98. Analogues of Sialic Acids as Potential Sialidase Inhibitors
Synthesis of 2-C-Hydroxymethyl Derivatives of *N*-Acetyl-6-amino-2,6-dideoxy-neuraminic Acid

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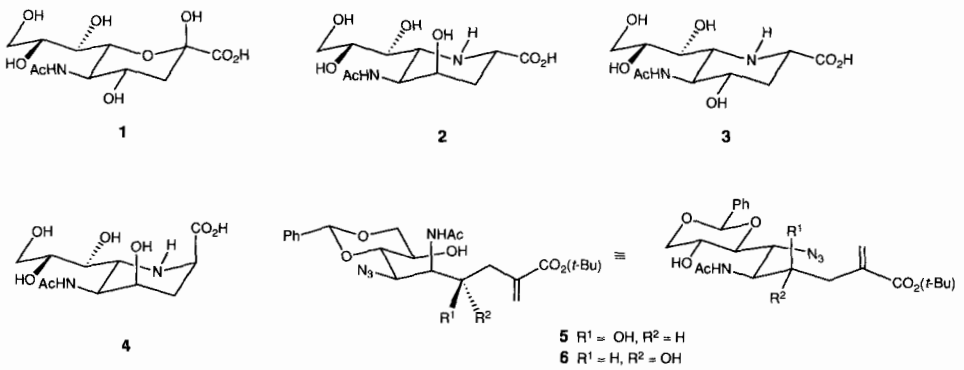
The intramolecular cycloaddition of the previously described azidoalkene **16**, the related diacetates **7** and **13**, and the monoacetate **8** led diastereoselectively to the (2*R*)- and (2*S*)-configurated hydropyridotriazoles **17**, **9** and **11**, **14** and **15**, and **10** and **12**, respectively (*Scheme 1*). Thermolysis of **16** gave also the aziridine **18**, its proportion increasing with reaction time. The diastereoselectivity of the cycloaddition is rationalized on the basis of steric interactions and of H-bonds in the transition state. Photolysis in benzene partially transformed **9** into the aziridine **19**. Treatment of **9** with aqueous AcOH gave **19** and the tetrahydrofuran **20**, with AcOH in benzene **20** and the triacetate **23**, and with aqueous H_2SO_4 in THF, the primary alcohol **22** (room temperature) or **19** and **22** (0°). Deacetylation of **9** followed by reaction with pyridinium hydrochloride led to the tetrahydrofuran **21** and the chloride **24** (*Scheme 2*). The diacetate **22** and the triacetate **23** gave the triol **25** which was deprotected to **26**. Reduction of the keto-aziridine **18** ($NaBH_4$) gave the alcohols **27** and **29** which were acetylated to give **28** and **19**, respectively (*Scheme 3*). Treatment of the aziridine **28** with AcOH in benzene followed by deacetylation gave **30** and hence **31**. AcOH in benzene transformed the triazoline **15** first into the aziridine **32** and hence into **33**, which was deprotected to give the triol **34** and hence **35**. The 2-(hydroxymethyl)piperidines **26**, **31**, and **35** inhibited *Vibrio cholerae* sialidase with $K_i = 3.8 \cdot 10^{-2}$ M, $3.4 \cdot 10^{-3}$ M, and $1.5 \cdot 10^{-4}$ M, respectively. The conformation of the glycerol side chain of these compounds and of the unbranched piperidines **2**–**4** deviates from the one of Neu5Ac (and Neu2en5Ac). This finding is rationalized by an H-bond between OH–C(8) and NH–C(6). The conformations and the K_i values of **26**, **31**, and **35** correlate with each other.

Introduction and Problem. – We have described three syntheses of *N*-acetylneuraminic acid (Neu5Ac, **1**) [1–3] which were conceived to elaborate strategies and methods suitable for the preparation of a variety of Neu5Ac analogues and particularly of potential inhibitors of sialidases[1]). One of these syntheses [1] has been used for the preparation of 4-deoxy-Neu5Ac [5] and of the 6-amino-2,6-dideoxy analogues of Neu5Ac **2**–**4** [6]. The piperidines **2** and **3** are reasonably good inhibitors of sialidases from *Vibrio cholerae* (K_i(**2**) = $1.9 \cdot 10^{-4}$ M, K_i(**3**) = $1.2 \cdot 10^{-4}$ M). To investigate the influence of additional C-substituents on the piperidine ring of **2** and **3** on the inhibition of sialidases, we intended to prepare C(2)-branched derivatives of *N*-acetyl-6-amino-2,6-dideoxyneuraminic acid. To this end, we studied the intramolecular 1,3-dipolar cycloaddition of the unsaturated azides **5** and **6**, intermediates in the above mentioned synthesis of 6-amino-2,6-dideoxy analogues of **1**. Intramolecular azide-olefin cycloadditions are well known [7–33] and have been used for the preparation of *N*-(ribofuranos-5-yl)triazoles [34] and pyrrolidin-1-yl (but not, to the best of our knowledge, for the preparation of piperidino) derivatives of carbohydrates [35] [36]. From **5** and **6**, we expected the initial formation of hydropyridotriazoles, which we hoped to transform into the corresponding aziridines[2]), the latter being of interest both as synthetic intermediates and as potential sialidase inhibitors.

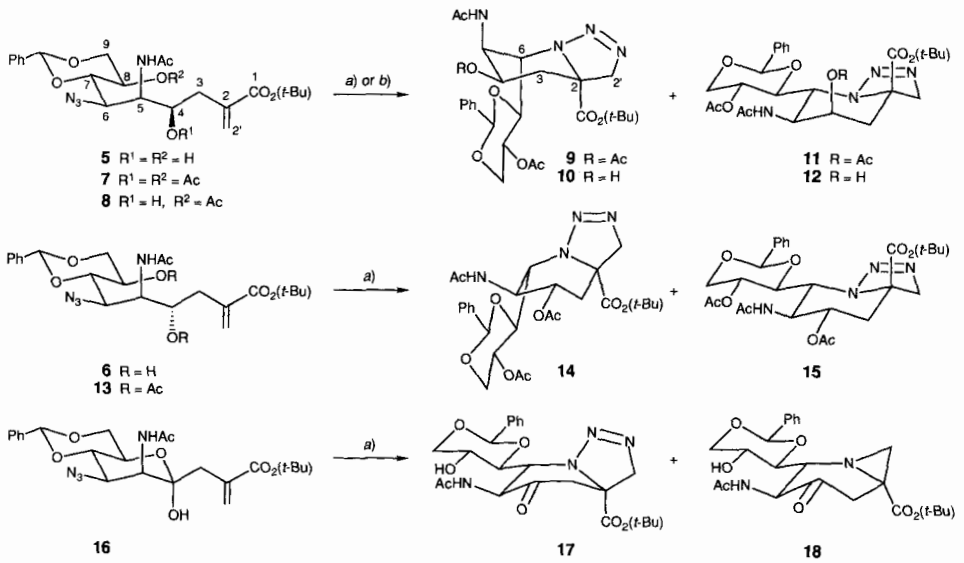
[1]) For leading references about sialidases and sialidase inhibitors, see [4].

[2]) For the preparation of aziridine inhibitors of coffee bean galactosidase and of α- and β-glucosidases by a different approach, see [37].



Results and Discussion.– The intramolecular cycloaddition of the azido-olefines **5–8**, **13**, and **16** (*Scheme 1*) can *a priori* lead in each case to four products, *viz.* two regioisomers and two diastereoisomers. Thermolysis of the diols **5** and **6** in benzene under reflux gave mixtures of unstable products. The diacetate **7**, however, gave regioselectively the dihydrotriazoles **9** (68%) and **11** (25%). Thermolysis of the epimeric diacetate **13** gave **14** (19%) and **15** (69%). The monoacetate **8**, obtained from **5** (82%), underwent slow cyclisation already at room temperature yielding, according to ^{1}H-NMR spectroscopy, a mixture of **10** (15%), **12** (55%), and four unidentified by-products from which **10** was obtained pure. Attempted isolation of **12** by HPLC led to its decomposition. Upon

Scheme 1[3])



a) Benzene, reflux. *b*) For **8**: benzene, r.t.

[3]) In the *Tables* and in the *Theoretical Part*, the same numbering is used for the dihydrotriazoles and aziridines as for their precursors.

acetylation, the dihydrohydrooxytriazoles **10** and **12** were converted into **9** and **11**, respectively. Finally, thermolysis of **16** gave an inseparable mixture of the dihydrooxotriazole **17** and the aziridine **18** (44%, **17/18** 3.6:1) together with starting material **16** (30%) which was separated by partial crystallization or by prep. HPLC (*Zorbax Sil*). Both ketones **17** and **18** decomposed partially during chromatography on silica gel. Aqueous AcOH transformed **17** into **18** which was isolated in 88% yield by crystallization. The dihydrotriazoles **9** and **17** were both transformed into the same aziridine **19** (see below and *Scheme 3*) and thus have the same configuration at C(2). Spectroscopic data confirmed the proposed structures, configurations, and conformations of compounds **9–12**, **14**, **15**, **17**, and **18**.

The absence of the azido bands in the IR spectra of the dihydrotriazoles **9–12**, **14**, **15**, and **17** and the absence of the olefinic H- and C-signals in the ^{1}H- and ^{13}C-NMR spectra, respectively, indicate that cycloaddition had occurred. The strong bands between 250–265 nm (ε = 2800–4300) in the UV spectra suggest the presence of a dihydrotriazole moiety [38]. The chemical shifts of $CH_2(2')^3$) show values between 3.88 and 4.66 ppm (see *Table 1*). This evidences the formation of fused adducts where $CH_2(2')$ is attached to the azo moiety for which $\delta(CH_2)$ is usually found between 3.8 and 4.9 ppm (compare δ of CH_2 attached to the triligated N-atom: 3.1–3.8 ppm [39][40]). In the ^{13}C-NMR spectra (*Table 2*), the *s* of C(2) appears consistently at a considerably higher field (62.66–66.21 ppm) than the *t* of C(2') (73.48–82.52 ppm). This again indicates that C(2') and not C(2) is attached to the azo moiety [40]. As expected[4]), all these dihydrotriazoles are fused and not bridged. According to their CD spectra, the hydropyridotriazoles **11** and **15** (strong negative maxima at 239 nm and positive maxima at 265–267 nm) form a set of compounds possessing the same configuration at C(2), and **9**, **10**, and **14** (strong positive maxima at 232–237 nm and negative maxima at 258–260 nm) form another set of compounds possessing a configuration at C(2) opposite to the one of **11** and **15**. These assignments correlate well with the chemical shift of C(2'), with δ values at 74.9 and 74.0 ppm for **11**[5]) and **15** on the one hand, and between 81.9 and 82.5 ppm for **9**, **10**, and **14** on the other hand.

The coplanarity of the aminoazo function requires a pseudoequatorial orientation of C(2')[6]). Such an orientation is realized in a $^2C_5$-like conformation of the (2*S*)-configurated hydropyridotriazoles (**11**, **12**, **15**), where, moreover, the side chain attached at C(6) is also equatorially oriented. In the (2*R*)-configurated epimers, the equatorial orientation of C(2') in a $^5C_2$-like conformation entails a 1,3-diaxial interaction of the COO(*t*-Bu) substituent and the side chain at C(6). One might thus speculate that (2*R*)-configurated hydropyridotriazoles will avoid a $^5C_2$-like conformation. AM1 calculations predict, however, that both the (2*R*)- and (2*S*)-epimers possess a chair conformation, $^5C_2$ for the former, and $^2C_5$ for the latter epimers.

According to the ^{1}H-NMR spectrum, **15** possesses a $^2C_5$-like conformation characterized by large vicinal coupling constants (J(3a,4) = J(4,5) = J(5,6) = 11 Hz) and should thus belong to the (2*S*)-series. The same is valid for **11** and **12** which show large J(5,6) and small J(3a,4), J(3b,4), and J(4,5) coupling constants (see *Table 1*). Among the (2*R*)-configurated hydropyridotriazoles, **9** and **10** possess a $^5C_2$-like conformation with large J(3a,4) and small J(4,5) and J(5,6) values. The epimer **14**, however, possesses a $^{N,4}B$ conformation, avoiding the three 1,3-diaxial interactions of a $^5C_2$-conformation. According to UV, ^{13}C- and ^{1}H-NMR spectra, **17** is also a dihydrotriazole, belonging to the (2*R*)-series as evidenced by the δ value of C(2') of 79.75 ppm. According to J(5,6) = 8 Hz, **17** possesses neither a $^5C_2$- nor a $^{N,4}B$-, but rather a flattened $B_{2,5}$-conformation. The IR spectrum of **18** shows three C=O bands at 1740 (ketone), 1730 (ester), and 1645 cm^{-1} (amide). In the ^{13}C-NMR spectrum of **18**, *t* at 38.67 and 37.98 ppm (C(3) and C(2')) indicate an aziridine moiety [43–46]. As expected, the *s* of C(2) at 41.1 ppm is shifted upfield in comparison with the corresponding signals of the dihydrotriazoles **9–12**, **14**, and **15** (62.6–66.2 ppm). Similarly, $CH_2(2')$ of **18** is strongly shielded (1.76 and 2.58 ppm). AM1 calculations indicate that **18** possesses a $^4H_5$ conformation, consistent with J(5,6) = 8.2 Hz.

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[4]) As a rule, intramolecular cycloadditions of azidoalkenes lead to fused dihydrotriazoles. The formation of a bridged adduct has been postulated [41], although the ^{1}H-NMR data appear to agree better with the corresponding annulated adduct.

[5]) The acetate **11** has also been obtained from **12** (see above), δ (C(2')) for **12** = 73.5 ppm.

[6]) According to X-ray analysis, the central piperazine ring of dimeric allyl azide exhibits a chair-like conformation, and the methylene groups of the dihydrotriazole moieties are equatorially oriented [41].

