Synthesis of Fusion-Isomeric Imidazopyridines and Their Evaluation as Inhibitors of *syn*- and *anti*-Protonating Glycosidases

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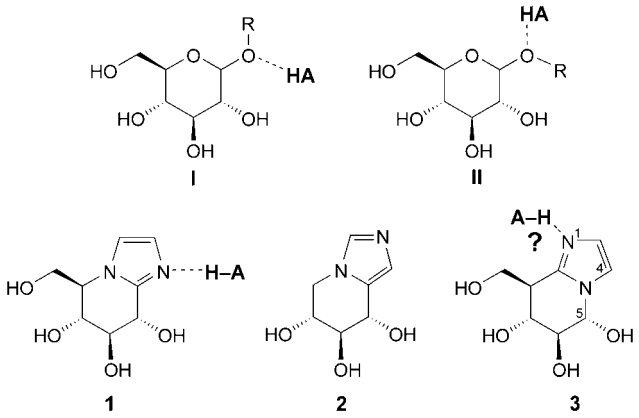
The *galacto*- and *gluco*-configured imidazopyridines **4** and **5** were synthesised as potential inhibitors of *syn*-protonating β-glycosidases. Methyl α-D-lyxopyranoside (**9**) was transformed into the 3,4-anhydro-β-L-riboside **16**, which, upon treatment with Et_2AlCN, gave the nitrile **17** (76–85%). Reaction of **17** with the dimethyl aluminate of aminoacetaldehyde dimethyl acetal led directly to the branched chain *lyxo*-configured imidazole **27** (53%) that was hydrolysed to an equilibrating mixture of **4** and **28**–**30**. Oxido reduction of **27** provided the *arabino*-configured imidazole **42** (*ca.* 48% from **27**). Hydrolysis of **42** led to the mixture **5**/**45** (63–90%). *anti*-Protonating β-galactosidases and β-glucosidases (families 1 and 2) were only weakly inhibited by **4**/**28**–**30** and **5**/**45**, respectively. Also the *syn*-protonating cellulase (Cel7A) was weakly inhibited by the monosaccharide mimics **5**/**45**, suggesting either that monosaccharide mimics are too small to inhibit Cel7A, or that fusion isomeric tetrahydroimidazo[1,2-*a*]pyridines are not a suitable scaffold for the inhibition of *syn*-protonating glycosidases.

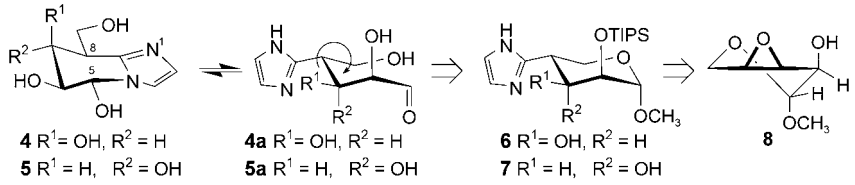
Introduction. – Selective inhibitors of *anti*- and *syn*-protonating glycosidases [1] will be useful to specify the (relative) position of the catalytic acid; they also have the potential of being highly selective. Of particular interest are complementary inhibitors of *syn*- and *anti*-protonating glycosidases possessing a common scaffold, as this would facilitate a comparative interpretation of the inhibitory activity. However, there are as yet no inhibitors selective for *syn*-protonating (α- or β-) glycosidases.

The anti- and *syn*-protonating glycosidases differ by the trajectory of the proton transfer from the catalytic acid AH to the glycosidic oxygen (**I** and **II**) and the tetrahydroimidazo[1,2-*a*]pyridines of type **1** are strong (about nanomolar) inhibitors of



anti-protonating β-glycosidases, interacting in a cooperative way with the catalytic acid and the catalytic base of the enzyme [2–17]. Tetrahydroimidazo[1,5-*a*]pyridines of type **2** [18–24] do not possess a 'glycosidic heteroatom' – a heteroatom that is located (more or less) in the same place as O–C(1) of glycosides – that could interact with the catalytic acid AH of either an *anti*- or a *syn*-protonating glycosidase. Not unexpectedly, these imidazoles are relatively weak glycosidase inhibitors. We wondered about the isomeric tetrahydroimidazo[1,2-*a*]pyridines of type **3**. These isomers do not have a 'glycosidic heteroatom' either, but N(1), although not ideally located, could interact with the catalytic acid AH of a *syn*-protonating glycosidase, provided the catalytic acid is (sufficiently) flexible, as it has indeed been advocated [25–27]. This consideration led us to first synthesise the monosaccharide-derived *galacto*- and *gluco*-configured imidazoles **4** and **5** (*Scheme 1*). These imidazoles will presumably exist in equilibrium with their open-chain aldehyde tautomers **4a** and **5a**, and be configurationally labile at HO–C(5). We were, however, confident that **4** and **5** would be sufficiently stable to be isolated and tested, and that, upon binding to a specific glycosidase, they would adapt their configuration at C(5) to the one of the preferred substrate.

Scheme 1



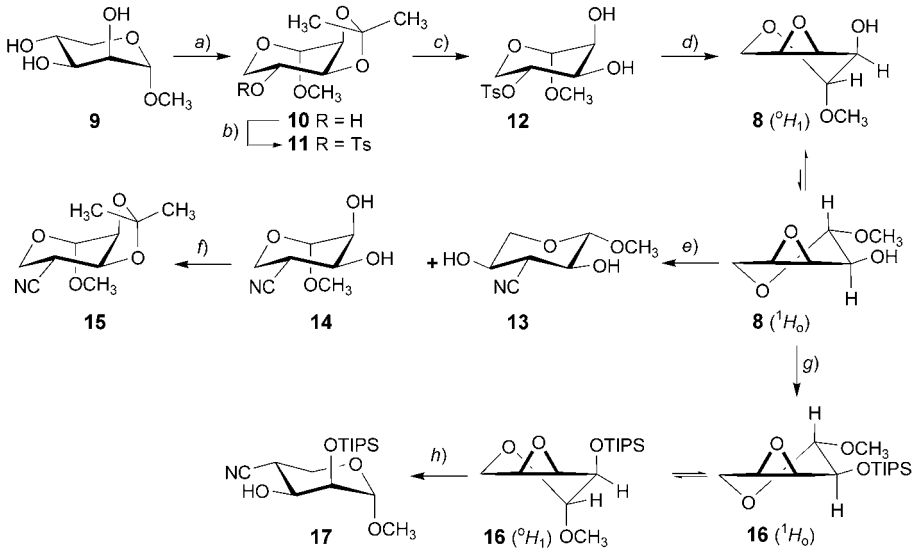
4 R^1= OH, R^2 = H
5 R^1 = H, R^2 = OH
4a R^1= OH, R^2 = H
5a R^1 = H, R^2 = OH
6 R^1= OH, R^2 = H
7 R^1 = H, R^2 = OH
8

The plan for the synthesis of the imidazopyridines **4** and **5** is outlined in *Scheme 1*. It is based on the assumption that glycoside hydrolysis of the branched-chain imidazolyl glycoside **6** or **7** is followed by equilibration of the resulting hemiacetals and corresponding hydroxyaldehydes **4a** and **5a**, and that further equilibration will lead to the desired tetrahydroimidazopyridines **4** and **5**. The branched-chain glycoside **6** should be obtained by regioselective ring opening of the known anhydroribo-β-L-pyranoside **8** [28] and transformed into its isomer **7**.

Results and Discussion. – 1. *Synthesis of the* galacto-*Imidazole* **4**. Methyl α-D-lyxopyranoside (**9**) [28] was obtained in a yield of 77% by *Fischer* glycosidation of D-lyxose with AcCl in anhydrous MeOH (*Scheme 2*). This controlled generation of HCl led to results that compare favourably with those of known procedures [28][29]. Isopropylidenation of **9** [30] with acetone and *Amberlyst-15* resulted consistently in yields of at least 85–90% of **10**. Tosylation to **11** [29] was followed by hydrolysis to the hydroxy toluenesulfonate **12**. Treatment of **12** with *t*-BuOK in THF provided the epoxide **8** in a maximal yield of 83–92% (33–40% from D-lyxose; 10–30-mmol scale). Lower yields resulted from using MeONa in MeOH [28].

The epoxide **8** in $CDCl_3$ adopts almost exclusively the $^{o}H_1$ conformation, as evidenced by $J(1,2) = 2.8$ Hz. The energy difference between the $^{1}H_o$ and $^{o}H_1$

Scheme 2



a) *Amberlyst-15*, 4-Å mol. sieves, Me_2CO. *b*) TsCl, pyridine; 84% from **9**. *c*) 80% aq. AcOH; 93%. *d*) ^{t}BuOK THF; 83%. *e*) Et_2AlCN, Et_2O. *f*) *Amberlyst-15*, Me_2CO, 4-Å mol. sieves; 17% of **15** and 20% of **13** from **8**. *g*) TIPSOTf (TIPS = (i-Pr)$_3$Si), 2,6-lutidine; 80–96%. *h*) Et_2AlCN, Et_2O; 76–85%.

conformers is small, and the barriers for their interconversion are low [31], so that *trans*-diaxial opening of the oxirane **8** is not sufficient to control regioselectivity. Ammonia and amines attack **8** preferentially at the less hindered C(4) [32], and treatment of **8** with HBr provided methyl 4-bromo-4-deoxy-D-lyxoside [28]. However, all attempts to introduce an imidazolyl moiety at C(4) (or at C(3)) by treating **8** with protected imidazolyl anions failed under a variety of conditions [11–13][33]. We, therefore, planned to introduce a CN group, and to transform it into the imidazolyl moiety *via* the corresponding amide and thioamide [2][4][6–8][34–36]. Treating the epoxide **8** with Et_2AlCN [37] resulted in an inseparable 1:1 mixture of the *trans*-hydroxy carbonitriles **13** and **14** (66%). Treatment of this mixture with acetone in the presence of *Amberlyst-15* transformed **14** to **15**, which was readily separated from **13**; this isopropylidenation establishes the constitution of **13** and **14**, and the configuration of **13** (*Scheme 2)*. Unlike in a related favourable case [38], complexation of Et_2AlCN with MeO–C(1) led neither to (regioselective) intramolecular delivery of cyanide nor to a sufficiently biased conformation. We then speculated that protection of HO–C(2) of **8** with the bulky (i-Pr)$_3$Si (TIPS) group would prevent the formation of a H-bond from HO–C(2) to the incipient oxyanion center, resulting from attack at C(3), that the TIPSO group would prefer a pseudoequatorial orientation, favour the ^1H_o conformation, and lead to a preferential attack of cyanide at C(4). The desired silyl ether **16** was readily obtained and characterised as a *ca.* 1:1 mixture of the $^oH_1$ and ^1H_o conformers by $J(1,2) = 4.6$ Hz. Opening of the oxirane ring of **16** by Et_2AlCN provided almost

exclusively **17**[1]). The minor regioisomer resulting from attack at C(3) of **16** was isolated in maximal 5% and desilylated to **13**. An alternative substitution of **16** with KCN in DMSO was inefficient and proceeded with concomitant *O*-desilylation; it led regioselectively to **14**.

The ^{1}H-NMR spectrum of **13** in CD_3OD and in $CDCl_3$ displayed a characteristic H–C(3) *t* with $J(2,3) \approx J(3,4) \approx 7.8$ Hz, evidencing that it is mostly adopting the $^1C_4$ conformation. The H–C(4) of **17** resonates at 3.01 ppm as a *td* with $J(3,4) = J(4,5_{ax}) = 9.6$; also $J(4,5_{eq}) = 4.5$ Hz. $J(1,2) = 2.4$, $J(2,3) = 3.0$ Hz are in agreement with a preferred $^4C_1$ conformation. The data are consistent with coupling constants calculated for the $^4C_1$ conformer of α-D-lyxose ($J(1,2) = 2.1$, $J(2,3) = 3.1$, $J(3,4) = 8.8$, $J(4, 5_{eq}) = 5.8$, $J(4,5_{ax}) = 10.5$ Hz) [40], which is more stable than the $^1C_4$ conformer by *ca.* 0.9 kcal/mol. These interpretations are supported by MM3 calculations [40]. Crystalline methyl α-D-lyxopyranoside also adopts the $^4C_1$ conformation [41].

According to a literature precedent [38], **17** was transformed to the amides **18** and **19** in ratios varying from 3:2 to 7:3, reflecting the migration of the TIPS group [42] (*Scheme 3*). Desilylation of the mixture **18**/**19** (TBAF · 3 H_2O)[2]) provided **20** in > 95% yield. Isopropylidenation of **20** gave **21** besides *ca.* 10% of the 1,3-oxazin-4-one **22**; formation of an oxazinone under such conditions appears to be unprecedented. *Lawesson*'s reagent transformed the amide **21** to the thioamide **23** (84%). Treatment of **23** with aminoacetaldehyde dimethyl acetal under a variety of conditions yielded neither an amidine nor an imidazole, but transformed **23** back to the nitrile **15**. We also attempted to synthesise an imidazole *via* the acetylated amide **24** and thioamide **25**. Treatment of **25** with aminoacetaldehyde dimethyl acetal in the presence of a variety of thiophilic reagents such as $Hg(OAc)_2$, HgO, and PbO afforded only the acetylated carbonitrile **26**. No reaction occurred in the absence of thiophilic reagents up to a temperature of 110°. An attempt to transform the carbonitriles **15**, **17**, and **26** to amidines by aminolysis of the corresponding nitrilium salts, generated under conditions of the *Pinner* reaction [43] or in the presence of a *Lewis* acid [44][45], and further to imidazoles also failed, as did the formation of an imidazole ring from the amides **21** or **24**.

Unexpectedly, however, the imidazole **27** was obtained (53%) in an attempt at transforming the carbonitrile **17** into the corresponding amidine by treatment with the aluminum amide derived from aminoacetaldehyde dimethyl acetal and Me_3Al (1:1), as suggested by the work of *Weinreb* and co-workers [46], *Garigipati* [47], and *Moss et al.* [48] (*Scheme 4*). This unprecedented one-pot synthesis of an imidazole from a carbonitrile is, however, not general and depends on the presence of the vicinal HO–C(3) group[3]). The lyxopyranoside **27** was hydrolysed with 20% aq. HCl in 80% aq. AcOH at 110° to provide a *ca.* 60:8:14:18 equilibrium mixture of the *galacto*-

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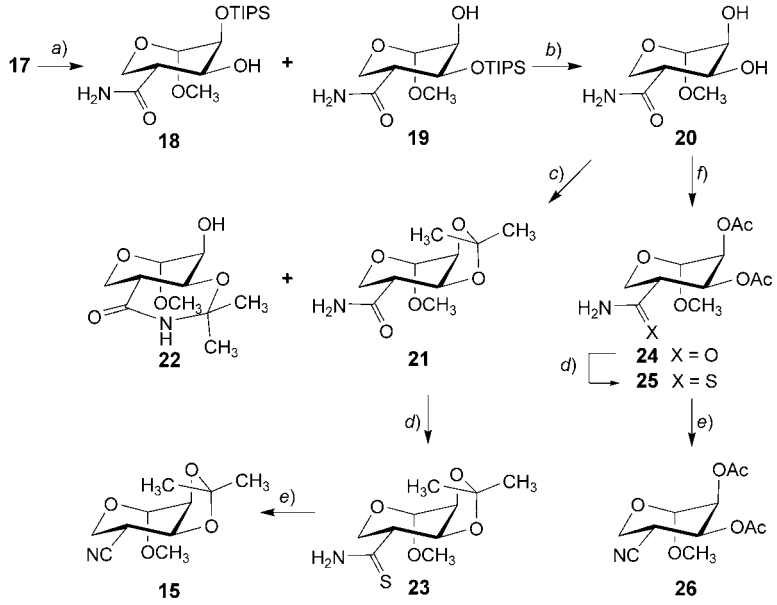
[1]) In an exploratory experiment, **16** was treated with Me_3SiCN in the presence of activated MgO or CaO [39]; this also led to regioselective opening at C(4) with simultaneous silylation of HO–C(3). The activation of MgO or CaO was essential to secure good yields. We thank *Florian Kleinbeck* for performing this experiment.

[2]) Less-satisfactory conditions include heating with 50% aq. AcOH and treatment with 20% aq. HCl in EtOH at 23°, the poor yield under hydrolysis conditions reflecting partial glycoside hydrolysis.

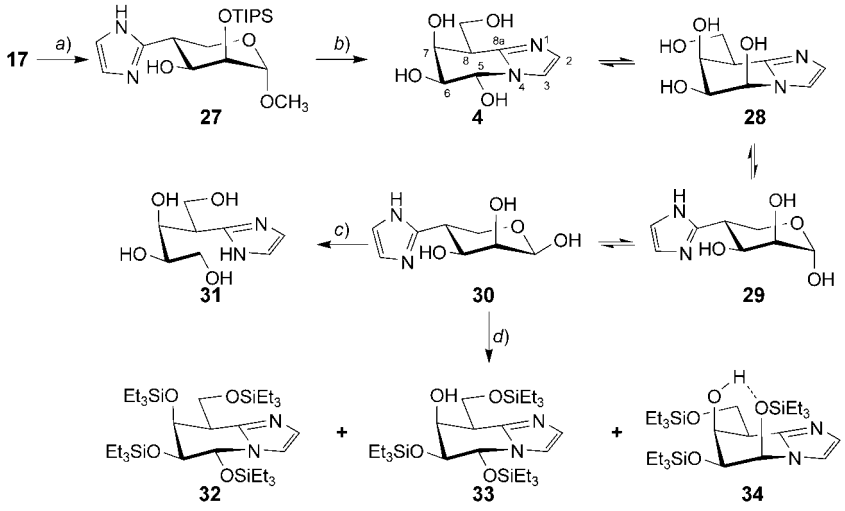
[3]) A similar treatment of a few representative carbonitriles lacking a corresponding OH group led (in high yields) to amidines.

Scheme 3



a) 30% H_2O_2, K_2CO_3, Me_2CO/H_2O 3:2; 86–95%. *b*) TBAF · 3 H_2O, THF; 85–95%, or 50% aq. AcOH; 50%, or 20% aq. HCl/EtOH 1:1; 50%. *c*) *Amberlyst-15*, Me_2CO, 4-Å mol. sieves; 81% of **21** and 12% of **22**. *d*) *Lawesson*'s reagent, toluene; 84% of **23**; 76% of **25**. *e*) $NH_2CH_2CH(OMe)_2$, $Hg(OAc)_2$, THF; 86% of **15**; > 95% of **26**. *f*) Ac_2O, 4-(dimethylamino)pyridine (DMAP), pyridine; 65%.

Scheme 4



a) Me_3Al, $NH_2CH_2CH(OMe)_2$, toluene; 46–53%. *b*) 20% aq. HCl, 80% aq. AcOH; 70%. *c*) $NaCNBH_3$, MeOH/AcOH; 90%. *d*) Et_3SiCl, 2,6-lutidine, pyridine; 16% of **32**, 22% of **33**, 8% of **34**.

