s*); 172.7 (*s*); 139.6 (*s*); 139.5 (*s*); 139.4 (*s*); 139.3 (*s*); 129.7–128.8 (*d*); 82.7 (*d*); 81.1 (*d*); 79.3 (*d*); 74.9 (*t*); 74.6 (*t*); 73.5 (*t*); 72.8 (*t*) 70.6 (*d*); 69.8 (*t*); 59. 0 (*t*); 58.4 (*d*, *t*); 23.1 (*q*). CI-MS: 609.5 ([*M* + 1 – CO_2]). Anal. calc. for $C_{39}H_{44}N_2O_7$ (652.75): C 71.75, H 6.79, N 4.29; found: C 71.65, H 6.55, N 4.29.

{(2'R,3'S,4'S)-3'-Acetamido-4'-hydroxy-2'-[(1"S,2"R)-1",2",3"-trihydroxypropyl]pyrrolidin-1'-yl}acetic Acid (**3**). A soln. of **40** (85 mg, 0.13 mmol) in MeOH (10 ml) and H_2O (2 ml) was hydrogenated in presence of 20% $Pd(OH)_2 \cdot H_2O$/C (30 mg) at 8 atm for 50 h. The filtered mixture was evaporated and freeze-dried to yield nearly colorless crystals of **3** (35 mg, 91%). R_f(acetone/H_2O 7:1) 0.2[9]). M.p. 154–158°. $[\alpha]_D$ = +13.4 (*c* = 3.0 H_2O). IR (KBr): 3700–2800 (br.), 1720*s*, 1680*s*, 1550*m*, 1400*s*, 1330*m*, 1080*m*, 1040*m*, 920*w*, 880*w*. ^{1}H-NMR (400 MHz, D_2O): 4.5 (*ddd* app. as *q*, *J* ≈ 4.7, H–C(4')); 4.43 (*t*, *J* = 5.0, H–C(3')); 4.08 (*dd*, *J* = 6.9, 5.1, H–C(1")); 4.11, 4.07, 3.95, 3.90 (*AB*, *J* = 16.0, CH_2(2)); 3.97 (*t*, *J* = 5.5, H–C(2')); 3.83 (*ddd*, *J* = 7.1, 5.5, 3.6, H–C(2")); 3.80 (*dd*, *J* = 11.6, 3.4, H_a–C(3")); 3.75 (*dd*, *J* = 12.4, 4.1, H_a–C(5')); 3.69 (*dd*, *J* = 12.5, 5.3, H_b–C(3")); 3.63 (*dd*, *J* = 12.3, 4.8, H_b–C(5')); 2.07 (*s*, Ac). ^{13}C-NMR (D_2O): 174.4 (*s*); 170.7 (*s*); 72.6 (*d*); 72.4 (*d*); 70.7 (*d*); 68.6 (*d*); 62.6 (*t*); 59.8 (*t*); 58.3 (*d*); 58.0 (*t*); 22.4 (*q*). CI-MS: 249.3 ([*M* + 1 – CO_2]) . Anal. calc. for $C_{11}H_{20}N_2O_7 \cdot H_2O$ (310.30): C 42.55, H 7.14, N 9.02; found: C 42.90, H 6.92, N 8.66.

Dibenzyl (Hydroxymethyl)phosphonate (**41**). A mixture of dibenzyl phosphite (7.9 g, 30 mmol); paraformaldehyde (1.0 g, 33.3 mmol), and Et_3N (0.45 ml, 3.2 mmol) was heated at 130° until the soln. turned colorless to give, after FC (AcOEt/hexane 3:1), **41** (5.2 g, 59%). Oil. R_f(AcOEt/hexane 3:2) 0.2. IR: 3600*w*, 3320*m*, 3100*w*, 3035*w*, 3020*w*, 3000*m*, 2960*w*, 2900*w*, 1600*w*, 1500*w*, 1455*m*, 1380*w*, 1230*s*, 1020*s*, 920*w*, 890*m* 690*m*. ^{1}H-NMR (300 MHz): 7.24–7.19 (*m*, 10 arom. H); 5.01–4.88 (*m*, 2 PhCH_2); 4.75–4.69 (*m*, OH); 3.84 (*t*, *J* = 5.9, CH_2P). ^{13}C-NMR: 136.0 (*s*); 135.9 (*s*); 128.5–127.9 (*d*); 68.0, 67.9 (*t*, *J*(P,C) = 6.8, PhCH_2); 58.9, 55.7 (*t*, *J*(P,C)= 160.8, CH_2P). ^{31}P-NMR: 25.7 (*s*). Anal. calc. for $C_{15}H_{17}N_2O_4P$ (292.27): C 61.64, H 5.86; found: C 61.80, H 6.00.