Table 1. *Selected ^{1}H-NMR* (400 MHz, $CDCl_3$) *Chemical Shifts* [ppm] *and Coupling Constants* [Hz] *for Compounds* **9**–**35**

H–Atom or J[3])	**9**	**10**	**14**	**17**	**11**	**12**	**15**	**18**	**27**[a])	**28**	**29**[a])[b])	**19**[c])	**32**
H_a–C(3)	1.55	1.38	1.82	2.41	1.71	1.55	1.49–1.56	2.92	2.14	2.43	2.34	2.56	1.96
H_b–C(3)	2.47	2.47	2.53	3.16	2.53	2.23	2.27	3.42	2.48	2.50	2.47	2.64	2.97
H–C(4)	5.57	2.72	4.30–4.43	–	5.14	3.94	5.26	–	3.69	5.00	3.96	5.16	4.99
H–C(5)	4.60–4.65	4.36	4.30–4.43	4.91	4.54	4.13	3.98	4.39	3.90	4.06	4.13	4.43	4.15
H–C(6)	4.96	5.02	4.70	4.87	4.30	4.41	4.40	3.51	3.21	2.98	3.24	2.85	3.36
H_a–C(2')	4.43	4.41	4.55	4.46	3.95	3.88	4.10	1.76	1.94	1.75	2.19	1.97	2.12
H_b–C(2')	4.43	4.48	4.66	4.64	4.14	4.08	4.22	2.58	2.14	2.32	2.51	2.34	2.35
J(3a,3b)	13.6	13.4	14.0	15.9	14.9	14.1	12.9	16.3	13.5	14.2	15.2	16.2	14.0
J(3a,4)	11.2	11.0	3.3	–	2.6	2.0	11.0	–	11.0	5.3	3.3	3.0	11.2
J(3b,4)	3.8	3.8	*ca.* 12.0	–	3.5	3.7	4.5	–	4.9	9.6	4.1	4.3	6.6
J(4,5)	4.1	4.3	[f])	–	2.7	2.4	11.0	–	9.8	9.5	2.8	2.8	10.7
J(5,6)	*ca.* 2.0	1.5	3.1	8.0	11.5	11.2	11.0	8.2	8.8	9.2	10.8	10.7	11.1
J(6,7)	3.2	3.5	3.0	2.1	3.2	3.4	3.6	3.0	1.6	1.7	1.6	1.5	2.1
$J(H_a,H_b)$	[f])	16.2	17.6	17.0	16.0	15.9	15.9	0.0	0.0	0.0	2.2	1.7	<0.3

H–Atom or J[3])	**20**[a])	**21**	**22**	**23**[d])	**24**	**25**[a])	**26**[e])	**30**[a])	**31**[e])	**33**	**34**[a])	**35**[e])
H_a–C(3)	1.76	1.76	1.70	1.70	1.95	1.68	2.12	1.37	1.93	1.60	1.46	1.75
H_b–C(3)	2.28	2.28	2.15	2.16	2.11	1.94	2.20	2.10	2.38	2.29	2.33	2.59
H–C(4)	4.34	4.38	5.10	5.15	4.36–4.40	3.99	4.14	3.64–3.72	3.93–4.05	5.01	3.50–3.60	3.70–3.82
H–C(5)	3.95	4.09	4.24	4.24	4.01	3.95	4.30	3.64–3.72	3.93–4.05	4.12	3.83	4.06
H–C(6)	3.32	2.92	2.81	3.11	3.40	3.35	3.77	3.02	3.58	3.08	3.20	3.70–3.82
H_a–C(2')	4.01	3.92	3.55	3.61	3.87	3.65	3.91	3.72	3.99	4.09	3.52	3.83
H_b–C(2')	4.15	4.17	3.80	5.20	4.47	4.24	4.47	3.79	3.99	4.16	3.57	3.94
J(3a,3b)	11.4	11.5	15.4	15.3	14.8	14.5	15.8	13.0	14.4	12.5	12.5	13.7
J(3a,4)	0.0	0.0	3.3	3.1	3.1	3.0	3.0	11.2	11.1	11.6	12.3	11.7
J(3b,4)	6.7	6.8	3.1	3.3	3.3	3.4	3.1	4.2	4.5	4.6	4.5	4.6
J(4,5)	0.9	<1.0	3.3	3.3	2.9	3.0	2.7	[f])	[f])	10.6	10.2	9.8
J(5,6)	*ca.* 9.0	9.5	10.5	11.0	10.6	10.8	11.6	*ca.* 9.6	10.5	10.5	10.6	9.8
J(6,7)	1.4	1.3	<1.5	1.2	2.3	1.3	<0.5	1.3	<0.5	1.6	1.3	0.7
$J(H_a,H_b)$	8.8	8.8	11.2	11.1	11.5	11.6	12.4	11.3	[f])	10.7	10.7	12.2

[a]) In CD_3OD. [b]) Long-range coupling (J = 1 Hz) between H_b–C(3) and H_a–C(2'). [c]) Long-range coupling (J = 0.9 Hz) between H_b–C(3) and H_b–C(2'). [d]) Long-range coupling (J = 1.2 Hz) between H_a–C(2') and NH. [e]) In D_2O. [f]) Not determined.

Table 2. *^{13}C-NMR* (50.6 MHz, $CDCl_3$) *Chemical Shifts* [Hz] *for Compounds* **7–35**

C-Atom[3])	**7**	**8**	**13**	**9**	**10**	**14**	**17**	**11**	**12**	**15**	**18**	**28**
C(1)	165.31	167.74	165.42	169.38[c])	169.64	169.57	169.67	168.94[c])	169.85	169.56[c])	169.26	169.58
C(2)	136.96	138.04	136.91	63.66	63.86	62.66	65.49	64.18	64.55	66.21	41.10	40.39
C(3)	34.97	37.38	35.19	29.49	32.23	33.88	43.59	32.54	36.23	34.26	38.67[c])	36.56
C(4)	71.45	71.90	71.31	66.17	64.04	67.82	202.75	70.18	67.20	69.30	204.28	69.96
C(5)	53.20	55.27	51.09	48.62	51.34	52.56	54.76	47.14	49.59	51.78	55.76	50.61
C(6)	56.69	57.12	59.64	59.51	59.12	62.73	60.01	54.53	53.03	56.40	62.00	63.08[c])
C(7)	78.43	78.79	77.95	81.16	81.51	80.57	81.48	76.73	76.74	76.06	82.18	78.48
C(8)	62.93	62.98	63.61	63.28	63.30	63.60	61.13	63.56	63.24	63.26	65.09	62.90[c])
C(9)	67.79	67.88	67.73	67.91	68.15	67.88	70.91	68.02	68.17	68.20	71.09	67.59
C(2')	127.48	128.03	127.49	81.91	82.03	82.52	79.75	74.88	73.48	73.97	37.98[c])	27.28
Ac	170.20	170.41	169.89	170.34	171.81	171.28	171.05	169.83[c])	170.27	170.42	170.76	171.23
	169.86	169.41	169.56	170.06	170.83	170.77	22.72	169.56	170.06	170.06	22.64	170.30
	169.03	23.18	169.30	169.50[c])	23.37	170.52		169.56[c])	23.23	169.02[c])		170.12
	23.11	20.57	23.18	23.27	20.71	23.09		23.24	20.89	23.33		23.23
	20.71		20.81	20.85		21.00		21.20		20.81		20.96
	20.53		20.69	20.63		20.71		20.87		20.71		20.86
t-Bu	80.71	81.54	81.08	83.86	83.87	83.27	84.27	82.50	82.12	83.54	82.50	81.12
	27.86	27.83	27.88	27.62	27.85	27.70	27.28	27.95	27.77	27.80	27.75	27.70
Benzylidene	101.59	101.36	101.35	102.25	102.61	103.02	101.95	101.67	101.61	101.84	101.59	101.26
	136.40	136.66	136.63	136.26	136.46	136.59	137.06	137.27	137.41	137.34	137.55	137.56
	129.62	129.50	129.07	128.49	128.83	128.85	128.67	128.82	128.71	128.83	129.05	128.76
	128.48	128.40	128.18	127.78	128.06	127.99	127.88	128.09	128.03	128.06	128.17	127.96
	125.92	125.85	125.95	125.98	126.04	126.26	126.34	126.29	126.35	126.45	126.08	126.25

Table 2 (cont.)

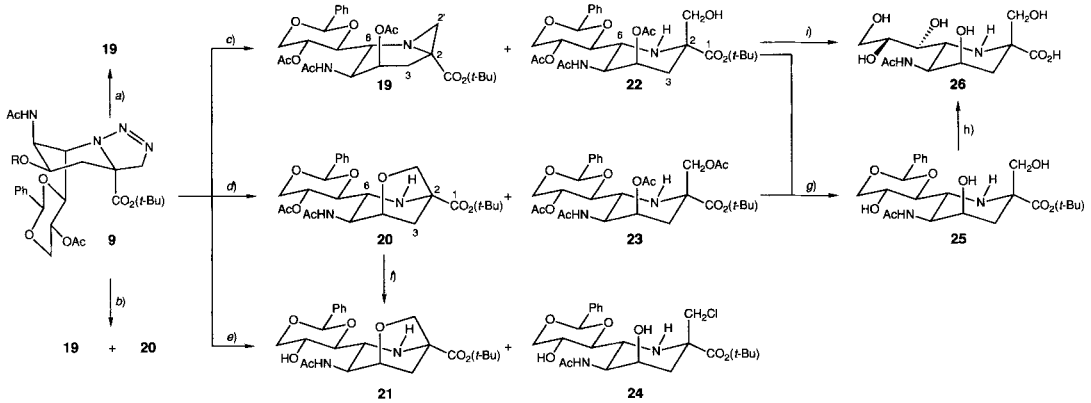
C-Atom[3])	**29**	**19**	**21**	**22**	**23**	**24**	**26**[a])	**30**[b])	**31**[a])	**34**[b])	**35**[a])
C(1)	170.70	169.51[c])	169.85	169.34[c])	169.46[c])	170.64	174.79[d])	173.93[c])	173.85[d])	174.02[c])	172.70[d])
C(2)	37.06	36.99	65.60	60.79	59.92	61.57	65.54	64.20	66.35	65.42	67.96
C(3)	40.50	38.71	42.55	34.04	34.87	37.22	33.46	40.62	34.03	38.90	34.60
C(4)	65.01	69.36	79.24[c])	71.33	71.27	66.67	65.26[c])	69.23	65.81[c])	70.61	65.76[c])
C(5)	49.27	44.64	49.30	46.17[d])	45.96	48.75	47.98	52.78	51.73	54.64[d])	51.70
C(6)	58.17	58.99	53.90	48.16[d])	48.04	50.96	50.78	55.16	54.16	54.88[d])	57.13
C(7)	81.65	78.71	79.93[c])	76.82	76.38	81.28	66.02[c])	81.03	66.43[c])	81.26	67.43[c])
C(8)	62.01	63.41	60.38	61.88	62.21	61.95	74.52	61.42	74.43	61.53	74.67
C(9)	71.07	67.56	71.29	67.88	67.89	70.90	62.43	72.25	60.42	69.00	65.38
C(2')	29.05	26.33	73.35	62.25	62.04	47.16	61.46	62.20	62.26	72.73	62.28
Ac	171.61	170.42	170.18	172.27	171.25	171.03	174.30[d])	174.14[c])	175.49[d])	174.22[c])	175.43[d])
	23.00	169.65[c])	23.36	169.84[c])	170.77	23.44	22.29	23.04	22.46	22.95	22.45
		169.56[c])		169.77[c])	170.12[c])						
		23.32		23.47	169.89[c])						
		21.27		21.39	23.51						
		20.96		20.89	21.47						
					21.14						
					20.33						
t-Bu	81.95	81.18	82.56	82.08	82.13	82.61		82.94		82.97	
	27.69	27.70	27.90	27.73	27.73	27.81		28.12		28.28	
Benzylidene	101.29	101.03	101.26	101.30	101.39	101.52		102.28		102.32	
	137.77	137.59	137.58	137.02	137.31	137.49		139.53		139.44	
	128.85	128.76	128.82	128.85	128.80	129.08		129.68		129.53	
	127.99	127.99	128.11	128.07	128.06	128.25		128.93		128.84	
	126.01	126.21	126.19	126.28	126.36	126.14		127.43		127.47	

[a]) In D_2O. [b]) In CD_3OD. [c]) [d]) Attribution may be interchanged.

The cycloadditions proceeded diastereoselectively. Thus, the (2*R*)-configurated addition products were preferentially formed from the diacetate **7** (d.e. 73%) and from the hemiacetal **16** (d.e. > 98%), while the (2*S*)-epimers were the major products from the monoacetate **8** (possessing the same configuration as **7**; d.e. 78%) and from the diacetate **13** (d.e. 78%). AM1 calculations show that the (2*S*)-epimers are more stable. That the (2*S*)-configurated **12** is preferentially formed in benzene at room temperature, and the (2*R*)-configurated **9** in benzene under reflux evidences the kinetic control of the cycloadditions. The diastereoselectivity may be rationalized as follows. In the (2*S*)-products, there is a 1,3-diaxial interaction between the C(2) and C(4) substituents. *Dreiding* models show that this interaction becomes effective at an early stage of the trajectory leading to the (2*S*)-configurated addition products. This interaction is energetically unfavourable in the case of the diacetate **7**, but may be favourable (H-bond to the carbonyl O-atom of COO(*t*-Bu)) in the case of the monoacetate **8**. In the (2*R*)-products **9** and **10**, there is a 1,3-diaxial interaction between the C(2) and C(6) substituents, but, again according to *Dreiding* models, this interaction becomes effective only at a considerably late stage of the reaction, probably after the transition state [43]. The models also show that a colinear approach of C(2) and N(1) of the azido function (corresponding to the pyrido N-atom in the product) on the reaction path leading to the (2*S*)-products (**11**, **12**, **15**) entails a quasi axial orientation of the C(5) acetamido function in a boat-like transition state and a destabilizing steric interaction of the 1,4-flagpole type between this group and the COO(*t*-Bu) function. This factor is particularly strong in the case of the hydroxy ketone derived from **16** and is responsible for the exclusive formation of a (2*R*)-hydropyridotriazole.

Photolysis, thermolysis, or acid treatment of dihydrotriazoles leads to aziridines, imines, or enamines and to secondary products. As a rule, photolysis is more selective than thermolysis and leads mainly to aziridines as the major products [39] [44–46]. Acid treatment of dihydrotriazoles gives rise to N_2 evolution and to secondary products which may stem from the intermediate formation of aziridines [46]. With catalytic amounts of acid in aprotic solvents, aziridines are indeed obtained in good-to-excellent yields [47]. The (2*R*)-hydropyridotriazole **9** was chosen as model compound for studying the transformation of hydropyridotriazoles into aziridines. Whereas thermolysis of **9** gave several products, sensitized irradiation at 366 nm for 70 min yielded the aziridine **19** (40%) together with starting material (50%; *Scheme 2*). Longer irradiation periods reduced the yield of **19** in favour of several secondary products. The transformation **9** → **19** could, however, be brought about advantageously with aqueous AcOH at room temperature giving **19** (71%) and the tetrahydrofuran **20** (15%), the latter arising from an acid-catalysed deacetylation and an intramolecular S_N2 reaction. The reaction of **9** with AcOH/C_6H_6 at room temperature afforded the triacetate **23** (66%) and **20** (18%). Treatment of **9** with 5% aqueous H_2SO_4 in THF at –20° gave a 2:1 mixture of the aziridine **19** and the primary alcohol **22**. After prolonged reaction (4 h) at room temperature, **22** was isolated in 50% yield. Deacetylation of **9** (NH_3 in MeOH) and treatment of the resulting diol with pyridinium hydrochloride in CH_2Cl_2 yielded the hydroxytetrahydrofuran **21** (78%) and the chloride **24** (15%). Deacetylation of **20** gave **21** as the only product, and deacetylation of **23** and of the diacetate **22** led to the triol **25**.

