132. Phosphonic-Acid Analogues of the *N*-Acetyl-2-deoxyneuraminic Acids: Synthesis and Inhibition of *Vibrio cholerae* Sialidase

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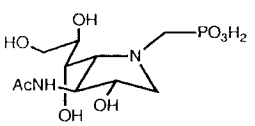
The phosphonic acids **3** and **4** were prepared to compare their inhibitory activity on *Vibrio cholerae* sialidase with the one of the corresponding *N*-acetyl-2-deoxyneuraminic acids **5** and **6**. Thus, hydrogenation and benzylation of methyl *N*-acetyl-2,3-didehydro-2-deoxyneuraminate (1MeNeu2en5Ac; **7**) gave a mixture of the fully *O*-benzylated benzyl and methyl esters **9** and **10**, the partially *O*-benzylated benzyl and methyl esters **11** and **12**, and the fully *O*- and *N*-benzylated benzyl and methyl esters **13** and **14** *(Scheme 1)*. Transesterification of **9** to **10** and hydrolysis of **10** gave the acid **15**. Oxidative decarboxylation of **15** with $Pb(OAc)_4$ gave a 1:9 mixture of the α- and β-D-*glycero*-D-*galacto*-acetates **16** and **17**. Phosphonoylation of **17** with $P(OMe)_3$ and Me_3SiOTf gave a 1.3:1 mixture of the phosphonates **18** and **19**, which were deprotected to give the (4-acetamido-2,4-dideoxy-D-*glycero*-α- and β-D-*galacto*-octopyranosyl)phosphonic acids **3** and **4**, respectively. The acid **6** was obtained by epimerization of the *tert*-butyl ester **23** with lithium *N*-cyclohexylisoproylamide and deprotection. The phosphonic acids **3** (K_i $5.5 \cdot 10^{-5}$ M) and **4** (K_i $2.3 \cdot 10^{-4}$ M) are stronger inhibitors of *Vibrio cholerae* sialidase than the anomeric *N*-acetyl-2-deoxyneuraminic acids **5** (K_i $2.6 \cdot 10^{-3}$ M) and **6**. Both **3** and **4** inhibit the *Vibrio cholerae* sialidase, while only the carboxylic acid **5**, possessing an equatorial COOH group is an inhibitor.

Introduction. – The phosphonic acid **1**, a pyrrolidine analogue of *N*-acetylneuraminic acid (Neu5Ac) is a notably stronger inhibitor of the *Vibrio cholerae* sialidase than the corresponding carboxylic acid **2** [1]. To probe the validity of the extrapolation according to which analogues of sialidase inhibitors possessing a phosphono (PO_3H_2) instead of a COOH group will be stronger inhibitors, we required the epimeric phosphonic acids **3** and **4** and the carboxylic acids **5** and **6**, which are more closely related to Neu5Ac than the pyrrolidines **1** and **2**. The relative inhibitory strength of the phosphonates **3** and **4** and of the carboxylates **5** and **6** is also of interest, as (2*S*)-6-amino-2,6-dideoxy-Neu5Ac possessing an equatorial COOH group is a moderatly strong inhibitor of the *N*-acetylneuraminidases from *Vibrio cholerae* and fowl plague virus, whilst the epimeric acid possessing axial COOH and HO–C(4) groups is not [2].



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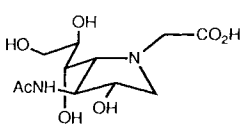

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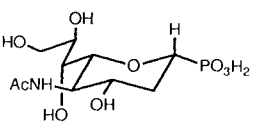

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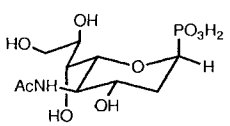

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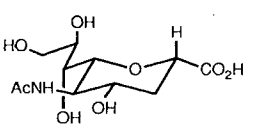

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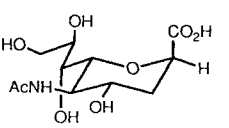

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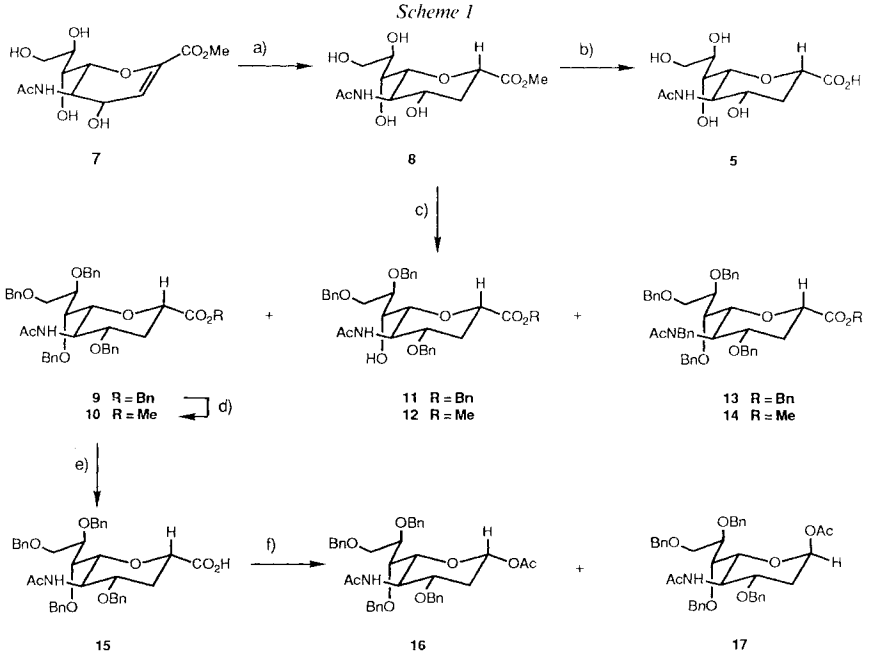
Plan. – The phosphonates **3** and **4** should be accessible from the glycosyl acetates **16** and **17** *(Scheme 1)* according to the method of *Meuwly* and *Vasella* [3]. The diastereoselectivity of this method which leads predominantly to 1,2-*cis*-configurated glycosylphosphonates from benzylated glycosyl acetates has been rationalized by a neighbouring effect of the 2-benzyloxy group[1]). 2-Deoxyglycosyl acetates such as **16** and **17** should, then, lead to mixtures of epimeric phosphonates. We hoped to obtain **16** and **17** by oxidative decarboxylation [5] of the benzylated 2-deoxy-Neu5Ac **15**. This acid may be prepared from Neu5Ac *via* the known methyl ester **7** of Neu2en5Ac [6–9]. The carboxylic acid **5** has been prepared by catalytic hydrogenation of Neu2en5Ac (83% [10]) and also by catalytic hydrogenation of protected Neu2en5Ac (95%) followed by deprotection [11]. A 1:4.5 [11] and a 1:10 [12] mixture of the acetylated methyl esters of **5** and **6** has been obtained by catalytic hydrogenation of acetochloro-Neu5Ac (79% [11], 55% from Neu5Ac [12]). Deprotection gave a mixture **5**/**6** [11]. We intended to prepare **6** by kinetic protonation of the enolate derived from the *tert*-butyl ester **23** *(Scheme 3)*[2]) (**23**→**24**) followed by hydrogenolysis (**24**→**25**) and hydrolysis of the ester.

Results and Discussion. – Neu5Ac, prepared by an improved procedure [9] according to *Kuhn* and *Baschang* [14], was converted into **7** (see [9] and ref. cit. therein). In

Scheme 1



a) 10% Pd/C, H_2, MeOH/H_2O, 100%. b) NaOH, H_2O, 92%. c) NaH, BnBr, DMF. d) NaOMe, MeOH, 61% from **8**. e) NaOH, MeOH, 100%. f) $Pb(OAc)_4$, Py, 60°, 65%, **16**/**17** = 1:9.

[1]) *Vaghefi et al.* [4] observed retention of configuration (in one case) and postulated a double inversion of configuration.

[2]) A similar epimerization of either one of the pure 2-epimers of protected 2-deoxy-KDO gave the axial and equatorial esters with a ratio of 4:1 [13].

agreement with previous work [10] [11], catalytic hydrogenation of **7** (10% Pd/C, aq. MeOH; *Scheme 1*) yielded exclusively the equatorial ester **8**, which was hydrolyzed to the acid **5** (92%). Benzylation of **8** ($PhCH_2Br$, NaH, DMF) gave a mixture of the fully *O*-benzylated benzyl and methyl esters **9** and **10**, the incompletely benzylated esters **11** and **12**, and small amounts of the *N*-benzylated esters **13** and **14**. Additional amounts of **9** and **10** were obtained by benzylation of **11** and **12**. Treatment of the combined mixtures **9**/**10** with NaOMe in MeOH gave the crystalline methyl ester **10** in 61% yield from **8**[3]). A mixture of the acetates **16** and **17** (65%, 1:9) was obtained by hydrolysis of **10** and decarboxylation of **15** with $Pb(OAc)_4$ in pyridine [5].

The chemical shifts in the ^{1}H-NMR spectra ($CDCl_3$) of **15** depend noticeably on the temperature (*Table 1*). At lower temperatures, the resonances of H–C(5), HN and CH_3CON are shifted to lower fields, in contrast to the signals of H–C(2), H–C(4), and H–C(6), which are shifted to higher fields. As the values of the coupling constants of H–C(2) to H–C(9) are hardly affected, this temperature dependence is presumably due to association phenomena and/or changes in the conformation of BnO groups.

The configuration at the anomeric center of **16** and **17** is evidenced both from the chemical shift of H–C(1) (*Table 2*), the coupling constants (*Table 3*), and the specific rotations. In the ^{1}H-NMR spectra of **16** and **17**, the chemical shifts of the anomeric protons are observed at 5.61 ppm for the α-D-anomer and at 6.28 ppm for the β-D-anomer. Given the $^1C_4$ conformation of **16** and **17** (*Table 3*), $^3J(1,2) = 10.2$ and 1.9 Hz in the spectra of **16**

Table 1. *^{1}H-NMR Data of* **15** *at Different Temperatures*

	Chemical shifts [ppm]				Coupling constants [Hz]		
	δ (298 K)	δ (283 K)	δ (273 K)		J(298 K)	J(283 K)	J(273 K)
H–C(2)	3.65	3.59	3.55	J (2,3ax)	12.3	12.3	12.2
H_{ax}–C(3)	1.57	1.56	1.55	J (2,3eq)	2.2	2.0	1.9
H_{eq}–C(3)	2.50	2.47	2.46	J (3ax, 3eq)	12.9	12.8	12.9
H–C(4)	3.60	3.46	3.41	J (3ax, 4)	10.7	11	11
H–C(5)	3.82–3.74	3.94	3.99	J (3eq, 4)	4.6	4.5	4.5
H–C(6)	3.82–3.74	3.62	3.57	J (4,5)	9.5	10.2	10.3
H–C(7)	3.82–3.74	3.79	3.79	J (5, N*H*)	8.6	9.4	9.6
H–C(8)	3.82–3.74	3.74	3.73	J (5,6)	–	11	10.5
H–C(9)	3.68	3.67	3.67	J (6,7)	–	0	0
H–C(9)	3.90	3.87	3.85	J (7,8)	–	8.6	8.9
AcN	1.84	1.90	1.92	J (8,9)	2.1	2.3	2.2
NH	4.82	4.93	4.97	J (8,9)	2.3	2.3	2.0
				J (9,9)	11	10.8	10.8

Table 2. *Spectroscopic Data of the Acetates and Phosphonates*

	^{1}H-NMR, chemical shifts [ppm]						
	δ (H–C(1))	δ (H_{ax}–C(2))	δ (H_{eq}–C(2))	δ (H–C(3))	δ (H–C(4))	δ (H–C(5))	δ (AcO)
16[a])	5.61	1.77	2.31	3.86–3.72	3.86–3.72	3.99	2.07
18[a])	3.70–3.87	1.79	2.43	3.87–3.70	3.87–3.70	3.87–3.70	
22[a])	3.80	1.97	2.30	5.01	3.99	3.66	
3[b])	3.85–3.78	1.69	2.26	3.85–3.78	3.85–3.78	3.62–3.57	
3[c])	3.80–3.69	1.70	2.24	3.80–3.69	3.80–3.69	3.49	
17[a])	6.28	1.84	2.25	4.01	3.93	4.32	1.86
19[a])	4.41	1.97	2.29	3.97	4.14	4.24	
4[b])	4.25	1.96	2.34	4.17	3.83–3.75	3.98	
4[c])	4.27–4.20	1.94	2.36	4.27–4.20	3.73	3.93	

[3]) See [1] and ref. cit. therein for similar results in the benzylation of methyl *N*-acetyl-2,3-didehydro-2-deoxyneuraminate.

Table 2 (cont.)

