40. Synthesis of Galactose- and *N*-Acetylglucosamine-Derived Tetrazoles and Their Evaluation as β-Glycosidase Inhibitors

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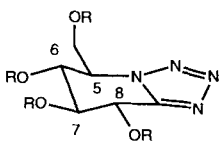
The title compounds **6** and **7** have been prepared from the known 2,3-di-*O*-benzyl-4,6-*O*-benzylidene-D-galactose (**18**) and N^2-acetyl-tri-*O*-benzyl-D-glucosamine oxime (**29**) in eight and six steps, respectively. The azidonitrile leading to the benzylated *galacto*-tetrazole **16** was prepared from **14** and cyclized under the conditions of its formation (*Scheme 1*). The alcohol **13** was obtained by oxidation of **10** followed by reduction. Better yields and diastereoselectivities were realized, when the benzylidene-protected D-*galacto*-alcohol **20** was subjected to oxido-reduction, yielding the L-*altro*-alcohol **22** *via* the ketone **21** (*Scheme 2*). Treatment of the corresponding tosylate **24** with NaN_3 yielded the tetrazole **25**, which was deprotected to **6**. The tetrabenzyl ether **16** (from **14**, or from **25** *via* **27**) was reduced to **28** and deprotected to give the known deoxygalactostatin **8** (*Scheme 2*). Oxidation of the hydroxynitrile **30**, derived from **29**, followed by reduction of **32** yielded mostly the L-*ido*-hydroxynitrile (*Scheme 3*), which was tosylated and treated with NaN_3 to give the tetrazole **35a** and its *manno*-isomer **36a**, while $Al(N_3)_3$ yielded (*E*)- and (*Z*)-**38** (*Scheme 4*). The intermediate azide **39** was isolated besides **40** when NH_4N_3/DMF was used; thermolysis of **39** gave mostly **35a**, which was deprotected to **7**, besides some elimination product **41**. Both **6** and **7** are stable in the pH range 1–10; at pH 12, **6** is unaffected but, **7** shows some epimerization to the *manno*-configurated isomer **43**. The tetrazole **6** is a competitive inhibitor of the β-galactosidases from *E. coli* (K_I = 1 μM, pH 6.8) and bovine liver (K_I = 0.8 μM, pH 7.0); the *N*-acetyl-β-D-glucosaminidase from bovine kidney is competitively inhibited by **7** ($K_I \approx 0.2$ μM, pH 4.1).

Introduction. – We have designed the *gluco*-tetrazole **1** [1] [2] and its *manno*-epimer **2** [2] as neutral transition-state analogues for the inhibition of β-glucosidases and β-mannosidases, respectively. These tetrazoles possess a half-chair conformation in the solid state; in solution, **1** is a half-chair ($^6H_7$) and **2** a sofa (S_7). A detailed kinetic study demonstrated that the inhibition is competitive and configurationally selective, and established these tetrahydrotetrazolopyridines (tetrahydropyridotetrazoles)[1]) as transition-state analogues [2]. The inhibitory properties of the *gluco*-tetrazole **1** parallel those of D-glucono-1,5-lactone, but, unlike the corresponding lactones, **1** and **2** are stable towards hydrolysis over a wide range of pH values, an advantage for co-crystallization [9] and for their potential use as templates in the generation of catalytic antibodies [10] [11]. Additionally, reduction of the tetra-*O*-benzyl-protected tetrazole **3** is a key step in a new route to deoxynojirimycin [1].

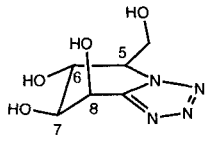
Galactose and *N*-acetylglucosamine derivatives possessing an sp^2-hybridized anomeric center, such as galactono-1,5-lactam **4** [12] and derivatives [13], the *N*-acetylglucosaminolactone **5** [14], the related lactone oximes [14] [15] and the lactam [14], are

[1]) For the preparation of carbohydrate-derived tetrazoloazepines, see [3] [4]. Aside from tetrazolo derivatives, some monosaccharide-derived imidazolopyridines were isolated [5] [6] or prepared [7] [8] and investigated for glycosidase inhibition.

quite potent inhibitors of the respective β-glycosidases. In this article, we describe the syntheses and enzyme assays of the *galacto*-tetrazole **6** and the *N*-acetylglucosamine-derived tetrazole **7**, and the conversion of a precursor of **6** to deoxygalactostatin **8** [16–19].



1 R = H
3 R = Bn



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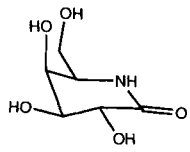

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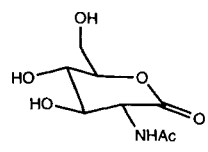

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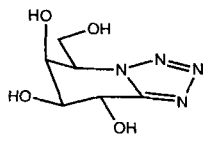

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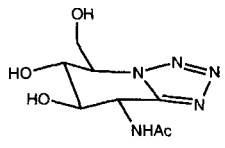

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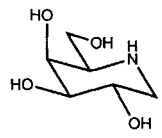

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To prepare **6** and **7**, we followed the synthetic route developed for the *gluco*-tetrazole **1**. This approach is based on the intramolecular 1,3-dipolar cycloaddition of a 5-azido-aldonitrile, obtained from a tetra-*O*-protected hydroxy-nitrile with formal retention of the configuration, involving a diastereoselective reduction as a key step.

Results and Discussion. — *Synthesis of the* galacto-*Tetrazole* **6**. Application of the original protecting-group strategy [1] proved unsatisfactory in the *galacto*-series (see *Scheme 1*)[2]). In particular, the inversion of the configuration at C(5) by oxido-reduction of **10** was disappointing, leading at best to a 1:1 ratio of the *galacto*/*altro*-derivatives **10** and **13**. We expected a higher diastereoselectivity for the reduction of the 4,6-*O*-benzylidenated ketone **21** (*Scheme 2*), based on the results of the reduction of 2-phenyl-1,3-dioxan-5-one obtained by *Wu* and *Houk* [21].

Thus, the oxime **19** was prepared in almost quantitative yield from 4,6-*O*-benzylidene-2,3-di-*O*-benzyl-D-galactose (**18**) [22] and converted to the nitrile **20** (79%) using PPh_3 and CBr_4 (*Scheme 2*). Cleavage of the benzylidene group was prevented by adding pyridine. Oxidation of **20** with pyridinium chlorochromate (PCC) gave the ketone **21** which streaked on TLC, preventing efficient chromatographic purification. The reaction mixture was worked up by filtration through silica gel. The crude ketone **21** was reduced with $NaBH_4$ in THF or MeOH to give a 1:5 mixture of the diastereoisomeric alcohols **20**/**22**, consistent with a predominant axial attack by this reagent. Complexing reagents such as $NaBH_4/CeCl_3$ [23], $LiBH_4$, or $Zn(BH_4)_2$ [24] led to reduced selectivity (*ca.* 1:2). The sterically more demanding $LiBH(Et)_3$, as expected, gave a selectivity greater than 98:2 in favor of the *galacto*-alcohol **20**, consistent with a preferred equatorial attack[3]). Separation of the alcohols **20** and **22** by flash chromatography failed, but the two diastereoiso-

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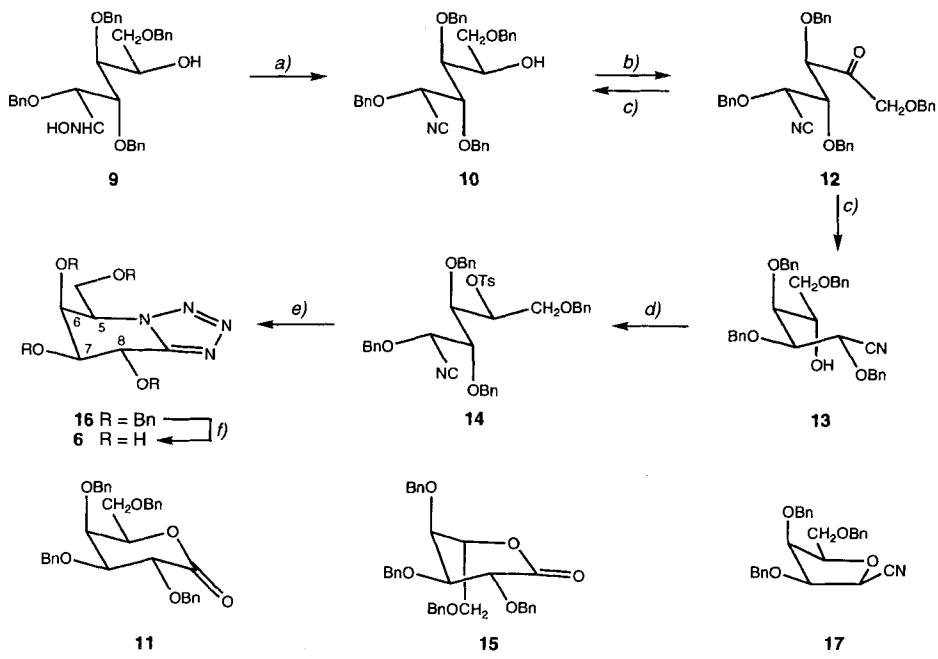
[2]) The schemes and figures in this paper indicate main conformers as deduced from vicinal coupling constants or, where necessary, molecular modelling (Macromodel V4.0, MM3 forcefield) [20].

[3]) A similar observation has been published by *Oshitari et al.* [25] in the synthesis of L-gulose from D-mannose.

Scheme 1



a) PPh_3, CBr_4, MeCN, 20 min, r.t.; 51% of **10** and 32% of **11**. *b*) PCC, CH_2Cl_2, 3-Å molecular sieves, 1.5 h, r.t.; 92%. *c*) $NaBH_4$, MeOH, 30 min, −60°; 39% of **10** and 40% of **13**. *d*) TsCl, pyridine, 20 h, 50°; 67%. *e*) NaN_3, DMSO, 16 h, 100°; 71%. *f*) H_2, 10% Pd/C, MeOH/AcOH, r.t., 48 h; 94%.

mers were unambiguously identified on the basis of their ^{1}H- and ^{13}C-NMR spectra, as detailed below. The tosylates **23**/**24** derived from the mixture **20**/**22** were separated by flash chromatography.

The structure of **20** is evidenced by the CN *s* at 117.34 ppm, the O*H*–C(5) *d* at 3.03 ppm (IR: 3570 cm^{-1}), and a PhC*H s* at 5.43 ppm. The coupling constant of the axial OH–C(5) is 11.5 Hz, indicating a bifurcated H-bond to O–C(4) and O–C(6) [26].

The crude ketone **21** shows a C=O resonance at 203.17 ppm and an IR band at 1740 cm^{-1}.

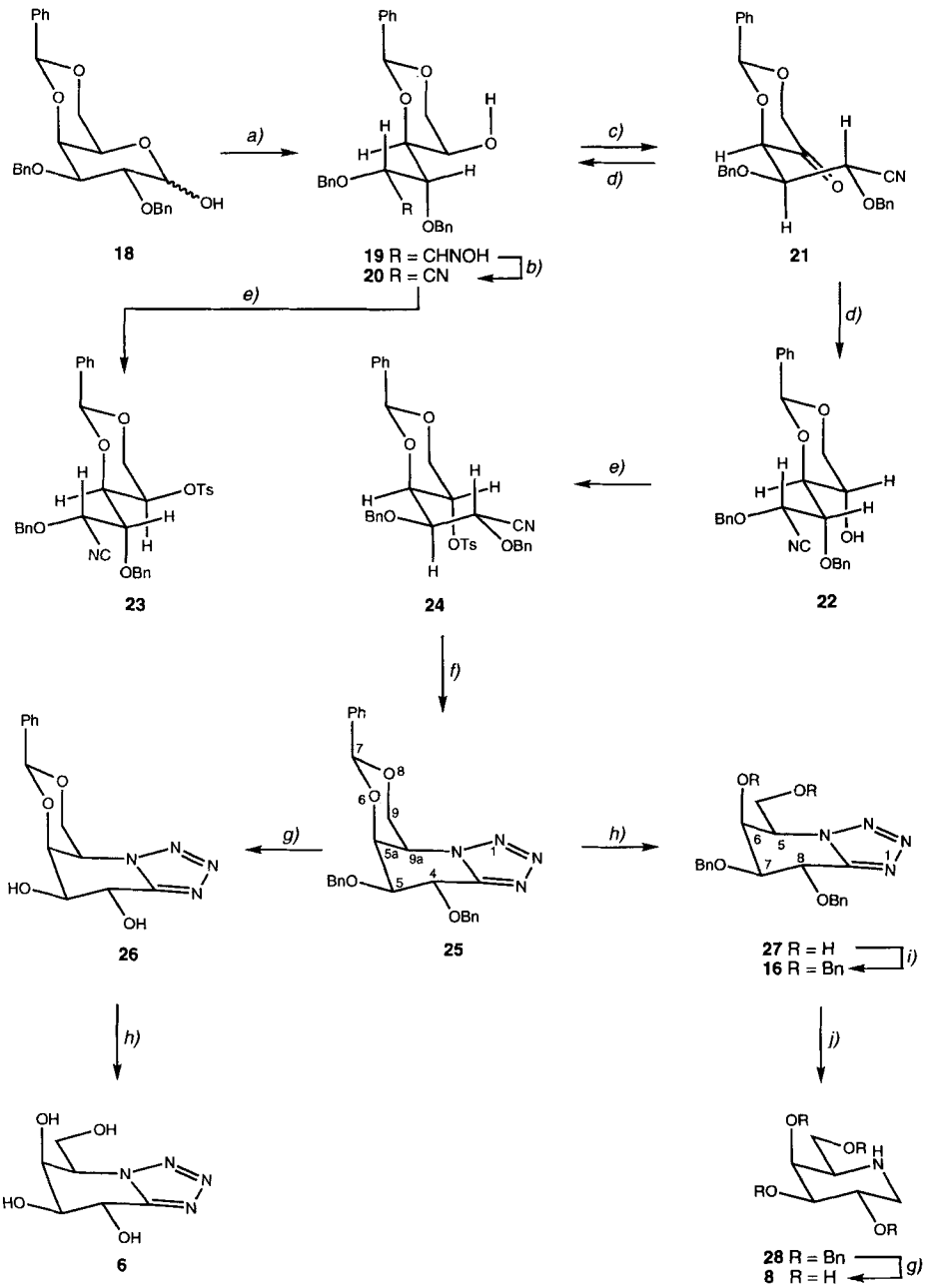
The ratio of the D-*galacto*-/L-*altro*-alcohols **20**/**22** was determined by comparing the integrations of the two O*H*–C(5) signals at 2.83 and 3.15 ppm, the *H*–C(2) *d*'s at 4.44 and 4.48 ppm, and the PhC*H's* at 5.40 and 5.28 ppm, respectively. The *J* values of the *altro*-alcohol **22** ($J(2,3) = 3.1$, $J(3,4) = 6.6$, $J(5,OH) \approx 0$ Hz) indicate that the main conformer has a H-bond between the equatorial OH–C(5) and the BnO–C(3) group of the side chain. In contrast, the *J* values of the *altro*-tosylate **24** ($J(2,3) = 8.1$, $J(3,4) = 1.2$ Hz) show that with the H-bond no longer available, the side chain reorients to avoid the 1,5-interaction between the BnO–C(3) and the equatorial TsO group.

Treatment of the tosylate **24** with NaN_3 gave the tetrazole **25** (77%; *Scheme 2*)[4]. The benzylidene group proved remarkably resistant to catalytic hydrogenolysis: after 1 week at 6 bar H_2 in the presence of 10% Pd/C, only *ca.* 10% of the material was fully deprotected to give **6**; 79% of the diol **26** was isolated[5]). However, **26** was debenzylide-

[4]) No participation from the BnO–C(2) group was observed, as in the case of the corresponding tetra-*O*-benzyl compound **14** (see *Exper. Part*).

[5]) A similar resistance of a benzylidene group has been noted, *e.g.*, by *Baumberger et al.* [27].

Scheme 2



a) NH_2OH, MeOH, 3 h, 55°; 99%. *b*) PPh_3, CBr_4, MeCN, pyridine, 20 min, r.t.; 79%. *c*) PCC, CH_2Cl_2, 3-Å mol. sieves, 1.5 h, r.t.; 73%. *d*) $NaBH_4$, THF, 3 h, −78°; 81% of **20**/**22** 1:5. *e*) TsCl, pyridine, 48 h, 75°; 69% of **24** and 13% of **23**. *f*) NaN_3, DMSO, 12 h, 120°; 77%. *g*) H_2, 10% Pd/C, MeOH/AcOH, r.t. *h*) HCl, MeOH, 60°. *i*) BnBr, NaH, 5 h, 60°; 80%. *j*) $LiAlH_4$, Et_2O, 5 h, r.t.; 78%.