Scheme 2[3])



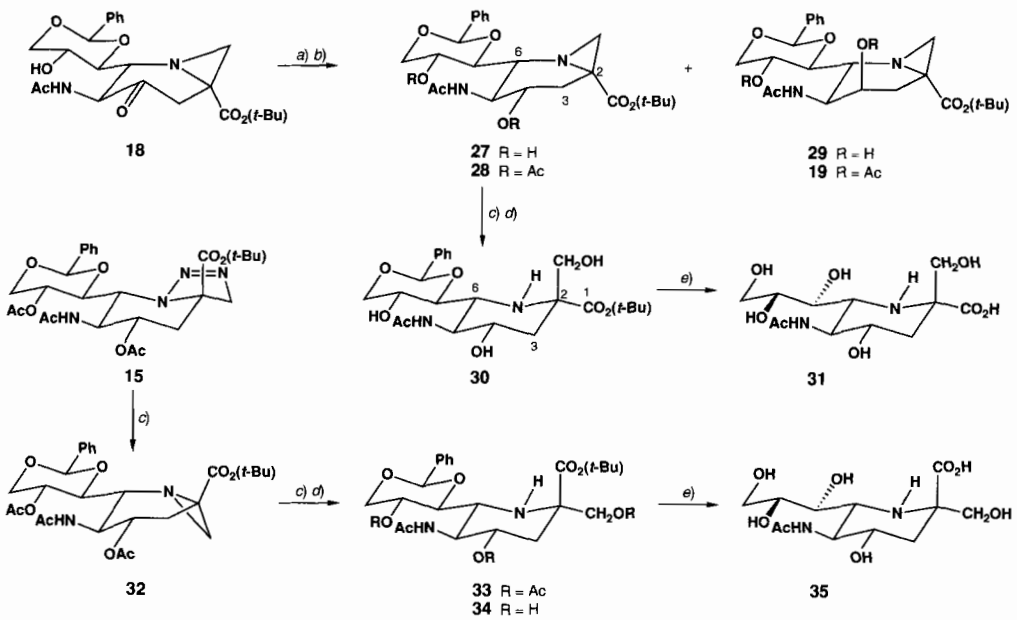
a) Benzophenone, benzene, hν, r.t. *b*) AcOH, THF/H_2O 2:1, r.t. *c*) 5% H_2SO_4, THF, –20° to r.t. *d*) AcOH/benzene 2:1, r.t. *e*) NH_3, MeOH, r.t.; pyridinium hydrochloride THF, r.t. *f*) NH_3, MeOH, r.t.; *g*) NaOMe, MeOH, r.t. *h*) CF_3COOH, r.t. *i*) 0.5M NaOH, MeOH, r.t. 2M HCO_2H, r.t.

The aziridine **19** shows characteristic signals for $CH_2(2')$[3]) [44] [47–50] in the ^{1}H- (1.97 ppm (*d* with J = 1.7 Hz) and 2.34 ppm (br. *s*)) and ^{13}C-NMR spectrum (26.3 ppm). The C(2) *s* occurs at 37.0 ppm. The coupling constants in the ^{1}H-NMR spectrum of **19** (J(5,6) = 10.7, J(3a,4) = 3.0, J(3b,4) = 4.3, and J(4,5) = 2.8 Hz) indicate an S_5-conformation [51]. The products **20–25** possess a $^2C_5$-conformation as evidenced by a large J(5,6) and a small J(4,5) (see *Table 1*). Whereas for **22–25** both J(3,4) have the same value of *ca.* 3.2 Hz, J(3,4; *cis*) is 6.7 and J(3,4; *trans*) is 0 Hz for the ethers **20** and **21**. In agreement with this, the values for J_{gem} of $CH_2(2')$ for **22–25** are in the range of 11–11.6 Hz, while the values of J_{gem} for **20** and **21** are significantly smaller (8.8 Hz) [52]. The formation of the two bridged products is an additional proof for the configuration at C(2). Compounds **20–24** may derive from an intermediate diazonium ion or (**22–24**) from nucleophilic opening of the aziridine ring.

Treatment of **25** with CF_3COOH cleaved both the benzylidene acetal and the COO-(*t*-Bu) group to give **26** as an amorphous powder in 82% yield after ion-exchange chromatography (*Dowex 1×8*, HCO_2^- form) and lyophilization (*Scheme 2*). The same compound **26** was also obtained in 64% yield by saponification of **22** (0.5M NaOH) followed by acetal cleavage with aqueous HCOOH. Reduction of the keto aziridine **18** with $NaBH_4$ gave the epimeric alcohols **27** (47%) and **29** (28%) (*Scheme 3*). Acetylation of the minor product **29** led to **19**. The ^{1}H-NMR data of **27** and of its acetate **28** are consistent with an S_5-conformation, as already postulated for **19** and **29**. The aziridine ring of **28** was opened by AcOH, and the product was deacetylated to the triol **30** (78%). Deprotection of **30** gave **31** (80%) as an amorphous powder. Finally, the dihydrotriazole **15** was transformed into the triacetate **33** (57%) by treatment with AcOH in CH_2Cl_2 for 48 h. After 25 h, the reaction mixture consisted of a 7:3 mixture of the aziridine **32** and of **33** (^{1}H-NMR) which were separated by flash chromatography. The ^{1}H-NMR spectrum of **32** (90% pure) showed a similar coupling pattern as **27** and **28**, indicating an S_5-conformation. Deacetylation of the triacetate **33** led to the triol **34** which, upon treatment with CF_3COOH, furnished **35** (41%).

The deprotected 2-(hydroxymethyl)piperidines **26**, **31**, and **35** possess a $^2C_5$-conformation as evidenced by the vicinal coupling constants (*Table 1*). Thus, the configuration at C(2) and the one at C(4) do not have a major impact on the conformation

Scheme 3[3])



a) $NaBH_4$, THF/H_2O 3:1, 0° *b*) Ac_2O, pyridine, 4-(dimethylamino)pyridine, CH_2Cl_2, r.t. *c*) AcOH, CH_2Cl_2, r.t. *d*) NaOMe, MeOH, r.t. *e*) CF_3COOH, r.t.

of the piperidine ring. A comparison of the coupling constants of the glycerol side chain of **2–4**, **26**, **31**, and **35** with those of Neu5Ac (**1**) and Neu2en5Ac [53] (*Table 3*) shows quite similar values for $J(6,7)$ and $J(8,9)$, while the values for $J(7,8)$ and $J(8,9')$ differ considerably, with $J(7,8)$ being smaller and $J(8,9')$ larger. The smaller $J(7,8)$ of **26** (3.4 Hz), **31** (3.6 Hz), and **35** (4.1 Hz) and to a lesser extend those of the unbranched piperidines **2** (6.0 Hz), **3** (6.0 Hz), and **4** (5.0 Hz) may be rationalized by postulating an H-bond between OH–C(8) and HN–C(6) or H_2N^+–C(6), as depicted in *Scheme 4* for OH–C(8) acting as a H-bond acceptor. The equilibrium between conformers **A** and **B** explains the coupling constants, assuming **A**/**B** ≈ 1:1 for compounds **2–4** and **A**/**B** ≈ 1:9 for **26**, **31**, and **35**. Conformer **A** corresponds to the one postulated by *Zbiral* and coworkers [54] for Neu5Ac, but our observations and rationalization are equally compatible with a conformer corresponding to the proposal of *Czarniecki* and *Thornton* [55] instead of **A**. *Zbiral* has shown the importance of the side-chain conformation for the ability of Neu5Ac and its epimers at C(7) and/or C(8) to act as substrates for the CMP-Neu5Ac synthetase, and a similarly important role of the side-chain conformation may well be anticipated for the action of sialidases. It may be that the relatively poor inhibition of *Vibrio cholerae* sialidase by **26** ($K_i = 3.8 \cdot 10^{-2}$), **31** ($K_i = 3.4 \cdot 10^{-3}$), and **35** ($K_i = 1.5 \cdot 10^{-4}$) [56] is codetermined by an unfavourable side-chain conformation. There is a correlation between the values of $J(7,8)$ of **26** and **31** and the pK_a values (pK_a (**26**) = 7.3; pK_a (**31**) = 6.3) and between the $J(7,8)$ values of **26**, **31**, and **35** and the K_i values; further investigations will have to show, how significant this correlation is.

Scheme 4

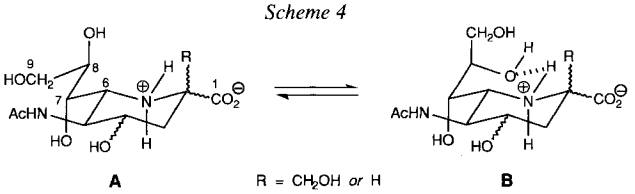


Table 3. *Comparison of the Coupling Constants of the Side Chain of the Unprotected Piperidines* **2–4**, **26**, **31** *and* **35** *with those of* **1** *and Neu2en5Ac*

Compound	Coupling Constant [Hz]			
	J(6,7)	*J*(7,8)	*J*(8,9)	*J*(8,9')
26	0.5	3.4	6.0	5.1
31	0.5	3.6	6.0	5.2
35	0.7	4.1	5.2	5.2
2 [6]	0	6.0	5.2	4.5
3 [6]	0	6.0	5.2	4.5
4 [6]	0	5.0	6.5	5.0
Neu5Ac (**1**) [54]	1.0	8.9	6.5	2.7
Neu2en5Ac	1.2	9.3	6.0	2.7

We thank the *Swiss National Science Foundation*, *F. Hoffmann-La Roche AG* and *Sandoz AG*, Basle, for generous support and Mr. *R. Wyler* for measuring the inhibition constants.

Experimental Part

General. Solvents were distilled before use. All reagents were obtained from *Fluka*. Solns. were evaporated at or below 50° in a *Büchi* rotary evaporator. Qual. TLC: *Merck* precoated silica gel *60 F-254* plates; detection by spraying the plates either with a soln. of 0.02M I_2 and 0.30M KI in 10% aq. H_2SO_4 soln. or with phosphomolybdic acid (10% in EtOH), followed in both cases by heating at *ca.* 200°. Flash chromatography (FC): silica gel *Merck 60* (40–63 μm). M.p.: uncorrected; *Büchi-510* apparatus. Optical rotations: *Perkin Elmer 241* spectrometer, 1-dm cell at 25° and 365, 436, 546, 578, and 589 nm; values at 589 nm from a regression curve. UV spectra: *Perkin Elmer 555* spectrometer; 1-cm cell. CD spectra: *Jasco J-500A* spectropolarimeter; *l* ($\Delta\varepsilon$) in nm. IR spectra: in KBr; *Perkin Elmer 298* spectrometer. ^{1}H- and ^{13}C-NMR spectra: at 400 MHz on a *Bruker-AM-400* (^{1}H) and at 50 MHz on *Varian-XL 200* spectrometer (^{13}C); chemical shifts in ppm rel. to tetramethylsilane as internal standart, coupling constants in Hz. Mass spectra: *Varian 112S* spectrometer; EI, 70 eV; CI, isobutane. For calculations, the AMPAC program (QCPE No. 506) was used. ^{13}C-NMR data see *Table 2*.

tert-*Butyl 5-Acetamido-4,8-di*-O-*acetyl-6-azido-7,9*-O-*benzylidene-2,3,5,6-tetradeoxy-2-methylidene*-D-glycero-D-talo-*nononate* (**7**). A mixture of Ac_2O (200 μl, 2.12 mmol) and pyridine (185 μl, 2.3 mmol) in CH_2Cl_2 (4 ml) was slowly added over 30 min to a stirred ice-cold soln. of **5** [6] (250 mg, 0.525 mmol) and a trace of 4-(dimethylamino)pyridine in dry CH_2Cl_2 (25 ml). After 2 h, TLC (AcOEt/hexane 4:1) showed the disappearance of **5**. The mixture was stirred for 1 additional h, diluted with AcOEt, washed successively with 5% aq. $NaHCO_3$ soln., H_2O, and brine, and dried ($MgSO_4$). Concentration of the soln. was followed by repeated evaporations with toluene. FC of the residue (80 g, AcOEt/hexane 4:1) gave **7** (276 mg, 94%). R_f (AcOEt/hexane 4:1) 0.33. M.p. 167–169° (dec.). $[\alpha]_D^{25} = -5.7$ ($c = 1.07$, $CHCl_3$). UV (EtOH): 248 (327), 254 (364), 259 (331), 265 (sh, 239). IR (KBr): 3440*s* (br.), 3270*m*, 3070*m*, 2970*m*, 2930*m*, 2880*m*, 2850*m*, 2120*m*, 1760*m*,

1745*s*, 1700*s*, 1655*s*, 1645*m*, 1560*m*, 1455*w*, 1420*w*, 1395*w*, 1370*m*, 1340*w*, 1320*m*, 1290*m*, 1275*m*, 1250*m*, 1235*s*, 1210*s*, 1140*s*, 1110*m*, 1085*m*, 1070*m*, 1055*m*, 1005*m*, 980*w*, 965*w*, 945*w*, 935*w*, 890*w*, 850*w*, 830*w*. ^{1}H-NMR (200 MHz): 1.46 (*s*, *t*-Bu); 1.80 (*s*, CH_3); 2.03 (*s*, CH_3); 2.07 (*s*, CH_3); 2.33 (*dd*, *J* = 13.8, 9.4, H–C(3)); 2.81 (br. *dd*, *J* = 13.7, 3.0, H–C(3)); 3.55 (*dd*, *J* = 4.7, 2.0, H–C(6)); 3.64 (*t*, *J* = 10.5, H_{ax}–C(9)); 4.23 (*dd*, *J* = 9.3, 1.9, H–C(7)); 4.52 (*dd*, *J* = 10.5, 5.4, H_{eq}–C(9)); 4.74 (*td*, *J* = 9.4, 4.7; addn. of CD_3OD: *dd*, *J* = 9.4, 4.7, H–C(5)); 5.15 (*td*, *J* = 9.7, 5.3, H–C(8)); 5.21 (*td*, *J* = 9.2, 3.0, H–C(4)); 5.56 (br. *s*, 2 H, PhC*H*, 1 olef. H); 6.12 (*d*, *J* = 1.6, 1 olef. H); 6.49 (*d*, *J* = 9.7, NH, exchangeable with CD_3OD); 7.36–7.44 (*m*, 3 arom. H); 7.47–7.54 (*m*, 2 arom. H). Anal. calc. for $C_{27}H_{36}N_4O_9$ (560.60): C 57.85, H 6.47, N 9.99; found: C 57.83, H 6.40, N 10.00.

tert-*Butyl 5-Acetamido-8-*O*-acetyl-6-azido-7,9-*O*-benzylidene-2,3,5,6-tetradeoxy-2-methylidene-*D*-glycero-*D*-talo-nononate* (**8**). To a stirred ice-cold soln. of **5** (93 mg, 0.195 mmol) and a trace of 4-(dimethylamino)pyridine in dry CH_2Cl_2 (8 ml) was added, over 30 min, a mixture of Ac_2O (20.3 µl, 0.22 mmol) and pyridine (20.2 µl, 0.25 mmol) in CH_2Cl_2 (2 ml). The mixture was stirred for 20 min and worked up as usual. FC (60 g, AcOEt/hexane 4:1) gave pure **8** (83 mg, 82%) which was crystallized from AcOEt/hexane: colourless globular crystals. R_f (AcOEt/hexane 4:1) 0.28. M.p. 138–141° (dec.). $[\alpha]_D^{25}$ = –23.7 (*c* = 0.55, $CHCl_3$). UV (EtOH): 250 (531), 255 (561), 260 (515), 265 (sh, 411). IR (KBr): 3420*s*, 3400*s*, 2980*m*, 2940*w*, 2910*w*, 2870*w*, 2100*s*, 1745*s*, 1710*s*, 1660*s*, 1630*m*, 1525*s*, 1510*m*, 1440*m*, 1405*m*, 1395*m*, 1370*s*, 1355*m*, 1335*s*, 1315*m*, 1300*m*, 1275*m*, 1230*s*, 1180*m*, 1150*s*, 1135*s*, 1100*m*, 1085*s*, 1070*s*, 1050*s*, 1030*s*, 1020*s*, 985*s*, 965*w*, 945*m*, 925*w*, 900*w*, 885*w*, 875*w*, 850*w*, 815*w*. ^{1}H-NMR (400 MHz): 1.49 (*s*, *t*-Bu); 1.81 (*s*, CH_3); 2.10 (*s*, CH_3); 2.37 (*dd*, *J* = 14.2, 8.3, H–C(3)); 2.66 (*dd*, *J* = 14.2, 2.6, H–C(3)); 3.63–3.68 (*m*, H–C(4)); 3.67 (*t*, *J* = 10.4, H_{ax}–C(9)); 3.92 (*dd*, *J* = 4.8, 2.1, H–C(6)); 3.96 (*d*, *J* = 3.3, OH, exchangeable with CD_3OD); 4.46–4.52 (*m*, 2 H, H–C(5), H–C(7)); 4.52 (*dd*, *J* = 10.6, 5.4, H_{eq}–C(9)); 5.20 (*td*, *J* = 9.8, 5.3, H–C(8)); 5.56 (*s*, PhC*H*); 5.70 (br. *s*, 1 olef. H); 6.19 (*d*, *J* = 1.3, 1 olef. H); 6.44 (*d*, *J* = 9.6, NH, exchangeable with CD_3OD); 7.39–7.43 (*m*, 3 arom. H); 7.48–7.51 (*m*, 2 arom. H). CI-MS: 492 (55), 491 (100, $[M + 1]^+$), 474 (27), 473 (43), 371 (19), 373 (30). Anal. calc. for $C_{25}H_{34}N_4O_8$ (518.57): C 57.91, H 6.61, N 10.80; found: C 58.18, H 6.72, N 10.89.