	^{13}C-NMR, chemical shifts [ppm] and coupling constants [Hz]				
	δ (C(1))	J (C(1), P)	J (C(2), P)	J (C(3), P)	J (C(5), P)
16[a])	91.83				
18[a])	71.21	173.1	0	20.5	17.0
20[c])	72.38	174.2	0	20.5	17.0
22[a])	71.77	175.9	0	21.2	17.1
3[c])	73.59	167.1	0	19.8	15.4
17[a])	92.18				
19[a])	66.02	161.7	1.8	5.0	0
21[c])	70.04	156.2	3.9	0	0
4[c])	71.91	153.9	0	0	0

	^{31}P-NMR, chemical shifts [ppm] and coupling constants [Hz]			
	δ (P)	J (H–C(1), P)	J (H_{ax}–C(2), P)	J (H_{eq}–C(2), P)
18[a])	22.10	–	–	2.3
20[c])	24.07	–	–	0
22[a])	20.88	–	11	0
3[b])	19.11	11.4	11.4	0
19[a])	25.80	11.4	26.7	7.0
21[c])	27.20	–	–	–
4[b])	19.85	12.1	34.2	5.1

[a]) $CDCl_3$. [b]) D_2O. [c]) CD_3OD.

Table 3. *H,H-Coupling Constants*

	Acetates and phosphonates					
	J (1,2ax)	J (1,2eq)	J (2ax,3)	J (2eq,3)	J (3,4)	J (4,5)
16[a])	10.2	1.9	11.2	4.7	–	10.3
18[a])	–	2.3	–	4.6	–	–
22[a])	12.8	2.0	11.2	4.8	10.1	10.4
20[b])	–	–	–	–	11.3	11.3
3[c])	11.3	–	11.3	–	–	–
3[b])	11.4	–	11.4	–	–	9.2
17[a])	3.3	1.6	10.5	4.6	10.0	10.0
19[a])	5.7	5.7	8.6	4.1	8.0	7.7
21[b])	–	–	–	–	–	–
4[c])	7.7	1.3	11.2	5.1	9.8	10.2
4[b])	7.7	0	11.0	5.0	10.0	10.0

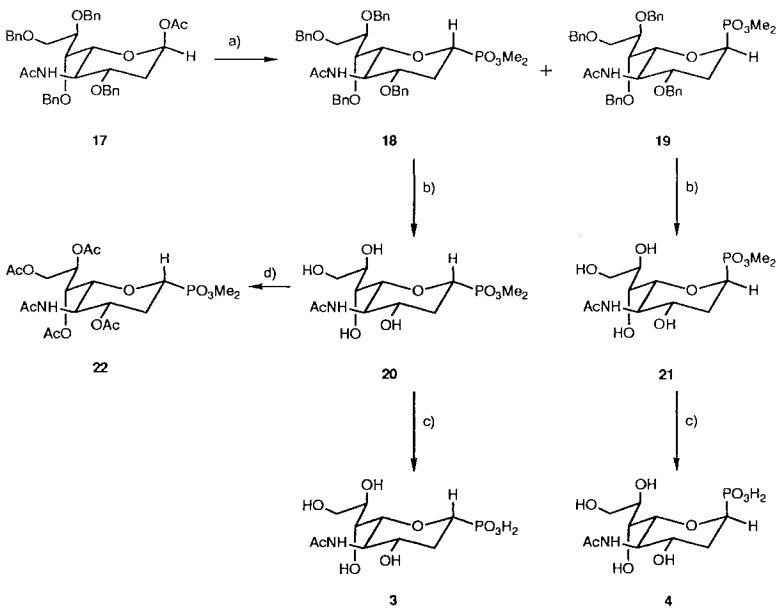
	Carboxylates					
	J (2,3ax)	J (2,3eq)	J (3ax,4)	J (3eq,4)	J (4,5)	J (5,6)
23[a])	12.1	1.9	11.6	4.8	9.8	9.8
8[c])	12.1	2.1	11.1	4.4	–	–
8[b])	12.2	2.2	–	4.3	–	10.0
5[c])	12.1	2.2	10.8	4.3	–	–
24[a])	6.1	2.5	11.0	4.2	9.6	10.0
25[c])	6.2	1.3	11.3	4.3	9	–
25[b])	6.5	1.2	11	4.4	10	9.9
6[c])	6.4	1.2	11.5	4.5	–	–

[a]) $CDCl_3$. [b]) CD_3OD. [c]) D_2O.

indicate the equatorial orientation of the AcO group (α-D-anomer), and $^3J(1,2) = 3.3$ and 1.6 Hz in the spectra of **17** an axial AcO group (β-D-anomer). A comparison of the specific rotation of **16** (+2.8°) and **17** (−35.7°) confirms this assignment [15].

Treatment of **17** with $P(OMe)_3$ and Me_3SiOTf [3] gave the dimethyl phosphonates **18** and **19** (68%, 1.3:1[1]); *Scheme 2*), which were separately subjected to hydrogenolysis (→**20** and **21**) and transesterification by Me_3SiBr. Hydrolysis of the silyl ester obtained from **18** and purification of the product by anion-exchange chromatography gave the phosphonic acid **3** (60% from **18**). Similarly, the axial phosphonate **19** yielded the phosphonic acid **4** (47% from **19**).

Scheme 2



a) $P(OMe)_3$, Me_3SiOTf, CH_2Cl_2, 0°, 68%, **18**/**19** = 1.3:1. b) 10% Pd/C, H_2 (8 bar), MeOH. c) Me_3SiBr, $MeOH/CH_2Cl_2$ 1:4, **3**: 60% from **18**, **4**: 47% from **19**. d) Ac_2O, Py, 52%.

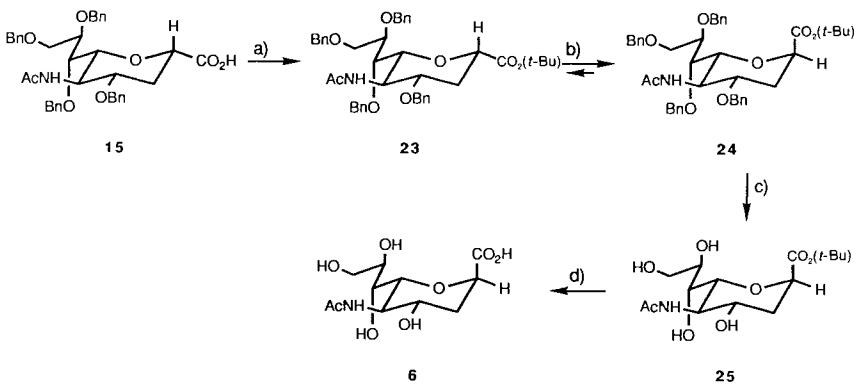
The acid **15** was converted to the *tert*-butyl ester **23** (90%, *Scheme 3*) [16]. This ester was epimerized under basic conditions to give a 1:4 mixture **23**/**24** (93%). Deprotection of **24** by hydrogenolysis (99%) followed by treatment with CF_3CO_2H and purification of the resulting acid by anion-exchange chromatography yielded 60% of **6**. The spectroscopic data (^1H- and ^{13}C-NMR) of **5** and **6** are in agreement with the published values [11].

The structures of the dimethyl phosphonates **18** and **19** were deduced from their NMR spectra (*Tables 2* and *3*). The dimethoxyphosphono group is evident from the signals at 25.80 and 22.10 ppm in the ^{31}P-NMR spectra. Correspondingly, one finds two typical *doublets* for the Me groups at 3.79–3.68 ppm ($^3J(H,P) = 10.4$–11.1 Hz, 6 H) in the ^1H-NMR spectra, and two signals (*dq*) at 53.66–52.36 ppm ($^2J(C,P) = 6.3$–7.1 Hz) in the ^{13}C-NMR spectra.

The assignment of the anomeric configuration[4]) is based on the rule that the ^1H-NMR signal of the anomeric axial proton (3.70–3.87 ppm for **18**) occurs at a higher field than the equatorial one (4.41 ppm for **19**) [3]. This

[4]) For a detailed discussion of the assignment of the anomeric configuration, and of the conformational behaviour of axial and equatorial glycosylphosphonates, see [3] [4] [17] [18] and ref. cit. therein.

Scheme 3



a) DMF, $(COCl)_2$, *t*-BuOH, Py, CH_3CN, 90%. b) Lithium *N*-cyclohexylisopropylamide, aq. NH_4Cl soln., THF, −50°, 93%, **23**/**24** = 1:4. c) 10% Pd/C, H_2, MeOH, 99%. d) CF_3CO_2H, 60%.

assignment is corroborated by the values of the coupling constants ^3J(1,2ax) (**22**: 11 Hz; **19**: 5.7 Hz) and ^3J(H–C(2),P) (**22**: 11 Hz; **19**: 26.7 Hz)[5]) [3]. In the ^{13}C-NMR spectra, the C(1) signals of **18** and **19** are found at 71.21 ppm with ^1J(C(1),P) = 173.1 Hz and 66.02 ppm with ^1J(C(1),P) = 161.7 Hz, respectively. The signal at a higher field and with the smaller coupling constant indicates an axial orientation of the P-substituent [3].

The ring conformations of the phosphonates and carboxylates have been examined on the basis of the vicinal H,H-coupling constants (see *Table 3*). The 'equatorial' compounds (*i.e.* equatorial substituent at C(1) or C(2)) **3**, **5**, **8**, **16**, **18**, **20**, **22**, and **23** show similar values for their coupling constants, which are as predicted for 'equatorial' 2-deoxyglycopyranosides [19]. This is not the case for the 'axial' (*i.e.* axial substituent at C(1) or C(2)) compounds, as expected[6]). Inspection of *Table 3* shows that the axial compounds **4**, **6**, **17**, **19**, **24**, and **25** form two groups. The acetate **17** adopts an almost perfect $^1C_4$ conformation. The other compounds adopt a more or less flattened chair conformation as indicated by the ^3J(1,2ax) coupling constants (5.7–7.7 Hz). The coupling constants of **19** (*Table 3*) are quite similar to those of dimethyl (4,6-di-*O*-acetyl-2,3-dideoxy-α-D-*erythro*-hexopyranosyl)phosphonate (^3J(1,2ax) = 4.4, ^3J(1,2eq) = 5.8, ^1J(H–C(1),P) = 12.0, ^3J(3ax,4) = 8.4, ^3J(4,5) = 8.0, and ^1J(C(1),P) = 160.0 Hz) [20], which have been rationalized by a $^1C_4 \rightleftarrows {}^4C_1$ equilibrium. According to the *Karplus*-type equations relating ^3J(H,P) of phosphonates to the dihedral angles [21] [22], one calculates a dihedral angle of 130–140° for **19** and one of 160–170° for **4** in agreement with a flattened chair conformation. Similar observations for axial phosphonates in the *gluco*- and *galacto*-series have been described [3] [4] [17]. An X-ray analysis of (α-D-glucopyranosyl)phosphonate [4] confirms the deviation of the phosphono group from an axial orientation.

The conformation in the side chain of the protected phosphonates and carboxylates are very similar to each other with the exception of the one of the axial phosphonate **19**

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[5]) The related coupling constants of **18** could not be determined from the ^{1}H-NMR spectrum.

[6]) *Altona* and *Haasnoot* predict ^3J (1,2ax; α-gluco) = 3.6 Hz [19]; *Meuwly* and *Vasella* found 6.2 Hz for ^3J (1,2ax) of the sodium salt of (α-D-glucopyranosyl)phosphonate [3], and *Vaghefi et al.* found 6.4 Hz for ^3J (1,2ax) of the corresponding acid [4].

Table 4. *H,H-Coupling Constants* [Hz] *of the Side Chain*

	Acetates and phosphonates				
	J (5,6)	*J* (6,7)	*J* (7,8)	*J* (7,8)	*J* (8,8)
18[a])	–	–	–	4.1	10.6
20[b])	–	–	–	7.4	10.3
22[a])	1.9	6.3	2.6	6.6	12.4
3[c])	0	9.3	–	–	–
3[b])	0	9.3	–	5.6	11.2
19[a])	3.6	5.9	–	–	–
21[b])	–	–	–	5.3	11.0
4[c])	1.2	8.8	–	6.3	11.6
4[b])	0	9.5	–	5.7	11.4
	Carboxylates				
	J (6,7)	*J* (7,8)	*J* (8,9)	*J* (8,9)	*J* (9,9)
23[a])	1.5	7.3	–	4.5	11.0
8[c])	0	9.0	–	–	–
8[b])	1.2	9.2	–	5.4	11.1
5[c])	0	9.4	–	–	–
24[a])	1.6	6.2	2.6	5.0	10.6
25[c])	0	8.4	2.8	6.0	11.6
25[b])	1.3	8.8	2.7	5.6	11.2
6[c])	0.9	8.9	–	6.4	11.9
Neu5Ac [23]	1.0	8.9	2.7	6.4	

[a]) $CDCl_3$. [b]) CD_3OD. [c]) D_2O.

where the distortion of the ring or the ring inversion correlates with a different conformation of the side chain as evidenced by a larger $^3J(5,6)$ value *(Table 4)*. The phosphonic and the carboxylic acids have the same coupling constants of the side chain as Neu5Ac indicating the same conformation for all these acids *(Table 4)*.