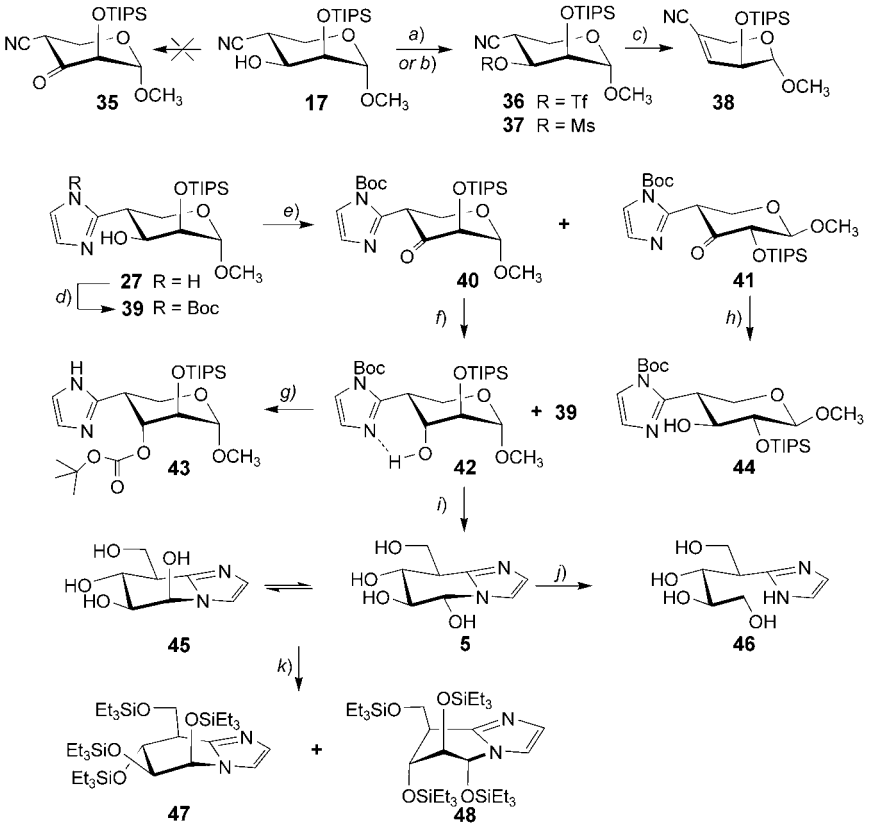
configured fused imidazole **4**, its *talo*-isomer **28**, and the branched-chain anomeric lyxopyranoses **29** and **30**. The desired *galacto*-imidazole **4** was the main component of this mixture between pH 5.5 and 8. In agreement with the interpretation of the complex NMR spectra of the hydrolysis products, reduction of the mixture **4**/**28**–**30** with $NaCNBH_3$ provided the tetrol **31** in high yields (90%). Triethylsilylation of **4**/**28**–**30** and flash chromatography provided the *galacto*-configured imidazoles **32** and **33**, and the *talo*-configured imidazole **34** in 16, 22, and 8% yield, respectively. As expected, desilylation of **32** and **34** with aq. HCl in CD_3OD at 24° for 36 h led in each case to the mixture **4**/**28**–**30**.

The H–C(4′) and H–C(5′) of the imidazole moiety of **27** give rise to a characteristic br. *s* at 6.97 ppm. The preferred $^4C_1$ conformation of **27** agrees well with $J(1,2) = 2.2$, $J(2,3) = 3.0$, $J(3,4) = 9.9$, $J(4,5_{ax}) = 10.5$, and $J(4,5_{eq}) = 4.8$ Hz. The C(4′) and C(5′) signals of the imidazole moiety of **27** appear as two broad *d*s at 127.83 and 115.19 ppm, respectively. Upon addition of a catalytic amount of AcOH they appear as a sharp *d* at 119 ppm. The constitution of **4** is evidenced by the characteristic *s* of C(8a) at 145.70, and by *d*s of C(2), C(3), and C(5) at 127.42, 118.23, and 81.58 ppm, respectively. $J(5,6) = 7.2$, $J(6,7) = 1.5$, $J(7,8) = 3.6$ Hz are in agreement with a $^7H_6$ as the predominant conformation and with the *galacto*-configuration of **4**. The tetrakis(triethylsilyl) ether **32** adopts the $^7H_6$ conformation in $CDCl_3$ solution in agreement with $J(5,6) = 6.9$, $J(6,7) = 1.5$, $J(7,8) = 3.0$ Hz. In CD_3OD solution, it exists as mixture of the $^7H_6$ and $^6H_7$ conformers with a predominant contribution from the $^7H_6$ conformer as indicated by $J(5,6) = 5.4$, $J(6,7) = 1.5$, $J(7,8) = 4.2$, $J(8,CH_a) = 7.2$, $J(8,CH_b) = 5.7$, and $J(CH_a,CH_b) = 9.9$ Hz. The *galacto*-alcohol **33** exists as *ca.* 2:1 mixture of $^7H_6$ and $^6H_7$ conformers, respectively, as evidenced by $J(5,6) = 4.5$, $J(6,7) = 2.1$, $J(7,8) = 6.3$, $J(8,CH_a) = 5.4$, $J(8,CH_b) = 8.4$, and $J(H–C(7),OH) = 4.2$ Hz. The $^7H_6$ conformation and *talo*-configuration of **34** is in agreement with $J(5,6) = 3.9$, $J(6,7) = 2.1$, $J(7,8) = 4.2$, $J(8,CH_a) = 4.2$, $J(8,CH_b) = 10.8$ Hz, and a $J(5,7)$ *w*-coupling of 1.8 Hz. The large value of $J(H–C(7),OH) = 7.2$ Hz for **34** indicates a H-bond between HO–C(7) and Et_3SiO–C(5).

2. *Synthesis of the* gluco-*Imidazole* **5**. Oxidation–reduction or inverting substitution at C(3) of **17** and subsequent transformations should provide the desired imidazole **5**, but both transformations proved difficult (*Scheme 5*). Oxidation of **17** with *Dess–Martin*'s periodinane [49], PCC, tetrapropylammonium perruthenate (TPAP) and NMO [50], or with DMSO/$(COCl)_2$ and Et_3N [51]) failed to provide the ketone **35**. *Mitsunobu* substitution with 4-nitrobenzoic acid [52] did not lead to a nitrobenzoate, but partially transformed **17** into a complex mixture. The readily prepared triflate **36** was stable to chromatography on silica gel and to prolonged storage at −20°, but reacted with $NaNO_2$, AcONa, AcOK, AcOCs, or Bu_4NOAc in DMF to provide only the unsaturated carbonitrile **38** without any indication of a substitution product. The corresponding methanesulfonate **37** was either not affected under the same conditions of attempted substitution, or also transformed to **38**, presumably on account of the acidity of H–C(4). As H–C(4) of imidazolyl analogues should be considerably less acidic, we used the (*tert*-butoxy)carbonyl (Boc) derivative **39** of **27** as the starting material.

While attempted substitution of HO–C(3) of **39** under *Mitsunobu* conditions either did not affect the starting material or gave intractable mixtures, *Dess–Martin*

Scheme 5



a) Tf_2O, DMAP, pyridine; >95%. *b*) MsCl, pyridine; 89%. *c*) CsOAc, DMF; 90%. *d*) Boc_2O, DMAP, MeCN. *e*) *Dess–Martin* periodinane, CH_2Cl_2; 58% of **40** and 11% of **41**, from **27**. *f*) $NaBH_4$, $CeCl_3 \cdot 7\,H_2O$, MeOH; 81% of **42**, or $NaBH_4$, MeOH; 48% of **39** and 26% of **42**. *g*) Et_3N, MeOH; 71%. *h*) $NaBH_4$, MeOH; 56%. *i*) 20% aq. HCl, 80% aq. AcOH; 63–90%. *j*) $NaCNBH_3$, AcOH/MeOH; 65%. *k*) Et_3SiCl, 2,6-lutidine, pyridine; 43% of **47**/**48**.

oxidation [49] gave readily the ulopyranoside **40** (58%) besides the doubly epimerised **41** (10%), and proved superior to oxidation under *Swern* conditions [51]. The ketone **41** was formed only during chromatography, as evidenced by the ^{1}H-NMR spectra of the crude, and its formation may be rationalised by a reversible elimination–addition of MeOH.

Reduction of **40** with $NaBH_4$ in the presence of $CeCl_3 \cdot 7\,H_2O$ [53] gave exclusively the α-D-arabinopyranoside **42** (80%), presumably as the consequence of the complexation of Ce^{III} with the C(3)=O and MeO–C(1) groups affecting the conformation of the pyranose ring and preventing the axial approach of hydride. Reduction of **40** with $NaBH_4$/MeOH gave a nearly 1:1 to 2:3 mixture of the *lyxo*-configured **39** and the *arabino*-configured **42**. Workup and chromatography, however, yielded typically 46% of **39** and 26% of **42**, and *ca.* 20% of a 4:1 to 9:1 mixture of *tert*-butyl carbonate **43** and

its epimer. The yields and ratio of **39** and **42** reflect the migration of the *N*-Boc group to HO–C(3) of **42** and, considerably more slowly, also of **39**. The migration is catalysed by base; treating pure **42** with Et_3N in MeOH yielded 71% of **43**. A related case of this type of *N*,*O*-carbonyl exocyclic rearrangement for *N*-carbonyl-oxazolidin-2-ones has been reported [54][55]. To confirm the structure, we reduced **41** with $NaBH_4$ in MeOH to the β-D-xylopyranoside **44** (56%).

The ulopyranoside **40** adopts a flattened $^4C_1$ conformation in agreement with $J(1,2) = 1.8$, $J(4,5_{eq}) = 6.6$, and $J(4,5_{ax}) = 11.1$ Hz. C(1) of **40** appears as *d* at 104.76, C(3) as *s* at 201.12 ppm. A C(1) *d* at 107.40, and $J(1,2) = 7.5$, $J(4,5_{eq}) = 6.3$, and $J(4,5_{ax}) =$ 11.4 Hz are consistent with a flattened $^4C_1$ conformation and with the configuration of **41**. The vicinal $J(1,2) \approx 1.2$, $J(2,3) = 3.0$, $J(3,4) = 2.1$, $J(4,5_{eq}) = 4.0$, $J(4,5_{ax}) = 11.1$, and a $J(3,5_{eq})$ *w*-coupling of 1.2 Hz are consistent with the $^4C_1$ conformation and the α-D-*arabino*-configuration of **42**. An intramolecular H-bond from HO–C(3) to N(3′) of **42** is evidenced by a *d* ($J = 5.4$ Hz) at 4.95 ppm. In the IR ($CHCl_3$) spectrum of **42**, the characteristic band at 3505 cm^{-1} for HO–C(3) did not change upon dilution (0.11M, 0.17M, 0.51M, 0.85M, 1.27M, 1.76M), evidencing an intramolecular H-bond. The disappearance of two *d*s at 7.34 ($J(4',5') = 1.8$, H–C(5′)) and 6.86 ppm ($J(4',5') = 1.8$, H–C(4′)), and the appearance of two br. *s* at 7.0 (H–C(4′)), and 6.96 ppm (H–C(5′)) in the ^{1}H-NMR spectrum of **43** evidences the migration of the *N*-Boc group to HO–C(3). A *ca.* 1:1 mixture of $^4C_1$ and $^1C_4$ conformers of **43** is evidenced by $J(1,2) =$ 4.5, $J(2,3) = 6.0$, $J(3,4) = 4.2$, $J(4,5_{eq}) = 4.2$, and $J(4,5_{ax}) = 6.0$ Hz. The β-D-*xylo*-configuration and the $^4C_1$-conformation of **44** agrees with $J(1,2) = 7.5$, $J(2,3) = 8.7$, $J(3,4) \approx$ $J(4,5_{ax}) \approx 10.5$, $J(4,5_{eq}) = 4.2$ Hz, and the downfield shift of C(1) at 105.46 ppm. J(H–C(3), HO) = 3.6 Hz agrees with an intramolecular H-bond to the equatorial imidazolyl or TIPSO group.

Hydrolysis of **42** (20% aq. HCl in 80% aq. AcOH) at 110° provided a *ca.* 1:1 equilibrium mixture of the D-*gluco*-configured **5** and its D-*manno*-isomer **45**, accounting for more than 95% of product. In keeping with the structure of **5**/**45**, reduction with $NaCNBH_3$ provided the tetrol **46** (66%). Silylation of **5**/**45** and chromatography gave the D-*manno*-imidazole **47** (27%) and the D-*gluco*-imidazole **48** (16%).

The D-*gluco*-configuration and predominant $^7H_6$ conformation of **5** is evidenced by $J(5,6) = 7.2$, $J(6,7) \approx J(7,8) \approx 9.3$ Hz; the *manno*-configuration of **45**, and its (prepondering) $^6H_7$ and $^7H_6$ conformations are in agreement with $J(5,6) = 3.6$, $J(6,7) = 8.4$, and $J(7,8) = 7.5$ Hz. The *gluco*-configured silyl ether **48** adopts a $^6H_7$ conformation with *pseudo*-axial silyloxy and (silyloxy)methyl groups as evidenced by $J(5,6) = 1.8$, $J(6,7) =$ 3.6, $J(7,8) \approx 1.2$, $J(8,CH_a) \approx 10.8$, $J(8,CH_b) = 5.4$ Hz, and a *w*-coupling of $J(5,7) \approx$ 0.9 Hz. There is precedent for the preferred axial orientation of silyloxy groups [56–63]. The *manno*-imidazole **47** adopts preferentially the $B_{5,8}$ conformation in accordance with $J(5,6) = 1.8$, $J(6,7) = 5.1$, $J(7,8) \approx 1.2$, $J(8,CH_a) = 5.1$, and $J(8,CH_b) = 10.5$ Hz.

Inhibition Studies. Exploratory inhibition experiments indicate that the D-*galacto*/D-*talo* and D-*lyxo*-configured imidazoles **4**/**28**–**30**, and D-*gluco*/D-*manno*-configured imidazoles **5**/**45** respectively, inhibit – at best – very weakly the *anti*-protonating β-glycosidases from family 1 and 2 (IC_{50} in the mM range). The mixture **4**/**28**–**30** containing the D-*galacto*-imidazole **4** was assayed against β-galactosidases from *E. coli* (family 2 [64]), bovine liver, and *A. oryzae* [65]). The β-galactosidases from *E. coli* and bovine liver were not inhibited by **4**/**28**–**30** up to a concentration of 7 mM, while the β-

galactosidase from *A. oryzae* was weakly inhibited ($IC_{50} \approx 1$ mM, [S] = 0.56 mM, 50 mM AcONa buffer, pH 4.9).

The β-glucosidase from *Caldocellum saccharolyticum* (family 1) and the β-glucosidases from sweet almonds were weakly inhibited by the D-*gluco*/D-*manno* mixture **5**/**45** ($IC_{50} \approx 500$ μM, [S] = 2.02 mM, 50 mM AcONa buffer, pH 4.9) and ($IC_{50} \approx$ 760 μM, [S] = 2.45 mM, 100 mM phosphate buffer, pH 6.9), respectively. Not unexpectedly, the monosaccharide imidazoles **5**/**45** inhibited the *syn*-protonating cellulase Cel7A from *T. reesei* (family 7) only weakly ($IC_{50} \approx 24$ mM at 50°; no inhibition up to 7.2 mM at 30°, [S] = 0.722 mM, 50 mM AcONa buffer, pH 4.9); a significant inhibition requires at least a disaccharide analogue [66–68].

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Experimental Part

General. All reactions were carried out under N_2 unless specified otherwise. THF and Et_2O were distilled over Na/benzophenone, and DMF, MeCN, and CH_2Cl_2 were distilled over CaH_2. TLC: *Alugram*® silica gel *60* GF_{254} plates; detection by heating with 'mostain' (400 ml of 10% aq. H_2SO_4 soln., 20 g of $(NH_4)_6Mo_7O_{24} \cdot 6\,H_2O$, 0.4 g of $Ce(SO_4)_2$) or 10% aq. H_2SO_4 soln. or 2% $KMnO_4$ in 4% aq. $NaHCO_3$ soln. Flash chromatography (FC): silica gel *Fluka 60* (0.04–0.063 mm). M.p.: uncorrected. Optical rotations: 1-dm cell at 25°, 589 nm. FT-IR spectra: KBr or *ca.* 2% soln. in $CHCl_3$; absorption in cm^{-1}. ^1H- and ^{13}C-NMR spectra: chemical shifts δ in ppm, referenced at 7.26 ppm for ^1H- and 77.1 ppm for ^{13}C-NMR, respectively, for $CHCl_3$; coupling constant J in Hz. MALDI- and HR-MALDI-MS: 2,5-dihydroxybenzoic acid (DHB). β-Galactosidase from bovine liver (3.2.1.23, as lyophilised powder), β-galactosidase from *E. coli* (3.2.1.23, as lyophilised powder), β-galactosidase from *A. oryzae* (3.2.1.23, as lyophilised powder), β-glucosidase from *Caldocellum saccharolyticum* (3.2.1.21, as lyophilised powder), and β-glucosidases from sweet almonds (3.2.1.21, as lyophilised powder), and all nitrophenyl β-D-glycopyranosides were purchased from *Sigma* and used without further purification.

Methyl α-D-*Lyxopyranoside* (**9**) [28][30]. To an ice cold soln. of D-lyxose (17.33 g, 115.5 mmol) in anh. MeOH (110 ml) was slowly added AcCl (*Fluka*, > 99%; 1 ml, 14.08 mmol). The resulting soln. (*ca.* 1% *w*/*v*) was heated under reflux for *ca.* 4 h until disappearance of D-lyxose. The cooled mixture was neutralised with Ag_2CO_3 (*ca.* 2 g, pH *ca.* 7), treated with activated charcoal, and filtered through a short plug of *Celite* (2 ∅ × 2 cm). The filtrate (*ca.* 160 ml, including washings with MeOH) was evaporated. The residue, solidifying upon cooling, was recrystallised in hot AcOEt (50 ml) to give pure **9** (14.6 g, first crop, 77%). Colourless solid. R_f ($CHCl_3$/MeOH 4:1) 0.48. M.p. 107.4–108° ([69]: 108–109°). $[\alpha]_D^{25} = +55.2$ ($c = 0.62$, H_2O). IR (KBr): 3302*s*, 3200*s*, 2992*m*, 2968*s*, 2921*s*, 2876*s*, 2840*m*, 1464*s*, 1454*s*, 1384*m*, 1352*s*, 1150*s*, 1128*s*, 1106*s*, 1060*s*, 1013*s*, 971*s*, 879*s*, 848*s*, 776*w*. ^1H-NMR (300 MHz, CD_3OD): 4.55 (*d*, $J = 3.6$, H–C(1)); 3.76–3.62 (*m*, H–C(2), H–C(3), H–C(4), H_{eq}–C(5)); 3.39 (*dd*, $J = 11.4$, 8.4, H_{ax}–C(5)); 3.30 (*s*, MeO). ^{13}C-NMR (75 MHz, D_2O): 102.01 (*d*, C(1)); 71.39 (*d*, C(3)); 70.21 (*d*, C(2)); 67.65 (*d*, C(4)); 63.28 (*t*, C(5)); 56.15 (*q*, MeO). Anal. calc. for $C_6H_{12}O_5$ (164.16): C 43.90, H 7.37; found: C 44.01, H 7.31.

