34. Analogues of Sialic Acids as Potential Sialidase Inhibitors. Synthesis of C_6 and C_7 Analogues of *N*-Acetyl-6-amino-2,6-dideoxyneuraminic Acid

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The piperidines **12**–**18**, piperidinose analogues of Neu5Ac (**1**) with a shortened side chain, were synthesized from *N*-acetyl-D-glucosamine *via* the azidoalkene **32** and tested as inhibitors of *Vibrio cholerae* sialidase. Deoxygenation at C(4) of the uronate **22**, obtained from the known D-GlcNAc derivative **20**, was effected by β-elimination (→ **23**), exchange of the AcO at C(3) with a (*t*-Bu)Me_2SiO group and hydrogenation (→**26**; *Scheme 1*). Chain extension of **26** by reaction with Me_3SiCH_2MgCl gave the D-*ido*-dihydroxysilane **28**, which was transformed into the unsaturated L-*xylo*-mesylate **29** and further into the L-*lyxo*-alcohol **30**, the mesylate **31**, and the L-*xylo*-azide **32**. The derivatives **29**–**31** prefer a sickle zig-zag and **32** mainly an extended zig-zag conformation (*Fig. 2*). The piperidinecarboxylate **15** was obtained from **32** by ozonolysis (→ **33**), intramolecular reductive amination (→ **34**), and deprotection, while reductive amination of **34** with glycolaldehyde (→ **35**) and deprotection gave **16** (*Scheme 2*). An intramolecular azide-olefin cycloaddition of **32** yielded exclusively the fused dihydrotriazole **36**, while the lactone **39** did not cyclize (*Scheme 3*). Treatment of **36** with AcOH (→ **37**) followed by hydrolysis (→ **38**) and deprotection led to the amino acid **18**. To prepare the (hydroxymethyl)piperidinecarboxylates **12** and **17**, **32** was first dihydroxylated (*Scheme 4*). The L-*gluco*-diol **40** was obtained as the major product, in agreement with *Kishi*'s rule. Silylation of **40** (→ **42**), oxidation with periodinane (→ **44**), and reductive amination gave the L-*gluco*-piperidine **45**. It was, on the one hand, deprotected to the amino acid **12** and, on the other hand, *N*-phenylated (→ **46**) and deprotected to **17**. While **45** and **12** adopt a $^2C_5$ conformation, the analogous *N*-Ph derivatives **46** and **17** adopt a $^5C_2$ and a $B_{3,6}$ conformation, respectively, on account of the allylic 1,3-strain. The conformational effects of this 1,3-strain are also evident in the carbamate **47**, obtained from **45** (*Scheme 5*), and in the C(2)-epimerized bicyclic ether **48**, which was formed upon treatment of **47** with (diethylamino)sulfur trifluoride (DAST). Fluorination of **40** with DAST (→ **49**) followed by treatment with AcOH led to the D-*ido*-fluorohydrin **50**. Oxidation of **50** (→ **51**) followed by a *Staudinger* reaction and reduction with $NaBH_3CN$ afforded the (fluoromethyl)piperidine **52**, while reductive amination of **51** with H_2/Pd led to the methylpiperidine **55**, which was similarly obtained from the keto tosylate **54** and from the dihydrotriazole **36**. Deprotection of **52** and **55** gave the amino acids **13** and **14**, respectively. The aniline **17** does not inhibit *V. cholerae* sialidase; the piperidines **12**–**16** and **18** are weak inhibitors, evidencing the importance of an intact 1,2,3-trihydroxypropyl side chain.

Introduction. – Several piperidine [1] and pyrrolidine [2] analogues of *N*-acetylneuraminic acid (Neu5Ac, **1**) are inhibitors of *Vibrio cholerae* neuraminidase. As shown in *Fig. 1*, the analogue **2** is the most active inhibitor, its epimer **3** is somewhat weaker, and the epimer **4**, possessing an axial COOH group, is not an inhibitor. The dependency of the inhibitory activity on the configuration at C(2) (systematic carbohydrate numbering) is significantly attenuated in the 2-hydroxymethylated piperidines **5** and **6** [3]. This may be due to an interaction of the CH_2OH group at C(2) with the COOH group and to a higher conformational flexibility of these branched-chain derivatives. A similar difference of the relative importance of the configuration at C(2) is observed for the epimeric 2-deoxy-*N*-acetylneuraminic acids **7** and **8** as compared to their phosphonic-acid analogues **9** and **10** [4]. The piperidine **11**, lacking the trihydroxypropyl side chain exists as a 2:1 mixture of

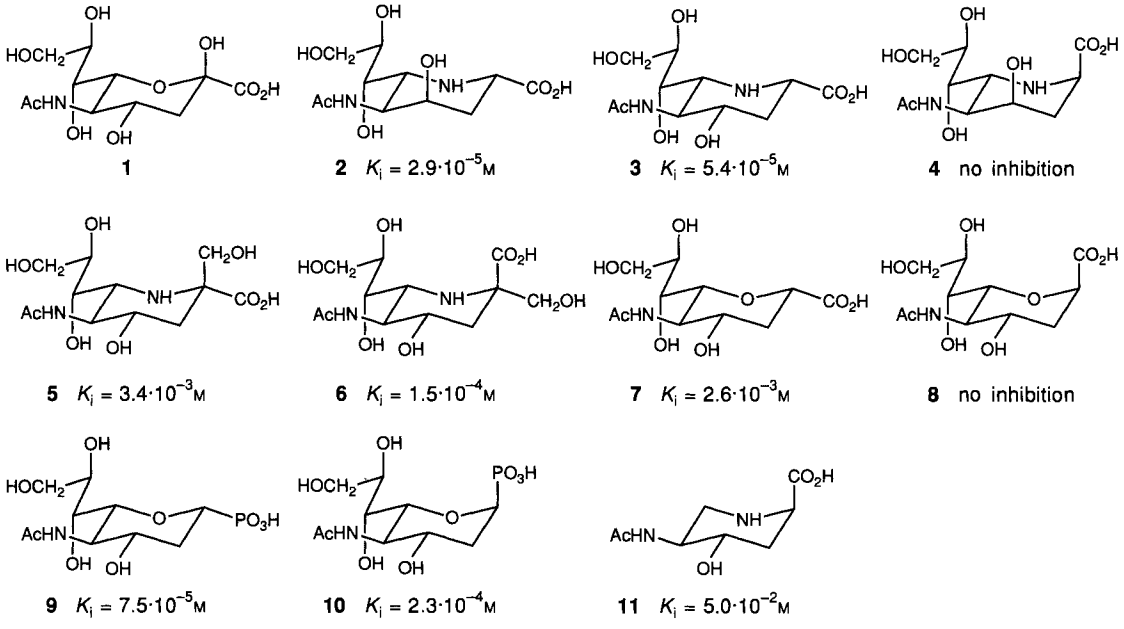

Fig. 1. *Neu5Ac* (**1**) *and some neuraminidase inhibitors with their* K_i *values*

the $^2C_5$ and $^5C_2$ conformers [5] and is still a (weak) inhibitor [6]. These observations, the different conformations of the trihydroxypropyl side chain of Neu5Ac and of its piperidine and pyrrolidine analogues [2], and the claim that this difference may influence the inhibitory activity illustrate the difficulties associated with the identification of the role of the side chain, of the configuration at C(2), and of the individual conformers of Neu5Ac analogues[1]). In this context, piperidine analogues of **11**, possessing an equatorial COOH group and a CH_2OH or CF_3 substituent at C(6) may contribute to assess the influence of the constitution of the side chain, of the OH group at C(7), of the configuration at C(6) and (indirectly) at C(2), and of the conformation of the piperidine ring. Such piperidine analogues with a shortened side chain may also be more easily accessible than the trihydroxypropyl-substituted analogues and thus be useful for the preparation of *N*-substituted derivatives. These could, in their turn, contribute to evaluate the role of *N*-protonation in the inhibition of sialidases, a factor known to be of importance in the inhibition of other glycosidases by piperidines and pyrrolidines [10].

Plan. – We intended to prepare the analogues **12**–**18** from the common intermediate **32** (*Scheme 1*). The azidoalkenoate **32** should be available from *N*-acetyl-D-glucosamine (= 2-(acetamido)-2-deoxy-D-glucopyranose; D-GlcNAc) by oxidation at C(6), deoxygenation at C(4), olefination and retentive substitution of OH–C(5) by an N_3 group.

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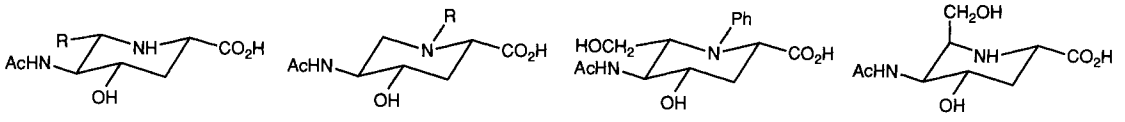
[1]) The importance of the 1,2,3-trihydroxypropyl side chain of Neu5Ac residues has been demonstrated by subjecting sialoglycoconjugates to the reaction first with periodate and then with borohydride to give octulose and heptulose derivatives [7] [8]. As a rule, progressive chain shortening led to a decrease of bacterial and viral sialidase action. The importance of the conformation of the side chain on the activity of a sialyl synthetase has been demonstrated and rationalized by *Zbiral et al.* [9].



12 R = CH_2OH
13 R = CH_2F
14 R = CH_3

15 R = H
16 R = CH_2CH_2OH

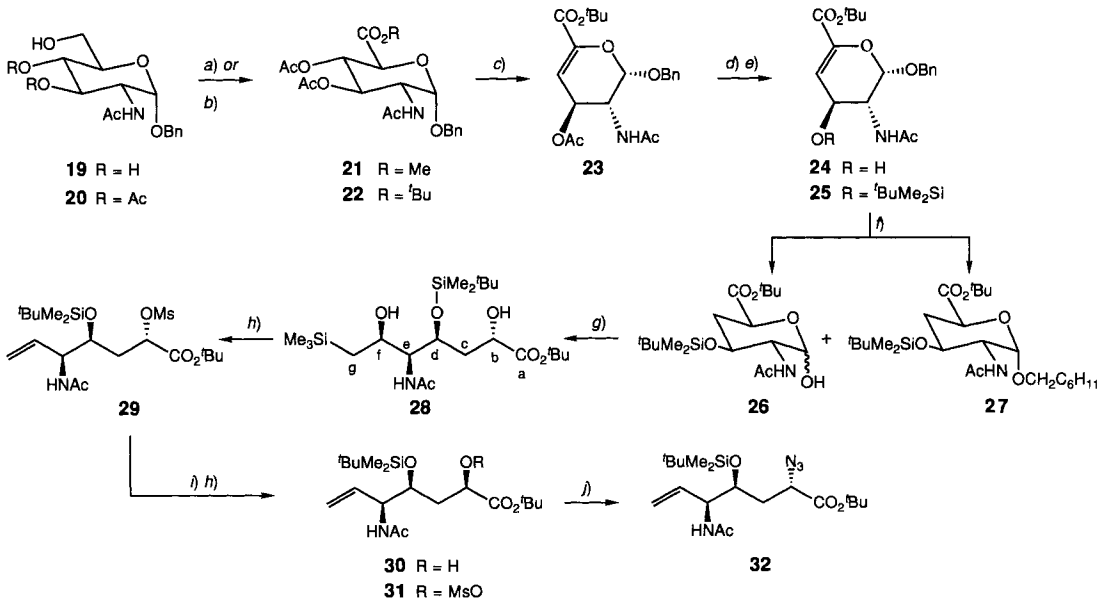
17

18

Ozonolysis of **32**, redutive amination, and deprotection should provide **15** and hence **16**, while an intramolecular azide-alkene 1,3-dipolar cycloaddition should lead to piperidines with a functionalized side chain. Inspection of *Dreiding* models of **32** indicate a small energy difference between the transition states leading to the diastereoisomeric cycloaddition products, depending on subtle conformational factors. As an alternative to the cycloaddition, dihydroxylation of the alkene and intramolecular formal substitution of OH–C(6) should also lead to the desired C_7 analogues **12–14**, **17**, and **18**.

In our synthesis of Neu5Ac (**1**) from *N*-acetylglucosamine, we had first introduced the trihydroxypropyl side chain and then removed the original OH–C(4) by β-elimination [11]. This reaction was followed by an alkoxyhalogenation. For the preparation of **32**, we intended to effect the deoxygenation at C(4) of D-GlcNAc by β-elimination followed by diastereoselective hydrogenation. Consequently, the chain extension by olefination had to be effected at a later stage.

Scheme 1



19 R = H
20 R = Ac

21 R = Me
22 R = ^{t}Bu

23

24 R = H
25 R = ^{t}BuMe$_2$Si

26

27

28

29

30 R = H
31 R = MsO

32

a) Pt/O_2, H_2O; MeI; DMF; Ac_2O, 4-(pyrrolidin-1-yl)pyridine, pyridine, 87%. *b*) CrO_3, pyridine, Ac_2O, *t*-BuOH, DMF/CH_2Cl_2, 80%. *c*) DBU, CH_2Cl_2, 71%; or 7-methyl-1,5,7-triazabicyclo[4.4.0]dec-5-ene, toluene, 93%. *d*) NaOMe, MeOH, 98%. *e*) *t*-$BuMe_2SiCl$, 2,6-dimethylpyridine, DMF, 93%. *f*) 10% Pd/C, H_2, MeOH; 75 (**26**) and < 5% (**27**). *g*) Me_3SiCH_2MgCl, THF, 85%. *h*) MsCl, Et_3N, CH_2Cl_2, 92%. *i*) KNO_2, DMF, 68%. *j*) NaN_3, DMF, 75%.

Results and Discussion. – 1. *Preparation of the Azidoalkenoate* **32.** Two routes were explored for the transformation of the D-glucosamine derivative **19** [12] into an appropriate ester of the corresponding uronic acid (*Scheme 1*). Catalytic oxygenation of **19** [12] [13], followed by esterification either with MeI or with CH_2N_2 and by acetylation, gave **21** in 87% yield [14] for batches of 1–5 g. Larger batches required large amounts of the Pt catalyst and longer reaction times, particularly when the catalyst was reused[2]). We preferred to transform **20**, readily available from **19** by tritylation, acetylation, and detritylation [15], into the *t*-Bu ester **22** by oxidation with CrO_3/pyridine in the presence of Ac_2O and *t*-BuOH [16] (62% from **19**). The oxidation proceeded cleanly, provided that **20** was added slowly to the reaction mixture. Both **21** and **22** are crystalline. The β-elimination [17] of AcOH from **22** was best effected with 7-methyl-1,5,7-triazabicyclo[4.4.0]dec-5-ene [18] in toluene and yielded 93% of the crystalline enoate **23**; 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) in CH_2Cl_2 gave lower yields.

The structure of **21**–**23** is evident from their elemental analysis and from spectroscopic data. Thus, the IR spectra showed no OH absorption but ester and amide bands at 1740, 1675, and 1545 cm^{-1} for **21**, at 1740, 1675, and 1510 cm^{-1} for **22**, and at 1740, 1680, and 1510 cm^{-1} for **23**. In the ^{1}H-NMR spectra of **21**–**23**, the CH_2(6) signals of **19** (3.47–3.54 ppm) and **20** (3.56 and 3.64 pm) are substituted by the MeO and *t*-BuO resonances of **21** (3.76 pm), **22** (1.46 ppm), and **23** (1.52 ppm), respectively. The ^{1}H- and ^{13}C-NMR spectra of **23** show signals for only 2 Ac groups, and H–C(4) now resonates at 5.91 ppm (*d*, J = 2.9 Hz), also the signal of the allylic H–C(3) of **23** is shifted to lower field (5.56 ppm) as compared to **21** and **22** (5.24 ppm). The large values of $J(2,3) = J(4,5) = 9.6$ Hz ($J(3,4)$ could not be measured) for **21** and **22** evidence their $^4C_1$ conformation. In **23**, the values for $J(1,2)$ (2.9 as compared to 3.7 Hz for **22**) and $J(2,3) = 8.8$ Hz indicate a $^2H_1$ conformation. The ^{13}C-NMR data confirm the structure. The shift values for C(4) (107.75 ppm) and C(5) (142.8 ppm) of **23** are characteristic for α,β-unsaturated hexuronates [11].

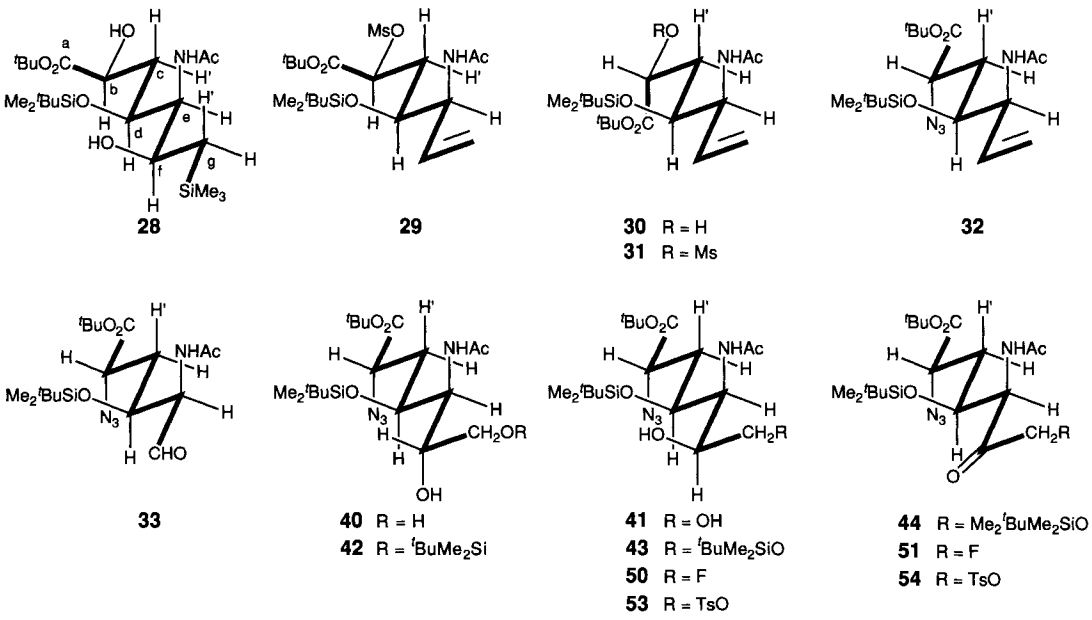


Fig. 2. *Preferred conformations of the open-chain compounds*

[2]) The catalyst was still active after having been used for seven times; a steady decrease of activity was observed.

The acetate **23** was deacetylated with NaOMe/MeOH. Silylation of the resulting alcohol **24** with *t*-BuMe$_2$SiCl gave **25** (91% from **23**). The olefinic double bond of **25** was rapidly and diastereoselectively hydrogenated in the presence of 10% Pd/C at atmospheric pressure, while the debenzylation was slow and required relatively large amounts of catalyst. The crystalline 4-deoxyhexuronate **26** was obtained in high yields. Formation of small amounts of the (cyclohexyl)methyl glycoside **27** was observed during hydrogenation on a larger scale. Olefination of **26** by (methylidene)triphenylphosphorane [19] failed, but the reaction of **26** with excess Me$_3$SiCH$_2$MgCl [20] [21] gave diastereoselective the D-*ido*-hydroxysilane **28** in a yield of 85%.

The ^{1}H-NMR spectrum (CD_3OD) of **26** showed that mainly the α-D-anomer was present (α/β = 6:1). The $^4C_1$ conformation of the α-anomer is evidenced by the values of 3.4, 10.2, 10.2, and 12.3 Hz for J(1,2), J(2,3), J(3,4$_{ax}$), and J(4$_{ax}$,5), respectively. These coupling constants also prove that H_2 had added from the side of the pseudoaxial BnO group, corresponding to an axial attack at C(5). This may be rationalized by assuming a preferred adsorption of the $^1H_2$ conformer of **25**, directed by the haptophilic acetamido group.

The structure of **28** is evident from its analytical data. The newly introduced Me$_3$SiCH$_2$ group gives rise to signals at 0.06, 0.74, and 0.84 ppm in the ^{1}H-NMR, and to a *q* at −0.8 and a *t* at 23.19 ppm in the ^{13}C-NMR spectrum (*Table 3*). The large values of J(b,c)[3], J(c,d), J(f,g'), and the medium-to-small values of J(b,c'), J(c',d), J(d,e), J(e,f), and J(f,g) (*Table 1*) are qualitatively compatible with the sickle zig-zag conformation depicted in *Fig. 2*. An H-bond between OH–C(f) and O–C(d) is indicated by the small value of the vicinal coupling constant (3.8 Hz) for the sharp *dd* of OH–C(f), coupling both with H–C(f) and with H–C(g) (W coupling, J = 1.1 Hz). The large value for J(f,g'), the small value for J(f,g), and the above mentioned W coupling are compatible with a D-*ido*- and a L-*gluco*-configuration. The L-*gluco*-configuration is, however, excluded by the small J(e,f) value.

Table 1. *Selected ^{1}H-NMR Chemical Shifts* [ppm] *and Coupling Constants* [Hz] *for the Open-Chain Compounds* **28–33**, **39–44**, **49–51**, **53**, *and* **54** (400 MHz, $CDCl_3$)[3])

H-Atom or J	**28**[a])	**29**	**30**[b])	**31**	**32**	**33**	**39**	**40**[c])	**42**
H–C(b)	4.07	4.94	4.11	5.01	3.82	3.82	4.35	3.78	3.75
H–C(c)	1.77	1.90–2.00	1.64	1.91	1.70	1.71–1.79	1.95	1.72	1.73
H′–C(c)	1.86		1.91	2.10	1.86		2.61	1.91	1.91
H–C(d)	4.17	3.98	4.07	3.97	3.95	4.49	4.62	4.29	4.37
H–C(e)	3.93	4.60	4.68	4.66	4.58	4.65	4.78	3.86	3.87
H–C(f)	4.00	5.83	5.81	5.79	5.85	9.73	5.88	3.60	3.51
H–C(g)	0.74	5.19	5.16	5.18	5.18	–	5.30	3.43	3.56
H′–C(g)	0.84	5.20	5.18	5.19	5.21	–	5.32	3.56	3.66
J(b,c)	9.6	8.8[g])	10.0	9.2	10.0	8.2[g])	10.7	8.0	8.6
J(b,c')	4.4	5.5[g])	3.6	4.0	4.8	6.3[g])	9.1	6.2	6.7
J(c,c')	14.3	[h])	14.0	14.6	14.0	[h])	13.4	14.1	13.8
J(c,d)	7.7	6.0	4.4	4.4	4.4	5.2[g])	9.9	6.7	6.2
J(c',d)	4.6	6.0	9.5	9.1	8.4	7.5[g])	6.0	6.7	6.9
J(d,e)	2.2	1.9	1.6	1.8	2.5	3.4	2.4	1.6	1.4
J(e,f)	3.6	5.0	5.0	5.2	4.8	–	6.0	9.4	9.2
J(e,g)	1.1	1.0	1.6	1.8	2.0	–	2.0	0	0
J(e,g')	–	1.0	1.6	1.8	2.0	–	1.5	0	0
J(f,g)	3.7	17.0	10.5	10.2	17.2	–	10.5	6.1	6.9
J(f,g')	10.2	10.8	17.0	17.4	10.5	–	17.3	3.2	3.3
J(g,g')	14.5	1.5	1.6	1.8	1.0	–	1.5	12.2	10.0

[3]) In the *General Part* and in the *Tables*, the C-atoms of the main chain are marked with letters starting from the carboxylic terminus.