Inspection of *Table 5*[7]) shows that both phosphonic acids are stronger inhibitors than the carboxylates and that the axial carboxylate is not an inhibitor. The fact that both the equatorial phosphonate and carboxylate are stronger inhibitors than the axial epimers (see also [2]) and the fact that Neu2en5Ac is a good inhibitor (K_i $1.6 \cdot 10^{-5}$ M; [24])[8]) is in keeping with a mechanism of *Vibrio cholerae* (and presumably other) sialidases, where,

Table 5. *pK'_a Values*[a]) *and Inhibitor Constants* (K_i Values)[b]) *of the Acids* **3**–**6**

	pK'_a (1)	pK'_a (2)	K_i [M]
3	1.63	6.35	$5.5 \cdot 10^{-5}$
4	1.67	6.30	$2.3 \cdot 10^{-4}$
5	2.33		$2.6 \cdot 10^{-3}$
6	2.30		no inhibition

[a]) Determined by titration of aqueous solutions of the acids with 0.1N NaOH.
[b]) Measured at pH 5.5 [24].

[7]) We thank *R. Wyler* for measuring the K_i values [24].
[8]) *Meindl* and *Tuppy* [10] found no inhibition of *Vibrio cholerae* sialidase by 2-deoxy-Neu5Ac and for Neu2en5Ac a K_i value of $1.0 \cdot 10^{-5}$ M.

along the reaction coordinate, the COOH group has to move from an axial towards an equatorial orientation. Among the here mentioned inhibitors, Neu2en5Ac appears to possess a geometry which is closest to the one of the transition state in agreement with the formation of a cationic – or rather zwitterionic – intermediate. The axial phosphonate **3** is a surprisingly good inhibitor. This may be partially rationalized by assuming that the PO_3H_2 group moves towards an equatorial position more easily than an axial COOH group, in agreement with the *A* values ($A(PO_3Me_2) = 1.99 \pm 0.11$ kcal/mol [20]; $A(CO_2Me) = 1.27$ kcal/mol [25]) and the small value for the anomeric effect of the $PO(OMe)_2$ group (0.56 kcal/mol [20]).

Experimental Part

General. The org. phase, obtained after aq. workup, was dried ($MgSO_4$) before evaporation *i.v.* below 40°. TLC: precoated silica gel plates (*Merck*, *Kieselgel 60 F_{254}*) with the solvent system indicated. Flash chromatography (FC): silica gel *Merck 60* (40–63 μm). M.p.: uncorrected. Optical rotations: 1-dm cell. IR spectra: KBr pellets or $CHCl_3$ solns. as indicated. ^{1}H-NMR spectra: at 400 MHz *(Bruker AM-400)*. ^{13}C-NMR spectra: at 50 MHz *(Varian XL-200)* or at 100 MHz *(Bruker AM-400)*. ^{31}P-NMR spectra: at 160 MHz *(Bruker AM-400)*. MS: by chemical ionisation (CI) or FAB.

*Methyl 5-Acetamido-2,6-anhydro-3,5-dideoxy-*D-erythro-L-gluco-*nononate* (**8**). A soln. of 23.5 g (77.0 mmol) of **7** in H_2O/MeOH (200 ml) 1:3 was hydrogenolyzed in the presence of 160 mg of 10% Pd/C under H_2 (8 bar) at r.t. for 24 h. Filtration of the mixture through *Celite* and evaporation gave 23.78 g (quant.) of **8**. An anal. sample was dried at r.t./10^{-2} mbar over P_2O_5 for 2 d. R_f (MeCN/H_2O 9:1) 0.26. $[\alpha]_D^{25} = -17.1$ (*c* = 1.04, MeOH). IR (KBr): 3450*s* (br.), 3320*s*, 2290*w*, 2960*w*, 2925*w*, 2890*w*, 1740*s*, 1660*m*, 1640*s*, 1550*m*, 1445*w*, 1390*w*, 1370*w*, 1315*w*, 1260*w*, 1225*m*, 1180*w*, 1155*m*, 1130*m*, 1095*w*, 1065*w*, 1035*m*, 965*w*, 890*m*, 775*w*, 725*w*, 610*w*, ^{1}H-NMR (400 MHz, D_2O): 4.30 (*dd*, *J* = 12.1, 2.1, H–C(2)); 3.90–3.79 (*m*, H–C(4,5,8,9)); 3.79 (*s*, CH_3O); 3.66–3.60 (*m*, H–C(6,9)); 3.49 (*d*, *J* = 9.0, H–C(7)); 2.41 (*ddd*, *J* = 12.9, 4.4, 2.2, H–C(3)); 2.03 (*s*, AcN); 1.64 (*td*, *J* = 12.2, 11.1, H–C(3)). ^{1}H-NMR (400 MHz, CD_3OD): 4.15 (*dd*, *J* = 12.2, 2.2, H–C(2)); 3.83–3.74 (*m*, H–C(4,5,8,9)); 3.75 (*s*, CH_3O); 3.62 (*dd*, *J* = 11.1, 5.4, H–C(9)); 3.53 (*dd*, *J* = 10.0, 1.3, H–C(6)); 3.42 (*dd*, *J* = 9.2, 1.2, H–C(7)); 2.31 (*ddd*, *J* = 12.7, 4.3, 2.2, H–C(3)); 2.00 (*s*, AcN); 1.57 (*m*, H–C(3)). ^{13}C-NMR (50 MHz, CD_3OD): 174.84, 172.96 (2*s*, C(1), CH_3CO); 78.19 (*d*); 75.25 (*d*); 71.66 (*d*); 71.03 (*d*); 70.36 (*d*); 65.02 (*t*, C(9)); 54.13 (*d*, C(5)); 52.76 (*q*, CH_3O); 38.13 (*t*, C(3)); 22.76 (*q*, CH_3CO). ^{13}C-NMR (50 MHz, D_2O): 175.30, 173.51 (2*s*, C(1), CH_3CO); 76.42 (*d*); 74.16 (*d*); 70.73 (*d*); 70.14 (*d*); 68.82 (*d*); 63.66 (*t*, C(9)); 53.37 (*q*, CH_3O); 52.56 (*d*, C(5)); 36.37 (*t*, C(3)); 22.60 (*q*, CH_3CO). CI-MS: 308.2 (100), 306.2 (10), 290.2 (6), 284.4 (3), 276.2 (4), 257.4 (3), 246.2 (4). Anal. calc. for $C_{12}H_{21}NO_8$ (307.30): C 46.90, H 6.89, N 4.56; found: C 46.68, H 7.10, N 4.60.

*Benzyl and Methyl 5-Acetamido-2,6-anhydro-4,7,8,9-tetra-*O*-benzyl-3,5-dideoxy-*D-erythro-L-gluco-*nononate* (**9** and **10**, resp.), *Benzyl and Methyl 5-Acetamido-2,6-anhydro-4,8,9-tri-*O*-benzyl-3,5-dideoxy-*D-erythro-L-gluco-*nononate* (**11** and **12**, resp.), *and Benzyl and Methyl 2,6-Anhydro-5-(*N*-benzylacetamido)-4,7,8,9-tetra-*O*-benzyl-3,5-dideoxy-*D-erythro-L-gluco-*nononate* (**13** and **14**, resp.). A mixture of 8.00 g (26.03 mmol) of **8** and of 16.0 g of molecular sieves (4 Å) in 120 ml of abs. DMF was stirred at 0° for 15 min, whereupon 2.60 g (108 mmol) of NaH and 20 ml (168 mmol) of $PhCH_2Br$ was added. After 4 h, additional 0.60 g (25 mmol) of NaH were added, and the mixture was left to warm up to r.t. After 12 h, excess NaH was destroyed with MeOH. The mixture was filtered through *Celite*, the filtrate evaporated, and the residue taken up in 200 ml of CH_2Cl_2 and washed with ice/H_2O. The aq. phase was extracted with CH_2Cl_2 (2 × 100 ml) and processed as usual. Purification of the residue by FC (AcOEt/hexane 1:2 and 1:1, then AcOEt) gave 6.81 g (37%) of **9**/**10**, 7.20 g (45%) of mainly **11**/**12**, which crystallized from AcOEt/hexane, and 2.20 g (11%) of **13**/**14** in a *ca.* 1:1 ratio.

A soln. of 7.20 g of **11**/**12** in abs. DMF (100 ml) was treated at 0° with 0.60 g (25 mmol) of NaH and 5 ml (42 mmol) of $PhCH_2Br$. After 2 h, 0.60 g (25 mmol) of NaH were added, and the soln. was left to warm up to r.t. After 24 h, workup and FC as described above gave 4.95 g (27%) of **9**/**10** and 0.60 g (3%) of **13**/**14** in *ca.* 1:1 ratio. Overall yield: 11.76 g (64%) of **9**/**10** (*ca.* 1:1) and 2.80 g (14%) of **13**/**14** (*ca.* 1:1).

To a soln. of 11.76 g of **9**/**10** in 100 ml of abs. MeOH, NaOMe (from 20 mg of Na and 5 ml of MeOH) was added. After 2 h, the soln. was neutralized with AcOH (0.1 ml), concentrated *i.v.*, and purified by FC (AcOEt/hexane 1:2; 2:3; 1:1): 10.59 g (61% from **8**) of **10** which crystallized from Et_2O/hexane.

Data of **9**: R_f (AcOEt/hexane 1:1) 0.42. $[\alpha]_D^{25} = -5.5$ ($c = 1.12$, $CHCl_3$). IR (KBr): 3400*m* (br.), 3270*w*, 3060*w*, 3030*w*, 2930*w*, 2870*w*, 1745*m*, 1655*s*, 1550*w*, 1500*w*, 1455*m*, 1370*w*, 1310*w*, 1270*w*, 1210*w*, 1175*w*, 1130*s*, 1095*s*, 1030*w*, 735*s*, 700*s*. ^{1}H-NMR (400 MHz, $CDCl_3$): 7.37–7.22 (*m*, 25 arom. H); 5.21, 5.12 (*AB*, $J = 12.2$, PhCH_2 (ester)); 4.65–4.38 (*m*, 4 PhCH_2); 4.49 (*d*, $J \approx 8$, NH); 3.96 (*dd*, $J = 10.4$, 1.5, H–C(6)); 3.94–3.91 (*m*, H–C(4,8)); 3.88 (*dd*, $J = 10.8$, 2.3, H–C(9)); 3.80 (*dd*, $J = 12.1$, 2.0, H–C(2)); 3.76 (*dd*, $J = 7.4$, 1.6, H–C(7)); 3.72 (*dd*, $J = 10.7$, 4.2, H–C(9)); 3.51 (*td*, $J = 9.9$, 8.5, H–C(5)); 2.45 (*ddd*, $J = 12.7$, 4.8, 2.0, H–C(3)); 1.69 (*s*, AcN); 1.67 (*q*, $J \approx 12$, H–C(3)). ^{13}C-NMR (50 MHz, $CDCl_3$): 169.98, 169.30 (2*s*, C(1), CH_3CO); 138.46, 138.29, 138.20, 135.35 (5*s*, arom. C); 129.2–127.4 (*m*, arom. C); 78.19 (*d*); 76.50 (*d*); 75.97 (*d*); 74.26 (*d*); 73.29 (*t*, PhCH_2); 73.06 (*t*, PhCH_2); 72.65 (*t*, PhCH_2); 70.82 (*t*, PhCH_2); 69.17 (*t*, C(9)); 66.72 (*t*, PhCH_2); 52.83 (*d*, C(5)); 33.70 (*t*, C(3)); 23.64 (*q*, CH_3CO). CI-MS: 744.4 (58), 668.3 (32), 654.3 (10), 426.2 (14), 412.2 (9), 181.1 (10), 147.1 (14), 123.1 (41), 107.1 (100), 105.0 (11). Anal. calc. for $C_{46}H_{49}NO_8$ (743.89): C 74.27, H 6.64, N 1.88; found: C 74.07, H 6.76, N 2.04.