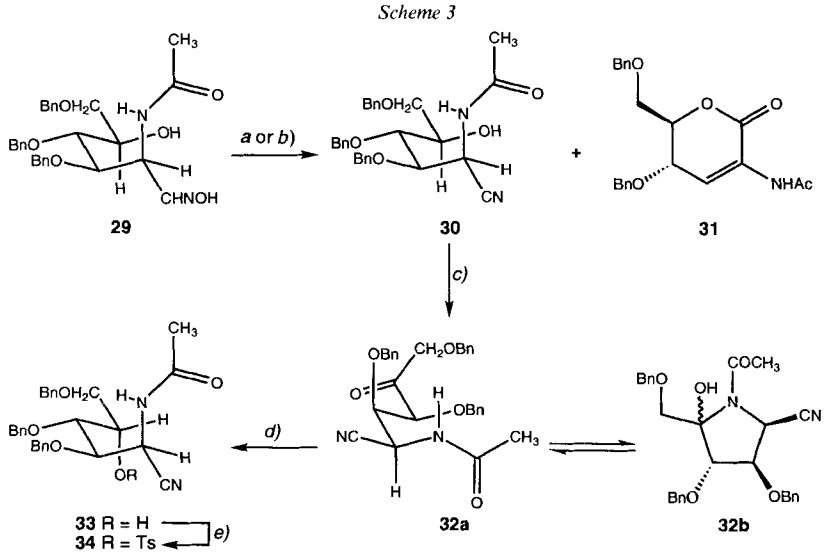
nated by treatment with *ca.* 0.1M methanolic HCl at 60°. The fully deprotected *galacto*-tetrazole **6** was purified by chromatography and obtained as a hygroscopic amorphous white solid which resisted attempts at crystallization. The structure of **6** was confirmed by the δ(C) of the tetrazole C(8a) (*s* at 157.28 ppm). The ^{1}H-NMR vicinal coupling ($J(7,8) = 9.0$, $J(6,7) = 2.1$, $J(5,6) = 2.8$ Hz) and the homoallylic coupling ($J(5,8) = 0.7$ Hz) indicated that **6** adopts a $^6H_7$ conformation in D_2O solution. In aqueous solution at neutral pH, **6** is stable indefinitely. Solutions of **6** at pH 1 and pH 12 were kept for 24 h, and showed no change in the ^{1}H-NMR spectrum or by TLC.

The 2,3-di-*O*-benzyl-diol **27** was prepared in almost quantitative yield from **25** by the same methanolic HCl treatment as above, and treated with NaH in benzyl bromide to give **16**, which was reduced by $LiAlH_4$ to tetra-*O*-benzyl-1-deoxygalactostatin (**28**; 78%). Catalytic hydrogenation gave deoxygalactostatin hydroacetate, which was converted to the known hydrochloride **8**·HCl by repeated evaporation of an aqueous solution of HCl. The ^{1}H-NMR spectrum and optical rotation of **8**·HCl compare satisfactorily with published data [16].

The structure of **25** was confirmed by a new resonance at 154.24 ppm, replacing the CN signal of **24** at 116.58 ppm. The chemical shift of the H–C(4) *d* (5.24 ppm) correlates well with the value for the corresponding proton of **16**. The equatorial H–C(9) shows a *dd* at 5.19 ppm, compared to 4.30 ppm for the axial proton. This large chemical-shift difference may be ascribed to the rigid conformation of the benzylidene ring, which forces the equatorial H–C(9) close to the aromatic tetrazole ring. In the ^{1}H-NMR spectrum of the diol **26** (CD_3OD), a *s* at 5.73 ppm and a *s* integrating for 5H at 7.29 ppm indicate the presence of the benzylidene group; a strong, broad OH band is observed at 3240 cm^{-1}. The diol **27** ($CDCl_3$) shows OH resonances at 3.00–3.04 ppm (IR: 3575 cm^{-1}) and signals of two Bn groups.

Synthesis of the N-*Acetylglucosamine-Derived Tetrazole* **7**. Dehydration of the oxime **29** [28] (CBr_4/PPh_3) led to poor yields of the nitrile **30** (36%) and the unsaturated lactone **31** (7%; *Scheme 3*). Treatment of **29** with diphenyl disulfide/PPh_3 [29], however, yielded

Scheme 3

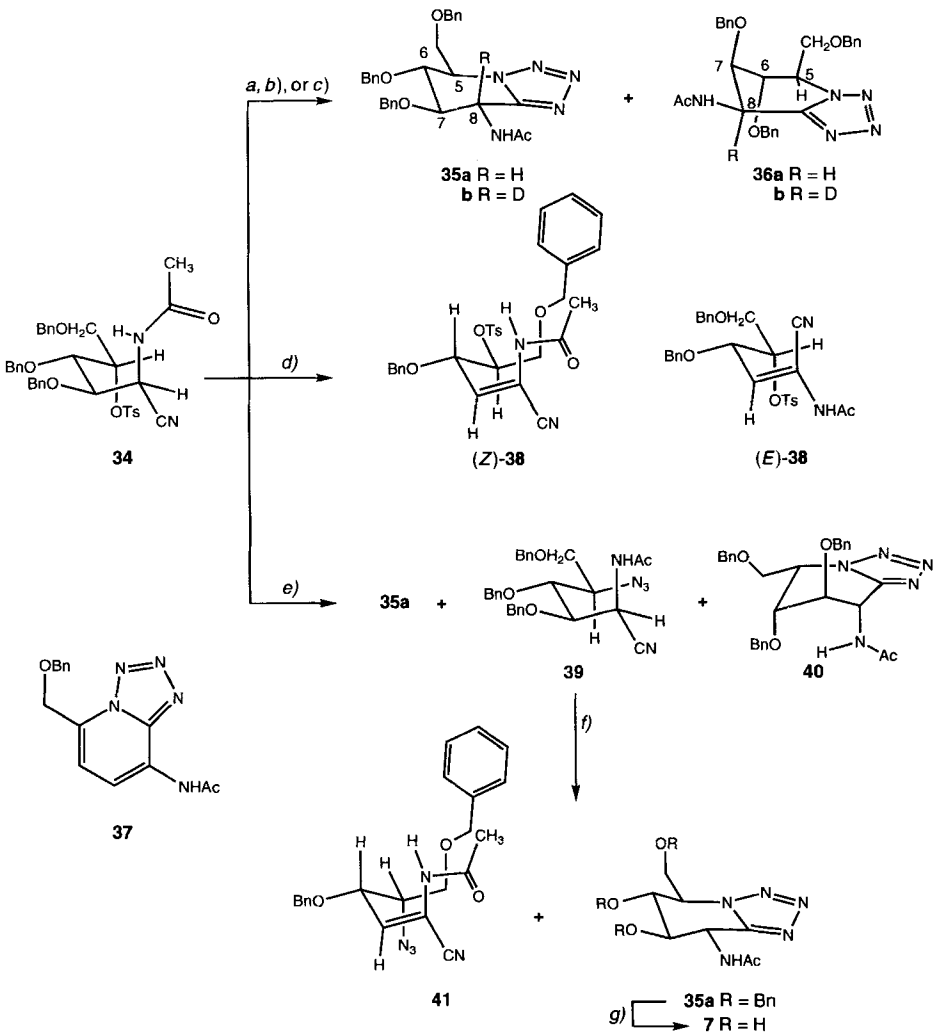


a) PPh_3, CBr_4, pyridine, MeCN/THF, 35 min, r.t.; 36% of **30** and 7% of **31**. *b*) $(PhS)_2$, Bu_3P, THF, 35 min, r.t.; 79% of **30**. *c*) Pyridine·SO_3, DMSO, Et_3N, r.t., 65 min; *ca.* 97%. *d*) $NaBH_4$, $CeCl_3 \cdot 6\,H_2O$, MeOH, –40 to –20°, 22 h; *ca.* 90%. *e*) TsCl, pyridine, 55–60°, 4.5 h; 85%.

79% of **30**. Oxidation (pyridine·SO_3, DMSO) of **30** gave the ketone **32**, which was reduced ($NaBH_4$, $CeCl_3 \cdot 6H_2O$, MeOH) to a 1:19 mixture of the D-*gluco*-alcohol **30** and the L-*ido*-alcohol **33** (91% from **30**), which could not be separated by flash chromatography. This mixture was tosylated, and the pure L-*ido*-tosylate **34** was isolated by chromatography (85%) and crystallization.

Treatment of **34** with NaN_3 in DMSO gave a mixture of products (*Scheme 4*). The desired tetrazole **35a** (29%) was isolated besides the D-*manno*-epimer **36a** (5%). The

Scheme 4



a) NaN_3, DMSO, 120–130°, 3 h; 29% of **35a** and 5% of **36a**. *b*) NaN_3, $MeOH/H_2O$, reflux, 16 h; 23% of **35a**/**36a** *ca.* 37:63. *c*) NaN_3, CD_3OD/D_2O, reflux, 16 h; 5% of **35b** and 5% of **36b**. *d*) $AlCl_3$, NaN_3, THF, reflux, 15 h; 50% of (*E*)- and (*Z*)-**38**. *e*) NH_4Cl, NaN_3, DMF, 60–65°, 28 h; **35a** (45%), **39** (12%), and **40** (1%). *f*) 110–120°, 2 h; 75% of **35a** and 9% of **41**. *g*) H_2, 10% Pd/C, MeOH/AcOH, r.t. 24 h; 91%.

reaction of **34** with other azides such as LiN_3 or *N,N,N',N'*-tetramethylguanidinium azide failed to produce higher yields of **35a**, as did NaN_3 in H_2O/MeOH, which led to the preferential formation of the D-*manno*-isomer **36a** (*ca.* 14%).

The complex ^{1}H-NMR spectrum indicates that **32** exists as a mixture of the ketone **32a** (CO band of medium intensity at 1732 cm^{-1}) and the cyclic tautomer **32b** (OH band at 3494 cm^{-1}). In the ^{1}H-NMR spectrum of the crude reduction product, a *d* at 2.48 ppm is assigned to OH–C(5) of **33**. The H–C(5) signal of **34** between 4.69 and 4.88 ppm is shifted to lower fields, as compared to the H–C(5) signal of **33** (3.98 ppm); the CN *s* of **34** is found at 117.47 ppm.

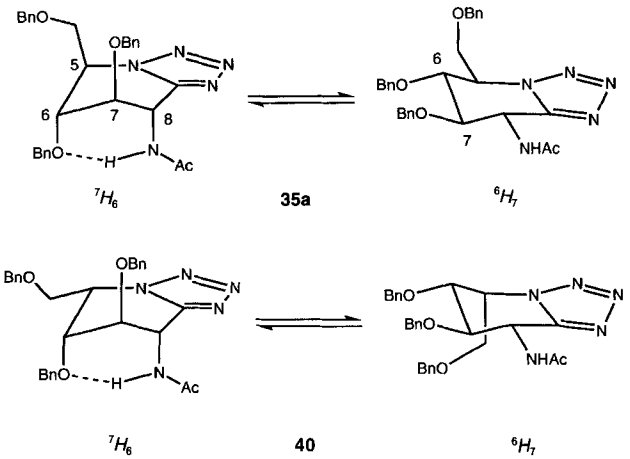
The structure and particularly the configuration of **35a** and **36a** were confirmed by their NMR spectra. The characteristic *s* of the tetrazole C-atom is observed at 151.14 (**35a**) or at 151.26 ppm (**36a**). The ^{1}H-NMR spectrum (*cf. Table*) of **35a** in $CDCl_3$ shows a concentration dependence: the geminal protons CH_2–C(5) are isochronous in the spectrum of a diluted solution (*ca.* 0.02M); in the spectrum of a more concentrated solution (*ca.* 0.08M), $\Delta\delta$ for CH,H'–C(5) is 0.06 ppm. The values of J(5,6), J(6,7), and J(7,8) indicate a preference for the $^7H_6$ conformation at either concentration in $CDCl_3$ solution. The preference is stronger at the lower concentration, suggesting that this conformer is stabilized by an intramolecular H-bond (NH···O–C(6); see *Scheme 5*). In keeping with this, **35a** adopts a $^6H_7$ conformation in CD_3OD solution, similarly to **3** [1].

Table. *Selected ^{1}H-NMR Chemical Shifts* δ [ppm] *and Coupling Constants* J [Hz] *of Tetrazoles*

	Solvent	Approx. conc.	NH	H–C(8)	H–C(7)	H–C(6)	H–C(5)	CH'–C(5)	CH–C(5)	AcN
35a	$CDCl_3$	0.02M	6.17	5.67	4.11	4.41	4.89	4.00	4.00	
	$CDCl_3$	0.08M	6.55	5.63	4.13	4.39	4.83	4.02	3.96	
	CD_3OD	0.015M	–	5.23	4.13	4.29	4.69	4.21	3.96	
35b	$CDCl_3$	0.011M	6.11	–	4.11	4.41	4.90	4.00	4.00	
3	$CDCl_3$			*ca.* 4.87	4.08	4.25	4.45	4.28	3.94	
36a	$CDCl_3$		6.30	5.80	4.15	4.42	4.86	4.09	3.73	
	CD_3OD		–	5.75	4.04	4.43	4.95	4.03	3.81	
36b	$CDCl_3$		6.18	–	4.14	4.41	4.87	4.09	3.73	
40	$CDCl_3$		5.90	5.79	4.04	4.30	4.83	4.57	3.97	
	CD_3OD		–	5.45	4.10	4.24	4.92	4.36	3.95	
7	CD_3OD		–	4.98	3.96	4.13	4.28	4.49	4.15	2.05
	D_2O		–	5.13	4.10	4.19	4.45	4.57	4.22	2.14
1	D_2O			4.86	3.87	4.05	4.37	4.48	4.13	
43	D_2O		–	5.67	4.30	4.44	4.67	4.25	4.13	2.10

	Solvent	Approx. conc.	J(8,NH)	J(7,8)	J(6,7)	J(5,6)	J(5,CH'–C(5))	J(5,CH–C(5))	^2J(CH_2–C(5))	J(5,8)
35a	$CDCl_3$	0.02M	8.9	3.5	5.4	3.1	6.3	6.3	–	
	$CDCl_3$	0.08M	8.9	4.2	5.8	3.8	6.7	4.9	9.6	
	CD_3OD	0.015M	–	6.9	8.0	6.8	4.2	3.3	10.3	
35b	$CDCl_3$	0.011M	–	–	5.4	3.0	6.4	6.4	–	
3	$CDCl_3$			6.9	8.8	7.5	3.9	2.6	10.3	
36a	$CDCl_3$		8.5	3.7	4.7	< 1	5.1	10.0	9.2	
	CD_3OD		–	4.0	*ca.* 4.3	*ca.* 1.3	5.8	9.0	9.3	
36b	$CDCl_3$		–	–	4.7	*ca.* 0.9	5.1	9.6	9.3	
40	$CDCl_3$		9.0	1.7	4.6	3.0	4.7	9.4	9.0	
	CD_3OD		–	3.8	6.1	3.9	4.5	7.2	9.6	
7	CD_3OD		–	9.0	9.0	*ca.* 8.7	2.7	2.4	12.0	0.9
	D_2O		–	9.5	9.5	*ca.* 9.3	2.5	2.4	12.8	1.0
1	D_2O			8.9	10.0	9.3	2.5	2.3	12.8	1.0
43	D_2O		–	4.6	6.3	3.6	4.6	4.7	12.4	

Scheme 5. Conformation of the Tetrazoles **35a** *and* **40**



The $CDCl_3$ and the CD_3OD spectra of the D-*manno*-isomer **36a** show only minor differences and do not allow assignment of configuration to this tetrazole. *A priori*, it could be D-*manno*, and result from an epimerization either at C(8) of **35a** or at C(2) of **34**, or alternatively L-*ido*, as the consequence of a neighboring-group participation of the acetamido group during the substitution of the tosyloxy group by azide, leading to a double inversion at C(5).

To check for epimerization at C(2)/C(8), **34** was treated with NaN_3 in D_3OD/D_2O. Partial deuteriation was evident from the reduced multiplicity of the signals of **35b** or **36b**, as compared with the corresponding signals in the spectra of **35a** and **36a**; the H–C(8) signal is no longer observed in the ^{1}H-NMR spectra of **35b** or **36b**. On the basis of this result, the D-*manno*-configuration was tentatively assigned to **36a**, assuming that the deuteration at C(8) is accompanied by partial epimerization. This is consistent with the observation that the *J* values in the ^{1}H-NMR spectra of **36a** are barely influenced by the solvent ($CDCl_3$, CD_3OD), suggesting a *trans*-orientation of NHAc and BnO–C(6) in **36a**.

The *manno*-tetrazole **36a** adopts a ^7S conformation, as indicated by the small vicinal coupling constants of the piperidine ring[6]).

The tetrazole **35a** was decomposed at temperatures > 265° (open capillary; melting at 113.5–114.5°). According to TLC, **35a** was not changed upon heating in DMSO at 110–120° for 3 h; addition of NaN_3, however, led to four products. On the basis of R_f values, two of them were tentatively identified as the *manno*-epimer **36a** and benzyl alcohol, suggesting elimination[7]).

To improve the synthesis of **35a**, we intended to subject the tosyloxynitrile **34** to an intermolecular 1,3-dipolar cycloaddition and to then close the piperidine ring by an intramolecular substitution. *Arnold* and *Thatcher* [31] described the formation of 5-substituted tetrazoles by the reaction of nitriles with *in situ* generated $Al(N_3)_3$ in boiling THF and demonstrated that this reagent does not displace a primary chloride. We thus treated **34** with $Al(N_3)_3$, but only obtained the unsaturated (*E*)- and (*Z*)-nitriles **38** (*Scheme 4*).