Thermolysis of **7**. A soln. of **7** (0.75 g, 1.34 mmol) in dry benzene (100 ml) was heated under reflux for 3 h. Removal of the solvent gave a residue which was purified by FC (160 g, AcOEt/hexane 4:1) to give **7** (30 mg, 4%), **11** (190 mg, 25%, crystallized from AcOEt/hexane as colourless needles), and **9** (510 mg, 68%, precipitated from AcOEt/hexane as an amorphous powder).

tert-*Butyl (3a*R,*5*R,*6*S,*7*R*)-6-Acetamido-5-acetoxy-7-[(4*S,*5*R*)-5-acetoxy-2-phenyl-1,3-dioxan-4-yl]-3,3a,4,5,6,7-hexahydropyrido[1,2-c][1,2,3]triazole-3a-carboxylate* (**9**): R_f (AcOEt) 0.19. $[\alpha]_D^{25}$ = +52.9 (*c* = 0.65, $CHCl_3$). UV (EtOH): 230 (sh, 3565), 237 (3670), 250 (sh, 3760), 256 (3973), 260 (sh, 3815). CD (EtOH): 212 (0), 234 (25.2),248 (0), 259 (–8.5), 291(0). IR (KBr): 3400*m* (br.), 3060*w*, 2980*w*, 2930*w*, 2860*w*, 1745*s*, 1680*m*, 1660*m*, 1535*m*, 1515*m*, 1450*m*, 1370*s*, 1285*m*, 1235*s*, 1160*s*, 1115*m*, 1090*m*, 1070*m*, 1050*s*, 1030*s*, 1010*m*, 920*w*, 840*w*. ^{1}H-NMR (400 MHz): 1.28 (*s*, *t*-Bu); 1.55 (*dd*, *J* = 13.5, 11.2, H–C(4)); 2.03 (*s*, 2 CH_3); 2.09 (*s*, CH_3); 2.47 (*dd*, *J* = 13.6, 3.8, H–C(4)); 3.68 (*t*, *J* = 10.3, H_{ax}–C(6')); 4.23 (*dd*, *J* = 9.8, 3.2, H–C(4')); 4.43 (*s*, 2 H–C(3)); 4.55 (*dd*, *J* = 10.4, 5.3, H_{eq}–C(6')); 4.60–4.65 (*m*, $w_{1/2}$ = 15.0; addn. of CD_3OD: br. *s*, $w_{1/2}$ = 7.0, H–C(6)); 4.96 (br. *t*, *J* ≈ 2.5, H–C(7)); 5.33 (*td*, *J* = 9.8, 5.2, H–C(5')); 5.57 (*dt*, *J* = 11.2, 4.1, H–C(5)); 5.60 (*d*, *J* = 7.9, NH, exchangeable with CD_3OD); 5.64 (*s*, H–C(2')); 7.27–7.37 (*m*, 3 arom. H); 7.52–7.56 (*m*, 2 arom. H). CI-MS: 561 (15, $[M + 1]^+$), 534 (26), 533 (100, $[M + 1 - N_2]^+$), 477 (31), 371 (15), 107 (86).

tert-*Butyl (3a*S,*5*R,*6*S,*7*R*)-6-Acetamido-5-acetoxy-7-[(4*S,*5*R*)-5-acetoxy-2-phenyl-1,3-dioxan-4-yl]-3,3a,4,5,6,7-hexahydropyrido[1,2-c][1,2,3]triazole-3a-carboxylate* (**11**): R_f (AcOEt) 0.30. M.p. 182–184° (dec.). $[\alpha]_D^{25}$ = –239.1 (*c* = 0.8, $CHCl_3$). UV (EtOH): 239 (3429), 255 (sh, 2794), 261 (2952), 265 (sh, 2889). CD (EtOH): 209 (0), 212 (3.4), 219 (0), 239 (–52.2), 254 (0), 267 (15.2), 306 (0). IR (KBr): 3460*m* (br.), 3350*s*, 3060*w*, 3030*w*, 2980*m*, 2940*w*, 2850*w*, 2900*w*, 2870*w*, 1750*s*, 1715*s*, 1680*s*, 1545*s*, 1500*m*, 1455*m*, 1430*m*, 1410*m*, 1380*s*, 1370*s*, 1340*m*, 1305*m*, 1280*m*, 1260*s*, 1250*s*, 1230*s*, 1150*s*, 1140*s*, 1130*s*, 1105*s*, 1080*m*, 1060*s*, 1030*s*, 1005*m*, 990*w*, 975*m*, 965*m*, 950*w*, 940*w*, 930*w*, 920*w*, 905*w*, 890*w*, 870*w*, 845*w*, 835*w*, 805*w*, 785*w*, 770*w*, 755*m*, 700*m*. ^{1}H-NMR (400 MHz): 1.43 (*s*, *t*-Bu); 1.71 (*dd*, *J* = 14.9, 2.6, H_{eq}–C(4)); 1.98 (*s*, CH_3); 2.08 (*s*, CH_3); 2.12 (*s*, CH_3) ; 2.53 (*dd*, *J* = 15.0, 3.5, H_{ax}–C(4)); 3.66 (*dd*, *J* = 10.3, 9.8, H_{ax}–C(6')); 3.95 (*d*, *J* = 16.0, H–C(3)); 4.14 (*d*, *J* = 16.0, H–C(3)); 4.30 (*dd*, *J* = 11.5, 3.2, H–C(7)); 4.44 (*dd*, *J* = 9.7, 3.1, H–C(4')); 4.52 (*dd*, *J* = 10.7, 5.1, H_{eq}–C(6')); 4.54 (*m*; addn. of CD_3OD: *dd*, *J* = 11.5, 2.7, H–C(6)); 5.14 (*q*, *J* = 2.9, H–C(5)); 5.44 (*td*, J = 9.5, 5.2, H–C(5')); 5.50 (*s*, H–C(2')); 5.58 (*d*, *J* = 8.4, NH, exchangeable with CD_3OD); 7.30–7.37 (*m*, 3 arom. H); 7.47–7.53 (*m*, 2 arom. H). Anal. calc. for $C_{27}H_{36}N_4O_9$ (560.60): C 57.85, H 6.47, N 9.99; found: C 57.81, H 6.45, N 10.00.

Thermolysis of **8**. A soln. of **8** (100 mg, 0.193 mmol) in dry benzene (5 ml) was left at r.t. for 7 d, when crystals separated from the mixture[7]). The mother liquor was decanted off, and the crystalline material (60 mg, enriched in three main products) was subjected to repeated FC (CH_2Cl_2/MeOH 95:5 or AcOEt) to give **12** (50 mg; 70% pure, could not be purified further) and pure **10** (6 mg, precipitated from AcOEt/hexane as an amorphous powder). Acetylation (1.5 equiv. of Ac_2O, 1.7 equiv. of pyridine, trace of 4-(dimethylamino)pyridine, CH_2Cl_2, r.t., 16 h) of **10** and **12** (70% pure) gave **9** and **11** (70% pure), resp., which were purified by FC.

tert-*Butyl (3a*R,5R,6S,7R*)-6-Acetamido-7-[(4*S,5R*)-5-acetoxy-2-phenyl-1,3-dioxan-4-yl]-3,3a,4,5,6,7-hexahydro-5-hydroxypyrido[1,2-c][1,2,3]triazole-3a-carboxylate* (**10**): R_f (AcOEt) 0.10, R_f (CH_2Cl_2/MeOH 95:5) 0.21. $[\alpha]_D^{25}$ = +50.7 (*c* = 0.40, $CHCl_3$). UV (EtOH): 238 (3843), 250 (sh, 3999), 246 (4263), 260 (sh, 4258). CD (EtOH): 211 (0), 235 (31.3), 248 (0), 258 (–8.9), 296 (0). IR ($CHCl_3$): 3560*w*, 3440*m*, 3000*w*, 2940*w*, 2870*w*, 1740*s*, 1670*m*, 1500*m*, 1370*s*, 1290*m*, 1190*s*, 1155*s*, 1095*m*, 1065*s*, 1050*s*, 1020*s*, 915*w*, 840*w*. ^{1}H-NMR (400 MHz): 1.34 (*s*, *t*-Bu); 1.38 (*dd*, *J* = 13.4, 11.0, H–C(4)); 2.03 (*s*, CH_3); 2.09 (*s*, CH_3); 2.47 (*dd*, *J* = 13.4, 3.8, H–C(4)); 2.72 (br. *s*, OH); 3.68 (*t*, *J* = 10.3, H_{ax}–C(6')); 4.22 (*dd*, *J* = 9.8, 3.5, H–C(4')); 4.37 (br. *t*; *J* ~ 5.3, H–C(6)); 4.42 (*d*, *J* = 16.2, H–C(3)); 4.48 (*d*, *J* = 16.2, H–C(3)); 4.49–4.55 (*m*, H–C(5); 4.52 (*dd*, *J* = 10.3, 5.3, H_{eq}–C(6')); 5.02 (*dd*, *J* = 3.4, 1.4, H–C(7)); 5.34 (*td*, *J* = 10.0, 5.4, H–C(5')), 5.56 (*s*, H–C(2')); 5.83 (*d*, *J* = 6.4, NH); 7.33–7.41 (*m*, 5 arom. H). ^{1}H-NMR ($CDCl_3$/CD_3OD 9:1, 400 MHz): 1.27 (*s*, *t*-Bu); 1.44 (*dd*, *J* = 13.6, 10.6, H–C(4)); 1.97 (*s*, CH_3); 2.03 (*s*, CH_3); 2.36 (*dd*, *J* = 13.6, 3.6, H–C(4)); 3.63 (*t*, *J* = 10.3, H_{ax}–C(6')); 4.17 (*dd*, *J* = 9.8, 3.4, H–C(4')); 4.22 (br. *dd*, *J* ≈ 4.2, 2.0, H–C(6)); 4.34 (*dt*, *J* = 10.6, 4.0, H–C(5)); 4.35 (*d*, *J* = 16.2, H–C(3)); 4.42 (*d*, *J* = 16.2, H–C(3)); 4.45 (*dd*, *J* = 10.3, 5.2, H_{eq}–C(6')); 4.90 (*dd*, *J* = 3.3, 2.2, H–C(7)); 5.27 (*td*, *J* = 10.0, 5.2, H–C(5')); 5.54 (*s*, H–C(2')); 7.24–7.30 (*m*, 3 arom. H); 7.34–7.37 (*m*, 2 arom. H). CI-MS: 493 (34), 492 (100, $[M + 1 - N_2]^+$), 474 (12), 435 (12), 107 (34).

tert-*Butyl (3a*S,5R,6S,7R*)-6-Acetamido-7-[(4*S,5R*)-5-acetoxy-2-phenyl-1,3-dioxan-4-yl]-3,3a,4,5,6,7-hexahydro-5-hydroxypyrido[1,2-c][1,2,3]triazole-3a-carboxylate* (**12**): R_f (AcOEt) 0.17, R_f (CH_2Cl_2/MeOH 95:5) 0.35. ^{1}H-NMR (400 MHz): 1.43 (*s*, *t*-Bu); 1.55 (*dd*, *J* = 14.0, 2.0, H–C(4)); 1.89 (br. *s*, OH, exchangeable with CD_3OD); 1.97 (*s*, CH_3); 2.12 (*s*, CH_3); 2.23 (*dd*, *J* = 14.2, 3.7, H–C(4)); 3.64 (*t*, *J* ≈ 10.2, H_{ax}–C(6')); 3.88 (*d*, *J* = 15.9, H–C(3)); 3.94 (br. *s*, $w_{1/2}$ = 8.0, H–C(5)); 4.08 (*d*, *J* = 15.9, H–C(3)); 4.13 (*ddd*, *J* = 11.2, 8.9, 2.4; addn. of CD_3OD: *dd*, *J* = 11.2, 2.4, H–C(6)); 4.29 (*dd*, *J* = 9.8, 3.4, H–C(4')); 4.41 (*dd*, *J* = 11.2, 3.3, H–C(7)); 4.50 (*dd*, *J* = 10.4, 5.2, H_{eq}–C(6')); 5.45 (*td*, *J* = 9.8, 5.1, H–C(5')); 5.48 (*s*, H–C(2')); 6.28 (*d*, *J* = 8.9, NH, exchangeable with CD_3OD); 7.29–7.38 (*m*, 3 arom. H); 7.54–7.56 (*m*, 2 arom. H).

tert-*Butyl 5-Acetamido-4,8-di-*O*-acetyl-6-azido-7,9-*O*-benzylidene-2,3,5,6-tetradeoxy-2-methylidene-*D-glycero-D-galacto-*nononate* (**13**). To an ice-cold soln. of **6** [6] (100 mg, 0.21 mmol) and a trace of 4-(dimethylamino)pyridine in abs. CH_2Cl_2 (5 ml) was added a mixture of Ac_2O (60 µl, 0.64 mmol) and pyridine (81 µl, 1 mmol) in CH_2Cl_2 (5 ml), dropwise within 30 min. The mixture was stirred at 0° for 6 h and at –20° overnight. Workup as usual followed by FC (25 g , AcOEt/hexane 4:1) gave pure **13** (88 mg, 75%; crystallized from AcOEt/hexane). R_f (AcOEt/hexane 4:1) 0.19. M.p. 137–142°. $[\alpha]_D^{25}$ = –68.3 (*c* = 0.64, $CHCl_3$). UV (EtOH): 249 (sh, 580), 255 (676), 260 (682), 264 (sh, 596). IR (KBr): 3400*m* (br.), 3280*m*, 3070*w*, 2980*m*, 2930*w*, 2870*w*, 2110*s*, 1755*s*, 1745*s*, 1695*s*, 1650*s*, 1565*m*, 1555*m*, 1455*w*, 1395*m*, 1370*s*, 1320*m*, 1280*m*, 1235*s*, 1225*s*, 1150*s*, 1100*m*, 1075*m*, 1045*s*, 1015*m*. ^{1}H–NMR (200 MHz): 1.50 (*s*, *t*-Bu); 1.98 (*s*, CH_3); 2.05 (*s*, CH_3); 2.11 (*s*, CH_3); 2.48 (*dd*, *J* = 13.6, 8.7, H–C(3)); 2.61 (*dd*, *J* = 13.6, 4.5, H–C(3)); 3.29 (*dd*, *J* = 7.4, 2.1, H–C(6)); 3.63 (*t*, *J* = 10.3, H_{ax}–C(9)); 4.15 (*dd*, *J* = 9.6, 2.2, H–C(7)); 4.53 (*dd*, *J* = 10.6, 5.3 H_{eq}–C(9)); 4.67 (*ddd*, *J* = 9.8, 7.4, 3.6; addn of CD_3OD:*dd*, *J* = 7.4, 3.6, H–C(5)); 5.12 (*td*, *J* = 9.7, 5.2, H–C(8)); 5.41–5.50 (*m*, H–C(4)); 5.51 (*s*, PhC*H*); 5.56 (br. *s*, 1 olef. H); 6.04 (*d*, *J* = 9.5, NH, exchangeable with CD_3OD); 6.14 (*d*, *J* = 1.5, 1 olef. H); 7.34–7.44 (*m*, 3 arom. H); 7.49–7.56 (*m*, 2 arom. H). Anal. calc. for $C_{27}H_{36}N_4O_9$ (560.60): C 57.85,H 6.47, N 9.99; found: C 57.76, H 6.64, N 9.84.

