Inhibition of Glycosidases by Lactam Oximes: Influence of the Aglycon in Disaccharide Analogues

by **Stefan Vonhoff**, **Tom D. Heightman**, and **Andrea Vasella***

Laboratorium für Organische Chemie, ETH-Zentrum, Universitätstrasse 16, CH-8092 Zürich

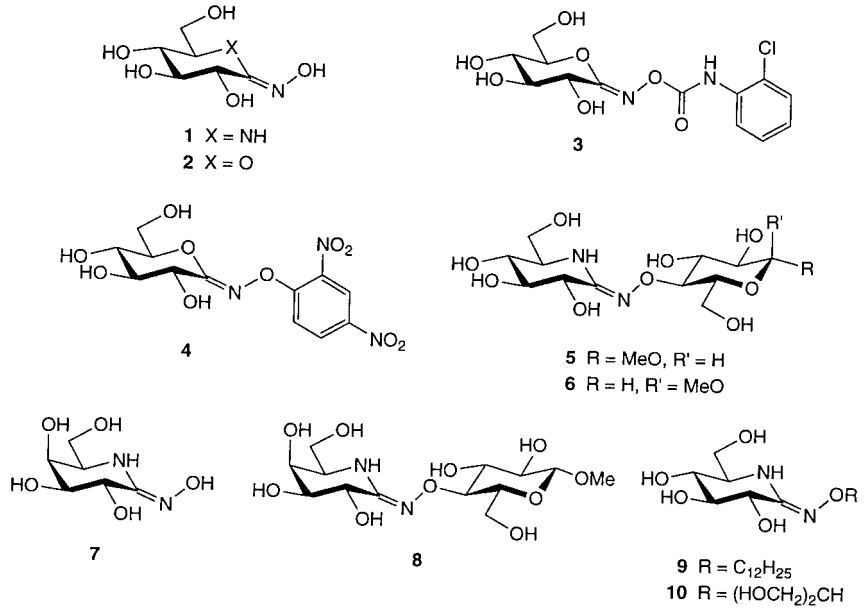
The influence of a substituent at the hydroximo function of the lactam analogue **1** on the inhibition of β- and α-glucosidases is evaluated. In contrast to **1**, the *O*-alkyl oximes **5**, **6**, **9**, and **10** are selective inhibitors of β-glucosidases. Alkylation of the D-gluconohydroximo-1,5-lactam **19** with the triflate **12**, or condensation of the thiogluconolactam **20** with the hydroxylamines **14** or **18** afforded the benzylated cellobioside analogues **21** and **23**, respectively. The *O*-alkyl oximes **33** and **39** were prepared similarly (*Scheme 3*). Deprotection afforded the cellobioside analogues **5** and **6**, and the *O*-alkyl oximes **9** and **10**. The lactam *O*-alkyl oximes **5**, **6**, **9**, and **10** are strong inhibitors of the β-glucosidase from *C. saccharolyticum* ($IC_{50} = 0.3-8$ μM) and, with exception of the dodecyl analogue **9** ($IC_{50} = 2$ μM), moderate-to-weak inhibitors of β-glucosidases from sweet almond ($IC_{50} = 60-1000$ μM; see *Table*). In contrast to the strong inhibition of α-glucosidase from brewer's yeast by **1** ($K_i = 2.9$ μM), the ethers **5**, **6**, and **10** are weak inhibitors of this enzyme (IC_{50} between 2500 and > 5000 μM). Similarly, the D-galactohydroximo-1,5-lactam **7** is a potent inhibitor of the α-galactosidase from coffee beans and of the β-galactosidases from bovine liver and *E. coli* ($K_i = 5$, 10, and 0.1 μM, resp.), while the lactoside analogue **8** is a strong inhibitor of the *E. coli* β-galactosidase ($K_i = 0.1$ μM), but a moderate-to-weak inhibitor of coffee-bean α-galactosidase and bovine-liver β-galactosidase ($K_i = 250$ μM and $IC_{50} = 2500$ μM, resp.). The *galacto*-configured lactam oximes **7** and **8** are good inhibitors of the β-glucosidase isolated from *C. saccharolyticum* ($K_i = 2.5$ and 3.3 μM, resp.).

Introduction. – The weakly basic hydroximolactam **1** (pK_{HA} *ca.* 5) is a stronger inhibitor of the β-glucosidases from sweet almonds and from *Agrobacterium faecalis* than the neutral hydroximolactone **2**, but it is less selective, inhibiting yeast α-glucosidase about as strongly ($K_i = 2.9$ μmol) as the *Agrobacterium* β-glucosidase ($K_i = 0.6$ μmol) [1][2][1]). The higher potency and the lack of selectivity have been traced back to the higher basicity of the hydroximolactam, and to the position of the exocyclic N-center relative to the mean plane of the ring [7]. The higher basicity and the position of the basic center allow this inhibitor to interact with the catalytic acid of β- and (less well) also of α-glucosidases. *O*-Acylation of the hydroximolactone, as in the carbamate **3**, increases its inhibitory potency, both against sweet-almond β-glucosidases that have an affinity for hydrophobic aglyca and against the *Agrobacterium* β-glucosidase [8]; it also decreases the α/β-selectivity. The 2,4-dinitrophenyl ether **4** is even a stronger inhibitor of yeast α-glucosidase than of sweet-almond β-glucosidase [9].