Treatment of **34** with NH_4Cl/NaN_3 at 60–65° in DMF[8]) [32–34] yielded 45% of **35a** as the main product, besides the new L-*ido*-tetrazole **40** (1%), starting material (*ca.* 9%),

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[6]) A similar conformation has been calculated for the *manno*-pyranosyl cation by *Winkler* and *Holan* [30].

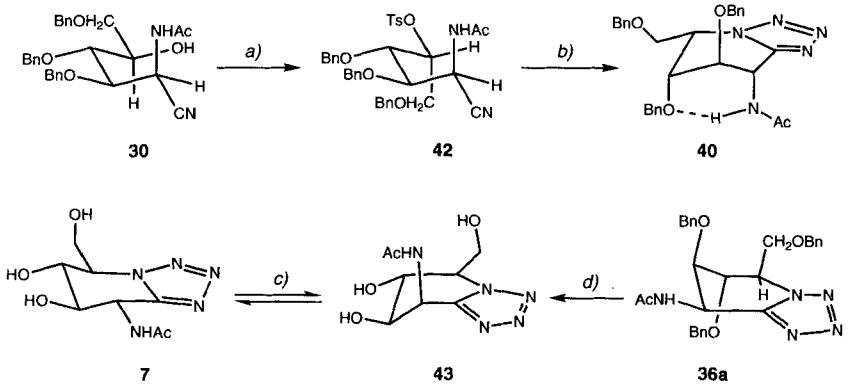
[7]) Prolonged heating of **35a** in DMSO in the presence of NaN_3 led to the tetrazolopyridine **37** (see *Scheme 4*).

[8]) In an exploratory experiment, the tetrazole **35a** was heated at 110–120° in DMF in the presence of NH_4Cl/NaN_3. This led to a transformation of **35a** similar to, but slower than that observed upon treatment with NaN_3 in hot DMSO.

and the azido-nitrile **39** (*ca.* 12%). Thermolysis of **39** gave **35a** (75%) and the unsaturated nitrile **41** (9%).

The ^{1}H-NMR spectra of $CDCl_3$ and CD_3OD solutions of **40** (*cf. Table*) again show solvent-dependent *J* values (although the differences are less pronounced than those observed for **35a**), indicating a *cis*-orientation of NHAc and BnO–C(6). This is consistent with an L-*ido*-configuration of **40**, which was evidenced by treating the D-*gluco*-tosylate **42** (derived from **30**) with NaN_3 to give **40** in poor yield (11%; *Scheme 6*).

Scheme 6



a) TsCl, pyridine, 55–60°, 4.5 h; 75%. *b*) NaN_3, DMSO, 110–120°, 3 h; 12%. *c*) 0.01M aq. NaOH. *d*) H_2, 10% Pd/C, MeOH/AcOH, r.t., 18 h; 93%.

In $CDCl_3$ solution, the $^7H_6$ conformation is mainly populated, while in CD_3OD solution, **40** exists as a mixture of the $^7H_6$ and $^6H_7$ conformers (*Scheme 5*). The azide band of **39** is observed at 2103 cm^{-1}; the CN *s* appears at 117.60 ppm; the signal of H–C(5) of **39** is found at 3.64 ppm and is shifted to higher field ($\Delta\delta$ *ca.* 1 ppm), as compared with the corresponding resonance of **34**. The conversion of **39** to **35a** evidences the D-*gluco*-configuration of **39**.

The azide band of **41** is observed at 2106 cm^{-1}; the CN *s* and a *s* indicating the presence of a C=C bond are at 114.26 and 114.36 ppm. The signal of H–C(4) of **41** shows a strong NOE upon irradiation of the NH signal at 7.82 ppm. On the basis of this observation, the (*Z*)-configuration is unambiguously assigned to **41**. The configuration of the (*E*)- and (*Z*)-isomers of **38** is assigned by comparing the chemical shift values of *Me*CO*NH*, H–C(3), and of C(2) with the corresponding values found for **41**.

The *Me*CONH groups of **41** and (*Z*)-**38** resonate at unusually high field (1.53 and 1.55 ppm, resp.). This shift (*cf.* (*E*)-**38**; 2.06 ppm), and the downfield shifts of the MeCO*NH* resonances of (*Z*)-**38** and **41** (7.95 and 7.82 ppm, resp.), as compared with (*E*)-**38** (*ca.* 7.4 ppm), suggest that **41** and (*Z*)-**38** adopt a preferred conformation in which the MeCONH and BnO–C(6) groups are in close proximity.

The isolation of the azide **39** indicates that the conversion of **34** with *in situ* generated NH_4N_3 proceeds (at least partially) by a single S_N2-type displacement at C(5) and subsequent 1,3-dipolar cycloaddition. The L-*ido*-tetrazole **40** is the product of a double inversion at C(5) of **34**, proceeding either *via* a chloride or involving neighboring-group participation by the NHAc group. The observation that the *manno*-epimer **36** was not formed indicates that under these conditions, Cl^- acts as a nucleophile rather than as a base, in keeping with the formation of **40** *via* intermolecular displacement of the tosyloxy group of **34** by Cl^-.

Hydrogenolytic debenzylation of **35a** afforded the *N*-acetylglucosamine-derived tetrazole **7** (91%). The large vicinal coupling constants of the piperidinose ring as well as a

homoallylic coupling ($J(5,8)$ *ca.* 1 Hz) indicate a $^6H_7$ conformation in D_2O solution, and compare well with the values found for the *gluco*-tetrazole **1** [1] [2]. The tetrazole **7** is stable in D_2O, in 0.1M aqueous HCl, or in 10^{-4} M aqueous NaOH at room temperature (no change in the ^{1}H-NMR after 1 d); in 10^{-2} M aqueous NaOH, however, **7** epimerized, leading to a *ca.* 4:1 mixture of **7** and **43** after 1 d. The ManNAc tetrazole **43** (*cf. Scheme 6*) was obtained as a pure compound by debenzylation of **36a**. A sample of **7** decomposed in an open capillary at temperatures > 230°.

Determination of Inhibition Constants. The tetrazole **6** is a competitive inhibitor of the β-galactosidases from *E. coli* and bovine liver. The former enzyme was studied according to the protocol of *Lehmann et al.* [35]. We found it necessary to modify the K_M determination by narrowing the range of substrate concentrations since at the high extreme of concentration, the enzyme was saturated, and at the low extreme, substrate consumption was significant, giving rise to non-steady-state kinetics. The K_I of **6** was found to be 1 μM at pH 6.8 which compares favorably with the value of 70 μM for the galactonolactam **4** [12]. The inhibition kinetics for the latter enzyme were studied according to *Withers* [2], resulting in a K_I of 0.8 μM at pH 7.0 for **6**.

As shown by preliminary kinectic measurements, β-glucosaminidase from bovine kidney is competitively inhibited by **7** with a K_I of *ca.* 0.2 μM (pH 4.1). This K_I value compares well – as expected – with the value measured for the lactone **5** which shows a K_I of 0.16 μM at pH 4.25 [14] against this enzyme; the corresponding 1,5-lactam shows a K_I of 1.8 μM [14].

We thank the *Swiss National Science Foundation* and *F. Hoffmann-La Roche AG*, Basel for generous support.

Experimental Part

General. Solvents were distilled before use. Normal workup implies distribution of the crude product between the indicated org. solvent and H_2O, drying of the org. layer ($MgSO_4$), filtration, and evaporation of the filtrate. TLC: *Merck* silica gel *60F-254* plates; detection by heating with 5% vanillin in conc. H_2SO_4 or with 'mostain' [36] (400 ml of 10% H_2O soln., 20 g of $(NH_4)_6Mo_7O_{24}\cdot 6H_2O$, 0.4 g of $Ce(SO_4)_2$). Flash chromatography (FC): silica gel (*Merck 60* (0.04 – 0.063 mm). M.p.: uncorrected. ^{1}H- (300 MHz, if not indicated otherwise) and ^{13}C-NMR (75 MHz, if not indicated otherwise): chemical shift δ in ppm and coupling constants J in Hz. FAB- and CI-Mass spectra: 3-nitrobenzyl alcohol and NH_3 as the matrixes, resp., unless indicated otherwise.

2,3,4,6-Tetra-O-benzyl-D-galactononitrile (**10**) *and 2,3,4,6-Tetra-O-benzyl-D-galactono-1,5-lactone* (**11**). A soln. of tetra-*O*-benzylgalactose oximes **9** (4.34 g, 7.81 mmol) [37] and PPh_3 (4.28 g, 16.3 mmol) in MeCN (80 ml) was treated with a soln. of CBr_4 (6.76 g, 20.4 mmol) in MeCN (10 ml). The soln. was stirred for 20 min at r.t., quenched with MeOH (15 ml), and evaporated. FC (hexane/AcOEt 4:1) afforded **10** (2.16 g, 51%) as a white crystalline solid and **11** (1.35 g, 32%) as a colorless oil.

Data of **10**: R_f (hexane/AcOEt 2:1) 0.52. M.p. 66–67°. $[\alpha]_D^{25} = +31.2$ ($c = 1.0$, $CHCl_3$). IR ($CHCl_3$): 3565*w*, 3090*w*, 3065*m*, 3010*m*, 2870*m*, 1950*w*, 1875*w*, 1810*w*, 1495*m*, 1455*s*, 1395*m*, 1340*m*, 1260*m*, 1100*s*, 1030*s*, 930*w*, 910*w*. ^{1}H-NMR ($CDCl_3$): 2.44 (*d*, $J = 7.5$, OH–C(5)); 3.50 (*dd*, $J = 9.5$, 6.2, H–C(6)); 3.59 (*dd*, $J = 9.5$, 6.2, H′–C(6)); 3.87 (*dd*, $J = 8.1$, 1.9, H–C(4)); 4.07 (*dd*, $J = 8.1$, 2.9, H–C(3)); 4.13 (*m*, H–C(5)); 4.34 (*d*, $J = 11.2$, 1 H, PhCH_2); 4.42 (*d*, $J = 11.2$, 1 H, PhCH_2); 4.49 (*d*, $J = 11.8$, 1 H, PhCH_2); 4.54 (*d*, $J = 11.5$, 1 H, PhCH_2); 4.53–4.54 (*m*, 2 H, H–C(2), PhCH_2); 4.80 (*d*, $J = 10.8$, 1 H, PhCH_2); 4.95 (*d*, $J = 11.5$, 1 H, PhCH_2); 4.98 (*d*, $J = 10.7$, 1 H, PhCH_2); 7.09–7.12 (*m*, 2 arom. H); 7.29–7.45 (*m*, 18 arom. H). ^{13}C-NMR ($CDCl_3$): 67.46 (*d*); 69.01 (*d*); 71.07 (*t*); 72.52 (*t*); 73.41 (*t*); 74.24 (*t*); 75.11 (*t*); 76.96 (*d*); 78.71 (*d*); 117.41 (*s*); 127.88–128.72 (several *d*); 135.58 (*s*); 137.18 (*s*); 137.41 (*s*); 137.79 (*s*). CI-MS: 538 (1, $[M + H]^+$), 446 (4), 181 (4), 91 (100). Anal. calc. for $C_{34}H_{35}NO_5$ (537.66): C 75.95, H 6.56, N 2.61; found: C 76.04, H 6.68, N 2.59.

Data of **11**: R_f (toluene/AcOEt 9:1) 0.36. IR ($CHCl_3$): 3090*w*, 3070*w*, 3010*m*, 2935*w*, 2875*w*, 1880*w*, 1745*s*, 1602*w*, 1500*m*, 1455*m*, 1360*m*, 1248*m*, 1105*s*, 1064*m*, 1028*m*, 910*w*. ^{1}H-NMR ($CDCl_3$): 3.68–3.77 (*m*, 2H–C(6)); 3.92 (*dd*, *J* = 9.6, 2.2, H–C(3)); 4.20 (*t*, *J* ≈ 1.8, H–C(4)); 4.37 (*ddd*, *J* = 5.9, 5.7, 1.5, H–C(5)); 4.48 (*d*, *J* = 11.8, 1H, PhCH_2); 4.52 (*d*, *J* = 9.6, H–C(2)); 4.54 (*d*, *J* = 11.8, 1H, PhCH_2); 4.64 (*d*, *J* = 11.2, 1H, PhCH_2); 4.72 (*d*, *J* = 11.8, 1H, PhCH_2); 4.79 (*d*, *J* = 11.8, 1H, PhCH_2); 4.82 (*d*, *J* = 11.5, 1H, PhCH_2); 4.97 (*d*, *J* = 11.4, 1H, PhCH_2); 5.22 (*d*, *J* = 11.0, 1H, PhCH_2); 7.25–7.47 (*m*, 20 arom. H). ^{13}C-NMR ($CDCl_3$): 67.57 (*t*); 72.58 (*d*); 72.86 (*t*); 73.70 (*t*); 74.78 (*t*); 75.34 (*t*); 77.36 (2*d*); 80.16 (*d*); 127.58–128.54 (several *d*); 137.14 (*s*); 137.29 (*s*); 137.53 (2*s*); 169.74 (*s*). CI-MS: 556 (6, $[M + NH_4]^+$), 539 (1, $[M + H]^+$), 447 (3), 355 (5), 341 (3), 267 (4), 249 (3), 181 (29), 163 (25), 91 (100).

*2,3,4,6-Tetra-*O*-benzyl-*L*-arabino-hex-5-ulosononitrile* (**12**). A soln. of **10** (2.42 g, 4.50 mmol) in CH_2Cl_2 (50 ml) was added to a suspension of PCC (2.16 g, 10.0 mmol; dried *i.v.*) and 3-Å molecular sieves (2.0 g; powdered, dried overnight at 120° *i.v.*) in dry CH_2Cl_2 (5 ml) under Ar. The mixture was stirred at r.t. for 1.5 h and filtered through silica gel. The filtrate was concentrated and purified by FC (hexane/AcOEt 6:1): **12** (2.22 g, 92%). Colorless oil. R_f (hexane/AcOEt 4:1) 0.42. IR ($CHCl_3$): 3090*w*, 3070*w*, 3040*w*, 3000*w*, 2870*m*, 1955*w*, 1880*w*, 1810*w*, 1735*s*, 1603*w*, 1495*m*, 1455*s*, 1397*m*, 1335*m*, 1252*m*, 1100*s*, 1030*s*, 910*m*. ^{1}H-NMR ($CDCl_3$): 4.23–4.83 (*m*, 13H); 7.24–7.33 (*m*, 20 arom. H). ^{13}C-NMR ($CDCl_3$): 67.22 (*d*); 72.86 (*t*); 73.11 (*t*); 73.78 (*t*); 74.15 (*t*); 74.20 (*t*); 79.69 (*d*); 80.91 (*d*); 116.7 (*s*); 127.90–128.76 (several *d*); 135.31 (*s*); 136.65 (*s*); 136.73 (*s*); 137.38 (*s*); 206.0 (*s*). CI-MS: 626 (58), 553 (94, $[M + NH_4]^+$), 536 (67, $[M + H]^+$), 386 (11), 323 (15), 283 (21), 181 (36), 91 (100).

*2,3,4,6-Tetra-*O*-benzyl-*L*-altrononitrile* (**13**) *and* **10**. A stirred soln. of **12** (214 mg, 0.40 mmol) in MeOH (20 ml) at −60° was treated with $NaBH_4$ (45 mg, 1.19 mmol). After 30 min, remaining $NaBH_4$ was destroyed by addition of acetone (1 ml). The mixture was treated with *Celite* (1 g) and concentrated. FC (hexane/AcOEt 4:1) gave **13** (86 mg, 40%) and **10** (83 mg, 39%). **13**: R_f (hexane/AcOEt 1:2) 0.60. $[\alpha]_D^{25}$ = +14.5 (*c* = 0.9, $CHCl_3$). IR ($CHCl_3$): 3565*m*, 3090*w*, 3070*m*, 3010*m*, 2870*m*, 1950*w*, 1810*w*, 1605*w*, 1495*m*, 1455*m*, 1395*m*, 1340*m*, 1250*m*, 1070*s*, 1030*m*, 910*w*. ^{1}H-NMR ($CDCl_3$): 2.64 (*d*, *J* = 5.2, OH–C(5)); 3.63 (*d*, *J* = 4.6, 2H–C(6)); 3.88 (*dd*, *J* = 7.0, 4.1, H–C(4)); 4.14 (*dd*, *J* = 5.9, 4.1, H–C(3)); 4.22 (*m*, H–C(5)); 4.44 (*d*, *J* = 11.8, 1H, PhCH_2); 4.50 (*s*, PhCH_2); 4.51 (*d*, *J* = 11.8, 1H, PhCH_2); 4.55 (*d*, *J* = 11.5, 1H, PhCH_2); 4.62 (*d*, *J* = 5.9, H–C(2)); 4.73 (*d*, *J* = 11.3, 1H, PhCH_2); 4.83 (*d*, *J* = 11.3, 1H, PhCH_2); 4.87 (*d*, *J* = 11.5, 1H, PhCH_2); 7.14–7.36 (*m*, 20 arom. H). ^{13}C-NMR ($CDCl_3$): 69.32 (*d*); 70.14 (*d*); 71.08 (*t*); 73.11 (*t*); 73.59 (*t*); 73.67 (*t*); 75.00 (*t*); 79.15 (*d*); 79.46 (*d*); 117.50 (*s*); 128.07–129.19 (several *d*); 136.33 (*s*); 137.96 (*s*); 138.31 (*s*); 138.23 (*s*). CI-MS: 628 (58), 555 (63, $[M + NH_4]^+$), 538 (100, $[M + H]^+$), 446 (30), 430 (30), 240 (31), 181 (35), 108 (49), 91 (97). Anal. calc. for $C_{34}H_{35}NO_5$ (537.66): C 75.95, H 6.56, N 2.61; found: C 75.79, H 6.78, N 2.54.