Methyl 2,3-O-*Isopropylidene*-α-D-*lyxopyranoside* (**10**) [28][29]. To a soln. of **9** (8.97 g, 54.70 mmol) in anh. acetone were added powdered molecular sieves (4 Å; 11.21 g) and *Amberlyst-15* (H^+ form, 807 mg). The resulting suspension was stirred at 23° for 4 h (consumption of **9**), and filtered through a short plug of *Celite* (3.8 ø × 4 cm; washing with additional 100 ml of acetone). Evaporation of the combined filtrate and washings gave **10** as viscous oil (11.4 g, quant.), which solidified upon storage. It was used for the next step without any further purification. A pure sample of **10** was obtained by FC (hexane/AcOEt 3:1). Colourless solid. R_f (hexane/AcOEt 3:2) 0.55. M.p. 51.4–52.6° ([29]: 40–41°; [28]: 49–52°). $[\alpha]_D^{25} = +48.3$ ($c = 0.8$, EtOH). IR (2%, $CHCl_3$): 3580*w* (sh), 3450*w*, 2992*w*, 2938*w*, 2839*w*, 1602*w*, 1450*w*, 1384*m*, 1374*m*, 1164*m*, 1140*m*, 1095*s*, 1073*s*, 1009*s*, 982*m*, 954*m*, 908*w*, 871*w*, 854*m*. ^1H-NMR (300 MHz, $CDCl_3$): 4.63 (*d*, $J = 3.0$, H–C(1)); 4.20 (*dd*, $J = 6.0$, 4.8, H–C(3)); 4.10 (*dd*, $J = 6.0$, 2.7, H–C(2)); 3.82–3.76 (*m*, addn. of $D_2O \rightarrow$ change, H–C(4), H_{eq}–C(5)); 3.67 (*dd*, $J = 12.9$, 6.9, H_{ax}–C(5)); 3.44 (*s*, MeO); 3.18 (*d*, $J = 7.5$, exchanged with D_2O, HO–C(4));

1.49, 1.34 (2*s*, Me_2C). ^{13}C-NMR (75 MHz, $CDCl_3$): 109.51 (*s*, Me_2C); 99.88 (*d*, C(1)); 77.36 (*d*, C(3)); 74.45 (*d*, C(2)); 63.29 (*t*, C(5)); 62.29 (*d*, C(4)); 55.58 (*q*, MeO); 27.69, 25.73 (2*q*, *Me*$_2$C). Anal. calc. for $C_9H_{16}O_5$ (204.22): C 43.90, H 7.37; found: C 44.01, H 7.31.

*Methyl 2,3-*O*-Isopropylidene-4-*O*-[(4-methylphenyl)sulfonyl]-α-*D*-lyxopyranoside* (**11**) [28][29]. A soln. of **10** (11.40 g, 55.88 mmol) in dry pyridine (14 ml) was treated with TsCl (15.34 g, 80.46 mmol). The resulting thick slurry was stirred at 23° for 22 h, diluted with AcOEt (150 ml), washed with 10% aq. HCl (2 × 25 ml), H_2O (2 × 25 ml), and brine (25 ml), dried (Na_2SO_4), and evaporated. FC (*ca.* 150 g of silica gel; *ca.* 300 ml of hexane/AcOEt 13:7) and two crystallisations from CH_2Cl_2/hexane gave **11** (16.45 g, 84% from **9**). Colourless solid. R_f (hexane/AcOEt 13:7) 0.66. M.p. 105–106° ([29]: 105–106°. $[\alpha]_D^{25} = -14.8$ ($c = 0.91$, EtOH) ([29]: $[\alpha]_D^{25} = -18.3$ ($c = 0.91$, EtOH)). IR ($CHCl_3$): 3028*w*, 2992*w*, 2938*w*, 1599*w*, 1451*w*, 1446*w*, 1375*s*, 1308*w*, 1176*m*, 1140*m*, 1095*s*, 1019*s*, 1017*s*, 995*m*, 962*w*, 925*m*, 830*s*. ^{1}H-NMR (300 MHz, $CDCl_3$): 7.83 (*d*, $J = 8.4$, 2 arom. H); 7.34 (*d*, $J = 8.4$, 2 arom. H); 4.71 (*d*, $J = 1.5$, H–C(1)); 4.39 (*ddd*, $J = 9.6$, 6.9, 5.1, H–C(4)); 4.14 (*dd*, $J = 6.3$, 5.4, H–C(3)); 4.04 (*dd*, $J = 5.4$, 1.5, H–C(2)); 3.77 (*dd*, $J = 12.0$, 5.1, H_{eq}–C(5)); 3.63 (*dd*, $J = 12.0$, 9.3, H_{ax}–C(5)); 3.38 (*s*, MeO); 2.44 (*s*, Me); 1.25, 1.17 (2*s*, Me_2C). ^{13}C-NMR (75 MHz, $CDCl_3$): 144.92, 133.08 (2*s*); 129.93 (*d*, 2 C); 128.2 (*d*, 2 C); 109.91 (*s*, Me_2C); 98.66 (*d*, C(1)); 76.95, 75.59, 74.62 (3*d*, C(2), C(3), C(4)); 58.54 (*t*, C(5)); 55.58 (*q*, MeO); 27.57, 26.29 (2*q*, *Me*$_2$C); 21.84 (*q*, Me). Anal. calc. for $C_{16}H_{22}O_7S$ (358.41): C 53.62, H 6.19; found: C 53.73, H 6.16.

*Methyl 4-*O*-[(4-Methylphenyl)sulfonyl]-α-*D*-lyxopyranoside* (**12**) [28][29]. A soln. of **11** (11.18 g, 31.22 mmol) in glacial AcOH (48 ml) was warmed to 100–110°, stirred for 5 min, treated with H_2O (12 ml), and stirred for 25 min at 100–110° when TLC showed completion of the reaction. Evaporation without any further heating gave a solid, which was crystallised from CH_2Cl_2/hexane to give **12** (8.89 g, 89%). Colourless solid. R_f (hexane/AcOEt 2:3) 0.28. M.p. 93.4–94.2° ([29]: 94–95°). $[\alpha]_D^{25} = 59.2$ ($c = 0.86$, EtOH) ([29]: $[\alpha]_D^{25} = 61.21$ ($c = 0.88$, EtOH)). IR ($CHCl_3$): 3569*m*, 3390*w* (sh), 3038*w*, 2937*w*, 2837*w*, 1598*m*, 1495*w*, 1465*w*, 1446*w*, 1403*m*, 1369*m*, 1177*s*, 1134*s*, 1100*s*, 1060*s*, 1017*s*, 976*s*, 956*m*, 824*s*. ^{1}H-NMR (300 MHz, $CDCl_3$): 7.82 (*d*, $J = 8.4$, 2 arom. H); 7.35 (*d*, $J = 8.4$, 2 arom. H); 4.62 (*d*, $J = 2.7$, H–C(1)); 4.60 (*td*, $J = 8.4$, 5.7, H–C(4)); 3.96 (*dt*, $J = 8.1$, 3.7, addn. of $D_2O \rightarrow$ *dd*, $J = 8.1$ 3.7, H–C(3)); 3.90 (*q*, $J = 3.0$, addn. of $D_2O \rightarrow$ *t*, $J = 3.0$, H–C(2)); 3.64 (*dd*, $J =$ 11.6, 5.2, H_{eq}–C(5)); 3.58 (*dd*, $J = 11.6$, 8.8, H_{ax}–C(5)); 3.37 (*s*, MeO); 2.93 (*d*, $J = 3.9$, exchanged with D_2O, HO–C(3)); 2.58 (*d*, $J = 3.0$, exchanged with D_2O, HO–C(2)); 2.46 (*s*, Me). ^{13}C-NMR (75 MHz, $CDCl_3$): 145.33, 132.86 (2*s*); 129.98 (*d*, 2 C); 127.94 (*d*, 2 C); 100.42 (*d*, C(1)); 77.25 (*d*, C(4)); 70.27, 68.85 (2*d*, C(2), C(3)); 59.78 (*t*, C(5)); 55.59 (*q*, MeO); 21.85 (*q*, Me). HR-MALDI-MS: 341.0668 ($[M + Na]^+$, $C_{13}H_{18}NaO_7S^+$; calc. 341.0665). Anal. calc. for $C_{13}H_{18}O_7S$ (318.34): C 49.05, H 5.70; found: C 48.97, H 5.82.

*Methyl 3,4-Anhydro-β-*L*-ribopyranoside* (**8**) [28]. A mixture of anh. THF (25 ml)) in a flame-dried 100-ml two-necked flask and *t*-BuOK (2.77 g, 24.70 mmol), under N_2, was cooled to *ca.* 3°, and treated with a soln. of **13** (6.45 g, 20.6 mmol) in anh. THF (45 ml) over a period of 15 min. The mixture was stirred for 45 min at 3°. During this time, stirring became sluggish. After dilution with anh. THF (40 ml), the mixture was stirred for 20 min, poured into sat. aq. NH_4Cl soln. (15 ml), and stirred for *ca.* 30 min. The liquid phase was decanted and filtered through a short pad of *Celite* (2 ø × 2 cm). The residue was treated with AcOEt (150 ml) and filtered. Evaporation of the combined filtrate and filtration through silica gel (*ca.* 20 g; *ca.* 120 ml of hexane/AcOEt 2:3) gave **8** (2.77 g, 92%; homogeneous by ^{1}H-NMR spectroscopy). An anal. sample was obtained by FC (hexane/AcOEt 3:2). Colourless oil. R_f (hexane/AcOEt 11:9) 0.24. M.p. < r.t. $[\alpha]_D^{25} = +542.8$ ($c = 1.01$, $CHCl_3$) ([28]: $[\alpha]_D^{25} = +98.6$ ($c = 1.4$, Me_2CO)). IR ($CHCl_3$): 3554*m*, 3027*m*, 3013*m*, 2960*m*, 2946*m*, 2919*m*, 2869*w*, 2839*w*, 1602*w*, 1466*w*, 1448*m*, 1405*m*, 1351*m*, 1327*w*, 1251*m*, 1149*s*, 1096*s*, 1071*s*, 1046*s*, 1017*s*, 1003*m*, 985*s*, 955*m*, 866*s*, 845*m*. ^{1}H-NMR (300 MHz, $CDCl_3$): 4.36 (*d*, $J = 2.5$, H–C(1)); 3.96 (*dd*, $J = 13.3$, 1.25, H_{eq}–C(5)); 3.90 (br. *d*, $J = 13.3$, H_{ax}–C(5)); 3.75 (*ddd*, $J = 9.9$, 4.4, 2.5, addn. of $D_2O \rightarrow$ *dd*, $J = 4.4$, 2.5, H–C(2)); 3.49 (*t*, $J = 4.4$, H–C(3)); 3.39 (*s*, MeO); 3.34 (*ddd*, $J = 4.4$, 1.5, 0.9, H–C(4)); 2.66 (*d*, $J = 9.9$, exchanged with D_2O, HO–C(2)). ^{13}C-NMR (75 MHz, $CDCl_3$): 99.84 (*d*, C(1)); 64.86 (*d*, C(2)); 58.06 (*t*, C(5)); 55.63 (*q*, MeO); 51.86, 51.57 (2*d*, C(3), C(4)). Anal. calc. for $C_6H_{10}O_4$ (146.14): C 49.31, H, 6.90; found: C 49.30, H 6.85.

*Methyl 3-Cyano-3-deoxy-β-*L*-xylopyranoside* (**13**) *and Methyl 4-Cyano-4-deoxy-2,3-*O*-isopropylidene-α-*D*-lyxopyranoside* (**15**). A cooled soln. (*ca.* −15°) of **8** (557 mg, 3.82 mmol) in anh. Et_2O (10 ml, 0.38M) was slowly treated with *ca.* 1M soln. of Et_2AlCN (7.5 ml, 7.5 mmol, 1.96 equiv.) in toluene. The mixture was allowed to warm to r. t. and then boiled under reflux for *ca.* 4 h. After the disappearance of **8**, the mixture was cooled in an ice-bath, treated dropwise (*caution:* exothermic reaction!) with sat. aq. NH_4Cl soln. (*ca.* 20 ml), and diluted with AcOEt (50 ml). The org. layer was washed with 10% aq. HCl (20 ml) and H_2O (25 ml), dried (Na_2SO_4), and evaporated. A soln. of the residue was dissolved in hexane/AcOEt 1:2, and passed through a short plug of silica gel (8 g of silica gel; hexane/AcOEt 1:2) to give a mixture of **13** and **14** (421 mg), which could not be separated and was used for the next step without further purification.

A soln. of the above mixture (421 mg, 21.9 mmol, *ca.* 90% pure) in dry acetone (25 ml) was treated with powdered molecular sieves (4 Å; *ca.* 3.2 g) and *Amberlyst-15* (H^+ form, 171 mg), stirred for *ca.* 11 h at 24°, and filtered through a short plug of *Celite* (washings with additional acetone). Evaporation and FC (8 g of silica gel; hexane/AcOEt 7:3 → 1:2) gave **15** (142 mg, 17% from **8**) and **13** (135 mg, 21% from **8**).

Data of **13**: Colourless solid. R_f (hexane/AcOEt 1:4) 0.57. M.p. 121.4–121.8° (CH_2Cl_2/hexane). $[\alpha]_D^{25} = +85.4$ ($c = 0.48$, $CHCl_3$). IR ($CHCl_3$): 3602*m*, 3370*w*, 3018*w*, 2935*w*, 2249*w*, 1449*w*, 1256*w* 1154*m*, 1101*s*, 1067*s*, 1037*s*, 984*w*, 878*w*, 833*w*. ^{1}H-NMR (300 MHz, $CDCl_3$): 4.31 (*d*, $J = 5.4$, H–C(1); 4.12 (*dd*, $J = 12.0$, 3.9, H_{eq}–C(5)); 4.04 (*m*, addn. of D_2O → change, H–C(4)); 3.72 (*dt*, $J = 7.8$, 5.1, irrad. at 4.31 → *dd*, $J = 7.8$, 4.8, addn. of D_2O → *dd*, $J = 7.8$, 4.8, H–C(2)); 3.52 (*s*, MeO); 3.43 (*dd*, $J = 11.7$, 6.9, H_{ax}–C(5)); 2.92 (*d*, $J = 4.8$, exchanged with D_2O, HO–C(2)); 2.87 (*t*, $J = 7.8$, H–C(3)); 2.70 (*d*, $J = 5.7$, exchanged with D_2O, HO–C(4)). ^{1}H-NMR (300 MHz, CD_3OD): 4.08 (*d*, $J = 7.5$, H–C(1)); 3.91 (*dd*, $J = 11.1$, 4.8, H_{eq}–C(5)); 3.80 (*td*, $J \approx 10.2$, 4.8, H–C(4)); 3.46 (*s*, MeO); 3.42 (*dd*, $J = 10.5$, 7.2, H–C(2)); 3.21 (*dd*, $J = 11.1$, 9.9, H_{ax}–C(5)); 2.64 (*t*, $J \approx 10.2$, H–C(3)). ^{13}C-NMR (75 MHz, CD_3OD): 120.17 (*s*, CN); 106.19 (*d*, C(1)); 70.44, 69.29 (2*d*, C(2), C(4)); 67.73 (*t*, C(5)); 57.25 (*q*, MeO); 44.07 (*d*, C(3)). Anal. calc. for $C_7H_{11}NO_4$ (173.16): C 48.55, H 6.40, N 8.09; found: C 48.64, H 6.43, N 8.00.

Data of **15**: Colourless solid. R_f (hexane/AcOEt 4:1) 0.32. M.p. 85.5–85.8°(hexane). $[\alpha]_D^{25} = +9.0$ ($c = 1.0$, $CHCl_3$). IR ($CHCl_3$): 3027*m*, 2993*s*, 2938*s*, 2841*w*, 2246*w*, 1602*w*, 1465*w*, 1385*m*, 1375*m*, 1350*w*, 1288*w*, 1245*m*, 1162*m*, 1140*s*, 1128*s*, 1097*s*, 1063*m*, 1018*m*, 980*w*, 956*w*, 893*m*, 850*m*. ^{1}H-NMR (300 MHz, $CDCl_3$): 4.87 (*d*, $J = 1.2$, H–C(1)); 4.38 (*dd*, $J = 8.4$, 5.1, H–C(3)); 4.04 (*dd*, $J = 5.1$, 1.2, H–C(2)); 3.78 (*d*, $J = 7.2$, 2 H–C (5)); 3.41 (*s*, MeO); 2.66 (*q*, $J \approx 7.8$, H–C(4)); 1.54, 1.37 (2*s*, Me_2C). ^{13}C-NMR (75 MHz, $CDCl_3$): 118.04 (*s*, C≡N); 110.28 (*s*, Me_2C); 98.40 (*d*, C(1)); 72.88, 72.22, (2*d*, C(2), C(3)); 56.62 (*t*, C(5)); 55.62 (*q*, MeO); 32.29 (*d*, C(4)); 28.28, 26.23 (2*q*, Me_2C). Anal. calc. for $C_{11}H_{15}NO_4$ (173.17): C 56.33, H 7.09, N 6.57; found: C 56.55, H 7.05, N 6.35.

*Methyl 3,4-Anhydro-2-*O*-(triisopropylsilyl)-β-*L*-ribopyranoside* (**16**). A soln. of **8** (2.77 g, 18.99 mmol) in anh. DMF (5 ml) was treated with 2,6-lutidine (4.4 ml, 37.8 mmol), cooled to 3°, slowly treated with triisopropylsilyl (TIPS) triflate (5.3 ml, 19.65 mmol) over a period of 15 min, and stirred at 3° until disappearance of **8** (*ca.* 3.5 h). The mixture was diluted with AcOEt (100 ml) and washed with 25% aq. $CuSO_4$ soln. (2 × 25 ml), H_2O (25 ml), and brine (25 ml), dried (Na_2SO_4), and evaporated. FC (*ca.* 65 g of silica gel; hexane/AcOEt 19:1 → 9:1) gave **16** (4.71 g, 76% from **12**). Colourless oil. R_f (hexane/AcOEt 17:1) 0.40. M.p. < r.t. $[\alpha]_D^{25} = +98.6$ ($c = 0.94$, $CHCl_3$). IR ($CHCl_3$): 3028*w*, 3006*w*, 2945*s*, 2868*s*, 1465*m*, 1390*w*, 1319*w*, 1146*s*, 1122*s*, 1093*w*, 1054*m*, 997*s*, 957*w*, 882*m*. ^{1}H-NMR (300 MHz, $CDCl_3$): 4.30 (*d*, $J = 4.2$, H–C(1)); 4.05 (*dd*, $J = 13.2$, 2.4, H_{eq}–C(5)); 3.93 (*dt*, $J = 13.5$, 1.0, H_{ax}–C(5); 3.92 (*dd*, $J = 4.5$, 3.0, H–C(2)); 3.39 (br. *dd*, $J = 6.6$, 0.5, H–C(4)); 3.39 (*s*, MeO); 3.36 (*ddd*, $J = 6.9$, 2.7, 0.9, H–C(3)). ^{13}C-NMR (75 MHz, $CDCl_3$): 101.84 (*d*, C(1)); 68.93 (*d*, C(2)); 60.81 (*t*, C(5)); 56.35 (*q*, MeO); 54.32, 53.17 (2*d*, C(3), C(4)); 18.11, 18.08 (2*q*, $(Me_2CH)_3Si$); 12.48 (*d*, $(Me_2CH)_3Si$). Anal. calc. for $C_{15}H_{30}O_4Si$ (302.48): C 59.56, H, 10.00; found: C 59.64, H 10.01.