Thermolysis of **13**. A soln. of **13** (260 mg, 0.464 mmol) in dry benzene (40 ml) was heated under reflux for 4 h. The residue obtained after evaporation was subjected to FC (30 g, AcOEt/hexane 4:1) to give **15** (179 mg, 69%; crystallized from AcOEt/hexane as fine colourless needles). Further elution gave crude **14** (64 mg, contaminated with **15** and **13**) and pure **13** (5 mg). Crude **14** was chromatographed twice (AcOEt and AcOEt/toluene 4:1, resp.) to give pure **14** (50 mg, 19%; crystallized from AcOEt/hexane) and **13** (5 mg; total 10 mg, 4%).

tert-*Butyl (3a*R,5S,6S,7R*)-6-Acetamido-5-acetoxy-7-[(4*S,5R*)-5-acetoxy-2-phenyl-1,3-dioxan-4-yl]-3,3a,4,5,6,7-hexahydropyrido[1,2-c][1,2,3]triazole-3a-carboxylate* (**14**): R_f (AcOEt) 0.30. M.p. 130–133°. $[\alpha]_D^{25}$ = +75.4 (*c* = 0.40, $CHCl_3$). UV (EtOH): 244 (3639), 249 (sh, 3653), 255 (3696), 260 (sh, 3582). CD (EtOH): 199 (0), 203(–7.0), 213 (0), 232 (15.7), 237 (16.6), 256 (0), 260 (0.9), 266 (0), 279 (0.9), 303 (0).

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[7]) ^{1}H-NMR (400 MHz) of the crude thermolysate showed the presence of **10** (15%), **12** (55%), and 4 unidentified by-products (30%).

IR ($CHCl_3$): 3430*w*, 3000*w*, 2990*w*, 2940*w*, 2885*w*, 1740*s*, 1680*s*, 1510*m*, 1370*s*, 1155*s*, 1090*m*, 1080*m*, 1065*m*, 1050*s*, 1015*m*, 980*m*, 920*w*, 905*w*, 840*w*. ^{1}H-NMR (400 MHz): 1.38 (*s*, *t*-Bu); 1.82 (*dd*, *J* = 14.0, 3.3, H_{eq}–C(4)); 1.99 (*s*, CH_3); 2.04 (*s*, CH_3); 2.09 (*s*, CH_3); 2.53 (br. *t*, *J* ≈ 13.0, H_{ax}–C(4)); 3.65 (*t*, *J* = 10.3, H_{ax}–C(6')); 4.30–4.43 (*m*, simplified after addn. of CD_3OD, H–C(5), H–C(6)); 4.44 (*dd*, *J* = 9.8, 3.0, H–C(4')); 4.53 (*dd*, *J* = 10.4, 5.3, H_{eq}–C(6')); 4.55 (*d*, *J* = 17.7, H–C(3)); 4.66 (*d*, *J* = 17.6, H–C(3); 4.70 (*t*, *J* = 3.1, H–C(7)); 5.31 (*td*, *J* = 10.0, 5.3, H–C(5')); 5.63 (*s*, H–C(2')); 6.41 (*d*, *J* = 6.9, NH, exchangeable with CD_3OD); 7.34–7.40 (*m*, 3 arom. H); 7.46–7.49 (*m*, 2 arom. H). CI-MS: 561 (19, $[M + 1]^+$), 534 (25), 533 (100, $[M + 1 - N_2]^+$), 477 (23), 400 (12), 373 (16), 371 (14). Anal. calc. for $C_{27}H_{36}N_4O_9$ (560.60): C 57.85, H 6.47, N 9.99; found: C 58.10, H 6.77, N 10.15.

tert-*Butyl (3a*S,5S,6S,7R)-*6-Acetamido-5-acetoxy-7-[(4*S,5R)-*5-acetoxy-2-phenyl-1,3-dioxan-4-yl]-3,3a,4,5,6,7-hexahydropyrido[1,2-c][1,2,3]triazole-3a-carboxylate* (**15**): R_f (AcOEt) 0.36. M.p. 190–191° (dec.). $[\alpha]_D^{25}$ = –205 (*c* = 0.5, $CHCl_3$). UV (EtOH): 239 (4217), 255 (sh, 3358), 260 (3438), 265 (sh, 3303). CD (EtOH): 208 (0), 239 (–56.3), 253 (0), 265 (17.0), 303 (0). IR (KBr): 3400*s* (br.), 3000*w*, 2970*w*, 2940*w*, 2880*w*, 1740 s, 1690*s*, 1525*m*, 1485*m*, 1455*w*, 1440*m*, 1410*w*, 1370*s*, 1305*m*, 1285*m*, 1240*s*, 1220*s*, 1165*m*, 1155*m*, 1150*m*, 1120*m*, 1110*m*, 1090*m*, 1060*m*, 1025*s*, 1005*m*, 995*m*, 985*m*, 920*w*, 880*w*, 840*w*. ^{1}H-NMR (400 MHz): 1.49–1.56 (*m*, H–C(4)); 1.52 (*s*, *t*-Bu); 1.99 (*s*, CH_3); 2.01 (*s*, CH_3); 2.10 (s, CH_3); 2.27 (*dd*, *J* = 12.9, 4.5, H–C(4)); 3.64 (*t*, *J* = 10.1, H_{ax}–C(6')); 3.98 (br. *q*, *J* ≈ 10.0; addn. of. CD_3OD: *t*, *J* = 11.0, H–C(6)); 4.10 (*d*, *J* = 15.9, H–C(3)); 4.22 (*d*, *J* = 16.0, H–C(3)); 4.29 (*dd*, *J* = 9.9, 3.6, H–C(4')); 4.40 (*dd*, *J* = 11.0, 3.6, H–C(7)); 4.52 (*dd*, *J* = 10.4, 5.2, H_{eq}–C(6')); 5.26 (*td*, *J* = 11.0, 4.5, H–C(5)); 5.45 (*td*, *J* = 9.9, 5.2, H–C(5')); 5.47 (*d*, *J* = 9.6, NH, exchangeable with CD_3OD); 5.49 (*s*, H–C(2')); 7.35–7.39 (*m*, 3 arom. H); 7.55–7.59 (*m*, 2 arom. H). CI-MS: 561 (45, $[M + 1]^+$), 534 (30), 533 (100, $[M + 1 - N_2]^+$), 478 (14), 477 (53), 473 (19), 417 (23), 371 (15). Anal. calc. for $C_{27}H_{36}N_4O_9$(560.60): C 57.85, H 6.47, N 9.99; found: C 58.06, H 6.31, N 10.09.

tert-*Butyl (3a*R,6S,7R)-*6-Acetamido-3,3a,4,5,6,7-hexahydro-7-[(4*S,5R)-*5-hydroxy-2-phenyl-1,3-dioxan-4-yl]-5-oxopyrido[1,2-c][1,2,3]triazole-3a-carboxylate* (**17**) *and* tert-*Butyl (3*R,4S,6*a*R)-*4-Acetamido-1,3,4,5,6,6a-hexahydro-3-[(4*S,5R)-*5-hydroxy-2-phenyl-1,3-dioxan-4-yl]-5-oxoazirino[1,2-a]pyridine-6a-carboxylate* (**18**). A soln. of **16** [6] (500 mg) in dry benzene (100 ml) was heated under reflux for 12 h and the light brown soln. stored in the refrigerator for 5 d. The white precipitate of **17/18** (220 mg, 44%; **17/18** = 3.6:1 (integration of H-C(2') *s*)) was filtered off. Attempted further separation of **17/18** by chromatography led to partial decompositon. The concentrated mother liquor was cooled, affording a precipitate of **16** (52 mg). Prep. HPLC (*Zorbax Sil*, AcOEt/hexane 2:1, 12 ml/min) of the mother liquor gave a second crop of **16** (102 mg; total 154 mg, 30%). UV (EtOH): 230, 248 (sh), 254 (sh), 260 (sh), 265 (sh), 320. IR (KBr): 3400*s* (br.) 3060*w*, 2980*m*, 2930*w*, 2860*w*, 2105*w*, 1730*s*, 1660*s*, 1520*m*, 1450*m*, 1395*m*, 1370*s*, 1310*m*, 1280*m*, 1255*m*, 1225*m*, 1155*s*, 1075*s*, 1030*s*, 985*m*, 920*w*, 885*w*, 840*w*. ^{1}H-NMR (400 MHz, only data of **17** listed): 1.21 (*s*, *t*-Bu); 2.08 (*s*, CH_3); 2.41 (*d*, *J* = 15.9, H–C(4)); 3.16 (*d*, *J* = 15.8, H–C(4)); 3.72 (*t*, *J* = 10.4, H_{ax}–C(6')); 4.10 (*dd*, *J* = 9.4, 2.1, H–C(4')); 4.24 (*m*; addn. of CD_3OD: simplification, H–C(5')); 4.39 (*dd*, *J* = 10.7, 5.3, H_{eq}–C(6')); 4.46 (*d*, *J* = 17.0, H–C(3)); 4.64 (*d*, *J* = 17.0, H–C(3)); 4.87 (*dd*, *J* = 8.0, 2.1, H–C(7)); 4.91 (*dd*, *J* = 8.1, 6.5; addn. of CD_3OD: *d*, *J* = 8.1, H–C(6)); 5.56 (*s*, H–C(2')); 6.37 (*d*, *J* = 6.5, NH, exchangeable with CD_3OD); 7.31–7.36 (*m*, 3 arom. H); 7.43–7.50 (*m*, 2 arom. H). CI-MS: 447 ($[M + 1 - N_2]^+$), 391.

tert-*Butyl (3*R,4S,6*a*R)-*4-Acetamido-1,3,4,5,6,6a-hexahydro-3-[(4*S,5R)-*5-hydroxy-2-phenyl-1,3-dioxan-4-yl]-5-oxoazirino[1,2-a]pyridine-6a-carboxylate* (**18**). A soln. of **17/18** (1.22 g, 2.61 mmol) in THF (50 ml), H_2O (25 ml), and AcOH (0.5 ml) was stirred at r.t. for 2.5 h by which time N_2 evolution had ceased. The mixture was basified with 1% aq. $NaHCO_3$ soln. and extracted with AcOEt. Usual workup gave **18** (pure by TLC; 1.02 g, 88%). Recrystallization from AcOEt/hexane gave colourless globular crystals. R_f (CH_2Cl_2/MeOH 9:1) 0.41, R_f (CH_2Cl_2/MeOH 95:5) 0.17. M.p. 194–195°. $[\alpha]_D^{25}$ = +122.3 (*c* = 0.5, $CHCl_3$). UV (EtOH): 248 (sh, 562), 255 (530), 260 (462), 264 (sh, 356), 274 (sh, 218). IR (KBr): 3420*m* (br.), 3265*m*, 3060*w*, 2970*w*, 2930*w*, 2860*w*, 1740*s*, 1730*s*, 1645*s*, 1550*m*, 1455*w*, 1430*w*, 1400*m*, 1370*m*, 1345*w*, 1305*m*, 1270*s*, 1260*m*, 1220*m*, 1170*m*, 1160*m*, 1140*w*, 1130*w*, 1110*s*, 1095*w*, 1085*s*, 1075*s*, 1035*w*, 1020*m*, 1010*m*, 970*w*, 940*w*, 910*w*, 880*w*, 845*w*, 820*w*. ^{1}H-NMR (400 MHz): 1.44 (*s*, *t*-Bu); 1.76 (*s*, H–C(1)); 1.89 (*s*, CH_3); 2.58 (*s*, H–C(1)); 2.92 (*d*, *J* = 16.3, H–C(6)); 3.42 (*d*, *J* = 16.3, H–C(6)); 3.51 (*dd*, *J* = 8.3, 2.9, H–C(3)); 3.68 (*t*, *J* = 10.5, H_{ax}–C(6')); 3.89 (br. *s*, OH, exchangeable with CD_3OD); 4.17 (*dd*, *J* = 9.2, 3.0, H–C(4')); 4.25–4.31 (br. *m*; addn. of CD_3OD: *td*, *J* = 9.7, 4.8, H–C(5')); 4.38 (*dd*, *J* = 10.8, 5.1, H_{eq}–C(6')); 4.39 (*dd*, *J* = 8.2, 6.1; addn. of CD_3OD: *d*, *J* = 8.2, H–C(4)); 5.53 (*s*, H–C(2')); 6.19 (*d*, *J* = 6.2, NH, exchangeable with CD_3OD); 7.34–7.38 (*m*, 3 arom. H); 7.43–7.46 (*m*, 2 arom. H). CI-MS: 447 (100, $[M + 1]^+$), 391 (98). Anal. calc. for $C_{23}H_{30}N_2O_7$ (446.50): C 61.87, H 6.77, N 6.27; found: C 62.03, H 6.93, N 6.04.