Introduction into an inhibitor of a substituent that more specifically mimicks the aglycon can lead to improved selectivity and provide information about the binding of

[1]) D-Glucono-1,5-lactone and its neutral analogues such as D-glucono-1,5-lactam (nojirilactam) and (5*R*,6*R*,7*S*,8*S*)-6,7,8-tris(benzyloxy)-5-[(benzyloxy)methyl]-5,6,7,8-tetrahydrotetrazolo[1,5-*a*]pyridine (nojiritetrazole) are also selective inhibitors of β-glucosidases with K_i values in the micromolar range [3–6].

the aglycon moiety [10–13][2]). An analogous modification should improve the inhibitory selectivity of the hydroximolactam **1**. The oxime function is particularly suitable for the introduction of substituents, and oxime-linked neoglycoproteins and oximes derived from C(1)-*O*-amino monosaccharides have been reported [24][25]. The disaccharide analogues **5** and **6**, related to **1**, should provide information about the influence of the aglycon on the selectivity of the inhibition of α- and β-glucosidases. Similarly, **8** may be a more selective inhibitor of β-galactosidases than the monosaccharide **7**. For the sake of comparison, the *O*-dodecyl oxime **9** and the 1,3-dihydroxypropan-2-yl derivative **10** were also prepared and evaluated.



Results and Discussion. – 1. *Synthesis.* Two approaches to the methyl β-cellobioside analogue **5** were investigated (*Scheme 1*), *viz*. alkylation of the hydroximolactam **19** [2] with the triflate **12** [16], and condensation of the thiogluconolactam **20** [26] with the hydroxylamine **14**.

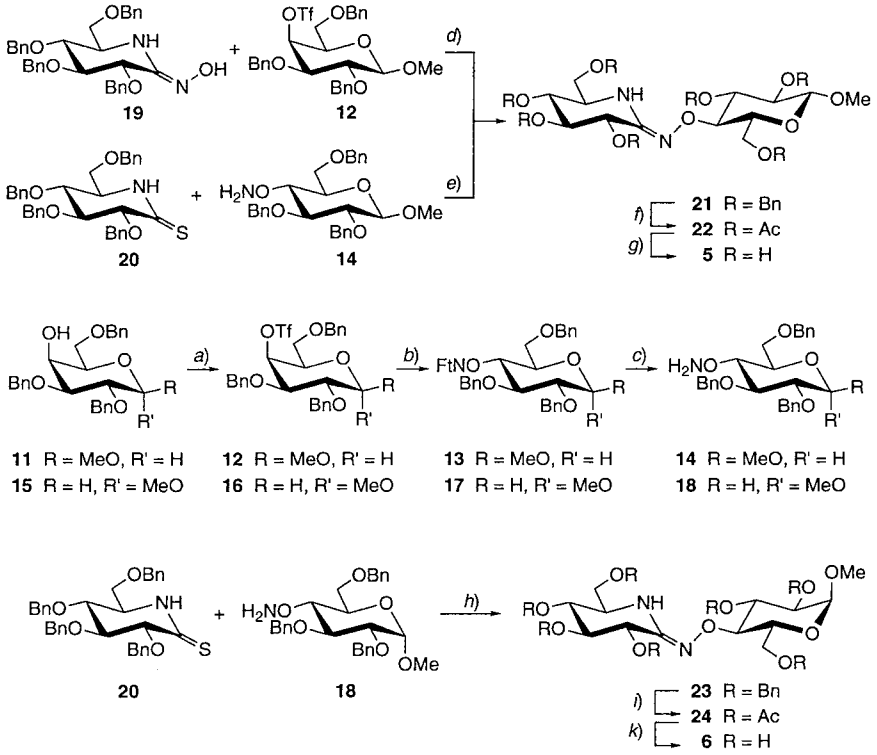
The *galacto*-configured triflate **12** was obtained in 93% yield from the readily available galactopyranoside **11** [27][3]). *O*-Alkylation of **19** under phase-transfer conditions [29] yielded 59% of **21**. Debenzylation of **21** with Li in $EtNH_2$ [30] afforded the pseudo-disaccharide **5**, which was purified *via* the acetate **22**. Attempted debenzylation of **21** using Na in NH_3 and THF as cosolvent [31] did not affect the starting material; prolonging the reaction time led to decomposition products from which methyl 2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranoside was isolated after acetylation.

The hydroxylamine **14** was prepared in two steps and 80% yield from the triflate **12** by base-promoted substitution with *N*-hydroxyphthalimide in DMPU (1,3-dimethyl-

[2]) For related disaccharide analogues, see [14–23].

[3]) The substitution of carbohydrate triflates by oximes has been reported [28].

Scheme 1



a) Tf_2O, pyridine, CH_2Cl_2; 93% (**12**), 90% (**16**). *b*) *N*-Hydroxyphthalimide (FtNOH), DMPU, Et(i-Pr)$_2$N or Et_3N; 91% (**13**), 76% (**17**). *c*) $N_2H_4 \cdot H_2O$, EtOH; 90% (**14**), 80% (**18**). *d*) NaOH, Et_4NBr, toluene; 59%. *e*) $Hg(OAc)_2$, Et(i-Pr)$_2$N, THF; 72%. *f*) Li, $EtNH_2$, THF, $-70°$; Ac_2O, pyridine; 80%. *g*) NH_3, MeOH; 77%. *h*) $Hg(OAc)_2$, Et(i-Pr)$_2$N, THF; 70%. *i*) Na, NH_3, $-33°$; Ac_2O, pyridine; 41%. *k*) NaOMe, MeOH; 96%.