*Methyl 4-Cyano-4-deoxy-2-*O*-(triisopropylsilyl)-α-*D*-lyxopyranoside* (**17**). A cooled soln. (*ca.* 3°) of **16** (4.71 g, 15.88 mmol) in anh. Et_2O (58 ml, 0.27M) was slowly treated with *ca.* 1M soln. of Et_2AlCN in toluene (19 ml, 19 mmol), allowed to warm to r.t., and then heated under reflux for *ca.* 4 h until disappearance of **16**. The mixture was cooled in an ice-bath and treated dropwise with sat. aq. NH_4Cl soln. (*ca.* 20 ml) (*caution:* exothermic reaction!). The mixture was stirred for an additional 2 h, the liquid phase was decanted, and the solid was thoroughly washed with AcOEt (2 × 25 ml). Evaporation of the combined filtrate, washings, and FC (100 g of silica gel; hexane/AcOEt 9:1 → 17:3) gave **17** (4.52 g, 88%). Colourless solid. R_f (hexane/AcOEt 17:3) 0.34; R_f (hexane/AcOEt 9:1) 0.46. M.p. 78–78.3° (MeOH/H_2O). $[\alpha]_D^{25} = -17.1$ ($c = 1.01$, $CHCl_3$). IR ($CHCl_3$): 3562*w*, 3018*w*, 2946*s*, 2869*s*, 2249*w*, 1464*m*, 1389*w*, 1369*w*, 1149*s*, 1132*s*, 1070*s*, 1030*s*, 998*w*, 973*w*, 883*m*. ^{1}H-NMR (300 MHz, $CDCl_3$): 4.61 (*d*, $J = 2.4$, H–C(1)); 4.03 (*td*, $J = 9.6$, 3.0, addn. of D_2O → *dd*, $J = 9.6$, 3.0, H–C(3)); 3.98 (*dd*, $J = 3.0$, 2.4, irrad. at 4.61 → *d*, $J = 3.0$, H–C(2)); 3.87 (*dd*, $J = 11.1$, 4.5, H_{eq}–C(5)); 3.78 (*dd*, $J = 11.1$, 10.2, H_{ax}–C(5)); 3.38 (*s*, MeO), 3.01 (*td*, $J \approx 9.6$, 4.5, H–C(4)); 2.44 (*d*, $J = 9.3$, exchanged with D_2O, HO–C(3)); 1.08 (br. *s*, $(Me_2CH)_3Si$). ^{13}C-NMR (75 MHz, $CDCl_3$): 118.28 (*s*, CN); 101.31 (*d*, C(1)); 69.94, 68.41 (2*d*, C(2), C(3)); 59.01 (*t*, C(5)); 55.63 (*q*, MeO); 32.53 (*d*, C(4)); 18.18, 18.10 (2*q*, $(Me_2CH)_3Si$); 12.65 (*d*, $(Me_2CH)_3Si$). MALDI-MS: 681.4 ($[2M + Na]^+$, $C_{32}H_{62}N_2NaO_8Si_2^+$; calc. 681.3937). Anal. calc. for $C_{16}H_{31}NO_4Si$ (329.51): C 58.32, H 9.48, N 4.25. found: C 58.18, H 9.59, N 4.22.

*Methyl 4-Carbamoyl-4-deoxy-2-*O*-(triisopropylsilyl)-α-*D*-lyxopyranoside* (**18**) *and Methyl 4-Carbamoyl-4-deoxy-3-*O*-(triisopropylsilyl)-α-*D*-lyxopyranoside* (**19**). A cold (0–5°) soln. of **17** (2.01 g, 6.10 mmol) in Me_2CO/H_2O 3:2 (50 ml) was treated with 1M aq. K_2CO_3 soln. (12.5 ml, 12.5 mmol) and 30% aq. H_2O_2 (3 ml, 26.4 mmol), warmed to 25°, stirred for *ca.* 16 h (disappearance of **17**), and treated with sat. aq. $NaHSO_3$ soln. (5 ml). After evaporation, the residue was taken up in AcOEt (200 ml), washed with 20% aq. HCl soln. (40 ml), H_2O (20 ml), and brine (20 ml), and dried (Na_2SO_4). Evaporation gave crude **18**/**19** *ca.* 1:1 (2.21 g), which was used for the

next step without further purification. Colourless solid. R_f (AcOEt/hexane 3:2) 0.22. IR ($CHCl_3$): 3525*m*, 3494*m*, 3406*m*, 3360*w*, 3194*w*, 3007*m*, 2946*s*, 2868*s*, 1684*s*, 1559*m*, 1464*m*, 1407*w*, 1386*m*, 1366*m*, 1148*s*, 1107*s*, 1061*s*, 1014*s*, 973*s*, 919*w*, 883*w*, 862*w*. ^{1}H-NMR (300 MHz, $CDCl_3$; **18**/**19** *ca.* 1:1): 6.73, 6.30, 6.13, 6.10 (4 br. *s*, slowly exchanged with D_2O, NH_2); 4.68 (*d*, J = 1.8, 0.5 H), 4.62 (*d*, J = 2.1, 0.5 H) (H–C(1)); 4.40 (*dd*, J = 9.3, 3.0, 0.5 H), 4.01 (*td*, J = 9.9, 3.6, addn. of D_2O → *dd*, J = 9.9, 3.3, 0.5 H) (H–C(3)); 3.91 (br. *q*, $J \approx 1.8$, addn. of D_2O → br. *t*, $J \approx 1.8$, 0.5 H–C(2)); 3.84 (br. *dd*, J = 12.0, 5.1, 0.5 H_{eq}–C(5)); 3.80–3.63 (*m*, 0.5 H–C(2), 0.5 H_{eq}–C(5), H_{ax}–C(5)); 3.32, 3.31 (2*s*, MeO); 2.82 (*td*, J = 10.8, 5.1, 0.5 H), 2.75 (*td*, J = 10.5, 5.4, 0.5 H) (H–C(4)); 2.73 (*d*, J = 9.3, exchanged with D_2O, 0.5 HO–C(3)); 2.66 (*d*, J = 1.8, exchanged with D_2O, 0.5 HO–C(2); 1.09–1.01 (*m*, $(Me_2CH)_3Si$). ^{13}C-NMR (75 MHz, $CDCl_3$; **18**/**19** *ca.* 1:1): 174.27, 173.54 (2*s*, C=O); 101.05, 100.84 (2*d*, C(1)); 70.49, 69.58, 68.88, 67.69 (4*d*, C(2), C(3)); 60.21, 59.35 (2*t*, C(5)); 55.11, 55.08 (2*q*, MeO); 46.34, 44.51 (2*d*, C(4)); 18.43, 18.08 (2*q*, $(Me_2CH)_3Si$); 12.62 (*d*, $(Me_2CH)_3Si$).

*Methyl 4-Carbomyl-4-deoxy-α-*D*-lyxopyranoside* (**20**). A stirred soln. of **18**/**19** *ca.* 1:1 (2.21 g, 6.35 mmol) and TBAF · 3 H_2O (2.6 g, 8.34 mmol) in dry THF (10 ml) was kept for 3 h at 83°. Evaporation, FC (24 g of silica gel; AcOEt → AcOEt/MeOH 9:1), and recrystallisation in AcOEt/MeOH gave **20** (916 mg, 78% from **17**). Colourless solid. R_f (MeOH/AcOEt 1:9) 0.24. M.p. 128.7–129.8°(MeOH/AcOEt). $[\alpha]_D^{25} = +52.3$ (c = 0.52 EtOH). IR (KBr): 3409*s*, 3225*s*, 3175*s*, 3007*m*, 2956*s*, 2938*s*, 2885*m*, 1682*s*, 1641*s*, 1621*s*, 1439*s*, 1384*s*, 1355*s*, 1250*s*, 1142*s*, 1126*s*, 1089*s*, 1059*s*, 1009*s*, 964*s*, 941*w*, 881*w*, 846*w*. ^{1}H-NMR (300 MHz, D_2O): 4.65 (*d*, J = 2.1, H–C(1)); 3.98 (*dd*, J = 10.8, 3.0, irrad. at 2.79 → change, H–C(3)); 3.73 (*dd*, J = 3.0, 2.1, H–C(2)); 3.71 (*dd*, J = 11.1, 5.4, irrad. at 2.79 → change, H_{eq}–C(5)); 3.62 (*t*, $J \approx 11.1$, irrad. at 2.79 → change, H_{ax}–C(5)); 3.27 (*s*, MeO); 2.79 (*td*, $J \approx 11.1$, 5.4, irrad. at 3.98 → *dd*, J = 11.1, 5.4, H–C(4)). ^{13}C-NMR (75 MHz, D_2O): 175.54 (*s*, C=O); 101.05 (*d*, C(1)); 67.96, 66.07 (2*d*, C(2), C(3)); 59.63 (*t*, C(5)); 54.74 (*q*, MeO); 44.86 (*d*, C(4)). Anal. calc. for $C_{10}H_{17}O_5N$ (231.25): C 51.94, H 7.41; N 6.06; found: C 52.07, H 7.27, N 6.02.

Isopropylidenation of **20**. A soln. of **20** (592 mg, 3.1 mmol) in anh. Me_2CO (20 ml) was treated with powdered molecular sieves (4 Å; 670 mg) and *Amberlyst-15* (H^+ form, 215 mg), stirred at 24° for 4 h, and filtered through a short plug of *Celite* (washing with 15 ml of Me_2CO). Evaporation and FC (*ca.* 15 g of silica gel; 300 ml of hexane/AcOEt 4:1) gave **21** (582 mg, 81%), and **22** (85 mg, 12%, containing traces of **21**).

*Methyl 4-Carbamoyl-4-deoxy-2,3-*O*-isopropylidene-α-*D*-lyxopyranoside* (**21**). Colourless solid. R_f (hexane/AcOEt 2:3) 0.21. M.p. 159–159.8° (CH_2Cl_2/hexane). $[\alpha]_D^{25} = +21.0$ (c = 1.01, $CHCl_3$). IR (*ca.* 3%, $CHCl_3$): 3502*m*, 3386*m*, 3007*m*, 2937*m*, 2838*m*, 1682*s*, 1589*s*, 1466*w*, 1385*s*, 1370*s*, 1248*w*, 1142*s*, 1093*s*, 1057*s*, 1006*m*, 908*w*, 953*w*, 851*m*. ^{1}H-NMR (300 MHz, $CDCl_3$): 6.28, 5.36 (2 br. *s*, exchanged with D_2O, NH_2); 4.88 (br. *s*, J < 1.5, H–C(1)); 4.36 (*dd*, J = 9.3, 5.4, H–C(3)); 4.02 (*dd*, J = 5.4, 1.8, H–C(2)); 3.84 (*dd*, J = 12.3, 4.8, H_{eq}–C(5)); 3.72 (*dd*, J = 12.3, 10.8, H_{ax}–C(5)); 3.39 (*s*, MeO); 2.66 (*ddd*, $J \approx 10.5$, 9.3, 4.8, H–C(4)); 1.58, 1.37 (2*s*, Me_2C). ^{13}C-NMR (75 MHz, $CDCl_3$): 173.84 (*s*, C=O); 109.68 (*s*, Me_2C); 98.54 (*d*, C(1)); 73.52, 72.94 (2*d*, C(2), C(3)); 57.11 (*t*, C(5)); 55.14 (*q*, MeO); 44.46 (*d*, C(4)); 28.42, 26.30 (2*q*, Me_2C). Anal. calc. for $C_{10}H_{17}O_5N$ (231.245): C 51.94, H 7.41, N 6.06; found: C 52.07, H 7.27, N 6.02.

*Methyl 4-Carbamoyl-4-deoxy-3-*O*,4′-*N*-isopropylidene-α-*D*-lyxopyranoside* (**22**). Colourless oil. R_f (hexane/AcOEt 2:3) 0.21. $[\alpha]_D^{25} = +43.0$ (c = 0.7, $CHCl_3$). IR ($CHCl_3$): 3599*w*, 3500*w*, 3396*w*, 3017*m*, 2936*w*, 1667*s*, 1591*w*, 1426*m*, 1389*w*, 1373*w*, 1215*s*, 1161*m*, 1125*m*, 1091*w*, 1055*s*, 1017*m*, 999*m*. ^{1}H-NMR (300 MHz, $CDCl_3$): 6.70 (br. *s*, slowly exchanged with D_2O, NH); 4.74 (*d*, J = 1.5, H–C(1)); 4.02 (*dd*, J = 11.7, 4.8, H_{eq}–C(5)); 4.01 (*dd*, J = 10.8, 2.7, H–C(3)); 3.94 (*td*, $J \approx 3.0$, 1.5, addn. of D_2O → *dd*, $J \approx 3.0$, 1.5, H–C(2)); 3.62 (*t*, $J \approx 11.4$, H_{ax}–C(5)); 3.37 (*s*, MeO); 2.66 (*td*, $J \approx 11.1$, 4.8, H–C(4)); 2.41 (*d*, J = 3.0, exchanged with D_2O, HO–C(2)); 1.49, 1.48 (2*s*, Me_2C). ^{13}C-NMR (75 MHz, $CDCl_3$): 168.84 (*s*, C=O); 100.86 (*d*, C(1)); 85.90 (*s*, Me_2C); 68.25, 67.61 (2*d*, C(2), C(3)); 57.76 (*t*, C(5)); 55.16 (*q*, MeO); 37.61 (*d*, C(4)); 31.21, 27.78 (2*q*, Me_2C). HR-EI-MS: 216.0873 ($[M-Me]^+$, $C_9H_{14}NO_4^+$; calc. 216.0877).

*Methyl 4-(Aminothiocarbonyl)-4-deoxy-2,3-*O*-isopropylidene-α-*D*-lyxopyranoside* (**23**). A soln. of **21** (30 mg, 0.129 mmol) in dry toluene (1 ml) was treated with *Lawesson*'s reagent (35.4 mg, 0.88 mmol) at 23°, heated to 70°, and stirred for 15 min (disappearance of **21**). Evaporation and FC (*ca.* 2 g of silica gel; hexane/AcOEt 7:3) gave **23** (27 mg, 84%). Yellowish solid. R_f (hexane/AcOEt 7:3) 0.22. M.p. 139–139.5° (CH_2Cl_2/hexane). $[\alpha]_D^{25} = -8.2$ (c = 0.96, $CHCl_3$). IR (*ca.* 1%, $CHCl_3$): 3468*w*, 3337*w*, 2992*m*, 2937*w*, 1601*m*, 1400*m*, 1385*m*, 1370*w*, 1246*w*, 1161*w*, 1140*m*, 1092*s*, 1055*s*, 1005*m*, 954*w*, 894*w*, 856*m*. ^{1}H-NMR (300 MHz, $CDCl_3$): 7.78, 7.59 (2 br. *s*, exchanged slowly with D_2O, NH_2); 4.88 (br. *s*, J < 1, H–C(1)); 4.39 (*dd*, J = 8.7, 5.4, H–C(3)); 4.03 (*dd*, J = 5.4, 0.5, H–C(2)); 3.88 (*dd*, J = 12.1, 4.8, H_{eq}–C(5)); 3.80 (*dd*, J = 12.1, 9.6, H_{ax}–C(5)); 3.39 (*s*, MeO); 2.83 (*ddd*, $J \approx 9.6$, 8.7, 4.8, H–C(4)); 1.57, 1.36 (2*s*, Me_2C). ^{13}C-NMR (75 MHz, $CDCl_3$): 207.82 (*s*, C=S); 109.62 (*s*, Me_2C); 98.45 (*d*, C(1)); 74.92, 73.67 (2*d*, C(2), C(3)); 59.33 (*t*, C(5)); 55.22 (*q*, MeO); 50.06 (*d*, C(4)); 28.53, 26.29 (2*q*, Me_2C). HR-MALDI-MS: 232.0644 ($[M-Me]^+$, $C_9H_{14}NO_4S^+$; calc. 232.0628). Anal. calc. for $C_{10}H_{17}NO_4S$ (249.30): C 48.57, H 6.93, N 5.66; found: C 49.11, H 7.04, N 5.54.

Transformation of **23** *to* **15**. At $-15°$, a soln. of **23** (10 mg, 0.0405 mmol) in THF (1 ml) was treated with aminoacetaldehyde dimethyl acetal (87 µl, 0.81 mmol) and then with $Hg(OAc)_2$ (13 mg, 0.41 mmol). The mixture was stirred for 35 min (complete consumption of **23**), and filtered through a short plug of *Celite* (washed with AcOEt). The combined org. layers (*ca.* 15 ml) were washed with sat. aq. $NaHCO_3$ soln., dried (Na_2SO_4), and evaporated. FC (silica gel, hexane/AcOEt 4:1) gave **15** (7 mg, 81%), which could not be distinguished from a sample of **15** prepared from **8**.

Methyl 2,3-Di-O-*acetyl-4-carbamoyl-4-deoxy-α*-D-*lyxopyranoside* (**24**). A mixture of **20** (83 mg, 0.43 mmol) in dry pyridine (1 ml) was treated with Ac_2O (0.3 ml, 0.88 mmol) and DMAP (2 mg, 0.016 mmol), stirred for 16 h at 23.5°, diluted with AcOEt (25 ml), washed with H_2O (5 ml) and 5% aq. HCl (5 ml), dried (Na_2SO_4), and filtered through a short column (*ca.* 1 g of silica gel). Evaporation of the filtrate and crystallisation from (CH_2Cl_2/hexane) gave **24** (92 mg, 74%). Colourless solid. R_f (hexane/AcOEt 3:2) 0.70. M.p. 192–193.3° (CH_2Cl_2/hexane). $[\alpha]_D^{25} = +13.3$ ($c = 0.35$, $CHCl_3$). IR (*ca.* 1%, $CHCl_3$): 3408*w*, 3015*w*, 2876*w*, 2839*w*, 1749*s*, 1692*m*, 1592*w*, 1374*m*, 1255*w*, 1134*m*, 1076*m*, 1048*m*, 1024*s*, 973*w*, 904*w*, 877*m*. ^{1}H-NMR (300 MHz, $CDCl_3$): 5.63 (br. *s*, exchanged with D_2O, NH); 5.49 (*dd*, $J = 11.1$, 3.3, H–C(3)); 5.43 (br. *s*, exchanged with D_2O, NH); 5.21 (*dd*, $J = 3.3$, 1.8, H–C(2)); 4.67 (*d*, $J = 1.8$, H–C(1)); 3.95 (*t*, $J \approx 11.4$, H_{ax}–C(5)); 3.86 (*dd*, $J = 11.4$, 5.1, H_{eq}–C(5)); 3.39 (*s*, MeO); 3.00 (*td*, $J \approx 11.1$, 4.8, H–C(4)); 2.14, 2.01 (2*s*, 2 AcO). ^{13}C-NMR (75 MHz, $CDCl_3$): 171.66 (*s*, $H_2NC{=}O$); 169.99, 169.54 (2*s*, 2 OC=O); 98.92 (*d*, C(1)); 67.76 (*d*, C(2), C(3)); 60.23 (*t*, C(5)); 55.26 (*q*, MeO); 44.55 (*d*, C(4)); 20.94, 20.82 (2*q*, 2 Me). HR-MALDI-MS: 298.0893 ($[M + Na]^+$, $C_{11}H_{17}NNaO_7^+$; calc. 298.0897). Anal. calc. for $C_{11}H_{17}NO_7$ (275.26): C 48.00, H 6.22, N 5.09; found: C 48.17, H 6.20, N 5.02.