Dibenzyl{[(trifluoromethanesulfonyl)oxy]methyl}phosphonate (**42**) *and Tetrabenzyl Oxybis(methylen)-bis[phosphonate]* (**43**). A stirred suspension of 99% granular NaH (170 mg, 7.0 mmol) in Et_2O (12 ml) was treated with a soln. of TfCl (1.03 g, 6.1 mmol) in Et_2O (2 ml) and cooled to –20°. Immediately afterwards, a soln. of **41** (1.5 g, 5.1 mmol) in Et_2O (4 ml) was added dropwise, while keeping the temp. between –15 and –20°. After stirring the mixture for 1 h at –20°, it was rapidly filtered through *Celite*, extracted with sat. aq. $NaHCO_3$ soln. (3 × 5 ml) and evaporated. FC (AcOEt/hexane 3:1) of the residue gave **42** (930 mg, 43 %) and **43** (360 mg, 25 %) as syrups.

Data of **42**: R_f(AcOEt/hexane 3:2) 0.7. IR: 3080*w*, 3060*w*, 3040*w*, 3000*w*, 2950*w*, 2900*w*, 1420*s*, 1250*s*, 1190*s*, 990*s*, 840*m*, 690*m*. ^{1}H-NMR (300 MHz): 7.32–7.26 (*m*, 10 arom. H); 5.03 (*m*, 2 PhCH_2); 4.34 (*d*, *J* = 8.9, PCH_2). ^{13}C-NMR: 134.9 (*s*); 134.8 (*s*); 129.8–127.6 (*d*); 69.4, 69.2(*t*, *J*(P,C) = 6.5, PhCH_2); 68.2, 64.9 (*t*, *J*(P,C) = 169.0, CH_2P). ^{31}P-NMR: 13.8 (*s*). CI-MS: 425.1 ([*M* + 1]$^+$). Anal. calc. for $C_{16}H_{16}F_3O_6PS$ (424.34): C 45.28, H 3.80, F 13.43; found: C 45.01, H 4.05, F 13.69.

Data of **43**: R_f(AcOEt/hexane 3:2) 0.4. IR: 3450*w*, 3090*w*, 3070*w*, 3030*w*, 3000*m*, 2950*w*, 2900*w*, 1730*s*, 1490*w*, 1450*m*, 1420*w*, 1350*w*, 1340*s*, 1240*s*, 1080*m*, 1000*s*, 970*s*, 915*m*, 890*m*, 850*m*, 690*m*, 660*m*. ^{1}H-NMR (300 MHz): 7.34–7.26 (*m*, 20 arom. H); 5.13 (*m*, 4 PhCH_2); 4.35 (*d*, *J* = 8.5, PCH_2). ^{13}C-NMR: 135.5 (*s*); 135.4 (*s*); 128.6–128.0 (*d*); 68.4, 62.2 (*t*, *J*(P,C) = 6.2, PhCH_2); 62.8, 59.4 (*t*, *J*(P,C)= 169.1, CH_2P). ^{31}P-NMR: 18.52 (*s*). Anal. calc. for $C_{30}H_{32}O_7P$ (566.53): C 63.60, H 5.69; found: C 63.36, H 5.77.