Table 1 (cont.)

H-Atom or *J*	**41**	**43**	**44**	**49**	**50**[c])	**51**	**53**	**54**
H–C(b)	3.80	3.79	3.75	3.85	3.78	3.79	3.79	3.74
H–C(c)	1.82	1.80	1.71	1.64	1.95	1.68–1.80	1.77	1.60–1.70
H′–C(c)	1.97	2.02	1.65	1.72	2.06		1.95	
H–C(d)	3.97–4.06	3.99	4.30	4.12	3.97	4.33	3.88–4.01	4.26
H–C(e)		3.82	4.75	4.01[d])	4.06[e])	4.84[f])		4.69
H–C(f)		4.09	–	4.60[d])	4.17–4.31	–	4.29	–
H–C(g)	3.45–3.57	3.40	4.37	4.35[d])		4.96[f])	3.88–4.01	4.66
H′–C(g)		3.52	4.60	4.50[d])		5.16[f])		5.04
J(b,c)	9.8	11.3	10.1	11.0	11.2	8.7[g])	10.5	7.3
J(b,c′)	5.0	3.3	4.5	3.4	3.3	6.1[g])	4.0	7.3
J(c,c′)	14.4	14.3	14.3	14.0	14.5	[h])	14.2	[h])
J(c,d)	4.4	2.6	3.3	2.9	2.3	5.2[g])	3.5	5.5[g])
J(c′,d)	7.8	10.1	8.7	9.6	10.5	7.7[g])	9.1	7.1[g])
J(d,e)	[h])	4.1	2.9	2.0	4.5	2.7	[h])	3.2
J(e,f)	[h])	0	–	5.5	1.5	–	[h])	–
J(e,g)	–	–	–	–	–	–	–	–
J(e,g′)	–	–	–	–	–	–	–	–
J(f,g)	[h])	10.0	–	5.5	[h])	–	[h])	–
J(f,g′)	[h])	4.0	–	2.5	[h])	–	[h])	–
J(g,g′)	[h])	10.0	18.7	10.4	[h])	16.7	[h])	14.4

[a]) δ(OH–C(b)) = 3.77 ppm, *J*(b,OH) = 7.4 Hz; δ (OH–C(f)) = 2.79 ppm, *J*(f,OH) = 3.8 Hz, *J*(g,OH) = 1.1 Hz. [b]) δ(OH–C(b)) = 3.0 ppm, *J*(b,OH) = 4.7 Hz. [c]) In CD_3OD. [d]) ^4J(F,e) = 1.0, ^3J(F,f) = 21.8, ^2J(F,g) = ^2J(F,g′) = 47.5 Hz. [e]) ^4J(F,e) = 1.3 Hz. [f]) ^4J(F,e) = 1.0, ^2J(F,g) = 47.1, ^2J(F,g′) = 47.3 Hz. [g]) Assignment may be reversed. [h]) Not determined.

Table 2. *Selected ^{1}H-NMR Chemical Shifts* [ppm] *and Coupling Constants* [Hz] *for the Piperidines* **12**–**18**, **34**–**38**, **45**–**48**, **52**, *and* **55** (400 MHz, $CDCl_3$)[3])

H-Atom or *J*	**34**	**35**	**15**[a])	**16**[a])	**36**	**37**	**38**	**18**[b])
H–C(b)	3.27	3.12	3.74	3.46	4.82	3.41	3.40	3.60
H–C(c)	1.70	1.93	1.76	1.79	2.09	2.03	2.00	1.78
H′–C(c)	2.15	2.02	2.59	2.38	2.33	2.09	2.23	2.31
H–C(d)	3.61–3.67	3.67	3.84	3.76	4.03	4.05	3.91	3.83
H–C(e)		3.80	3.92	3.96	4.10	3.15	3.78	3.92
H–C(f)	2.40	2.14	2.87	2.62	4.13	3.62	3.56	3.54
H–C(g)	–	–	–	–	3.75	3.95	3.45	3.63–3.70
H′–C(g)	3.45[k])	3.48[k])	3.49[k])	3.51[k])	4.36	4.11	3.57	
J(b,c)	9.0	7.3	13.2	12.3	7.7	6.4	7.4	8.2
J(b,c′)	4.0	4.9	3.3	3.0	1.4	2.8	1.9	4.2
J(c,c′)	13.8	13.5	13.9	12.7	14.8	14.4	14.5	13.8
J(c,d)	8.6	7.3	11.0	12.0	2.9	3.2	3.2	8.2
J(c′,d)	4.0	4.0	4.6	3.4	2.5	3.2	3.2	4.2
J(d,e)	[l])	7.3	10.2	11.8	3.0	3.2	3.2	8.2
J(e,f)	8.1	7.3	11.8	11.8	2.9	2.3	2.0	4.2
J(f,g)	–	–	–	–	12.6	2.1	10.5	8.5
J(f,g′)	3.6[m])	3.5[m])	4.8[m])	4.6[m])	11.4	2.2	5.0	8.5
J(g,g′)	12.6[n])	11.8[n])	12.8[n])	12.0[n])	15.9	11.5	12.5	[l])

Table 2 (cont.)

H-Atom or *J*	**45**	**12**[c])	**46**	**46**[d])	**17**[d])[e])	(*E*)-**47**	(*Z*)-**47**
H–C(b)	3.27	3.61	4.29	4.20	4.08	4.55	4.71
H–C(c)	1.52	1.77	2.12	2.17–2.20	1.93	1.97	1.97
H′–C(c)	2.20	2.57	2.38[h])		2.42	2.34	2.41
H–C(d)	3.63	3.80	4.09	3.90	3.60	*ca.* 4.08	*ca.* 4.08
H–C(e)	3.38	3.82	4.39[h])	4.35	3.84	4.33	4.33
H–C(f)	2.72	3.09	3.75	3.51	3.94	3.82	3.71
H–C(g)	3.59	3.69	3.80	3.72	3.58	4.00–4.15	3.90
H′–C(g)	3.69	3.78	4.09	3.85	3.81		*ca.* 4.05
J(b,c)	12.0	13.4	7.4	6.1	12.0	8.2	8.2
J(b,c′)	2.5	2.5	3.5	6.1	6.6	2.0	2.0
J(c,c′)	12.0	13.4	14.3	[l])	12.0	14.7	14.7
J(c,d)	11.0	10.7	3.5	4.4	12.0	3.1	3.1
J(c′,d)	4.7	3.8	4.5	5.9	3.7	< 2	< 2
J(d,e)	10.0	10.7	3.4	5.9	6.5	3.7	3.7
J(e,f)	9.7	10.7	4.1	4.4	4.0	0	0
J(f,g)	7.5	6.1	[l])	3.4	6.5	3.8	4.8
J(f,g′)	2.9	2.5	10.7	7.8	4.0	8.4	9.8
J(g,g′)	10.0	12.5	10.7	10.5	10.5	[l])	9.8

H-Atom or *J*	(*E*)-**48**	(*Z*)-**48**	**52**[d])	**13**[f])	**55**	**14**[g])
H–C(b)	4.52	4.66	3.34	4.02	3.31	3.63
H–C(c)	1.96	1.94	1.44	1.79	1.50	1.70
H′–C(c)	2.30	2.39	2.23	2.60	2.21	2.51
H–C(d)	4.53	4.43	3.70	3.85	3.60	3.67–3.74
H–C(e)	4.22	4.25	3.50	3.81	3.29	
H–C(f)	4.84	4.73	2.82[i])	3.47[j])	2.69	3.11
H–C(g)	3.83	3.81	4.38[i])	4.64[j])	1.17	1.27
H′–C(g)	4.39	4.31	4.45[i])	4.68[j])	–	–
J(b,c)	9.4	9.4	12.5	13.6	12.3	13.6
J(b,c′)	0	0	2.6	3.1	2.6	3.7
J(c,c′)	14.8	14.8	12.5	13.6	12.3	13.6
J(c,d)	0.9	0.9	10.7	10.3	11.0	11.0
J(c′,d)	4.5	4.5	4.9	4.3	4.8	3.7
J(d,e)	4.1	4.1	10.0	10.0	9.6	[l])
J(e,f)	3.8	3.8	10.0	10.0	10.0	10.9
J(f,g)	3.2	3.2	6.1	5.4	6.4	6.6
J(f,g′)	0	0	2.9	3.0	–	–
J(g,g′)	9.2	9.2	9.5	11.1	–	–

[a]) In D_2O.
[b]) In CD_3OD/D_2O 3:1.
[c]) In CD_3OD/D_2O 4:1.
[d]) In CD_3OD.
[e]) As sodium salt.
[f]) In CD_3OD/D_2O 95:5.
[g]) In CD_3OD/D_2O 1:3.
[h]) J(c′,e) = 1.0 Hz.
[i]) ^3J(F,f) = 20.2, ^2J(F,g) = 47.9, ^2J(F,g′) = 47.0 Hz.
[j]) ^3J(F,f) = 20.9, ^2J(F,g) = 47.2, ^2J(F,g′) = 46.7 Hz.
[k]) Value of H′–C(f).
[l]) Not determined.
[m]) Value of J(e,f′).
[n]) Value of J(f,f′).

Table 3. *^{13}C-NMR Chemical Shifts* [ppm] *for Open-Chain Compounds* **28–33**, **39–42**, **44**, **49–51**, **53**, *and* **54** (50.6 MHz, $CDCl_3$)[3])

C-Atom	**28**	**29**	**30**	**31**	**32**	**33**	**39**[a])	**40**
C(a)	171.76	168.12[b])	169.60	167.42[b])	169.42[b])	169.08	175.33	169.14
C(b)	73.10	75.65	67.68	75.29	58.91	58.69	59.14	59.06
C(c)	39.46	37.09	38.79	36.32	34.87	35.01	32.38	36.44
C(d)	70.87	70.46	71.14	70.39	70.03	67.49	80.14	70.12
C(e)	59.13	54.65	53.15	53.21	54.55	62.57	55.03	53.70
C(f)	68.65	135.38	136.58	136.00	134.97	199.48	134.89	66.76
C(g)	23.19	116.10	115.76	115.89	115.81	–	118.60	62.55
AcNH	173.62	169.75[b])	173.88	169.45[b])	169.55[b])	170.36	173.68	171.89
	23.35	23.24	23.18	23.12	23.03	22.90	22.83	23.05
t-BuO	82.07	83.82	82.40	83.41	82.84	83.32	–	83.28
	27.98	27.82	27.88	27.75	27.78	27.87	–	27.87
t-BuMe$_2$Si	17.97	18.01	17.93	17.85	17.86	17.84	–	18.03
	25.82	25.82	25.78	25.69	25.70	25.65	–	25.89
	–4.23	–4.26	–4.47	–4.66	–4.40	–4.71	–	–4.48
	–4.60	–4.62	–4.65	–4.69	–4.60	–4.93	–	–4.83
Other C	–0.80[f])	39.07[g])	–	38.83[g])	–	–	–	–

C-Atom	**42**	**41**	**44**	**49**	**50**	**51**	**53**	**54**
C(a)	169.44[b])	169.77	169.23	169.43	169.78	168.96	169.79	168.92
C(b)	59.05	59.06	59.88[b])	58.77	59.12	59.70[b])	59.10	58.52
C(c)	35.94	34.45	35.05	32.87	34.31	34.83	34.07	34.12
C(d)	70.73	68.86[b])	68.15	68.49	68.57	68.01	68.51	68.09
C(e)	53.38	52.87	58.77[b])	70.98[c])	52.05[d])	58.70[b])	52.90	60.36
C(f)	67.07	68.75[b])	205.32	78.05[c])	66.84[d])	202.07[e])	66.10	198.43
C(g)	65.05	64.21	69.32	83.74[c])	84.73[d])	84.66[e])	71.89	71.30
AcNH	169.81[b])	171.77	170.03	165.01	170.71	170.19	170.56	170.01
	23.26	22.97	23.08	13.46	25.70	22.96	23.01	22.72
t-BuO	83.08	82.92	82.27	82.78	83.00	83.47	82.97	83.27
	27.92	27.80	27.93	27.76	27.91	27.88	27.89	27.74
t-BuMe$_2$Si	18.09	17.76	17.95	17.76	17.84	17.84	17.77	17.71
	25.94	25.63	25.73	25.53	23.07	25.72	25.69	25.62
	–4.68	–4.53	–4.30	–4.31	–4.54	–4.59	–4.55	–4.59
	–5.42	–4.97	–5.35	–5.19	–4.92	–5.07	–5.02	–5.44
Other C	[h])	–	[i])	–	–	–	[j])	[k])

[a]) In CD_3OD. [b]) Assignment may be reversed. [c]) ^3J(F,e) = 4.5, ^2J(F,f) = 18.6, ^1J(F,g) = 175.8 Hz. [d]) ^3J(F,e) = 5.8, ^2J(F,f) = 20.2, ^1J(F,g) = 170.3 Hz. [e]) ^2J(F,f) = 16.9, ^1J(F,g) = 185.3 Hz. [f]) Me_3Si. [g]) $MeSO_2$. [h]) Signals of an additional *t*-BuMe$_2$Si group at 18.19, 25.80, –4.68, and –5.48 ppm. [i]) Signals of an additional *t*-BuMe$_2$Si group at 18.36, 25.74, –5.10, and –5.47 ppm. [j]) Signals of TsO at 145.05, 132.31, 129.89, 128.74, 127.92, 125.85, and 21.52 ppm. [k]) Signals of TsO at 145.21, 132.43, 129.81, 127.86, and 21.44 ppm.

Table 4. *^{13}C-NMR Chemical Shifts* [ppm] *for Piperidines* **12–18**, **34–38**, **45–48**, **52**, *and* **55** (50.6 MHz, $CDCl_3$)[3])

C-Atom	**34**	**35**	**15**[a])	**16**[a])	**36**	**37**	**38**	**18**[a])
C(a)	169.72	169.95	174.57	174.87	169.64	174.03	173.37	175.07
C(b)	56.80	62.59	57.52	67.91	54.53[d])	54.26[d])	53.51[d])	54.70[d])
C(c)	36.51	34.52	33.64	35.61	29.08	28.48	29.46	33.20
C(d)	70.61	68.93	68.03	68.36	67.81	70.03	67.31	64.72
C(e)	53.07	51.42	49.57	50.82	49.72[d])	52.98[d])	50.32[d])	53.68[d])
C(f)	46.44	50.07	43.52	52.73	49.44[d])	40.52	49.81[d])	51.46[d])
C(g)	–	–	–	–	64.77	68.85	64.07	56.79

Table 4 (cont.)

C-Atom	**34**	**35**	**15**[a])	**16**[a])	**36**	**37**	**38**	**18**[a])
AcNH	171.49	171.79	172.61	172.95	170.27	157.01	170.37	173.55
	23.22	23.27	21.92	22.98	22.98	21.35	23.48	22.37
t-BuO	81.12	81.31	–	–	82.02	80.64	81.40	–
	27.81	28.07	–	–	28.09	28.18	28.48	–
t-BuMe$_2$Si	17.72	18.08	–	–	18.32	18.59	18.72	–
	25.52	25.76	–	–	25.89	26.17	26.36	–
	–4.42	–4.45	–	–	–4.97	–4.53	–4.43	–
	–4.89	–4.81	–	–	–5.03	–4.89	–4.61	–
Other C	–	[g])	–	[h])	–	–	–	–

C-Atom	**45**	**12**[a])	**46**	**17**[b])	(*E*)-**47**	(*Z*)-**47**	(*E*)-**48**	(*Z*)-**48**
C(a)	169.73	175.42	168.94	174.02	169.07	168.81	170.19	170.24
C(b)	56.79[d])	57.81[d])	53.88[d])	62.50[d])	57.35	57.65	52.03[d])	51.60[d])
C(c)	38.09	34.09	30.03	35.30	27.52	27.36	27.19	27.09
C(d)	72.41	69.16	66.72	69.69	65.71	65.86	71.54	71.42
C(e)	55.45	51.57	49.01	49.28	51.11	50.73	50.60	50.36
C(f)	59.74[d])	58.55[d])	59.45[d])	55.71[d])	46.83	46.41	54.56[d])	54.94[d])
C(g)	64.14	67.06	60.98	64.54	61.52	62.33	68.05	67.90
AcNH	170.77	173.36	171.80	174.02	170.61	170.41	170.53	170.53
	23.60	22.56	23.41	22.66	23.32	23.32	23.20	23.20
t-BuO	81.41	–	81.34	–	81.60	81.60	82.20	82.20
	27.94	–	27.94	–	27.94	27.94	27.82	27.90
t-BuMe$_2$Si	17.78	–	18.49	–	18.11	18.11	–	–
	25.58	–	25.92	–	25.84	25.84	–	–
	–4.73	–	–4.75	–	–4.07	–4.07	–	–
	–5.43	–	–5.45	–	–4.73	–4.73	–	–
Other C	[i])	–	[j])[k])	[l])	[m])	[m])	[n])	[n])

C-Atom	**52**	**13**[a])	**55**	**14**[a])[c])
C(a)	170.23[d])	175.23	169.90	179.85
C(b)	56.57	58.10	57.08[d])	59.28[d])
C(c)	38.37	34.45	38.81	37.71
C(d)	71.71	69.35	72.16	71.74
C(e)	54.82[e])	50.97[f])	53.99	53.52
C(f)	58.01[e])	57.02[f])	60.17[d])	58.57[d])
C(g)	84.65[e])	80.92[f])	19.01	17.81
AcNH	170.83[d])	173.60	171.17	175.00
	23.44	22.56	23.68	22.54
t-BuO	81.65	–	81.60	–
	27.89	–	27.96	–
t-BuMe$_2$Si	17.72	–	17.80	–
	25.12	–	25.58	–
	–4.21	–	–4.15	–
	–4.79	–	–4.74	–
Other C	–	–	–	–

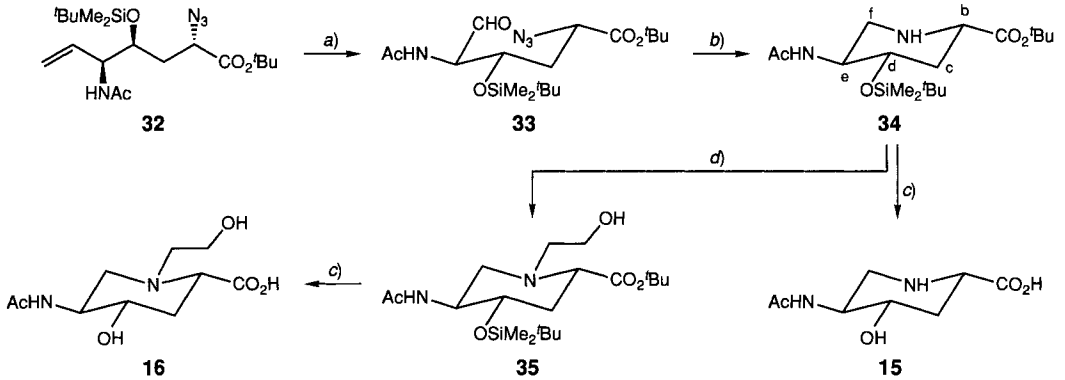
[a]) In D_2O. [b]) In CD_3OD. [c]) As sodium salt. [d]) Assignments may be reversed. [e]) ^3J(F,e) = 5.9, ^2J(F,f) = 18.0, ^1J(F,g) = 167.7 Hz. [f]) ^3J(F,e) = 4.0, ^2J(F,f) = 18.6, ^1J(F,g) = 169.7 Hz. [g]) Signals of NCH_2CH_2OH at 56.95 and 58.91 ppm. [h]) Signals of NCH_2CH_2OH at 56.86 and 58.26 ppm. [i]) Signals of an additional *t*-BuMe$_2$Si group at 18.20, 25.89, –4.18, and –4.78 ppm. [j]) Signals of an additional *t*-BuMe$_2$Si group at 18.41, 26.06, –4.20, and –4.80 ppm. [k]) Signals of PhN at 148.44, 129.21, 118.61, and 113.92 ppm. [l]) Signals of PhN at 150.04, 130.06, 122.13, and 119.80 ppm. [m]) Signals of an additional *t*-BuMe$_2$Si group at 18.53, 26.03, –4.07, and –4.66 ppm; signals of BnOCO at 156.71/156.38, 67.73/67.83, 135.92/136.06, and 128.17–128.53 ppm. [n]) Signals of BnOCO at 156.9/157.0, 68.97/68.87, 136.06/136.40, and 128.65–128.03 ppm.

A variety of acidic conditions failed to transform **28** into the ald-6-enonate **29**. Only deprotected or lactonized products were obtained. Mesylation of **28** in the presence of Et_3N, however, afforded the unsaturated L-*xylo*-mesylate **29** in high yields. Treatment of **29** with KNO_2 in DMF[4]) at 100° for 1 h gave the L-*lyxo*-alcohol **30** which was transformed into the mesylate **31** (72% from **29**). The desired L-*xylo*-azide **32** was obtained by a second nucleophilic substitution at C(2) in 75% yield.

The constitutional changes in the transformation of **29** to **32** are obvious from the analytical data, particularly from the IR spectra where the sulfonyl bands at 1360 and 1175 cm^{-1} (**29** and **31**), the OH band of **30**, and the sharp absorption at 2105 cm^{-1} for the azide **32** evidence the functional group interchanges. The ^{1}H-NMR spectra of **29**–**32** show the typical signal pattern for monosubstituted alkenes (see *Table 1*). The inversion at C(b) is reflected in the ^{1}H-NMR spectra of **29**–**32**. Their interpretation is delicate, as **29**–**32** assume different conformations. The 2-OH and the 2-MsO derivatives **29**–**31** prefer a sickle zig-zag conformation (synclinal arrangement of C(a) and C(d), similar to **28**), whereas the azide **32** prefers an extended zig-zag conformation. The vicinal coupling constants of **30**–**32** are compatible with the conformations depicted in *Fig. 2*. The values J(c,d) = J(c',d) = 6 Hz for **29** show that an additional conformer obtained by rotation around C(c)–C(d), also devoid of a 1,3-parallel arrangement of C(a) and the silyloxy group, contributes significantly to the conformational equilibrium.

2. *Preparation of the Piperidinecarboxylic Acids* **15** *and* **16**. Ozonolysis of **32** and reductive workup with PPh_3 gave the aldehyde **33** in 96% yield (*Scheme 2*). Intramolecu-

Scheme 2



a) O_3/O_2, CH_2Cl_2; PPh_3, 96%. *b*) $NH_4(HCO_2)$, 10% Pd/C, MeOH, 80%. *c*) Aq. CF_3CO_2H; 87 (**15**) or 79% (**16**). *d*) $OHCCH_2OH$, 10% Pd/C, H_2, MeOH, 90%.

lar reductive amination yielded 80% of the crystalline piperidine **34** which was deprotected by treatment with aqueous CF_3CO_2H. The piperidinecarboxylic acid **15** (87%) was isolated by ion-exchange chromatography followed by lyophilization. Reductive amination of **34** with glycolaldehyde led to the crystalline (2-hydroxyethyl)amino ester **35** which was deprotected to the amino acid **16**.