3,4,5,6-tetrahydropyrimidin-2(1*H*)-one)[4]) followed by deprotection of the resulting phthalimide **13** with hydrazine hydrate in boiling EtOH [34] (*Scheme 1*)[5]). The hydroxylamine **14** was condensed with **20** in the presence of $Hg(OAc)_2$. This yielded 72% of **21**; no epimerization was observed (*cf.* [26] for a similar condensation). Thus, the two syntheses of **21** are about equivalent.

Attempts to prepare the α-D-configured disaccharide analogue **23** by *O*-alkylation of the hydroximolactam **19** with the triflate **16** [16][35] failed under conditions that proved successful for the preparation of the anomeric analogue **21**. Decomposition of the triflate **16** proceeded more rapidly than its substitution by the hydroximolactam **19**, while milder methods, such as treatment with NaH, [18]crown-6 ether in THF or in THF/DMPU at 23° [28], or with *Hünig*'s base and DMPU did not promote substitution. Higher temperatures led to degradation of the triflate, while the lactam oxime was recovered. However, at 22°, the triflate **16** was smoothly converted to the

---

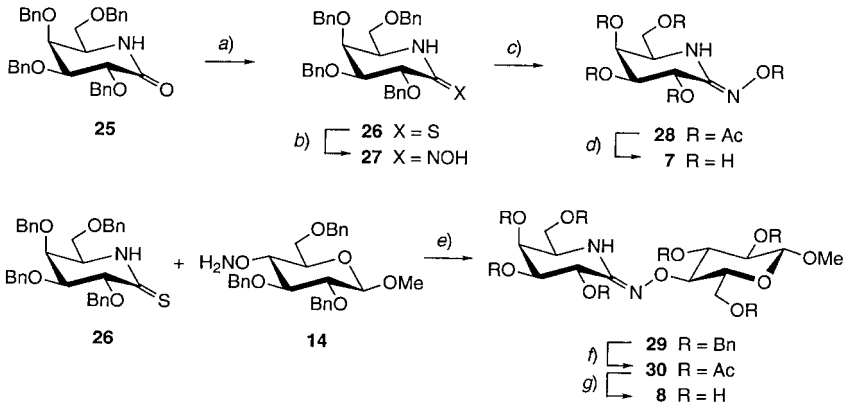
[4]) Alkylation in DMF or DMSO was slower and afforded the phthalimide **13** in lower yield.

[5]) For syntheses of other monosaccharide derived hydroxylamines, see [32][33].

phthalimide **17**. The hydroxylamine **18**, resulting from hydrazinolysis of **17**, was condensed with the thiogluconolactam **20** to afford 70% of the methyl α-cellobioside analogue **23**. Debenzylation with Li/$EtNH_2$ and purification *via* the heptaacetate **24** gave the α-cellobioside analogue **6** in 40% yield.

The *galacto*-hydroximolactam **7** [36] was conveniently prepared by analogy to the *gluco*-analogue **1** [2] (*Scheme 2*). Thus, treatment of the lactam **25** [37] with *Lawesson*'s reagent afforded the thiogalactonolactam **26** which was condensed with NH_2OH according to *Hoos et al.* [2] to give the hydroximolactam **27** in 78% yield. Debenzylation under *Birch* conditions produced the *galacto*-hydroximolactam **7**, which was purified *via* the pentaacetate **28**. The benzyl(Bn)-protected analogue **29** of methyl β-lactoside was synthesized by condensing the thionolactam **26** and the hydroxylamine **14**[6]). Deprotection of the heptabenzyl ether **29**, again under *Birch* conditions, afforded 83% of the desired β-lactoside analogue **8**.

Scheme 2



a) *Lawesson*'s reagent, toluene; 88%. *b*) $NH_2OH \cdot HCl$, $NaHCO_3$, MeOH; 89%. *c*) Li, $EtNH_2$, THF, $-60°$; Ac_2O, pyridine; 69%. *d*) NH_3, MeOH; 91%. *e*) $Hg(OAc)_2$, $Et(i\text{-}Pr)_2N$, THF; 80%. *f*) Li, $EtNH_2$, THF, $-60°$; Ac_2O, pyridine; 88%. *g*) NH_3, MeOH; 94%.