Dibenzyl {{(2'R,3'S,4'S)-3'-Acetamido-4'-(benzyloxy)-2'-[(1"S,2"R)-1",2",3"-tris(benzyloxy)propyl]-pyrrolidin-1'-yl}methyl}phosphonate (**44**). A soln. of **42** (140 mg, 0.32 mmol) and **33** (130 mg, 0.21 mmol) in Et_2O (10 ml) was stirred at r.t. After 4 d, the mixture was washed with 2N NaOH (5 ml), H_2O, and dried. FC (AcOEt/hexane 3:2) of the residue, gave **44** (105 mg, 55%). Oil. R_f(AcOEt/hexane 3:1) 0.3. $[\alpha]_D$ = –3.3 (*c* = 8.5). IR: 3290*w*, 3090*w*, 3060*w*, 3040*w*, 3000*m*, 2940*w*, 2910*w*, 2860*w*, 1730*s*, 1550*w*, 1500*w*, 1450*m*, 1370*m*, 1230*m*, 1100*s*, 1039*s*, 990*s*, 920*w*, 880*w*, 690*w*, 660*m*. ^{1}H-NMR (400 MHz): 7.61 (*d*, *J* = 7.1, AcNH); 7.35–7.19 (*m*, 30 arom. H); 5.05–4.45 (*m*, 6 PhCH_2); 4.39 (*d*, *J* = 7.1, H–C(3')); 3.98 (*dd*, *J* = 2.7, 9.5, H–C(1")); 3.86 (*d*, *J* = 3.6, H–C(4')); 3.74 (*m*, H–C(2"), H_a–C(2)); 3.64 (*m*, H_a–C(3"), H_b–C(2)); 3.32 (*dd*, *J* = 3.2, 7.0, H–C(2')); 3.26 (*dd*, *J* = 6.4, 16.4, H_b–C(3")); 3.16 (*m*, CH_2(5')); 1.88 (*s*, Ac). ^{13}C-NMR: 169.1 (*s*); 138.9 (*s*); 138.3 (*s*); 138.2 (*s*); 138.1 (*s*); 135.8 (*s*); 135.75 (*s*); 135.72 (*s*); 135.6 (*s*); 128.9–127.0 (*d*); 83.0 (*d*); 82.5 (*d*); 79.9 (*d*); 74.4 (*t*); 73.0 (*t*); 71.9 (*t*); 70,8 (*t*); 69.7 (*t*); 68.4 (*d*); 68.3 (*t*); 67.0 (*t*); 66.9 (*t*); 66.8 (*t*); 66.7 (*t*); 66.6 (*t*); 56.3 (*d*); 56.0 (*t*); 50.7, 48.3 (*t*, *J*(P,C(2)) = 124.6, C(2)); 23.0 (*q*). ^{31}P-NMR: 30.53 (*s*). CI-MS: 870.0 ([*M* + 1]). Anal. calc. for $C_{52}H_{57}N_2O_8P$ (869.01): C 71.87, H 6.61, N 3.22; found: C 71.80, H 6.82, N 3.02.

{{(2'R,3'S,4'S)-3'-Acetamido-4'-hydroxy-2'-[(1"S,2"R)-1",2",3"-trihydroxypropyl]pyrrolidin-1'-yl}methyl}phosphonic Acid (**4**). A soln. of **44** (155 mg, 0.178 mmol) in MeOH (15 ml) and H_2O (3 ml) was hydrogenated in the presence of 20% $Pd(OH)_2 \cdot H_2O$ (60 mg) at 8 atm for 60 h. The filtered catalyst was washed with MeOH. The combined filtrate and washings were evaporated. A soln. of the residue in 5 ml of H_2O was freeze-dried to yield **4**. R_f(Aceton/H_2O 3:1) 0.2. M.p. 193–197°. $[\alpha]_D$ = +19.7 (*c* = 1.5, H_2O). IR (KBr):

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[9]) The spot was revealed by treatment with 0.1M $KMnO_4$/1M H_2SO_4 and heating at *ca.* 250°.

3700–2700(br.), 1650*s*, 1550*m*, 1430*m*, 1380*m*, 1310*m*, 1170*m*, 1070*s*, 920*m*, 760*m*. ^{1}H-NMR (400 MHz, D_2O): 4.45 (*ddd* app. as *q*, *J* ≈ 3.4, H–C(2")); 4.37 (*t*, *J* = 3.4, H–C(1")); 4.07 (*t*, *J* = 6.2, H–C(3')); 4.02 (*t*, *J* = 5.7, H–C(2')); 3.83 (*ddd*, *J* = 3.7, 5.6, 9.3, H–C(4')); 3.77 (*m*, CH_2(3")); 3.79, 3.76, 3.67, 3.64 (*AB*, *J* = 11.8, CH_2(2)); 3.64 (*t*, *J* = 11.8, H_a–C(5')); 3.50 (*dd* app. as *t*, *J* ≈ 11.6, H_b–C(5')); 2.01 (*s*, Ac). ^{13}C-NMR (D_2O): 174.3 (*s*); 73.3 (*d*); 72.6 (*d*); 72.5 (*d*); 68.4 (*d*); 62.5 (*t*); 59.8 (*t*); 58.0 (*d*); 54.3, 51.6 (*t*, *J*(P,C(2)) = 135.3, C(2)); 22.3 (*q*). ^{31}P-NMR (81 MHz, D_2O): 8.5 (*s*). FAB-MS: 347.3 ([*M* + 1]). Anal. calc. for $C_{10}H_{21}N_2O_8P \cdot H_2O$ (346.28): C 34.68, H 6.69, N 8.09; found: C 34.48, H 6.59, N 8.08.