Data of **10**: R_f (AcOEt/hexane 1:1) 0.37. $[\alpha]_D^{25} = -8.6$ ($c = 1.12$, $CHCl_3$). M.p. 88.5°. IR (KBr): 3450*m* (br.), 3250*m*, 3070*w*, 3030*w*, 2930*w*, 2860*w*, 1955*w*, 1880*w*, 1810*w*, 1750*m*, 1730*m*, 1650*s*, 1565*m*, 1495*w*, 1455*m*, 1440*w*, 1370*w*, 1330*w*, 1315*w*, 1285*w*, 1220*w*, 1165*w*, 1120*m*, 1090*s*, 1050*w*, 1030*w*, 995*w*, 955*w*, 905*w*, 890*w*, 785*w*, 740*s*, 700*s*, 610*w*. ^{1}H-NMR (400 MHz, $CDCl_3$): 7.39–7.25 (*m*, 20 arom. H); 4.72–4.39 (*m*, 4 PhCH_2); 4.45 (*d*, $J = 8.2$, NH); 3.99–3.90 (*m*, H–C(4,6,8,9)); 3.80–3.72 (*m*, H–C(2,7,9)); 3.72 (*s*, CH_3O); 3.46 (*td*, $J = 9.9$, 8.3, H–C(5)); 2.47 (*ddd*, $J = 12.8$, 4.9, 2.0, H–C(3)); 1.68 (*s*, AcN); 1.64 (*td*, $J = 12.2$, 11.5, H–C(3)). ^{13}C-NMR (50 MHz, $CDCl_3$): 170.05, 169.99 (2*s*, C(1), CH_3CO); 138.40, 138.23, 138.18 (3*s*, arom. C); 129.96–127.51 (*m*, arom. C); 77.95 (*d*); 76.37 (*d*); 75.81 (*d*); 74.18 (2*d*); 73.32 (*t*, PhCH_2); 73.08 (*t*, PhCH_2); 72.45 (*t*, PhCH_2); 70.73 (*t*, PhCH_2); 69.11 (*t*, C(9)); 52.82 (*d*, C(5)); 52.03 (*q*, CH_3O); 33.76 (*t*, C(3)); 23.59 (*q*, CH_3CO). CI-MS: 668.7 (100), 560.6 (46), 488.6 (7), 470.6 (21), 380.4 (11), 91.2 (22). Anal. calc. for $C_{40}H_{45}NO_8$ (667.79): C 71.94, H 6.79, N 2.10; found: C 71.81, H 6.59, N 2.08.

Data of **11**: R_f (AcOEt/hexane 1:1) 0.19. $[\alpha]_D^{25} = +7.2$ ($c = 1.00$, $CHCl_3$). M.p. 149°. IR (KBr): 3435*m* (br.), 3265, 3090*m*, 3065*m*, 3035*w*, 2930*w*, 2875*m*, 2820*w*, 1950*w*, 1870*w*, 1810*w*, 1730*s*, 1645*s*, 1605*w*, 1570*m*, 1500*m*, 1455*m*, 1410*w*, 1400*w*, 1375*w*, 1365*m*, 1345*w*, 1325*m*, 1315*w*, 1270*s*, 1245*m*, 1215*w*, 1185*m*, 1165*w*, 1140*m*, 1115*w*, 1100*s*, 1080*w*, 1065*s*, 1025*m*, 1015*m*, 970*w*, 905*w*, 875*w*, 785*w*, 745*s*, 735*m*, 700*s*, 615*w*. ^{1}H-NMR (400 MHz, $CDCl_3$): 7.41–7.15 (*m*, 20 arom. H); 5.25, 5.15 (*AB*, $J = 12.2$, PhCH_2 (ester)); 5.01 (*d*, $J = 7.8$, NH); 4.72–4.36 (*m*, 3 PhCH_2); 4.60 (*d*, $J = 5.1$, OH); 3.94–3.86 (*m*, H–C(5,8,9)); 3.78 (*dd*, $J = 12.1$, 2.2, H–C(2)); 3.70 (*dd*, $J = 10.6$, 4.9, H–C(9)); 3.59 (*ddd*, $J = 9.7$, 5.1, 1.3, H–C(7)); 3.44 (*td*, $J = 10.5$, 4.6, H–C(4)); 3.31 (*dd*, $J = 10.3$, 1.4, H–C(6)); 2.54 (*ddd*, $J = 13.0$, 4.7, 2.2, H–C(3)); 1.90 (*s*, AcN); 1.80 (*td*, $J = 12.3$, 11.6, H–C(3)). ^{13}C-NMR (50 MHz, $CDCl_3$): 172.50, 172.43 (2*s*, CH_3CO); 169.30 (*s*, C(1)); 138.66, 138.52, 137.90, 135.23 (4*s*, arom. C); 128.58–127.33 (*m*, arom. C); 78.11 (*d*); 77.00 (*d*); 76.04 (*d*); 74.16 (*d*); 73.19 (*t*, PhCH_2); 72.96 (*t*, PhCH_2); 70.10 (*t*, PhCH_2); 69.82 (*t*, C(9)); 67.69, 67.59 (2*d*, C(7)); 66.96 (*t*, PhCH_2); 51.28, 51.19 (2*d*, C(5)); 33.17 (*t*, C(3)); 23.04, 22.98 (2*q*, CH_3CO). CI-MS: 654.6 (100), 578.6 (15), 564.5 (7), 546.5 (81), 454.4 (11), 415.4 (10), 382.3 (23), 366.3 (22), 364.3 (13), 348.3 (7), 276.2 (17), 181.2 (17), 147.2 (27), 108.1 (34), 107.1 (23), 105.1 (11). Anal. calc. for $C_{39}H_{43}NO_8$ (653.77): C 71.65, H 6.63, N 2.14; found: C 71.83, H 6.47, N 1.99.

Data of **12**: R_f (AcOEt/hexane 1:1) 0.11. $[\alpha]_D^{25} = +8.4$ ($c = 1.03$, $CHCl_3$). M.p. 173°. IR (KBr): 3430*m* (br.), 3280*m*, 3080*m*, 3030*w*, 2950*m*, 2865*m*, 1955*w*, 1870*w*, 1810*w*, 1750*s*, 1645*s*, 1605*w*, 1565*m*, 1500*m*, 1465*w*, 1455*m*, 1435*m*, 1395*w*, 1385*m*, 1365*m*, 1350*w*, 1325*w*, 1315*m*, 1305*w*, 1270*m*, 1250*w*, 1235*w*, 1220*m*, 1190*w*, 1170*m*, 1130*s*, 1100*s*, 1065*m*, 1030*m*, 1010*w*, 965*w*, 890*w*, 880*w*, 780*w*, 735*s*, 695*m*, 620*w*. ^{1}H-NMR (400 MHz, $CDCl_3$): 7.41–7.25 (*m*, 15 arom. H); 5.05 (*d*, $J = 7.8$, NH); 4.77–4.37 (*m*, 3 PhCH_2); 4.59 (*m*, OH); 3.93–3.86 (*m*, H–C(5,8,9)); 3.77 (*s*, CH_3O); 3.76 (*dd*, $J = 12.0$, 2.3, H–C(2)); 3.70 (*dd*, $J = 10.6$, 5.0, H–C(9)); 3.59 (*dd*, $J = 9.5$, 3.7, H–C(7)); 3.46 (*td*, $J = 10.5$, 4.6, H–C(4)); 3.31 (*dd*, $J = 10.3$, 1.3, H–C(6)); 2.55 (*ddd*, $J = 12.9$, 4.7, 2.2, H–C(3)); 1.91 (*s*, AcN); 1.77 (*td*, $J = 12.5$, 11.2, H–C(3)). ^{13}C-NMR (50 MHz, $CDCl_3$): 172.48 (*s*, CH_3CO); 169.97 (*s*, C(1)); 138.67, 138.47, 137.87, (3*s*, arom. C); 128.57–127.32 (*m*, arom. C); 78.11 (*d*); 76.79 (*d*); 76.00 (*d*); 74.20 (*d*); 73.22 (*t*, PhCH_2); 72.84 (*t*, PhCH_2); 70.14 (*t*, PhCH_2); 69.72 (*t*, C(9)); 67.68 (*d*, C(7)); 52.18 (*q*, CH_3O); 51.28 (*d*, C(5)); 33.26 (*t*, C(3)); 23.03 (*q*, CH_3CO). CI-MS: 578.5 (100), 546.5 (3), 488.4 (3), 391.4 (6), 308.2 (3). Anal. calc. for $C_{33}H_{39}NO_8$ (577.67): C 68.61, H 6.80, N 2.42; found: C 68.78, H 6.81, N 2.29.

Data of **13**: R_f (AcOEt/hexane 1:1) 0.73. $[\alpha]_D^{25} = +31.6$ ($c = 1.07$, $CHCl_3$). IR ($CHCl_3$): 3090*w*, 3065*w*, 3000*m*, 2930*w*, 2870*m*, 1955*w*, 1875*w*, 1810*w*, 1755*s*, 1640*s*, 1495*m*, 1450*s*, 1410*w*, 1400*w*, 1360*m*, 1305*w*, 1265*m*, 1150*m*, 1110*s*, 1025*m*, 985*w*, 940*w*, 910*w*, 690*m*. ^{1}H-NMR (400 MHz, $CDCl_3$): 7.36–7.16 (*m*, 30 arom. H); 5.18 (*s*, PhCH_2); 5.05, 3.97 (*AB*, $J = 15.3$, PhCH_2); 4.80–4.40 (*m*, 3 PhCH_2); 4.27, 3.66 (*AB*, $J = 11.2$, PhCH_2); 4.05 (*t*, $J = 9.8$, H–C(5)); 4.01 (*m*, H–C(8)); 3.98 (*m*, H–C(6)); 3.89 (*dd*, $J = 10.8$, 2.0, H–C(9)); 3.66 (*m*, H–C(7)); 3.61 (*dd*, $J = 12.3$, 1.7, H–C(2)); 3.61 (*dd*, $J = 10.7$, 5.0, H–C(9)); 3.26 (*td*, $J = 10.2$, 4.7, H–C(4)); 2.43 (*ddd*, $J = 12.8$, 4.8, 2.0, H–C(3)); 2.11 (*s*, AcN); 1.58 (*td*, $J = 12.4$, 11.0, H–C(3)). ^{13}C-NMR (50 MHz, $CDCl_3$): 173.66, 168.96

(2*s*, CH_3CO, C(1)); 138.88, 138.59, 138.06, 138.03, 137.62, 135.10 (6*s*, arom. C); 128.53–126.81 (*m*, arom. C); 77.56 (*d*); 76.77 (*d*); 75.57 (*d*); 74.75 (*d*); 74.31 (*d*); 73.15 (2*t*, PhCH_2); 72.54 (*t*, PhCH_2); 72.44 (*t*, PhCH_2); 69.74 (*t*, C(9)); 66.70 (*t*, PhCH_2); 58.93 (*d*, C(5)); 44.56 (*t*, PhCH_2); 33.64 (*t*, C(3)); 22.32 (*q*, CH_3CO). CI-MS: 726.4 (9), 516.4 (5), 424.2 (5), 410.3 (19), 338.2 (13), 107.1 (100), 91.1 (18). Anal. calc. for $C_{53}H_{55}NO_8$ (834.02): C 76.33, H 6.65, N 1.68; found: C 76.50, H 6.84, N 1.60.

Data of **14**: R_f (AcOEt/hexane 1:1) 0.68. $[\alpha]_D^{25} = +38.8$ ($c = 1.06$, $CHCl_3$). IR ($CHCl_3$): 3090*w*, 3065*w*, 3000*m*, 2950*w*, 2930*w*, 2870*m*, 1955*w*, 1875*w*, 1810*w*, 1755*s*, 1640*s*, 1495*m*, 1450*s*, 1415*w*, 1355*m*, 1305*w*, 1265*m*, 1150*w*, 1105*s*, 1025*m*, 985*w*, 940*w*, 910*w*, 690*m*. ^{1}H-NMR (400 MHz, $CDCl_3$): 7.36–7.17 (*m*, 25 arom. H); 5.05, 4.00 (*AB*, $J = 15.5$, PhCH_2); 4.80–4.38 (*m*, 3 PhCH_2); 4.30, 3.68 (*AB*, $J = 11.1$, PhCH_2); 4.06 (*t*, $J = 9.9$, H–C(5)); 4.01 (*m*, H–C(8)); 3.98 (*dd*, $J = 10.0$, 1.6, H–C(6)); 3.92 (*dd*, $J = 10.8$, 2.0, H–C(9)); 3.67 (*dd*, $J = 7.7$, 1.5, H–C(7)); 3.63 (*dd*, $J = 10.8$, 5.0, H–C(9)); 3.61 (*dd*, $J = 12.2$, 2.1, H–C(2)); 3.27 (*td*, $J = 10.2$, 4.8, H–C(4)); 2.45 (*ddd*, $J = 12.8$, 4.8, 2.0, H–C(3)); 2.11 (*s*, AcN); 1.57 (*td*, $J = 12.5$, 10.9, H–C(3)). ^{13}C-NMR (50 MHz, $CDCl_3$): 173.78, 169.76 (2*s*, CH_3CO, C(1)); 139.04, 138.74, 138.20, 138.11, 137.76 (5*s*, arom. C); 128.45–127.03 (*m*, arom. C); 77.83 (*d*); 77.00 (*d*); 75.85 (*d*); 74.82 (*d*); 74.42 (*d*); 73.33 (2*t*, PhCH_2); 72.86 (*t*, PhCH_2); 72.56 (*t*, PhCH_2); 69.82 (*t*, C(9)); 59.11 (*d*, C(5)); 52.11 (*q*, CH_3O); 44.72 (*t*, PhCH_2); 33.81 (*t*, C(3)); 23.45 (*q*, CH_3CO). CI-MS: 758.6 (100), 668.4 (6), 650.4 (17), 634.4 (19), 588.4 (6), 107.1 (31), 91.1 (33). Anal. calc. for $C_{47}H_{51}NO_8$ (757.92): C 74.48, H 6.78, N 1.85; found: C 74.31, H 6.91, N 2.05.