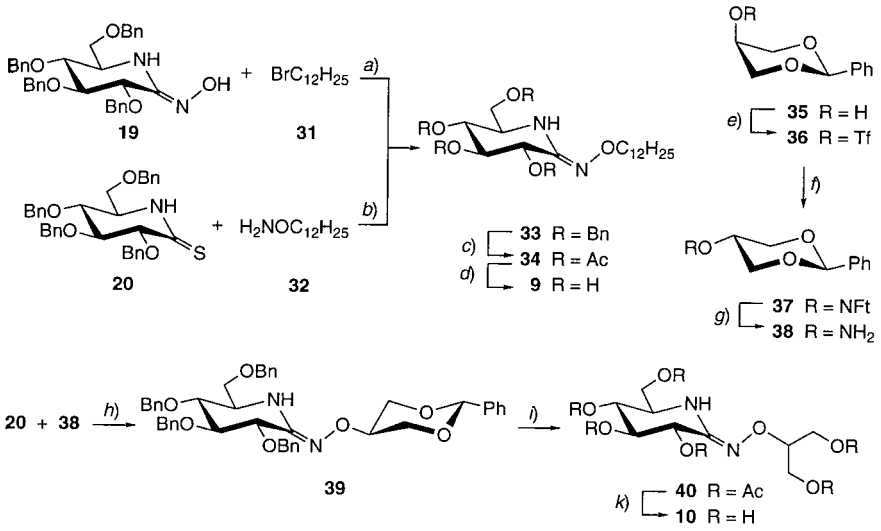
The Bn-protected lactam *O*-dodecyl oxime **33** was obtained in good yield either by alkylation of the lactam oxime **19** with 1-bromododecane (**31**) under phase-transfer conditions, or by condensation of the thiogluconolactam **20** with *O*-dodecylhydroxylamine (**32**) [38] (*Scheme 3*). Debenzylation and purification *via* the tetraacetate **34** yielded 70% of the lactam *O*-dodecyl oxime **9**[7]). The protected D-gluconolactam *O*-(1,3-dihydroxypropan-2-yl) oxime **39** was prepared in 81% yield by the $Hg(OAc)_2$-promoted [26] condensation of the thiogluconolactam **20** with the hydroxylamine **38**. This hydroxylamine was obtained by transforming *cis*-2-phenyl-1,3-dioxan-5-ol (**35**) [39] *via* the triflate **36** into the *N*-alkoxyphthalimide **37**, followed by dephthaloylation.

---

6) Alternatively, **29** was obtained in moderate yield by coupling the hydroximolactam **27** with the triflate **12**.

7) Homologues of **33** with longer alkyl chains proved less soluble in $EtNH_2$. A 12-tricosyl homologue of the lactam *O*-dodecyl oxime **9** was synthesized by condensing the Ac-protected analogue of the thiogluconolactam **20** [7] with the appropriate hydroxylamine by *in situ* activation with $Hg(OAc)_2$ and deprotection. It was very poorly soluble in H_2O.

Scheme 3



a) NaOH, Et_4NBr, toluene; 67%. *b*) $NaHCO_3$, MeOH; 73%. *c*) Li, $EtNH_2$, THF, $-78°$; Ac_2O, pyridine; 74%. *d*) NaOMe, MeOH; 97%. *e*) Tf_2O, pyridine, CH_2Cl_2; 88%. *f*) *N*-Hydroxyphthalimide (FtNOH), DMPU, Et_3N; 77%. *g*) $N_2H_4 \cdot H_2O$, EtOH; 75%. *h*) $Hg(OAc)_2$, $Et(i\text{-}Pr)_2N$, THF; 81%. *i*) Li, $EtNH_2$, $-78°$; Ac_2O, pyridine; 79%. *k*) NaOMe, MeOH; 95%.

The correponding tosylate [40] did not react with *N*-hydroxyphthalimide under otherwise identical conditions. Deprotection of **39** with Li/$EtNH_2$ and purification of the *O*-alkyl oxime **10** *via* the hexaacetate **40** proceeded in 75% yield.

Triflation of **11** and **15** is evidenced by the H–C(4) signal of **12** and **16** at 5.40 and 5.42 ppm, respectively, which is shifted to 4.45 and 4.38 ppm for the phthalimides **13** and **17**. The H–C(4) signal for the hydroxylamines **14** and **18** is observed at 3.84 and 4.07 ppm, respectively. The benzylated *O*-alkyl oximes **21** and **23** are characterized by an exchangeable NH signal at 5.44 (5.45) ppm and by $J(1,2) = 7.8$ (3.7) Hz. The imino group gives rise to a C(1) *s* at 149.05 (148.93) ppm, characteristic for the (*Z*)-configuration [2], and a C=N band at 1653 (1651) cm^{-1}.

$J(2',3') = 5.8$, $J(3',4') = 5.8$, and $J(4',5') = 9.3$ Hz in the ^{1}H-NMR spectrum ($CDCl_3$) of the acetylated cellobioside analogue **22** indicate a $B_{2,5}$ conformation of the lactam-oxime moiety, as reported for penta-*O*-acetyl-D-gluconohydroximo-1,5-lactam [2]; the *J* values for the anomer **24** are similar ($J(2',3') = 6.2$, $J(3',4') = 6.2$, and $J(4',5') = 8.4$ Hz). The *J* values of the anomeric deprotected cellobioside analogues **5** ($J(2',3') = 8.4$, $J(3',4') = 8.6$, and $J(4',5') = 9.1$ Hz) and **6** ($J(2',3') = 8.5$, $J(3',4') = 8.5$, and $J(4',5') = 9.2$ Hz) in CD_3OD are in agreement with a flattened $^4C_1$ conformation of the lactam-oxime moiety.