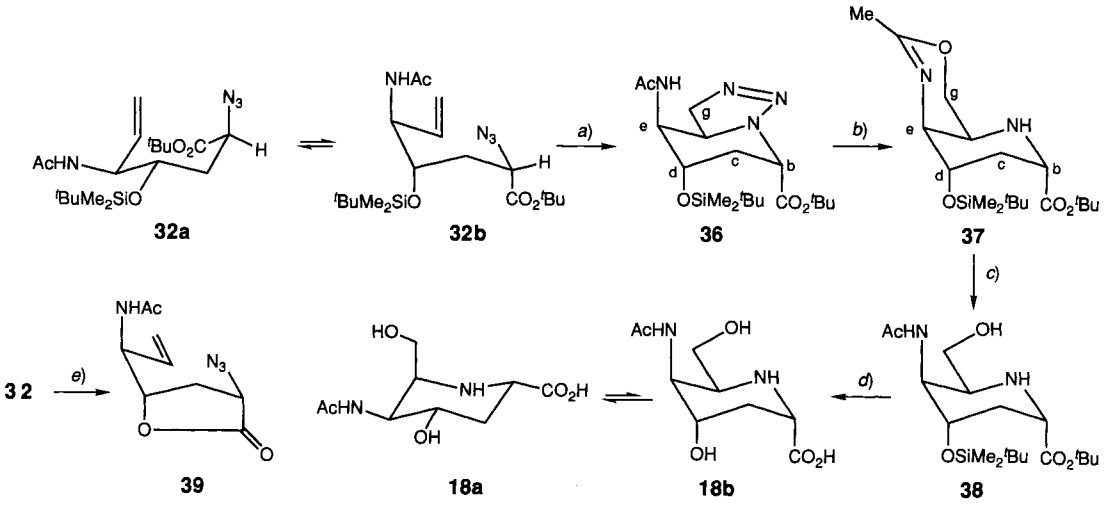
The aldehyde **33**, a somewhat unstable oil, shows IR bands at 3420, 2105, 1735, and 1675 cm^{-1}, evidencing the presence of acetamido, azido, and formyl groups. The predominant conformation of **33** appears to be similar to the one of **32**, although an additional conformer must be present, as evidenced by the J values (*Table 1*). H–C(d)

[4]) Other reagents like KO_2 (DMSO/DMF, 0°, 1 h, 15%) [22], KNO_2 (DMF, 20°, 48 h, 40%), or $NaNO_2$ (DMF, 45°, 12 h, 30%) [23] gave low yields, whereas $Bu_4N^+CF_3CO_2^-$ (DMF, 80°, 4 h, 45%) gave a 3:1 mixture of epimeric alcohols.

resonating at 4.49 ppm lies in the deshielding zone of the formyl group (*s* at 9.73 ppm) and is shifted by 0.54 ppm to lower field as compared to H–C(d) of **32**. Signals of an additional CH_2 group appear in the ^1H- and ^{13}C-NMR spectra (*Tables 2* and *3*, resp.) of **34** (2.40 and 3.45 ppm; 46.44 ppm), while **35** gives rise to signals for 4 CH_2 groups (1.93 and 2.02, 2.14 and 3.48, 2.53 and 2.82, and 3.54 and 3.64 ppm; 34.52, 50.07, 56.95 and 58.91 ppm). The values of J(b,c), J(c,d), J(d,e), and J(e,f) are 7.3 Hz for **35** ($CDCl_3$), 8.1–9.0 Hz for **34** ($CDCl_3$), 10.2–13.2 Hz for **15** (D_2O), and 11.8–12.7 Hz for **16** (D_2O). The amino acids **15** ($pK_{HA} = 8.3$) and **16** ($pK_{HA} = 7.9$) exist mostly as zwitterions and appear to adopt a $^2C_5$ conformation. The relatively small J values for **34** and particularly for **35** are indicative of either a flattened $^2C_5$ conformation or a *ca.* 3:1 equilibrium between the $^2C_5$ and $^5C_2$ conformers.

3. *Preparation of Piperidinecarboxyclic Acid* **18**. Thermolysis of the azidoalkenoate **32** in toluene under reflux gave in 83% yield a single crystalline dihydrotriazole **36** (see *Scheme 3*). The formation of fused adducts is expected [3]. Surprisingly, thermolysis of the conformationally biased γ-lactone **39** under a range of different conditions failed to give cycloaddition products.

Scheme 3



a) Toluene, 110%, 83%. *b*) AcOH, toluene, 87%. *c*) Aq. AcOH, toluene, 61%. *d*) Aq. CF_3CO_2H, 83%. *e*) CF_3CO_2H, THF, 94%.

The absence of an N_3 band in the IR spectrum of **36** and of olefinic H and C signals in its NMR spectra, and the UV maxima at 240 ($\varepsilon = 1539$) and 266 nm ($\varepsilon = 122$) evidence the formation of a dihydrotriazole (see [3] and lit. cit. therein). The signals of CH_2(g) occur at 3.75 and 4.36 ppm, and show the large geminal (15.9 Hz) and vicinal (J(f,g) = 12.6, J(f,g') = 11.3 Hz) coupling constants which are characteristic for such bicyclic dihydrotriazoles [24]. Since the coplanarity of the aminoazo function requires a pseudoequatorial orientation of CH_2(g) [3], the configuration at C(f) of **36** can be deduced from the vicinal coupling constants of the piperidine moiety. All values of these vicinal coupling constants are small except for J(b,c) = 7.7 Hz (see *Table 2*). This indicates a more or less axial orientation of the substituents, hence a $^5C_2$ conformation and an (*R*)-configuration at C(f). The *t* of C(c) (29.08 ppm) is shifted upfield as compared with the $^2C_5$ configurated piperidines **15**, **16**, **34**, and **35**, due to the axially oriented AcNH group (*gauche* effect).

The exclusive formation of **36** may be understood by comparing the plausible transition states leading from **32** to the isomeric cycloadducts. A parallel approach of the azido function to the alkenyl group of the conformer **32a** entails severe steric interactions between the ester function and particularly the alkenyl group. A parallel approach of the

N_3 function to the *re*-side of the alkenyl group of the conformer **32b** appears to generate no major steric interaction up to a distance of *ca.* 2 Å between C(f) and N(α) of the N_3 function, while such an approach of the N_3 function to the *si*-side of the alkenyl group without notable build-up of strain is possible only up to a distance of *ca.* 2.7 Å between C(f) and N(α). *Dreiding* models similarly suggest a build-up of strain in the analogous approach of the N_3 and the alkenyl groups in **39** at a distance of *ca.* 2.7 Å[5]). Calculations suggest distances of 2.25–2.35 Å between the functional groups in the transition states of the related cycloadditions of diazoalkane, nitrone, ozone, and carbonyl ylide to ethylene [25].

In the presence of AcOH, **36** evolved N_2 and gave the acid-labile product **37** which was isolated in 87% yield by chromatography on silica gel treated with Et_3N. The formation of **37** by a neighboring group participation of the axial acetamido group confirms the *cis*-relation of C(g) and the acetamido group in **36**. Mild acid hydrolysis of **37** gave the crystalline hydroxyacetamide **38** (61%), which was deprotected with CF_3CO_2H yielding 83% of the amino acid **18**.

The IR spectrum of **37** is characterized by weak NH absorptions between 3300 and 3600 cm^{-1} and strong bands for the CO and the imino groups at 1725 and at 1675 cm^{-1}. The ^1H- and ^{13}C-NMR spectra show the presence of *t*-$BuMe_2SiO$ and *t*-BuOCO groups. The imino-ether moiety in **37** is characterized by a Me *s* at 1.93 ppm and a *s* for the *OC*=N group at 157.01 ppm. Its presence is proven by the transformation of **37** into **38**, which shows the typical signals for an OH and an NHAc group (IR: 3600–3420, 1665, and 1500 cm^{-1}; ^1H-NMR: 1.99 (*s*, Me); 1.98–2.00 (OH); 6.16 ppm (*d*, NH); ^{13}C-NMR: 170.37 and 23.48 ppm (NHAc)). The conformation of the *cis*-oxaazadecalin **37** is evidenced by the small values of all vicinal coupling constants (with the exception of J(b,c) = 6.4 Hz). A comparison of the vicinal coupling constants for **36**–**38** (*Table 2*) shows that the conformation of the piperidine ring is fairly constant, corresponding to $^5C_2$. The coupling constants for the (zwitterionic) amino acid **18**, however, are best explained by assuming the presence of a *ca.* 2:1 mixture of the $^2C_5$ and $^5C_2$ conformers, **18a** and **18b**, respectively.

4. *Preparation of the (Hydroxymethyl)piperidinecarboxylic Acids* **12** *and* **17**. Dihydroxylation of **32** with OsO_4/*N*-methylmorpholine *N*-oxide gave two diastereoisomers **40** and **41** in a ratio of 7:1 (79%) which were silylated to **42** and **43**, respectively (*Scheme 4*).

Silylation hardly affects the coupling constants for **40** and **41**. The C(a)-to-C(e) part of the minor isomer **41** and of **43** adopts fairly exactly an extended zig-zag conformation. This is not the case for the major isomer **40** and for **42**. The values of J(e,f) for **40** (9.3 Hz) and for **42** (9.2 Hz) differ markedly from the one of **43** (0 Hz) suggesting an antiperiplanar arrangement of H–C(e) and H–C(f) in **40** and **42**, and a corresponding dihedral angle of *ca.* 90° in **41** and **43**. The chemical-shift values of H–C(d) (**40**: 4.29, **42**: 4.37, **41**: 4.03, **43**: 3.99 ppm) suggest that H–C(d) in **40** and in **42** is deshielded by a 1,3-parallel arrangement of H–C(d) and OH–C(f). These values for the coupling constants and the chemical shifts are in agreement with the configurations and conformations depicted in *Fig. 2* which imply the possibility of an intramolecular H-bond between OH–C(f) and O–C(d) in **43**. The IR spectrum of **43** indeed shows a relatively strong band at 3560 and a weak one at 3300–3500 cm^{-1}, while the relative intensities of these bands are interchanged for **42**. The formation of an L-*gluco*-configurated main product is in agreement with *Kishi*'s rule [26].

Intramolecular reductive amination (H_2, Pd/C) of the azido ketone **44**, obtained in 94% yields from **42** by oxidation with periodinane (= 3-oxo-1*H*-1λ^5,2-benziodoxol-1,1,1-triyl triacetate) [27], proceeded smoothly to give the crystalline piperidine **45** (79%). Deprotection of **45** with aqueous CF_3CO_2H gave the piperidinecarboxylic acid **12** (85%). The piperidine **45** was *N*-phenylated using $Ph_3Bi(OAc)_2$ [28] in the presence of $Cu(OAc)_2$

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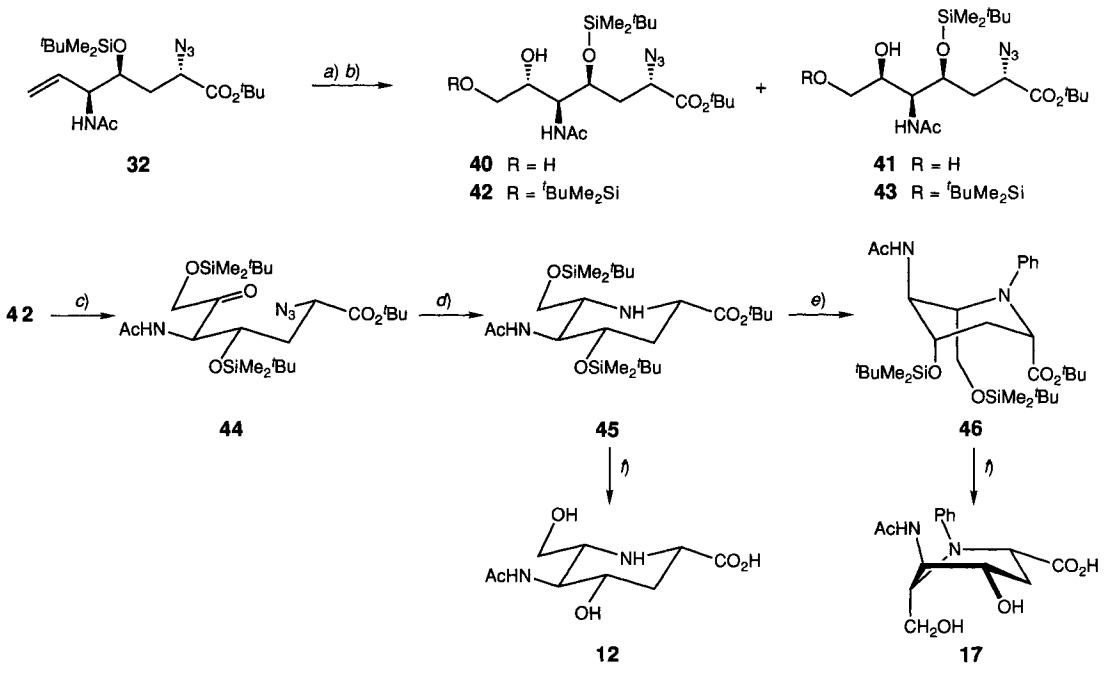
[5]) We found no example in the literature where (*cis*-1-azido-3-allyl)-substituted cyclopentanes or tetrahydrofurans led to dihydrotriazoles in an intramolecular cycloaddition.

Scheme 4



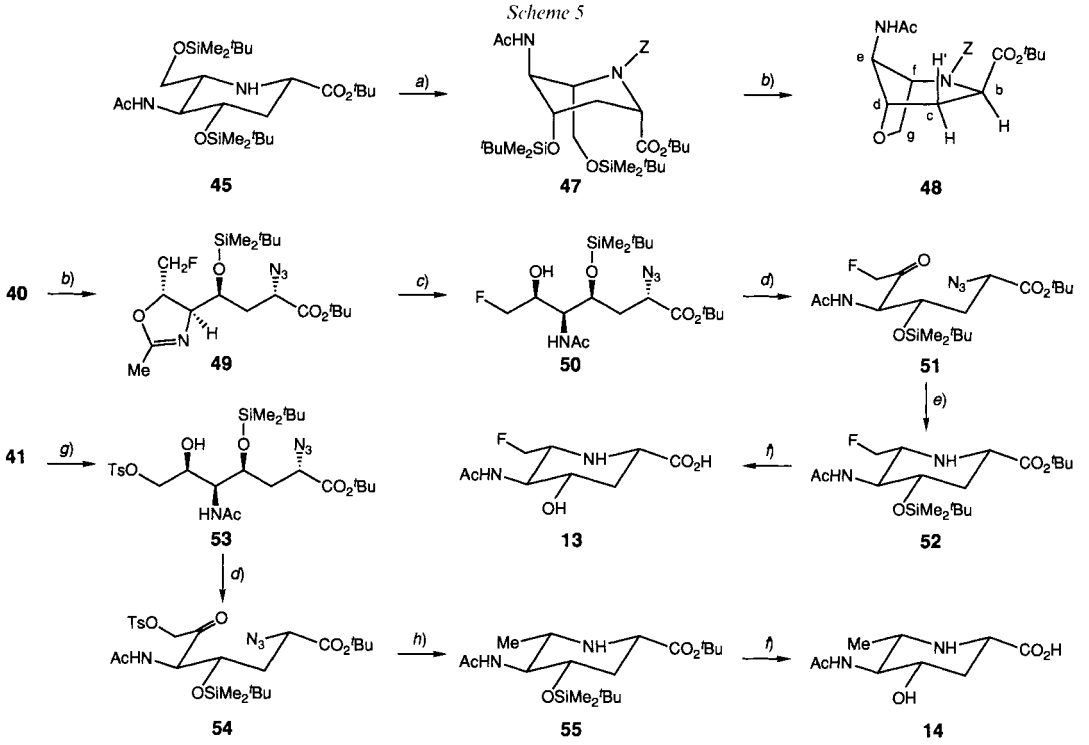
a) OsO_4, *N*-methylmorpholine *N*-oxide, acetone, 69%. *b*) *t*-$BuMe_2SiCl$, 2,6-dimethylpyridine, DMF, 95%. *c*) Periodinane, CH_2Cl_2, 94%. *d*) 10% Pd/C, H_2, MeOH, 79%. *e*) $Ph_3Bi(OAc)_2$, $Cu(OAc)_2$, CH_2Cl_2, 39%. *f*) Aq. CF_3CO_2H; 85 (**12**) or 80% (**17**).

according to *Barton et al.* [29]. The reaction did not go to completion. Adding further reagents, increasing the temperature, or using degassed solvents had no effect, and *ca.* 50% of starting material was recovered. The aniline **46** was obtained in 39% yield and deprotected to the *N*-phenylpiperidinecarboxylic acid **17**.

The large vicinal coupling constants in the ^{1}H-NMR spectra of **45** and **12** (*Table 2*) prove both the L-*gluco*-configuration and the $^2C_5$ conformation. The *J* values of **46** are best rationalized by assuming a flattened $^5C_2$ conformation with pseudoaxial substituents at C(b), C(d), C(e), and C(f). The flattening results from the sp^2 ring N-atom and reduces the unfavorable 1,3-diaxial interaction between the substituents. The $^5C_2$ conformation was evidenced by a long-range coupling (W coupling) between the pseudoequatorial H′–C(c) and H–C(e) and by a NOE of 3% between the pseudoaxial H–C(c) and the NH of the AcNH group. Driving force for this chair inversion is the allylic 1,3-strain [30] [31] between the Ph group and the equatorial substituents at C(b) and C(f). The preference for the $^5C_2$ conformation of **46** is weaker in CD_3OD (larger *J* values) than in $CDCl_3$. The ^{1}H-NMR spectrum of the sodium salt of **17** in CD_3OD is characterized by large values (12 Hz) for *J*(b,c) and *J*(c,d) and by medium values (3.7–6.6 Hz) for *J*(b,c′), *J*(c′,d), *J*(d,e), and *J*(e,f). These *J* values agree well with a flattened $B_{3,6}$ conformation which allows good solvation of the pseudoequatorial carboxylate moiety. Flattening reduces the unfavorable steric interaction of the CH_2OH group with H_{ax}–C(3) (both in a flagpole position).

5. *Preparation of the Piperidinecarboxylic Acids* **13** *and* **14**. The *N*-(benzyloxycarbonyl) piperidine **47**, obtained from **45** (*Scheme 5*), reacted with (diethylamino)sulfur trifluoride (DAST) [32] to give the tetrahydrofuran derivative **48** (40%). According to the ^{1}H- and ^{13}C-NMR spectra, **47** and **48** are each mixtures of rotamers with (*E*)/(*Z*) ratios of 55:45

Scheme 5



a) $PhCH_2OCOCl$ (ZCl), CH_2Cl_2, aq. $Na_2CO_3/NaHCO_3$, 81%. *b*) DAST, CH_2Cl_2; 40 (**48**) or 52% (**49**). *c*) Aq. AcOH, AcOEt, 90%. *d*) Periodinane, CH_2Cl_2; 80 (**51**) or 75% (**54**). *e*) PPh_3, THF; $HCO_2H/Na(HCO_2)$, MeOH; $NaBH_3CN$, Et_2O, 69%. *f*) Aq. CF_3CO_2H, 75 (**13**) or 76% (**14**). *g*) TsCl, pyridine, 81%. *h*) 10% Pd/C, H_2, MeOH, 68%.

(**47**) and 60:40 (**48**). The assignment is based upon *Paulsen*'s rule that the H-atoms next to the N-atom of the substituent *cis* to the O-atom in *N,N*-disubstituted acetamides resonate at lower field than the corresponding H-atoms of the *trans*-substituent [33].

X-Ray analyses of *cis*-2,6-disubstituted *N*-acylpiperidines [34] or of *N*-acylpipecolic-acid derivatives [35] show that these compounds possess a flattened chair conformation with pseudoaxial substituents in 2- and 6-position or a pseudoaxial COOH group on account of the allylic 1,3-strain [30] in the inverted chair conformation. Indeed, the small vicinal J(H,H) (*Table 2*) of (*E*)- and (*Z*)-**47** agree well with a flattened $^5C_2$ conformation. That no inversion of configuration had occurred during *N*-acylation was proven by the regeneration of **45** upon hydrogenolysis of **47**. The absence of the characteristic heteronuclear H,F and C,F couplings show that **48** does not contain F. According to the IR and NMR spectra, **48** possesses an AcNH, a BnOCO, and a *t*-BuOCO, but no silyl groups. The absence of OH bands in the IR spectrum suggests the formation of a cyclic ether which is facilitated by the pseudoaxial position of the silyloxy and the silyloxymethyl groups in **47**. The presence of an oxaazabicyclo [3.2.1]octane skeleton in **48** is deduced from the downfield shifts of H–C(d) and H–C(f) and from the small values of $J(f,g_{exo})$ (3.2 Hz) and especially of $J(f,g_{endo})$ (0 Hz). In agreement with these observations, the value of $J(g,g')$ decreased from 9.8 Hz (**47**) to 9.2 Hz (**48**). *Dreiding* models suggest that the presence of the sp^2 ring N-atom induces conformations of the piperidine ring close to a ^5S [36], a flattened $^{2,5}B$, or a flattened $^5C_2$. The strongly different values of J(b,c) = 9.4 and J(c,d) = 0.9 Hz are incompatible with a b,d-*cis*-configuration, and can only be explained by assuming an epimerization at C(b), presumably as the consequence of a strongly destabilizing interaction between the *t*-BuOCO and the ZN group. The deshielding of NH in **48** (5.64 and 5.75 ppm; **47**: 5.38 and 5.45 ppm) may indicate a H-bond between the AcNH and the COOR group.

The open-chain diol **40** (*Scheme 4*) reacted with DAST to give the fluorinated dihydrooxazole **49**, which was partially converted to the desired fluoride **50** during chromatography on silica gel and completely by treatment with AcOH (80% from **40**). According to combustion analysis, **49** ($C_{19}H_{35}FN_4O_4Si$) contains one F-atom.

The large heteronuclear coupling constants $^2J(F,H-C(g)) = {}^2J(F,H'-C(g)) = 47.5$ Hz and $^1J(F,CH_2(g)) = 169.7$ Hz show that the F-atom of **49** is bound to the terminal CH_2 group. The additional characteristic heteronuclear coupling constants which are expected by analogy with 6-deoxy-6-fluorohexoses [37] are listed in *Table 2* and *4*. The absence of OH and NH bands, and the presence of an imino band at 1670 cm^{-1} in the IR spectrum of **49** suggest a dihydrooxazole moiety in agreement with a downfield shift of C(e) (70.98 ppm) and C(f) (78.05 ppm) and with an upfield shift of the C signals of the 'isoacetamido' group (165.01 and 13.46 ppm). The configuration at C(f) can not be determined from $J(e,f) = 5.5$ Hz, as this J value is compatible with either a *cis*- or a *trans*-substitution. The D-*ido*-configuration of the fluorohydrin **50** (and hence also of **49**), is revealed by comparison of its $J(H,H)$ values with the ones of **43** (*Table 1* and *Fig. 2*). Thus, ring closure to the dihydrooxazole **49** has occurred with inversion at C(f).