*2,3,4,6-Tetra-*O*-benzyl-5-*O*-(tol-4-ylsulfonyl)-*L*-altrononitrile* (**14**), **11**, *and 2,3,4,6-Tetra-*O*-benzyl-*L*-altrono-1,5-lactone* (**15**). A soln. of toluene-4-sulfonyl chloride (426 mg, 2.23 mmol) and **13** (120 mg, 0.223 mmol) in pyridine (2 ml) was stirred at 50° for 20 h and then concentrated until formation of a precipitate. The suspension was treated with sat. aq. $NaHCO_3$ soln., stirred for 30 min, and then worked up as usual ($CHCl_3$, sat. $NaHCO_3$ soln., H_2O). TLC analysis showed a mixture of **14** (104 mg, 67%), **11** (10 mg, 8%), and **15** (8 mg, 7%) of similar R_f which were analyzed and separated by HPLC (*Si60 S5W*, 20 × 250 mm; hexane/AcOEt 9:2, 16 ml/min; UV 254 nm).

Data of **14**: R_f (toluene/AcOEt 9:1) 0.56. $[\alpha]_D^{25}$ = +29.3 (*c* = 1.0, $CHCl_3$). IR ($CHCl_3$): 3065*w*, 3010*w*, 2870*w*, 1810*w*, 1600*w*, 1495*w*, 1455*m*, 1400*w*, 1365*m*, 1260*w*, 1175*s*, 1095*s*, 1030*m*, 955*m*, 915*m*. ^{1}H-NMR ($CDCl_3$): 2.34 (*s*, Me); 3.64 (*d*, *J* = 5.6, 2H–C(6)); 3.86 (*dd*, *J* = 7.9, 3.0, H–C(3)); 3.99 (*dd*, *J* = 7.9, 2.4, H–C(4)); 4.26 (*d*, *J* = 10.9, 1H, PhCH_2); 4.30 (*s*, PhCH_2); 4.42 (*d*, *J* = 3.0, H–C(2)); 4.43 (*d*, *J* = 11.5, 1H, PhCH_2); 4.60 (*d*, *J* = 10.9, 1H, PhCH_2); 4.65 (*d*, *J* = 11.1, 1H, PhCH_2); 4.82 (*d*, *J* = 11.6, 1H, PhCH_2); 4.87 (*d*, *J* = 11.0, 1H, PhCH_2); 5.09 (*td*, *J* = 5.6, 2.4, H–C(5)); 7.08–7.16 (*m*, 4 arom. H); 7.24–7.37 (*m*, 18 arom. H); 7.69–7.72 (*d*, *J* = 8.4, 2 arom. H). ^{13}C-NMR ($CDCl_3$): 21.35 (*q*); 66.75 (*d*); 67.72 (*t*); 72.19 (*t*); 72.91 (*t*); 73.44 (*t*); 73.90 (*t*); 77.05 (*d*); 78.17 (*d*); 80.42 (*d*); 117.00 (*s*); 127.08–128.36 (several *d*); 129.33 (*d*); 133.33 (*s*); 135.32 (*s*); 136.63 (*s*); 136.85 (*s*); 137.25 (*s*); 144.32 (*s*). CI-MS: 692 (1, $[M + H]^+$), 600 (1), 430 (1), 338 (3), 181 (11), 91 (100). Anal. calc. for $C_{41}H_{41}NO_7S$ (691.85): C 71.18, H 5.97, N 2.02, S 4.63; found: C 71.21, H 6.07, N 2.20, S 4.52.

Data for **15**: R_f (toluene/AcOEt 9:1) 0.39. IR ($CHCl_3$): 3090*w*, 3065*w*, 3010*w*, 2920*w*, 2870*w*, 1950*w*, 1880*w*, 1740*s*, 1500*w*, 1455*m*, 1360*w*, 1285*w*, 1250*w*, 1115*s*, 1030*m*, 910*w*. ^{1}H-NMR (200 MHz, $CDCl_3$): 3.68 (*d*, *J* = 3.3, 2H–C(6)); 4.02 (*dd*, *J* = 6.2, 2.6, H–C(3)); 4.16 (*dd*, *J* = 6.4, 2.6, H–C(4)); 4.25 (*d*, *J* = 6.2, H–C(2)); 4.47 (*d*, *J* = 12.0, 1H, PhCH_2); 4.55–4.70 (*m*, 7H, PhCH_2, H–C(5)); 4.96 (*d*, *J* = 11.5, 1H, PhCH_2); 7.22–7.34 (*m*, 20 arom. H). ^{13}C-NMR (50 MHz, $CDCl_3$): 69.09; 72.45; 72.84; 73.10; 73.84; 73.88; 74.87; 76.00; 78.45; 128.21–129.03; 137.69; 137.85; 138.04; 138.08; 169.19. CI-MS: (NH_3): 556 (3, $[M + NH_4]^+$), 539 (2, $[M + H]^+$), 447 (4), 355 (3), 267 (3), 181 (28), 163 (21), 91 (100).

(5R,6S,7S,8S)-6,7,8-Tris(benzyloxy)-5-[(benzyloxy)methyl]-5,6,7,8-tetrahydrotetrazolo[1,5-a]pyridine (**16**) *and 2,5-Anhydro-3,4,6-tri-O-benzyl-D-galactononitrile* (**17**). A soln. of **14** (100 mg, 0.145 mmol) and NaN_3 (150 mg, 2.31 mmol) in dry DMSO (5 ml) was stirred at 100° for 16 h, diluted with H_2O, and worked up as usual (AcOEt, H_2O). FC (hexane/AcOEt 4:1) afforded **16** (58 mg, 71%) as a colorless oil which crystallized on standing *i.v.* and **17** (4 mg, 6%) as a colourless oil.

Data of **16**: R_f (hexane/AcOEt 2:1) 0.63. M.p. 48–49°. $[\alpha]_D^{25} = +55.8$ ($c = 0.6$, $CHCl_3$). IR ($CHCl_3$): 3090*w*, 3065*w*, 3010*w*, 2960*w*, 2870*w*, 1955*w*, 1815*w*, 1605*w*, 1495*w*, 1455*m*, 1400*w*, 1355*m*, 1330*w*, 1310*w*, 1260*m*, 1100*s* (br.), 1030*s* (br.), 910*w*. ^{1}H-NMR ($CDCl_3$): 3.97 (*dd*, $J = 9.2, 8.5$, CH–C(5)); 4.02 (*dd*, $J = 7.5, 1.7$, H–C(7)); 4.35 (*dd*, $J = 9.3, 5.3$, CH′–C(5)); 4.46 (*dd*, $J = 3.3, 1.7$, H–C(6)); 4.53–4.66 (*m*, 4H, H–C(5), PhCH_2); 4.73 (*d*, $J = 12.1$, 1H, PhCH_2); 4.81 (*d*, $J = 11.9$, 1H, PhCH_2); 4.88 (*d*, $J = 11.1$, 1H, PhCH_2); 4.96 (*d*, $J = 11.2$, 1H, PhCH_2); 5.09 (*d*, $J = 7.4$, H–C(8)); 5.30 (*d*, $J = 11.2$, 1H, PhCH_2); 7.16–7.45 (*m*, 20 arom. H). ^{13}C-NMR ($CDCl_3$): 58.98 (*d*); 66.43 (*t*); 71.21 (*d*); 73.49 (*t*); 73.49 (*d*); 73.82 (*t*); 73.92 (*t*); 74.77 (*t*); 80.53 (*d*); 127.67–128.45 (several *d*); 137.10 (*s*); 137.25 (*s*); 137.31 (*s*); 137.44 (*s*); 152.65 (*s*). CI-MS: 563 (4, $[M + H]^+$), 471 (17), 203 (15), 138 (7), 91 (100). Anal. calc. for $C_{34}H_{34}N_4O_4$ (562.67): C 72.58, H 6.09, N 9.96; found: C 72.46, H 5.94, N 9.82.

Data of **17**: R_f (hexane/AcOEt 2:1) 0.40. ^{1}H-NMR ($CDCl_3$): 3.73 (*dd*, $J = 10.1, 6.6$, H–C(6)); 3.80 (*dd*, $J = 10.1, 5.9$, H′–C(6)); 4.12 (*t*, $J = 3.8$, H–C(4)); 4.16–4.21 (*m*, H–C(5)); 4.19 (*dd*, $J = 7.2, 3.8$, H–C(3)); 4.47 (*d*, $J = 11.8$, 1H, PhCH_2); 4.56 (*d*, $J = 11.8$, 1H, PhCH_2); 4.63 (*d*, $J = 11.8$, 1H, PhCH_2); 4.69 (*s*, PhCH_2); 4.72 (*d*, $J = 7.1$, H–C(2)); 4.98 (*d*, $J = 11.8$, 1H, PhCH_2); 7.26–7.40 (*m*, 15 arom. H). ^{13}C-NMR (50 MHz, $CDCl_3$): 67.05; 68.88; 73.67; 73.86 (2); 76.31; 80.27; 81.29; 117.17; 128.07–129.07; 137.00; 138.27 (2). CI-MS: 520 (23), 447 (63, $[M + NH_4]^+$), 430 (88, $[M + H]^+$), 338 (82), 246 (20), 181 (16), 105 (19), 91 (100).

(5R,6S,7S,8S)-5,6,7,8-Tetrahydro-5-(hydroxymethyl)tetrazolo[1,5-a]pyridine-6,7,8-triol (**6**). *a*) A soln. of **16** (230 mg, 0.41 mmol) in MeOH (8 ml) was treated with AcOH (*ca.* 0.05 ml) and 10% Pd/C (300 mg), followed by hydrogenation at 6 bar for 48 h at r.t. The suspension was filtered through *Celite* and the solid residue washed with MeOH. Evaporation of the filtrate followed by FC (AcOEt/MeOH 19:1) afforded **6** (78 mg, 94%) as a white solid.

b) A stirred soln. of **26** (530 mg, 1.83 mmol) in MeOH (25 ml) was treated with 1N aq. HCl (1 ml) and heated at 60° for 6 h. The soln. was concentrated and purified by FC (AcOEt/MeOH 19:1): **6** (336 mg, 91%). White solid. R_f (AcOEt/MeOH 3:1) 0.50. $[\alpha]_D^{25} = +10.6$ ($c = 0.5$, H_2O). IR (KBr): 3420*vs* (br.), 2920*s*, 1635*m*, 1630*m*, 1615*m*, 1460*m*, 1435*m*, 1420*m*, 1340*m*, 1160*m*, 1110*s*, 1055*s*, 985*m*, 920*m*, 890*w*, 850*m*, 805*m*, 720*m*. ^{1}H-NMR (500 MHz, D_2O): 4.11 (*dd*, J = 9.0, 2.1, H–C(7)); 4.16 (*dd*, $J = 11.9, 6.3$, CH–C(5)); 4.39 (*dd*, $J = 11.9, 5.5$, CH′–C(5)); 4.60 (*t*, $J \approx 2.4$, H–C(6)); 4.72 (*tdd*, $J = 5.9, 2.8, 0.7$, H–C(5)); 5.09 (*dd*, $J = 9.0, 0.7$, H–C(8)). ^{13}C-NMR (D_2O): 61.90 (*t*); 63.53 (*d*); 66.90 (*d*); 72.09 (*d*); 75.61 (*d*); 157.28 (*s*). FAB-MS (glycerol): 427 (10, $[2M + Na]^+$), 225 (55, $[M + Na]^+$), 203 (100, $[M + H]^+$), 107 (30), 89 (36), 77 (39).

(E)- and (Z)-2,3-Di-O-benzyl-4,6-O-benzylidene-D-galactose Oximes (**19**). $NH_2OH \cdot HCl$ (41.0 g, 590 mmol) was added to a stirred soln. of Na (7.0 g, 304 mmol) in abs. EtOH (100 ml) at 55°. Stirring was continued for 5 min followed by addition of 2,3-di-*O*-benzyl-4,6-*O*-benzylidene-D-galactopyranose (**18**) [22] (33.0 g, 73.6 mmol). The mixture was stirred at 55° for 3 h and filtered. The residue was washed with AcOEt, and the combined filtrate and washings were concentrated. Normal workup (AcOEt) gave crystalline **19** (33.9 g, 99%). Recrystallization ($CHCl_3$/pentane) afforded pure **19** for analysis. R_f (hexane/AcOEt 2:1) 0.34. M.p. 138–139°. $[\alpha]_D^{25} = +62.2$ ($c = 0.9$, $CHCl_3$). IR ($CHCl_3$): 3580*m*, 3345*w*, 3070*w*, 3010*m*, 2865*m*, 1730*w*, 1600*w*, 1495*w*, 1455*m*, 1395*m*, 1340*w*, 1310*w*, 1260*w*, 1090*s*, 1060*s*, 1030*s*, 1010*s*, 930*w*. ^{1}H-NMR ($CDCl_3$, (*E*)/(*Z*) 3:1): 3.05 (*d*, $J = 11.2$, 0.75H, OH–C(5)); 3.11 (*d*, $J = 11.6$, 0.25H, OH–C(5)); 3.87 (br. *d*, $J = 10.7$, H–C(5)); 3.89 (*dd*, $J = 9.0, 3.0$, 0.75H, H–C(3)); 4.07 (*d*, $J = 11.9$, H–C(6)); 4.18 (br. *d*, $J \approx 9.0$, H–C(4)); 4.18 (*m*, 0.25H, H–C(3)); 4.27 (*dd*, $J = 8.0, 3.0$, 0.75H, H–C(2)); 4.28 (*dd*, $J = 11.9, 1.8$, H′–C(6)); 4.38 (*d*, $J = 12.0$, 0.75H, PhCH_2); 4.40 (*d*, $J = 11.9$, 0.25H, PhCH_2); 4.69 (*d*, $J = 10.9$, 1H, PhCH_2); 4.71 (*d*, $J = 12.1$, 1H, PhCH_2); 4.77 (*d*, $J = 10.9$, 0.25H, PhCH_2); 4.82 (*d*, $J = 11.1$, 0.75H, PhCH_2); 5.00 (*dd*, $J = 5.8, 1.7$, 0.25H, H–C(2)); 5.39 (*s*, 0.75H, PhC*H*); 5.41 (*s*, 0.25H, PhC*H*); 7.02 (*d*, $J = 5.8$, 0.25H, H–C(1)); 7.15–7.40 (*m*, 15 arom. H); 7.48 (*d*, $J = 7.9$, 0.75H, H–C(1)); 8.20 (*s*, 0.75H, NOH); 8.62 (*s*, 0.25H, NOH). ^{13}C-NMR ($CDCl_3$, (*E*)/(*Z*) 3:1): (*E*)-isomer: 63.15 (*d*); 71.12 (*t*); 72.62 (*t*); 75.08 (*d*); 75.43 (*t*); 77.58 (*d*); 78.56 (*d*); 101.09 (*d*); 125.84 (*d*); 127.94–128.96 (several *d*); 137.38 (*s*); 137.47 (*s*); 137.63 (*s*); 152.88 (*d*); (*Z*)-isomer: 63.01, 70.81; 72.41; 101.01; 150.47. FAB-MS: 464 (31, $[M + H]^+$), 358 (11), 91 (100). Anal. calc. for $C_{27}H_{29}NO_6$ (463.53): C 69.96, H 6.31, N 3.02; found: C 69.87, H 6.28, N 3.01.