Extrusion of N_2 from **9**. a) A soln. of **9** (30 mg, 0.056 mmol) and benzophenone (30 mg, 0.165 mmol) in benzene (8 ml) was degassed thoroughly (Ar) and irradiated (externally) in a *Pyrex* tube for 70 min using a 366-nm light source. The solvent was removed and the residue washed well with hexane. ^{1}H-NMR of the crude product (30 mg): **19** (40%) and **9** (50%) as main components.

b) A mixture of **9** (10 mg, 0.018 mmol), THF (2 ml), H_2O (1 ml), and AcOH (50 µl, 0.874 mmol; 0.29M in the reaction mixture) was stirred at r. t. for 7.5 h. The mixture was basified with 10% $NaHCO_3$ soln. and worked up as usual: 10 mg of crude mixture of **19** (75%), **9** (10%), and **20** (7%; according to 200-MHz ^{1}H-NMR).

c) A mixture of **9** (103 mg, 0.184 mmol), THF (20 ml), H_2O (10 ml), and AcOH (0.5 ml, 8.74 mmol, 0.29M in the reaction mixture) was stirred at r. t. for 25 h . Usual workup gave 104 mg of crude mixture. Crystallization from Et_2O/hexane gave **19** (59 mg). FC of the mother liquor (silica gel treated with 2% $NaHCO_3$, AcOEt) gave an additional crop (10 mg) of **19** (total 69 mg, 71%) and **20** (14 mg, 15%)[8]).

d) A mixture of **9** (50 mg, 0.089 mmol), benzene (1 ml), and AcOH (0.5 ml) was stirred at r.t. for 7 h. The mixture was diluted with AcOEt and poured into aq. $NaHCO_3$ soln. Usual workup gave 51 mg of crude product. Crystallization from AcOEt/hexane gave **23** (30 mg) as fine colourless needles. FC (8 g, AcOEt) of the mother liquor gave a second crop of **23** (5 mg; total 35 mg, 66%) and **20** (8 mg, 18 %, crystallized from AcOEt/hexane).

e) To a soln. of **9** (150 mg, 0.268 mmol) in freshly distilled THF (24 ml) at –20° was added 5% aq. H_2SO_4 soln. (10 ml, 4.893 mmol; 0.144M in the reaction mixture) over 5 min. The mixture was stirred at –20° for 15 min, at 0° for 2 h, and at r. t. for 4 h, basified with solid $NaHCO_3$ and worked up. FC (42 g, CH_2Cl_2/MeOH 95:5) gave pure **22** (74 mg, 50%, crystallized from AcOEt/hexane) as globular crystals.

f) As *e*. The reaction was stopped after stirring at 0° for 1 h 45 min. ^{1}H-NMR (200 MHz): a 65:35 mixture **19/22** which was completely transformed into **22** by several treatments with aq. H_2SO_4 soln. according to *e*.

g) To a sat. soln. of NH_3 in dry MeOH at 0° was added **9** (50 mg, 0.089 mmol). The mixture was stirred for 6 h at 0° and 24 h at r.t., till only one product was observed on TLC. The solvent was removed and freshly dried pyridinium hydrochloride (60 mg, 0.52 mmol) added to the dried residue in dry CH_2Cl_2 (5 ml). After stirring for 1 h, basic workup followed by FC (silica gel treated with 2% $NaHCO_3$, CH_2Cl_2/MeOH 9:1) gave **21** (33 mg, 82%, precipitated from Et_2O/hexane as an amorphous powder) and **24** (6.5 mg, 15%, precipitated from Et_2O/hexane as an amorphous powder).

tert-*Butyl (3*R,*4*S,*5*R,*6a*R)-*4-Acetamido-5-acetoxy-3-[(4*S,*5*R)-*5-acetoxy-2-phenyl-1,3-dioxan-4-yl]-1,3,4,5,6,6a-hexahydroazirino[1,2-a]pyridine-6a-carboxylate* (**19**): M.p. 195–195.5°. $[\alpha]_D^{25}$ = –49.5 (*c* = 0.24, $CHCl_3$). R_f (AcOEt/toluene 4:1) 0.10. IR (KBr): 3460*m* (br.), 3260*m*, 3070*w*, 2980*m*, 2940*w*, 2870*w*, 1745*s*, 1720*s*, 1650*s*, 1565*m*, 1550*m*, 1455*m*, 1440*w*, 1380*m*, 1370*s*, 1310*m*, 1285*m*, 1230*s*, 1150*s*, 1105*s*, 1085*m*, 1080*m*, 1050*s*, 1025*s*, 985*w*, 975*w*, 950*w*, 930*w*, 890*w*, 850*w*. ^{1}H-NMR (400 MHz): 1.36 (*s*, *t*-Bu); 1.97 (*d*, *J* = 1.7, H–C(1)); 1.99 (*s*, CH_3); 2.10 (*s*, CH_3); 2.11 (*s*, CH_3); 2.34 (br. *s*, $w_{1/2}$ = 4.0, H–C(1)); 2.56 (*dd*, *J* = 16.2, 3.0, H–C(6)); 2.64 (*ddd*, *J* = 16.3, 4.3, 1.0, H–C(6)); 2.85 (*dd*, *J* = 10.7, 1.5, H–C(3)); 3.64 (*t*, *J* = 10.2, H_{ax}–C(6')); 3.86 (*dd*, *J* = 9.2, 1.4, H–C(4')); 4.43 (*ddd*, *J* = 10.7, 8.8, 2.8; after addn. of CD_3OD: *dd*, *J* = 10.7, 2.8, H–C(4)); 4.45 (*dd*, *J* = 10.6, 5.4, H_{eq}–C(6')); 5.16 (*dt*, *J* = 4.1, 3.0, H–C(5)); 5.40 (*d*, *J* = 8.8, NH, exchangeable with CD_3OD); 5.47 (*td*, *J* = 9.4, 4.3, H–C(5')); 5.50 (*s*, H–C(2')); 7.31–7.35 (*m*, 3 arom. H); 7.48–7.51 (*m*, 2 arom. H). CI-MS: 533 (100, $[M + 1]^+$), 477 (40), 371 (50). Anal. calc. for $C_{27}H_{36}N_2O_9$ (532.59): C 60.89, H 6.81, N 5.26; found: C 60.92, H 6.96, N 5.09.

tert-*Butyl 5-Acetamido-8-*O*-acetyl-2-amino-2-*N,*6-anhydro-7,9-*O*-benzylidene-2,3,5-trideoxy-2-*C,*4-*O*-methylene-*D-erythro-L-allo-*nononate* (**20**): R_f (AcOEt) 0.22. $[\alpha]_D^{25}$ = –63.8 (*c* = 0.41, $CHCl_3$). IR ($CHCl_3$): 3430*m*, 3340*w*, 2980*m*, 2940*m*, 2910*w*, 2870*w*, 1735*s*, 1675*s*, 1500*s*, 1455*m*, 1395*m*, 1370*s*, 1330*m*, 1310*s*, 1300*m*, 1290*m*, 1165*s*, 1135*s*, 1100*s*, 1050*s*, 1025*s*, 975*m*, 915*m*, 885*w*, 840*m*. ^{1}H-NMR (400 MHz): 1.47 (*s*, *t*-Bu); 1.76 (*d*, *J* = 11.5, H–C(3)); 2.0–2.12 (br. *s*, NH, exchangeable with CD_3OD); 2.04 (*s*, CH_3); 2.09 (*s*, CH_3); 2.28 (*dd*, *J* = 11.5, 6.8, H–C(3)); 2.92 (br. *d*, *J* = 9.5, H–C(6)); 3.57 (*t*, *J* = 10.3, H_{ax}–C(9)); 3.84 (*dd*, *J* = 9.8, 1.3, H–C(7)); 3.92 (*d*, *J* = 8.8, 1 H, CH_2–C(2)); 4.09 (br. *t*, *J* ≈ 9.5; after addn. of CD_3OD: br. *d*, *J* ≈ 9.5, H–C(5)); 4.17 (*d*, *J* = 8.8, 1 H, CH_2–C(2)); 4.38 (br. *d*, *J* = 6.7, H–C(4)); 4.52 (*dd*, *J* = 10.6, 5.3, H_{eq}–C(9)); 5.14 (*td*, *J* = 9.9, 5.3, H–C(8)); 5.53 (*s*, PhC*H*); 5.77 (*d*, *J* = 9.5, NH, exchangeable with CD_3OD); 7.34–7.37 (*m*, 3 arom. H); 7.51–7.53 (*m*, 2 arom. H). CI-MS: 491 (100, $[M + 1]^+$), 431 (4).

tert-*Butyl 5-Acetamido-2-amino-2-*N,*6-anhydro-7,9-*O*-benzylidene-2,3,5-trideoxy-2-*C,*4-*O*-methylene-*D-erythro-L-allo-*nononate* (**21**): R_f (CH_2Cl_2/MeOH 9:1) 0.42. $[\alpha]_D^{25}$ = –51.1 (*c* = 0.46, $CHCl_3$). IR (KBr): 3680–3120*s* (br.), 2980*m*, 2930*m*, 2860*m*, 1730*s*, 1655*s*, 1540*m*, 1450*m*, 1395*m*, 1370*s*, 1330*m*, 1305*m*, 1250*s*, 1165*s*, 1130*s*, 1090*s*, 1070*s*, 1030*s*, 975*w*, 920*w*, 860*w*, 840*w*. ^{1}H-NMR (400 MHz, CD_3OD): 1.46 (*s*, *t*-Bu); 1.76 (*d*, *J* = 11.3, H–C(3)); 1.98 (*s*, CH_3); 2.28 (*dd*, *J* = 11.6, 6.7, H–C(3)); 3.32 (*dd*, *J* ≈ 9.0, 1.2, H–C(6)); 3.55

[8]) Deacetylation of **20** (dry MeOH/NH_3, 0°, 6 h, r.t., 16 h) gave **21**.

(*t*, *J* = 10.5, H_{ax}–C(9)); 3.57 (*dd*, *J* = 9.5, 1.4, H–C(7)); 3.94 (*td*, *J* = 10.0, 5.3, H–C(8)); 3.95 (br. *d*, *J* = 9.5, H–C(5)); 4.01 (*d*, *J* = 8.8, 1 H CH_2–C(2)); 4.15 (*d*, *J* = 8.8, 1 H CH_2–C(2)); 4.23 (*dd*, *J* = 10.6, 5.3, H_{eq}–C(9)); 4.34 (*dd*, *J* = 5.8, 0.9, H–C(4)); 5.48 (*s*, PhC*H*); 7.33–7.36 (*m*, 3 arom. H); 7.47–7.49 (*m*, 2 arom. H). CI-MS: 449 ([*M* + 1]$^+$). Anal. calc. for $C_{23}H_{32}N_2O_7$ (448.52): C 61.59, H 7.19, N 6.25; found: C 61.35, H 7.30, N 6.08.

tert-*Butyl 5-Acetamido-4,8-di-*O*-acetyl-2-amino-2-*N*,6-anhydro-7,9-*O*-benzylidene-2,3,5-trideoxy-2-*C*-(hydroxymethyl)-*D-erythro-L-allo-*nononate* (**22**): R_f (CH_2Cl_2/MeOH 95:5) 0.31. M.p. 178–179°. $[\alpha]_D^{25}$ = –74.2 (*c* = 0.83, $CHCl_3$). UV (EtOH): 248 (83), 254 (124), 260 (119), 265 (45). IR (KBr): 3540*m*, 3440*m* (br.), 3270*m*, 3060*w*, 2980*m*, 2940*w*, 2880*w*, 1740*s*, 1645*s*, 1550*m*, 1455*m*, 1430*w*, 1400*m*, 1370*s*, 1285*m*, 1235*s*, 1165*s*, 1130*m*, 1100*s*, 1080*m*, 1050*s*, 1030*s*, 990*m*, 980*m*, 950*w*, 915*w*, 895*w*, 880*w*, 845*w*. ^{1}H-NMR (400 MHz): 1.43 (*s*, *t*-Bu); 1.70 (*dd*, *J* = 15.4, 3.3, H–C(3)); 2.07 (*s*, CH_3); 2.13 (*s*, CH_3); 2.15 (*s*, CH_3); 2.15 (*dd*, *J* = 15.4, 3.1, H–C(3)); 2.59 (br. *d*, *J* = 12.7, NH, exchangeable with CD_3OD); 2.81 (br. *t*, *J* ≈ 11.6; after addn. of CD_3OD: br. *d*, *J* ≈ 11.6, H–C(6)); 3.05 (br. *d*, *J* = 11.3, OH, exchangeable with CD_3OD); 3.55 (*t*, *J* = 11.2; after addn. of CD_3OD: *d*, *J* = 11.2, 1 H, CH_2–C(2)); 3.67 (*t*, *J* = 10.5, H_{ax}–C(9)); 3.80 (br. *d*, *J* ≈ 10.7, H–C(7), 1 H, CH_2–C(2)); 4.24 (*ddd*, *J* = 10.5, 9.8, 3.3; after addn. of CD_3OD: *dd*, *J* = 10.5, 3.3, H–C(5)); 4.36 (*dd*, *J* = 10.6, 5.5, H_{eq}–C(9)); 5.10 (*q*, *J* = 3.2, H–C(4)); 5.43 (*d*, *J* = 9.5, NH, exchangeable with CD_3OD); 5.47 (*s*, PhC*H*); 5.53 (*td*, *J* = 9.9, 5.5, H–C(8)); 7.32–7.42 (*m*, 3 arom. H); 7.55–7.58 (*m*, 2 arom. H). CI-MS: 551 (100, [*M* + 1]$^+$), 533 (5), 519 (7), 491 (10). Anal. calc. for $C_{27}H_{38}N_2O_{10}$ (550.61): C 58.90, H 6.96, N 5.09; found: C 59.09, H 7.18, N 4.90.

tert-*Butyl 5-Acetamido-2-*C*-(acetoxymethyl)-4,8-di-*O*-acetyl-2-amino-2-*N*,6-anhydro-7,9-*O*-benzylidene-2,3,5-trideoxy-D-*erythro-L-allo-*nononate* (**23**): R_f (AcOEt) 0.32. M.p. 202°. $[\alpha]_D^{25}$ = –64.7 (*c* = 0.53, $CHCl_3$). IR (KBr): 3400*m* (br.), 2980*w*, 2930*w*, 2850*w*, 1745*s*, 1660*w*, 1525*w*, 1450*w*, 1370*m*, 1240*s*, 1165*m*, 1135*m*, 1100*m*, 1055*m*, 1045*m*, 1030*m*, 950*w*, 900*w*, 880*w*, 845*w*, 800*w*. ^{1}H-NMR (400 MHz): 1.43 (*s*, *t*-Bu); 1.70 (*dd*, *J* = 15.3, 3.1, H–C(3)); 1.98 (*s*, CH_3); 2.07 (*s*, CH_3); 2.15 (*s*, CH_3); 2.16 (*dd*, *J* = 15.4, 3.3, H–C(3)); 2.21 (*s*, CH_3); 2.40 (br. *d*, *J* = 12.4, NH, exchangeable with CD_3OD); 3.11 (br. *t*, *J* ≈ 11.2; after addn. of CD_3OD: br. *d*, *J* ≈ 11.2, H–C(6)); 3.49 (*t*, *J* = 10.3, H_{ax}–C(9)); 3.61 (*dd*, *J* = 11.1, 1.2; after addn. of CD_3OD: *d*, *J* = 11.1, 1 H, CH_2–C(2)); 3.82 (*dd*, *J* = 9.7, 1.2, H–C(7)); 4.24 (*ddd*, *J* = 10.8, 9.8, 3.3; after addn. of CD_3OD: *dd*, *J* = 10.8, 3.3, H–C(5)); 4.54 (*dd*, *J* = 10.5, 5.3, H_{eq}–C(9)); 5.06 (*td*, *J* = 9.9, 5.3, H–C(8)); 5.15 (*q*, *J* = 3.2, H–C(4)); 5.20 (*d*, *J* = 11.1, 1 H, CH_2–C(2)); 5.45 (*s*, PhC*H*); 5.50 (*d*, *J* = 9.7, NH, exchangeable with CD_3OD); 7.33–7.40 (*m*, 3 arom. H); 7.54–7.57 (*m*, 2 arom. H). CI-MS: 593 (100, [*M* + 1]$^+$), 533 (9), 491 (12), 415 (9). Anal. calc. for $C_{29}H_{40}N_2O_{11}$ (592.64): C 58.77, H 6.80, N 4.73; found: C 58.57, H 6.69, N 4.58.