*5-Acetamido-2,6-anhydro-4,7,8,9-tetra-*O*-benzyl-3,5-dideoxy-*D-erythro-L-gluco-*nononic Acid* (**15**). To a soln. of 6.68 g (10.0 mmol) of **10** in 90 ml of MeOH were added 10 ml of 2N NaOH. After 1 h at r.t., the mixture was neutralized with AcOH and concentrated *i.v.* The residue was taken up in CH_2Cl_2 (200 ml) and washed with ice/H_2O (500 ml). The H_2O phase was extracted with CH_2Cl_2 (2 × 100 ml) and processed as usual yielding 6.53 g (100%) of **15**. R_f (MeCN/H_2O 9:1) 0.47. $[\alpha]_D^{25} = -27.0$ ($c = 1.11$, $CHCl_3$). IR (KBr): 3460*m* (br.), 3090*w*, 3065*w*, 3030*w*, 2930*w*, 2870*w*, 1955*w*, 1880*w*, 1810*w*, 1730*s*, 1655*s*, 1560*m*, 1495*m*, 1455*m*, 1370*m*, 1320*w*, 1265*w*, 1210*w*, 1185*w*, 1160*w*, 1130*s*, 1095*s*, 1070*m*, 1030*m*, 915*w*, 880*w*, 850*w*, 820*w*, 740*s*, 700*s*, 610*w*. ^{1}H-NMR (400 MHz, $CDCl_3$, 298 K): 7.38–7.24 (*m*, 20 arom. H); 4.82 (*d*, $J = 8.6$, NH); 4.69–4.37 (*m*, 4 PhCH_2); 3.90 (*dd*, $J = 10.8$, 2.1, H–C(9)); 3.82–3.74 (*m*, H–C(5,6,7,8)); 3.68 (*dd*, $J = 11.5$, 2.3, H–C(9)); 3.65 (*dd*, $J = 12.3$, 2.2, H–C(2)); 3.60 (*ddd*, $J = 10.7$, 9.5, 4.5, H–C(4)); 2.50 (*ddd*, $J = 12.9$, 4.6, 2.3, H–C(3)); 1.84 (*s*, AcN); 1.57 (*td*, $J = 12.5$, 11.2, H–C(3)). ^{1}H-NMR (400 MHz, $CDCl_3$, 283 K): 7.39–7.23 (*m*, 20 arom. H); 4.93 (*d*, $J = 9.4$, NH); 4.70–4.35 (*m*, 4 PhCH_2); 3.94 (*q*, $J = 9.9$, H–C(5)); 3.87 (*dd*, $J = 10.8$, 2.3, H–C(9)); 3.79 (*d*, $J = 8.6$, H–C(7)); 3.74 (*dt*, $J = 8.6$, 2.2, H–C(8)); 3.67 (*dd*, $J = 10.8$, 2.3, H–C(9)); 3.62 (*d*, $J \approx 11$, H–C(6)); 3.59 (*dd*, $J = 12.3$, 2.0, H–C(2)); 3.46 (*td*, $J = 10.2$, 4.5, H–C(4)); 2.47 (*ddd*, $J = 12.8$, 4.5, 2.1, H–C(3)); 1.90 (*s*, AcN); 1.56 (*td*, $J = 12.4$, 11.4, H–C(3)). ^{1}H-NMR (400 MHz, $CDCl_3$, 273 K): 7.39–7.22 (*m*, 20 arom. H); 4.97 (*d*, $J = 9.6$, NH); 4.71–4.34 (*m*, 4 PhCH_2); 3.99 (*q*, $J = 10.0$, H–C(5)); 3.85 (*dd*, $J = 10.7$, 2.2, H–C(9)); 3.79 (*d*, $J = 8.9$, H–C(7)); 3.73 (*dt*, $J = 8.9$, 2.1, H–C(8)); 3.67 (*dd*, $J = 10.8$, 2.0, H–C(9)); 3.57 (*d*, $J = 10.5$, H–C(6)); 3.55 (*dd*, $J = 12.2$, 1.8, H–C(2)); 3.41 (*td*, $J = 10.3$, 4.5, H–C(4)); 2.46 (*ddd*, $J = 12.9$, 4.5, 2.0, H–C(3)); 1.92 (*s*, AcN); 1.55 (*td*, $J = 12.4$, 11.4, H–C(3)). ^{13}C-NMR (50 MHz, $CDCl_3$): 171.27, 170.54 (2*s*, C(1), CH_3CO); 138.05, 137.80, 137.68 (3*s*, arom. C); 129.12–127.68 (*m*, arom. C); 77.64 (*d*); 76.22 (*d*); 75.88 (*d*); 74.39 (*d*); 73.74 (*d*); 73.50 (*t*, PhCH_2); 73.43 (*t*, PhCH_2); 72.11 (*t*, PhCH_2); 70.70 (*t*, PhCH_2); 68.26 (*t*, C(9)); 52.35 (*d*, C(5)); 33.42 (*t*, C(3)); 23.53 (*q*, CH_3CO). CI-MS: 654.8 (100), 546.6 (4), 475.7 (13), 338.6 (14), 123.2 (21), 107.2 (59), 91.2 (19). Anal. calc. for $C_{39}H_{43}NO_8$ (653.77): C 71.65, H 6.63, N 2.14; found: C 71.50, H 6.85, N 2.14.

*4-Acetamido-3,6,7,8-tetra-*O*-benzyl-2,4-dideoxy-*D-glycero-α-*and-β-*D-galacto-*octopyranosyl Acetate* (**16** and **17**, resp.). A mixture of 3.50 g (5.35 mmol) of **15** and 7.0 g (15.8 mmol) of $Pb(OAc)_4$ in 35 ml of abs. pyridine was stirred under N_2 at 60° for 2.5 h. The mixture was poured into ice/H_2O/CH_2Cl_2 (200 ml/100 ml), acidified with 4N HCl (pH *ca.* 2) and filtered through *Celite*. The aq. phase was extracted with CH_2Cl_2 (2 × 50 ml) and processed as usual. The β-D-anomer **17** crystallized from Et_2O. After several crops of **17** were obtained, the α-D-anomer **16** crystallized from the mother liquor. Yield: 2.331 g (65%), with **16**/**17** *ca.* 1:9 (HPLC).

Data of **16**: R_f (AcOEt/hexane 1:1) 0.46. $[\alpha]_D^{25} = +2.8$ ($c = 1.03$, $CHCl_3$). M.p. 130–131°. IR (KBr): 3390*m* (br.), 3270*m*, 3090*w*, 3065*m*, 3030*m*, 2970*w*, 2930*w*, 2920*m*, 2870*m*, 1955*w*, 1875*w*, 1810*w*, 1755*s*, 1650*s*, 1605*w*, 1565*m*, 1545*m*, 1495*m*, 1455*m*, 1400*w*, 1365*m*, 1330*w*, 1315*m*, 1230*s*, 1130*s*, 1090*s*, 1050*s*, 1030*w*, 975*w*, 960*w*, 940*w*, 910*w*, 895*w*, 885*w*, 735*s*, 695*s*, 605*m*. ^{1}H-NMR (400 MHz, $CDCl_3$): 7.39–7.26 (*m*, 20 arom. H); 5.61 (*dd*, $J = 10.2$, 1.9, H–C(1)); 4.66–4.40 (*m*, 4 PhCH_2); 4.50 (*d*, $J = 8.5$, NH); 3.99 (*d*, $J = 10.3$, H–C(5)); 3.86–3.72 (*m*, H–C(3,4,6,7,8)); 3.68 (*dd*, $J = 10.8$, 3.4, H–C(8)); 2.31 (*ddd*, $J = 12.2$, 4.7, 2.0, H–C(2)); 2.07 (*s*, AcO); 1.77 (*q*, $J = 11.2$, H–C(2)); 1.77 (*s*, AcN). ^{13}C-NMR (50 MHz, $CDCl_3$): 169.98, 169.11 (2*s*, CH_3CO); 138.53, 138.12, 138.08 (3*s*, arom. C); 129.38–127.51 (*m*, arom. C); 91.83 (*d*, C(1)); 77.34 (*d*); 75.37 (*d*); 73.96 (*d*); 73.77 (*t*, PhCH_2); 73.31 (*t*, PhCH_2); 72.95 (*d*); 72.76 (*t*, PhCH_2); 70.84 (*t*, PhCH_2); 68.32 (*t*, C(8)); 51.69 (*d*, C(4)); 35.42 (*t*, C(2));

23.70 (*q*, *C*H_3CO); 21.01 (*q*, *C*H_3CO). CI-MS: 500.2 (100), 410.2 (4); 91.1 (11), 61.1 (12), 57.1 (69), 43.0 (21). Anal. calc. for $C_{40}H_{45}NO_8$ (667.79): C 71.94, H 6.79, N 2.10; found: C 71.86, H 6.83, N 2.05.

Data of **17**: R_f (AcOEt/hexane 1:1) 0.46. $[\alpha]_D^{25} = -35.7$ (*c* = 1.02, $CHCl_3$). M.p. 104.5–105.5°. IR (KBr): 3460*m* (br.), 3390*m*, 3060*w*, 3030*w*, 2930*w*, 2910*w*, 2860*w*, 1960*w*, 1880*w*, 1820*w*, 1745*s*, 1680*s*, 1605*w*, 1585*w*, 1510*m*, 1500*m*, 1470*w*, 1455*m*, 1395*w*, 1365*m*, 1385*w*, 1310*m*, 1260*w*, 1235*m*, 1190*m*, 1130*m*, 1100*s*, 1075*m*, 1040*w*, 1030*w*, 1000*m*, 950*m*, 920*w*, 900*w*, 825*w*, 745*s*, 700*s*, 620*w*. ^{1}H-NMR (400 MHz, $CDCl_3$): 7.38–7.25 (*m*, 20 arom. H); 6.28 (*dd*, *J* = 3.3, 1.6, H–C(1)); 4.71 (*d*, *J* = 8.6, NH); 4.69–4.41 (*m*, 4 PhCH_2); 4.32 (*d*, *J* = 10.0, H–C(5)); 4.01 (*td*, *J* = 10.2, 4.6, H–C(3)); 3.93 (*q*, *J* = 9.9. H–C(4)); 3.85 (*dd*, *J* = 8.4, 0.9, H–C(6)); 3.80–3.75 (*m*, H–C(7,8)); 3.69 (*dd*, *J* = 11.3, 3.8, H–C(8)); 2.25 (*ddd*, *J* = 13.5, 4.5, 1.6, H–C(2)); 1.86 (*s*, AcO); 1.84 (*ddd*, *J* = 13.4, 10.5, 3.4, H–C(2)); 1.81 (*s*, AcN). ^{13}C-NMR (50 MHz, $CDCl_3$): 170.06, 169.18 (2*s*, CH_3*C*O); 138.59, 138.34, 138.03 (3*s*, arom. C); 129.22–127.23 (*m*, arom. C); 92.18 (*d*, C(1)); 77.44 (*d*); 74.34 (*d*); 74.04 (*t*, Ph*C*H_2); 73.47 (*d*); 73.32 (*t*, Ph*C*H_2); 72.11 (*t*, Ph*C*H_2); 71.02 (*d*); 70.90 (*t*, Ph*C*H_2); 67.96 (*t*, C(8)); 51.77 (*d*, C(4)); 34.22 (*t*, C(2)); 23.78 (*q*, *C*H_3CO); 20.77 (*q*, *C*H_3CO). CI-MS: 590.7 (3), 500.6 (100), 410.5 (2), 392.5 (5). Anal. calc. for $C_{40}H_{45}NO_8$ (667.79): C 71.94, H 6.79, N 2.10; found: C 71.69, H 7.00, N 2.14.