2,3-Di-O-benzyl-4,6-O-benzylidene-D-galactononitrile (**20**). A stirred soln. of **19** (1.22 g, 2.63 mmol), PPh_3 (2.42 g, 9.23 mmol), and pyridine (0.5 ml, 6 mmol) in MeCN (20 ml) was treated with a soln. of CBr_4 (1.83 g, 5.52 mmol) in MeCN (5 ml). After 20 min, the soln. was diluted with H_2O (30 ml) and extracted with $CHCl_3$ (2 × 60 ml). Normal workup and FC (hexane/AcOEt 4:1) afforded **20** (925 mg, 79%). White crystals. R_f (hexane/AcOEt 2:1) 0.50. M.p. 127–128°. $[\alpha]_D^{25} = +84.4$ ($c = 1.0$, $CHCl_3$). IR ($CHCl_3$): 3570*m*, 3090*m*, 3070*m*, 3010*m*, 2920*m*, 2875*m*, 1955*w*, 1810*w*, 1605*w*, 1500*m*, 1455*s*, 1400*s*, 1360*m*, 1340*m*, 1310*m*, 1260*m*, 1120*s*, 1085*s*, 1060*s*, 1030*s*, 1005*s*, 950*m*,

915*m*, 905*m*. ^{1}H-NMR ($CDCl_3$): 3.03 (*d*, *J* = 11.5, OH–C(5)); 3.85 (*d*, *J* = 11.2, H–C(5)); 3.99–4.15 (*m*, H–C(3), H–C(4), H–C(6)); 4.29 (*dd*, *J* = 12.0, 1.6, H′–C(6)); 4.40 (*d*, *J* = 1.6, H–C(2)); 4.57 (*d*, *J* = 12.2, 1 H, PhCH_2); 4.90 (*d*, *J* = 10.5, 1 H, PhCH_2); 4.98 (*d*, *J* = 12.2, 1 H, PhCH_2); 5.08 (*d*, *J* = 10.5, 1 H, PhCH_2); 5.43 (*s*, PhC*H*); 7.25–7.54 (*m*, 15 arom. H). ^{13}C-NMR ($CDCl_3$): 62.34 (*d*); 65.65 (*d*); 72.15 (*t*); 72.22 (*t*); 75.38 (*t*); 76.44 (*d*); 76.85 (*d*); 100.77 (*d*); 117.34 (*s*); 125.66–128.89 (several *d*); 135.23 (*s*); 136.94 (*s*); 136.98 (*s*). FAB-MS: 446 (51, $[M + H]^+$), 91 (100). Anal. calc. for $C_{27}H_{27}NO_5$ (445.52): C 72.79, H 6.11, N 3.14; found: C 72.49, H 6.14, N 2.87.

2,3-Di-O-*benzyl-4,6*-O-*benzylidene*-L-arabino-*hex-5-ulosononitrile* (**21**). A soln. of **20** (1.082 g, 2.43 mmol) in CH_2Cl_2 (5 ml) was added to a suspension of PCC (1.00 g, 4.64 mmol; dried *i.v.*) and 3-Å molecular sieves (1 g; powdered, dried overnight at 120° *i.v.*) in dry CH_2Cl_2 (10 ml) under Ar. The mixture was stirred at r.t. for 1.5 h and filterered through silica gel (eluting with AcOEt/hexane 1:4 (5 × 20 ml)). Evaporation gave crude **21** (796 mg, 73%). White solid. R_f (hexane/AcOEt 2:1). 0.65. IR ($CHCl_3$): 3485*w*, 3070*w*, 3040*w*, 2930*w*, 2875*w*, 1800*w*, 1740*m*, 1600*w*, 1495*w*, 1455*m*, 1400*m*, 1340*w*, 1315*w*, 1115*s*, 1030*m*, 985*m*, 915*w*. ^{1}H-NMR ($CDCl_3$): 4.36 (*dd*, *J* = 6.9, 2.4, H–C(3)); 4.39 (*s*, 2 H); 4.55 (*d*, *J* = 6.9, H–C(2)); 4.56 (*d*, *J* = 11.5, 1 H); 4.75 (*d*, *J* = 11.5, 1 H); 4.83 (*d*, *J* = 2.4, H–C(4)); 4.85 (*d*, *J* = 11.6, 1 H); 4.86 (*d*, *J* = 11.3, 1 H); 5.90 (*s*, PhC*H*); 7.28–7.61 (*m*, 15 arom. H). ^{13}C-NMR ($CDCl_3$): 67.74; 72.36; 72.93; 74.22; 78.24; 81.88; 99.44; 116.30; 125.93–129.34; 135.37; 136.47; 136.90; 203.17. FAB-MS: 444 (5, $[M + H]^+$), 327 (3), 307 (3), 289 (3), 281 (3), 221 (3), 207 (4), 91 (100).

20 *and 2,3-Di*-O-*benzyl-4,6*-O-*benzylidene*-L-*altrononitrile* (**22**). A stirred soln. of **21** (796 mg, 1.79 mmol) in THF (10 ml) at −78° was treated with $NaBH_4$ (380 mg, 10.0 mmol). After 3 h, remaining $NaBH_4$ was destroyed with acetone (1 ml) and the mixture adsorbed onto silica gel. FC (hexane/AcOEt 4:1) gave **20**/**22** 1:5 (647 mg, 81%) as indicated by ^{1}H-NMR analysis. R_f (hexane/AcOEt 2:1) 0.50. IR ($CHCl_3$): 3565*m*, 3090*w*, 3070*w*, 3010*m*, 2875*m*, 1955*w*, 1880*w*, 1810*w*, 1605*w*, 1495*m*, 1455*m*, 1395*m*, 1360*m*, 1340*m*, 1315*m*, 1290*m*, 1250*m*, 1115*s*, 1085*s*, 1030*s*, 1005*s*, 950*m*, 915*m*. ^{1}H-NMR ($CDCl_3$; **20**/**22** 1:5): signals of **22**: 3.15 (*s*, 0.85 H, OH–C(5)); 3.57 (*dd*, *J* = 10.9, 9.7, 0.85 H, H–C(6)); 3.79–3.83 (*m*, 1.7 H, H–C(4), H–C(5)); 4.03 (*dd*, *J* = 6.6, 3.1, 0.85 H, H–C(3)); 4.30 (*dd*, *J* = 10.9, 4.7, 0.85 H, H′–C(6)); 4.48 (*d*, *J* = 3.1, 0.85 H, H–C(2)); 4.62 (*d*, *J* = 12.0, 0.85 H, PhCH_2); 4.87 (*d*, *J* = 11.0, 0.85 H, PhCH_2); 5.00 (*d*, *J* = 12.9, 0.85 H, PhCH_2); 5.08 (*d*, *J* = 11.0, 0.85 H, PhCH_2); 5.28 (*s*, 0.85 H, PhC*H*); 7.24–7.53 (*m*, 15 arom. H); signals of **20**: 2.83 (*d*, *J* = 11.4, 0.15 H, OH–C(5)); 4.44 (*d*, *J* = 1.3, 0.15 H, H–C(2)); 5.40 (*s*, 0.15 H, PhC*H*). ^{13}C-NMR ($CDCl_3$; **20**/**22** 1:5): signals of **22**: 63.52; 66.04; 70.25; 72.48; 74.72; 77.96; 81.42; 100.96; 117.23; 125.76–129.02 (several); 135.26; 136.22; 136.97; signals of **20**: 62.41; 65.68; 72.28; 75.47; 76.57; 101.02; 117.34; 135.38; 137.06. FAB-MS: 446 (16), 91 (100).

2,3-Di-O-*benzyl-4,6*-O-*benzylidene-5*-O-*(tol-4-ylsulfonyl)*-D-*galactononitrile* (**23**) *and 2,3-Di*-O-*benzyl-4,6*-O-*benzylidene-5*-O-*(tol-4-ylsulfonyl)*-L-*altrononitrile* (**24**). A mixture of toluene-4-sulfonyl chloride (700 mg, 3.67 mmol), 4-(dimethylamino)pyridine (20 mg, cat.), and **20**/**22** 1:5 (164 mg, 0.368 mmol) in pyridine (10 ml) was stirred at 75° for 48 h and then concentrated until formation of a precipitate. The residue was treated with sat. aq. $NaHCO_3$ soln., stirred for 30 min, and then worked up as usual ($CHCl_3$, sat. aq. $NaHCO_3$ soln., H_2O). FC (toluene/AcOEt 33:1) afforded **23** (28 mg, 13%) as colorless crystals and **24** (153 mg, 69%) as a colourless oil.

Data of **23**: R_f (hexane/AcOEt 2:1) 0.57. M.p. 113–114°. $[\alpha]_D^{25} = +7.7$ (*c* = 1.0, $CHCl_3$). IR ($CHCl_3$): 3070*m*, 3040*m*, 2880*m*, 1955*w*, 1710*w*, 1600*m*, 1500*m*, 1455*m*, 1400*m*, 1365*s*, 1340*s*, 1305*m*, 1175*s*, 1150*m*, 1120*s*, 1095*s*, 1045*s*, 1030*s*, 1000*s*, 950*m*, 900*s*. ^{1}H-NMR ($CDCl_3$): 2.43 (*s*, Me); 3.93 (*d*, *J* = 13.3, H–C(6)); 4.13 (*dd*, *J* = 9.2, 1.5, H–C(3)); 4.21 (*dd*, *J* = 9.2, 1.2, H–C(4)); 4.38 (*dd*, *J* = 13.3, 1.6, H′–C(6)); 4.45 (*d*, *J* = 1.3, H–C(2)); 4.54 (*d*, *J* = 12.0, 1 H, PhCH_2); 4.85 (*d*, *J* = 9.9, 1 H, PhCH_2); 4.93 (*d*, *J* = 12.0, 1 H, PhCH_2); 5.00 (br. *s*, H–C(5)); 5.09 (*d*, *J* = 9.9, 1 H, PhCH_2); 5.37 (*s*, PhC*H*); 7.18–7.55 (*m*, 17 arom. H); 7.87 (*d*, *J* = 8.4, 2 arom. H). ^{13}C-NMR ($CDCl_3$): 21.69 (*q*); 65.18 (*d*); 68.45 (*t*); 71.55 (*d*); 72.51 (*t*); 74.69 (*t*); 75.80 (*d*); 76.43 (*d*); 101.40 (*d*); 117.33 (*s*); 126.10–129.97 (several *d*); 134.66 (*s*); 135.30 (*s*); 136.83 (*s*); 136.96 (*s*); 145.06 (*s*). FAB-MS: 600 (4, $[M + H]^+$), 375 (4), 181 (8), 91 (100). Anal. calc. for $C_{34}H_{33}NO_7S$ (599.70): C 68.10, H 5.55, N 2.34; found: C 68.02, H 5.58, N 2.57.

Data of **24**: R_f (hexane/AcOEt 2:1) 0.63. $[\alpha]_D^{25} = +6.7$ (*c* = 1.0, $CHCl_3$). IR ($CHCl_3$): 3070*w*, 3010*m*, 2960*w*, 2875*w*, 1695*m*, 1600*w*, 1495*w*, 1455*m*, 1395*w*, 1340*m*, 1260*s*, 1175*s*, 1095*s*, 1030*s*, 930*w*, 905*m*. ^{1}H-NMR ($CDCl_3$): 2.38 (*s*, Me); 3.80 (*dd*, *J* = 10.6, 10.0, H–C(6)); 3.93 (*dd*, *J* = 8.1, 1.2, H–C(3)); 4.22 (*dd*, *J* = 9.5, 1.2, H–C(4)); 4.33 (*d*, *J* = 8.1, H–C(2)); 4.44 (*dd*, *J* = 10.6, 5.3, H′–C(6)); 4.47 (*d*, *J* = 11.3, 1 H, PhCH_2); 4.70 (*d*, *J* = 11.8, 1 H, PhCH_2); 4.78 (*d*, *J* = 11.5, 1 H, PhCH_2); 4.79 (*d*, *J* = 11.4, 1 H, PhCH_2); 4.99 (*td*, *J* = 9.7, 5.3, H–C(5)); 5.51 (*s*, PhC*H*); 7.18–7.50 (*m*, 17 arom. H); 7.72 (*d*, *J* = 8.3, 2 arom. H). ^{13}C-NMR ($CDCl_3$): 21.70 (*q*); 68.57 (*t*); 69.02 (*d*); 69.18 (*d*); 73.10 (*t*); 74.76 (*t*); 78.70 (*d*); 78.92 (*d*); 101.81 (*d*); 116.58 (*s*); 125.38–130.17 (several *d*); 132.75 (*s*); 135.92 (*s*); 136.56 (*s*); 137.37 (*s*); 145.63 (*s*). FAB-MS: 600 (13, $[M + H]^+$), 181 (20), 91 (100). Anal. calc. for $C_{34}H_{33}NO_7S$ (599.70): C 68.10, H 5.55, N 2.34; found: C 68.23, H 5.72, N 2.18.

*(4*S*,5*S*,5a*S*,7*S*,9a*R*)-4,5-Bis(benzyloxy)-5,5a,9,9a-tetrahydro-7-phenyl-4*H*,7*H*-[1,3]dioxino[4,5-e]tetrazolo[1,5-a]pyridine* (**25**). A soln. of **24** (112 mg, 0.187 mmol) and NaN_3 (150 mg, 2.31 mmol) in dry DMSO (5 ml) was stirred at 120° for 12 h. After cooling, the soln. was diluted with H_2O (10 ml) and worked up as usual (AcOEt,

H_2O), affording a pale yellow oil. Crystallization from $CHCl_3$/pentane afforded pure **25** (68 mg, 77%). R_f (hexane/AcOEt 1:1) 0.41. M.p. 153–154°. $[\alpha]_D^{25} = +76.3$ ($c = 1.0$, $CHCl_3$). IR ($CHCl_3$): 3070*m*, 3010*m*, 2870*m*, 1955*w*, 1605*w*, 1500*w*, 1455*m*, 1395*m*, 1365*m*, 1325*m*, 1295*w*, 1260*m*, 1160*m*, 1095*s*, 1040*s*, 1030*s*, 990*m*, 915*w*. ^{1}H-NMR ($CDCl_3$): 3.97 (*dd*, $J = 8.5, 1.9$, H–C(5)); 4.22–4.23 (*m*, H–C(9a)); 4.30 (*dd*, $J = 12.9, 1.8$, H–C(9)); 4.64 (*t*, $J = 1.9$, H–C(5a)); 4.83 (*d*, $J = 12.1$, 1 H, PhCH_2); 4.92 (*d*, $J = 12.1$, 1 H, PhCH_2); 5.01 (*d*, $J = 10.9$, 1 H, PhCH_2); 5.19 (*dd*, $J = 12.9, 1.3$, H′–C(9)); 5.24 (*d*, $J = 8.5$, H–C(4)); 5.48 (*d*, $J = 10.8$, 1 H, PhCH_2); 5.57 (*s*, H–C(7)); 7.26–7.50 (*m*, 15 arom. H). ^{13}C-NMR ($CDCl_3$): 52.14 (*d*); 67.22 (*t*); 72.14 (*d*); 73.45 (*t*); 73.94 (*d*); 74.77 (*t*); 78.60 (*d*); 101.34 (*d*); 126.11–129.48 (several *d*); 136.41 (*s*); 137.31 (*s*); 137.41 (*s*); 154.24 (*s*). FAB-MS: 471 (85, $[M + H]^+$), 91 (100). Anal. calc. for $C_{27}H_{26}N_4O_4$ (470.53): C 68.92, H 5.57, N 11.91; found: C 69.16, H 5.63, N 11.90.

*(4*S*,5*S*,5a*S*,7*S*,9a*R*)-5,5a,9,9a-Tetrahydro-7-phenyl-4*H*,7*H*-[1,3]dioxino[4,5-*e*]tetrazolo[1,5-*a*]pyridine-4,5-diol* (**26**). A soln. of **25** (1.13 g, 2.40 mmol) and AcOH (0.1 ml) in MeOH (20 ml) was treated with 10% Pd/C (500 mg) and hydrogenated at 6 bar for 7 d. The suspension was diluted with MeOH and filtered through *Celite* which was washed thoroughly with MeOH. Evaporation of the combined filtrate and washings followed by FC (AcOEt) afforded **26** (552 mg, 79%) as a colorless glass and **6** (43 mg, 9%) as a white solid. **26**: R_f (AcOEt) 0.27. M.p. 178–179°. $[\alpha]_D^{25} = +10.3$ ($c = 0.8$, MeOH). IR (KBr): 3240*vs* (br.), 2870*m*, 1975*w*, 1910*w*, 1840*w*, 1720*w*, 1700*w*, 1685*w*, 1655*w*, 1635*w*, 1540*m*, 1520*w*, 1500*m*, 1450*s*, 1395*s*, 1370*m*, 1345*m*, 1325*m*, 1305*m*, 1265*m*, 1245*m*, 1225*m*, 1160*s*, 1135*s*, 1110*s*, 1085*s*, 1025*s*, 990*s*, 950*m*, 930*m*. ^{1}H-NMR (CD_3OD): 4.04 (*dd*, $J = 8.9, 2.0$, H–C(5)); 4.48 (*dd*, $J = 12.9, 1.9$, 1 H, H–C(9)); 4.60 (*m*, H–C(9a)); 4.79 (*t*, $J = 2.1$, H–C(5a)); 5.06 (br. *d*, $J = 8.9$, H–C(4)); 5.08 (*dd*, $J = 12.9, 1.5$, 1 H, H′–C(9)); 5.73 (*s*, H–C(7)); 7.29 (*s*, 5 arom. H). ^{13}C-NMR (CD_3OD): 54.19 (*d*); 66.39 (*d*); 68.30 (*t*); 74.01 (*d*); 77.58 (*d*); 102.35 (*d*); 127.27 (2*d*); 129.19 (2*d*); 130.24 (*d*); 138.83 (*s*); 157.17 (*s*). FAB-MS: 581 (9, $[2M + H]^+$), 291 (100, $[M + H]^+$). Anal. calc. for $C_{13}H_{14}N_4O_4$ (290.28): C 53.79, H 4.86, N 19.30; found: C 53.59, H 5.00, N 19.19.