Several attempts to oxidize **50** failed (CrO_3/pyridine/Ac_2O [38]; pyridinium chlorochromate, pyridinium dichromate; *Swern* oxidation), but oxidation with periodinane [27] yielded 80% of the fluoro ketone **51**. A *Staudinger* reaction [39] [40] of **51** with Ph_3P gave the phosphazo intermediate, which was reduced *in situ* with cyanoborohydride[6]) in the presence of a formate buffer (pH 3.6) to the desired fluorinated 2,6-*cis*-piperidine **52** (69%). Reductive amination of **51** in the presence of Pd/C led predominantly to the corresponding defluorinated piperidine **55**. The defluorination may be rationalized by the intermediate formation of an aziridine or an aziridinium cation. In agreement with this hypothesis, catalytic hydrogenation of the keto tosylate **54** led also to **55** (*ca.* 70%). The ketone **54** was obtained in 60% yield from **41** by selective tosylation (→ **53**) and oxidation with periodinane. The piperidine **55** was also obtained by hydrogenation of the dihydrotriazole **36** (*Scheme 3*). This reaction occurred with inversion of configuration at C(f), presumably by diastereoselective reduction of an intermediate imine or enamine [42]. Deprotection of **52** and **55** under usual conditions gave the free amino acids **13** and **14**, respectively.

The configuration and the $^2C_5$ conformation of **52**, **55**, **13**, and **14** are evident from the vicinal coupling constants (*Table 2*). They are similar to those of **12** and **45**. The acyclic derivatives **51**, **53**, and **54** adopt an extended zig-zag conformation (*Table 1* and *Fig. 2*).

6. *Inhibition of the Sialidase from* Vibrio cholerae. The results of the inhibition of *Vibrio cholerae* sialidase by the piperidinecarboxylic acids **12**–**18** [43] are listed in *Table 5*. The aniline **17** is not an inhibitor; all the other piperidines are poor inhibitors. As expected, the C_6 analogue **16** possessing an equatorial COOH group is a somewhat better inhibitor than the isomer **11** possessing an axial COOH group. Alkylation of the ring N-atom (see **16**) reduces the inhibition. Similar K_i values were measured for the C_7 analogues. The better inhibition by the alcohol **12** than by the fluoride **13** indicates that the OH group at C(7) may act as a H-donor rather than a H-acceptor. The surprisingly good inhibition by **18** may be due to a H-bond between OH–C(7) and the binding site for OH–C(8) of Neu5Ac [9] of the sialidase. The poor inhibition of these C_6 and C_7 piperidine analogues shows the importance of an intact trihydroxypropyl side chain also in the piperidine series.

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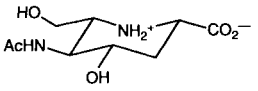
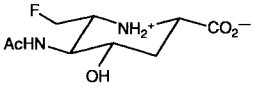
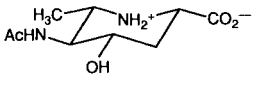
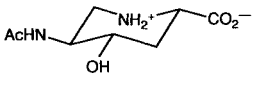
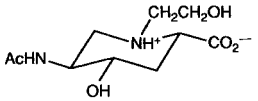
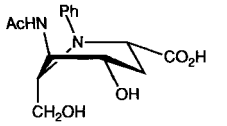
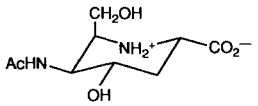
[6]) See [41] for similar reductions of fluoro azides.

Table 5. *K_i Values of the Piperidinecarboxylic Acids* **12**–**18** *in the Inhibition of* Vibrio cholerae *Sialidase*

Compound		pK_{HA}	Inhibition [%][a]	K_i
	**(12)**	7.3	54	$6.1 \cdot 10^{-3}$ M
	**(13)**	6.8	18	$2.7 \cdot 10^{-2}$ M
	**(14)**	8.4	36	$9.6 \cdot 10^{-3}$ M
	**(15)**	8.3	41	$1.0 \cdot 10^{-2}$ M
	**(16)**	7.9	19	$3.0 \cdot 10^{-2}$ M
	**(17)**	4.5	0	–
	**(18)**	7.6	68	$3.2 \cdot 10^{-3}$ M

[a]) Inhibition at 0.01M concentration of inhibitor and at $2 \cdot 10^{-4}$ M concentration of the substrate.

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

Experimental Part

General. See [2]. TLC: compounds were detected by spraying the plates with a 5% vanillin soln. in conc. H_2SO_4 soln., or by 2% ninhydrin soln. in EtOH, followed by heating to *ca.* 200°. Unless indicated otherwise, $CDCl_3$ was used as solvent for NMR and $CHCl_3$ for IR spectroscopy.

General Procedure for the Cleavage of tert-*Butoxy- and (*tert-*Butyl)dimethylsilyloxy Groups (Procedure A).* For each 0.2 mmol of starting material, a mixture of CF_3CO_2H/H_2O 4:1 (2.5 ml) was used. The soln. was stirred at r.t., until TLC indicated the disappearance of the starting material. The solvent was evaporated, the residue dissolved in MeOH (5 ml) and evaporated (3×). A soln. of the residue was taken up in bidest. H_2O (1 ml) and extracted with CH_2Cl_2. The aq. phase was lyophilized, the residue taken up in bidest. H_2O (1 ml), and the pH of the soln. adjusted to *ca.* 9 by the addition of 0.5M NaOH. Ion-exchange chromatography was performed on *Dowex 1 × 8* (formate form, 1 g resin for 10 mg ob substance; elution with 0.05M, 0.1M, and 0.3M HCO_2H). The products were obtained as microcrystalline solids by freeze-drying of the appropriate fractions.

*General Procedure for the Oxidation with 3-Oxo-1*H*-1λ^5,2-benziodoxol-1,1,1-triyl Triacetate (= Periodinane)* [27] *(Procedure B).* Periodinane (*Aldrich*; 1.5 mmol) was added to a stirred soln. of starting material (1 mmol) in dry CH_2Cl_2 (30 ml). The mixture was stirred at r.t., until TLC indicated completion of the reaction. The suspension

was evaporated, the residue treated with AcOEt (15 ml), and the precipitate removed and washed with AcOEt. Evaporation of the combined org. layers and FC (AcOEt/hexane 1:3) of the residue gave the products.

*Benzyl 2-acetamido-3,4-di-*O*-acetyl-2-deoxy-α-*D*-glucopyranoside* (**20**) was synthesized from **19** [12] (100 g, 0.32 mol) according to [15]. FC (AcOEt/hexane 1:1, AcOEt) and recrystallization in acetone/Et_2O gave **20** in 78% yield. R_f (AcOEt) 0.38. M.p. 164–166°. $[\alpha]_D^{25} = +124.5$ ($c = 1.3$, $CHCl_3$) ([15]: m.p. 165–167°, $[\alpha]_D^{25} = +125$ ($c = 1.07$, $CHCl_3$)). IR: 3600–3440*s* (br.), 3440*m*, 3000*w*, 2930*w*, 2880*w*, 1745*s*, 1680*s*, 1510*m*, 1380*m*, 1370*m*, 1240–1200*s*, 1120*m*, 1090*m*, 1050*s*, 1025*s*, 950*w*, 910*w*. ^{1}H-NMR (300 MHz): 1.89 (*s*, Ac); 2.02 (*s*, Ac); 2.06 (*s* Ac); 2.41 (*t*, $J = 5.9$, exchanged with D_2O, OH); 3.56 (*ddd*, $J = 3.9, 5.9, 12.4$, H_a–C(6)); 3.64 (*ddd*, $J = 2.4, 5.9, 12.4$, H_b–C(6)); 3.79 (*ddd*, $J = 2.4, 3.9, 9.7$, H–C(5)); 4.33 (*ddd*, $J = 3.7, 9.5, 10.7$; after exchange with D_2O: *dd*, $J = 3.8, 10.7$, H–C(2)); 4.52 (*d* $J = 11.8$), 4.72 (*d*, $J = 11.8$, PhCH_2); 4.96 (*d*, $J = 3.7$, H–C(1)); 5.06 (*t*, $J = 9.7$, H–C(4)); 5.30 (*dd*, $J = 9.7, 10.7$, H–C(3)); 5.70 (*d*, $J = 9.5$, exchanged with D_2O, AcN*H*); 7.30–7.42 (*m*, 5 arom. H); ^{13}C-NMR: 20.52 (*q*); 20.60 (*q*); 22.95 (*q*); 51.83 (*d*); 60.89 (*t*); 68.50 (*d*); 69.93 (*t*); 70.08 (*d*); 70.89 (*d*); 96.44 (*d*); 128.04 (*d*); 128.17 (*d*); 128.50 (*d*); 136.53 (*s*); 169.88 (*s*); 170.15 (*s*); 171.23 (*s*).

*Methyl (Benzyl 2-Acetamido-3,4-di-*O*-acetyl-2-deoxy-α-*D*-glucopyranosid)uronate* (**21**). PtO_2 (3.30 g) was suspended in H_2O (130 ml) and hydrogenated at r.t./1 atm. for 14 h. The suspension was treated with H_2O (200 ml), **19** (3.11 g, 10 mmol) and $NaHCO_3$ (1.34 g). The mixture was vigourously stirred (vibromixer) and heated at 80–90° under a continuous O_2 stream for 2–3 h. The cooled mixture was filtered, the filtrate evaporated, and the residue powdered and dried over P_4O_{10}. MeI (3.1 ml) was added to a soln. of the residue in dry DMF (27.5 ml). After stirring the mixture for 6 h at 40°, excess MeI was evaporated, and 4-(pyrrolidin-1-yl)pyridine (0.25 g), pyridine (3.7 ml, 30 mmol), and Ac_2O (2.8 ml, 30 mmol) were added. The mixture was stirred at r.t. for 4 h and poured into ice-water (200 ml). The precipitate was filtered off, washed with ice-cold H_2O and dried: **21** (3.66 g, 87%). R_f (AcOEt/hexane 4:1) 0.40. M.p. 139°. $[\alpha]_D^{25} = +110.6$ ($c = 1.1$, $CHCl_3$) ([14]: m.p. 141.5°, $[\alpha]_D^{25} = +112.2$ ($c = 1.7$, $CHCl_3$)). IR (KBr): 3310*s*, 3060*w*, 2960*w*, 2920*w*, 1740*s*, 1675*s*, 1545*s*, 1500*w*, 1455*m*, 1440*m*, 1370*s*, 1340*w*, 1310*w*, 1285*w*, 1240*s* (br.), 1210*m* (br.), 1165*w*, 1120*s*, 1070*s*, 1030*s*, 990*m*, 900*m*, 840*w*. ^{1}H-NMR (200 MHz): 1.87 (*s*, AcN); 2.03 (*s*, 2 AcO); 3.76 (*s*, MeO); 4.31 (*d*, $J = 9.5$, H–C(5)); 4.38 (*dt*, $J = 3.9, 9.5$, H–C(2)); 4.52 (*d*, $J = 11.9$), 4.76 (*d*, $J = 11.9$, PhCH_2); 5.03 (*d*, $J = 3.9$, H–C(1)); 5.20–5.28 (*m*, H–C(3), H–C(4)); 5.61 (*d*, $J = 9.5$, AcN*H*); 7.32–7.41 (*m*, 5 arom. H). ^{13}C-NMR: 20.45 (*q*); 20.65 (*q*); 23.00 (*q*); 51.53, 52.80 (*d*,*q*); 68.85 (*d*); 69.20 (*d*); 70.41 (*d*); 70.51 (*t*); 96.66 (*d*); 128.20 (*d*); 128.41 (*d*); 128.66 (*d*); 136.16 (*s*); 167.99 (*s*); 169.29 (*s*); 169.74 (*s*); 171.28 (*s*).

tert-*Butyl (Benzyl 2-Acetamido-3,4-di-*O*-acetyl-2-deoxy-α-*D*-glucopyranosid)uronate* (**22**). CrO_3 (32 g, 320 mmol) and dry pyridine (52 ml, 640 mmol) were added to a stirred and cooled (ice) mixture of dry CH_2Cl_2/DMF 4:1 (640 ml). The mixture was stirred at r.t. for 30 min and treated with Ac_2O (60 ml, 640 mmol) and *t*-BuOH (160 ml, 1.72 mol) [16]. A soln. of **20** (34 g, 86 mmol) in dry CH_2Cl_2/DMF 4:1 (160 ml) was added dropwise at r.t. over 4 h. The resulting mixture was stirred at r.t. for 24 h and then cooled to 10°. MeOH (200 ml) was added and stirring continued for 30 min at r.t. The mixture was concentrated to 200 ml and filtered through a short column of SiO_2 (prepared with Et_2O, AcOEt as eluent). Concentration of the eluate, FC of the residue (AcOEt/hexane 1:1), and recrystallization in toluene gave **22** (32.0 g, 80%). R_f (AcOEt) 0.59. M.p. 126–127°. $[\alpha]_D^{25} = +102.5$ ($c = 1.5$, $CHCl_3$). IR: 3440*m*, 3020*w*, 3005*w*, 2995*m*, 2940*w*, 2880*w*, 1740*s*, 1675*s*, 1510*m*, 1455*w*, 1370*s*, 1305*m*, 1225*s*, 1155*m*, 1125*m*, 1050*s*, 1020*m*, 970*w*, 910*w*, 840*w*. ^{1}H-NMR (300 MHz): 1.46 (*s*, *t*-Bu); 1.87 (*s*, Ac); 2.01 (*s*, Ac); 2.02 (*s*, Ac); 4.19 (*d*, $J = 9.6$, H–C(5)); 4.36 (*dt*, $J = 3.7, 9.6$, H–C(2)); 4.53 (*d*, $J = 11.9$, 4.77 (*d*, $J = 11.9$, PhCH_2); 5.00 (*d*, $J = 3.7$, H–C(1)); 5.20–5.29 (*m*, H–C(3), H–C(4)); 5.65 (*d*, $J = 9.3$, AcN*H*); 7.32–7.41 (*m*, 5 arom. H). ^{13}C-NMR: 20.59 (*q*); 20.67 (*q*); 23.00 (*q*); 27.75 (*q*); 51.49 (*d*); 69.11 (*d*); 69.74 (*d*); 70.44 (*t*); 70.90 (*d*); 82.88 (*s*); 96.71 (*d*); 128.19 (*d*); 128.36 (*d*); 128.66 (*d*); 136.38 (*s*); 166.51 (*s*); 168.82 (*s*); 169.87 (*s*); 171.28 (*s*). CI-MS: 466 ([$M + 1$]$^+$). Anal. calc. for $C_{23}H_{31}NO_9$ (465.50): C 59.35, H 6.71, N 3.01; found: C 59.07, H 6.96, N 3.03.

tert-*Butyl (Benzyl 2-Acetamido-3-*O*-acetyl-2,4-dideoxy-β-*L*-threo-hex-4-enopyranosid)uronate* (**23**). *a*) To a suspension of **22** (22 g, 47.3 mmol) in dry toluene containing 4 g of ground molecular sieves (4 Å), 7-methyl-1,5,7-triazabicyclo[4.4.0]dec-5-ene (8.8 ml, 61.3 mmol) was added. The suspension was held under reflux for 3 h, cooled to r.t., and treated with 1M $KHSO_4$. The org. phase was separated and the aq. phase extracted twice with AcOEt. The combined org. phases were washed with brine, dried ($MgSO_4$), and evaporated. FC of the residue (AcOEt/hexane 1:1) yielded **23** (17.8 g, 93%) as a foam.

b) To a soln. of **22** (15 g, 32.22 mmol) in dry CH_2Cl_2 (100 ml), 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU; 19 ml, 127.5 mmol) was added. The mixture was boiled under reflux for 8 h, cooled, treated with 1M $KHSO_4$, and extracted twice with CH_2Cl_2. Processing the org. phase as usual and FC (AcOEt/hexane 1:1) gave **23** (9.3 g, 71%) as an oil which solidified upon standing at r.t. R_f (AcOEt/hexane 4:1) 0.54. M.p. 49–51°. $[\alpha]_D^{25} = +222.5$ ($c = 2.4$, $CHCl_3$). IR: 3440*m*, 3020*w*, 3005*m*, 2995*m*, 2940*w*, 2880*w*, 1740*s*, 1680*s*, 1510*s*, 1455*w*, 1370*s*, 1345*w*, 1320*m*, 1220*s*, 1140*s*, 1100*s*, 1035*m*, 1010*m*, 980*w*, 950*w*, 930*w*, 840*m*. ^{1}H-NMR (300 MHz): 1.52 (*s*, *t*-Bu); 1.92 (*s*, Ac); 2.08 (*s*,

Ac); 4.40 (*td*, J = 8.8, 2.7, H–C(2)); 4.64 (*d*, J = 11.9), 4.87 (*d*, J = 11.9, PhCH_2); 5.20 (*d*, J = 2.7, H–C(1)); 5.56 (*dd*, J = 2.9, 8.8, H–C(3)); 5.73 (*d*, J = 8.7, AcN*H*); 5.91 (*d*, J = 2.9, H–C(4)); 7.30–7.41 (*m*, 5 arom. H); ^{13}C-NMR: 20.93 (*q*); 23.05 (*q*); 27.89 (*q*); 49.40 (*d*); 66.79 (*d*); 70.82 (*t*); 82.47 (*s*); 97.27 (*d*); 107.75 (*d*); 127.97 (*d*); 128.11 (*d*); 128.47 (*d*); 136.48 (*s*); 142.86 (*s*); 160.43 (*s*); 170.04 (*s*); 170.94 (*s*). CI-MS: 346 ([M + 1 – AcOH]$^+$). Anal. calc. for $C_{21}H_{27}NO_7$ (405.45): C 62.21, H 6.71, N 3.45; found: C 62.18, H 6.90, N 3.34.

tert-*Butyl (Benzyl 2-Acetamido-2,4-dideoxy-β*-L-threo-*hex-4-enopyranosid)uronate* (**24**). At r.t., 2.5M NaOMe/MeOH (3 ml) was added to a stirred soln. of **23** (20 g, 49.32 mmol) in dry MeOH (200 ml). After 20 h, solid CO_2 was added, the solvent evaporated, and the resulting syrup dissolved in CH_2Cl_2 and washed with H_2O. The org. phase was processed as usual. FC of the residue (AcOEt/hexane 4:1) gave **24** (17.5 g, 98%). Foam. R_f (AcOEt/hexane 4:1) 0.34. M.p. 50–51°. $[\alpha]_D^{25}$ = +129.5 (c = 1.1, $CHCl_3$). IR: 3600*w*, 3440–3300*m* (br.), 3005*m*, 2990*m*, 2940*w*, 1740*s*, 1670*s*, 1510*m*, 1455*w*, 1390*w*, 1370*s*, 1340*w*, 1320*m*, 1250–1200*m*, 1135*s*, 1100*m*, 1050*m*, 1035*m*, 910*w*, 840*w*. ^{1}H-NMR (300 MHz): 1.51 (*s*, *t*-Bu); 1.96 (*s*, Ac); 3.8–4.2 (br. *s*, exchanged with D_2O, OH); 4.16 (*dt*, J = 2.5, 7.5; after exchange with D_2O: *dd*, J = 2.5, 7.7, H–C(2)); 4.35 (*dd*, J = 3.0, 7.6, H–C(3)); 4.64 (*d*, J = 11.9), 4.88 (*d*, J = 11.9, PhCH_2); 5.16 (*d*, J = 2.6, H–C(1)); 5.97 (*d*, J = 7.5, exchanged with D_2O, AcN*H*); 6.06 (*d*, J = 3.0, H–C(4)); 7.30–7.38 (*m*, 5 arom. H). ^{13}C-NMR: 20.03 (*q*); 27.89 (*q*); 52.69 (*d*); 65.31 (*d*); 70.73 (*t*); 82.19 (*s*); 97.00 (*d*); 111.76 (*d*); 127.97 (*d*); 128.06 (*d*); 128.46 (*d*); 136.60 (*s*); 141.43 (*s*); 160.95 (*s*); 171.49 (*s*). CI-MS: 364 ([M + 1]$^+$). Anal. calc. for $C_{19}H_{25}NO_6$ (363.41): C 62.80, H 6.93, N 3.85; found: C 62.56, H 7.01, N 3.71.

tert-*Butyl (Benzyl 2-Acetamido-3*-O-*[(*tert-*butyl)dimethylsilyl]-2,4-dideoxy-β*-L-threo-*hex-4-enopyranosid)-uronate* (**25**). At 0°, 2,6-dimethylpyridine (10.85 ml, 93.45 mmol) and *t*-BuMe_2SiCl (8.5 g, 56.39 mmol) were added to a stirred soln. of **24** (17 g, 46.78 mmol) in dry DMF (40 ml) at 0°. After stirring at r.t. for 24 h, the solvent was evaporated at 0.5 Torr, the residue dissolved in CH_2Cl_2 (200 ml) and washed with H_2O, and the org. phase processed as usual. FC (AcOEt/hexane 1:1) of the residue gave crystalline **25** (20.8 g, 93%), which was recrystallized in Et_2O/hexane. R_f (AcOEt/hexane 2:1) 0.74. M.p. 123°. $[\alpha]_D^{25}$ = +163.5 (c = 1.6, $CHCl_3$). IR: 3440*m*, 3000*m*, 2990*m*, 2980*m*, 2960*m*, 2940*m*, 2895*w*, 2860*m*, 1735*s*, 1680*s*, 1510*m*, 1470*w*, 1465*w*, 1460*w*, 1390*w*, 1370*s*, 1330*w*, 1310*m*, 1295*m*, 1255*m*, 1150*m*, 1110*w*, 1095*m*, 1070*m*, 1045*w*, 1010*w*, 940*w*, 930*w*, 875*w*, 845*s*. ^{1}H-NMR (200 MHz): 0.11 (*s*, Me_2Si); 0.85 (*s*, *t*-BuSi); 1.53 (*s*, *t*-Bu); 1.94 (*s*, Ac); 4.14 (*dddd*, J = 0.5, 2.0, 5.5, 7.8, H–C(2)); 4.29 (*dd*, J = 3.9, 5.5, H–C(3)); 4.69 (*d*, J = 12.0), 4.94 (*d*, J = 12.0, PhCH_2); 5.10 (*d*, J = 2.0, H–C(1)); 5.61 (*d*, J = 7.8, AcN*H*); 5.98 (*dd*, J = 0.5, 3.9, H–C(4)); 7.33 (*s*, 5 arom. H). ^{13}C-NMR: –4.58 (*q*); –4.55 (*q*); 17.85 (*s*); 23.18 (*q*); 25.60 (*q*); 27.92 (*q*); 52.25 (*d*); 65.28 (*d*); 70.89 (*t*); 82.16 (*s*); 96.96 (*d*); 111.34 (*d*); 127.97 (*d*); 128.02 (*d*); 128.09 (*d*); 128.44 (*d*); 136.60 (*s*); 142.21 (*s*); 161.21 (*s*); 169.96 (*s*). CI-MS: 478 (19, [M + 1]$^+$), 346 (100). Anal. calc. for $C_{25}H_{39}NO_6Si$ (477.68): C 62.86, H 8.23, N 2.93; found: C 63.09, H 8.08, N 3.00.