Methyl {(2'R,3'S,4'S)-3'-Acetamido-4'-(benzyloxy)-2'-[(1"S,2"R)-1",2",3"-tris(benzyloxy)propyl]-pyrrolidin-1'-yl}oxoacetate (**45**) *and Methyl {(2'R,3'S,4'S)-3'-[*N*-Acetyl-*N*-(methoxalyl)amino]-4'-(benzyloxy)-2'-[(1"S,2"R)-1",2",3"- tris(benzyloxy)propyl]pyrrolidin-1'-yl}oxoacetate* (**46**). To a stirred soln. of **33** · HCl at r.t., prepared from **33** (600 mg, 1 mmol) in CH_2Cl_2 (40 ml), were added a soln. of methoxalyl chloride (170 mg, 0.128 ml, 1.4 equiv.) in CH_2Cl_2 (17 ml) and then a soln. of Et_3N (170 mg, 0.236 ml, 1.7 equiv.) in CH_2Cl_2 (8.5 ml). After 20 min, further methoxalyl chloride (30 mg) and, after 30 min, MeOH (1 ml) were added. Usual workup and FC (AcOEt/hexane 3:1) gave **46** (76 mg, 11%) and **45** (476 mg, 70%), both as oils. Upon washing the mixture obtained after addition of MeOH with 1N NaOH, **46** was converted into **45**, which was isolated in a yield of 78%.

Data of **45**: R_f(AcOEt/hexane 1:1) 0.50. $[\alpha]_D$ = –0.5 (*c* = 4.3). IR: 3430*w*, 3300*w*, 3060*w*, 3030*w*, 2990*w*, 2950*m*, 2865*m*, 1735*s*, 1650*s*, 1490*s*, 1450*s*, 1425*m*, 1364*s*, 1325*m*, 1250–1200*s*, 1100*s*, 1025*m*, 910*w*, 690*w*. ^{1}H-NMR (400 MHz): 7.49–7.16 (*m*, 20 arom. H); 5.57 (*d*, *J* = 6, AcN*H*); 4.63 (*d*, *J* = 10.2, H–C(2)); 4.69–4.41 (*m*, 4 PhC*H*$_2$, H–C(3')); 4.04 (*dd*, *J* = 10.2, 3.0, H–C(1")); 4.04 (*d*, *J* = 6.3, H–C(4')); 3.84 (*dd*, *J* = 14.3, 6.3, H_a–C(5')); 3.75–3.62 (*m*, H–C(6), H_a–C(3")); 3.59 (*dd*, *J* = 9.0, 3.8, H_b–C(3")); 3.48 (*s*, MeO); 3.46 (*d*, *J* = 14.3, H_b–C(5')); 1.77 (*s*, Ac). ^{13}C-NMR: 169.8 (*s*); 161.8 (*s*); 159.6 (*s*); 138.1 (*s*); 138.0 (*s*); 137.3 (*s*); 137.0 (*s*); 129.0–127.1 (*d*); 79.9 (2*d*); 75.6 (*d*); 74.3 (*t*); 73.1 (*t*); 72.1 (*t*); 71.1 (*t*); 68.9 (*t*); 63.9 (*d*); 56.2 (*d*); 51.9 (*q*); 51.4 (*t*); 22.6 (*q*). CI-MS: 681.5 (100, $[M + 1]^+$). Anal. calc. for $C_{40}H_{44}N_2O_8$ (680.77): C 70.57, H 6.52, N 4.11; found: C 70.44, H 6.57, N 4.10.