The thiogalactonolactam **26** is characterized by a *s* at 201.6 ppm, and a C=S band at 1514 cm^{-1}. Conversion of **26** to the hydroximolactam **27** is confirmed by the replacement of the C=S *s* at 201.6 ppm by a *s* at 150.1 ppm, by the shift of the NH signal to 5.80 ppm, and by a new OH resonance at 8.09 ppm. (*Z*)-Configuration of **27** is indicated by the C(1) *s* at 150.1 ppm (*cf.* [2]). The hepta-*O*-benzyl-lactose analogue **29** shows resonances consistent with those of **21** and **23**, with a MeO *s* at 3.60 ppm, and a NH *s* at 5.63 ppm. A *d* at 104.8 and a *s* at 149.6 ppm evidence the presence of the anomeric and oxime C-atoms, respectively; the analogous signals for the deprotected lactose analogue **8** are a *d* at 105.7 and a *s* at 155.5 ppm. $J(2,3) = 8.9$ and $J(2',3') = 8.7$ Hz indicate that both rings of **8** have a $^4C_1$ conformation in CD_3OD.

Similarly, the lactam *O*-alkyl oximes **33** and **39** are characterized by an exchangeable NH signal at 5.47 and 5.36 ppm and a C(1) *s* at 148.90 and 150.10 ppm, respectively. The $B_{2,5}$ conformation of the acetylated gluconolactam oxime **40** is evidenced by $J(2,3) = 5.9$, $J(3,4) = 6.2$, and $J(4,5) = 9.6$ Hz. The same conformation is indicated for the dodecyl ether **34** ($J(2,3) = 5.3$, $J(3,4) = 5.9$, and $J(4,5) = 9.3$ Hz). A $^4C_1$ conformation is indicated for the gluconolactam *O*-alkyl oximes **9** and **10** by $J(2,3) = 8.3$, $J(3,4) = 8.4$, and $J(4,5) = 9.2$ as well as $J(2,3) = 8.3$, $J(3,4) = 8.5$, and $J(4,5) = 8.8$ Hz, respectively.

2. *Evaluation of the Lactam Oximes* **5**–**10** *as Inhibitors of Glucosidases and Galactosidases.* The β-glucosidases from sweet almonds are equally well inhibited by the lactam oxime **1** and the β-D-anomer **5** of the disaccharide analogue, while the α-D-anomer **6** is *ca.* 16 times weaker (*Table*)[8]. This difference must reflect the structure of the active site. Although the complete amino-acid sequence of the sweet-almond β-glucosidases is not known, they have recently been classified as family-1 enzymes on the basis of the active-site residues [43]. The known three-dimensional structure of another glycosidase of family 1, cyanogenic β-glucosidase from white clover, shows several hydrophobic residues at the aglycon binding site (*i.e.*, Trp-185, Phe-197, Val-254, and Trp-369 [44]) of which Trp-369 is likely to π-stack with an aromatic glycosyl substrate. Sweet-almond and white clover β-glucosidases have a comparable substrate specificity. It may well be that the flatter aglycon moiety of the methyl β-cellobioside analogue **5** fits better into the aglycon binding site than the one of the α-cellobioside analogue **6**.

Table. *Inhibition Constants* K_i *and* IC_{50} *Values for the Lactam Oximes* **1** *and* **5**–**10**

Enzyme	K_M[a])	pH	K_i [μM] or, in italics, IC_{50} values [μM]						
			1[b])	**5**	**6**	**7**	**8**	**9**	**10**
β-Glucosidases from sweet almonds	3.0 (1.2)	6.8	16	*60*	*1000*			*2*	*150*
β-Glucosidase from *C. saccharolyticum*	1.2 (1.2)	6.8	3.3	*3.6*	*2*	2.5	3.3	*0.3*	*8*
α-Glucosidase from brewer's yeast	1.2 (1.2)	6.8	2.9	*2500*	*>5000*			*40*	*4000*
β-Galactosidase from bovine liver	0.24 (0.24)	7.0				10[c])	*2500*		
β-Galactosidase from *E. coli*	0.04	6.8				0.1	0.1		
α-Galactosidase from coffee beans	0.19	6.0				5	250		

[a]) K_M values [mM] for corresponding 4-nitrophenyl hexopyranosides. In parenthesis, start concentration of the substrate [mM]. [b]) Values taken from [7]. [c]) Value taken from [36].

The cellobioside analogues **5** and **6** inhibit the β-glucosidase from *Caldocellum saccharolyticum* about as strongly as the parent hydroximolactam **1**.

The cellobioside analogues **5** and **6** show a *ca.* 1000-fold weaker binding efficiency against yeast α-glucosidase than the parent hydroximolactam **1**. The β-cellobioside analogue **5** inhibits yeast α-glucosidase 40 times more weakly than sweet-almond β-glucosidases and 700 times more weakly than the β-glucosidase from *C. saccharolyticum*. Thus, the methyl β-cellobioside analogue **5** shows a marked selectivity for the inhibition of β-glucosidases, while the methyl α-cellobioside **6** is inactive against yeast α-glucosidase and even differentiates between β-glucosidases.

The *galacto*-configured hydroximolactams **7** and **8** are potent competitive inhibitors of the *E. coli* β-galactosidase (family 2) with a K_i of 100 nM, suggesting that the glucosyl ring of **8** does not interfere with the binding of the hydroximolactam unit in the active site. The comparable inhibition by **7** and **8** is not surprising given that lactose is the natural substrate for the *E. coli* enzyme. Molecular modelling suggests that, despite the

---

[8]) The methyl α-cellobioside analogue **6** was also examined as a potential inhibitor of glycogen phosphorylase b (GPb) from rabbit muscle. No inhibition was observed at a concentration of 1.0 mM [41]. This contrasts with the moderate inhibition of GPb by D-gluconohydroximo-1,5-lactone (**2**; K_i = 0.92 mM) [41][42].

larger distance between the two rings, the lactose analogue **8** adopts a conformation similar to that of lactose.