*Dimethyl (4-Acetamido-3,6,7,8-tetra-*O*-benzyl-2,4-dideoxy-*D-glycero-α- *and* -β-D-galacto-*octopyranosyl)-phosphonates* (**18** and **19**, resp.). To a soln. of 1.336 g (2.00 mmol) of **17** and 0.6 ml (5.1 mmol) of $P(OMe)_3$ in 5 ml of dry CH_2Cl_2 under N_2 at 0°, 0.6 ml (3.3 mmol) of Me_3SiOTf were added. After 2 h, 0.3 ml (2.5 mmol) of $P(OMe)_3$ and 0.3 ml (1.7 mmol) of Me_3SiOTf were added. After additional 2 h at 0°, the mixture was poured into ice/H_2O (100 ml), extracted with CH_2Cl_2 (1 × 40 ml, 2 × 20 ml), and processed as usual. FC (AcOEt/hexane 1:1, 2:1, and 1:0) gave 554 mg (38%) of **18** and 427 mg (30%) of **19**.

Data of **18**: R_f (AcOEt) 0.39. $[\alpha]_D^{25} = +14.4$ (*c* = 0.99, $CHCl_3$). IR ($CHCl_3$): 3670*w*, 3430*m*, 3400*w* (br.), 3090*w*, 3065*w*, 3035*w*, 2995*m*, 2955*w*, 2930*w*, 2860*m*, 2460*w*, 1955*w*, 1875*w*, 1810*w*, 1680*s*, 1605*w*, 1510*m*, 1495*m*, 1455*m*, 1365*m*, 1325*w*, 1305*w*, 910*w*, 860*w*, 820*w*, 690*w*. ^{1}H-NMR (400 MHz, $CDCl_3$): 7.37–7.27 (*m*, 20 arom. H); 4.74 (*d*, *J* = 8.0, NH); 4.71–4.38 (*m*, 4 PhCH_2); 3.87–3.70 (*m*, H–C(1,3,4,5,6,7,8)); 3.79 (*d*, *J* = 10.4, $POCH_3$); 3.74 (*d*, *J* = 10.5, $POCH_3$); 3.66 (*dd*, *J* = 10.6, 4.1, H–C(8)); 2.43 (*ddt*, *J* = 13.0, 4.6, 2.3, H–C(2)); 1.79 (*m*, H–C(2)); 1.79 (*s*, AcN). ^{13}C-NMR (50 MHz, $CDCl_3$): 169.99 (*s*, CH_3*C*O); 138.35, 138.01, 137.88, (3*s*, arom. C); 128.11–127.04 (*m*, arom. C); 78.29 (*dd*, *J*(C,P) = 17.0); 77.89 (*d*); 76.80 (*dd*, *J*(C,P) = 20.5); 74.69 (*d*); 73.37 (*t*, Ph*C*H_2); 73.09 (*t*, Ph*C*H_2); 72.49 (*t*, Ph*C*H_2); 71.21 (*dd*, *J*(C,P) = 173.1, C(1)); 70.34 (*t*, Ph*C*H_2); 68.88 (*t*, C(8)); 53.66 (*dq*, *J*(C,P) = 7.1, $POCH_3$); 52.89 (*dq*, *J*(C,P) = 6.3, $POCH_3$); 51.62 (*d*, C(4)); 31.07 (*t*, C(2)); 23.37 (*q*, *C*H_3CO). ^{31}P-NMR (160 MHz, $CDCl_3$): 22.10. CI-MS: 718.5 (49), 610.4 (6), 400.3 (14), 338.4 (10), 197.2 (24), 107.1 (70), 91.1 (30), 57.1 (100), 43.1 (17). Anal. calc. for $C_{40}H_{48}NO_9P$ (717.79): C 66.93, H 6.74, N 1.95, P 4.32; found: C 66.80, H 6.99, N 1.75, P 4.15.

Data of **19**: R_f (AcOEt) 0.20. $[\alpha]_D^{25} = -9.6$ (*c* = 1.00, $CHCl_3$). IR ($CHCl_3$): 3670*w*, 3430*w*, 3310*m* (br.), 3090*w*, 3060*w*, 3030*w*, 2995*m*, 2955*w*, 2930*w*, 2860*w*, 2460*w*, 1955*w*, 1875*w*, 1810*w*, 1675*s*, 1495*m*, 1455*m*, 1370*m*, 1310*w*, 960*w*, 915*w*, 880*w*, 835*m*, 690*w*. ^{1}H-NMR (400 MHz, $CDCl_3$): 7.39–7.24 (*m*, 20 arom. H); 5.48 (*d*, *J* = 8.8, NH); 4.75–4.48 (*m*, 4 PhCH_2); 4.41 (*dt*, *J* = 11.4, 5.7, H–C(1)); 4.24 (*ddd*, *J* = 7.7, 3.6, 1.3, H–C(5)); 4.14 (*q*, *J* = 8.1, H–C(4)); 4.00 (*dd*, *J* = 5.9, 3.7, H–C(6)); 3.97 (*td*, *J* = 8.0, 4.1, H–C(3)); 3.92–3.85 (*m*, H–C(7,8)); 3.70 (*d*, *J* = 11.1, $POCH_3$); 3.70 (*m*, H–C(8)); 3.68 (*d*, *J* = 10.8, $POCH_3$); 2.29 (*ddt*, *J* = 14.0, 7.0, 4.7, H–C(2)); 1.97 (*dddd*, *J* = 26.7, 14.1, 8.6, 5.7, H–C(2)); 1.85 (*s*, AcN). ^{13}C-NMR (50 MHz, $CDCl_3$): 169.60 (*s*, CH_3*C*O); 138.36, 138.06, 137.95, 137.87 (4*s*, arom. C); 128.46–127.12 (*m*, arom. C); 78.26 (*d*); 75.35 (2*d*); 74.23 (*t*, Ph*C*H_2); 73.55 (*dd*, *J*(C,P) = 5.0); 73.01 (*t*, Ph*C*H_2); 71.92 (*t*, Ph*C*H_2); 70.97 (*t*, Ph*C*H_2); 68.70 (*t*, C(8)); 66.02 (*dd*, *J*(C,P) = 161.7, C(1)); 52.84 (*dq*, *J*(C,P) = 7.1, $POCH_3$); 52.36 (*dq*, *J*(C,P) = 6.9, $POCH_3$); 49.51 (*d*, C(4)); 28.03 (*dt*, *J*(C,P) = 1.8, C(2)); 23.18 (*q*, *C*H_3CO). ^{31}P-NMR (160 MHz, $CDCl_3$): 25.80. CI-MS: 718.5 (100), 610.4 (9), 491.4 (6), 338.5 (17), 147.2 (15), 123.1 (10), 107.1 (24), 91.1 (35). Anal. calc. for $C_{40}H_{48}NO_9P$ (717.79): C 66.93, H 6.74, N 1.95, P 4.32; found: C 66.74, H 6.56, N 1.76, P 4.21.

*Dimethyl (4-Acetamido-2,4-dideoxy-*D-glycero-α-D-galacto-*octopyranosyl)phosphonate* (**20**). A soln. of 366 mg (0.51 mmol) of **18** in 18 ml of dry MeOH was hydrogenolyzed in the presence of 180 mg of 10% Pd/C under H_2 (8 bar) at r.t. for 24 h. Filtration of the mixture through *Celite* and concentration of the filtrate *i.v.* gave 188 mg (quant.) of **18**. An anal. sample was dried at r.t./10^{-2} mbar over P_2O_5 for 2 d. R_f ($MeCN/H_2O$ 9:1) 0.15. $[\alpha]_D^{25} = +2.3$ (*c* = 1.00, MeOH). IR (KBr): 3400*s* (br.), 2960*m*, 2930*w*, 2860*w*, 1645*s*, 1560*m*, 1445*w*, 1375*w*, 1320*w*, 1225*m*, 1035*s*, 945*w*, 900*w*, 835*m*, 760*w*. ^{1}H-NMR (400 MHz, CD_3OD): 4.79 (*s*, 1 H); 4.00 (*t*, *J* = 11.3, H–C(4)); 3.84 (*d*, *J* = 10.3, $POCH_3$); 3.83 (*d*, *J* = 10.2, $POCH_3$); 3.75 (*m*, 3 H); 3.63 (*dd*, *J* = 10.3, 7.4, H–C(8)); 3.51 (*s*, 1 H); 3.43 (*d*, *J* = 8.3); 2.19 (*d*, *J* = 11.3, H–C(2)); 2.02 (*s*, AcN); 1.72 (*m*, H–C(2)). ^{13}C-NMR (50 MHz, CD_3OD): 175.21 (*s*, CH_3*C*O); 80.60 (*dd*, *J*(C,P) = 17.0); 72.38 (*dd*, *J*(C,P) = 174.2, C(1)); 71.70 (*d*); 71.00 (*dd*, *J*(C,P) = 20.5); 70.54 (*d*); 65.38 (*t*, C(8)); 54.97 (*dq*, *J*(C,P) = 6.8, $POCH_3$); 54.53 (*dq*, *J*(C,P) = 6.1, $POCH_3$); 54.46 (*d*, C(4)); 35.65 (*t*, C(2)); 23.09 (*q*, *C*H_3CO). ^{31}P-NMR (160 MHz, CD_3OD): 24.07. FAB-MS: 380.2 (47), 372.3 (20), 358.2 (100),

344.3 (11), 340.2 (50), 316.2 (10), 248.2 (6), 231.2 (14), 230.2 (5), 185.2 (12), 137.1 (18), 121.1 (24), 115.1 (10), 93.1 (30), 75.1 (10), 57.1 (10). Anal. calc. for $C_{12}H_{24}NO_9P$ (329.24): C 40.34, H 6.77, N 3.92, P 8.67; found: C 40.20, H 6.89, N 3.72, P 8.58.

*Dimethyl (4-Acetamido-2,4-dideoxy-*D*-glycero-β-*D*-galacto-octopyranosyl)phosphonate* (**21**). A soln. of 261 mg (0.36 mmol) of **19** in 13 ml of dry MeOH was hydrogenolyzed in the presence of 130 mg of 10% Pd/C under H_2 (8 bar) at r.t. for 24 h. Filtration of the mixture through *Celite* and evaporation gave 132 mg (quant.) of **19**. An anal. sample was dried at r.t./10^{-2} mbar over P_2O_5 for 2 d. R_f (MeCN/H_2O 9:1) 0.17. $[\alpha]_D^{25} = -15.2$ ($c = 1.00$, MeOH). IR (KBr): 3400*s* (br.), 2960*m*, 2860*w*, 1645*s*, 1560*m*, 1445*w*, 1375*m*, 1320*w*, 1225*m*, 1100*m*, 1040*s*, 900*w*, 835*m*, 785*m*. ^{1}H-NMR (400 MHz, CD_3OD): 4.78 (*m*, 1 H); 4.48 (*m*, 1 H); 4.09 (*m*, 1 H); 3.94 (*m*, 1 H); 3.86 (*d*, $J = 10.6$, $POCH_3$); 3.81 (*d*, $J = 10.6$, $POCH_3$); 3.77 (*m*, 2 H); 3.61 (*dd*, $J = 11.0$, 5.3, H–C(8)); 3.43 (*m*, 1 H); 2.26 (*m*, H–C(2)); 2.01 (*s*, AcN); 1.93 (*m*, H–C(2)). ^{13}C-NMR (50 MHz, CD_3OD): 175.23 (*s*, CH_3CO); 76.34 (*d*); 71.97 (*d*); 70.76 (*d*); 70.04 (*dd*, J(C,P) = 156.2, C(1)); 67.94 (*d*); 65.29 (*t*, C(8)); 54.71 (*dq*, J(C,P) = 6.9, $POCH_3$); 54.47 (*d*, C(4)); 53.71 (*dq*, J(C,P) = 7.6, $POCH_3$); 34.12 (*dt*, J(C,P) = 3.9, C(2)); 23.03 (*q*, CH_3CO). ^{31}P-NMR (160 MHz, CD_3OD): 27.20. FAB-MS: 380.2 (31), 358.2 (100), 342.2 (11), 340.2 (6), 207.2 (6), 185.2 (26), 155.1 (10), 115.1 (19), 93.1 (53), 75.1 (13), 57.1 (10). Anal. calc. for $C_{12}H_{24}NO_9P$ (357.29): C 40.34, H 6.77, N 3.92, P 8.67; found: C 40.10, H 6.93, N 3.72, P 8.54.