tert-*Butyl 2-Acetamido-3*-O-*[(*tert-*butyl)dimethylsilyl]-2,4-dideoxy*-D-xylo-*hexopyranuronate* (**26**). Under Ar, 10% Pd/C (0.7 g) was added to a soln. of **25** (1.3 g, 2.72 mmol) in dry MeOH (50 ml). After hydrogenation at 1 atm. for 24 h, additional 10% Pd/C (0.4 g) was added and hydrogenation continued for another 24 h. The suspension was filtered through *Celite* and washed with AcOEt. Evaporation and recrystallization in cyclohexane gave **26** (1.01 g, 96%) as colorless needles (α-D-anomer). R_f (AcOEt) 0.32. M.p. 78–79°. $[\alpha]_D^{25}$ = +45.7 (c = 1.9, $CHCl_3$, after 10 min)→58.3 (after 26 h, final). IR: 3600*w*, 3440*w* (br.), 3000*w*, 2990*w*, 2960*w*, 2930*s*, 2910*w*, 2860*m*, 1740*s*, 1675*s*, 1510*m*, 1470*w*, 1460*w*, 1450*w*, 1395*w*, 1370*m*, 1310*w*, 1255*m*, 1160*m*, 1135*s*, 1080*m*, 1040*w*, 905*m*, 870*m*, 840*s*. ^{1}H-NMR (CD_3OD): α-D-anomer: 0.08 (*s*, Me_2Si); 0.86 (*s*, *t*-BuSi); 1.47 (*s*, *t*-Bu); 1.57 (*ddd*, J = 10.2, 12.3, 12.8, H_{ax}–C(4)); 1.95 (*s*, Ac); 2.19 (*ddd*, J = 4.8, 2.5, 12.8, H_{eq}–C(4)); 3.85 (*dd*, J = 3.4, 10.2, H–C(2)); 4.01 (*dt*, J = 4.8, 10.2, H–C(3)); 4.47 (*dd*, J = 2.5, 12.3, H–C(5)); 5.10 (*d*, J = 3.4, H–C(1)). ^{1}H-NMR of crude mixture: β-D-anomer at 5.50 (*d*, J = 8.8, H–C(1)). ^{13}C-NMR: –4.84 (*q*); –4.38 (*q*); 17.77 (*s*); 23.39 (*q*); 25.53 (*q*); 27.91 (*q*); 37.26 (*t*); 54.78 (*d*); 67.17 (2*d*); 82.11 (*s*); 92.65 (*d*); 170.19 (*s*); 170.32 (*s*). CI-MS: 390 ([M + 1]$^+$). Anal. calc. for $C_{18}H_{35}NO_6Si$ (389.57): C 55.50, H 9.06, N 3.60; found: C 55.52, H 9.32, N 3.49.

tert-*Butyl {(Cyclohexyl)methyl 2-Acetamido-3*-O-*[(*tert-*butyl)dimethylsilyl]-2,4-dideoxy*-α-D-xylo-*hexopy-ranosid}uronate* (**27**). Similarly to the above mentioned reaction, a soln. of **25** (16.4 g, 34.33 mmol) in dry MeOH (300 ml) was hydrogenated in the presence of 10% Pd/C (8 g) for 8 d. FC (AcOEt/hexane 2:1) gave **26** (11.77 g, 88%) and **27** (0.83 g, 5%), which was crystallized from Et_2O/hexane. R_f (AcOEt/hexane 2:1) 0.66. M.p. 137–138°. $[\alpha]_D^{25}$ = +92.3 (c = 1.1, $CHCl_3$). IR: 3430*w*, 2990*w*, 2910*s*, 2850*s*, 1740*s*, 1670*s*, 1500*w*, 1440*w*, 1370*m*, 1310*w*, 1250*w*, 1115*s*, 1075*m*, 1020*m*, 905*w*, 890*w*, 840*m*. ^{1}H-NMR (200 MHz): 0.04 (*s*, MeSi); 0.06 (*s*, MeSi); 0.83–0.86 (*m*, 11 H); 1.16–1.27 (*m*, 4 H); 1.47 (*s*, *t*-Bu); 1.62–1.78 (*m*, 6 H); 1.96 (*s*, Ac); 2.12 (*ddd*, J = 2.7, 4.8, 12.8, H_{eq}–C(4)); 3.20 (*dd*, J = 6.1, 9.8), 3.47 (*dd*, J = 6.8, 9.8, $C_6H_{11}CH_2$); 3.80 (*dt*, J = 4.8, 10.1, H–C(3)); 4.03 (*dt*, J = 3.6, 9.5, H–C(2)); 4.16 (*dd*, J = 2.5, 12.0, H–C(5)); 4.85 (*d*, J = 3.6, H–C(1)); 5.38 (*d*, J = 9.5, AcN*H*). ^{13}C-NMR: –4.77 (*q*); –4.24 (*q*); 17.80 (*s*); 23.47 (*q*); 25.41 (*q*); 25.54 (*t*); 25.67 (*t*); 25.71 (*t*); 27.98 (*q*); 29.90 (*t*); 30.01 (*t*); 37.22 (*t*); 37.64 (*d*); 54.37 (*d*); 67.76 (*d*); 73.74 (*t*); 81.79 (*s*); 98.43 (*d*); 169.40 (*s*); 169.50 (*s*). CI-MS: 486 ([M + 1]$^+$). Anal. calc. for $C_{25}H_{47}NO_6Si$ (485.74): C 61.82, H 9.75, N 2.88; found: C 61.85, H 9.97, N 2.76.

tert-*Butyl* *5-Acetamido-4-*O*-[(*tert*-butyl)dimethylsilyl]-3,5,7-trideoxy-7-*C*-(trimethylsilyl)-*D*-ido-heptonate* (**28**). A soln. of **26** (5 g, 12.8 mmol) in dry THF (20 ml) was added dropwise at 0° over 30 min under Ar to a soln. of Me_3SiCH_2MgCl (prepared from Mg (1.55 g, 64.17 mmol) and Me_3SiCH_2Cl (8.92 ml, 64.17 mmol)) in dry THF (30 ml). The mixture was stirred for 1 h at 0° and then for 3 h at r.t., diluted with AcOEt (50 ml), poured into an ice-cold sat. NH_4Cl soln., and extracted with AcOEt. The org. phase was washed with sat. NH_4Cl soln. (pH 6) and processed as usual. The residue was co-evaporated with toluene. FC (AcOEt/hexane 4:1) yielded **28** (5.20 g, 85%), which was crystallized from Et_2O. R_f (AcOEt/hexane 4:1) 0.54. M.p. 138°. $[\alpha]_D^{25} = +15.5$ ($c = 1.3$, $CHCl_3$). IR: 3510*m* (br.), 3440*m*, 2990*w*, 2960*s*, 2940*m*, 2890*w*, 2860*w*, 1730*s*, 1655*s*, 1500*s*, 1465*w*, 1390*w*, 1370*m*, 1315*w*, 1280*m*, 1250*s*, 1200*m*, 1160*m*, 1130*m*, 1085*s*, 1020*w*, 970*w*, 915*w*, 860*m*, 840*s*. ^{1}H-NMR (400 MHz): 0.06 (*s*, Me_3Si); 0.15 (*s*, MeSi); 0.16 (*s*, MeSi); 0.74 (*ddd*, $J = 1.0$, 3.7, 14.5; after exchange with D_2O: *dd*, $J = 3.7$, 14.5, H_a–C(7)); 0.84 (*dd*, $J = 10.2$, 14.5, H_b–C(7)); 0.92 (*s*, *t*-BuSi); 1.48 (*s*, *t*-Bu); 1.77 (*ddd*, $J = 7.7$, 9.6, 14.3, H_a–C(3)); 1.86 (*td*, $J = 4.6$, 14.3, H_b–C(3)); 2.10 (*s*, Ac); 2.79 (*dd*, $J = 1.1$, 3.8, exchanged with D_2O, OH–C(6)); 3.77 (*d*, $J = 7.4$, exchanged with D_2O, OH–C(2)); 3.93 (*ddd*, $J = 2.2$, 3.6, 9.1; after exchange with D_2O: *dd*, $J = 2.2$, 3.6, H–C(5)); 4.00 (br. *qd*, $J = 3.8$, 10.5; after exchange with D_2O: br. *td*, $J \approx 3.8$, 10.5, H–C(6)); 4.07 (*ddd*, $J = 4.6$, 7.3, 9.6; after exchange with D_2O: *dd*, $J = 4.2$, 9.7, H–C(2)); 4.17 (*ddd*, $J = 2.2$, 4.8, 7.7, H–C(4)); 6.19 (*d*, $J = 9.1$, exchanged with D_2O, AcN*H*). ^{13}C-NMR: *Table 3*. CI-MS: 478 ($[M + 1]^+$). Anal. calc. for $C_{22}H_{47}NO_6Si_2$ (477.79): C 55.31, H 9.92, N 2.93; found: C 55.23, H 10.13, N 2.93.

tert-*Butyl* *5-Acetamido-4-*O*-[(*tert*-butyl)dimethylsilyl]-3,5,6,7-tetradeoxy-2-*O*-(methylsulfonyl)-*L*-xylo-hept-6-enonate* (**29**). Et_3N (3.6 ml, 25.82 mmol) and methanesulfonyl chloride (1.32 ml, 17 mmol) were added under Ar at −20° to a stirred soln. of **28** (3 g, 6.23 mmol) in dry CH_2Cl_2 (20 ml). After 5 min, the suspension was poured into sat. $NaHCO_3$ soln. at 0°. The mixture was extracted with CH_2Cl_2 and the org. phase washed with sat. NH_4Cl soln. and processed as usual to yield a crude oil (2.7 g, 92%) which was used for the next transformation. FC (AcOEt/hexane 1:1) of 150 mg gave an anal. sample of **29** (88%). Colorless oil. R_f (AcOEt/hexane 1:1) 0.34. $[\alpha]_D^{25} = -51.5$ ($c = 0.9$, $CHCl_3$). IR: 3450*m*, 2990*m*, 2960*m*, 2940*m*, 2860*m*, 1740*s*, 1675*s*, 1500*s*, 1370*s*, 1360*s*, 1330*m*, 1255*m*, 1175*s*, 1155*s*, 1110–1090*m*, 1005*w*, 970*s*, 840*s*. ^{1}H-NMR (400 MHz): 0.11 (*s*, MeSi); 0.15 (*s*, MeSi); 0.91 (*s*, *t*-BuSi); 1.5 (*s*, *t*-Bu); 1.90–2.00 (*m*, CH_2(3)); 2.06 (*s*, Ac); 3.16 (*s*, Ms); 3.98 (*dt*, $J = 1.9$, 6.0, H–C(4)); 4.60 (*tddd*, $J = 0.9$, 1.9, 5.0, 9.1; after exchange with D_2O: *m*, H–C(5)); 4.94 (*dd*, $J = 5.5$, 8.0, H–C(2)); 5.19 (*ddd*, $J = 0.9$, 1.5, 17.0, H_a–C(7)); 5.20 (*ddd*, $J = 0.9$, 1.5, 10.8, H_b–C(7)); 5.71 (*d*, $J = 9.1$, exchanged with D_2O, AcN*H*); 5.83 (*ddd*, $J = 5.0$, 10.8, 17.0, H–C(6)). ^{13}C-NMR: *Table 3*. CI-MS: 466 ($[M + 1]^+$). Anal. calc. for $C_{20}H_{39}NO_7SSi$ (465.68): C 51.59, H 8.44, N 3.01, S 6.88; found: C 51.30, H 8.29, N 3.24, S 6.95.

tert-*Butyl* *5-Acetamido-4-*O*-[(*tert*-butyl)dimethylsilyl]-3,5,6,7-tetradeoxy-*L*-lyxo-hept-6-enonate* (**30**). A mixture of crude **29** (*ca.* 6.3 mmol) and finely powdered and dried ($CaCl_2$) KNO_2 (2.7 g, 31.7 mmol) in dry DMF (20 ml) was vigorously stirred at 100° for 1 h. The resulting gel was diluted with DMF (5 ml), cooled to r.t., diluted with CH_2Cl_2 (100 ml), and filtered through a Na_2SO_4 pad. The filtrate was evaporated: **30** (1.7 g, 68%). FC (200 mg of crude **30**, AcOEt/hexane 1:1) gave a pure sample of **30**. Oil. R_f (AcOEt/hexane 1:1) 0.32. $[\alpha]_D^{25} = -23.6$ ($c = 1.0$, $CHCl_3$). IR: 3520–3480*m* (br.), 3440*m*, 2990*m*, 2960*m*, 2940*m*, 2900*w*, 2860*m*, 1725*s*, 1670*s*, 1500*s*, 1475*w*, 1460*w*, 1370*s*, 1285*m*, 1255*s*, 1200*m*, 1160*m*, 1085*s*, 910*m*, 840*s*. ^{1}H-NMR (400 MHz): 0.06 (*s*, MeSi); 0.07 (*s*, MeSi); 0.88 (*s*, *t*-BuSi); 1.47 (*s*, *t*-Bu); 1.64 (*ddd*, $J = 4.3$, 10.0, 14.0, H_a–C(3)); 1.91 (*ddd*, $J = 3.6$, 9.5, 14.0, H_b–C(3)); 2.05 (*s*, Ac); 3.00 (*d*, $J = 4.7$, exchanged with D_2O, OH); 4.07 (*ddd*, $J = 1.6$, 4.4, 9.5, H–C(4)); 4.11 (*ddd*, $J = 3.6$, 4.7, 10.0; after exchange with D_2O: *dd*, $J = 3.6$, 10.1, H–C(2)); 4.68 (*tdd*, $J = 1.6$, 5.0, 9.3; after exchange with D_2O: *m*, H–C(5)); 5.16 (*td*, $J = 1.6$, 10.5, H_a–C(7)); 5.18 (*td*, $J = 1.6$, 17.0, H_b–C(7)); 5.81 (*ddd*, $J = 5.1$, 10.5, 17.0, H–C(6)); 5.86 (*d*, $J = 9.4$, exchanged with D_2O, AcN*H*). ^{13}C-NMR: *Table 3*. CI-MS: 388 ($[M + 1]^+$). Anal. calc. for $C_{19}H_{37}NO_5Si$ (387.60): C 58.88, H 9.62, N 3.61; found: C 58.59, H 9.46, N 3.85.

tert-*Butyl* *5-Acetamido-4-*O*-[(*tert*-butyl)dimethylsilyl]-3,5,6,7-tetradeoxy-2-*O*-(methylsulfonyl)-*L*-lyxo-hept-6-enonate* (**31**). Crude **30** (*ca.* 4.2 mmol) was mesylated under the same conditions as described for **29**, using Et_3N (1.8 ml, 12.9 mmol) and methanesulfonyl chloride (0.7 ml, 9 mmol) in CH_2Cl_2 (25 ml). Workup as usual and FC (AcOEt/hexane 1:1) gave **31** (2.1 g, 72% from **28**). Colorless oil. R_f (AcOEt/hexane 1:1) 0.42. $[\alpha]_D^{25} = -8.7$ ($c = 1.0$, $CHCl_3$). IR: 3450*m*, 2995*m*, 2960*m*, 2940*m*, 2900*w*, 2870*m*, 1750*s*, 1675*s*, 1500*s*, 1475*w*, 1460*w*, 1375*s*, 1365*s*, 1335*s*, 1255*m*, 1175*s*, 1155*s*, 1090*m* (br.), 1020*w*, 970*s*, 910*s*, 895*w*, 840*s*. ^{1}H-NMR (400 MHz): 0.07 (*s*, MeSi); 0.10 (*s*, MeSi); 0.89 (*s*, *t*-BuSi); 1.49 (*s*, *t*-Bu); 1.91 (*ddd*, $J = 4.4$, 9.3, 14.6, H_a–C(3)); 2.05 (*s*, Ac); 2.10 (*ddd*, $J = 4.0$, 9.1, 14.6, H_b–C(3)); 3.15 (*s*, $MeSO_2$); 3.97 (*ddd*, $J = 1.8$, 4.4, 9.1, H–C(4)); 4.66 (*tdd*, $J = 1.8$, 5.2, 8.9, H–C(5)); 5.01 (*dd*, $J = 4.0$, 9.2, H–C(2)); 5.18 (*td*, $J = 1.8$, 10.1, H_a–C(7)); 5.19 (*td*, $J = 1.8$, 17.5, H_b–C(7)); 5.74 (*d*, $J = 8.9$, AcN*H*); 5.79 (*ddd*, $J = 5.2$, 10.1, 17.5, H–C(6)). ^{13}C-NMR: *Table 3*. CI-MS: 466 (25, $[M + 1]^+$), 410 (100). Anal. calc. for $C_{20}H_{39}NO_7SSi$ (465.68): C 51.59, H 8.44, N 3.01, S 6.88; found: C 51.48, H 8.32, N 3.20, S 7.10.

tert-*Butyl 5-Acetamido-2-azido-4-*O*-[(*tert*-butyl)dimethylsilyl]-2,3,5,6,7-pentadeoxy-*L*-xylo-hept-6-enonate* (**32**). NaN_3 (1.9 g, 30 mmol) was added to a soln. of **31** (2.8 g, 6 mmol) in dry DMF (30 ml). The mixture was stirred at r.t. for 12 h. After evaporation under high vacuum, the residue was taken up in CH_2Cl_2 (100 ml) and filtered through a Na_2SO_4 pad. The filtrate was evaporated. FC (AcOEt/hexane 1:3) gave **32** (1.87 g, 75%). Colorless oil. R_f (AcOEt/hexane 1:1) 0.73. $[\alpha]_D^{25} = -71.1$ ($c = 1.0$, $CHCl_3$). IR: 3450*w*, 2950*w*, 2960*m*, 2940*m*, 2900*w*, 2860*w*, 2105*s*, 1735*s*, 1675*s*, 1500*s*, 1475*m*, 1375*s*, 1300*w*, 1255*s*, 1200*s*, 1155*s*, 1100*s*, 1005*w*, 995*w*, 975*w*, 940*w*, 925*w*, 900*w*, 840*s*. ^{1}H-NMR (400 MHz): 0.11 (*s*, MeSi); 0.12 (*s*, MeSi); 0.90 (*s*, *t*-BuSi); 1.50 (*s*, *t*-Bu); 1.70 (*ddd*, $J = 4.4$, 10.0, 14.0, H_a–C(3)); 1.86 (*ddd*, $J = 4.8$, 8.4, 14.0, H_b–C(3)); 2.05 (*s*, Ac); 3.82 (*dd*, $J = 4.8$, 10.0, H–C(2)); 3.95 (*ddd*, $J = 2.5$, 4.4, 8.4, H–C(4)); 4.58 (*ddddd*, $J = 1.0$, 2.0, 2.5, 4.8, 8.8, H–C(5)); 5.18 (*ddd*, $J = 1.0$, 2.0, 17.2, H_a–C(7)); 5.21 (*td*, $J = 1.0$, 10.5, H_b–C(7)); 5.72 (*d*, $J = 8.8$, AcN*H*); 5.85 (*ddd*, $J = 4.8$, 10.6, 17.2, H–C(6)). ^{13}C-NMR: *Table 3*. CI-MS: 413 ($[M + 1]^+$). Anal. calc. for $C_{19}H_{36}N_4O_4Si$ (412.61): C 55.31, H 8.79, N 13.58; found: C 55.09, H 8.94, N 13.46.

tert-*Butyl 2-Acetamido-5-azido-3-*O*-[(*tert*-butyl)dimethylsilyl]-2,4,5-trideoxy-*D*-xylo-hexuronate* (**33**). A stream of O_3/O_2 was passed into a cooled (−78°) mixture of **32** (300 mg, 0.727 mmol), CH_2Cl_2 (40 ml), and solid $NaHCO_3$ (35 mg) until it turned blue (5 min). The soln. was purged with O_2 (10 min) and N_2 (5 min). After the addition of a soln. of Ph_3P (152 mg, 0.581 mmol) in CH_2Cl_2 (1 ml), the mixture was warmed to r.t., stirred for 1 h and evaporated. FC (AcOEt/hexane 1:3→1:1) gave **33** (290 mg, 96%) as a colorless oil, which was immediately used for the next step. R_f (AcOEt/hexane 1:1) 0.59. $[\alpha]_D^{25} = -95.2$ ($c = 0.9$, $CHCl_3$). IR: 3430*m*, 2980*m*, 2960*m*, 2930*m*, 2860*w*, 2710*w*, 2105*s*, 1735*s*, 1675*s*, 1490*m*, 1470*m*, 1460*m*, 1370*m*, 1300*w*, 1250*s*, 1200*s*, 1105*m*, 1005*s*, 840*s*. ^{1}H-NMR (400 MHz): 0.16 (*s*, MeSi); 0.17 (*s*, MeSi); 0.90 (*s*, *t*-BuSi); 1.50 (*s*, *t*-Bu); 1.71–1.79 (*m*, CH_2(4)); 2.09 (*s*, Ac); 3.82 (*dd*, $J = 6.3$, 8.2, H–C(5)); 4.49 (*ddd*, $J = 3.4$, 5.2, 7.7, H–C(3)); 4.65 (*dd*, $J = 3.4$, 7.3, H–C(2)); 6.20 (*d*, $J = 7.3$, AcN*H*); 9.73 (*s*, H–C(1)). ^{13}C-NMR: *Table 3*. CI-MS: 415 ($[M + 1]^+$). Anal. calc. for $C_{18}H_{34}N_4O_5Si$ (414.58): C 52.15, H 8.27, N 13.51; found: C 52.14, H 8.44, N 13.30.

tert-*Butyl (2*S*,4*S*,5*S*)-5-Acetamido-4-[(*tert*-butyl)dimethylsilyloxy]piperidine-2-carboxylate* (**34**). NH_4(HCOO) (350 mg, 5.55 mmol) and 10% Pd/C (50 mg) were added under Ar to a soln. of **33** (230 mg, 0.555 mmol) in MeOH (12 ml). The mixture was stirred at r.t. for 3 h, diluted with AcOEt (20 ml), and filtered through *Celite*. The filtrate was evaporated, a soln. of the residue in AcOEt (30 ml) washed with 1M NaOH, and the org. phase processed as usual. FC (CH_2Cl_2/MeOH 9:1) of the residue and crystallization from Et_2O afforded **34** (165 mg, 80%). R_f (AcOEt/EtOH 85:15) 0.20. M.p. 197°. $[\alpha]_D^{25} = +34.4$ ($c = 1.1$, $CHCl_3$). IR: 3440*m*, 3000*m*, 2995*m*, 2960*m*, 2930*m*, 2860*m*, 1735*s*, 1675*s*, 1500*m*, 1460*w*, 1370*s*, 1305*w*, 1270*m*, 1250*s*, 1200*m*, 1155*s*, 1115*s*, 1085*s*, 1015*w*, 1005*s*, 895*w*, 840*s*. ^{1}H-NMR (400 MHz): 0.09 (*s*, MeSi); 0.10 (*s*, MeSi); 0.88 (*s*, *t*-BuSi); 1.47 (*s*, *t*-Bu); 1.70 (*td*, $J \approx 8.6$, 13.8, H_{ax}–C(3)); 1.96 (*s*, Ac); 2.15 (*td*, $J = 4.0$, 13.8, H_{eq}–C(3)); 2.40 (*dd*, $J = 8.1$, 12.6, H_{ax}–C(6)); 3.27 (*dd*, $J = 4.0$, 9.0, H–C(2)); 3.45 (*dd*, $J = 3.6$, 12.6, H_{eq}–C(6)); 3.61–3.67 (*m*, H–C(4), H–C(5)); 5.59 (br. *d*, $J = 4.3$, exchanged with D_2O, AcN*H*). ^{13}C-NMR: *Table 4*. CI-MS: 373 ($[M + 1]^+$). Anal. calc. for $C_{18}H_{36}N_2O_4Si$ (372.58): C 58.03, H 9.74, N 7.52; found: C 58.30, H 9.90, N 7.54.