Methyl 2,3-Di-O-*acetyl-4-(aminothiocarbonyl)-4-deoxy-α*-D-*lyxopyranoside* (**25**). A stirred mixture of **24** (102 mg, 0.37 mmol) and *Lawesson*'s reagent (95 mg, 0.225 mmol) in dry toluene (2 ml) was kept at 98° for 20 min (disappearance of **24**). Evaporation and FC (*ca.* 3 g of silica gel; hexane/AcOEt 7:3 → 2:3) gave **25** (82 mg, 76%). Colourless solid. R_f (hexane/AcOEt 3:2) 0.48. M.p. 195–197° (CH_2Cl_2/hexane). $[\alpha]_D^{25} = +3.6$ ($c = 1.08$, $CHCl_3$). IR (*ca.* 1%, $CHCl_3$): 3488*w*, 3373*w*, 3197*w*, 3017*w*, 2839*w*, 1748*s*, 1603*m*, 1426*w*, 1374*m*, 1320*w*, 1294*w*, 1240*s*, 1133*m*, 1075*s*, 1022*s*, 977*w*, 909*w*, 861*m*. ^{1}H-NMR (300 MHz, $CDCl_3$): 7.61 (br. *s*, exchanged with D_2O, NH); 7.14 (br. *s*, exchanged with D_2O, NH); 5.58 (*dd*, $J = 11.1$, 3.3, H–C(3)); 5.22 (*dd*, $J = 3.2$, 1.8, H–C(2)); 4.68 (*d*, $J = 1.8$, H–C(1)); 4.03 (*t*, $J \approx 11.1$, H_{ax}–C(5)); 3.88 (*dd*, $J = 11.1$, 4.8, H_{eq}–C(5)); 3.40 (*s*, MeO); 2.83 (*td*, $J \approx 11.1$, 4.8, H–C(4)); 2.14, 1.98 (2*s*, 2 AcO). ^{13}C-NMR (75 MHz, $CDCl_3$): 204.76 (*s*, C=S); 169.79, 169.48 (2*s*, 2 C=O); 99.05 (*d*, C(1)); 69.85, 68.02 (2*d*, C(2), C(3)); 62.94 (*t*, C(5)); 55.47 (*q*, MeO); 50.39 (*d*, C(4)); 21.12, 20.91 (2*q*, 2 Me). Anal. calc. for $C_{11}H_{17}NO_6S$ (291.32): C 45.35, H 5.88, N 4.78; found: C 45.17, H 5.66, N 4.78.

Methyl 2,3-Di-O-*acetyl-4-cyano-4-deoxy-α*-D-*lyxopyranoside* (**26**). A soln. of **25** (52 mg, 0.178 mmol) in THF (2 ml) was cooled to 0°, treated with $NH_2CH_2CH(OMe)_2$ (100 µl, 0.93 mmol) and $Hg(OAc)_2$ (81 mg, 0.254 µmol), stirred for 5 h (consumption of **25**), diluted with AcOEt (25 ml), and filtered through a short plug of *Celite* (AcOEt). The filtrate (*ca.* 25 ml) was washed with H_2O (5 ml) and brine (25 ml), dried (Na_2SO_4), and evaporated. FC (*ca.* 2 g of silica gel; hexane/AcOEt 7:3) gave **26** (33 mg, 77%). Colourless solid. R_f (hexane/AcOEt 7:3) 0.38. M.p. 121–122°. $[\alpha]_D^{25} = +9.4$ ($c = 0.9$, $CHCl_3$). IR ($CHCl_3$): 3038*w*, 2961*w*, 2928*s*, 2841*w*, 2250*w*, 1751*s*, 1602*w*, 1463*w*, 1375*m*, 1295*w*, 1261*m*, 1156*m*, 1134*s*, 1077*s*, 1026*m*, 978*w*, 920*w*, 903*w*, 875*w*, 850*m*. ^{1}H-NMR (300 MHz, $CDCl_3$): 5.40 (*dd*, $J = 11.4$, 3.0, H–C(3)); 5.19 (*dd*, $J = 3.0$, 2.1, H–C(2)); 4.67 (*d*, $J = 2.1$, H–C(1)); 3.98 (*dd*, $J = 11.4$, 6.3, H_{eq}–C(5)); 3.94 (*dd*, $J = 11.4$, 10.5, H_{ax}–C(5)); 3.41 (*s*, MeO); 3.26 (*ddd*, $J =$ 11.4, 10.5, 6.0, H–C(4)); 2.14, 2.08 (2*s*, 2 Me). ^{13}C-NMR (75 MHz, $CDCl_3$): 169.53, 169.09 (2*s*, 2 C=O); 116.44 (*s*, CN); 98.81 (*s*, C(1)); 67.02, 66.64 (2*d*, C(2), C(3)); 58.78 (*t*, C(5)); 55.71 (*q*, MeO); 29.22 (*d*, C(4)); 20.95, 20.77 (2*q*, 2 Me). Anal. calc. for $C_{11}H_{15}NO_6$ (257.2399): C 51.36, H 5.88, N 5.44; found: C 51.48, H 5.76, N 5.43.

*Methyl 4-Deoxy-4-(1*H-*imidazol-2-yl)-2*-O-*(triisopropylsilyl)-α*-D-*lyxopyranoside* (**27**). A cold (3°) soln. of **17** (4.3 g, 13.06 mmol) in anh. toluene (40 mmol) was treated with a premixed soln. of Me_3Al and $NH_2CH_2CH(OMe)_2$ in toluene (24 ml, 21.6 mmol, *ca.* 0.9M), warmed slowly to 23°, and kept for 26 h at 90°. The mixture was allowed to cool and treated carefully with a sat. aq. NH_4Cl soln. (25 ml) to allow precipitation of the aluminium salts. After filtration and washing with AcOEt (350 ml), the combined org. layers were washed with H_2O (2 × 40 ml) and brine, dried (Na_2SO_4), and evaporated. FC (*ca.* 105 g, hexane/AcOEt 9:1 → 7:3) gave **17** (620 mg, 14%) and **27** (2.54 g, 53%). Yellow solid. R_f (AcOEt) 0.34. M.p. 113.9–114.8° (hexane). $[\alpha]_D^{25} =$ +3.0 ($c = 1.01$, $CHCl_3$). UV (EtOH, qualitative, λ_{max}): 210 nm. IR (1.5%, $CHCl_3$): 3551*m*, 3423*m*, 2946*s*, 2869*s*, 1541*m*, 1464*m*, 1437*m*, 1371*m*, 1268*m*, 1132*s*, 1111*s*, 1086*m*, 1070*s*, 1020*s*, 998*m*, 967*m*, 910*m*, 884*m*, 838*w*. ^{1}H-NMR (400 MHz, $CDCl_3$; assignment based on a DQFCOSY and a HSQC spectrum): 9.98 (br. *s*, NH, exchanged with D_2O); 6.97 (br. *s*, H–C(4′), H–C(5′)); 4.68 (*d*, $J = 2.2$, H–C(1)); 4.16 (*dd*, $J = 11.7$, 5.1, H_{eq}–C(5)); 4.05 (br. *s*, addn. of $D_2O \rightarrow$ *dd*, $J = 9.9$, 3.0, H–C(3)); 3.96 (*t*, $J \approx 2.5$, H–C(2)); 3.85 (*dd*, $J = 11.7$,

10.5, H_{ax}–C(5a)); 3.37 (*s*, MeO); 3.29 (*td*, $J \approx 10.5, 4.8$, H–C(4)); 2.78 (br. *s*, exchanged with D_2O, HO–C(3)); 1.14–1.04 (*m*, $(Me_2CH)_3Si$). ^{13}C-NMR (100 MHz, $CDCl_3$): 146.73 (*s*, C(2′)); 127.83 (br. *d*, C(4′)); 115.19 (br. *d*, C(5′)); 101.34 (*d*, C(1)); 70.56 (*d*, C(2)); 69.82 (*d*, C(3)); 60.33 (*t*, C(5)); 55.04 (*q*, MeO); 38.02 (*d*, C(4)); 17.94 (*q*, $(Me_2CH)_3Si$); 12.57 (*d*, $(Me_2CH)_3Si$). HR-MALDI-MS: 393.2172 ($[M+Na]^+$, $C_{18}H_{34}N_2NaO_4Si^+$; calc. 393.2180). Anal. calc. for $C_{18}H_{34}N_2O_4Si$ (370.23): C 58.34, H 9.25, N 7.56; found: C 58.26, H 9.18, N 7.58.

*(5*R/S*,6*S*,7*R*,8*R*)-5,6,7,8-Tetrahydro-8-(hydroxymethyl)imidazo[1,2-*a*]pyridine-5,6,7-triol* (**4**/**28**) *and 4-Deoxy-4-(1*H*-imidazol-2-yl)-α/β-*D*-lyxopyranoside* (**29**/**30**). A stirred soln. of **27** (365 mg, 0.78 mmol) in 80% aq. AcOH (6.8 ml) was treated with 20% aq. HCl (1.15 ml, *ca.* 2.3 mmol) was kept at 113°. After stirring for 2.5 h, it was cooled to 24°. Evaporation and FC (9 g of silica gel; AcOEt/MeOH/H_2O 13:6:1) gave pure **4**/**28**/**29**/**30** (182 mg, 95%), which was filtered through a short plug of *Amberlite-CG 120* (H^+ form, 2% NH_4OH) and lyophilised. Hygroscopic solid. R_f (AcOEt/MeOH/H_2O 13:6:1) 0.52. R_f (AcOEt/MeOH/H_2O 7:2:1) 0.65. $[\alpha]_D^{25} = +0.4$ (*c* = 1.55, EtOH). IR (KBr): 3460*s*, 2925*w*, 2855*w*, 1631*w*, 1488*w*, 1452*w*, 1263*w*, 1172*w*, 1092*w*, 1041*w*, 928*w*, 833*w*. ^{1}H-NMR (300 MHz, CD_3OD; **4**/**28**/**29**/**30** *ca.* 60:8:14:18): 7.08 (br. *s*, 0.68 H, H–C(2) of **4**/**28**); 6.90–6.87 (3 br. *s*, 1.68 H, H–C(3) of **4**/**28**, H–C(4′) and H–C(5′) of **29**/**30**); 5.47 (*d*, *J* = 3.6, 0.8 H), 5.32 (*d*, *J* = 7.2, 0.60 H) (H–C(5) of **4**/**28**); 5.06 (*d*, *J* = 4.8, 0.14 H), 4.67 (br. *s*, 0.18 H) (H–C(1) of **29**/**30**); 4.40–3.15 (*m*) (H–C(6), H–C(7), and CH_2–C(8) of **4**, and H–C(2), H–C(3), H–C(4), H–C(5_{ax}), and H–C(5_{eq}) of **29**/**30**); 4.35 (*dd*, *J* = 3.6, 1.5, 0.60 H, H–C(7) of **4**)); 4.20 (*dd*, *J* = 10.8, 4.2, 0.60 H, CH_2–C(8) of **4**); 3.84 (*dd*, *J* = 10.8, 9.3, 0.60 H, CH_2–C(8) of **4**); 3.73 (*dd*, *J* = 7.2, 1.5, 0.60 H, H–C(6) of **4**); 3.35–3.15 (*m*, 0.32 H, H–C(4) of **29**/**30**); 3.05–2.98 (*m*), 3.01 (br. *ddd*, *J* = 8.4, 4.2, 3.6, 0.6 H) (H–C(8) of **4**/**28**). ^{13}C-NMR (75 MHz, CD_3OD, **4**/**28**/**29**/**30** *ca.* 60:8:14:18): 147.39 (*s*, 0.18 C), 146.91(*s*, 0.14 C), 145.70 (*s*, 0.6 C), 144.36 (*s*, 0.08 C), (C(8a) of **4**/**28** and C(2′) of **29**/**30**); 128.29 (*d*, 0.08 C), 127.42 (*d*, 0.6 C) (C(2) of **4**/**28**); 122.33 (*d*, 0.28 C), 121.82 (*d*, 0.36 C) (C(4′) and C(5′) of **29**/**30**); 119.68 (*d*, 0.08 C), 118.23 (*d*, 0.6 C) (C(3) of **4**/**28**); 96.86 (*d*, 0.14 C), 96.04 (*d*, 0.18 C) (C(1) of **29**/**30**); 81.58 (*d*, 0.6 C), 79.24 (*d*, 0.08 C) (C(5) of **4**/**28**); 75.14 (*d*, 0.6 C, C(6) of **4**); 71.72 (*d*, 0.08 C), 71.30 (*d*, 0.18 C), 70.85, (*d*, 0.14 C), 69.42 (*d*, 0.18 C), 69.30 (*d*, 0.14 C), 69.15 (*d*, 0.08 C) (C(6) and C(7) of **28**, C(2) and C(3) of **29**/**30**); 70.04 (*d*, 0.6 C, C(7) of **4**); 61.44 (*t*, 0.32 C), 61.43 (*t*, 0.6 C), 60.99 (*t*, 0.08 C) (CH_2–C(8) of **4**/**28** and C(5) of **29**/**30**); 42.81 (*d*, 0.6 C), 42.31 (*d*, 0.14 C), 40.75 (*d*, 0.08 C), 39.97 (*d*, 0.18 C) (C(8) of **4**/**28** and C(4) of **29**/**30**). HR-MALDI-MS of the HCl salts: 201.0871 ($[M+H-HCl]^+$, $C_8H_{13}N_2O_4^+$; calc. 201.0870).

*2-Deoxy-2-(1*H*-imidazol-2-yl)-*D*-arabinitol* (**31**). A soln. of **4**/**28**–**30** (41 mg, 0.203 mmol) in dry MeOH (1 ml) was treated with AcOH (100 µl) and $NaCNBH_3$ (53 mg, 0.84 mmol), stirred for 60 h at 26°, and evaporated. FC (*ca.* 6 g of silica gel; AcOEt → AcOEt/MeOH 9:1 → AcOEt/MeOH/NH_4OH 7:2:1) gave **31** (34 mg, 90%). Colourless syrup. R_f (AcOEt/MeOH/H_2O 7:2:1) 0.45. $[\alpha]_D^{25} = -15.1$ (*c* = 0.1, EtOH). ^{1}H-NMR (300 MHz, CD_3OD): 6.91 (br. *s*, H–C(4′), H–C(5′)); 3.90 (*dd*, *J* = 10.8, 7.8, irrad. at 3.44 → change, H_a–C(5)); 3.88 (*dd*, *J* = 9.0, 2.7, irrad. at 3.44 → change, irrad. at 3.11 → change, H–C(3)); 3.80 (*dd*, *J* = 10.8, 6.6, irrad. at 3.44 → change, H_b–C(5)); 3.67 (*dd*, *J* = 11.4, 3.6, irrad. at 3.11 → *d*, *J* = 10.8, H_b–C(1)); 3.51 (*dd*, *J* = 11.4, 6.3, irrad. at 3.11 → *d*, *J* = 10.8, H_a–C(1)); 3.44 (*ddd*, *J* = 7.8, 6.6, 2.7, H–C(4)); 3.11 (*ddd*, *J* = 9.6, 6.3, 3.6, irrad. at 3.51 → change, H–C(2)). ^{13}C-NMR (75 MHz, CD_3OD): 147.94 (*s*, C(2′)); 122.16 (br. *s*, C(4′), C(5′)); 73.82, 71.94 (2*d*, C(3), C(4)); 65.21. 63.66 (2*t*, C(1), C(5)); 45.0 (*d*, C(2)). HR-MALDI-MS: 242.2839 ($[M+K]^+$, $C_8H_{14}KN_2O_4^+$; calc. 242.0669); 225.0846 ($[M+Na]^+$, $C_8H_{14}N_2NaO_4^+$; calc. 225.0840); 203.1026 ($[M+H]^+$, $C_8H_{15}N_2O_4^+$; calc. 203.1026).

Silylation of **4**/**28**–**30**. A soln. of **4**/**28**–**30** (470 mg, 1.99 mmol) in dry pyridine (8 ml) at 2° was treated with 2,6-lutidine (1 ml, 8.41 mmol) and Et_3SiCl (3.0 ml, 17.88 mmol). The mixture was stirred for 24 h at 27°, diluted with AcOEt (200 ml), washed with H_2O (5 × 20 ml) and brine (5 ml), dried (Na_2SO_4), and evaporated. FC (*ca.* 12 g of silica gel; *ca.* 50 ml of AcOEt/hexane 1:4) gave **32** (212 mg, 16%), **33** (230 mg, *ca.* 90% pure, 22%,) and **34** (85 mg, 8%).

*(5*R*,6*S*,7*R*,8*R*)-5,6,7,8-Tetrahydro-5,6,7-tris(triethylsilyloxy)-8-[(triethylsilyloxy)methyl]imidazo[1,2-*a*]pyridine* (**32**). Colourless oil. R_f (hexane/AcOEt 7:3) 0.81. $[\alpha]_D^{25} = +0.5$ (*c* = 2.9, $CHCl_3$). IR ($CHCl_3$): 2958*s*, 2913*s*, 2878*s*, 1525*w*, 1490*w*, 1458*w*, 1414*w*, 1381*w*, 1255*m*, 1156*m*, 1139*m*, 1093*s*, 1008*s*, 962*w*, 885*w*, 862*w*. ^{1}H-NMR (300 MHz, CD_3OD): 7.00 (*d*, *J* = 1.5, H–C(2)); 6.90 (*d*, *J* = 1.2, H–C(3)); 5.50 (*d*, *J* = 5.4, H–C(5)); 4.49 (*dd*, *J* = 4.2, 1.5, H–C(7)); 4.09 (*dd*, *J* = 9.9, 5.7, CH_a–C(8)); 3.93 (*dd*, *J* = 9.9, 7.2, CH_b–C(8)); 3.87 (*dd*, *J* = 5.7, 1.5, H–C(6)); 3.20 (*ddd*, *J* = 7.2, 5.7, 4.2, H–C(8)); 1.03–0.61 (*m*, 4 $(MeCH_2)_3Si$). ^{1}H-NMR (300 MHz, $CDCl_3$): 6.94 (*d*, *J* = 1.5, H–C(2)); 6.91 (*d*, *J* = 1.2, H–C(3)); 5.46 (*d*, *J* = 6.9, H–C(5)); 4.41 (*dd*, *J* = 3.0, 1.5, H–C(7)); 4.27 (*dd*, *J* = 9.9, 5.1, CH_a–C(8)); 3.93 (*t*, $J \approx 9.6$, CH_b–C(8)); 3.87 (*dd*, *J* = 6.6, 1.5, H–C(6)); 2.93 (br. *ddd*, $J \approx 9.0$, 5.1, 3.0, H–C(8)); 1.03–0.56 (*m*, 4 $(MeCH_2)_3Si$). ^{13}C-NMR (75 MHz, CD_3OD, assignment based on a HSQC spectrum): 146.11 (*s*, C(8a)); 128.89 (*d*, C(2)); 118.30 (*d*, C(3)); 82.69 (*d*, C(5)); 77.82 (*d*,

C(6)); 70.86 (*d*, C(7)); 61.55 (*t*, CH_2−C(8)); 45.68 (*d*, C(8)); 7.60, 7.56, 7.42, 7.39 (4*q*, 4 (*Me*CH_2)$_3$Si); 6.28, 5.59 (2*t*, 4 (*Me*CH_2)$_3$Si). HR-MALDI-MS: 657.4336 ($[M+H]^+$, $C_{32}H_{69}N_2O_4Si_4^+$; calc. 657.4329).