*Dimethyl (4-Acetamido-3,6,7,8-tetra-*O*-acetyl-2,4-dideoxy-*D*-glycero-α-*D*-galacto-octopyranosyl)phosphonate* (**22**). A suspension of 29 mg (0.08 mmol) of **20** in 1 ml of pyridine and 1 ml of Ac_2O was kept at r.t. for 24 h. At 0°, 0.5 ml of MeOH were added. After 1 h, the mixture was poured into 50 ml of ice/H_2O, extracted with CH_2Cl_2 (3 × 20 ml) and processed as usual. Prep. TLC (AcOEt) yielded 22 mg (52%) of **22**. R_f (AcOEt) 0.07. ^{1}H-NMR (400 MHz, $CDCl_3$): 5.49 (*d*, $J = 9.9$, NH); 5.33 (*ddd*, $J = 6.3$, 1.9, 0.6, H–C(6)); 5.22 (*td*, $J = 6.4$, 2.5, H–C(7)); 5.01 (*td*, $J = 10.6$, 5.0, H–C(3)); 4.42 (*dd*, $J = 12.4$, 2.6, H–C(8)); 4.10 (*dd*, $J = 12.4$, 6.6, H–C(8)); 3.99 (*q*, $J = 10.1$, H–C(4)); 3.85 (*d*, $J = 10.6$, $POCH_3$); 3.80 (*d*, $J = 10.7$, $POCH_3$); 3.80 (*m*, H–C(1)); 3.66 (*dd*, $J = 10.4$, 2.0, H–C(5)); 2.30 (*ddt*, $J = 13.0$, 4.7, 2.0, H–C(2)); 2.12 (*s*, AcO); 2.07 (*s*, AcO); 2.03 (*s*, AcO); 2.03 (*s*, AcO); 1.97 (*tdd*, $J = 12.8$, 11.2, 10.0, H–C(2)); 1.89 (*s*, AcN). ^{13}C-NMR (100 MHz, $CDCl_3$): 170.83 (*s*, CH_3CO); 170.47 (*s*, CH_3CO); 170.17 (*s*, CH_3CO); 170.14 (*s*, CH_3CO); 169.93 (*s*, CH_3CO); 78.88 (*dd*, J(C,P) = 17.1); 71.77 (*dd*, J(C,P) = 175.9, C(1)); 71.40 (*dd*, J(C,P) = 21.2); 70.52 (*d*); 67.74 (*d*); 62.19 (*t*, C(8)); 54.03 (*q*, $POCH_3$); 53.02 (*q*, $POCH_3$); 49.90 (*d*, C(4)); 31.25 (*t*, C(2)); 23.10 (*q*, CH_3CO); 20.76 (*q*, CH_3CO); 20.69 (*q*, CH_3CO); 20.63 (*q*, CH_3CO). ^{31}P-NMR (160 MHz, $CDCl_3$): 20.88.

*(4-Acetamido-2,4-dideoxy-*D*-glycero-α-*D*-galacto-octopyranosyl)phosphonic Acid* (**3**). A suspension of 40 mg (0.11 mmol) of **20** in CH_2Cl_2 (1 ml) was treated under N_2 at 0° with Me_3SiBr (400 µl, 3.1 mmol). After 48 h at r.t., MeOH (0.5 ml) was added, the mixture concentrated *i.v.*, the residue taken up in H_2O (5 ml), and the mixture lyophilized. The procedure was repeated in 0.5 ml of MeOH/CH_2Cl_2 (abs.) (1:4). Purification of the combined residues by anion-exchange chromatography (*Dowex 1 × 8* ($HCOO^-$); 0–0.7M HCOOH) gave 44 mg (60%) of **3**. An anal. sample was dried at r.t./10^{-2} mbar over P_2O_5 for 2 d. R_f (PrOH/NH_3 (25%)/H_2O 6:3:1) 0.24. $[\alpha]_D^{25} = -3.9$ ($c = 1.03$, H_2O). p$K_1 = 1.63$, p$K_2 = 6.35$. IR (KBr): 3380*s* (br.), 2940*w*, 1640*m*, 1560*m*, 1430*w*, 1380*w*, 1320*w*, 1085*m*, 1030*m*, 935*w*, 900*w*, 815*w*. ^{1}H-NMR (400 MHz, D_2O): 3.85–3.78 (*m*, H–C(1,3,4,7,8)); 3.62–3.57 (*m*, H–C(5,8)); 3.47 (*d*, $J = 9.3$, H–C(6)); 2.26 (*d*, $J = 12.7$, H–C(2)); 2.03 (*s*, AcN); 1.69 (*quint*, $J = 11.3$, H–C(2)). ^{1}H-NMR (400 MHz, CD_3OD): 3.80–3.69 (*m*, H–C(1,3,4,7,8)); 3.60 (*dd*, $J = 11.2$, 5.6, H–C(8)); 3.49 (*d*, $J = 9.2$, H–C(5)); 3.43 (*d*, $J = 9.3$, H–C(6)); 2.24 (*d*, $J = 12.7$, H–C(2)); 2.01 (*s*, AcN); 1.70 (*quint*, $J = 11.4$, H–C(2)). ^{13}C-NMR (100 MHz, CD_3OD): 175.33 (*s*, CH_3CO); 80.06 (*dd*, J(C,P) = 15.4); 73.59 (*dd*, J(C,P) = 167.1, C(1)); 71.71 (*d*); 71.61 (*dd*, J(C,P) = 19.8); 70.71 (*d*); 65.36 (*t*, C(8)); 54.68 (*d*, C(4)); 36.20 (*t*, C(2)); 23.04 (*q*, CH_3CO). ^{31}P-NMR (160 MHz, D_2O): 19.11. FAB-MS: 352.2 (47), 344.2 (11), 330.2 (100), 312.2 (26), 288.2 (6), 277.3 (12), 223.1 (7), 207.1 (27). Anal. calc. for $C_{10}H_{20}NO_9P$ (329.24): C 36.48, H 6.12, N 4.25, P 9.41; found: C 36.20, H 6.40, N 4.06, P 9.15.

*(4-Acetamido-2,4-dideoxy-*D*-glycero-β-*D*-galacto-octopyranosyl)phosphonic Acid* (**4**). Under N_2, Me_3SiBr (100 µl, 0.77 mmol) was added to a soln. of 60 mg (0.17 mmol) of **21** in 0.3 ml of DMF at 0°. After 12, 24, and 36 h, 100 µl (0.77 mmol) of Me_3SiBr were added at 0°. After 48 h, the mixture was treated with 0.5 ml of MeOH, concentrated *i.v.*, taken up in H_2O (5 ml), and lyophilized. Purification by anion-exchange chromatography (*Dowex 1 × 8* ($HCOO^-$); 0–0.7M HCOOH) gave 26 mg (47%) of **4**. An anal. sample was dried at r.t./10^{-2} mbar over P_2O_5 for 2 d. R_f (PrOH/NH_3 (25%)/H_2O 6:3:1) 0.33. $[\alpha]_D^{25} = -16.5$ ($c = 1.03$, H_2O). p$K_1 = 1.67$, p$K_2 = 6.30$. IR (KBr): 3400*s* (br.), 2930*w*, 1640*m*, 1560*m*, 1435*w*, 1380*w*, 1320*w*, 1120*m*, 1040*m*, 920*w*, 900*w*, 685*w*. ^{1}H-NMR (400 MHz, D_2O): 4.25 (*dd*, $J = 12.1$, 6.7, H–C(1)); 4.17 (*ddd*, $J = 11.1$, 9.8, 5.1, H–C(3)); 3.98 (*d*, $J = 10.2$, H–C(5)); 3.83–3.75 (*m*, H–C(4,7,8)); 3.58 (*dd*, $J = 11.6$, 6.3, H–C(8)); 3.48 (*dd*, $J = 8.8$, 1.2, H–C(6)); 2.34 (*dtd*, $J = 13.8$, 5.1, 1.3, H–C(2)); 2.01 (*s*, AcN); 1.96 (*dddd*, $J = 34.2$, 13.9, 11.3, 7.7, H–C(2)). ^{1}H-NMR (400 MHz, CD_3OD): 4.27–4.20 (*m*, H–C(1,3)); 3.93 (*d*, $J = 10.0$, H–C(5)); 3.82–3.75 (*m*, H–C(7,8)); 3.73 (*t*, $J = 10.0$, H–C(4)); 3.62

(*dd*, J = 11.4, 5.7, H–C(8)); 3.47 (*d*, J = 9.5, H–C(6)); 2.36 (*dt*, J = 13.4, 5.0, H–C(2)); 2.01 (*s*, AcN); 1.94 (*dddd*, J = 35.0, 13.6, 11.0, 7.7, H–C(2)). ^{13}C-NMR (100 MHz, CD_3OD): 175.60 (*s*, CH_3CO); 75.95 (*d*); 72.72 (*d*); 71.91 (*dd*, J(C,P) = 153.9, C(1)); 70.62 (*d*); 68.23 (*d*); 64.95 (*t*, C(8)); 54.91 (*d*, C(4)); 34.38 (*t*, C(2)); 22.90 (*q*, CH_3CO). ^{31}P-NMR (160 MHz, D_2O): 19.85. FAB-MS: 352.1 (27), 330.2 (100), 314.2 (10), 312.2 (6), 288.2 (6), 277.3 (5). Anal. calc. for $C_{10}H_{20}NO_9P$ (329.24): C 36.48, H 6.12, N 4.25, P 9.41; found: C 36.20, H 6.07, N 4.16, P 9.28.

5-Acetamido-2,6-anhydro-3,5-dideoxy-D-erythro-L-gluco-*nononic Acid* (**5**). A soln. of 100 mg (0.33 mmol) of **8** in H_2O (6 ml) were treated with 0.1M NaOH (4 ml). After 3 h, the mixture was diluted with H_2O (5 ml) and purified by anion-exchange chromatography (*Dowex 1* × *8* ($HCOO^-$); 0–0.5M HCOOH) yielding 88 mg (92%) of **5**. An anal. sample was dried at r.t./10^{-2} mbar over P_2O_5 for 2 d. R_f (PrOH/H_2O 7:3) 0.40. $[\alpha]_D^{25}$ = –9.1 (c = 1.02, H_2O). pK_1 = 2.33. IR (KBr): 3400*s* (br.), 2960*w*, 2930*w*, 1750*m*, 1740*s*, 1650*s*, 1635*m*, 1545*m*, 1430*w*, 1370*w*, 1345*w*, 1320*w*, 1260*w*, 1220*w*, 1190*w*, 1150*w*, 1135*m*, 1115*w*, 1100*w*, 1085*w*, 1065*w*, 1045*m*, 1025*w*, 955*w*, 910*w*, 900*w*, 875*w*, 740*w*, 685*w*, 620*w*. ^{1}H-NMR (400 MHz, D_2O): 4.24 (*dd*, J = 12.1, 2.1, H–C(2)); 3.90–3.78 (*m*, H–C(4,5,8,9)); 3.64–3.59 (*m*, H–C(6,9)); 3.48 (*d*, J = 9.4, H–C(7)); 2.41 (*ddd*, J = 12.8, 4.3, 2.3, H–C(3)); 2.03 (*s*, AcN); 1.64 (*td*, J = 12.4, 10.8, H–C(3)). ^{13}C-NMR (50 MHz, D_2O): 175.12, 174.92 (2*s*, C(1), CH_3CO); 76.09 (*d*); 73.92 (*d*); 70.61 (*d*); 69.99 (*d*); 68.74 (*d*); 63.59 (*t*, C(9)); 52.51 (*d*, C(5)); 36.48 (*t*, C(3)); 22.53 (*q*, CH_3CO). CI-MS: 318.1 (11), 294.1 (12), 276.1 (100), 258.1 (14), 234.1 (5). Anal. calc. for $C_{11}H_{19}NO_8$ (293.27): C 45.05, H 6.53, N 4.78; found: C 44.96, H 6.68, N 4.56.