The hydroximolactam **7** ($K_i = 10$ μM) binds bovine-liver β-galactosidase *ca.* 100 times more strongly than the hydroximolactam ether **8** (IC_{50} *ca.* 2.5 mM), in keeping with the strong preference of the bovine-liver enzyme for aryl pyranosides. This contrasts somewhat with the results for the inhibition of the sweet-almond β-glucosidases, which also have a preference for aryl-pyranoside substrates (see above). It would seem that the aromatic aglycon binding site in the bovine liver β-glycosidase is more selective than the one in the sweet-almond β-glucosidases.

The potent inhibition of coffee-bean α-galactosidase by the hydroximolactam **7** ($K_i = 5$ μM) is significantly weakened by the introduction of the glucosyl moiety in **8** ($K_i = 250$ μM), similarly to the results obtained for the *gluco*-configured lactam oximes **1** and **5**.

Finally, the K_i values of the D-galactonohydroximo-1,5-lactam **7** (2.5 μM) and the lactoside analogue **8** (3.3 μM) against the β-glucosidase from *C. saccharolyticum* (family 1) are similar to those for the *gluco*-analogues **1** and **5**, confirming that family-1 glucosidases are not selective for the configuration at C(4), and also that the aglycon binding site is adapted for hydrophilic as well as hydrophobic residues. This is in keeping with the role of the enzyme as an *exo*-cellulase [45].

To examine whether the increased α/β-glucosidase selectivity of the cellobioside analogues **5** and **6** is an aglycon specific effect, we evaluated the lactam *O*-alkyl oximes **9** and **10**, possessing a hydrophobic and a hydrophilic aglycon moiety with differing steric requirements. The dodecyl analogue **9** is a stronger inhibitor of the examined β-glucosidases than the parent hydroximolactam **1**, and inhibits the β-glucosidases from sweet almonds and *C. saccharolyticum* 30- and 10-fold more strongly than the cellobioside analogue **5**[9]). It inhibits yeast α-glucosidase 10 times more weakly than the hydroximolactam **1**, but 60 times more strongly than the disaccharide analogue **5**. Thus, the *O*-alkyl oxime **9** is a stronger inhibitor than **1**, **5**, and **6**. It is more highly selective than **1**, but less so than **5** and **6**. The propanediol derivative **10** is a weaker inhibitor of the examined α- and β-glucosidases than **1** and **5**, and partially weaker than **6**. It is almost as selective as **5**, but less so than **6**. Obviously, the selectivity is readily influenced by additional substituents at the hydroximo function.

We thank Dr. *N. G. Oikonomakos* for the evaluation of **6** as glycogen phosphorylase b inhibitor, Dr. *B. Bernet* for the critical reading of the manuscript, and the *Swiss National Science Foundation* and *F. Hoffmann-La Roche AG*, Basel, for generous support.

Experimental Part

1. *General*. Enzymes were purchased from *Sigma Chemical Co.* and used without further purification. Solvents were distilled before use. Moisture sensitive reactions were run under Ar or N_2 in dry solvents. TLC: *Merck* silica gel *60* F_{254} plates; detection by heating with 'mostain' (400 ml of 10% aq. H_2SO_4 soln., 20 g of $(NH_4)_6Mo_7O_{24} \cdot H_2O$, 0.4 g of $Ce(SO_4)_2$) or 20% aq. H_2SO_4. Flash chromatography (FC): silica gel *Merck 60*

[9]) The enhanced inhibition of **9** might be caused by the transfer of the hydrophobic alkyl chain from the aqueous phase onto the more lipophilic environment of the active site. The analogous hydrophobic *N*-dodecyl-β-D-glucosylamine [46] and N^1-dodecyl-D-gluconamidine [47][48] have been reported to be very strong inhibitors of bovine β-glucosidase ($IC_{50} = 1.5$ and 0.2 nM, resp.).

(0.040–0.063 mm). M.p.: uncorrected. Chemical shifts δ in ppm and coupling constants J in Hz. 3-NOBA = 3-nitrobenzyl alcohol.