tert-*Butyl 5-Acetamido-2-amino-2-*N*,6-anhydro-7,9-*O*-benzylidene-2-*C*-(chloromethyl)-2,3,5-trideoxy-*D-erythro-L-allo-*nononate* (**24**): R_f (CH_2Cl_2/MeOH 9:1) 0.33. $[\alpha]_D^{25}$ = –26.7 (*c* = 0.43, $CHCl_3$). IR ($CHCl_3$): 3610*w*, 3460–3240*m* (br.), 2960*s*, 2930*s*, 2860*m*, 1730*s*, 1670*s*, 1505*m*, 1450*m*, 1395*s*, 1370*s*, 1310*s*, 1290*s*, 1260*s*, 1150*s*, 1090*s*, 1030*s*, 915*m*. ^{1}H-NMR (400 MHz): 1.47 (*s*, *t*-Bu); 1.55–1.75 (br. *s*, NH, exchangeable with CD_3OD); 1.92 (*s*, CH_3); 1.95 (*dd*, *J* = 14.9, 3.1, H–C(3)); 2.11 (*dd*, *J* = 14.7, 3.3, H–C(3)); 2.52 (br. *s*, OH, exchangeable with CD_3OD); 3.40 (*dd*, *J* = 10.6, 2.3, H–C(6)); 3.63 (*t*, *J* = 10.4, H_{ax}–C(9)); 3.72 (*dd*, *J* = 9.3, 2.4, H–C(7)); 3.87 (*d*, *J* = 11.5, 1 H, CH_2–C(2)); 4.01 (ddd, *J* ≈ 10.5, 6.5, 2.9; after addn. of CD_3OD: *dd*, *J* = 10.5, 2.9, H–C(5)); 4.15 (*td*, *J* = 9.6, 5.2, H–C(8)); 4.35 (*dd*, *J* = 10.8, 5.3, H_{eq}–C(9)); 4.36–4.40 (m, H–C(4)); 4.47 (*d*, *J* = 11.5, 1 H, CH_2–C(2)); 5.46 (*s*, PhC*H*); 6.20 (br. *d*, *J* = 6.4, NH, exchangeable with CD_3OD); 7.36–7.39 (*m*, 3 arom. H); 7.48–7.50 (*m*, 2 arom. H). CI-MS: 487 (36) and 485 (36, [*M* + 1]$^+$), 469 (40) and 467 (81, [*M* – OH]$^+$), 450 (41), 449 (100, [*M* – Cl]$^+$), 371 (50).

tert-*Butyl 5-Acetamido-2-amino-2-*N*,6-anhydro-7,9-*O*-benzylidene-2,3,5-trideoxy-2-*C*-(hydroxymethyl)-*D-erythro-L-allo-*nononate* (**25**). A soln. of **22** (47 mg, 0.085 mmol) and NaOMe (0.5 mg, 0.01 mmol) in dry MeOH (9 ml) was stirred at r.t. for 24 h when the intermediate product (R_f 0.66) was completely transformed into **25**. The solvent was removed and the residue subjected to FC (12 g, CH_2Cl_2/MeOH 85:15): **25** (38 mg, 95%, crystallized from CH_2Cl_2/hexane) as fine colourless needles. R_f ($CHCl_3$/MeOH 4:1) 0.53. M.p. 200–204°(dec.). $[\alpha]_D^{25}$ = –64.4 (*c* = 0.49, $CHCl_3$). UV (EtOH): 249 (150), 255 (185), 260 (154), 265 (sh, 92). IR ($CHCl_3$): 3340*s* (br.), 2980*s*, 2940*m*, 2860*m*, 1730*s*, 1670*s*, 1505*m*, 1455*m*, 1400*m*, 1370*s*, 1310*m*, 1250*s*, 1160*s*, 1095*s*, 1070*s*, 1040*s*, 1030*s*, 975*m*, 915*w*, 890*w*, 865*w*, 845*w*. ^{1}H-NMR (400 MHz, CD_3OD): 1.44 (*s*, *t*-Bu); 1.68 (*dd*, *J* = 14.5, 3.0, H–C(3)); 1.94 (*dd*, *J* = 14.6, 3.4, H–C(3)); 2.01 (*s*, CH_3); 3.35 (*dd*, *J* = 10.8, 1.2, H–C(6)); 3.56 (*t*, *J* = 10.4, H_{ax}–C(9)); 3.62 (*dd*, *J* = 9.3, 1.4, H–C(7)); 3.65 (*d*, *J* = 11.6, 1 H, CH_2–C(2)); 3.95 (*dd*, *J* = 10.8, 3.0, H–C(5)); 3.99 (*q*, *J* = 3.2, H–C(4)); 4.12 (*td*, *J* = 9.8, 5.3, H–C(8)); 4.24 (*dd*, *J* = 10.5, 5.3, H_{eq}–C(9)); 4.24 (*d*, *J* = 11.5, 1 H, CH_2–C(2)); 5.44 (*s*, PhC*H*); 7.31–7.36 (*m*, 3 arom. H); 7.50–7.52 (*m*, 2 arom. H). CI-MS: 467 (28, [*M* + 1]$^+$), 449 (100, [*M* – OH]$^+$).

5-Acetamido-2-amino-2-N,*6-anhydro-2,3,5-trideoxy-2*-C-*(hydroxymethyl)*-D-erythro-L-allo-*nononic Acid* (**26**). a) *From* **22**. A mixture of **22** (9.5 mg, 0.017 mmol), MeOH (0.25 ml), and 0.5M aq. NaOH (0.5 ml) was stirred at r.t. for 48 h. TLC (CH_2Cl_2/MeOH 95:5): disappearance of **22**, product at R_f 0.08. After addition of 0.5M NaOH (2.25 ml), stirring was continued for 4 d at r.t. TLC (i-PrOH/MeOH/0.3M HCO_2H 6:1:3): disappearance of this product at R_f 0.78, new product at R_f 0.58. The solvent was evaporated and the residue dissolved in 2M HCO_2H (2 ml). After stirring at r. t. for 6 h, the mixture was washed with CH_2Cl_2, the aq. layer evaporated, and the residue basified with a few drops of 0.5M NaOH and chromatographed (*Dowex 1×8* (HCO_2^-), 2.5 g; H_2O (35 ml), 0.15M HCO_2H (30 ml), and 0.3M HCO_2H (100 ml)). The fractions eluted with 0.15M HCO_2H were combined, the solvent removed at < 36°, and the aq. soln. of the residue lyophilized: **26** (3.6 mg, 64%) as a foam.

b) *From* **25**. A mixture of **25** (41 mg, 0.088 mmol) and CF_3COOH (1.5 ml) was stirred at r.t. for 5.5 h. The solvent was removed and the dried (high vacuum) residue dissolved in H_2O (10 ml) and washed well with CH_2Cl_2. The aq. layer was evaporated and the residue dissolved in 0.5 ml of 0.5M NaOH (pH *ca.* 11) and chromatographed (*Dowex 1×8* (HCO_2^-), 8 g; 0.1, 0.2, and 0.3M aq. HCO_2H, each 250 ml). The fractions eluted with 0.1M HCO_2H were combined and evaporated at < 36°. An aq. soln. of the residue was lyophilized for 24 h: **26** (24.5 mg, 82%). R_f (i-PrOH/MeOH/0.3M HCO_2H 6:1:3) 0.24. $[\alpha]_D^{25}$ = –60.7 (*c* = 0.53, H_2O). pK_a (H_2O): 7.31. IR (KBr): 3700–2600*s* (br.), 1635*s* (br.), 1555*m* (br.), 1380*s*, 1350*w* (br.), 1320*w*, 1270*w*, 1155*w*, 1080*w*, 1045*m*, 955*w*, 895*w*, 860*w*, 830*w*. ^{1}H-NMR (400 MHz, D_2O): 2.05 (*s*, CH_3); 2.12 (*dd*, *J* = 15.8, 3.0, H–C(3)); 2.20 (*dd*, *J* = 15.9, 3.1, H–C(3)); 3.67 (*dd*, *J* = 11.8, 6.0, H–C(9)); 3.72 (*dd*, *J* = 11.9, 5.1, H–C(9)); 3.77 (*d*, *J* = 11.6, H–C(6); irradiation at 4.47: NOE of 22%); 3.91 (*d*, *J* = 12.4, 1 H, CH_2–C(2); irradiation at 4.47: NOE of 30%); 3.93 (*d*, *J* = 3.4, H–C(7); irradiation at 3.77: NOE of 4%); 4.04 (br. *q*, *J* ≈ 4.0, H–C(8)); 4.14 (*q*, *J* = 2.9, H–C(4)); 4.30 (*dd*, *J* = 11.5, 2.7, H–C(5)); 4.47 (*d*, *J* = 12.5, 1 H, CH_2–C(2); irradiation at 3.77: NOE of 12%). CI-MS: 305 (77, $[M - OH]^+$), 287 (100, $[M - H_2O - OH]^+$). Anal. calc. for $C_{12}H_{22}N_2O_8 \cdot 0.5H_2O$ (331.32): C 43.50, H 7.00, N 8.45; found: C 43.35, H 6.75, N 8.41.

Reduction of **18**. To a soln. of **18** (830 mg, 1.86 mmol) in THF (60 ml) and H_2O (20 ml) at 0° was added $NaBH_4$ (0.42 g, 11.05 mmol) in small portions over 45 min. The mixture was stirred for 45 min and worked up. FC (silica gel treated with 2% $NaHCO_3$, CH_2Cl_2/MeOH 9:1) gave **29** (234 mg, 28%) and **27** (393 mg, 47%) which, upon acetylation (1.5 equiv. of Ac_2O, 1.7 equiv. of pyridine, trace of 4-(dimethylamino)pyridine, CH_2Cl_2, r.t., 16 h), gave **19** and **28** (precipitated from CH_2Cl_2/hexane as colourless amorphous powder), resp., in quantitative yields.

tert-*Butyl (3*R,*4*S,*5*S,*6a*R)-*4-Acetamido-1,3,4,5,6,6a-hexahydro-5-hydroxy-3-[(4*S,*5*R)*]-5-hydroxy-2-phenyl-1,3-dioxan-4-yl]azirino[1,2-*a*]pyridine-6a-carboxylate* (**27**): colourless solidified foam. R_f (AcOEt) 0.26. $[\alpha]_D^{25}$ = +39.1 (*c* = 0.75, $CHCl_3$). IR ($CHCl_3$): 3620*w*, 3390*m* (br.), 3000*m*, 2980*m*, 2930*m*, 2870*m*, 1725*s*, 1660*s*, 1515*m*, 1455*m*, 1440*m*, 1390*m*, 1370*s*, 1345*m*, 1290*s*, 1150*s*, 1100*s*, 1085*s*, 1030*s*, 915*w*, 875*w*, 845*m*. ^{1}H-NMR (400 MHz, CD_3OD): 1.39 (*s*, *t*-Bu); 1.94 (*s*, H–C(1)); 1.95 (*s*, CH_3); 2.14 (*s*, H–C(1)); 2.14 (*dd*, *J* = 13.5, 11.0, H–C(6)); 2.48 (*dd*, *J* = 13.8, 4.9, H–C(6)); 3.21 (*dd*, *J* = 8.8, 1.6, H–C(3)); 3.49 (*dd*, *J* = 9.0, 1.6, H–C(4')); 3.54 (*t*, *J* = 10.3, H_{ax}–C(6')); 3.69 (*td*, *J* = 10.4, 4.9, H–C(5)); 3.90 (*t*, *J* = 9.4, H–C(4)); 4.21 (*dd*, *J* = 10.3, 5.4, H_{eq}–C(6')); 4.27 (*ddd*, *J* = 10.1, 9.2, 5.4, H–C(5')); 5.47 (*s*, H–C(2')); 7.28–7.34 (*m*, 3 arom. H); 7.48–7.52 (*m*, 2 arom. H). CI-MS: 450 (26), 449 (100, $[M + 1]^+$), 431 (11), 393 (54).

tert-*Butyl (3*R,*4*S,*5*S,*6a*R)-*4-Acetamido-5-acetoxy-3-[(4*S,*5*R)*]-5-acetoxy-2-phenyl-1,3-dioxan-4-yl]-1,3,4,5,6,6a-hexahydroazirino[1,2-*a*]pyridine-6a-carboxylate* (**28**): R_f (AcOEt) 0.23. $[\alpha]_D^{25}$ = –29.8 (*c* = 0.35, $CHCl_3$). IR (KBr): 3600–3160*m* (br.), 3060*w*, 2980*m*, 2930*w*, 2870*w*, 1740*s*, 1660*s*, 1550*m*, 1450*m*, 1390*m*, 1370*s*, 1315*m*, 1285*m*, 1235*s*, 1170*s*, 1150*s*, 1120*m*, 1100*m*, 1075*m*, 1040*s*, 1030*s*, 980*m*, 900*w*, 850*w*. ^{1}H-NMR (400 MHz): 1.39 (*s*, *t*-Bu); 1.75 (*s*, H–C(1)); 1.96 (*s*, CH_3); 2.04 (*s*, CH_3); 2.09 (*s*, CH_3); 2.32 (*s*, H–C(1)); 2.43 (*dd*, *J* = 14.2, 5.3, H–C(6)); 2.50 (*dd*, *J* = 14.2, 9.6, H–C(6)); 2.98 (*dd*, *J* = 9.2, 1.7, H–C(3)); 3.60 (*t*, *J* = 10.2, H_{ax}–C(6')); 3.84 (*dd*, *J* = 9.3, 1.7, H–C(4')); 4.06 (*q*, *J* = 9.1; after addn. of CD_3OD: *t*, H–C(4)); 4.47 (*dd*, *J* = 10.4, 5.3, H_{eq}–C(6')); 5.00 (*td*, *J* = 9.5, 5.3, H–C(5)); 5.48 (*td*, *J* = 9.6, 5.2, H–C(5')); 5.52 (*s*, H–C(2'); 5.52 (br. *d*, *J* = 9.2, NH, exchangeable with CD_3OD); 7.34–7.37 (*m*, 3 arom. H); 7.49–7.52 (*m*, 2 arom. H). CI-MS: 534 (7), 533 (3, $[M + 1]^+$), 372 (13), 175 (16), 101 (17), 91 (25), 86 (14), 85 (20), 83 (22), 81 (36), 79 (100). Anal. calc. for $C_{27}H_{36}N_2O_9$ (532.59): C 60.89, H 6.81, N 5.26; found: C 60.60, H 7.10, N 5.38.

tert-*Butyl (3*R,*4*S,*5*R,*6a*R)-*4-Acetamido-1,3,4,5,6,6a-hexahydro-5-hydroxy-3-[(4*S,*5*R)*]-5-hydroxy-2-phenyl-1,3-dioxan-4-yl]azirino[1,2-*a*]pyridine-6a-carboxylate* (**29**): colourless solidified foam. R_f (AcOEt) 0.35. $[\alpha]_D^{25}$ = +44.9 (*c* = 1.12, $CHCl_3$). IR ($CHCl_3$): 3620*w*, 3400*m* (br.), 3000*m*, 2980*m*, 2930*m*, 2870*m*, 1725*s*, 1665*s*, 1510*m*, 1455*m*, 1445*m*, 1390*m*, 1370*s*, 1345*m*, 1290*s*, 1145*s*, 1105*s*, 1080*s*, 1060*s*, 1030*s*, 1020*m*, 1000*m*, 985*m*, 945*m*, 915*w*, 875*w*, 845*m*. ^{1}H-NMR (400 MHz, CD_3OD): 1.37 (*s*, *t*-Bu); 1.95 (*s*, CH_3); 2.19 (br. *d*, *J* ≈ 1.7, H–C(1)); 2.34 (*dd*, *J* = 15.2, 3.3, H–C(6)); 2.47 (*ddd*, *J* = 15.1, 4.1, 0.9, H–C(6)); 2.51 (*d*, *J* = 2.2,