*(5*R*,6*S*,7*S*,8*S*)-7,8-Bis(benzyloxy)-5-(hydroxymethyl)-5,6,7,8-tetrahydrotetrazolo[1,5-*a*]pyridin-6-ol* (**27**). A soln. of **25** (1.64 g, 3.49 mmol) in MeOH (50 ml) was treated with aq. 1N HCl (5 ml) and stirred at 60° for 6 h. After cooling and treatment with sat. aq. $NaHCO_3$ soln., normal workup (AcOEt, H_2O) and FC (hexane/AcOEt 3:1) afforded **27** (1.31 g, 98%) as a colorless oil which crystallized after several h *i.v.* R_f (hexane/AcOEt 1:1) 0.17. M.p. 107–108°. $[\alpha]_D^{25} = +52.0$ ($c = 1.0$, $CHCl_3$). IR ($CHCl_3$): 3575*s*, 3420*m* (br.), 3090*m*, 3070*m*, 3010*m*, 2875*m*, 1955*w*, 1880*w*, 1810*w*, 1600*m*, 1495*m*, 1455*s*, 1400*m*, 1361*m*, 1330*m*, 1260*m*, 1100*s*, 1030*s*, 1015*s*, 910*m*. ^{1}H-NMR ($CDCl_3$): 3.00–3.04 (*m*, OH–C(6), OHCH_2–C(5)); 4.00 (*dd*, $J = 7.2, 2.2$, H–C(7)); 4.27 (*ddd*, $J = 12.2, 9.0, 4.9$, CH–C(5)); 4.40 (*ddd*, $J = 12.3, 5.3, 4.5$, CH′–C(5)); 4.50 (*m*, H–C(5)); 4.60 (*dd*, $J = 5.3, 2.8$, H–C(6)); 4.76 (*d*, $J = 11.7$, 1 H, PhCH_2); 4.84 (*d*, $J = 11.7$, 1 H, PhCH_2); 5.00 (*d*, $J = 11.4$, 1 H, PhCH_2); 5.04 (*d*, $J = 7.2$, H–C(8)); 5.31 (*d*, $J = 11.4$, 1 H, PhCH_2); 7.29–7.49 (*m*, 10 arom. H). ^{13}C-NMR ($CDCl_3$): 60.23 (*d*); 60.75 (*t*); 68.00 (*d*); 71.30 (*d*); 73.46 (*t*); 74.36 (*t*); 80.23 (*d*); 128.36–128.94 (several *d*); 137.40 (2*d*); 153.48 (*s*). FAB-MS: 383 (100, $[M + H]^+$), 91 (94). Anal. calc. for $C_{20}H_{22}N_4O_4$ (382.42): C 62.82, H 5.80, N 14.65; found: C 63.10, H 5.91, N 14.60.

*(5*R*,6*S*,7*S*,8*S*)-6,7,8-Tris(benzyloxy)-5-[(benzyloxy)methyl]-5,6,7,8-tetrahydrotetrazolo[1,5-*a*]pyridine* (**16**). A stirred soln. of **27** (398 mg, 1.04 mmol) in benzyl bromide (1.5 ml) was treated with NaH (100 mg, 4.17 mmol) and heated at 60° for 5 h. Excess NaH was destroyed with MeOH (5 ml) and the soln. evaporated. FC (hexane/AcOEt 9:1→4:1) afforded **16** (469 mg, 80%) as a colorless oil which crystallized *i.v.*

*2,3,4,6-Tetra-*O*-benzyl-1,5-dideoxy-1,5-imino-*D*-galactitol* (**28**). A soln. of **16** (460 mg, 0.818 mmol) in dry Et_2O (20 ml) was added dropwise to a stirred suspension of $LiAlH_4$ (400 mg, 10.5 mmol) in Et_2O (20 ml). After 5 h, the mixture was poured onto ice-water (100 ml), to which were added Et_2O (100 ml) and aq. NaOH soln. (5 g in 100 ml). Normal workup (Et_2O, H_2O, brine), evaporation, and FC (hexane/AcOEt 1:1) afforded **28** (334 mg, 78%). Colorless oil. R_f (AcOEt) 0.52. $[\alpha]_D^{25} = +12.5$ ($c = 1.0$, $CHCl_3$). IR: 3065*w*, 3010*m*, 2870*m*, 1940*w*, 1875*w*, 1805*w*, 1605*w*, 1495*w*, 1455*m*, 1365*m*, 1260*m*, 1095*s*, 1030*m*, 910*w*. ^{1}H-NMR ($CDCl_3$): 1.66 (br. *s*, NH); 2.49 (*dd*, $J = 12.9, 10.4$, H_a–C(1)); 2.79 (*td*, $J \approx 6.8, 1.1$, H–C(5)); 3.28 (*dd*, $J = 12.8, 5.3$, H_e–C(1)); 3.55 (*dd*, $J = 9.8, 7.2$, H–C(6)); 3.48 (*dd*, $J = 8.8, 6.5$, H′–C(6)); 3.49 (*dd*, $J = 9.4, 2.4$, H–C(3)); 3.90 (*td*, $J \approx 9.3, 5.2$, H–C(2)); 3.98 (*dd*, $J = 1.3, < 1$, H–C(4)); 4.43 (*d*, $J = 11.8$, 1 H, PhCH_2); 4.49 (*d*, $J = 11.8$, 1 H, PhCH_2); 4.57 (*d*, $J = 11.3$, 1 H, PhCH_2); 4.68 (*d*, $J = 11.6$, 1 H, PhCH_2); 4.76–4.84 (*m*, 3 H, PhCH_2); 4.97 (*d*, $J = 11.3$, 1 H, PhCH_2); 7.26–7.43 (*m*, 20 arom. H). ^{13}C-NMR ($CDCl_3$): 48.82 (*t*); 58.33 (*d*); 70.04 (*t*); 72.44 (*t*); 72.92 (*t*); 73.26 (*t*); 74.26 (*t*); 74.68 (*d*); 77.10 (*d*); 84.71 (*d*); 127.29–128.25 (several *d*); 137.81 (*s*); 138.71 (3*s*). FAB-MS: 524 (73, $[M + H]^+$), 402 (18), 91 (100). Anal. calc. for $C_{34}H_{37}NO_4$ (523.67): C 77.98, H 7.12, N 2.67; found: C 78.00, H 7.40, N 2.44.

*1,5-Dideoxy-1,5-imino-*D*-galactitol* (**8**). A soln. of **28** (134 mg, 0.256 mmol) and AcOH (*ca.* 0.05 ml) in MeOH (5 ml) was treated with 10% Pd/C (200 mg) and hydrogenated at 6 bar for 48 h at r.t. The suspension was filtered through *Celite* and the solid residue washed with MeOH. Evaporation of the filtrate followed by FC (NH_3 in $CHCl_3$/MeOH 3:1) and precipitation from MeOH/acetone gave **8**·HOAc, which was treated with 1N aq. HCl and

lyophilized several times, affording **8**·HCl (47 mg, 92%). Hygroscopic white solid. $[\alpha]_D^{25} = +41.7$ ($c = 0.3$, H_2O; [16]: $[\alpha]_{D'} = +46.1$ (H_2O)). ^{1}H-NMR (500 MHz, D_2O): 2.87 (*dd*, $J = 12.4, 11.6$, H_a–C(1)); 3.41 (*ddd*, $J = 8.8, 4.8, 1.3$, H–C(5)); 3.51 (*dd*, $J = 12.5, 5.4$, H_e–C(1)); 3.63 (*dd*, $J = 9.7, 3.0$, H–C(3)); 3.80 (*dd*, $J = 12.2, 8.8$, H–C(6)); 3.87 (*dd*, $J = 12.2, 4.8$, H′–C(6)); 4.07 (*ddd*, $J = 11.5, 9.7, 5.4$, H–C(2)); 4.16 (*dd*, $J = 3.0, 1.3$, H–C(4)).

Dehydration of **29**. *a*) A suspension of **29** (3.0 g, 5.9 mmol) [28] and PPh_3 (4.65 g, 17.7 mmol) in MeCN/THF 1:3 (120 ml) was treated with pyridine (1.8 g, 22.8 mmol) and warmed until a clear soln. was formed. A soln. of CBr_4 (5.88 g, 17.7 mmol) in MeCN (30 ml) was added dropwise over 10 min (exothermic reaction→40°), and stirring was continued for 25 min. The soln. was treated with MeOH (90 ml), stirred for 15 min, and evaporated. FC (hexane/AcOEt 1:1) gave **30** (1.058 g, 36%) and **31** (0.153 g, 7%).

b) A mixture of **29** (9.2 g, 18.2 mmol) and diphenyl disulfide (12.0 g, 55 mmol) was dried *i.v.* for 40 min, dissolved in dry THF (140 ml), and treated with a soln. of Bu_3P (*ca.* 85%; 13.0 g, 55 mmol) in THF (40 ml). After stirring at r.t. for 35 min, MeOH (180 ml) was added and stirring continued for 10 min. The soln. was concentrated and filtered through silica gel (hexane→hexane/AcOEt 2:3) to give a greenish oil. FC (hexane/AcOEt 1:1) yielded **30** (7.0 g, 79%). Yellow oil.

*2-Acetamido-3,4,6-tri-*O*-benzyl-2-deoxy-*D*-gluconolactone* (**30**): R_f (hexane/AcOEt 2:3) 0.30. $[\alpha]_D^{25} = +20.3$ ($c = 0.56$, $CHCl_3$). IR ($CHCl_3$): 3565*m*, 3428*m*, 3089*w*, 3067*w*, 3007*m*, 2925*m*, 2870*m*, 1952*w*, 1878*w*, 1811*w*, 1684*s*, 1496*s*, 1454*m*, 1399*m*, 1369*m*, 1095*s*, 1028*m*, 909*m*. ^{1}H-NMR (200 MHz, $CDCl_3$): 1.86 (*s*, AcN); 2.71 (*d*, $J = 7.1$, OH–C(5)); 3.57–3.66 (*m*, H–C(4), 2H–C(6)); 3.84 (*tt*, $J \approx 5.6, 7.2$, H–C(5)); 4.02 (*dd*, $J = 3.2, 5.5$, H–C(3)); 4.49 (*d*, $J = 12.0$, 1H, PhCH_2); 4.52 (*d*, $J = 11.3$, 1H, PhCH_2); 4.55 (*d*, $J = 12.6$, 1H, PhCH_2); 4.63 (*d*, $J = 11.3$, 1H, PhCH_2); 4.79 (*s*, PhCH_2); 5.23 (*dd*, $J = 3.2, 8.3$, H–C(2)); 6.22 (*d*, $J = 8.2$, NH); 7.20–7.40 (*m*, 15 arom. H). ^{13}C-NMR ($CDCl_3$): 22.61 (*q*); 41.99 (*d*); 70.30 (*t*); 70.47 (*d*); 73.41 (*t*); 74.37 (*t*); 75.05 (*t*); 78.30 (*d*); 78.95 (*d*); 117.81 (*s*); 127.75–128.53 (several *d*); 136.86 (*s*); 137.36 (2*s*); 169.67 (*s*). FAB-MS: 977 (7, $[2M + H]^+$), 490 (35), 489 (99, $[M + H]^+$), 462 (11), 381 (14), 306 (15), 288 (10), 181 (27), 91 (100). Anal. calc. for $C_{29}H_{32}N_2O_5$ (488.58): C 71.29, H 6.60, N 5.73; found: C 71.34, H 6.65, N 5.72.

*2-Acetamido-4,6-di-*O*-benzyl-2,3-dideoxy-*D*-gluc-2-eno-1,5-lactone* (**31**). An anal. sample was crystallized from Et_2O/hexane. R_f (hexane/AcOEt 2:3) 0.56. M.p. 63–65°. IR ($CHCl_3$): 3400*m*, 3090*w*, 3067*w*, 3007*m*, 2869*m*, 1725*s*, 1695*s*, 1655*w*, 1511*s*, 1454*m*, 1395*m*, 1371*m*, 1341*m*, 1309*m*, 1172*m*, 1074*m* (br.), 1028*m*. ^{1}H-NMR (200 MHz, $CDCl_3$): 2.14 (*s*, AcN); 3.69 (*dd*, $J = 3.8, 10.6$, H–C(6)); 3.76 (*dd*, $J = 3.5, 10.5$, H′–C(6)); 4.46–4.65 (*m*, 5H, H–C(4), H–C(5), PhCH_2); 4.70 (*d*, $J = 11.4$, 1H, PhCH_2); 7.25–7.41 (*m*, 10 arom. H); 7.63 (*d*, $J = 3.7$, H–C(3)); 7.78 (br. *s*, NH). ^{13}C-NMR ($CDCl_3$): 24.45 (*q*); 68.11 (*t*); 68.38 (*d*); 71.15 (*t*); 73.44 (*t*); 80.26 (*d*); 120.94 (*d*); 125.11 (*s*); 127.61–128.46 (several *d*); 136.99 (*s*); 137.31 (*s*); 161.12 (*s*); 169.08 (*s*). CI-MS: 382 (2, $[M + H]^+$), 290 (16), 108 (20), 91 (100).

*2-Acetamido-3,4,6-tri-*O*-benzyl-*D*-xylo-hex-5-ulosononitrile* (**32**). A soln. of **30** (6.37 mg, 13.1 mmol) in dry DMSO (70 ml) was treated with Et_3N (10.6 g, 105 mmol) and cooled to 15° (→turbid mixture). A soln. of pyridine·SO_3 (11.7 g, 73.5 mmol) in DMSO (50 ml) was added over 15 min ($T < 20°$). Stirring at r.t. was continued for 65 min, toluene/H_2O 2:1 (300 ml) was added to the slightly cooled soln., and the mixture was vigorously stirred for 20 min. Normal workup (toluene, H_2O, sat. aq. NaCl soln.) and filtration of the crude through silica gel (hexane/AcOEt 2:3) afforded **32** (6.16 g, *ca.* 97%). IR ($CHCl_3$): 3494*m*, 3433*m*, 3090*w*, 3067*m*, 3008*m*, 2927*m*, 2872*m*, 1953*w*, 1877*w*, 1812*w*, 1732*m*, 1660*s* (br.), 1497*m*, 1454*m*, 1384*s*, 1104*s* (br.), 1028*m*, 913*m*. ^{1}H-NMR (200 MHz, $CDCl_3$): 1.75–2.13 (several *s*, 3H); 3.42–5.61 (*m*, 12H); 7.13–7.38 (*m*, 15 arom. H). CI-MS (NH_3); 487 (5, $[M + H]^+$), 427 (7), 379 (6), 181 (6), 108 (11), 91 (100).

*2-Acetamido-3,4,6-tri-*O*-benzyl-2-deoxy-*L*-idononitrile* (**33**). A soln. of **32** (5.95 g, 12.2 mmol) and $CeCl_3 \cdot 6\,H_2O$ (4.3 g, 12.2 mmol) in MeOH (200 ml) was cooled to −35 to −40°. $NaBH_4$ (1.4 g, 37.8 mmol) was added in portions over 25 min. Upon warming to −25° within 25 min, the evolution of gas stopped. The soln. was kept at −20° for 22 h and poured onto phosphate buffer (200 ml; prepared by the addn. of aq. NaOH soln. to a soln. of 10 g of $NaH_2PO_4 \cdot 2\,H_2O$ in 100 ml of H_2O until pH *ca.* 6). After concentration to about half its volume, the remaining mixture was diluted with phosphate buffer and worked up as usual (AcOEt, phosphate buffer, sat. aq. NaCl) to give **33**/**30** 95:5 (5.71 g, 96%). The **33**/**30** ratio was determined by HPLC (*Si60 S5W*, 4 × 250 mm; THF/hexane 2:8, 2 ml/min; UV 254 nm). R_f (hexane/AcOEt 2:3) 0.29. IR ($CHCl_3$); 3570*m*, 3429*m*, 3090*w*, 3067*m*, 3007*m*, 2920*m*, 2868*m*, 1953*w*, 1877*w*, 1812*w*, 1688*s*, 1496*s*, 1454*m*, 1371*m*, 1276*m*, 1092*s*, 1028*m*, 914*w*. ^{1}H-NMR ($CDCl_3$): 1.93 (*s*, AcN); 2.48 (*d*, $J = 6.9$, OH–C(5)); 3.40 (*dd*, $J = 6.1, 9.3$, H–C(6)); 3.52 (*dd*, $J = 6.4, 9.3$, H′–C(6)); 3.62 (*dd*, $J = 2.3, 7.1$, H–C(4)); 3.98 (*dq*, $J \approx 2.1, 6.1$, H–C(5)); 4.06 (*dd*, $J = 2.7, 7.1$, H–C(3)); 4.44 (*d*, $J = 11.8$, 1H, PhCH_2); 4.50 (*d*, $J = 11.8$, 1H, PhCH_2); 4.53 (*d*, $J = 11.2$, 1H, PhCH_2); 4.71 (*d*, $J = 11.4$, 1H, PhCH_2); 4.75 (*d*, $J = 10.9$, 1H, PhCH_2); 4.82 (*d*, $J = 10.7$, 1H, PhCH_2); 5.25 (*dd*, $J = 2.7, 8.9$, H–C(2)); 6.39 (*d*, $J = 9.0$, NH); 7.22–7.40 (*m*, 15 arom. H); irrad. at 5.25→6.39 (*s*); 4.06 (*d*, $J = 7.1$). ^{13}C-NMR ($CDCl_3$): 22.65 (*q*); 41.25 (*d*); 68.62 (*d*); 70.61 (*t*); 73.26 (*t*); 74.80 (*t*); 75.09 (*t*); 77.98 (*d*); 78.10 (*d*); 117.78 (*s*); 127.81–128.51 (several *d*); 136.74 (*s*);

137.29 (*s*); 137.57 (*s*); 169.65 (*s*). FAB-MS: 977 (2, $[2M + H]^+$), 490 (13), 489 (33, $[M + H]^+$), 381 (11), 181 (25), 91 (100).