Data of **46**: R_f(AcOEt/hexane 1:1) 0.75. $[\alpha]_D$ = +26.2 (*c* = 3.2). IR: 3090*w*, 3070*w*, 3040*w*, 3000*w*, 2950*w*, 2870*w*, 1740*s*, 1690*s*, 1660*s*, 1455*m*, 1435*m*, 1425*m*, 1365*m*, 1250–1200*s*, 1090*s*, 1070*s*, 1025*m*, 690*w*. ^{1}H-NMR (200 MHz, (D_6)DMSO, 22°): 3.80, 3.78 (2*s*, 2 MeO); 2.16, 2.09 (2*s*, Ac); ratio of the two rotamers *ca.* 1:3, coalescence at 120°. ^{13}C-NMR major isomer: 173.9 (*s*); 163.4 (*s*); 162.1 (*s*); 161.3 (*s*); 158.9 (*s*); 137.9–136.8 (*s*); 129.4–127.5 (*d*); 80.3 (*d*); 78.1 (*d*); 77.1 (*d*); 73.5 (*t*); 73.4 (*t*); 73.3 (*t*); 73.1 (*t*); 70.4 (*t*); 63.9 (*d*); 57.1 (*d*); 52.9 (*q*); 52.8 (*q*); 52.4 (*q*); 51.7 (*t*); 23.2 (*q*); minor isomer: 173.7 (*s*); 163.4 (*s*); 162.1 (*s*); 161.7 (*s*); 158.6 (*s*); 137.9–136.8 (*s*); 129.4–127.5 (*d*); 79.8 (*d*); 78.8 (*d*); 78.3 (*d*); 74.3 (*t*); 73.4 (*t*); 72.8 (*t*) 72.5 (*t*); 68.1 (*t*); 66.3 (*d*); 60.2 (*d*); 52.9 (*q*); 52.8 (*q*); 52.4 (*q*); 49.7 (*t*); 23.3 (*q*).

{(2'R,3'S,4'S)-3'-Acetamido-4'-(benzyloxy)-2'-[(1"S,2"R)-1",2",3"-tris(benzyloxy)propyl]pyrrolidin-1'-yl}oxoacetatic Acid (**47**). At r.t., 2M NaOH (1.5 ml) was added to a stirred soln. of **45** (990 mg, 1.45 mmol) in MeOH (50 ml). After 2 h, the mixture was filtered over charcoal and neutralized with solid CO_2. A soln. of the residue of the filtrate in CH_2Cl_2 was washed with 0.5M H_2SO_4 (10 ml) and H_2O, dried, and evaporated: **47** (727 mg, 75%) as a foam. R_f(AcOEt/AcOH/H_2O 9:2:2) 0.80. $[\alpha]_D$ = –19.6 (*c* = 6.9). IR: 3430*w*, 3290*w*, 3090*w*, 3060*w*, 3030*w*, 3000*w*, 2930*w*, 2870*w*, 1780*w*, 1740*w*, 1675*s*, 1660*s*, 1645*s*, 1490*m*, 1452*m*, 1370*m*, 1330*m*, 1310*m*, 1100*s*, 1045*m*, 1025*m*, 690*w*. ^{1}H-NMR (400 MHz): 7.33–7.21 (*m*, 18 arom. H); 7.13–7.08 (*m*, 2 arom. H); 5.91 (*d*, *J* = 6.0, AcNH); 4.87–4.39 (*m*, 4 PhC*H*$_2$, H–C(3'), H–C(2')); 4.11 (*dd*, *J* = 9.7, 4.4, H–C(1")); 4.08 (*d*, *J* = 5.5, H–C(4')); 3.86 (*dd*, *J* = 14.4, 5.5, H_a–C(5')); 3.78–3.71 (*m*, H–C(6), H_a–C(3")); 3.59 (*d*, *J* = 9.6, 3.7, H_b–C(3")); 3.51 (*d*, *J* = 14.4, H_b–C(5')); 1.80 (*s*, Ac). ^{13}C-NMR: 170.5 (*s*); 161.2 (*s*); 160.1 (*s*); 138.0 (2*s*); 137.4 (*s*); 136.4 (*s*); 128.9–127.3 (*d*); 80.3 (*d*); 79.9 (*d*); 75.3 (*d*); 74.4 (*t*); 73.2 (*t*); 72.3 (*t*); 71.4 (*t*); 68.7 (*t*); 64.5 (*d*); 57.4 (*d*); 52.3 (*t*); 22.7 (*q*).