*(2*S*,4*S*,5*S*)-5-Acetamido-4-hydroxypiperidine-2-carboxylic Acid* (**15**). According to *Procedure A*, **34** (70 mg, 0.188 mmol) afforded **15** (33 mg, 87%) after 1 h. R_f (i-PrOH/H_2O 7:3) 0.40. M.p. 282–284°. $[\alpha]_D^{25} = +16.0$ ($c = 0.5$, H_2O). pK_{HA} (H_2O) 8.3. IR (KBr): 3550*m*, 3420*m*, 1660*s*, 1630*s*, 1600*s*, 1460*m*, 1400*s*, 1370*m*, 1350*w*, 1325*w*, 1275*w*, 1160*m*, 1085*s*, 985*w*, 950*w*, 930*w*. ^{1}H-NMR (400 MHz, D_2O): 1.76 (*ddd*, $J = 11.0$, 13.2, 13.9, H_{ax}–C(3)); 1.92 (*s*, Ac); 2.59 (*ddd*, $J = 3.3$, 4.6, 13.9, H_{eq}–C(3)); 2.87 (*dd*, $J = 11.8$, 12.8, H_{ax}–C(6)); 3.49 (*dd*, $J = 4.8$, 12.8, H_{eq}–C(6)); 3.74 (*dd*, $J = 3.3$, 13.2, H–C(2)); 3.84 (*ddd*, $J = 4.6$, 10.2, 11.8, H–C(4)); 3.92 (*ddd*, $J = 4.8$, 10.2, 11.8, H–C(5)). ^{13}C-NMR: *Table 4*. CI-MS: 203 ($[M + 1]^+$). Anal. calc. for $C_8H_{14}N_2O_4 \cdot 1H_2O$ (220.22): C 43.63, H 7.32, N 12.72; found: C 43.43, H 7.11, N 12.43.

tert-*Butyl (2*S*,4*S*,5*S*)-5-Acetamido-4-[(*tert*-butyl)dimethylsilyloxy]-1-(2-hydroxyethyl)piperidine-2-carboxylate* (**35**). Glycolaldehyde (100 mg, 1.67 mmol) and 10% Pd/C (40 mg) were added under Ar to a soln. of **34** (100 mg, 0.268 mmol) in MeOH (10 ml). The mixture was hydrogenated at r.t./1 atm. for 12 h. Filtration of the diluted suspension (AcOEt, 20 ml) through *Celite*, evaporation of the filtrate, and FC (AcOEt, AcOEt/EtOH 95:5, 85:15) afforded **35** (100 mg, 90%) as an oil, which crystallized in contact with $CHCl_3$ and H_2O. R_f (AcOEt/EtOH 85:15) 0.53. M.p. 73–75°. $[\alpha]_D^{25} = +4.4$ ($c = 1.9$, $CHCl_3$). IR: 3600–3300*m* (br.), 3440*m*, 2980*m*, 2960*m*, 2935*s*, 2890*m*, 2860*m*, 1725*s*, 1670*s*, 1500*m*, 1460*m*, 1390*w*, 1370*s*, 1300*w*, 1280*w*, 1250*s*, 1200*m*, 1155*s*, 1120*s*, 1090*s*, 1065*m*, 1050*m*, 1005*w*, 910*s*, 840*s*. ^{1}H-NMR (400 MHz): 0.09 (*s*, MeSi); 0.10 (*s*, MeSi); 0.88 (*s*, *t*-BuSi); 1.47 (*s*, *t*-Bu); 1.93 (*d*, $J = 7.3$, 13.5, H_a–C(3)); 1.97 (*s*, Ac); 2.04 (*td*, $J \approx 4.5$, 13.4, H_b–C(3)); 2.14 (*dd*, $J = 7.3$, 11.8, H_a–C(6)); 2.53 (*ddd*, $J = 3.7$, 4.6, 13.4, H_a–C(1′)); 2.82 (*ddd*, $J = 4.0$, 7.9, 13.3, H_b–C(1′)); 3.12 (*dd*, $J = 4.9$, 7.3, H–C(2)); 3.48 (*dd*, $J = 3.5$, 11.8, H_b–C(6)); 3.54 (*ddd*, $J = 4.1$, 5.1, 11.1, H_a–C(2′)); 3.64 (*ddd*, $J = 3.5$, 7.7, 11.2, H_b–C(2′)); 3.67 (*dt*, $J = 4.0$, 7.3, H–C(4)); 3.80 (*dq*, $J = 3.5$, 7.3, H–C(5)); 5.72 (*d*, $J = 7.3$, AcN*H*). ^{13}C-NMR: see *Table 4*.

CI-MS: 417 ($[M + 1]^+$). Anal. calc. for $C_{20}H_{40}N_2O_5Si$ (416.64): C 57.66, H 9.68, N 6.72; found: C 57.76, H 9.68, N 6.95.

(2S,4S,5S)-5-Acetamido-4-hydroxy-1-(2-hydroxyethyl)piperidine-2-carboxylic Acid (**16**). According to *Procedure A*, **35** (100 mg, 0.24 mmol) gave **16** (46.7 mg, 79%) after 2 h. R_f (i-PrOH/H_2O 7:3) 0.51. $[\alpha]_D^{25} = +4.5$ ($c = 1.9$, H_2O). pK_{HA} (H_2O): 7.9. IR (KBr): 3600–3300*s* (br.), 2950*w*, 2860*w*, 1635*s*, 1600*s*, 1350*s*. ^{1}H-NMR (400 MHz, D_2O): 1.79 (br. *q*, $J \approx 12.3$, H_{ax}–C(3)); 2.02 (*s*, Ac); 2.38 (*ddd*, $J = 3.0$, 3.4, 12.7, H_{eq}–C(3)); 2.62 (*t*, $J = 12.0$, H_{ax}–C(6)); 2.88–2.92 (*m*, H_a–C(1′)); 3.18–3.23 (*m*, H_b–C(1′)); 3.46 (br. *d*, $J \approx 12.2$, H–C(2)); 3.51 (*dd*, $J = 4.6$, 12.0, H_{eq}–C(6)); 3.76 (*dt*, $J = 3.4$, 11.8, H–C(4)); 3.80–3.86 (*m*, CH_2(2′)); 3.96 (*dt*, $J = 4.6$, 11.8, H–C(5)). ^{13}C-NMR: *Table 4*. CI-MS: 229 ($[M + 1 - H_2O]^+$). Anal. calc. for $C_{10}H_{18}N_2O_5$ (246.27): C 48.77, H 7.37, N 11.38; found: C 48.94, H 7.37, N 11.43.

tert-*Butyl* *(3aR,4S,5S,7S)-4-Acetamido-5-[(*tert*-butyl)dimethylsilyloxy]-3,3a,4,5,6,7-hexahydropyrido-[1,2-c][1,2,3]triazole-7-carboxylate* (**36**). A soln. of **32** (100 mg, 0.242 mmol) in dry toluene (20 ml) was boiled under reflux for 4 h, cooled, and evaporated. FC of the resulting gel (SiO_2 treated with 2% of Et_3N, AcOEt) gave **36** (83 mg, 83%) as a solid. R_f (AcOEt/EtOH 95:5) 0.52. M.p. 144–146°. $[\alpha]_D^{25} = -2.0$ ($c = 0.75$, $CHCl_3$). UV (EtOH): 240 (1539), 266 (1922). CD (EtOH): 199 (0), 233 (21.0), 248 (0), 265 (−12.8), 300 (0). IR: 3430*m*, 3000*m*, 2980*s*, 2960*s*, 2940*s*, 2900*w*, 2860*m*, 1735*s*, 1680*s*, 1500*s*, 1475*m*, 1370*s*, 1310*w*, 1260*s*, 1200*m*, 1155*s*, 1090*s*, 1050*w*, 1005*w*, 985*w*, 910*w*, 865*w*, 840*s*. ^{1}H-NMR (400 MHz): 0.11 (*s*, MeSi); 0.13 (*s*, MeSi); 0.89 (*s*, *t*-BuSi); 1.45 (*s*, *t*-Bu); 1.99 (*s*, Ac); 2.09 (*ddd*, $J = 2.9$, 7.7, 14.8, H_a–C(6)); 2.33 (*ddd*, $J = 1.4$, 2.5, 14.8, H_b–C(6)); 3.75 (*dd*, $J = 12.6$, 15.9, H_a–C(3)); 4.03 (*q*, $J = 3.0$, H–C(5)); 4.10 (*td*, $J = 2.9$, 8.8, H–C(4)); 4.13 (*ddd*, $J = 2.9$, 11.4, 12.6, H–C(3a)); 4.36 (*dd*, $J = 11.3$, 15.9, H_b–C(3)); 4.82 (br. *d*, $J \approx 7.7$, H–C(7)); 5.53 (*d*, $J = 8.8$, AcN*H*). ^{13}C-NMR: *Table 4*. CI-MS: 385 ($[M + 1 - N_2]^+$). Anal. calc. for $C_{19}H_{36}N_4O_4Si$ (412.61): C 55.31, H 8.79, N 13.58; found: C 55.35, H 8.94, N 13.33.

tert-*Butyl* *(4aS,6S,8S,8aS)-8-[(*tert*-Butyl)dimethylsilyloxy]-4a,5,6,7,8,8a-hexahydro-2-methyl-4H-pyrido-[3,2-d][3,1]oxazine-6-carboxylate* (**37**). A 10% (*v*/*v*) soln. of AcOH in toluene (160 µl) was added dropwise to a soln. of **36** (70 mg of the crude product of the thermolysis of **32**, 0.17 mmol) in toluene (15 ml), until the development of N_2 ceased (10 min). After neutralization with sat. Na_2CO_3 soln., the org. phase was processed as usual. Co-evaporation with toluene (2×) and FC (SiO_2 treated with 2% of Et_3N, AcOEt) of the residue gave **37** (57 mg, 87%). Acid- and H_2O-labile oil. R_f (AcOEt/EtOH 95:5) 0.36. $[\alpha]_D^{25} = +2.2$ ($c = 0.9$, $CHCl_3$). IR: 2980*s*, 2960*s*, 2940*s*, 2900*m*, 2860*m*, 1725*s*, 1675*s*, 1605*w*, 1495*m*, 1480*w*, 1465*m*, 1390*m*, 1370*m*, 1250*s*, 1200*s*, 1155*s*, 1130*m*, 1115*m*, 1095*s*, 1080*s*, 1020*w*, 980*w*, 970*w*, 940*w*, 910*s*, 860*m*, 840*s*. ^{1}H-NMR (400 MHz): 0.06 (*s*, MeSi); 0.08 (*s*, MeSi); 0.88 (*s*, *t*-BuSi); 1.46 (*s*, *t*-Bu); 1.93 (*s*, Me); 2.03 (*ddd*, $J = 3.0$, 6.6, 14.2, H_a–C(7)); 2.09 (*td*, $J \approx 3.0$, 14.4, H_b–C(7)); 2.32 (br. *s*, NH); 3.15 (br. *s*, H–C(8a)); 3.41 (*dd*, $J = 2.6$, 6.4, H–C(6)); 3.62 (*q*, $J = 2.2$, H–C(4a)); 3.95 (*dd*, $J = 2.1$, 11.5, H_a–C(4)); 4.05 (*q*, $J = 3.2$, H–C(8)); 4.11 (*dd*, $J = 2.2$, 11.5, H_b–C(4)). ^{13}C-NMR: *Table 4*. CI-MS: 385 ($[M + 1]^+$).

tert-*Butyl* *(2S,4S,5S,6S)-5-Acetamido-4-[(*tert*-butyl)dimethylsilyloxy]-6-(hydroxymethyl)piperidine-2-carboxylate* (**38**). A soln. of 80% aq. AcOH (180 µl) in toluene (320 µl) was added dropwise to a soln. of **36** (70 mg, 0.17 mmol) in toluene (15 ml). After stirring for 20 min and neutralization as described above, FC (AcOEt/EtOH 95:5, 85:15) afforded **38** (4.17 mg, 61%) which was crystallized from Et_2O. R_f (AcOEt/EtOH 95:5) 0.13. M.p. 155–156°. $[\alpha]_D^{25} = +24.6$ ($c = 0.5$, $CHCl_3$). IR: 3600–3420*m* (br.), 2980*m*, 2960*m*, 2930*m*, 2860*m*, 1725*s*, 1665*s*, 1500*m*, 1460*w*, 1370*s*, 1260*s*, 1150*s*, 1090*s*, 1075*m*, 1005*w*, 970*w*, 840*s*. ^{1}H-NMR (400 MHz): 0.10 (*s*, MeSi); 0.12 (*s*, MeSi); 0.89 (*s*, *t*-BuSi); 1.47 (*s*, *t*-Bu); 1.99 (*s*, Ac); 1.98–2.00 (*s*, exchanged with D_2O, OH); 2.00 (*ddd*, $J = 3.2$, 7.4, 14.5, H_a–C(3)); 2.23 (br. *d*, $J \approx 14.5$, H_b–C(3)); 3.40 (*dd*, $J = 1.9$, 7.4, H–C(2)); 3.45 (*dd*, $J = 10.5$, 12.5, H_a–C(1′)); 3.56 (*ddd*, $J = 2.0$, 5.0, 10.5, H–C(6)); 3.57 (*dd*, $J = 5.0$, 12.5, H_b–C(1′)); 3.78 (*ddd*, $J = 2.0$, 3.2, 8.4; after exchange with D_2O: *m*, H–C(5)); 3.91 (*q*, $J = 3.2$, H–C(4)); 6.16 (*d*, $J = 8.4$, exchanged with D_2O, AcN*H*). ^{13}C-NMR: *Table 4*. CI-MS: 403 ($[M + 1]^+$). Anal. calc. for $C_{19}H_{38}N_2O_5Si$ (402.61): C 56.68, H 9.51, N 6.96; found: C 56.67, H 9.26, N 6.79.

(2S,4S,5S,6S)-5-Acetamido-4-hydroxy-6-(hydroxymethyl)piperidine-2-carboxylic Acid (**18**). According to *Procedure A*, **38** (60 mg, 0.152 mmol) afforded **18** (29.2 mg, 83%) after 5 h. R_f (i-PrOH/H_2O 7:3) 0.30. M.p. 196–199°. $[\alpha]_D^{25} = +29.1$ ($c = 0.4$, H_2O). pK_{HA} (H_2O) 7.6. IR (KBr): 3450–3400*s* (br.), 2940*m*, 1635*s*, 1600*s*, 1405*m*, 1380*m*, 1350*m*, 1320*m*, 1090*w*, 1060*m*. ^{1}H-NMR (400 MHz, CD_3OD/D_2O 3:1): 1.78 (*td*, $J = 8.2$, 13.8, H_{ax}–C(3)); 2.01 (*s*, Ac); 2.31 (*td*, $J = 4.2$, 13.8, H_{eq}–C(3)); 3.54 (*dt*, $J = 4.2$, 8.5, H–C(6)); 3.60 (*dd*, $J = 4.2$, 8.2, H–C(2)); 3.63–3.70 (*m*, CH_2–C(6)); 3.83 (*dt*, $J = 4.2$, 8.2, H–C(4)); 3.92 (*dd*, $J = 4.2$, 8.2, H–C(5)). ^{13}C-NMR: *Table 4*. FAB-MS (glycerol): 233 ($[M + 1]^+$). Anal. calc. for $C_9H_{16}N_2O_5$ (232.24): C 46.55, H 6.94, N 12.06; found: C 46.61, H 6.95, N 11.94.

*5-Acetamido-2-azido-2,3,5,6,7-pentadeoxy-*L*-xylo-hept-6-enono-1,4-lactone* (**39**). CF_3CO_2H (1 ml) was added to a soln. of **32** (100 mg, 0.242 mmol) in THF (5 ml). The mixture was stirred at 50° for 5 h, cooled to r.t., diluted with MeOH, evaporated, and co-evaporated twice with toluene/MeOH. FC (AcOEt) of the residue gave **39** (51 mg,

94%) as a syrup. R_f (AcOEt/EtOH 95:5) 0.36. $[\alpha]_D^{25} = -151.0$ ($c = 2.5$, EtOH). IR: 3430*m*, 2980*m*, 2950*w*, 2920*m*, 2850*m*, 2105*s*, 1785*s*, 1725*m*, 1675*s*, 1600*m*, 1490*m*, 1370*m*, 1260*s*, 1145*s*, 1095*s*, 1015*m*. ^{1}H-NMR (400 MHz): 1.95 (*ddd*, $J = 10.0, 10.6, 13.4$, H_a–C(3)); 2.08 (*s*, Ac); 2.61 (*ddd*, $J = 6.0, 9.1, 13.3$, H_b–C(3)); 4.35 (*dd*, $J = 9.1, 10.8$, H–C(2)); 4.62 (*ddd*, $J = 2.4, 6.0, 9.8$, H–C(4)); 4.78 (*qdd*, $J \approx 2.0, 6.0, 9.2$, H–C(5)); 5.30 (*ddd*, $J = 1.5, 2.0, 10.5$, H_a–C(7)); 5.32 (*td*, $J = 1.5, 17.3$, H_b–C(7)); 5.63 (br. *d*, $J \approx 9.1$, AcN*H*); 5.88 (*ddd*, $J = 6.0, 10.6, 17.0$, H–C(6)). ^{13}C-NMR: *Table 3*. CI-MS: 225 ($[M + 1]^+$).

tert-*Butyl 5-Acetamido-2-azido-4*-O-*[(*tert-*butyl)dimethylsilyl]-2,3,5-trideoxy*-L-gluco-*heptonate* (**40**) *and* tert-*Butyl 5-Acetamido-2-azido-4*-O-*[(*tert-*butyl)dimethylsilyl]-2,3,5-trideoxy*-D-ido-*heptonate* (**41**). *N*-Methylmorpholine *N*-oxide (984 mg, 7.22 mmol) and OsO_4 (30 mg) were added to a soln. of **32** (2 g, 4.86 mmol) in dry acetone (15 ml) and stirred at r.t. for 16 h. Addition of sat. $NaHSO_3$ soln. gave a precipitate. Stirring was continued for 30 min. The mixture was filtered through *Celite* and charcoal, the filtrate evaporated, the residue diluted with CH_2Cl_2 and washed with 1M HCl, and the org. phase processed as usual. FC (AcOEt/hexane 4:1, AcOEt, AcOEt/EtOH 95:5) afforded **40** (1.44 g, 69%) as an oil and **41** (200 mg, 10%) as a solid.

Data of **40**: R_f (AcOEt/hexane 4:1) 0.29. $[\alpha]_D^{25} = -28.6$ ($c = 0.8$, $CHCl_3$). IR: 3550*m*, 3435*s*, 3400*m* (br.), 2980*m*, 2960*s*, 2930*s*, 2890*m*, 2860*m*, 2105*s*, 1735*s*, 1660*s*, 1600*w*, 1500*s*, 1470*m*, 1460*m*, 1390*w*, 1370*s*, 1310*m*, 1250*s*, 1200*s*, 1150*s*, 1090*s*, 1075*s*, 1035*m*, 1005*w*, 975*w*, 840*s*. ^{1}H-NMR (300 MHz, CD_3OD): 0.11 (*s*, MeSi); 0.13 (*s*, MeSi); 0.90 (*s*, *t*-BuSi); 1.47 (*s*, *t*-Bu); 1.72 (*ddd*, $J = 6.7, 8.0, 14.1$, H_a–C(3)); 1.91 (*ddd*, $J = 6.2, 6.7, 14.1$, H_b–C(3)); 1.98 (*s*, Ac); 3.43 (*dd*, $J = 6.1, 12.2$, H_a–C(7)); 3.56 (*dd*, $J = 3.2, 12.2$, H_b–C(7)); 3.60 (*ddd*, $J = 3.2, 6.2, 9.4$, H–C(6)); 3.78 (*dd*, $J = 6.2, 8.0$, H–C(2)); 3.86 (*dd*, $J = 1.6, 9.4$, H–C(5)); 4.29 (*dt*, $J = 1.6, 6.7$, H–C(4)). ^{13}C-NMR: *Table 3*. CI-MS: 447 ($[M + 1]^+$). Anal. calc. for $C_{19}H_{38}N_4O_6Si$ (446.62): C 51.09, H 8.58, N 12.54; found: C 50.85, H 8.81, N 12.32.