*2-Acetamido-3,4,6-tri-*O*-benzyl-2-deoxy-5-*O*-(tol-4-ylsulfonyl)-*L*-idononitrile* (**34**). A soln. of **33** (4.5 g, 9.2 mmol) in pyridine (180 ml) was treated with toluene-4-sulfonyl chloride (18.0 g, 94.4 mmol) and stirred at 55–60° for 4.5 h. The soln. was concentrated to *ca.* 60 ml and poured onto sat. aq. $NaHCO_3$ soln. (600 ml). After 15 min of vigorous stirring, the mixture was worked up as usual ($CHCl_3$, sat. aq. $NaHCO_3$ soln.). The residue was co-evaporated with toluene. FC (toluene/AcOEt 5:1) yielded **34** (5.0 g, 85%). An anal. sample was crystallized in EtOH/H_2O and recrystallized from AcOEt/Et_2O/hexane. R_f (toluene/AcOEt 5:1) 0.21. M.p. 87–87.5°. $[\alpha]_D^{25} = 0.0$ ($c = 0.88$, $CHCl_3$). IR ($CHCl_3$): 3431*m*, 3090*w*, 3067*w*, 3007*m*, 2927*m*, 2872*m*, 1952*m*, 1810*m*, 1689*s*, 1599*m*, 1496*s*, 1455*m*, 1402*w*, 1369*s*, 1308*w*, 1282*w*, 1177*s*, 1095*m*, 1040*s*, 1028*m*, 975*w*, 907*m*. ^{1}H-NMR ($CDCl_3$): 1.86 (*s*, AcN); 2.43 (*s*, Me); 3.44 (*dd*, $J = 4.9$, 10.6, H–C(6)); 3.62 (*dd*, $J = 5.8$, 10.5, H′–C(6)); 3.78 (*dd*, $J = 3.7$, 7.3, H–C(4)); 3.96 (*dd*, $J = 2.4$, 7.3, H–C(3)); 4.28 (*s*, PhCH_2); 4.61 (*d*, $J = 11.3$, 1 H, PhCH_2); 4.68 (*d*, $J = 11.5$, 1 H, PhCH_2); 4.69–4.88 (*m*, 3 H, H–C(5), PhCH_2); 5.08 (*dd*, $J = 2.4$, 9.0, H–C(2)); 5.89 (*d*, $J = 8.8$, NH); 7.14–7.39 (*m*, 17 arom. H); 7.79–7.82 (*m*, 2 arom. H); irrad. at 5.08→5.89 (*s*); 3.96 (*d*, $J = 7.4$). ^{13}C-NMR ($CDCl_3$): 21.66 (*q*); 22.52 (*q*); 41.14 (*d*); 67.11 (*t*); 73.06 (*t*); 75.08 (*t*); 75.65 (*t*); 76.75 (*d*); 78.10 (*d*); 78.23 (*d*); 117.47 (*s*); 127.62–129.95 (several *d*); 133.07 (*s*); 136.61 (*s*); 137.18 (2*s*); 145.27 (*s*); 169.43 (*s*). FAB-MS: 1285 (1, $[2M + H]^+$), 644 (10), 643 (22, $[M + H]^+$), 181 (15), 91 (100). Anal. calc. for $C_{36}H_{38}N_2O_7S$ (642.77): C 67.27, H 5.96, N 4.36; found: C 67.24, H 6.08, N 4.20.

Treatment of **34** *with* NaN_3. *a*) A soln. of **34** (368 mg, 0.57 mmol) and NaN_3 (394 mg, 6 mmol) in DMSO (3.5 ml) was stirred at 120–130° for 3 h and worked up as usual (AcOEt, H_2O). FC (hexane/AcOEt 2:3) gave **36a** (16 mg, 5%) and **35a** (86 mg, 29%).

b) A soln. of **34** (110 mg, 0.17 mmol) in MeOH (6 ml) was treated with NaN_3 (2.0 g, 31 mmol) and H_2O (4 ml) and boiled under reflux for 16 h. The solvent was partially distilled off. Normal workup (AcOEt, H_2O) and FC (hexane/AcOEt 2:3) yielded **36a** (9 mg, 10%) and **36a**/**35a** 1:2 (11 mg, 13%).

*(5*R*,6*R*,7*R*,8*S*)-8-Acetamido-6,7-bis(benzyloxy)-5-[(benzyloxy)methyl]-5,6,7,8-tetrahydrotetrazolo[1,5-*a*]-pyridine* (**35a**): R_f (hexane/AcOEt 2:3) 0.13. M.p. 113.5–114.5°. (AcOEt/hexane). $[\alpha]_D^{25} = +12.7$ ($c = 0.66$, $CHCl_3$). IR ($CHCl_3$): 3437*m*, 3089*w*, 3067*w*, 3007*m*, 2928*w*, 2872*m*, 1954*w*, 1877*w*, 1810*w*, 1681*s*, 1603*w*, 1498*s*, 1455*m*, 1370*m*, 1340*m*, 1295*w*, 1261*w*, 1099*s*, 1028*m*. ^{1}H-NMR ($CDCl_3$; *ca.* 0.02M): 1.87 (*s*, AcN); 4.00 (*d*, $J = 6.3$, CH_2–C(5)); 4.11 (*dd*, $J = 3.6$, 5.4, H–C(7)); 4.41 (*dd*, $J = 3.1$, 5.4, H–C(6)); 4.50 (*s*, PhCH_2); 4.59 (*d*, $J = 11.4$, 1 H, PhCH_2); 4.63 (*d*, $J = 12.1$, 1 H, PhCH_2); 4.67 (*d*, $J = 12.0$, 1 H, PhCH_2); 4.75 (*d*, $J = 11.8$, 1 H, PhCH_2); 4.89 (*dt*, $J \approx 3.0$, 6.3, H–C(5)); 5.67 (*dd*, $J = 3.4$, 8.9, H–C(8)); 6.17 (*d*, $J = 8.8$, NH); 7.17–7.38 (*m*, 15 arom. H); irrad. at 5.67→6.17 (*s*); 4.11 (*d*, $J = 5.4$). ^{1}H-NMR (200 MHz, $CDCl_3$; *ca.* 0.08M): *Table*. ^{1}H-NMR (CD_3OD; *ca.* 0.015M): *Table*; irrad. at 5.23→4.13 (*d*, $J = 8.0$). ^{13}C-NMR (50 MHz, $CDCl_3$; *ca.* 0.08M): 22.94 (*q*); 44.02 (*d*); 59.71 (*d*); 67.82 (*t*); 73.32 (*t*); 73.47 (2*t*); 73.69 (*d*); 77.20 (*d*); 127.78–128.67 (several *d*); 136.47 (*s*); 136.83 (s); 137.12 (*s*); 151.14 (*s*); 169.38 (*s*). FAB-MS: 1027 (1, $[2M + H]^+$), 515 (14), 514 (40, $[M + H]^+$), 91 (57). Anal. calc. for $C_{29}H_{31}N_5O_4$ (513.60): C 67.82, H 6.08, N 13.64; found: C 67.72, H 6.16, N 13.60.

*(5*R*,6*R*,7*R*,8*R*)-8-Acetamido-6,7-bis(benzyloxy)-5-[(benzyloxy)methyl]5,6,7,8-tetrahydrotetrazolo[1,5-*a*]-pyridine* (**36a**): R_f (hexane/AcOEt 2:3) 0.19 M.p. 89–90° (AcOEt/hexane). $[\alpha]_D^{25} = +5.8$ ($c = 0.33$, $CHCl_3$). IR ($CHCl_3$): 3441*m*, 3276*w*, 3089*w*, 3067*w*, 3007*m*, 2928*w*, 2871*m*, 1953*w*, 1878*w*, 1811*w*, 1681*s*, 1602*w*, 1498*s*, 1455*s*, 1369*m*, 1341*w*, 1273*m*, 1136*m*, 1076*s*, 1028*m*, 993*m*, 913*w*. ^{1}H-NMR ($CDCl_3$; *ca.* 0.02M): 1.95 (*s*, AcN); 3.73 (*dd*, $J \approx 9.2$, 10.0, CH–C(5)); 4.09 (*dd*, $J = 5.1$, 9.1, CH′–C(5)); 4.15 (*t*, $J \approx 4.0$, H–C(7)); 4.23 (*d*, $J = 11.8$, 1 H, PhCH_2); 4.37 (*d*, $J = 11.7$, 1 H, PhCH_2); 4.42 (br. *d*, $J = 4.7$, H–C(6)); 4.45 (*d*, $J = 11.8$, 1 H, PhCH_2); 4.59 (*d*, $J = 11.8$, 1 H, PhCH_2); 4.61 (*d*, $J = 12.1$, 1 H, PhCH_2); 4.67 (*d*, $J = 12.1$, 1 H, PhCH_2); 4.86 (br. *dd*, $J \approx 5.2$, 10.1, H–C(5)); 5.80 (*dd*, $J = 3.7$, 8.4, H–C(8)); 6.30 (*d*, $J = 8.5$, NH); 7.05–7.09 (*m*, 2 arom. H); 7.25–7.39 (*m*, 13 arom. H); irrad. at 5.80→6.30 (*s*); 4.15 (*d*, $J = 4.5$); irrad. at 4.86→4.09 (changed), 3.73 (changed). ^{1}H-NMR (CD_3OD): *Table*; irrad. at 5.75→4.04 (*d*, $J = 4.7$); irrad. at 4.95→4.43 (*d*, $J = 4.7$), 4.03 (changed), 3.81 (changed). ^{13}C-NMR (100 MHz, $CDCl_3$): 22.97 (*q*); 43.70 (*d*); 59.60 (*d*); 69.22 (*t*); 70.24 (*d*); 71.99 (*t*); 73.01 (*t*); 73.60 (*t*); 74.82 (*d*); 127.91–128.78 (several *d*); 136.34 (*s*); 136.42 (*s*); 137.12 (*s*); 151.26 (*s*); 169.96 (*s*). FAB-MS: 1027 (3, $[2M + H]^+$), 515 (39), 514 (100, $[M + H]^+$), 91 (97). Anal. calc. for $C_{29}H_{31}N_5O_4$ (513.60): C 67.82, H 6.08, N 13.64; found: C 67.62, H 6.17, N 13.55.

*(5*R*,6*R*,7*R*,8*S*)-8-Acetamido-6,7-bis(benzyloxy)-5-[(benzyloxy)methyl](8-^{2}H)-5,6,7,8-tetrahydrotetrazolo-[1,5-*a*]pyridine* (**35b**) *and (5*R*,6*R*,7*R*,8*R*)-8-Acetamido-6,7-bis(benzyloxy)-5-[(benzyloxy)methyl](8-^{2}H)-5,6,7,8-tetrahydrotetrazolo[1,5-*a*]pyridine* (**36b**). The tosylate **34** (110 mg, 0.17 mmol) was converted into **35b** and **36b** by the procedure described for **35a**/**36a** but using CD_3OD and D_2O instead of MeOH and H_2O, resp. FC (hexane/AcOEt 2:3) afforded **36b** (4 mg, 5%) and **35b** (4 mg, 5%). *Data of* **35b**: ^{1}H-NMR ($CDCl_3$; *ca.* 0.011M); *Table*. *Data of* **36b**: ^{1}H-NMR ($CDCl_3$): *Table*.

8-Acetamido-5-[(benzyloxy)methyl]tetrazolo[1,5-a]pyridine (**37**). A soln. of **35a** (23 mg, 0.045 mmol) and NaN_3 (27 mg, 0.41 mmol) in DMSO (0.25 ml) was stirred for 24 h at 120°. Dilution of the soln. (AcOEt) and prep. TLC (silica gel *60F-254*, 2 mm; hexane/AcOEt 2:3) afforded a colourless oil, which was crystallized from Et_2O/hexane; **37** (6 mg, 45%). Evaporation of the mother liquor gave a further sample of **37** (impure; 5 mg, *ca.* 38%). R_f (hexane/AcOEt 2:3) 0.30. M.p. 112–113°. IR ($CHCl_3$): 3408*m*, 3295*w*, 3090*w*, 3007*m*, 2924*w*, 2866*m*, 1705*s*, 1642*w*, 1548*s*, 1498*s*, 1454*m*, 1412*m*, 1369*m*, 1329*m*, 1290*m*, 1153*w*, 1116*m*, 1087*m*, 1050*m*, 1006*m*, 908*m*, 846*m*. ^{1}H-NMR ($CDCl_3$): 2.35 (*s*, AcN); 4.78 (*s*, CH_2); 5.08 (*s*, CH_2); 7.29–7.43 (*m*, 6H); 8.59 (*d*, J = 7.8, 1H); 8.66 (br. *s*, NH). FAB-MS: 595 (4, $[2M + H]^+$), 299 (23), 298 (100, $[M + H]^+$), 91 (54).

*(E)- and (Z)-2-Acetamido-4,6-di-O-benzyl-2,3-dideoxy-5-O-(tol-4-ylsulfonyl)-*L-threo-*hex-2-enononitrile* ((*E*)- and (*Z*)-**38**, resp.). A soln. of **34** (100 mg, 0.16 mmol) in dry THF (5 ml) was added to a mixture of $AlCl_3$ (62 mg, 0.47 mmol) and NaN_3 (91 mg, 1.40 mmol). The mixture was heated under reflux for 15 h and worked up as usual (AcOEt, sat. aq. $NaHCO_3$ soln.). FC (hexane/AcOEt 6:4) afforded (*Z*)-**38** (13 mg, 16%) and (*E*)-**38** (28 mg, 34%).

(*Z*)-**38**: R_f (hexane/AcOEt 1:1) 0.33. IR ($CHCl_3$): 3350*m* (br.), 3067*w*, 3038*m*, 2926*w*, 2872*m*, 2233*w*, 2110*w*, 1708*s*, 1640*m*, 1598*m*, 1481*m*, 1455*m*, 1368*s*, 1259*m*, 1176*s*, 1098*m*, 909*m*. ^{1}H-NMR ($CDCl_3$): 1.55 (*s*, AcN); 2.42 (*s*, Me); 3.69 (*dd*, J = 4.2, 11.5, H–C(6)); 3.88 (*dd*, J = 3.7, 11.5, H′–C(6)); 4.34 (*d*, J = 11.5, 1H, PhCH_2); 4.42 (*dd*, J = 6.5, 7.9, H–C(4)); 4.44 (d, J = 11.5, 1H, PhCH_2); 4.46 (*d*, J = 11.5, 1H, PhCH_2); 4.55 (*d*, J = 11.0, 1H, PhCH_2); 4.69 (*td*, $J \approx 4.0$, 6.4, H–C(5)); 5.56 (*dd*, J = 0.8, 8.0, H–C(3)); 7.13–7.38 (*m*, 12 arom. H); 7.74–7.79 (*m*, 2 arom. H); 7.95 (br. *s*, NH). ^{13}C-NMR ($CDCl_3$): 21.72 (*q*); 22.31 (*q*); 68.90 (*t*); 72.28 (*t*); 73.53 (*d*); 74.43 (*t*); 80.88 (*d*); 114.16 (*s*); 114.71 (*s*); 127.57–129.86 (several *d*); 132.93 (*s*); 136.17 (*s*); 136.75 (*s*); 145.42 (*s*); 167.70 (*s*). FAB-MS: 536 (9), 535 (28, $[M + H]^+$), 91 (100).

(*E*)-**38**: R_f (hexane/AcOEt 1:1) 0.19. IR ($CHCl_3$): 3537*w*, 3427*w*, 3344*w*, 3066*w*, 2926*m*, 2869*m*, 2232*w*, 2107*w*, 1705*s*, 1637*m*, 1599*m*, 1496*m*, 1454*m*, 1369*s*, 1175*s*, 1097*s*. 913*s*. ^{1}H-NMR ($CDCl_3$): 2.06 (*s*, AcN); 2.37 (*s*, Me); 3.58 (*dd*, J = 5.4, 10.9, H–C(6)); 3.68 (*dd*, J = 4.5, 10.9, H′–C(6)); 4.33 (*d*, J = 11.9, 1H, PhCH_2); 4.36 (*d*, J = 11.6, 1H, PhCH_2); 4.39 (*d*, J = 12.0, 1H, PhCH_2); 4.55 (*dd*, J = 4.8, 9.7, H–C(4)); 4.56 (*d*, J = 12.0, 1H, PhCH_2); 4.73 (*q*, $J \approx 4.9$, H–C(5)); 6.55 (br. *d*, J = 9.7, H–C(3)); 7.16–7.34 (*m*, 12 arom. H); 7.40 (br. *s*, NH); 7.72–7.76 (*m*, 2 arom. H); irrad. at 6.55→4.55 (*d*, J = 5.1); irrad. at 4.73→3.58 (*d*, J = 10.7), 3.68 (*d*, J = 10.7), 4.55 (*d*, J = 8.1). ^{13}C-NMR ($CDCl_3$): 21.67 (*q*); 23.57 (*q*); 68.09 (*t*); 71.56 (*t*); 73.35 (*t*); 75.49 (*d*); 81.39 (*d*); 112.89 (*s*); 113.58 (*s*); 127.73–129.61 (several *d*); 133.48 (*s*); 136.98 (*s*); 137.39 (*s*); 144.78 (*s*); 168.50 (*s*). FAB-MS: 625 (3), 557 (5, $[M + Na]^+$), 536 (4), 535 (12, $[M + H]^+$), 427 (7), 91 (100).