{(2'R,3'S,4'S)-3'-Acetamido-4'-hydroxy-2'-[(1"S,2"R)-1",2",3"-trihydroxypropyl]pyrrolidin-1'-yl}oxoacetic Acid (**5**). A soln. of **47** (290 mg, 0.43 mmol) in MeOH (40 ml) and H_2O (5 ml) was hydrogenated in the presence of 20% $Pd(OH)_2 \cdot H_2O$/C (100 mg) at 8 atm for 48 h. The soln. was filtered over *Celite* and evaporated. Freeze-drying of the aq. soln. of the residue gave **5** (124 mg, 93%) as a microcrystalline solid. R_f(AcOEt/AcOH/H_2O 9:2:2) 0.05[9]. M.p. 228–229°. $[\alpha]_D$ = +61.8 (*c* = 1.6, H_2O). IR (KBr): 3400*s*, 1760*s*, 1690*s*, 1660–1640*s*, 1550*m*, 1455*m*, 1380*m*, 1310*m*, 1235*m*, 1195*m*, 1135*m*, 1085*m*, 1045*m*, 970*w*. ^{1}H-NMR (400 MHz, D_2O): 4.48 (*t*, *J* = 6.8, H–C(3')); 4.28–4.11 (*m*, H–C(2'), H–C(4')); 3.90 (*dd*, *J* = 11.3, 7.0, H_a–C(5')); 3.82 (*dd*, *J* = 11.5, 2.0, H_a–C(3")); 3.68 (*dd*, *J* = 9.2, 1.4, H–C(1")); 3.59 (*dd*, *J* = 11.5, 6.3, H_b–C(3")); 3.54 (*ddd*, *J* = 9.2, 6.3, 2.1, H–C(2")); 3.36 (*dd*, *J* = 11.3, 9.3, H_b–C(5')); 2.01 (*s*, Ac). ^{13}C-NMR: 174.8 (*s*); 158.6 (*s*); 153.6 (*s*); 83.4 (*d*); 73.1 (*d*); 70.1 (*d*); 61.3 (*t*); 58.9 (*d*); 57.8 (*d*); 49.7 (*t*); 22.6 (*q*).

N-{(1S,7S,8S,8aR)-1-[(1'R)-1',2'-Dihydroxyethyl]-3,4,6,7,8,8a-hexahydro-7-hydroxy-3,4-dioxo-1H-pyrrolo[1,2-d][1,4]oxazin-8-yl}acetamide (**48**). Freeze-dried **5** (194 mg) was dissolved at 80° in AcOH (4 ml). After 5 min, the lactone **48** started to precipitate. The mixture was cooled to +5° and filtered after 12 h. The precipitate was washed with AcOH and Et_2O: **48** (134 mg, 87%). R_f(AcOEt/AcOH/H_2O 3:2:2) 0.4. M.p. 230–231° (dec.). $[\alpha]_D$ = +39 (5 min), +63 (12 h); (*c* =1.0, H_2O). IR (KBr): 4430*s*, 3380*s*, 3360*s*, 3220w, 3020*w*, 2860*w*, 2840*m*, 2790*w*, 1770*s*, 1705*s*, 1650*s*, 1560*s*, 1470*m*, 1460*m*, 1430*w*, 1410*w*, 1385*w*, 1340*m*, 1330*m*, 1310*m*, 1060*m*, 1030*s*, 1010*m*, 970*m*, 960*w*, 940*w*, 930*w*, 880*w*, 870*w*, 820*w*, 800*w*, 730*w*, 710*w*, 690*w*, 650*w*. ^{1}H-NMR (400 MHz, (D_6)DMSO): 8.15 (*d*, *J* = 8.0, AcNH); 5.48 (*s*, OH–C(7)); 5.25 (*d*, *J* = 4.4, OH–C(1')); 4.71 (*dd*, *J* = 2.7, 10.7, H–C(1)); 4,57 (*s*, HO–C(2)); 4.18 (*dd*, *J* = 5.7, 10.9, H–C(8)); 4.05 (*m*, H–C(7), H–C(8a)); 3.71 (*s*, H–C(1')); 3.52 (*m*, CH_2(6), H_a–C(2")); 3.42 (*dd*, *J* = 6.4, 16.7, H_b–C(2")); 1.89 (*s*, Ac). ^{13}C-NMR ((D_6)DMSO): 169.8 (*s*); 157.4 (*s*); 151.9 (*s*); 83.2 (*d*); 72.6 (*d*); 70.1 (*d*); 61.5 (*t*); 59.6 (*d*); 57.7 (*d*); 50.3 (*t*); 23.0 (*q*). Anal. calc. for $C_{11}H_{16}N_2O_7$ (288.25): C 45.83, H 5.59, N 9.72; found: C 45.56, H 5.54, N 9.57.

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