H–C(1)); 3.24 (*dd*, *J* = 10.8, 1.5, H–C(3)); 3.50 (*dd*, *J* = 9.2, 1.7, H–C(4')); 3.56 (*t*, *J* = 10.4, H_{ax}–C(6')); 3.96 (br. *q*, *J* ≈ 3.4, H–C(5)); 4.13 (*dd*, *J* = 10.8, 2.8, H–C(4)); 4.25 (*dd*, *J* = 10.5, 5.4, H_{eq}–C(6')); 4.27 (*td*, *J* = 9.7, 5.4, H–C(5')); 5.43 (*s*, H–C(2')); 7.27–7.34 (*m*, 3 arom. H); 7.45–7.50 (*m*, 2 arom. H). CI-MS: 450 (21), 449 (100, $[M + 1]^+$), 431 (8), 393 (7).

tert-*Butyl 5-Acetamido-2-amino-2*-N,*6-anhydro-7,9*-O-*benzylidene-2,3,5-trideoxy-2*-C-*(hydroxymethyl)*-D-erythro-L-gluco-*nononate* (**30**). A soln. of **28** (196 mg, 0.439 mmol) and AcOH (0.3 ml) in CH_2Cl_2 (7 ml) was stirred at r.t. for 24 h. TLC (CH_2Cl_2/MeOH 9:1): one major product at R_f 0.43. After basic workup, the crude product (210 mg) was dissolved in dry MeOH (5 ml) containing NaOMe (22 mmol) and stirred for 24 h at r.t. The solvent was removed and FC of the residue (CH_2Cl_2/MeOH 9:1) gave **30** (158 mg, 78%; crystallized from CH_2Cl_2/hexane) as colourless globular crystals. R_f (CH_2Cl_2/MeOH 9:1) 0.15. M.p. 163–166° (dec.). $[\alpha]_D^{25}$ = –40.6 (*c* = 0.35, $CHCl_3$). IR (KBr): 3560*s*, 3460*s* (br.), 3360*s* (br.), 3270*s* (br.), 3090*m*, 2980*m*, 2940*m*, 2880*w*, 2850*w*, 1725*s*, 1655*m*, 1620*s*, 1560*m*, 1475*m*, 1450*m*, 1445*m*, 1395*s*, 1385*s*, 1370*s*, 1365*s*, 1330*m*, 1320*m*, 1310*m*, 1280*s*, 1255*m*, 1240*m*, 1230*m*, 1210*m*, 1160*s*, 1150*s*, 1120*m*, 1105*m*, 1090*s*, 1070*s*, 1060*s*, 1050*s*, 1035*s*, 1025*s*, 990*w*, 980*w*, 975*w*, 945*w*, 915*w*, 900*w*, 885*w*, 845*m*. ^{1}H-NMR (400 MHz, CD_3OD): 1.37 (*dd*, *J* = 13.0, 11.4, H_{ax}–C(3)); 1.45 (*s*, *t*-Bu); 2.01 (*s*, CH_3); 2.10 (*dd*, *J* = 13.0, 4.2, H_{eq}–C(3)); 3.02 (br. *d*, *J* ≈ 9.6, H–C(6)); 3.55 (*t*, *J* = 10.5, H_{ax}–C(9)); 3.61 (*dd*, *J* = 9.4, 1.3, H–C(7)); 3.64–3.74 (*m*, H–C(4), H–C(5)); 3.72 (*d*, *J* = 11.3, 1 H, CH_2–C(2)); 3.79 (*d*, *J* = 11.2, 1 H, CH_2–C(2)); 4.06 (*td*, *J* = 9.9, 5.3, H–C(8)); 4.23 (*dd*, *J* = 10.5, 5.4, H_{eq}–C(9)); 5.45 (*s*, PhC*H*); 7.31–7.35 (*m*, 3 arom. H); 7.52–7.54 (*m*, 2 arom. H). CI-MS: 467 (100, $[M + 1]^+$), 411 (38).

5-Acetamido-2-amino-2-N,*6-anhydro-2,3,5-trideoxy-2*-C-*(hydroxymethyl)*-D-erythro-L-gluco-*nononic Acid* (**31**). A soln. of **30** (102 mg, 0.219 mmol) in CF_3COOH (2 ml) was stirred at r.t. for 8 h. The solvent was removed and the dried (high vacuum) residue dissolved in H_2O (10 ml) and washed well with CH_2Cl_2. The aq. soln. was evaporated and the residue dissolved in 1 ml of 1M NaOH (pH *ca.*11) and chromatographed (*Dowex 1×8* (HCO_2^-), 8 g; 250 ml of 0.1, 0.2, and 0.3M aq. HCO_2H). The first 40 ml (eluant) of 0.1M HCO_2H were evaporated. An aq. soln. of the residue was lyophilized for 48 h: **31** (56 mg, 80%) as a foam. R_f (i-PrOH/MeOH/0.3M HCO_2H 6:1:3) 0.26. $[\alpha]_D^{25}$ = –22.9 (*c* = 0.28, H_2O). pK_a 6.33. IR (KBr): 3680–2640*s* (br.), 1630*s* (br.), 1560*m* (br.), 1430*m*, 1375*s*, 1315*m*, 1260*m*, 1150*w*, 1095*m*, 1060*m*, 1040*m*, 925*w*, 875*w*. ^{1}H-NMR (400 MHz, D_2O): 1.93 (*dd*, *J* = 14.4, 11.1, H_{ax}–C(3)); 2.05 (*s*, CH_3); 2.38 (*dd*, *J* = 14.5, 4.5, H_{eq}–C(3)); 3.58 (br. *d*, *J* = 10.5, H–C(6)); 3.63 (*dd*, *J* = 11.7, 6.0, H–C(9)); 3.67 (*dd*, *J* = 11.7, 5.2, H–C(9)); 3.93 (br. *d*, *J* = 3.6, H–C(7)); 3.93–4.05 (*m*, 3 H); 3.99 (*s*, CH_2–C(2)). CI-MS: 305 (4, $[M - OH]^+$), 287 (100, $[M - H_2O - OH]^+$), 189 (19). Anal. calc. for $C_{12}H_{22}N_2O_8 \cdot H_2O$ (340.33): C 42.35, H 7.10, N 8.25; found: C 42.11, H 6.86, N 8.00.

tert-*Butyl 5-Acetamido-2-amino-2*-N,*6-anhydro-7,9*-O-*benzylidene-2,3,5-trideoxy-2*-C-*(hydroxymethyl)*-D-erythro-L-manno-*nononate* (**34**). A soln. of **15** (191 mg, 0.341 mmol) and AcOH (0.75 ml) in dry CH_2Cl_2 (3 ml) was stirred at r.t. for 48 h. After evaporation, the main product (**33**, R_f (AcOEt) 0.44) was separated by FC (AcOEt), dissolved in dry MeOH (5 ml) containing a trace of NaOMe, and stirred at r.t. for 48 h. Usual workup followed by FC (CH_2Cl_2/MeOH 9:1) gave **34** (90 mg, 57%; precipitated from AcOEt/hexane as an amorphous colourless powder). R_f (CH_2Cl_2/MeOH 9:1) 0.40. $[\alpha]_D^{25}$ = –6.8 (*c* = 0.15, $CHCl_3$). IR (KBr): 3600–3150*s*, 2980*m*, 2930*m*, 2860*m*, 1720*s*, 1650*s*, 1565*m*, 1555*m*, 1455*m*, 1395*m*, 1370*s*, 1315*m*, 1250*m*, 1235*m*, 1150*s*, 1090*s*, 1075*s*, 1030*s*, 900*m*, 845*m*. ^{1}H-NMR (400 MHz, CD_3OD): 1.46 (*t*, *J* = 12.3, H_{ax}–C(3)); 1.50 (*s*, *t*-Bu); 2.00 (*s*, CH_3); 2.33 (*dd*, *J* = 12.5, 4.5, H_{eq}–C(3)); 3.20 (*dd*, *J* = 10.6, 1.3, H–C(6)); 3.5–3.6 (*m*, H–C(4)); 3.52 (*d*, *J* = 10.7, 1 H, CH_2–C(2)); 3.54 (*t*, *J* = 10.2, H_{ax}–C(9)); 3.57 (*d*, *J* = 10.7, 1 H, CH_2–C(2)); 3.58 (*dd*, *J* = 9.6, 1.3, H–C(7)); 3.83 (*t*, *J* = 10.4, H–C(5)); 3.97 (*td*, *J* = 9.8, 5.2, H–C(8)); 4.26 (*dd*, *J* = 10.6, 5.3, H_{eq}–C(9)); 5.43 (*s*, PhC*H*); 7.20–7.32 (*m*, 3 arom. H); 7.53–7.55 (*m*, 2 arom. H). CI-MS: 467 ($[M + 1]^+$).

In a similar reaction, a soln. of **15** (59 mg, 0.1 mmol) and AcOH (0.1 ml) in dry CH_2Cl_2 (2 ml) was stirred at r.t. for 25 h. After evaporation, FC (16 g, AcOEt) of the residue gave **33** (14 mg, 22%; R_f 0.44) and **32** (33 mg, 59%; R_f 0.40).

tert-*Butyl (3*R,*4*S,*5*S,*6a*S*)-4-Acetamido-5-acetoxy-3-[(4*S,*5*R*)]-5-acetoxy-2-phenyl-1,3-dioxan-4-yl]-1,3,4,5,6,6a-hexahydroazirino[1,2-*a*]pyridine-6a-carboxylate* (**32**): ^{1}H-NMR (400 MHz): 1.40 (*s*, *t*-Bu); 1.96 (*dd*, *J* = 13.9, 11.2, H–C(6)); 1.99 (*s*, CH_3); 2.05 (*s*, CH_3); 2.10 (*s*, CH_3); 2.12 (*s*, H–C(1)); 2.35 (*s*, H–C(1)); 2.97 (*dd*, *J* = 14.1, 6.6, H–C(6)); 3.36 (*dd*, *J* = 11.1, 2.1, H–C(3)); 3.57 (*t*, *J* = 10.3, H_{ax}–C(6')); 3.93 (*dd*, *J* = 9.8, 2.2, H–C(4')); 4.15 (*td*, *J* = 10.8, 9.4; after addn. of CD_3OD: *t*, *J* = 10.7, H–C(4)); 4.55 (*dd*, *J* = 10.4, 5.2, H_{eq}–C(6')); 4.99 (*td*, *J* = 10.9, 6.6, H–C(5)); 5.37 (*d*, *J* = 9.4, NH, exchangeable with CD_3OD); 5.38 (*td*, *J* = 9.9, 5.0, H–C(5')); 5.41 (*s*, H–C(2')); 7.33–7.40 (*m*, 3 arom. H); 7.53–7.56 (*m*, 2 arom. H).

tert-*Butyl 5-Acetamido-2*-C-*(acetoxymethyl)-4,8-di*-O-*acetyl-2-amino-2*-N,*6-anhydro-7,9*-O-*benzylidene-2,3,5-trideoxy*-D-erythro-L-manno-*nononate* (**33**). ^{1}H-NMR (400 MHz): 1.46 (*s*, *t*-Bu); 1.60 (*t*, *J* = 12.3, 3.1, H–C(3)); 1.64 (br. *s*, NH, exchangeable with CD_3OD); 1.99 (*s*, CH_3); 2.00 (*s*, CH_3); 2.05 (*s*, CH_3); 2.12 (*s*, CH_3);

2.29 (*dd*, *J* = 12.5, 4.6, H–C(3)); 3.08 (br. *d*, *J* ≈ 10.0; after addn. of CD_3OD: sharper *d*, *J* ≈ 10.9, H–C(6)); 3.60 (*t*, *J* = 10.2, H_{ax}–C(9)); 3.84 (*dd*, *J* = 9.8, 1.6, H–C(7)); 4.09 (*d*, *J* = 10.7, 1 H, CH_2–C(2)); 4.12 (*q*, *J* = 10.2; after addn. of CD_3OD: *t*, *J* = 10.6, H–C(5)); 4.16 (*d*, *J* = 10.7, 1 H, CH_2–C(2)); 4.47 (*dd*, *J* = 10.4, 5.2, H_{eq}–C(9)); 5.01 (*ddd*, *J* = 11.6, 10.6, 4.6, H–C(4)); 5.20 (*td*, *J* = 9.9, 5.2, H–C(8)); 5.37 (*d*, *J* = 9.4, NH, exchangeable with CD_3OD); 5.47 (*s*, PhC*H*); 7.32–7.38 (*m*, 3 arom. H); 7.56–7.59 (*m*, 2 arom. H).

*5-Acetamido-2-amino-2-*N*,6-anhydro-2,3,5-trideoxy-2-*C*-(hydroxymethyl)-*D*-erythro-*L*-manno-nononic Acid* (**35**). A soln. of **34** (70 mg, 0.15 mmol) in CF_3COOH (2 ml) was stirred at r.t. for 7 h. The solvent was removed and the dried (high vacuum) residue dissolved in H_2O (10 ml) and washed well with CH_2Cl_2. After evaporation of H_2O, the residue was dissolved in 1 ml of 1M NaOH (pH *ca.* 11) and chromatographed (*Dowex 1×8* (HCO_2^-), 8 g; 250 ml of 0.1, 0.2, and 0.3M aq. HCO_2H). The first 20 ml (eluant) of 0.1M HCO_2H were evaporated, and the residue was dissolved in H_2O and lyophilized for 48 h: **35** (21 mg, 41%) as colourless powder. R_f (i-PrOH/MeOH/0.3M HCO_2H 6:1:3) 0.49. M.p. 200–205° (dec.). $[\alpha]_D^{25} = -3.9$ (*c* = 0.41, H_2O). IR (KBr): 3700–2500*s*, 1635*s*, 1575*s*, 1440*m*, 1375*s*, 1325*m*, 1275*m*, 1130*m*, 1100–1075*m*, 1030*m*, 930*w*, 880*w*, 845*m*. ^{1}H-NMR (400 MHz, D_2O): 1.75 (*dd*, *J* = 13.7, 11.7, H_{ax}–C(3)); 2.10 (*s*, CH_3); 2.59 (*dd*, *J* = 13.7, 4.6, H_{eq}–C(3)); 3.70–3.82 (*m*, 4 H); 3.83 (*d*, *J* = 12.2, 1 H, CH_2–C(2)); 3.94 (*d*, *J* = 12.2, 1 H, CH_2–C(2)); 3.94 (*dd*, *J* = 4.1, 0.8, H–C(7)); 4.06 (*t*, *J* = 9.8, H–C(5)); 4.08 (*td*, *J* = 5.2, 4.2, H–C(8)). FAB-MS: 323 (100, $[M+1]^+$), 277 (95). Anal. calc. for $C_{12}H_{22}N_2O_8 \cdot 0.5\ H_2O$ (331.32): C 43.50, H 7.00, N 8.45; found: C 43.52, H 7.29, N 8.17.

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