Data of **41**: R_f (AcOEt/hexane 4:1) 0.25. M.p. 78–79°. $[\alpha]_D^{25} = -31.7$ ($c = 1.1$, $CHCl_3$). IR: 3600–3300*s* (br.), 3435*s*, 3000*w*, 2990*m*, 2960*s*, 2930*s*, 2880*m*, 2860*m*, 2105*s*, 1735*s*, 1665*s*, 1500*s*, 1460*m*, 1390*m*, 1370*s*, 1310*w*, 1255*s*, 1200*s*, 1150*s*, 1100*s*, 1050*s*, 1005*w*, 975*w*, 910*m*, 840*s*. ^{1}H-NMR (400 MHz): 0.14 (*s*, MeSi); 0.16 (*s*, MeSi); 0.90 (*s*, *t*-BuSi); 1.51 (*s*, *t*-Bu); 1.82 (*ddd*, $J = 4.4, 9.8, 14.2$, H_a–C(3)); 1.97 (*ddd*, $J = 5.0, 7.8, 14.2$, H_b–C(3)); 2.05 (*s*, Ac); 2.95 (br. *s*, exchanged with D_2O, OH); 3.10 (br. *s*, exchanged with D_2O, OH); 3.45–3.57 (*m*; after exchange with D_2O: *d*, $J = 4.9$, CH_2(7)); 3.80 (*dd*, $J = 5.0, 9.8$, H–C(2)); 3.97–4.06 (*m*, H–C(4), H–C(5), H–C(6)); 6.12 (*d*, $J = 8.4$, exchanged with D_2O, AcN*H*). ^{13}C-NMR: *Table 3*. CI-MS: 447 ($[M + 1]^+$). Anal. calc. for $C_{19}H_{38}N_4O_6Si$ (446.62): C 51.09, H 8.58, N 12.54; found: C 51.35, H 8.80, N 12.40.

tert-*Butyl 5-Acetamido-2-azido-4,7-bis*-O-*[(*tert-*butyl)dimethylsilyl]-2,3,5-trideoxy*-L-gluco-*heptonate* (**42**). A mixture of **40** (600 m g, 1.34 mmol) in DMF (25 ml), *t*-$BuMe_2SiCl$ (222 mg, 1.48 mmol), and 2,6-dimethylpyridine (350 µl, 2.69 mmol) was stirred at r.t. for 3 h and worked up as described for **25**. FC (AcOEt/hexane 1:3) of the residue yielded **42** (720 mg, 96%). Oil. R_f (AcOEt/hexane 1:3) 0.43. $[\alpha]_D^{25} = -22.3$ ($c = 0.9$, $CHCl_3$). IR (3580–3300*m* (br.), 3430*m*, 2990*m*, 2950*s*, 2930*s*, 2880*m*, 2860*s*, 2105*s*, 1735*s*, 1670*s*, 1500*s*, 1470*m*, 1465*m*, 1390*m*, 1370*s*, 1300*w*, 1250*s*, 1200*s*, 1150*s*, 1090*s*, 1050*s*, 1005*w*, 975*w*, 910*w*, 890*w*, 840*s*. ^{1}H-NMR (400 MHz): 0.07 (*s*, MeSi); 0.08 (*s*, MeSi); 0.15 (*s*, MeSi); 0.17 (*s*, MeSi); 0.90 (*s*, *t*-BuSi); 0.92 (*s*, *t*-BuSi); 1.51 (*s*, *t*-Bu); 1.73 (*ddd*, $J = 6.2, 8.6, 13.8$, H_a–C(3)); 1.91 (*dt*, $J \approx 6.8, 13.8$, H_b–C(3)); 2.01 (*s*, Ac); 2.79 (*d*, $J = 3.3$, exchanged with D_2O, OH–C(6)); 3.51 (*tdd*, $J = 3.3, 6.9, 9.2$; after exchange with D_2O: *ddd*, $J = 3.3, 6.9, 9.2$, H–C(6)); 3.56 (*dd*, $J = 6.9, 10.0$, H_a–C(7)); 3.66 (*dd*, $J = 3.3, 10.0$, H_b–C(7)); 3.75 (*dd*, $J = 6.7, 8.6$, H–C(2)); 3.87 (*dt*, $J = 1.4, 9.2$; after exchange with D_2O: *dd*, $J = 1.4, 9.2$, H–C(5)); 4.37 (*ddd*, $J = 1.4, 6.2, 6.9$, H–C(4)); 5.73 (*d*, $J = 9.1$, exchanged with D_2O, AcN*H*). ^{13}C-NMR: *Table 3*. CI-MS: 561 ($[M + 1]^+$). Anal. calc. for $C_{25}H_{52}N_4O_6Si_2$ (560.89): C 53.54, H 9.34, N 9.99; found: C 53.41, H 9.18, N 9.90.

tert-*Butyl 5-Acetamido-2-azido-4,7-bis*-O-*[(*tert-*butyl)dimethylsilyl]-2,3,5-trideoxy*-D-ido-*heptonate* (**43**). As described for **42**, **41** (30 mg, 0.067 mmol) was transformed to **43** (36 mg, 95%). Solid. R_f (AcOEt/hexane 1:3) 0.41. M.p. 75°. $[\alpha]_D^{25} = -41.6$ ($c = 0.5$, $CHCl_3$). IR: 3560*s* (br.), 3440*m*, 2980*m*, 2960*s*, 2930*s*, 2880*m*, 2860*s*, 2105*s*, 1730*s*, 1670*s*, 1500*s*, 1470*m*, 1430*m*, 1390*m*, 1370*s*, 1315*m*, 1250*s*, 1200*s*, 1155*s*, 1135*s*, 1100*s*, 1005*m*, 975*m*, 940*w*, 910*m*, 840*s*. ^{1}H-NMR (400 MHz): 0.07 (*s*, MeSi); 0.075 (*s*, MeSi); 0.13 (*s*, MeSi); 0.18 (*s*, MeSi); 0.90 (*s*, *t*-BuSi); 0.91 (*s*, *t*-BuSi); 1.51 (*s*, *t*-Bu); 1.80 (*ddd*, $J = 2.6, 11.3, 14.3$, H_a–C(3)); 2.00 (*s*, Ac); 2.02 (*ddd*, $J = 3.3, 10.1, 14.3$, H_b–C(3)); 2.75 (*s*, exchanged with D_2O, OH–C(6)); 3.40 (*t*, $J = 10.0$, H_a–C(7)); 3.52 (*dd*, $J = 4.0, 10.0$, H_b–C(7)); 3.79 (*dd*, $J = 3.3, 11.3$, H–C(2)); 3.82 (*dd*, $J = 4.1, 8.0$; after exchange with D_2O: *d*, $J = 4.1$, H–C(5)); 3.99 (*ddd*, $J = 2.6, 4.1, 10.0$, H–C(4)); 4.09 (*dd*, $J = 4.0, 10.0$, H–C(6)); 6.10 (*d*, $J = 8.0$, exchanged with D_2O, AcN*H*). CI-MS: 561 ($[M + 1]^+$).

tert-*Butyl 5-Acetamido-2-azido-4,7-bis*-O-*[(*tert-*butyl)dimethylsilyl]-2,3,5-trideoxy*-L-xylo-*6-heptulosonate* (**44**). According to *Procedure B*, **42** (350 mg, 0.624 mmol) and periodinane (390 mg, 0.919 mmol) gave **44** (330 mg, 94%) after 4 h. Colorless oil. R_f (AcOEt/hexane 1:3) 0.45. $[\alpha]_D^{25} = -83.6$ ($c = 1.6$, $CHCl_3$). IR: 3420*m*, 2980*m*, 2960*s*, 2930*s*, 2900*m*, 2880*m*, 2860*s*, 2110*s*, 1735*s*, 1675*s*, 1495*s*, 1470*m*, 1465*m*, 1430*w*, 1390*m*, 1370*s*, 1335*w*,

1295*m*, 1255*s*, 1200*m*, 1150*s*, 1100*s*, 1050*m*, 1005*w*, 960*w*, 940*w*, 840*s*. ^{1}H-NMR (400 MHz): 0.09 (*s*, MeSi); 0.10 (*s*, MeSi); 0.15 (*s*, MeSi); 0.18 (*s*, MeSi); 0.92 (*s*, *t*-BuSi); 0.93 (*s*, *t*-BuSi); 1.48 (*s*, *t*-Bu); 1.65 (*ddd*, J = 4.5, 8.7, 14.3, H_a–C(3)); 1.71 (*ddd*, J = 3.7, 10.1, 14.3, H_b–C(3)); 2.04 (*s*, Ac); 3.75 (*dd*, J = 4.5, 10.1, H–C(2)); 4.30 (*td*, J = 3.3, 8.7, H–C(4)); 4.37 (*d*, J = 18.7, H_a–C(7)); 4.60 (*d*, J = 18.7, H_b–C(7)); 4.75 (*dd*, J = 2.9, 7.4, H–C(5)); 6.32 (*d*, J = 7.4, AcN*H*). ^{13}C-NMR: *Table 3*. CI-MS: 559 ([M + 1]$^+$). Anal. calc. for $C_{25}H_{50}N_4O_6Si_2$ (558.87): C 53.73, H 9.02, N 10.02; found: C 53.56, H 9.24, N 10.22.

tert-*Butyl* *(2S,4S,5S,6R)-5-Acetamido-4-[(*tert-*butyl)dimethylsilyloxy)-6-*{*[(*tert-*butyl)dimethylsilyloxy]-methyl*}*piperidine-2-carboxylate* (**45**). A soln. of **44** (230 mg, 0.41 mmol) in MeOH (15 ml) was hydrogenated for 4 h at 1 atm in the presence of 10% Pd/C (50 mg). The suspension was diluted with AcOEt, filtered through *Celite*, and evaporated. FC (AcOEt/hexane 1:1) of the residue (85% pure) and recrystallization in Et_2O/hexane gave **45** (168 mg, 79%). Needles. R_f (AcOEt/hexane 1:1) 0.43. M.p. 186°. $[\alpha]_D^{25}$ = +7.3 (c = 0.8, $CHCl_3$). IR: 3440*m*, 2950*s*, 2930*s*, 2880*m*, 2850*m*, 1725*s*, 1675*s*, 1650*m*, 1500*s*, 1460*m*, 1390*w*, 1370*s*, 1250*s*, 1200*m*, 1150*s*, 1110*s*, 1080*s*, 1040*m*, 1005*w*, 940*w*, 840*s*. ^{1}H-NMR (400 MHz): 0.03 (*s*, MeSi); 0.04 (*s*, MeSi); 0.05 (*s*, MeSi); 0.06 (*s*, MeSi); 0.85 (*s*, *t*-BuSi); 0.88 (*s*, *t*-BuSi); 1.45 (*s*, *t*-BuSi); 1.52 (*q*, $J \approx$ 12.0, H_{ax}–C(3)); 1.94 (*s*, Ac); 2.20 (*ddd*, J = 2.5, 4.7, 12.0, H_{eq}–C(3)); 2.72 (*ddd*, J = 2.8, 7.5, 10.0, H–C(6)); 3.27 (*dd*, J = 2.5, 11.9, H–C(2)); 3.38 (*q*, J = 9.7, H–C(5)); 3.59 (*dd*, J = 7.5, 10.0, H_a–C(1′)); 3.63 (*dt*, J = 4.7, 10.0, H–C(4)); 3.69 (*dd*, J = 2.9, 10.0, H_b–C(1′)); 5.21 (*d*, J = 9.3, AcN*H*). ^{13}C-NMR: *Table 4*. CI-MS: 517 ([M + 1]$^+$). Anal. calc. for $C_{25}H_{52}N_2O_5Si_2$ (516.88): C 58.10, H 10.14, N 5.42; found: C 58.29, H 10.23, N 5.60.

(2S,4S,5S,6R)-5-Acetamido-4-hydroxy-6-(hydroxymethyl)piperidine-2-carboxylic Acid (**12**). According to *Procedure A*, **45** (80 mg, 0.155 mmol) gave **12** (30.6 mg, 85%) after 12 h. R_f (i-PrOH/H_2O 7:3) 0.22. M.p. 220–223°. $[\alpha]_D^{25}$ = −9.6 (c = 0.4, H_2O). pK_{HA} (H_2O) 7.3. IR (KBr): 3600–300*s* (br.), 2930*w*, 1670*s*, 1635*s*, 1400*m*, 1380*m*, 1340*m*, 1260*w*, 1210*w*, 1175*w*, 1150*w*, 1090*w*, 1015*w*, 990*w*, 935*w*. ^{1}H-NMR (400 MHz, CD_3OD/D_2O 4:1): 1.77 (*dt*, J = 10.7, 13.4, H_{ax}–C(3)); 2.03 (*s*, Ac); 2.57 (*ddd*, J = 2.5, 3.8, 13.6, H_{eq}–C(3)); 3.05–3.15 (*m*, H–C(6)); 3.61 (*dd*, J = 2.5, 13.2, H–C(2)); 3.69 (*dd*, J = 6.1, 12.5, H_a–C(1′)); 3.78 (*dd*, J = 2.5, 12.5, H_b–C(1′)); 3.80 (*dt*, J = 3.8, 10.7, H–C(4)); 3.82 (*t*, J = 10.7, H–C(5)). ^{13}C-NMR: *Table 4*. CI-MS: 197 ([M + 1 − H_2O − OH]$^+$). Anal. calc. for $C_9H_{16}N_2O_5$ (232.24): C 46.55, H 6.94, N 12.06; found: C 46.72, H 6.82, N 11.97.

tert-*Butyl* *(2S,4S,5S,6R)-5-Acetamido-4-[(*tert-*butyl)dimethylsilyloxy]-6-*{*[(*tert-*butyl)dimethylsilyloxy]-methyl*}*-1-phenylpiperidine-2-carboxylate* (**46**). A mixture of **45** (100 mg, 0.193 mmol), $Ph_3Bi(OAc)_2$ [28] (151 mg, 0.29 mmol) and anh. $Cu(OAc)_2$ (9 mg) in dry CH_2Cl_2 (10 ml) was stirred at r.t. for 72 h [29]. The suspension was diluted with CH_2Cl_2 (20 ml) and washed with 1M NaOH. The org. phase was processed as usual. FC (AcOEt/hexane 1:3) of the residue gave **46** (44.5 mg, 39%) as a solid and **45** (50 mg, 50%); **46** was recrystallized in Et_2O. R_f (AcOEt/hexane 1:3) 0.40. R_f (AcOEt/hexane 1:1) 0.34. M.p. 160–162°. $[\alpha]_D^{25}$ = −6.6 (c = 0.6, $CHCl_3$). UV (EtOH): 226 (3485), 251 (12222). CD (EtOH): 199 (0), 211 (6.56), 229 (0.27), 242 (1.32), 249 (0), 258 (−1.59), 271 (−0.65), 293 (−1.95), 319 (0). IR: 3690*w*, 3430*m*, 2950*s*, 2930*s*, 2880*m*, 2860*s*, 1730*s*, 1715*s*, 1670*s*, 1600*m*, 1490*s*, 1460*m*, 1390*w*, 1365*s*, 1310*w*, 1270*m*, 1250*s*, 1200*s*, 1140*s*, 1110*s*, 1090*s*, 1050*s*, 1005*w*, 985*w*, 940*w*, 910*w*, 840*s*. ^{1}H-NMR (400 MHz, $CDCl_3$): 0.03 (*s*, MeSi); 0.06 (*s*, MeSi); 0.13 (*s*, MeSi); 0.19 (*s*, MeSi); 0.91 (*s*, *t*-BuSi); 0.92 (*s*, *t*-BuSi); 1.33 (*s*, *t*-Bu); 1.93 (*s*, Ac); 2.12 (*ddd*, J = 3.5, 7.5, 14.3; irrad. at 2.38: *dd*, J = 3.5, 7.5, H_a–C(3)); 2.38 (*dtd*, $J \approx$ 1.0, 4.0, 14.3; irrad. at 4.39; *ddd*, J = 3.4, 4.3, 14.3; NOE (14%) upon irrad. at 2.12, H_b–C(3)); 3.75–3.80 (*m*, changed upon irrad. at 4.39, H–C(6), H_a–C(1′)); 4.09 (*t*, $J \approx$ 10.7, H_b–C(1′)); 4.09 (*q*, $J \approx$ 4.0; irrad. at 2.38: *t*, $J \approx$ 3.5; irrad. at 4.39: *t*, $J \approx$ 3.7; NOE (7%) upon irrad. at 2.12, H–C(4)); 4.29 (*dd*, J = 3.6, 7.4; irrad. at 2.38, *d*, J = 7.4; NOE (6%) upon irrad. at 2.12, H–C(2)); 4.35–4.42 (*m*; irrad. at 2.38: *ddd*, J = 3.4, 4.1, 7.4, H–C(5)); 5.56 (*d*, J = 7.7; irrad. at 4.39: *s*; NOE (3%) upon irrad. at 2.12, AcN*H*); 6.80–6.84 (*m*, 3 arom. H); 7.22–7.28 (*m*, 2 arom. H). ^{1}H-NMR (400 MHz, CD_3OD): 0.00 (*s*, MeSi); 0.01 (*s*, MeSi); 0.12 (*s*, MeSi); 0.16 (*s*, MeSi); 0.88 (*s*, *t*-BuSi); 0.91 (*s*, *t*-BuSi); 1.27 (*s*, *t*-Bu); 1.90 (*s*, Ac); 2.17–2.20 (*m*, CH_2(3)); 3.51 (*ddd*, J = 3.4, 4.4, 7.8, H–C(6)); 3.72 (*dd*, J = 3.4, 10.5, H_a–C(1′)); 3.85 (*dd*, J = 7.8, 10.5, H_b–C(1′)); 3.90 (*dt*, J = 4.4, 5.9, H–C(4)); 4.20 (*t*, J = 6.1, H–C(2)); 4.35 (*dd*, J = 4.4, 5.9, H–C(5)); 6.86 (*t*, J = 6.4, 1 arom. H); 6.92 (*d*, J = 8.0, 2 arom. H); 7.20–7.24 (*m*, 2 arom. H). ^{13}C-NMR: *Table 4*. CI-MS: 593 ([M + 1]$^+$). Anal. calc. for $C_{31}H_{56}N_2O_5Si_2$ (592.97): C 62.79, H 9.52, N 4.72; found: C 62.93, H 9.29, N 4.82.

(2S,4S,5S,6R)-5-Acetamido-4-hydroxy-6-(hydroxymethyl)-1-phenylpiperidine-2-carboxylic Acid (**17**). According to *Procedure A*, **46** (40 mg, 0.068 mmol) yielded after 12 h **17** (16.7 mg, 80%). R_f (i-PrOH/H_2O 7:3) 0.58. $[\alpha]_D^{25}$ = +67.2 (c = 0.5, MeOH). pK_{HA} (H_2O) 4.45. IR (KBr): 3500–3150*m* (br.), 2950*w*, 1675*m*, 1600*w*, 1570*m*, 1540*m*, 1425*m*, 1140*m*, 985*w*, 940*w*, 910*w*. ^{1}H-NMR (400 MHz, CD_3OD; sodium salt, obtained by treatment of a MeOH soln. of **17** with 1M NaOH, evaporation of the solvent, and precipitation of the salt from CD_3OD/Et_2O): 1.93 (*q*, J = 12.0, H_a–C(3)); 1.97 (*s*, Ac); 2.42 (*ddd*, J = 3.7, 6.6, 12.0, H_b–C(3)); 3.58 (*dd*, J = 6.5, 10.5, H_a–C(1′)); 3.60 (*ddd*, J = 3.7, 6.5, 12.0, H–C(4)); 3.81 (*dd*, J = 4.0, 10.5, H_b–C(1′)); 3.84 (*dd*, J = 4.0, 6.5, H–C(5)); 3.94 (*td*, J = 4.0, 6.5, H–C(6)); 4.08 (*dd*, J = 6.6, 12.0, H–C(2)); 6.68 (*t*, J = 7.3, 1 arom. H); 6.85 (*d*, J = 8.1, 2 arom. H);

7.10–7.14 (*m*, 2 arom. H). ^{13}C-NMR: *Table 4*. CI-MS: 291 ($[M - H_2O + 1]^+$). Anal. calc. for $C_{15}H_{20}N_2O_5 \cdot 1H_2O$ (326.44): C 55.19, H 6.80, N 8.59; found: C 54.94, H 6.61, N 8.88.

tert-*Butyl (2S,4S,5S,6R)-5-Acetamido-1-[(benzyloxy)carbonyl]-4-[(*tert-*butyl)dimethylsilyloxy]-6-{[(*tert-*butyl)dimethylsilyloxy]methyl}piperidine-2-carboxylate* (**47**). A suspension of **45** (20 mg, 0.04 mmol) in CH_2Cl_2 (1 ml) was treated with 1M aq. $NaHCO_3$ (10 µl), 1M aq. Na_2CO_3 (10 µl), and (benzyloxy)carbonyl chloride (13.2 mg, 0.077 mmol). The mixture was stirred at r.t. for 1 h, diluted with CH_2Cl_2 (10 ml), and washed with 1M $NaHCO_3$. The org. phase was processed as usual. FC (hexane, AcOEt/hexane 1:3) gave **47** (20.6 mg, 81%). Solid. R_f (AcOEt/hexane 4:1) 0.37. M.p. 144–145°. $[\alpha]_D^{25} = +4.3$ ($c = 0.8$, $CHCl_3$): IR: 3440*m*, 2950*s*, 2930*s*, 2880*m*, 2860*m*, 1725*s*, 1690*s*, 1680*s*, 1600*w*, 1500*m*, 1470*m*, 1460*m*, 1450*w*, 1405*s*, 1390*s*, 1370*s*, 1325*m*, 1305*s*, 1250*s*, 1200*s*, 1155*s*, 1090*s*, 1030*w*, 1005*m*, 995*m*, 940*m*, 905*m*, 880*m*, 835*s*. ^{1}H-NMR (400 MHz, $(Z)/(E) = 11:9$): 0.07–0.19 (*m*, 4 MeSi); 0.84 (*s*, 4 H), 0.90 (*s*, 14 H, 2 *t*-BuSi); 1.36 (*s*, 5 H), 1.40 (*s*, 4 H, *t*-Bu); 1.94 (*s*, Ac); 1.97 (*ddd*, $J = 3.1, 8.2, 14.7$, H_a–C(3)); 2.34 (br. *d*, $J \approx 14.7$, 0.55 H), 2.41 (br. *d*, $J \approx 14.7$, 0.45 H, H_b–C(3)); 3.71 (br. *dd*, $J \approx 4.8, 9.8$, 0.45 H; extinguished upon irrad. at 3.82; irrad. at 3.90: br. *d*, $J \approx 9.8$), 3.82 (br. *dd*, $J \approx 3.8, 8.4$, 0.55 H; irrad. at 3.90: br. *d*, $J \approx 8.4$, H–C(6)); 3.90 (br. *dd*, $J \approx 4.8, 9.8$, 0.45 H; irrad. at 3.71: br. *d*, $J \approx 9.8$, 0.45, H_a–C(1′)); 4.00–4.15 (*m*, 2.55 H, H–C(4), H_b–C(1′), and 0.55 H_a–C(1′)); 4.32–4.42 (*m*; addition of CD_3OD: 4.33, *d*, $J = 3.7$, H–C(5)); 4.55 (br. *dd*, $J = 2.0, 8.5$, 0.55 H; irrad. at 1.97: br. *s*), 4.71 (br. *dd*, $J = 2.0, 8.5$, 0.45 H; irrad. at 1.97: br. *s*, H–C(2)); 5.11 (*d*, $J = 12.2$, 0.55 H), 5.14 (*d*, $J = 12.2$, 0.45 H), 5.20 (*d*, $J = 12.2$, 0.55 H), 5.26 (*d*, $J = 12.2$, 0.45 H, PhCH_2); 5.38 (br. *d*, $J \approx 7.1$, 0.45 H, exchanged with CD_3OD), 5.45 (br. *d*, $J \approx 7.2$, 0.55 H, exchanged with CD_3OD, AcN*H*); 7.33–7.43 (*m*, 5 arom. H). ^{13}C-NMR: *Table 4*. CI-MS: 651 ($[M + 1]^+$).