*(5*R*,6*S*,7*R*,8*R*)-5,6,7,8-Tetrahydro-5,6-bis(triethylsilyloxy)-8-[(triethylsilyloxy)methyl]imidazo[1,2-*a*]pyridin-7-ol* (**33**). Colourless oil. R_f (hexane/AcOEt 7:3) 0.61. IR ($CHCl_3$): 3411*w*, 2959*s*, 2813*s*, 2878*s*, 1525*w*, 1458*m*, 1414*m*, 1338*w*, 1251*m*, 1128*s*, 1090*s*, 1055*s*, 885*m*, 861*w*. ^{1}H-NMR (300 MHz, $CDCl_3$; *ca.* 90% pure): 7.00 (*d*, *J* = 1.5, H−C(2)); 6.87 (*d*, *J* = 1.5, H−C(3)); 5.46 (*d*, *J* = 4.5, H−C(5)); 4.50 (*ddd*, *J* = 6.3, 4.2, 2.1, irrad. at 3.36 → change, irrad. at 4.19 → *dd*, *J* = 6.3, 2.1, addn. of D_2O → *dd*, *J* = 6.3, 2.1, H−C(7)); 4.30–4.28 (*m*, irrad. at 3.36 → *s*, CH_2−C(8)); 4.19 (*d*, *J* = 3.9, HO−C(7), exchanged with D_2O); 4.01 (*dd*, *J* = 4.8, 2.1, irrad. at 5.46 → *d*, *J* = 2.1, H−C(6)); 3.36 (*ddd*, *J* = 8.4, 6.9, 5.4, irrad. at 4.50 → br. *dd*, *J* = 7.8, 7.2, H−C(8)); 1.00–0.94 (*m*, 3 (*Me*CH_2)$_3$Si); 0.71–0.66 (*m*, 3 (MeC*H*$_2$)$_3$Si). ^{13}C-NMR (75 MHz, $CDCl_3$): 143.17 (*s*, C(8a)); 128.99 (*d*, C(2)); 117.15 (*d*, C(3)); 81.16 (*d*, C(5)); 76.31 (*d*, C(6)); 68.76 (*d*, C(7)); 64.10 (*t*, CH_2−C(8)); 40.35 (*d*, C(8)); 6.99, 6.93, 6.88 (3*q*, 3 (*Me*CH_2)$_3$Si); 5.19, 5.17, 4.46 (3*t*, 3 (Me*C*H$_2$)$_3$Si). HR-MALDI-MS: 565.3283 ($[M+Na]^+$, $C_{26}H_{54}O_5N_2NaSi_3^+$; calc. 565.3284).

*(5*S*,6*S*,7*R*,8*R*)-5,6,7,8-Tetrahydro-5,6-bis(triethylsilyloxy)-8-[(triethylsilyloxy)methyl]imidazo[1,2-*a*]pyridin-7-ol* (**34**). Colourless solid. R_f (hexane/AcOEt 7:3) 0.33. $[\alpha]_D^{25} = -17.0$ (*c* = 0.65, $CHCl_3$). IR ($CHCl_3$): 3506*w*, 2958*s*, 2913*s*, 2878*s*, 1488*m*, 1458*m*, 1378*w*, 1263*m*, 1143*s*, 1119*s*, 1103*s*, 1078*s*, 1007*s*, 976*s*, 956*m*, 864*m*. ^{1}H-NMR (300 MHz, $CDCl_3$): 7.01 (*d*, *J* = 1.2, H−C(2)); 6.87 (*d*, *J* = 1.5, H−C(3)); 5.60 (*dd*, *J* = 3.9, 1.8, H−C(5)); 4.46 (*dd*, *J* = 9.6, 4.5, CH_a−C(8)); 4.37 (*m*, addn. of D_2O → *dt*, *J* ≈ 3.9, 2.1, H−C(7)); 4.14 (*dd*, *J* = 10.6, 9.6, CH_b−C(8)); 4.19 (*d*, *J* = 7.2, HO−C(7)); 3.99 (*dd*, *J* = 3.3, 2.4, H−C(6)); 2.93 (*dt*, *J* = 10.8, 4.2, H−C(8)); 1.04–0.94 (*m*, 3 (*Me*CH_2)$_3$Si); 0.73–0.64 (*m*, 3 (MeC*H*$_2$)$_3$Si). ^{13}C-NMR (75 MHz, $CDCl_3$): 142.64 (*s*, C(8a)); 129.38 (*d*, C(2)); 117.42 (*d*, C(3)); 80.38 (*d*, C(5)); 70.70, 69.35 (2*d*, C(6), C(7)); 59.32 (*t*, CH_2−C(8)); 42.95 (*d*, C(8)); 6.99, 6.87, 6.70 (3*q*, 3 (*Me*CH_2)$_3$Si); 5.08, 4.62 (2*t*, 3 (Me*C*H$_2$)$_3$Si). HR-MALDI-MS: 543.3469 ($[M+H]^+$, $C_{26}H_{55}N_2O_4Si_3^+$; calc. 565.3464).

*Methyl 4-Cyano-4-deoxy-3-*O*-[(trifluoromethyl)sulfonyl]-2-*O*-(triisopropylsilyl)-α-*D*-lyxopyranoside* (**36**). At −15°, a soln. of **17** (409 mg, 1.24 mmol) in pyridine (2 ml) was treated dropwise with Tf_2O (307 µl, 1.86 mmol). The mixture was stirred for 7 h (disappearance of **17**), diluted with CH_2Cl_2 (30 ml), washed with 10% aq. HCl soln. (5 ml), H_2O (5 ml) and brine (5 ml), and dried (Na_2SO_4). Evaporation and FC (20 g of silica gel; AcOEt/hexane 1:19 → 3:17) gave **36** (548 mg, 99%). Colourless oil. R_f (hexane/AcOEt 17:3) 0.46. $[\alpha]_D^{25} = -28.2$ (*c* = 0.54, $CHCl_3$). IR ($CHCl_3$): 2946*m*, 2893*w*, 2869*m*, 2254*w*, 1464*m*, 1421*s*, 1370*w*, 1339*m*, 1168*s*, 1144*s*, 1067*s*, 1041*m*, 1013*w*, 963*s*, 909*m*, 882*m*, 858*s*. ^{1}H-NMR (300 MHz, $CDCl_3$): 5.17 (*dd*, *J* ≈ 11, 2.4, H−C(3)); 4.65 (*d*, *J* = 1.8, H−C(1)); 4.29 (*t*, *J* ≈ 2.4, H−C(2)); 4.0 (*dd*, *J* = 11.4, 5.1, H_{eq}−C(5)); 3.85 (*t*, *J* ≈ 11.1, H_{ax}−C(5)); 3.57 (*td*, *J* ≈ 11.1, 5.1, H−C(4)); 3.39 (*s*, MeO); 1.29–1.06 (*m*, (Me_2CH)$_3$Si). ^{13}C-NMR (75 MHz, $CDCl_3$): 118.38 (*q*, ^1J(C,F) = 317, CF_3); 115.32 (*s*, C≡N); 101.27 (*d*, C(1)); 82.97 (*d*, C(3)); 69.04 (*d*, C(2)); 59.13 (*t*, C(5)); 55.56 (*q*, MeO); 29.18 (*d*, C(4)); 17.92, 17.89 (2*q*, (*Me*$_2$CH)$_3$Si); 12.58 (*d*, (Me_2C*H*)$_3$Si).

*Methyl 4-Cyano-3,4-dideoxy-2-*O*-(triisopropylsilyl)-β-*L*-*glycero*-pent-3-enopyranoside* (**38**). At 2°, a soln. of **36** (325 mg, 0.704 mmol) in dry DMF (2 ml) was treated slowly with CsOAc (157 mg, 0.82 mmol), stirred for 3 h (disappearance of **36**), diluted with AcOEt (25 ml), washed with H_2O (2 × 10 ml) and brine (10 ml), and dried (Na_2SO_4). Evaporation and FC (*ca.* 6 g of silica gel; AcOEt/hexane 3:97) gave **38** (198 mg, 90%). Colourless oil. R_f (AcOEt/hexane 1:9) 0.51. $[\alpha]_D^{25} = +175.5$ (*c* = 0.78, $CHCl_3$). IR ($CHCl_3$): 3026*w*, 2946*s*, 2868*s*, 2226*w*, 1464*m*, 1412*w*, 1391*w*, 1371*w*, 1216*s* 1152*s*, 1102*s*, 1050*s*, 918*w*, 882*m*. ^{1}H-NMR (300 MHz, $CDCl_3$): 6.54 (*dtd*, *J* ≈ 3.6, 2.1, 0.6, H−C(3)); 4.62 (br. *d*, *J* = 3.0, H−C(1)); 4.21 (*dt*, *J* ≈ 16.2, 2.2, H−C(5)); 4.20 (*dt*, *J* ≈ 16.2, 2.2, H′−C(5)); 4.08 (*ddt*, *J* ≈ 3.6, 3.0, 2.2, H−C(2)); 3.47 (*s*, MeO); 1.15–1.03 (*m*, Me_2(CH)$_3$Si). ^{13}C-NMR (75 MHz, $CDCl_3$): 141.37 (*d*, C(3)); 115.75 (*s*, C≡N); 113.73 (*s*, C(4)); 102.08 (*d*, C(1)); 65.12 (*d*, C(2)); 60.21 (*t*, C(5)); 56.44 (*q*, MeO); 18.10, 18.07 (2*q*, (*Me*$_2$CH)$_3$Si); 12.40 (*d*, (Me_2C*H*)$_3$Si). Anal. calc. for $C_{16}H_{29}NO_3Si$ (311.49): C 61.69, H 9.38, N 4.50; found: C 61.63, H 9.43, N 4.69.

*Methyl 4-Cyano-4-deoxy-3-*O*-(methylsulfonyl)-2-*O*-(triisopropylsilyl)-α-*D*-lyxopyranoside* (**37**). An ice-cold soln. of **17** (353 mg, 1.07 mmol) in pyridine (2 ml) was treated dropwise with MsCl (160 µl, 2.06 mmol), warmed to 23° (*ca.* 2 h) and stirred for 20 h (disappearance of **17**). The mixture was diluted with AcOEt (30 ml), washed with 10% aq. HCl soln., H_2O (10 ml) and brine (5 ml), and dried ($MgSO_4$). Evaporation and FC (2 g of silica gel; AcOEt/hexane/ (3:15) gave **37** (389 mg, 89%). Colourless solid. R_f (hexane/AcOEt 3:17) 0.10. M.p. 73.1–73.8°. $[\alpha]_D^{25} = -19.6$ (*c* = 0.55, $CHCl_3$). IR ($CHCl_3$): 3015*w*, 2945*s*, 2892*m*, 2869*s*, 2250*w*, 1464*m*, 1412*w*, 1371*s*, 1351*m*, 1179*s*, 1166*m*, 1066*s*, 1044*m*, 1013*m*, 990*m*, 964*s*, 909*m*, 882*m*, 844*s*. ^{1}H-NMR (300 MHz, $CDCl_3$): 5.01 (*dd*, *J* = 11.1, 2.7, H−C(3)); 4.62 (*d*, *J* = 1.8, H−C(1)); 4.26 (*t*, *J* ≈ 2.4, H−C(2)); 3.97 (*dd*, *J* = 11.1, 5.1, H_{eq}−C(5)); 3.86 (*t*, *J* ≈ 11.1, H_{ax}−C(5)); 3.48 (*td*, *J* ≈ 11.4, 5.4, H−C(4)); 3.39 (*s*, MeO); 3.18 (*s*, MsO); 1.29–1.06 (*m*, (Me_2CH)$_3$Si). ^{13}C-NMR (75 MHz, $CDCl_3$): 117.21 (*s*, C≡N); 101.60 (*d*, C(1)); 76.05 (*d*, C(3)); 69.24 (*d*,

C(2)); 59.19 (*t*, C(5)); 55.67 (*q*, MeO); 38.83 (*q*, MsO); 29.14 (*d*, C(4)); 18.15 (*q*, (*Me*$_2$CH)$_3$Si); 12.62 (*d*, (Me$_2$*C*H)$_3$Si). Anal. calc. for $C_{17}H_{33}NO_6SSi$ (407.598): C 50.09, H 8.16, N 3.44; found: C 50.21, H 8.03, N 3.40.

*Methyl 4-[1-[(*tert*-Butoxy)carbonyl]-1*H*-imidazol-2-yl]-4-deoxy-2-*O*-(triisopropylsilyl)-α-*D*-lyxopyranoside* (**39**). A soln. of **27** (1.288 g, 3.48 mmol) in anh. MeCN (12 ml) was treated with Boc_2O (987 mg, 4.5 mmol) and DMAP (47 mg, 0.385 mmol). The mixture was stirred at 24° for 4 h (disappearance of **27**), and evaporated. A soln. of the residue in AcOEt (30 ml) was washed with H_2O (10 ml) and brine (10 ml), dried (Na_2SO_4), and evaporated. The resulting thick oil was used for the next step without further purification. An anal. sample of **39** was obtained by FC (silica gel; hexane/AcOEt 4:1). Colourless oil. R_f (hexane/AcOEt 7:3) 0.42. $[\alpha]_D^{25} = +20.5$ ($c = 0.7$, $CHCl_3$). IR ($CHCl_3$): 3556*w*, 2945*s*, 2868*m*, 1750*s*, 1465*m*, 1414*m*, 1372*m*, 1307*s*, 1264*w*, 1142*s*, 1068*s*, 1021*s*, 971*w*, 908*s*. ^{1}H-NMR (300 MHz, $CDCl_3$): 7.28 (*d*, $J = 1.8$, H–C(5′)); 6.88 (*d*, $J = 1.8$, irrad. at 7.29 → *s*, H–C(4′)); 4.68 (*d*, $J = 1.8$, irrad. at 4.09 → *s*, H–C(1)); 4.26–4.18 (*m*, addn. of D_2O → change, irrad. at 3.97 → change, H–C(3), H–C(4)); 4.09 (*t*, $J \approx 2.2$, irrad. at 4.68 → *d*, $J = 2.4$, irrad. at 4.20 → br. *s*, H–C(2)); 3.97 (*t*, $J \approx 10.8$, irrad. at 4.20 → *d*, $J = 10.8$, H_{ax}–C(5)); 3.81 (*dd*, $J = 10.8$, 3.6, irrad. at 4.20 → *d*, $J = 10.8$, irrad. at 3.97 → change, H_{eq}–C(5)); 3.36 (*s*, MeO); 2.81 (*d*, $J = 9.3$, irrad. at 4.20 → br. *s*, exchanged with D_2O, HO–C(3)); 1.60 (*s*, Me_3C); 1.14–1.08 (*m*, (Me$_2$CH)$_3$Si). ^{13}C-NMR (75 MHz, $CDCl_3$): 149.07 (*s*, C=O); 148.26 (*s*, C(2′)); 127.68 (*d*, C(4′)); 118.72 (*d*, C(5′)); 102.04 (*d*, C(1)); 85.68 (*s*, Me$_3$*C*); 71.18, 70.93 (2*d*, C(2), C(3)); 61.68 (*t*, C(5)); 55.02 (*q*, MeO); 38.59 (*d*, C(4)); 28.01 (*q*, *Me*$_3$C); 18.20, 18.18 (2*q*, (*Me*$_2$CH)$_3$Si); 12.74 (*d*, (Me$_2$*C*H)$_3$Si). HR-MALDI-MS: 493.2700 ([*M* + Na]$^+$, $C_{23}H_{42}N_2NaO_6Si^+$; calc. 493.2704). Anal. calc. for $C_{23}H_{42}N_2O_6Si$ (470.68): C 58.69, H, 8.99, N 5.95; found: C 58.70, H, 8.94, N 5.85.

Oxidation of **39** *with Periodinane.* At 3°, a soln. of **39** (1.2 g of crude product, 3.48 mmol) in anh. CH_2Cl_2 (8 ml) was treated with *Dess–Martin*'s periodinane (1.24 g, 2.91 mmol). The mixture was stirred until disappearance of **39** (*ca.* 3–4 h), diluted with Et_2O (50 ml), and treated with sat. aq. $NaHCO_3$ soln. (20 ml). The aq. layer was washed with Et_2O (50 ml). The combined org. layers were washed with sat. aq. $NaHCO_3$ soln. (3 × 20 ml), dried (Na_2SO_4), and evaporated. FC (22 g of silica gel; hexane/AcOEt 4:1) gave **40** (975 mg, 60% from **27**) and a mixture of **40** and **41** (522 mg, 32% from **27**).

*Methyl 4-[1-[(*tert*-Butoxy)carbonyl]-1*H*-imidazol-2-yl]-4-deoxy-2-*O*-(triisopropylsilyl)-α-*D*-*threo*-pentopyranosid-3-ulose* (**40**). Colourless solid. R_f (hexane/AcOEt 7:3) 0.45. M.p. 83.8–85.1°. $[\alpha]_D^{25} = +64.1$ ($c = 1.0$, $CHCl_3$). IR (3%, $CHCl_3$): 2945*s*, 2868*m*, 1761*s*, 1741*s*, 1542*w*, 1499*w*, 1465*m*, 1412*m* 1372*s*, 1339*s*, 1309*s*, 1264*w*, 1165*s*, 1141*s*, 1066*s*, 1044*s*, 1004m, 941*w*, 883*m*, 844*m*. ^{1}H-NMR (300 MHz, $CDCl_3$; assignment based on a DQFCOSY and a HSQC spectrum): 7.32 (*d*, $J = 1.8$, H–C(5′)); 6.90 (*d*, $J = 1.8$, H–C(4′)); 5.27 (*dd*, $J = 11.1$, 6.6, H–C(4)); 4.87 (*d*, $J = 2.4$, H–C(1)); 4.53 (*t*, $J \approx 11.0$, H_{ax}–C(5)); 4.28 (*dd*, $J = 11.1$, 6.6, H_{eq}–C(5)); 4.11 (*d*, $J = 1.8$, H–C(2)); 3.41 (*s*, MeO); 1.54 (*s*, Me_3C); 1.19–1.13 (*m*, (Me$_2$C*H*)$_3$Si)); 1.11, 1.09 (2*d*, $J = 6.6$, (*Me*$_2$CH)$_3$Si). ^{13}C-NMR (75 MHz, $CDCl_3$): 201.12 (*s*, C(3)); 148.25 (*s*, C(2′)); 147.18 (*s*, OC=O); 127.76 (*d*, C(4′)); 118.71 (*d*, C(5′)); 104.76 (*d*, C(1)); 85.08 (*s*, Me$_3$*C*); 76.67 (*d*, C(2)); 62.57 (*t*, C(5)); 55.15 (*q*, MeO); 47.80 (*d*, C(4)); 27.92 (*q*, *Me*$_3$C); 18.04 (br. *q*, (*Me*$_2$CH)$_3$Si); 12.27 (*d*, (Me$_2$*C*H)$_3$Si). HR-MALDI-MS: 492.2587 ([*M* + Na]$^+$, $C_{23}H_{40}N_2NaO_6Si^+$; calc. 492.2593). Anal. calc. for $C_{23}H_{40}N_2O_6Si$ (468.66): C 58.94, H 8.60, N 5.98; found: C 58.89, H 8.44, N 5.92.