2. *Preparation of* **5**. *Methyl 2,3,6-Tri*-O-*benzyl-4*-O-*[(trifluoromethyl)sulfonyl]-β*-D-*galactopyranoside* (**12**) [16]. At $-15°$, Tf_2O (8.6 g, 5.0 ml, 32.7 mmol) was added dropwise within 20 min to a stirred suspension of **11** [27] (7.6 g, 16.0 mmol), pyridine (2.6 ml, 32.7 mmol), and 3-Å molecular sieves (0.2 g) in CH_2Cl_2 (50 ml). The suspension was warmed to 0° within 3 h, poured into cold 1M aq. HCl soln. (50 ml), and the org. layer was washed with H_2O (3 × 40 ml). Evaporation and FC (hexane/AcOEt 4:1) gave **12** (8.9 g, 93%). Colourless oil. R_f (hexane/AcOEt 2:1) 0.45. IR (CH_2Cl_2): 3033*w*, 2875*w*, 1497*w*, 1454*m*, 1407*s*, 1210*s*, 1143*s*, 1105*s*, 1081*s*, 1029*m*, 921*s*, 630*m*. ^{1}H-NMR ($CDCl_3$, 300 MHz): 3.57 (*s*, MeO); 3.61–3.77 (*m*, H–C(2), H–C(3), H–C(5), 2 H–C(6)); 4.32 (*d*, J = 7.5, H–C(1)); 4.46 (*d*, J = 11.5), 4.61 (*d*, J = 11.5), 4.65 (*d*, J = 11.2), 4.74 (*d*, J = 10.9), 4.86 (*d*, J = 10.9), 4.89 (*d*, J = 11.8, 6 PhC*H*); 5.40 (*d*, J = 2.2, H–C(4)); 7.26–7.42 (*m*, 15 arom. H). ^{13}C-NMR ($CDCl_3$, 75 MHz): 57.28 (*q*, MeO); 66.99 (*t*, C(6)); 71.02 (*d*, C(4)); 72.91, 73.69, 75.40 (3*t*, 3 Ph*C*H$_2$); 77.73 (*d*, C(5)); 78.36 (*d*, C(2)); 81.66 (*d*, C(3)); 104.83 (*d*, C(1)); 118.60 (*q*, ^1J(C,F) = 319, CF_3); 127.80–128.63 (several *d*); 137.19, 137.35, 138.22 (3*s*). ^{19}F-NMR ($CDCl_3$, 282 MHz): −73.76. FAB-MS (3-NOBA): 596 (35, $[M]^+$), 595 (100, $[M-H]^+$), 505 (20), 181 (37), 91 (27).

Methyl 2,3,6-Tri-O-*benzyl-4*-O-*phthalimido-β*-D-*glucopyranoside* (**13**). A soln. of **12** (5.3 g, 8.9 mmol) and *N*-hydroxyphthalimide (1.8 g, 11.0 mmol) in DMPU (20 ml) and Et_3N (1.6 ml, 11.0 mmol) was stirred at 22°. After 24 h, the mixture was poured into H_2O (80 ml), and extracted with Et_2O (4 × 25 ml). The org. layer was washed with H_2O (2 × 25 ml), dried ($MgSO_4$), and evaporated to afford, after FC (hexane/AcOEt 4:1) **13** (4.8 g, 91%). Colourless solid. R_f (hexane/AcOEt 7:3) 0.42. M.p. 78.6–79.3° (hexane/Et_2O). IR (CH_2Cl_2): 3033*w*, 2927*m*, 2873*m*, 1791*m*, 1734*s*, 1497*m*, 1468*m*, 1454*m*, 1373*m*, 1360*m*, 1189*s*, 1170*m*, 1121*s*, 1082*s*, 1028*s*, 1018*s*, 990*m*, 878*m*. ^{1}H-NMR ($CDCl_3$, 300 MHz): 3.49 (*dd*, $J \approx$ 8.4, 7.8, H–C(2)); 3.60 (*s*, MeO); 3.83 (*ddd*, J = 9.5, 5.9, 1.8, H–C(5)); 3.91 (*dd*, J = 10.9, 6.2, H–C(6)); 4.10 (*t*, $J \approx$ 8.5, H–C(3)); 4.17 (*dd*, J = 10.9, 1.6, H′–C(6)); 4.42 (*d*, J = 7.8, H–C(1)); 4.45 (*dd*, J = 9.3, 8.4, H–C(4)); 4.62 (*d*, J = 11.2), 4.63 (*d*, J = 11.7, 2 PhC*H*); 4.64 (*s*, PhCH_2); 4.93 (*d*, J = 11.2), 5.01 (*d*, J = 11.5, 2 PhC*H*); 6.97–7.07 (*m*, 4 arom. H); 7.23–7.38 (*m*, 12 arom. H); 7.53–7.61 (*m*, 3 arom. H). ^{13}C-NMR ($CDCl_3$, 75 MHz): 57.05 (*q*, MeO); 70.03 (*t*, C(6)); 72.95 (*d*, C(5)); 73.58 (*t*, PhCH_2); 74.13 (*t*, 2 PhCH_2); 82.37 (*d*); 82.68 (*d*); 82.76 (*d*); 104.24 (*d*, C(1)); 123.25–128.43 (several *d*); 128.70 (2*s*); 134.14 (2*d*); 138.31, 138.41, 138.69 (3*s*); 163.19 (*s*, 2 C=O). FAB-MS (3-NOBA): 608 (77), 470 (81), 181 (66), 91 (100).