tert-*Butyl 5-Acetamido-2,6-anhydro-4,7,8,9-tetra*-O-*benzyl-3,5-dideoxy*-D-erythro-L-gluco-*nononate* (**23**). To a soln. of 0.9 ml (11.67 mmol) of DMF and 50 ml of dry CH_2Cl_2 at 0°, 1.0 ml (11.64 mmol) of oxalyl chloride and after 30 min, 4.869 g (7.45 mmol) of **15** were added. After additional 30 min at 0°, a mixture of 1.8 ml (22.32 mmol) of pyridine and 2.2 ml (23.45 mmol) of abs. *t*-BuOH were added. The mixture was kept for 12 h at r.t., then it was poured into ice/H_2O (100 ml), acidified with 1M H_2SO_4 (pH *ca.* 2), extracted with CH_2Cl_2 (1 × 50 ml, 2 × 20 ml), and processed as usual. FC (AcOEt/hexane 1:1) gave 4.756 g (90%) of **23**, which crystallized from Et_2O/hexane. R_f (AcOEt/hexane 1:1) 0.48. $[\alpha]_D^{25}$ = –2.2 (c = 1.12, $CHCl_3$). M.p. 87–88°. IR (KBr): 3460*m* (br.), 3240*m*, 3065*m*, 3030*w*, 2980*w*, 2930*m*, 2865*m*, 1955*w*, 1880*w*, 1815*w*, 1750*s*, 1720*m*, 1645*s*, 1560*m*, 1495*w*, 1455*m*, 1390*w*, 1370*m*, 1315*w*, 1275*w*, 1235*w*, 1210*w*, 1155*s*, 1135*s*, 1085*s*, 1030*m*, 990*w*, 955*w*, 920*w*, 880*w*, 845*w*, 810*w*, 745*s*, 735*m*, 700*s*, 610*m*. ^{1}H-NMR (400 MHz, $CDCl_3$): 7.38–7.27 (*m*, 20 arom. H); 4.71–4.40 (*m*, 4 PhCH_2); 4.52 (*d*, J = 8.5, NH); 3.98–3.89 (*m*, H–C(4,6,8,9)); 3.77 (*dd*, J = 7.3, 1.5, H–C(7)); 3.74 (*dd*, J = 11.0, 4.5, H–C(9)); 3.69 (*dd*, J = 12.1, 1.9, H–C(2)); 3.52 (*td*, J = 9.8, 8.6, H–C(5)); 2.39 (*ddd*, J = 12.7, 4.8, 1.9, H–C(3)); 1.69 (*s*, AcN); 1.61 (*q*, J = 12.0, H–C(3)); 1.46 (*s*, *t*-Bu). ^{13}C-NMR (50 MHz, $CDCl_3$): 169.74, 168.15 (2*s*, C(1), CH_3CO); 138.24, 138.05, 138.00, 137.85 (4*s*, arom. C); 128.58–126.68 (*m*, arom. C); 81.00 (*s*, $(CH_3)_3C$); 77.84 (*d*); 76.58 (*d*); 76.26 (*d*); 74.49 (*d*); 74.28 (*d*); 72.89 (*t*, PhCH_2); 72.78 (*t*, PhCH_2); 72.23 (*t*, PhCH_2); 70.22 (*t*, PhCH_2); 68.88 (*t*, C(9)); 51.74 (*d*, C(5)); 33.29 (*t*, C(3)); 27.53 (*q*, $(CH_3)_3C$); 23.11 (*q*, CH_3CO). CI-MS: 710.3 (100), 654.2 (46), 602.2 (6), 57.1 (59), 43.0 (13). Anal. calc. for $C_{43}H_{52}NO_8$ (709.87): C 72.76, H 7.24, N 1.97; found: C 72.85, H 7.32, N 1.95.

tert-*Butyl 5-Acetamido-2,6-anhydro-4,7,8,9-tetra*-O-*benzyl-3,5-dideoxy*-D-erythro-L-manno-*nononate* (**24**). To a soln. of 0.7 ml (4.16 mmol) of *N*-cyclohexylisopropylamine and 10 ml of dry THF under Ar at –50°, 2.8 ml (1.45M, 4.06 mmol) of BuLi were added. After 30 min at 0°, the mixture was cooled to –80°, and 710 mg (1.00 mmol) of **23** were added. The mixture was kept for 3 h at –50°, cooled to –80°, treated with 2 ml of sat. NH_4Cl soln., warmed up to r.t., poured into ice/H_2O (100 ml), acidified with 1M H_2SO_4 (pH *ca.* 2), extracted with CH_2Cl_2 (3 × 25 ml), and processed as usual. FC (AcOEt/hexane 1:2, 2:3) gave 652 mg (93%) of **24**/**23** (4:1, HPLC). R_f (AcOEt/hexane 1:1) 0.55. $[\alpha]_D^{25}$ = –33.3 (c = 1.06, $CHCl_3$). IR (KBr): 3400*s* (br.), 3290*m* (br.), 3080*w*, 3060*w*, 3030*m*, 3000*w*, 2975*m*, 2925*s*, 2865*m*, 1950*w*, 1875*w*, 1810*w*, 1740*s*, 1660*s*, 1545*w*, 1525*w*, 1495*m*, 1455*s*, 1390*w*, 1370*s*, 1310*w*, 1250*w*, 1200*w*, 1130*s*, 1095*s*, 1030*m*, 910*w*, 845*w*, 740*s*, 700*s*. ^{1}H-NMR (400 MHz, $CDCl_3$): 7.44–7.25 (*m*, 20 arom. H); 4.78 (*d*, J = 8.8, NH); 4.75–4.42 (*m*, 4 PhCH_2); 4.45 (*dd*, J = 5.8, 2.4, H–C(2)); 4.32 (*dd*, J = 10.0, 1.6, H–C(6)); 3.97 (*ddd*, J = 6.2, 5.0, 2.4, H–C(8)); 3.93 (*dd*, J = 10.6, 2.6, H–C(9)); 3.81 (*q*, J = 9.4, H–C(5)); 3.78 (*dd*, J = 6.2, 1.8, H–C(7)); 3.75 (*dd*, J = 10.6, 5.0, H–C(9)); 3.65 (*ddd*, J = 10.8, 9.6, 4.2, H–C(4)); 2.46 (*ddd*, J = 13.1, 4.2, 2.5, H–C(3)); 1.85 (*ddd*, J = 13.1, 11.1, 6.1, H–C(3)); 1.79 (*s*, AcN); 1.45 (*s*, *t*-Bu). ^{13}C-NMR (50 MHz, $CDCl_3$): 170.09, 169.81, (2*s*, C(1), CH_3CO); 138.76, 138.31, 138.17, 138.11 (4*s*, arom. C); 129.16–127.28 (*m*, arom. C); 81.65 (*s*, $(CH_3)_3C$); 78.88 (*d*); 75.04 (*d*); 74.05 (*d*); 73.89 (*t*, PhCH_2); 73.56 (*d*); 73.02 (*t*, PhCH_2); 72.53 (*t*, PhCH_2); 71.66 (*d*); 70.58 (*t*, PhCH_2); 69.37 (*t*, C(9)); 51.79 (*d*, C(5)); 31.70 (*t*, C(3)); 27.90 (*q*, $(CH_3)_3C$); 23.49 (*q*, CH_3CO). CI-MS: 710.5 (75), 654.5 (8), 230.2 (14), 147.2 (15), 110.1 (18), 107.1 (42), 91.1 (100). Anal. calc. for $C_{43}H_{51}NO_8$ (709.87): C 72.76, H 7.24, N 1.97; found: C 72.73, H 7.18, N 1.84.

tert-*Butyl 5-Acetamido-2,6-anhydro-3,5-dideoxy*-D-erythro-L-manno-*nononate* (**25**). A soln. of 500 mg (0.704 mmol) of **24** in 25 ml of dry MeOH was hydrogenolyzed in the presence of 100 mg of 10% Pd/C under H_2 (8 bar) at r.t. for 24 h. After filtration of the mixture through *Celite*, concentration of the filtrate *i.v.*, the residue was taken

up in H_2O (5 ml) and lyophilized yielding 245 mg (99%) of **25**. An anal. sample was dried at r.t./10^{-2} mbar over P_2O_5 for 2 d. R_f ($MeCN/H_2O$ 9:1) 0.47. $[\alpha]_D^{25} = -26.1$ ($c = 1.04$, MeOH). M.p. 178° (dec.). IR (KBr): 3550*s*, 3385*s*, 3330*s*, 2990*w*, 2960*w*, 2930*w*, 1730*s*, 1640*s*, 1565*s*, 1455*w*, 1435*m*, 1390*w*, 1380*m*, 1370*m*, 1345*w*, 1320*m*, 1310*m*, 1295*w*, 1280*m*, 1245*s*, 1220*w*, 1160*m*, 1150*s*, 1135*s*, 1110*m*, 1095*s*, 1065*w*, 1050*m*, 1040*s*, 1010*m*, 975*w*, 945*w*, 910*m*, 890*w*, 880*w*, 850*w*, 840*m*, 830*w*, 755*m*, 735*w*, 680*w*, 655*w*, 635*w*. ^{1}H-NMR (400 MHz, D_2O): 4.65 (*dd*, $J = 6.1, 1.0$, H–C(2)); 3.88 (*dd*, $J = 11.6, 2.8$, H–C(9)); 3.86–3.81 (*m*, H–C(5,6,8)); 3.77 (*td*, $J = 8.3, 4.0$, H–C(4)); 3.67 (*dd*, $J = 11.6, 6.0$, H–C(9)); 3.56 (*d*, $J = 8.4$, H–C(7)); 2.54 (*ddd*, $J = 13.5, 4.3, 1.6$, H–C(3)); 2.06 (s, AcN); 1.90 (*ddd*, $J = 13.3, 11.3, 6.3$, H–C(3)); 1.54 (*s*, *t*-Bu). ^{1}H-NMR (400 MHz, CD_3OD): 4.52 (*dd*, $J = 6.5, 1.0$, H–C(2)); 3.81 (*dd*, $J \approx 12, 2.7$, H–C(9)); 3.78 (*ddd*, $J = 8.7, 5.5, 3.0$, H–C(8)); 3.72 (*t*, $J = 9.8$, H–C(5)); 3.65 (*td*, $J = 10.5, 4.5$, H–C(4)); 3.65 (*dd*, $J = 9.9, 1.4$, H–C(6)); 3.62 (*dd*, $J = 11.2, 5.6$, H–C(9)); 3.47 (*dd*, $J = 8.8, 1.3$, H–C(7)); 2.48 (*ddd*, $J = 13.3, 4.3, 1.4$, H–C(3)); 1.99 (*s*, AcN); 1.85 (*ddd*, $J = 13.2, 11.7, 6.5$, H–C(3)); 1.51 (*s*, *t*-Bu). ^{13}C-NMR (50 MHz, CD_3OD): 175.40, 173.21 (2*s*, C(1), CH_3CO); 84.46 (*s*, $(CH_3)_3C$); 75.75 (*d*); 74.09 (*d*); 73.05 (*d*); 70.44 (*d*); 68.86 (*d*); 64.85 (*t*, C(9)); 54.60 (*d*, C(5)); 36.20 (*t*, C(3)); 28.55 (*q*, $(CH_3)_3C$); 22.98 (*q*, CH_3CO). FAB-MS: 372.3 (4), 350.3 (21), 294.2 (100), 276.2 (6). Anal. calc. for $C_{15}H_{27}NO_8$ (349.38): C 51.57, H 7.79, N 4.01; found: C 51.66, H 8.04, N 3.83.

5-Acetamido-2,6-anhydro-3,5-dideoxy-D-erythro-L-manno-*nononic Acid* (**6**). For 3 h, 100 mg (0.286 mmol) of **25** were kept in CF_3CO_2H (3 ml) at r.t. The mixture was concentrated *i.v.*, taken up in H_2O (5 ml), and lyophilized. Purification by anion-exchange chromatography (*Dowex 1 × 8* ($HCOO^-$); 0–0.7M HCOOH) gave 50 mg (60%) of **6**. An anal. sample was dried at r.t./10^{-2} mbar over P_2O_5 for 2 d. R_f (PrOH/H_2O 7:3) 0.57. $[\alpha]_D^{25} = -28.5$ ($c = 0.82$, H_2O). $pK_1 = 2.30$. IR (KBr): 3400*s* (br.), 2930*w*, 1705*m*, 1635*m*, 1565*m*, 1425*w*, 1380*w*, 1315*w*, 1260*w*, 1205*w*, 1130*m*, 1050*w*, 960*w*, 905*w*, 800*w*, 640*w*. ^{1}H-NMR (400 MHz, D_2O): 4.70 (*dd*, $J = 6.3, 1.1$, H–C(2)); 3.85–3.75 (*m*, H–C(5,6,8,9)); 3.72 (*m*, H–C(4)); 3.61 (*dd*, $J = 11.9, 6.4$, H–C(9)); 3.52 (*dd*, $J = 8.9, 0.9$, H–C(7)); 2.52 (*ddd*, $J = 13.4, 4.5, 1.4$, H–C(3)); 2.01 (*s*, AcN); 1.90 (*ddd*, $J = 13.4, 11.5, 6.5$, H–C(3)). ^{13}C-NMR (50 MHz, D_2O): 175.34, 175.20 (2*s*, C(1), CH_3CO); 74.01 (*d*); 72.39 (*d*); 71.53 (*d*); 68.61 (*d*); 67.87 (*d*); 63.41 (*t*, C(9)); 52.78 (*d*, C(5)); 33.91 (*t*, C(3)); 22.46 (*q*, CH_3CO). CI-MS: 318.3 (24), 300.3. (4), 294.3 (10), 276.2 (100), 258.2 (34), 250.3 (14), 240.2 (5), 234.2 (14), 232.3 (5), 216.2 (15). Anal. calc. for $C_{11}H_{19}NO_8 \cdot 1.6\ H_2O$ (322.09): C 41.02, H 6.95, N 4.35; found: C 40.95, H 6.93, N 4.11.

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