Regeneration of **45** *from* **47**. A soln. of **47** (3 mg) in MeOH (1 ml) was hydrogenated for 1 h in the presence of 10% Pd/C (10 mg). The mixture was filtered through *Celite* and the filtrate concentrated and dried *i.v.* yielding **45** (3 mg). ^{1}H-NMR: identical with the one from a sample prepared from **44**.

tert-*Butyl 5-Acetamido-2-*N,*6:4,7-dianhydro-2-{[(benzyloxy)carbonyl]amino}-2,3,5-trideoxy-*L-manno-*heptonate* (**48**). A soln. of **47** (10 mg, 0.0154 mmol) and (diethylamino)sulfur trifluoride (DAST; 100 µl, 0.75 mmol) in CH_2Cl_2 (1 ml) was kept at r.t. for 9 d. After the addition of MeOH (1 ml) at 0° and stirring for 30 min, the solvent was evaporated. A soln. of the residue in CH_2Cl_2 (5 ml) was washed with NH_4Cl soln. and concentrated to afford **48** (2.6 mg, 40%). Syrup. R_f (AcOEt/hexane 4:1) 0.20. $[\alpha]_D^{25} = +1.3$ ($c = 0.9$, $CHCl_3$). IR: 3430*m*, 3330*w*, 3030*w*, 2995*m*, 2980*m*, 2960*m*, 2930*m*, 2890*w*, 1735*s*, 1700–1685*s* (br.), 1500*s*, 1450*m*, 1430*s*, 1405*s*, 1370*s*, 1330*s*, 1285*m*, 1240*m*, 1200*m*, 1150*s*, 1110*m*, 1070*s*, 1050*m*, 1020*m*, 995*w*, 960*w*, 915*w*, 855*m*. ^{1}H-NMR (400 MHz, $(Z)/(E) = 6:4$): 1.41 (*s*, 5.4 H), 1.47 (*s*, 3.6 H, *t*-Bu); 1.95 (*s*, 1.2 H), 2.01 (*s*, 1.8 H, Ac); 1.94 (*ddd*, $J = 0.9, 9.4, 14.8, 0.4$ H), 1.96 (*ddd*, $J = 0.9, 9.4, 14.8, 0.6$ H, H_a–C(3)); 2.30 (*dd*, $J = 4.5, 14.8, 0.6$ H), 2.39 (*dd*, $J = 4.5, 14.8, 0.4$ H, H_b–C(3)); 3.81 (*dd*, $J = 3.2, 9.2, 0.4$ H), 3.83 (*dd*, $J = 3.2, 9.2, 0.6$ H, H_a–C(7)); 4.22 (*td*, $J \approx 4.0, 6.0, 0.6$ H), 4.25 (*td*, $J \approx 4.0, 6.8, 0.4$ H, H–C(5)); 4.29 (*d*, $J = 9.3, 0.6$ H), 4.31 (*d*, $J = 9.3, 0.4$ H, H_b–C(7)); 4.43 (br. *t*, $J \approx 4.8, 0.4$ H), 4.53 (br. *t*, $J \approx 4.8, 0.6$ H, H–C(4)); 4.52 (*d*, $J = 9.4, 0.6$ H), 4.66 (*d*, $J = 9.4, 0.4$ H, H–C(2)); 4.73 (*t*, $J \approx 3.5, 0.4$ H), 4.84 (*t*, $J \approx 3.5, 0.6$ H, H–C(6)); 5.10 (*d*, $J = 12.2, 0.6$ H), 5.15 (*d*, $J = 12.3, 0.4$ H), 5.21 (*d*, $J = 12.2, 0.6$ H), 5.25 (*d*, $J = 12.3, 0.4$ H, PhCH_2); 5.64 (br. *d*, $J = 6.8, 0.4$ H), 5.75 (br. *d*, $J = 5.8, 0.6$ H, AcN*H*); 7.28–7.36 (*m*, 5 arom. H). ^{13}C-NMR: *Table 4*. CI-MS: 405 ($[M + 1]^+$).

tert-*Butyl (2S,4S,4′S,5′S)-2-Azido-4-[(*tert-*butyl)dimethylsilyloxy]-4-[5′-(fluoromethyl)-4′,5′-dihydro-2′-methyl-1′,3′-oxazol-4′-yl]butyrate* (**49**). DAST (0.27 ml, 2.03 mmol) was added to a soln. of **40** (300 mg, 0.671 mmol) in CH_2Cl_2 (12 ml) at 0°. The mixture was stirred at r.t. for 2 h and cooled to 0°. After treatment with MeOH (2 ml), the mixture was stirred at r.t. for 30 min, diluted with CH_2Cl_2 (30 ml) and washed with sat. NH_4Cl soln. The org. phase was processed as usual. FC (AcOEt/hexane 1:3, 1:1) of the residue obtained after co-evaporation with toluene gave **49** (150 mg, 52%) as an oil and **50** (110 mg, 37%) as a crystalline compound.

Data of **49**: R_f (AcOEt/hexane 1:1) 0.78. $[\alpha]_D^{25} = -12.9$ ($c = 0.9$, $CHCl_3$). IR: 2980*m*, 2950*m*, 2900*w*, 2860*m*, 2105*s*, 1730*s*, 1670*s*, 1600*w*, 1460*w*, 1370*m*, 1250*s*, 1200*s*, 1150*s*, 1110*s*, 1065*w*, 1005*w*, 940*w*, 840*s*. ^{1}H-NMR (400 MHz): 0.12 (*s*, MeSi); 0.14 (*s*, MeSi); 0.90 (*s*, *t*-BuSi); 1.51 (*s*, *t*-Bu); 1.64 (*ddd*, $J = 2.9, 11.0, 14.0$, H_a–C(3)); 1.72 (*ddd*, $J = 3.4, 9.6, 14.0$, H_b–C(3)); 2.00 (*s*, Ac); 3.85 (*dd*, $J = 3.4, 11.0$, H–C(2)); 4.01 (*ddd*, $J = 1.0, 2.0, 5.5$, H–C(4′)); 4.13 (*ddd*, $J = 2.0, 2.9, 9.6$, H–C(4)); 4.35 (*ddd*, $J = 5.5, 10.4, 47.5$, CH_aF); 4.50 (*ddd*, $J = 2.6, 10.4, 47.5$, CH_bF); 4.60 (*tdd*, $J = 2.5, 5.5, 21.8$, H–C(5′)). ^{13}C-NMR: *Table 3*. CI-MS: 431 ($[M + 1]^+$). Anal. calc. for $C_{19}H_{35}FN_4O_4Si$ (430.60): C 53.00, H 8.19, N 13.01, F 4.41; found: C 52.96, H 8.34, N 12.89, F 4.39.

tert-*Butyl 5-Acetamido-2-azido-4-*O*-[(*tert-*butyl)dimethylsilyl]-2,3,5,7-tetradeoxy-7-fluoro-*D-ido-*heptonate* (**50**). A mixture of **49** (170 mg, 0.394 mmol), H_2O (20 µl), and AcOH (100 µl, 1.67 mmol) in AcOEt (3 ml) was stirred at r.t. for 24 h, diluted with AcOEt (20 ml), and washed with H_2O. The org. phase was processed as usual. FC (AcOEt/hexane 1:3, 1:1) of the residue obtained after co-evaporation with toluene gave **50** (160 mg, 90%). The solid was recrystallized in Et_2O/hexane. R_f (AcOEt/hexane 1:1) 0.54. M.p. 137°. $[\alpha]_D^{25} = -44.6$ ($c = 1.0$, $CHCl_3$). IR: 3610*m*, 3440*m*, 2980*m*, 2950*s*, 2930*s*, 2900*m*, 2860*s*, 2110*s*, 1730*s*, 1675*s*, 1495*s*, 1470*m*, 1390*w*, 1370*s*, 1320*w*,

1290*w*, 1250*s*, 1200*s*, 1150*s*, 1120*s*, 1090*s*, 1005*w*, 965*w*, 910*w*, 840*s*. ^{1}H-NMR (400 MHz, CD_3OD): 0.12 (*s*, MeSi); 0.18 (*s*, MeSi); 0.92 (*s*, *t*-BuSi); 1.50 (*s*, *t*-Bu); 1.95 (*ddd*, *J* = 2.3, 11.2, 14.5, H_a–C(3)); 1.98 (*s*, Ac); 2.06 (*ddd*, *J* = 3.3, 10.5, 14.5, H_b–C(3)); 3.78 (*dd*, *J* = 3.3, 11.2, H–C(2)); 3.97 (*ddd*, *J* = 2.3, 4.5, 10.5, H–C(4)); 4.06 (*ddd*, *J* = 1.0, 1.5, 4.5, H–C(5)); 4.17–4.31 (*m*, CH_2(7), H–C(6)). ^{13}C-NMR: *Table 3*. CI-MS: 431 ([*M* – H_2O + 1]$^+$). Anal. calc. for $C_{19}H_{37}FN_4O_5Si$ (448.61): C 50.87, H 8.31, N 12.49, F 4.23; found: C 50.80, H 8.02, N 12.56, F 3.98.

tert-*Butyl 5-Acetamido-2-azido-4-*O*-[(*tert-*butyl)dimethylsilyl]-2,3,5,7-tetradeoxy-7-fluoro-*L*-xylo-6-heptulosonate* (**51**). According to *Procedure B*, **50** (200 mg, 0.446 mmol) and periodinane (380 mg, 0.892 mmol) in CH_2Cl_2 (15 ml) gave, after 3 h and FC (AcOEt/hexane 1:3), **51** (160 mg, 80%). Syrup. R_f (AcOEt/hexane 1:1) 0.74. $[\alpha]_D^{25} = -103.3$ (*c* = 0.8, $CHCl_3$). IR: 3430*m*, 2980*w*, 2950*m*, 2930*m*, 2900*w*, 2890*w*, 2860*m*, 2110*s*, 1735*s*, 1675*s*, 1490*m*, 1470*m*, 1460*w*, 1390*w*, 1370*s*, 1250*s*, 1200*s*, 1150*s*, 1120*s*, 1095*s*, 1050*w*, 1005*w*, 910*w*, 840*s*. ^{1}H-NMR (400 MHz): 0.17 (*s*, MeSi); 0.18 (*s*, MeSi); 0.92 (*s*, *t*-BuSi); 1.51 (*s*, *t*-Bu); 1.68–1.80 (*m*, CH_2(3)); 2.08 (*s*, Ac); 3.79 (*dd*, *J* = 6.1, 8.7, H–C(2)); 4.33 (*ddd*, *J* = 2.7, 5.2, 7.7, H–C(4)); 4.84 (*ddd*, *J* = 1.3, 2.7, 7.5, H–C(5)); 4.96 (*dd*, *J* = 16.7, 47.1, H_a–C(7)); 5.16 (*dd*, *J* = 16.7, 47.3, H_b–C(7)); 6.30 (*d*, *J* = 7.5, AcN*H*). ^{13}C-NMR: *Table 3*. CI-MS: 447 ([*M* + 1]$^+$). Anal. calc. for $C_{19}H_{35}FN_4O_5Si$ (446.60): C 51.10, H 7.90, N 12.54, F 4.25; found: C 50.97, H 8.03, N 12.60, F 4.03.

*tert-Butyl (2*S*,4*S*,5*S*,6*R*)-5-Acetamido-4-[(*tert-*butyl)dimethylsilyloxy]-6-(fluoromethyl)piperidine-2-carboxylate* (**52**). Ph_3P (120 mg, 0.448 mmol) was added to a soln. of **51** (100 mg, 0.224 mmol) in THF (8 ml). The mixture was stirred at r.t. for 3 h, cooled to 0° and treated first with a mixture of $Na(HCO_2)$ (300 mg) and HCO_2H (250 µl) in MeOH (10 ml) and subsequently with a soln. of $NaCNBH_3$ (30 mg) in Et_2O (5 ml). After completion of the reaction (15 min), the mixture was diluted with toluene (40 ml) and AcOEt (10 ml) and stirred at r.t. for 5 min. The mixture was washed with H_2O (5 ml) and the aq. layer extracted with AcOEt (2 × 10 ml). Drying of the combined org. phases ($MgSO_4$), co-evaporation with toluene (2×), and FC (CH_2Cl_2/EtOH 15:1) gave **52** (62 mg, 69%), which was recrystallized in CH_2Cl_2/Et_2O. R_f (CH_2Cl_2/EtOH 15:1) 0.28. M.p. 226–227°. $[\alpha]_D^{25} = +24.2$ (*c* = 0.5, $CHCl_3$). IR: 3440*w*, 3330*w*, 2950*s*, 2930*s*, 2860*s*, 1730*s*, 1675*s*, 1490*w*, 1460*w*, 1440*w*, 1420*w*, 1390*w*, 1370*m*, 1250*m*, 1200*m*, 1145*s*, 1105*s*, 1040*w*, 1005*w*, 980*w*, 835*s*. ^{1}H-NMR (CD_3OD): 0.08 (*s*, MeSi); 0.09 (*s*, MeSi); 0.87 (*s*, *t*-BuSi); 1.44 (*dt*, *J* = 10.7, 12.5, H_{ax}–C(3)); 1.48 (*s*, *t*-Bu); 1.94 (*s*, Ac); 2.23 (*ddd*, *J* = 2.6, 4.9, 12.7, H_{eq}–C(3)); 2.82 (*dddd*, *J* = 2.9, 6.1, 10.5, 20.2, H–C(6)); 3.34 (*dd*, *J* = 2.6, 12.3, H–C(2)); 3.50 (*t*, *J* = 10.0, H–C(5)); 3.70 (*ddd*, *J* = 4.9, 10.0, 10.7, H–C(4)); 4.38 (*ddd*, *J* = 6.1, 9.5, 47.9, CH_aF); 4.45 (*ddd*, *J* = 2.9, 9.5, 47.0, CH_bF). ^{13}C-NMR: *Table 4*. CI-MS: 405 ([*M* + 1]$^+$). Anal. calc. for $C_{19}H_{37}FN_2O_4Si$ (404.60): C 56.40, H 9.22, N 6.92, F 4.70; found: C 56.64, H 8.99, N 6.67, F 4.53.

*(2*S*,4*S*,5*S*,6*R*)-5-Acetamido-6-(fluoromethyl)-4-hydroxypiperidine-2-carboxylic Acid* (**13**). According to *Procedure A*, **52** (50 mg, 0.124 mmol) gave after 12 h **13** (20 mg, 75%). R_f (i-PrOH/H_2O 7:3) 0.49. $[\alpha]_D^{25} = -11.8$ (*c* = 0.7, H_2O). pK_{HA} (H_2O/EtOH 1:1) 6.8. IR (KBr): 3400*s* (br.), 3280*s* (br.), 2820*m*, 2780*m*, 1635*s* (br.), 1405*m*, 1370*s*, 1355*s*, 1315*m*, 1270*w*, 1155*w*, 1100*w*, 1015*w*, 945*w*, 885*w*, 775*m*. ^{1}H-NMR (400 MHz, CD_3OD/D_2O 19:1; **13**·CF_3CO_2H obtained by treating a MeOH soln. of **13** with CF_3CO_2H and Et_2O): 1.79 (*dt*, *J* = 10.3, 13.6, H_{ax}–C(3)); 2.01 (*s*, Ac); 2.60 (*ddd*, *J* = 3.1, 4.3, 13.6, H_{eq}–C(3)); 3.47 (*dddd*, *J* = 3.0, 5.4, 10.0, 20.9, H–C(6)); 3.81 (*t*, *J* = 10.0, H–C(5)); 3.85 (br. *dt*, *J* = 4.3, 10.7, H–C(4)); 4.02 (*dd*, *J* = 3.0, 13.6, H–C(2)); 4.64 (*ddd*, *J* = 5.4, 11.1, 47.2, CH_aF); 4.68 (*ddd*, *J* = 3.0, 11.1, 46.7 (CH_bF). ^{13}C-NMR: *Table 4*. CI-MS: 235 ([*M* + 1]$^+$). Anal. calc. for $C_9H_{15}FN_2O_4 \cdot 1H_2O$ (252.24): C 42.86, H 6.79, N 11.11; found: C 42.70, H 6.91, N 11.40.

tert-*Butyl 5-Acetamido-2-azido-4-*O*-[(*tert-*butyl)dimethylsilyl]-2,3,5-trideoxy-7-*O*-(4-tolylsulfonyl)-*D*-ido-heptonate* (**53**). TsCl (154 mg, 0.807 mmol) was added at 0° to a soln. of **41** (300 mg, 0.672 mmol) in dry pyridine (5 ml). The mixture was stirred for 30 min at 0° and then for 12 h at r.t. The mixture was evaporated, and a soln. of the residue in CH_2Cl_2 (50 ml) was extracted with sat. $NaHCO_3$ soln. and H_2O. The org. phase was dried ($MgSO_4$) and pyridine removed by co-evaporation (2×) with toluene. FC (AcOEt/hexane 1:1) of the residue gave **53** (327 mg, 81%). Solid. R_f (AcOEt/hexane 1:1) 0.42. M.p. 95–96°. $[\alpha]_D^{25} = -22.4$ (*c* = 0.7, $CHCl_3$). IR: 3600*w*, 3440*m*, 3400–3350*m* (br.), 2980*m*, 2950*s*, 2930*s*, 2890*m*, 2860*s*, 2105*s*, 1730*s*, 1675*s*, 1600*m*, 1490*s*, 1470*m*, 1410*m*, 1365*s*, 1370*s*, 1250*s*, 1170*s*, 1150*s*, 1120*s*, 1095*s*, 1005*w*, 975*m*, 905*w*, 845*s*. ^{1}H-NMR (400 MHz): 0.11 (*s*, MeSi); 0.12 (*s*, MeSi); 0.87 (*s*, *t*-BuSi); 1.51 (*s*, *t*-Bu); 1.77 (*ddd*, *J* = 3.5, 10.5, 14.2, H_a–C(3)); 1.95 (*ddd*, *J* = 4.1, 9.1, 14.2, H_b–C(3)); 1.99 (*s*, Ac); 2.46 (*s*, Ms); 2.87 (*s*, exchanged with D_2O, OH); 3.79 (*dd*, *J* = 4.0, 10.5, H–C(2)); 3.88–4.01 (*m*, 4 H); 4.29 (*m*; after exchange with D_2O: *m*, H–C(6)); 6.00 (*d*, *J* = 8.5, exchanged with D_2O, AcN*H*); 7.36 (*d*, *J* = 8.1, 2 arom. H); 7.78 (*d*, *J* = 8.3, 2 arom. H). ^{13}C-NMR: *Table 3*. CI-MS: 601 ([*M* + 1]$^+$). Anal. calc. for $C_{26}H_{44}N_4O_8SSi$ (600.81): C 51.98, H 7.38, N 9.32; found: C 51.96, H 7.43, N 9.25.

tert-*Butyl 5-Acetamido-2-azido-4-*O*-[(*tert-*butyl)dimethylsilyl]-2,3,5-trideoxy-7-*O*-(4-tolylsulfonyl)-*L*-xylo-6-heptulosonate* (**54**). According to *Procedure B*, a mixture of **53** (150 mg, 0.25 mmol), CH_2Cl_2) (5 ml), and periodinane (150 mg, 0.354 mmol) afforded, after 3 h and FC (AcOEt/hexane 1:2), **54** (113 mg, 75%). Oil. R_f (AcOEt/hexane 1:1) 0.56. $[\alpha]_D^{25} = -60.7$ (*c* = 0.6, $CHCl_3$). IR: 3420*m*, 2970*m*, 2950*s*, 2930*s*, 2860*s*, 2100*s*, 1735*s*,

1675*s*, 1600*w*, 1485*m*, 1470*m*, 1455*m*, 1370*s*, 1305*w*, 1290*w*, 1250*m*, 1175*s*, 1150*s*, 1095*s*, 1030*m*, 1000*m*. 845*s*. ^{1}H-NMR (400 MHz): 0.16 (*s*, MeSi); 0.18 (*s*, MeSi); 0.89 (*s*, *t*-BuSi); 1.50 (*s*, *t*-Bu); 1.60–1.70 (*m*, CH_2(3)); 2.05 (*s*, Ac); 2.46 (*s*, Me); 3.74 (*t*, $J \approx 7.3$, H–C(2)); 4.26 (*ddd*, $J = 3.2, 5.5, 7.1$, H–C(4)); 4.66 (*d*, $J = 14.4$, H_a–C(7)); 4.69 (*dd*, $J = 3.2, 7.0$, H–C(5)); 5.04 (*d*, $J = 14.4$, H_b–C(7)); 6.29 (*d*, $J = 7.0$, AcN*H*); 7.36 (*d*, $J = 8.3$, 2 arom. H); 7.82 (*d*, $J = 8.3$, 2 arom. H). ^{13}C-NMR: *Table 3*. CI-MS: 599 ($[M + 1]^+$). Anal. calc. for $C_{26}H_{42}N_4O_8SSi_2$ (598.79): C 52.15, H 7.07, N 9.36; found: C 52.39, H 6.99, N 9.08.

tert-*Butyl* *(2S,4S,5S,6S)-5-Acetamido-4-[(*tert*-butyl)dimethylsilyloxy]-6-methylpiperidine-2-carboxylate* (**55**). A soln. of **54** (100 mg, 0.167 mmol) and Et_3N (50 µl) in MeOH (7 ml) was hydrogenated (r.t.) in the presence of 10% Pd/C (30 mg). Usual workup after 2 h and FC (AcOEt/EtOH 95:5) gave **55** (51 mg, 81%; 84% pure). Pure **55** was obtained by recrystallization in Et_2O/hexane. R_f (AcOEt/EtOH 85:15) 0.50. M.p. 212–215°. $[\alpha]_D^{25} = +20.2$ ($c = 0.6$, $CHCl_3$). IR: 3430*w*, 3400–3300*w* (br.), 2950*m*, 2930*s*, 2860*m*, 1740*s*, 1675–1650*s*, 1500*w*, 1460*w*, 1360*m*, 1250*m*, 1200*m*, 1175*s*, 1140*s*, 1110*s*, 1040*m*, 1005*w*, 845*s*. ^{1}H-NMR (400 MHz): 0.05 (*s*, MeSi); 0.07 (*s*, MeSi); 0.87 (*s*, *t*-BuSi); 1.17 (*d*, $J = 6.4$, Me); 1.47 (*s*, *t*-Bu); 1.50 (*dt*, $J = 11.0, 12.3$, H_{ax}–C(3)); 1.98 (*s*, Ac); 2.21 (*ddd*, $J = 2.6, 4.8, 12.6$, H_{eq}–C(3)); 2.69 (*qd*, $J = 6.3, 10.0$, H–C(6)); 3.29 (*dt*, $J = 9.6, 10.0$, H–C(5)); 3.31 (*dd*, $J = 2.6, 12.0$, H–C(2)); 3.61 (*ddd*, $J = 4.8, 9.6, 11.0$, H–C(4)); 5.09 (*d*, $J = 9.3$, AcN*H*). ^{13}C-NMR: *Table 4*. CI-MS: 387 ($[M + 1]^+$). Anal. calc. for $C_{19}H_{38}N_2O_4Si$ (386.61): C 59.03, H 9.91, N 7.25; found: C 58.84, H 10.09, N 7.43.

Hydrogenation of **51**. Hydrogenation of a soln. of **51** (30 mg, 0.07 mmol) in MeOH (5 ml) in the presence of 10% Pd/C (10 mg) for 20 min gave after workup **55** and **52** in a ratio of 97:3.

(2S,4S,5S,6S)-5-Acetamido-4-hydroxy-6-methylpiperidine-2-carboxylic Acid (**14**). According to *Procedure A*, **55** (40 mg, 0.1 mmol) gave after 15 h **14** (17 mg, 76%). R_f (i-PrOH/H_2O 7:3) 0.29. pK_{HA} (H_2O/EtOH 1:1) 8.4. $[\alpha]_D^{25} = -7.4$ ($c = 0.5$, H_2O). IR (KBr): 3500–3200*s* (br.), 1670*s*, 1620*s*, 1575*s*, 1460*w*, 1440*w*, 1400*s*, 1380*m*, 1350*w*, 1305*w*, 1250*m*, 1105*s*, 1035*w*, 930*w*, 850*m*, 790*w*. ^{1}H-NMR (D_2O/CD_3OD 3:1): 1.27 (*d*, $J = 6.4$, Me); 1.70 (*dt*, $J = 11.0, 13.6$, H_{ax}–C(3)); 1.98 (*s*, Ac); 2.51 (*td*, $J = 3.7, 13.6$, H_{eq}–C(3)); 3.11 (*qd*, $J = 6.6, 10.9$, H–C(6)); 3.63 (*dd*, $J = 3.7, 13.6$, H–C(2)); 3.67–3.74 (*m*, H–C(4); H–C(5)). ^{13}C-NMR: *Table 4*. CI-MS: 217 ($[M + 1]^+$). Anal. calc. for $C_9H_{16}N_2O_4$ (216.23): C 49.97, H 7.46, N 12.95; found: C 49.72, H 7.66, N 12.70.

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