Treatment of **34** *with* NH_4N_3. Molecular sieves (3 Å; *Union Carbide*, powdered; 12.0 g) were dried in the reaction vessel. After cooling to r.t., NaN_3 (10.5 g, 162 mmol), NH_4Cl (9.0 g, 168 mmol), and a soln. of **34** (3.86 g, 6 mmol) were added. The mixture was stirred at 60–65° for 28 h and filtered and the residue washed with AcOEt. Normal workup (AcOEt, H_2O) of the filtrate and drying *i.v.* at slightly elevated temperature gave a yellow oil (3.9 g). FC (hexane/AcOEt 2:3) afforded **34**/**39** (R_f (hexane/AcOEt 2:3) 0.4–0.55), **40** (34 mg, 1%), and **35a** (1.39 g, 45%) as a yellowish solid, which was recrystallized (AcOEt/hexane) to give colorless crystals (1.23 g, m.p. 113–115°). MPLC of **34**/**39** (silica gel *60*, 0.015–0.04 mm, 250 g; hexane/AcOEt 7:3, 10 ml/min; UV 254 nm) gave **39** (261 mg, 9%) and **34**/**39** 3:1 (443 mg, *ca.* 12%).

*2-Acetamido-5-azido-3,4,6-tri-*O*-benzyl-2,5-dideoxy-*D*-glucononitrile* (**39**): R_f (hexane/AcOEt 1:2) 0.50. IR ($CHCl_3$): 3428*m*, 3090*w*, 3067*w*, 3007*m*, 2917*m*, 2870*m*, 2103*s*, 1953*w*, 1878*w*, 1812*w*, 1688*s*, 1602*w*, 1496*s*, 1455*m*, 1399*w*, 1370*m*, 1272*m*, 1095*s*, 1028*m*, 914*w*. ^{1}H-NMR ($CDCl_3$): 1.87 (*s*, AcN); 3.64 (*td*, $J \approx 4.6$, 6.2, H–C(5)); 3.69–3.77 (*m*, H–C(4), H–C(6)); 3.85 (*dd*, J = 4.4, 9.9, H′–C(6)); 4.04 (*dd*, J = 2.9, 5.0, H–C(3)); 4.56 (*s*, PhCH_2); 4.57 (*d*, J = 11.1, 1H, PhCH_2); 4.66 (*d*, J = 11.2, 1H, PhCH_2); 4.77 (*s*, PhCH_2); 5.11 (*dd*, J = 2.8, 8.4, H–C(2)); 5.92 (*d*, J = 8.4, NH); 7.24–7.41 (*m*, 15 arom. H). ^{13}C-NMR ($CDCl_3$): 22.69 (*q*); 41.41 (*d*); 60.72 (*d*); 68.59 (*t*); 73.51 (*t*); 74.42 (*t*); 75.25 (*t*); 77.54 (*d*); 78.01 (*d*); 117.60 (*s*); 127.82–128.64 (several *d*); 136.54 (*s*); 137.01 (*s*); 137.12 (*s*); 169.54 (*s*). FAB-MS: 1027 (1, $[2M + H]^+$), 515 (9), 514 (25, $[M + H]^+$), 406 (7), 181 (7), 91 (100).

A sample of **39** (110 mg, 0.21 mmol) was kept at 120–130° for 2 h. FC (hexane/AcOEt 1:2) yielded **41** (7.5 mg, 9%) and **35a** (83 mg, 75%).

*(Z)-2-Acetamido-5-azido-4,6-di-*O*-benzyl-2,3,5-trideoxy-*D*-*erythro*-hex-2-enononitrile* (**41**): R_f (hexane/AcOEt 2:1) 0.20. IR ($CHCl_3$): 3355*m* (br.), 3090*w*, 3068*w*, 3008*m*, 2924*m*, 2871*m*, 2233*w*, 2106*s*, 1955*w*, 1812*w*, 1708*s*, 1640*m*, 1602*w*, 1496*m-s*, 1479*m*, 1455*m*, 1368*m*, 1320*m*, 1260*s*, 1164*m*, 1074*s*, 1028*m*, 988*m*. ^{1}H-NMR ($CDCl_3$): 1.53 (s, AcN); 3.46 (*dd*, J = 7.8, 10.6, H–C(6)); 3.66 (*dd*, J = 6.1, 10.6, H′–C(6)); 4.03 (*ddd*, J = 4.7, 6.0, 7.8, H–C(5)); 4.34 (*dd*, J = 4.7, 7.8, H–C(4)); 4.44 (*d*, J = 11.8, 1H, PhCH_2); 4.50 (*s*, PhCH_2); 4.64 (*d*, J = 11.7, 1H, PhCH_2); 5.82 (*dd*, $J \approx 1$, 7.8, H–C(3)); 7.21–7.40 (*m*, 10 arom. H); 7.82 (br. *s*, NH); NOE: irrad at 7.82→6.8% at 4.34, 5.8% at 1.53. ^{13}C-NMR ($CDCl_3$): 22.34 (*q*); 63.23 (*d*); 68.83 (*t*); 71.78 (*t*); 73.92 (*t*); 74.21 (*d*); 114.26 (*s*); 114.36 (*s*); 126.50–129.74 (several *d*); 136.42 (*s*); 136.52 (*s*); 167.58 (*s*). FAB-MS: 811 (3, $[2M + H]^+$), 407 (12), 406 (42, $[M + H]^+$), 91 (100).

*2-Acetamido-3,4,6-tri-*O*-benzyl-2-deoxy-5-*O*-(tol-4-ylsulfonyl)-*D*-glucononitrile* (**42**). The alcohol **30** (500 mg, 1.02 mmol) was converted into **42** by the procedure used for the synthesis of **34**. FC (hexane/AcOEt 65:35) afforded **42** (490 mg, 75%). R_f (hexane/AcOEt 1:1) 0.41. IR ($CHCl_3$): 3430*m*, 3090*w*, 3067*w*, 3007*m*, 2925*m*, 2875*m*, 1952*w*, 1809*w*, 1687*s*, 1598*m*, 1496*s*, 1455*m*, 1369*s*, 1275*m*, 1177*s*, 1096*s*, 1041*m*, 1027*m*, 963*m*, 911*m*. ^{1}H-NMR ($CDCl_3$): 1.99 (*s*, AcN); 2.43 (*s*, Me); 3.36 (*dd*, J = 5.0, 10.0, H–C(6)); 3.82 (*dd*, J = 6.7, 10.2, H′–C(6)); 3.95 (*dd*, J = 2.5, 6.9, H–C(3)); 4.07 (*dd*, J = 2.6, 6.9, H–C(4)); 4.31 (*d*, J = 11.8, 1 H, PhCH_2); 4.36 (*d*, J = 11.8, 1 H, PhCH_2); 4.62 (*ddd*, J = 2.7, 5.4, 6.9, H–C(5)); 4.68 (*d*, J = 11.1, 1 H, PhCH_2); 4.75 (*s*, PhCH_2); 4.87 (*d*, J = 11.1, 1 H, PhCH_2); 5.22 (*dd*, J = 2.5, 9.4, H–C(2)); 6.03 (*d*, J = 9.3, NH); 7.15–7.40 (*m*, 17 arom. H); 7.76–7.80 (*m*, 2 arom. H); irrad. at 5.22→6.03 (*s*); 3.95 (*d*, J = 6.9). ^{13}C-NMR ($CDCl_3$): 21.73 (*q*); 22.83 (*q*); 41.25 (*d*); 66.85 (*t*); 73.40 (*t*); 75.38 (*t*); 75.77 (*t*); 78.71 (*d*); 79.21 (*d*); 80.05 (*d*); 117.44 (*s*); 127.68–129.86 (several *d*); 133.15 (*s*); 136.75 (*s*); 136.99 (*s*); 137.47 (*s*); 145.03 (*s*); 169.85 (*s*). FAB-MS: 1285 (1, $[2M + H]^+$), 733 (1), 644 (10), 643 (24, $[M + H]^+$), 535 (4), 181 (12), 91 (100).

*(5*S*,6*R*,7*R*,8*S*)-8-Acetamido-6,7-bis(benzyloxy)-5-[(benzyloxy)methyl]-5,6,7,8-tetrahydrotetrazolo[1,5-a]-pyridine* (**40**). A soln. of **42** (390 mg, 0.61 mmol) and NaN_3 (390 mg, 6.0 mmol) in DMSO (4 ml) was stirred at 100–120° for 3 h and worked up as usual ($CHCl_3$, sat. aq. NaCl soln.). Drying *i.v.* (70°) and FC (hexane/AcOEt 2:3) afforded **40** (36 mg, 12%) as a colorless oil which was crystallized from Et_2O/hexane. R_f (hexane/AcOEt 2:3) 0.29. M.p. 81.5–83°. IR ($CHCl_3$): 3438*m*, 3090*w*, 3067*w*, 3007*m*, 2929*m*, 2873*m*, 1953*w*, 1810*w*, 1682*s*, 1497*s*, 1455*m*, 1396*w*, 1370*m*, 1332*m*, 1306*m*, 1095*s*, 1046*m*, 1028*m*, 992*w*, 908*m*. ^{1}H-NMR ($CDCl_3$): 1.78 (*s*, AcN); 3.97 (*t*, $J \approx 9.3$, CH–C(5)); 4.04 (*dd*, J = 1.8, 4.7, H–C(7)); 4.30 (*dd*, J = 3.0, 4.4, H–C(6)); 4.47 (*d*, J = 10.9, 1 H, PhCH_2); 4.57 (*dd*, J = 4.7, 9.0, CH′–C(5)); 4.58 (*d*, J = 10.9, 1 H, PhCH_2); 4.60 (*d*, J = 11.7, 1 H, PhCH_2); 4.65 (*d*, $J \approx 12$, 1 H, PhCH_2); 4.71 (*d*, J = 11.7, 1 H, PhCH_2); 4.82 (*d*, J = 11.8, 1 H, PhCH_2); 4.83 (*ddd*, J = 3.0, 4.9, 9.5, H–C(5)); 5.79 (*dd*, J = 1.6, 9.0, H–C(8)); 5.90 (*d*, J = 9.0, NH); 7.07–7.41 (*m*, 15 arom. H). ^{1}H-NMR (CD_3OD): *Table*; irrad at 5.45→4.10 (*d*, J = 6.2). ^{13}C-NMR (100 MHz, $CDCl_3$): 22.83 (*q*); 42.95 (*d*); 56.09 (*d*); 65.52 (*t*); 72.08 (*t*); 73.22 (*d*); 73.93 (*d*); 74.03 (*t*); 74.12 (*t*); 128.03–128.87 (several *d*); 136.37 (*s*); 136.72 (*s*); 137.11 (*s*); 150.93 (*s*); 168.83 (*s*). FAB-MS: 1027 (3, $[2M + H]^+$), 515 (26), 514 (70, $[M + H]^+$), 406 (9), 307 (19), 91 (100).

*(5*R*,6*R*,7*R*,8*S*)-8-Acetamido-5,6,7,8-tetrahydro-5-(hydroxymethyl)tetrazolo[1,5-a]pyridine-6,7-diol* (**7**). At r.t., a soln. of **35a** (800 mg, 1.56 mmol) and AcOH (1.7 ml) in MeOH (50 ml) was hydrogenated for 24 h at 6 bar in the presence of 10% Pd/C (800 mg). The mixture was filtered through *Celite* and the residue thoroughly washed with MeOH. The combined filtrate and washings were evaporated to give a colorless powder (415 mg) which was dissolved in hot EtOH/MeOH and filtered. Evaporation and crystallization from EtOH/AcOEt gave **7** (193 mg, 51%). FC (AcOEt/MeOH 8:2) of the mother liquor yielded a second crop of 7 (151 mg, 40%). The combined material was recrystallized in EtOH to give colorless crystals (200 mg); concentration of the mother liquor gave a colorless powder (144 mg). R_f (AcOEt/MeOH 8:2) 0.24. M.p. 235–240° (dec.). $[\alpha]_D^{25} = +51.7$ (c = 0.65, H_2O). IR (KBr): 3417*s*, 3251*s*, 2963*w*, 2926*w*, 2862*w*, 1652*s*, 1573*s*, 1527*m*, 1438*m*, 1382*m*, 1344*m*, 1326*m*, 1311*m*, 1243*w*, 1224*w*, 1199*m*, 1162*m*, 1132*m*, 1112*m*, 1083*m*, 1068*m*, 1042*m*, 1017*m*, 1007*m*, 987*m*, 853*m*, 765*m*, 742*m*, 637*m*, 602*m*. ^{1}H-NMR (CD_3OD): *Table*; irrad. at 4.98→4.28 (*td*, J = 2.5, 8.5) and 3.96 (*d*, J = 9.3). ^{1}H-NMR (400 MHz, D_2O): *Table*. ^{13}C-NMR (100 MHz, D_2O): 24.61 (*q*); 49.81 (*d*); 60.19 (*t*); 65.02 (*d*); 70.12 (*d*); 74.01 (*d*); 156.31 (*s*); 177.38 (*s*). FAB-MS (glycerol): 244 (6, $[M + H]^+$), 226 (3). Anal. calc. for $C_8H_{13}N_5O_4$ (243.22): C 39.51, H 5.39, N 28.69; found.: C 39.73, H 5.31, N 28.64.

*(5*R*,6*R*,7*R*,8*R*)-8-Acetamido-5,6,7,8-tetrahydro-5-(hydroxymethyl)tetrazolo[1,5-a]pyridine-6,7-diol* (**43**). At r.t., a soln. of **36a** (41 mg, 0.08 mmol) and AcOH (0.1 ml) in MeOH (3 ml) was hydrogenated for 18 h at 6 bar in the presence of 10% Pd/C (60 mg). The mixture was filtered through *Celite* and the residue thoroughly washed with MeOH. The combined filtrate and washings were evaporated. FC (AcOEt/MeOH 8:2) afforded **43** (18 mg, 93%). R_f (AcOEt/MeOH 3:1) 0.40. ^{1}H-NMR (D_2O): *Table*; irrad. at 5.67→4.30 (*d*, J = 6.2). ^{13}C-NMR (125 MHz, D_2O): 24.54 (*q*); 46.06 (*d*); 63.09 (*t*); 66.78 (*d*); 70.19 (*d*); 70.99 (*d*); 154.67 (*s*); 177.09 (*s*). FAB-MS: 509 (19, $[2M + Na]^+$), 267 (23), 266 (100, $[M + Na]^+$), 245 (16), 244 (70, $[M + H]^+$).

Enzyme-Inhibition Studies for **6**. β-*D*-Galactosidases from *E.coli* and bovine liver were purchased from *Boehringer Mannheim* and *Sigma*, resp., and used without further purification. 2-Nitrophenyl β-*D*-galactopyranoside was used as substrate (0.1 1 mM) in sodium phosphate buffer (200 mM, pH 6.8, 1 mM $MgCl_2$, 30° for the *E. coli* enzyme, and 50 mM, pH 7.0, 0.1% BSA (bovine albumine), 1 mM $MgCl_2$, 37° for the bovine enzyme). After addition of inhibitor soln. (1.0, 2.0, 4.0, 10.0, 20.0 μM) or H_2O, followed by enzyme soln. the amount of 2-nitrophenolate liberated was determined by continuous measurement of the UV/VIS absorption at 405 nm. K_I values were determined by *Lineweaver-Burke* plots.

Enzyme-Inhibition Studies for **7**. 4-Nitrophenyl 2-acetamido-2-deoxy-β-*D*-glucopyranoside (GlcNAc-Np) from *Sigma* (cat. No. N-9376) and β-*N*-acetylglucosaminidase EC 3.2.1.30 from bovine kidney from *Sigma* (cat. No. A-2415) were used. The suspension of the enzyme in 3.2M $(NH_4)_2SO_4$ (0.1 ml, 5 U) was centrifuged, and the

pellet was dissolved in H_2O. Citrate buffer (0.5M, pH 4.1; 100 µl), **7** (1.13, 0.23, 0.11 µM in H_2O; 300 µl), or H_2O (300 µl), resp., and enzyme soln. (52 mU in H_2O; 100 µl) were incubated at 37° for 5 min. After addition of GlcNAc-Np (5.0, 2.5, 1.6, 1.0, 0.5 mM in H_2O; 500 µl), incubation was continued for 3, 6, 9, or 12 min. The reaction was stopped by addition of borate buffer (0.2M, pH 9.2; 1000 µl). The amount of 4-nitrophenolate liberated was determined by measurement of the UV/VIS absortion at 400 nm.

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