*Methyl 4-[1-[(*tert*-Butoxy)carbonyl]-1*H*-imidazol-2-yl]-4-deoxy-2-*O*-(triisopropylsilyl)-β-*D*-erythro-pentopyranosid-3-ulose* (**41**). Colourless oil. R_f (hexane/AcOEt 4:1) 0.15. $[\alpha]_D^{25} = -14.3$ ($c = 0.2$, $CHCl_3$). IR ($CHCl_3$): 2945*m*, 2892*m*, 2868*m*, 1758*s*, 1603*w*, 1544*w*, 1465*m*, 1413*m* 1372*m*, 1340*m*, 1309*s*, 1261*w*, 1139*s*, 1116*s*, 1104*s*, 1070*m*, 1020*m*, 997*w*, 969*w*, 919*w*, 884*m*, 844*w*. ^{1}H-NMR (300 MHz, $CDCl_3$): 7.34 (*d*, $J = 1.8$, H–C(5′)); 6.87 (*d*, $J = 1.8$, H–C(4′)); 4.63 (*dd*, $J = 11.4$, 6.6, H–C(4)); 4.51 (*dd*, $J = 11.4$, 6.3, H_{eq}–C(5)); 4.34 (*d*, $J = 7.5$, H–C(1)); 4.30 (*d*, $J = 7.5$, H–C(2)); 4.13 (*t*, $J \approx 11.4$, H_{ax}–C(5)); 3.59 (*s*, MeO); 1.54 (*s*, Me_3C); 1.19–1.13 (*m*, (*Me*$_2$CH)$_3$Si). ^{13}C-NMR (75 MHz, $CDCl_3$): 200.62 (*s*, C(3)); 147.18 (*s*, OC=O); 143.53 (*s*, C(2′)); 127.76 (*d*, C(4′)); 118.95 (*d*, C(5′)); 107.40 (*d*, C(1)); 85.44 (*s*, Me$_3$*C*); 70.78 (*d*, C(2)); 63.65 (*t*, C(5)); 57.15 (*q*, MeO); 51.28 (*d*, C(4)); 27.93 (*q*, *Me*$_3$C); 18.02, 17.94 (2*q*, (*Me*$_2$CH)$_3$Si); 12.57 (*d*, (Me$_2$*C*H)$_3$Si). HR-MALDI-MS: 492.2587 ([*M* – Boc + Na]$^+$, $C_{23}H_{40}N_2NaO_6Si^+$; calc. 492.2593).

*Methyl 4-[1-[(*tert*-Butoxy)carbonyl)]-1*H*-imidazol-2-yl]-4-deoxy-2-*O*-(triisopropylsilyl)-α-*D*-arabinopyranoside* (**42**). *a*) At 3–5°, a soln. of **40** (975 mg, 2.08 mmol) in dry MeOH (10 ml) was treated with $NaBH_4$ (38 mg, 1.03 mmol). The mixture was stirred for 1 h (disappearance of **40**), treated with sat. aq. NH_4Cl soln. (10 ml), and evaporated. The aq. residue was diluted with AcOEt (100 ml). The org. layer was separated, washed with H_2O (20 ml) and brine (20 ml), dried (Na_2SO_4), and evaporated. FC (*ca.* 23 g of silica gel; hexane/AcOEt 7:3) gave **39** (469 mg, 48%), **42** (265 mg, 25%), and an inseparable mixture (240 mg, 25%).

b) At 0°, a soln. of **40** (155 mg, 0.33 mmol) in dry MeOH (2 ml) was treated with $CeCl_3 \cdot 7\,H_2O$ (130 mg, 0.35 mmol) and $NaBH_4$ (8.6 mg, 0.23 mmol), stirred for 20 min (disappearance of **40**), treated with sat. aq. NH_4Cl soln. (10 ml), and diluted with AcOEt (60 ml). The org. layer was separated, washed with brine (5 ml),

dried (Na_2SO_4), and evaporated. FC (3 g of silica gel, hexane/AcOEt 7:3) provided **42** (124 mg, 80%). Colourless oil. R_f (hexane/AcOEt 7:3) 0.34. $[\alpha]_D^{25} = -52.1$ ($c = 1.0$, EtOH). IR ($CHCl_3$): 3507*w*, 3342*w*, 2945*m*, 2868*m*, 1762*s*, 1602*w*, 1542*w*, 1464*w*, 1373*m*, 1305*s*, 1141*s*, 1101*m*, 1073*w*, 1038*m*, 882*w*. ^{1}H-NMR (300 MHz, $CDCl_3$; assignment based on a DQFCOSY and a HSQC spectrum): 7.34 (*d*, $J = 1.8$, H–C(5′)); 6.86 (*d*, $J = 1.8$, H–C(4′)); 4.95 (*d*, $J = 5.4$, exchanged with D_2O, HO–C(3)); 4.63 (br. *s*, H–C(1)); 4.29 (*t*, $J \approx 11.8$, irrad. at 3.70 → change, H_{ax}–C(5)); 4.28–4.22 (overlapped *m*, addn. of D_2O → change, H–C(3)); 4.15 (*ddd*, $J \approx 11.1$, 4.0, 2.1, irrad. at 3.70 → change, H–C(4)); 3.95 (*dd*, $J = 3.0$, 1.2, irrad. at 4.63 → *d*, $J = 3.3$, H–C(2)); 3.70 (*ddd*, $J \approx 10.8$, 4.0, 1.2, H_{eq}–C(5)); 3.39 (*s*, MeO); 1.62 (*s*, Me_3C); 1.08 (br. *s*, $(Me_2CH)_3Si$). ^{13}C-NMR (75 MHz, $CDCl_3$): 149.10 (*s*, OC=O); 147.27 (*s*, C(2′)); 127.11 (*d*, C(4′)); 118.69 (*d*, C(5′)); 101.88 (*d*, C(1)); 85.82 (*s*, Me_3C); 70.10 (*d*, C(2)); 69.14 (*d*, C(3)); 59.96 (*t*, C(5)); 55.85 (*q*, MeO); 36.10 (*d*, C(4)); 27.99 (*q*, Me_3C); 18.21, 18.06 (2*q*, $(Me_2CH)_3Si$); 12.40 (*d*, $(Me_2CH)_3Si$). HR-MALDI-MS: 493.2700 ($[M + Na]^+$, $C_{23}H_{42}O_6N_2NaSi^+$; calc. 493.2710). Anal. calc. for $C_{23}H_{42}N_2O_6Si \cdot 0.25\ H_2O$ (475.18): C 58.14, H 9.04, N 5.90; found: C 57.96, H 8.57, N 5.73.

*Methyl 3-*O*-[(*tert*-Butoxy)carbonyl)-4-deoxy-4-(1*H*-imidazol-2-yl)-2-*O*-(triisopropylsilyl)-α-*D*-arabinopyranoside* (**43**). A soln. of **42** (17 mg, 0.36 mmol) in dry MeOH/Et_3N 10:1 (1.1 ml) was stirred at 23° for 5 h (disappearance of **42**) and evaporated. FC (5 g of silica gel, hexane/AcOEt 7:3) gave **43** (12 mg, 71%). Colourless solid. M.p. 124.8–126.2°. R_f (hexane/AcOEt 7:3) 0.45. $[\alpha]_D^{25} = -32.9$ ($c = 0.30$, $CHCl_3$). IR ($CHCl_3$): 3246*w*, 2962*m*, 2946*m*, 2868*m*, 1744*s*, 1545*w*, 1464*m*, 1395*w*, 1370*w*, 1280*s*, 1262*s*, 1130*s*, 1099*s*, 1080*s*, 1040*s*, 999*s*, 919*w*, 882*m*, 846*m*, 821*m*. ^{1}H-NMR (300 MHz, $CDCl_3$, assignment based on a DQFCOSY and a HSQC spectrum): 7.00 (br. *s*, H–C(4′); 6.96 (br. *s*, H–C(5′)); 4.85 (*dd*, $J = 6.0$, 4.2, irrad. at 3.85 → change, H–C(3)); 4.40 (*d*, $J = 4.5$, irrad. at 3.85 → *s*, H–C(1)); 4.25 (*dd*, $J = 10.6$, 6.0, irrad. at 3.75 → change, H_{ax}–C(5)); 3.85 (*dd*, $J = 6.0$, 4.5, irrad. at 4.40 → *d*, $J = 6.0$, irrad. at 4.85 → *d*, $J = 4.5$, H–C(2)); 3.83 (*dt*, $J = 6.0$, 4.2, H–C(4)); 3.78 (*dd*, $J = 10.6$, 4.2, H_{eq}–C(5)); 3.46 (*s*, MeO); 1.45 (*s*, Me_3C); 1.08–1.04 (*m*, $(Me_2CH)_3Si$). ^{13}C-NMR (75 MHz, $CDCl_3$, assignment based on a DQFCOSY and a HSQC spectrum): 152.80 (*s*, OC=O); 144.96 (*s*, C(2′)); 128.22 (*d*, C(4′)); 115.80 (*d*, C(5′)); 103.50 (*d*, C(1)); 82.80 (*s*, Me_3C); 75.59 (*d*, C(3)); 69.67 (*d*, C(2)); 60.81 (*t*, C(5)); 56.39 (*q*, MeO); 36.94 (*d*, C(4)); 27.84 (*q*, Me_3C); 18.10 (*q*, $(Me_2CH)_3Si$); 12.37 (*d*, $(Me_2CH)_3Si$). HR-MALDI-MS: 471.2875 ($[M + H]^+$, $C_{23}H_{43}N_2O_6Si^+$; calc. 471.2885). Anal. calc. for $C_{23}H_{42}N_2O_6Si$ (470.68): C 58.69, H 8.99, N 5.95; found: C 58.94, H 9.07, N 5.90.

*Methyl 4-[1-[(*tert*-Butoxy)carbonyl]-1*H*-imidazol-2-yl]-4-deoxy-2-*O*-(triisopropylsilyl)-β-*D*-xylopyranoside* (**44**). A cold soln. of **41** (70 mg, 0.15 mmol) in dry MeOH (2 ml) was treated with $NaBH_4$ (6.5 mg, 0.17 mmol). The mixture was stirred for 1 h (disappearance of **41**), treated with sat. aq. NH_4Cl soln. (1 ml), and evaporated. The aq. residue was diluted with AcOEt (20 ml). The org. layer was separated and washed with H_2O (5 ml) and brine (5 ml), dried (Na_2SO_4), and evaporated. FC (*ca.* 6 g of silica gel, hexane/AcOEt 17:3) gave **44** (38 mg, 54%). Colourless oil. R_f (hexane/AcOEt 7:3) 0.45. $[\alpha]_D^{25} = +57.8$ ($c = 0.47$, $CHCl_3$). IR ($CHCl_3$): 3588*w*, 3018*w*, 2962*m*, 2945*m*, 2867*m*, 1760*m*, 1463*w*, 1372*m*, 1353*w*, 1306*s*, 1262*m*, 1140*s*, 1099*m*, 1071*m*, 1034*m*, 988*w*, 908*w*, 883*m*, 842*m*. ^{1}H-NMR (300 MHz, $CDCl_3$): 7.32 (*d*, $J = 1.8$, H–C(5′)); 6.91 (*d*, $J = 1.8$, H–C(4′)); 4.20 (*ddd*, $J = 10.5$, 8.7, 3.6, irrad. at 3.83 → change, irrad. at 3.59 → change, irrad. at 2.78 → *dd*, $J = 10.5$, 8.7, addn. of CD_3OD → *dd*, $J = 10.5$, 8.7, H–C(3)); 4.17 (*d*, $J = 7.5$, irrad. at 3.59 → change, H–C(1)); 4.13 (*dd*, $J = 11.1$, 4.2, irrad. at 3.80 → change, H_{eq}–C(5)); 3.80 (*td*, $J \approx 10.5$, 4.2, H–C(4)); 3.59 (*dd*, $J = 8.7$, 7.5, H–C(2)); 3.49 (*s*, MeO); 3.47 (*dd*, $J = 11.1$, 10.8, irrad. at 3.80 → change H_{ax}–C(5)); 2.78 (*d*, $J = 3.6$, exchanged with CD_3OD, HO–C(3)); 1.61 (*s*, Me_3C); 1.18–1.05 (*m*, $(Me_2CH)_3Si$)). ^{13}C-NMR (75 MHz, $CDCl_3$): 147.69, 147.20 (2*s*, C=O, C(2′)); 127.74 (*d*, C(4′)); 119.13 (*d*, C(5′)); 105.46 (*d*, C(1)); 86.0 (*s*, Me_3C); 76.63, 75.13 (*d*, C(2), C(3)); 65.01 (*t*, C(5)); 56.78 (*q*, MeO); 43.22 (*d*, C(4)); 27.94 (*q*, Me_3C); 18.26, 18.21 (2*q*, $(Me_2CH)_3Si$); 12.73 (*d*, $(Me_2CH)_3Si$). HR-MALDI-MS: 493.2587 ($[M + Na]^+$, $C_{23}H_{42}N_2NaO_6Si^+$; calc. 493.2593).

*(5*R*,6*S*,7*R*,8*R*)- and (5*S*,6*S*,7*R*,8*R*)-5,6,7,8-Tetrahydro-8-(hydroxymethyl)-imidazo[1,2-*a*]pyridine-5,6,7-triol* (**5** and **45**, resp.). A soln. of **42** (365 mg, 0.78 mmol) in 80% aq. AcOH (6.8 ml) was treated with 20% aq. HCl (1.15 ml, *ca.* 2.3 mmol). The stirred mixture was kept for 2.5 h at 113° and evaporated. FC (9 g of silica gel; AcOEt/MeOH/H_2O 13:6:1) and filtration through *Amberlite-CG-120* (H^+ form, 2% aq. NH_4OH) gave **5**/**45** (182 mg, 95%). Light yellow hygroscopic solid. M.p. 180–185° (dec.). ^{1}H-NMR (300 MHz, CD_3OD; **5**/**45** 47:53, >95% pure): 7.14 (*d*, $J = 1.2$, 0.47 H), 7.10 (*d*, $J = 1.5$, 0.53 H) (H–C(2)); 6.97 (*d*, $J = 1.5$, 0.53 H–C(3)); 6.89 (*d*, $J = 1.2$, 0.47 H–C(3)); 5.89 (*d*, $J = 3.6$, 0.53 H–C(5)); 5.15 (*d*, $J = 7.2$, 0.47 H–C(5)); 4.27 (*dd*, $J = 8.4$, 7.5, irrad. at 2.83 → change, 0.53 H, H–C(7)); 4.24 (*dd*, $J = 10.8$, 3.6, irrad. at 2.83 → change, 0.53 H), 4.17 (*dd*, $J = 10.5$, 3.9, irrad. at 2.83 → change, 0.53 H), 4.08 (br. *dd*, $J = 9.6$, 3.6, irrad. at 2.83 → change, 0.47 H), 4.04 (*dd*, $J = 10.5$, 3.9, irrad. at 2.83 → change, 0.47 H) (CH_2–C(8)); 3.93 (*t*, $J = 9.3$, 0.47 H–C(7)); 3.85 (*dd*, $J = 8.7$, 3.6, irrad. at 5.89 → *d*, $J = 8.7$, 0.53 H–C(6)); 3.64 (*dd*, $J = 9.6$, 7.2, 0.47 H–C(6)); 2.97–2.79 (*m*, H–C(8)).

Data for **5**/**45**·HCl: Hygroscopic solid. R_f (AcOEt/MeOH/H_2O 13:6:1) 0.52. $[\alpha]_D^{25} = -52.1$ ($c = 1.0$, EtOH). IR (KBr): 3400*w*, 2936*m*, 1634*s*, 1535*w*, 1490*m*, 1461*m*, 1376*m*, 1325*m*, 1267*m*, 1176*w*, 1131*s*, 1090*s*,

1067*s*, 1004*m*, 938*w*, 903*w*, 814*w*. ^{1}H-NMR (300 MHz, CD_3OD; **5**/**45** *ca.* 1:1): 7.22, 7.21 (2*d*, $J = 1.5$, H–C(2)); 7.04, 7.03 (2*d*, $J = 1.5$, H–C(3)); 5.72 (*d*, $J = 3.6$, 0.5 H, H–C(5) of **45**); 5.26 (*d*, $J = 6.6$, 0.5 H, H–C(5) of **5**); 4.26 (*dd*, $J = 11.4$, 3.3, 0.5 H, H–C(7) of **45**); 4.21 (*dd*, $J = 12.1$, 3.3, 0.5 H, CH_a–C(8) of **45**); 4.10 (*t*, $J \approx 9.0$, 0.5 H, H–C(7) of **5**); 3.98–3.90 (*m*, 1 H), 3.81–3.70 (*m*, 1.5 H), (CH_b–C(8) of **45**, CH_2–C(8) of **5**, H–C(6)); 3.04–2.97 (*m*, H–C(8)). ^{13}C-NMR (75 MHz, CD_3OD; **5**/**45** *ca.* 1:1): 145.95, 145.30 (2*s*, C(8a)); 128.58, 128.48 (2*d*, C(2)); 119.34, 117.81 (2*d*, C(3)); 82.44 (*d*, C(5) of **45**); 78.40 (*d*, C(5) of **5**); 76.53 (*d*, C(6) of **45**); 72.39 (*d*, C(6) of **5**); 71.84, 70.93, 70.79, 68.83 (4*d*, C(2), C(3)); 69.70, 67.55 (2*d*, C(7)); 62.47, 61.78 (2*t*, CH_2–C(8)); 45.05, 44.95 (2*d*, C(8)). HR-MS-MALDI: 201.0872 ($[M + H - HCl]^+$, $C_8H_{13}O_4N_2^+$; calc. 201.0870).

*4-Deoxy-4-(1*H*-imidazol-2-yl)-*D*-arabinitol* (**46**). A cold soln. of **5**/**45** (43 mg, 0.18 mmol) in MeOH (2 ml) was treated at 0° with AcOH (0.2 ml) and $NaCNBH_3$ (41 mg, 0.65 mmol), warmed to 28°, stirred at that temp. for 60 h, and co-evaporated with toluene. FC (AcOEt/MeOH/25% aq. NH_4OH 14:5:1) gave slightly impure **46**, which, upon additional FC (AcOEt/MeOH/25% NH_4OH, 7:2:1), gave **46** · HOAc (22 mg, 66%). Hygroscopic solid. $[\alpha]_D^{25} = -2.9$ ($c = 0.1$, EtOH). R_f (AcOEt/MeOH/25% aq. NH_4OH, 7:2:1) 0.26. IR (KBr): 3427*s*, 2925*w*, 2558*w*, 1666*s*, 1624*s*, 1442*m*, 1366*s*, 1032*w*, 1047*w*, 998*w*, 834*s*. ^{1}H-NMR (300 MHz, CD_3OD, **46** · HOAc): 7.11 (br. *s*, H–C(4′), H–C(5′)); 3.95–3.85 (*m*, 2 H–C(1)); 3.93 (*dd*, $J = 9.0$, 1.8, irrad. at 3.04 → *dd*, $J = 9.0$, H–C(3)); 3.48 (*dd*, $J = 10.8$, 6.0, H_a–C(5)); 3.41 (*dd*, $J = 10.8$, 6.0, irrad. at 3.04 → change, H_b–C(5)); 3.34 (*ddd*, $J \approx 9.0$, 6.3, 5.1, H–C(2)); 3.04 (*td*, $J = 6.0$, 1.8, H–C(4)); 1.83 (*s*, AcO). ^{13}C-NMR (75 MHz, CD_3OD, **46** · HOAc): 179.31 (*s*, C=O); 148.40 (*s*, C(1′)); 121.06 (*d*, C(4′), C(5′)); 72.97, 71.33 (2*d*, C(2), C(3)); 64.56, 63.32 (2*t*, C(1), C(5)); 45.83 (*d*, C(4)); 22.95 (*q*, Me). ESI-MS: 203.3 ($[M + H]^+$, $C_8H_{15}N_2O_4^+$; calc. 203.3).

Silylation of **5**/**45**. At 2°, a soln. of **5**/**45** (31 mg, 0.131 mmol) in dry pyridine (2.5 ml) was treated with 2,6-lutidine (0.07 ml) and Et_3SiCl (0.2 ml), stirred for 46 h at 26°, diluted with AcOEt (25 ml), washed with H_2O (2 × 5 ml) and brine (5 ml), dried (Na_2SO_4), and evaporated. FC (3 g of silica gel; *ca.* 50 ml of AcOEt/hexane 1:9) gave **47**/**48** *ca.* 1:4 (14 mg, 16%) and **47**/**48** *ca.* 85:17 (27 mg, 31%).

*(5*R*,6*S*,7*R*,8*R*)-5,6,7,8-Tetrahydro-5,6,7-tris(triethylsilyloxy)-8-[(triethylsilyloxy)methyl]imidazo[1,2-*a*]pyridine* (**48**): *Data for a* ca. *1:4 Mixture* **47**/**48**. Colourless oil. R_f (hexane/AcOEt 9:1) 0.31. $[\alpha]_D^{25} = +8.5$ ($c = 0.6$, $CHCl_3$). IR ($CHCl_3$): 2958*s*, 2913*s*, 2878*s*, 1526*w*, 1485*w*, 1458*m*, 1414*m* 1378*w*, 1259*w*, 1094*w*, 1007*s*, 973*w*, 921*w*, 887*w*, 833*m*. ^{1}H-NMR (300 MHz, $CDCl_3$; **47**/**48** *ca.* 1:4): 7.00 (*d*, $J = 1.5$, H–C(2)); 6.92 (*d*, $J = 1.2$, H–C(3)); 5.42 (*dd*, $J = 1.8$, 0.9, irrad. at 4.49 → *d*, $J = 1.8$, H–C(5)); 4.49 (*ddd*, $J \approx 3.6$, 1.2, 0.9, irrad. at 5.42 → *dd*, $J = 3.3$, 1.2, H–C(7)); 4.07 (*dd*, $J = 3.6$, 1.8, irrad. at 5.42 → *d*, $J = 3.9$, irrad. at 4.49 → *d*, $J = 1.8$, H–C(6)); 4.07 (*dd*, $J = 9.6$, 5.4, CH_a–C(8)); 3.75 (*dd*, $J = 11.0$, 9.6, irrad. at 4.07 → *d*, $J \approx 11.0$, CH_b–C(8)); 3.20 (*ddd*, $J = 10.5$, 5.1, 0.5, irrad. at 4.49 → *dd*, $J = 10.5$, 5.4, irrad at 4.07 → *dd*, $J = 10.5$, 0.5, H–C(8)); 1.04–0.55 (*m*, 4 ($MeCH_2$)$_3$Si). ^{13}C-NMR (75 MHz, $CDCl_3$; **47**/**48** *ca.* 1:4): 143.13 (*s*, C(8a)); 128.50 (*d*, C(2)); 117.59 (*d*, C(3)); 81.61 (*d*, C(5)); 73.94 (*d*, C(7)); 67.99 (*d*, C(6)); 64.02 (*t*, CH_2–C(8)); 46.19 (*d*, C(8)); 7.14, 7.06, 6.97 (3*q*, 4 (*Me*CH_2)$_3$Si); 5.09, 4.87, 4.60 (3*t*, 4 (Me*C*H_2)$_3$Si). HR-MALDI-MS: 657.4335 ($[M + H]^+$, $C_{32}H_{69}N_2O_4Si_4^+$; calc. 657.4329).

*(5*S*,6*S*,7*R*,8*R*)-5,6,7,8-Tetrahydro-5,6,7-tris(triethylsilyloxy)-8-[(triethylsilyloxy)methyl]imidazo[1,2-*a*]pyridine* (**47**): *Data for a 85:15 Mixture* **47**/**48**. Colourless oil. R_f (hexane/AcOEt 9:1) 0.26. $[\alpha]_D^{25} = -15.1$ ($c = 1.3$, $CHCl_3$). IR ($CHCl_3$): 3017*w*, 2958*s*, 2913*s*, 2878*s*, 1458*w*, 1414*w*, 1354*w*, 1264*w*, 1154*m*, 1092*w*, 1007*m*, 967*w*, 919*w*, 829*m*. ^{1}H-NMR (300 MHz, $CDCl_3$; **47**/**48** *ca.* 85:15): 6.99 (*d*, $J = 1.25$, H–C(2)); 6.92 (*d*, $J = 1.25$, H–C(3)); 5.70 (*d*, $J = 1.8$, H–C(5)); 4.51 (*dd*, $J = 5.1$, 1.2, irrad. at 2.98 → *d*, $J = 5.1$, H–C(7)); 4.18 (*dd*, $J = 9.6$, 5.1, irrad. at 2.98 → *d*, $J \approx 9.6$, CH_a–C(8)); 3.95 (*dd*, $J = 5.1$, 1.8, irrad. at 5.70 → *d*, $J = 5.1$, irrad. at 4.51 → *d*, $J = 1.8$, H–C(6)); 3.78 (*dd*, $J = 10.5$, 9.6, irrad. at 2.98 → *dd*, $J = 10.5$, CH_b–C(8)); 2.98 (*ddd*, $J = 10.5$, 5.1, 1.2, irrad. at 4.18 → br. *d*, $J = 10.5$, H–C(8)); 1.06–0.52 (*m*, 4 ($MeCH_2$)$_3$Si). ^{13}C-NMR (75 MHz, $CDCl_3$; **47**/**48** *ca.* 85:15): 143.71 (*s*, C(8a)); 127.56 (*d*, C(3)); 115.00 (*d*, C(4)); 78.37 (*d*, C(5)); 74.24 (*d*, C(7)); 68.06 (*d*, C(6)); 64.26 (*t*, CH_2–C(8)); 46.28 (*d*, C(8)); 7.03, 6.87 (2*q*, 4 (*Me*CH_2)$_3$Si); 5.05, 4.86, 4.55 (3*t*, 4 Me*C*H_2)$_3$Si). HR-MALDI-MS: 657.4319 ($[M + H]^+$, $C_{32}H_{69}N_2O_4Si_4^+$; calc. 657.4329).

Inhibition Studies. IC_{50} Values were determined at a substrate concentration near K_M value of the each enzyme by plotting the reciprocal value of the rate of substrate hydrolysis *vs.* the inhibitor concentration. After fitting a straight line to the data by linear regression, the negative [*I*]-intercept of this plot provided the appropriate IC_{50} value.

a) *Inhibition of* Escherichia coli *β-Galactosidase.* $K_M = 0.94$ mM ([70]: 0.18 mM). The assay was carried out at pH 6.9 (NaH_2PO_4/Na_2HPO_4 buffer 100 mM) and at 37°. The reaction was started by addition of 2-nitrophenyl *β*-D-galactopyranoside after preincubating the enzyme in the presence of the inhibitor for 15 min at 37°. After 20 min, the reaction was quenched by the addition of 400 mM Na_2CO_3 soln. The rate of hydrolysis was determined by measuring the absorption at *λ* 405 nm and subsequently subtracting the absorption of a blank probe (H_2O, buffer, and substrate).

b) *Inhibition of Bovine Liver β-Galactosidase.* $K_M = 1.45$ mM. The assay was carried out at pH 6.9 (NaH_2PO_4/Na_2HPO_4 buffer 100 mM) and at 37°. The reaction was started by addition of 2-nitrophenyl β-D-galactopyranoside after preincubating the enzyme in the presence of the inhibitor for 20 min at 50°. After 30 min, the reaction was quenched by the addition of 400 mM Na_2CO_3 soln. The rate of hydrolysis was determined by measuring the absorption at λ 405 nm and subsequently subtracting the absorption of a blank probe (H_2O, buffer, and substrate).

c) *Inhibition of* A. oryzae *β-Galactosidase.* $K_M = 2.5$ mM. The assay was carried out at pH 4.9 (AcONa buffer 50 mM) and at 30°. The reaction was started by addition of 2-nitrophenyl β-D-galactopyranoside after preincubating the enzyme in the presence of the inhibitor for 10 min at 30°. After 30 min, the reaction was quenched by the addition of 400 mM Na_2CO_3 soln. The rate of hydrolysis was determined by measuring the absorption at λ 405 nm and subsequently subtracting the absorption of a blank probe (H_2O, buffer, and substrate).

d) *Inhibition of* Caldocellum saccharolyticum *β-Glucosidase.* $K_M = 1.95$ mM ([71]: 0.51 mM). The assay was carried out at pH 4.9 (AcONa buffer 50 mM) and at 55°. The reaction was started by addition of 4-nitrophenyl β-D-galactopyranoside after preincubating the enzyme in the presence of the inhibitor for 10 min at 55°. After 20 min, the reaction was quenched by the addition of 400 mM Na_2CO_3 soln. The rate of hydrolysis was determined by measuring the absorption at λ 405 nm and subsequently subtracting the absorption of a blank probe (H_2O, buffer, and substrate).

e) *Inhibition of Sweet Almond β-Glucosidases.* $K_M = 3.2$ mM ([72]: 67–80 mM at pH 5.2–6.0). The assay was carried out at pH 6.9 (NaH_2PO_4/Na_2HPO_4 buffer 100 mM) and at 37°. The reaction was started by addition of 4-nitrophenyl β-D-galactopyranoside after preincubating the enzyme in the presence of the inhibitor for 10 min at 37°. After 30 min, the reaction was quenched by the addition of 400 mM Na_2CO_3 soln. The rate of hydrolysis was determined by measuring the absorption at λ 405 nm and subsequently subtracting the absorption of a blank probe (H_2O, buffer, and substrate).

f) *Inhibition of* T. ressei *Cellulase Cel7A*. $K_M = 0.63–0.88$ mM ([73]: 0.46 mM). The assay was carried out at pH 4.9 (AcONa buffer 50 mM) and at 50°. The reaction was started by addition of 4-nitrophenyl β-D-galactopyranoside after preincubating the enzyme in the presence of the inhibitor for 10 min at 50°. After 25 min, the reaction was quenched by the addition of 400 mM Na_2CO_3 soln. The rate of hydrolysis was determined by measuring the absorption at λ 405 nm and subsequently subtracting the absorption of a blank probe (H_2O, buffer, and substrate).

REFERENCES

[1] T. D. Heightman, A. T. Vasella, *Angew. Chem., Int. Ed.* **1999**, *38*, 750.
[2] T. Granier, N. Panday, A. Vasella, *Helv. Chim. Acta* **1997**, *80*, 979.
[3] N. Panday, T. Granier, A. Vasella, *Helv. Chim. Acta* **1998**, *81*, 475.
[4] N. Panday, A. Vasella, *Synthesis* **1999**, 1459.
[5] N. Panday, A. Vasella, *Helv. Chim. Acta* **2000**, *83*, 1205.
[6] N. Panday, M. Meyyappan, A. Vasella, *Helv. Chim. Acta* **2000**, *83*, 513.
[7] N. Panday, Y. Canac, A. Vasella, *Helv. Chim. Acta* **2000**, *83*, 58.
[8] M. Terinek, A. Vasella, *Helv. Chim. Acta* **2003**, *86*, 3482.
[9] K. Tatsuta, *Pure Appl. Chem.* **1996**, *68*, 1341.
[10] K. Tatsuta, S. Miura, H. Gunji, *Bull. Chem. Soc. Jpn.* **1997**, *70*, 427.
[11] K. Tatsuta, S. Miura, *Tetrahedron Lett.* **1995**, *36*, 6721.
[12] K. Tatsuta, S. Miura, S. Ohta, H. Gunji, *Tetrahedron Lett.* **1995**, *36*, 1085.
[13] K. Tatsuta, S. Miura, S. Ohta, H. Gunji, *J. Antibiot.* **1995**, *48*, 286.
[14] T. Aoyagi, H. Suda, K. Uotani, F. Kojima, T. Aoyama, K. Horiguchi, M. Hamada, T. Takeuchi, *J. Antibiot.* **1992**, *45*, 1404.
[15] T. Aoyama, H. Naganawa, H. Suda, K. Uotani, T. Aoyagi, T. Takeuchi, *J. Antibiot.* **1992**, *45*, 1557.
[16] M. Terinek, A. Vasella, *Helv. Chim. Acta* **2004**, *87*, 3035.
[17] M. Terinek, A. Vasella, *Helv. Chim. Acta* **2005**, *88*, 10.
[18] E. Dubost, T. Tschamber, J. Streith, *Tetrahedron Lett.* **2003**, *44*, 3667.
[19] A. Frankowski, C. Seliga, D. Bur, J. Streith, *Helv. Chim. Acta* **1991**, *74*, 934.
[20] A. Frankowski, D. Deredas, J. Streith, T. Tschamber, *Tetrahedron* **1998**, *54*, 9033.
[21] J. Streith, H. Rudyk, T. Tschamber, C. Tarnus, C. Strehler, D. Deredas, A. Frankowski, *Eur. J. Org. Chem.* **1999**, 893.

[22] J. Streith, A. Boiron, A. Frankowski, D. Lenouen, H. Rudyk, T. Tschamber, *Synthesis* **1995**, 944.
[23] F. Gessier, T. Tschamber, C. Tarnus, M. Neuburger, W. Huber, J. Streith, *Eur. J. Org. Chem.* **2001**, 4111.
[24] K. Weinberg, S. Jankowski, D. Le Nouen, A. Frankowski, *Tetrahedron Lett.* **2002**, *43*, 1089.
[25] C. V. Ramana, A. Vasella, *Helv. Chim. Acta* **2000**, *83*, 1599.
[26] G. J. Davies, L. Mackenzie, A. Varrot, M. Dauter, A. M. Brzozowski, M. Schülein, S. G. Withers, *Biochemistry* **1998**, *37*, 11707.
[27] G. Sulzenbacher, H. Driguez, B. Henrissat, M. Schülein, G. J. Davies, *Biochemistry* **1996**, *35*, 15280.
[28] P. W. Kent, P. F. V. Ward, *J. Chem. Soc.* **1953**, 416.
[29] J. P. Verheijden, P. J. Stoffyn, *Tetrahedron* **1957**, *1*, 253.
[30] C. V. Varaprasad, D. Averett, K. S. Ramasamy, *Tetrahedron* **1999**, *55*, 13345.
[31] J. G. Buchanan, R. Fletcher, K. Parry, W. A. Thomas, *J. Chem. Soc. B* **1969**, 377.
[32] W. G. Overend, A. C. White, N. R. Williams, *Chem. Ind. (London)* **1963**, 1840.
[33] T. Granier, A. Vasella, *Helv. Chim. Acta* **1995**, *78*, 1738.
[34] J. Spychala, *Synth. Commun.* **1997**, *27*, 3431.
[35] G. Levesque, J. C. Gressier, M. Proust, *Synthesis* **1981**, 963.
[36] D. H. Hua, F. Q. Zhang, J. S. Chen, P. D. Robinson, *J. Org. Chem.* **1994**, *59*, 5084.
[37] W. Nagata, M. Yoshioka, T. Okumura, *J. Chem. Soc. C* **1970**, 2365.
[38] A. Knierzinger, A. Vasella, *J. Chem. Soc., Chem. Commun.* **1984**, 9.
[39] K. Sugita, A. Ohta, M. Onaka, Y. Izumi, *Chem. Lett.* **1990**, 481.
[40] M. K. Dowd, W. M. Rockey, A. D. French, P. J. Reilly, *J. Carbohydr. Chem.* **2002**, *21*, 11.
[41] A. G. Evdokimov, F. Frolow, *Acta Crystallogr., Sect. C* **1996**, *52*, 3218.
[42] J. Alzeer, A. Vasella, *Helv. Chim. Acta* **1995**, *78*, 177.
[43] S. Patai, 'The Chemistry of Amidines and Imidates', John Wiley & Sons, London, 1975.
[44] G. Rousselet, P. Capdevielle, M. Maumy, *Tetrahedron Lett.* **1993**, *34*, 6395.
[45] J. I. Ogonor, *Tetrahedron* **1981**, *37*, 2909.
[46] J. I. Levin, E. Turos, S. M. Weinreb, *Synth. Commun.* **1982**, *12*, 989.
[47] R. S. Garigipati, *Tetrahedron Lett.* **1990**, *31*, 1969.
[48] R. A. Moss, W. Ma, D. C. Merrer, S. Xue, *Tetrahedron Lett.* **1995**, *36*, 8761.
[49] D. B. Dess, J. C. Martin, *J. Am. Chem. Soc.* **1991**, *113*, 7277.
[50] S. V. Ley, J. Norman, W. P. Griffith, S. P. Marsden, *Synthesis* **1994**, 639.
[51] A. J. Mancuso, D. Swern, *Synthesis* **1981**, 165.
[52] O. Mitsunobu, *Synthesis* **1981**, 1.
[53] J. L. Luche, *J. Am. Chem. Soc.* **1978**, *100*, 2226.
[54] S. P. Bew, S. D. Bull, S. G. Davies, E. D. Savory, D. J. Watkin, *Tetrahedron* **2002**, *58*, 9387.
[55] S. Knapp, P. J. Kukkola, S. Sharma, T. G. M. Dhar, A. B. J. Naughton, *J. Org. Chem.* **1990**, *55*, 5700.
[56] E. L. Eliel, H. Satici, *J. Org. Chem.* **1994**, *59*, 688.
[57] M. A. Tius, J. Busch-Petersen, *Tetrahedron Lett.* **1994**, *35*, 5181.
[58] T. Hosoya, Y. Ohashi, T. Matsumoto, K. Suzuki, *Tetrahedron Lett.* **1996**, *37*, 663.
[59] J. Xu, A. Egger, B. Bernet, A. Vasella, *Helv. Chim. Acta* **1996**, *79*, 2004.
[60] H. Yamada, M. Nakatani, T. Ikeda, Y. Marumoto, *Tetrahedron Lett.* **1999**, *40*, 5573.
[61] S. Shuto, M. Terauchi, Y. Yahiro, H. Abe, S. Ichikawa, A. Matsuda, *Tetrahedron Lett.* **2000**, *41*, 4151.
[62] S. Shuto, M. Terauchi, Y. Yahiro, H. Abe, S. Ichikawa, A. Matsuda, *Tetrahedron Lett.* **2004**, *45*, 6819.
[63] G. F. Painter, A. Falshaw, H. Wong, *Org. Biomol. Chem.* **2004**, *2*, 1007.
[64] R. H. Jacobson, X. J. Zhang, R. F. DuBose, B. W. Matthews, *Nature* **1994**, *369*, 761.
[65] M. Kurogochi, S. I. Nishimura, Y. C. Lee, *J. Biol. Chem.* **2004**, *279*, 44704.
[66] A. Varrot, C. A. Tarling, J. M. Macdonald, R. V. Stick, D. L. Zechel, S. G. Withers, G. J. Davies, *J. Am. Chem. Soc.* **2003**, *125*, 7496.
[67] S. Vonhoff, K. Piens, M. Pipelier, C. Braet, M. Claeyssens, A. Vasella, *Helv. Chim. Acta* **1999**, *82*, 963.
[68] J. M. Macdonald, R. V. Stick, D. M. G. Tilbrook, S. G. Withers, *Aust. J. Chem.* **2002**, *55*, 747.
[69] V. Popsavin, S. Grabe, B. Stojanovic, M. Popsavin, V. Pejanovic, D. Milkjkovic, *Carbohydr. Res.* **1999**, *312*, 110.
[70] S. A. Kuby, H. A. Lardy, *J. Am. Chem. Soc.* **1953**, *75*, 890.
[71] A. R. Plant, J. E. Oliver, M. L. Patchett, R. M. Daniel, H. W. Morgan, *Arch. Biochem. Biophys.* **1988**, *262*, 181.
[72] J. Schwartz, J. Sloan, *Arch. Biochem. Biophys.* **1970**, *137*, 122.
[73] J. Stahlberg, C. Divne, A. Koivula, K. Piens, M. Claeyssens, T. T. Teeri, T. A. Jones, *J. Mol. Biol.* **1996**, *264*, 337.

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