Methyl 4-O-*Amino-2,3,6-tri*-O-*benzyl-β*-D-*glucopyranoside* (**14**). A soln. of **13** (4.7 g, 7.9 mmol) in EtOH (100 ml) and hydrazine hydrate (80%, 10 ml) was kept under reflux for 3 h. Concentration to *ca*. 50 ml gave a colourless solid, which was removed by filtration. Further evaporation and FC of the residue (hexane/AcOEt 4:1) afforded **14** (3.4 g, 90%). Colourless solid. R_f (hexane/AcOEt 7:3) 0.15. M.p. 78.5–79.0° (hexane/Et_2O). $[\alpha]_D^{25} = -25.2$ (c = 0.98, $CHCl_3$). IR (CH_2Cl_2): 3089*w*, 3033*m*, 2913*m*, 2870*m*, 1587*m*, 1496*m*, 1454*m*, 1388*w*, 1359*m*, 1309*w*, 1209*m*, 1090*s*, 1056*s*, 1028*s*, 912*m*. ^{1}H-NMR ($CDCl_3$, 300 MHz): 3.45 (*dd*, J = 9.0, 7.8, H–C(2)); 3.60 (*s*, MeO); 3.54–3.62 (*m*), 3.66–3.73 (*m*, H–C(3), H–C(5), H–C(6)); 3.84 (*t*, $J \approx$ 9.0, H–C(4)); 3.86 (*dd*, $J \approx$ 10.4, 3.1, H′–C(6)); 4.32 (*d*, J = 7.8, H–C(1)); 4.64 (*s*, PhCH_2); 4.74 (*d*, J = 11.2), 4.79 (*d*, J = 11.5), 4.93 (*d*, J = 11.5), 4.95 (*d*, J = 11.2, 4 PhC*H*); 5.09 (*s*, exchange with D_2O, NH_2); 7.26–7.42 (*m*, 15 arom. H). ^{13}C-NMR ($CDCl_3$, 75 MHz): 57.01 (*q*, MeO); 69.97 (*t*, C(6)); 72.94 (*d*, C(5)); 73.51, 74.67, 74.77 (3*t*, 3 PhCH_2); 80.12 (*d*); 82.31 (*d*); 82.50 (*d*); 104.49 (*d*, C(1)); 127.67–128.43 (several *d*); 138.32, 138.66, 138.90 (3*s*). FAB-MS (3-NOBA): 959 (43, $[2M+H]^+$), 448 (71, $[M-HNO]^+$), 181 (28), 91 (100). Anal. calc. for $C_{28}H_{33}NO_6$ (479.57): C 70.13, H 6.94, N 2.92; found: C 70.28, H 7.02, N 2.73.

Methyl 4-O-*[(Z)-(5-Amino-2,3,4,6-tetra*-O-*benzyl-5-deoxy*-D-*glucopyranosylidene)amino]-2,3,6-tri*-O-*benzyl-β*-D-*glucopyranoside* (**21**). a) *From* **12** *and* **19**. A vigorously stirred mixture of **19** [2] (1.31 g, 2.37 mmol), **12** (1.30 g, 2.37 mmol), Et_4NBr (50 mg) in toluene (50 ml), and an aq. soln. of NaOH (4.0 g in 25 ml) was heated to reflux for 24 h. The layers were separated, and the aq. layer was extracted with CH_2Cl_2 (2 × 25 ml). Drying of the combined org. layers ($MgSO_4$), evaporation, and FC (hexane/AcOEt 4:1) afforded **21** (1.41 g, 59%).

b) *From* **14** *and* **20**. At 22°, a soln. of **20** [26] (1.32 g, 2.40 mmol) and **14** (1.15 g, 2.40 mmol) in THF (40 ml, freshly distilled) was treated with Et(i-Pr)$_2$N (1.43 ml, 8.40 mmol) and $Hg(OAc)_2$ (1.14 g, 3.59 mmol). After 16 h at 20°, the mixture was filtered through *Celite* and evaporated. The residue was dissolved in CH_2Cl_2 (50 ml), and washed with sat. aq. $NaHCO_3$ soln. (2 × 35 ml). Drying of the org. phase ($MgSO_4$), evaporation, and FC (hexane/AcOEt 9:1) afforded **21** (1.74 g, 72%). Colourless oil. R_f (hexane/AcOEt 4:1) 0.25, R_f (hexane/AcOEt 7:3) 0.80. $[\alpha]_D^{25} = +27.5$ (c = 2.3, $CHCl_3$). IR (CH_2Cl_2): 3422*w*, 3068*s*, 2987*s*, 2868*m*, 1653*m*, 1604*w*, 1551*w*, 1496*m*, 1453*s*, 1422*s*, 1361*m*, 1288*s*, 1213*m*, 1094*s*, 1060*s*, 1028*m*, 989*m*, 896*s*. ^{1}H-NMR ($CDCl_3$, 500 MHz): 3.39 (*dd*, J = 9.7, 6.5, H–C(6′)); 3.41–3.44 (*m*, H–C(5)); 3.43 (*dd*, J = 8.9, 8.0, H–C(2)); 3.60 (*s*, MeO); 3.63–3.67 (*m*, H–C(4′), H′–C(6′)); 3.71 (*ddd*, J = 9.4, 6.4, 2.8, H–C(5′)); 3.86 (*t*, $J \approx$ 3.2, H–C(3′)); 3.86–3.89

(*m*, H–C(4)); 3.98–4.06 (*m*, H–C(2′), H–C(3), 2 H–C(6)); 4.31 (*d*, *J* = 11.6), 4.35 (*d*, *J* = 10.9, 2 PhC*H*); 4.37 (*d*, *J* = 7.8, H–C(1)); 4.40 (*d*, *J* = 12.0), 4.43 (*d*, *J* = 12.0), 4.45 (*d*, *J* = 12.1), 4.51 (*d*, *J* = 11.7), 4.52 (*d*, *J* = 11.6, 5 PhC*H*); 4.57 (*s*, PhCH_2); 4.61 (*d*, *J* = 12.0), 4.62 (*d*, *J* = 11.2), 4.69 (*d*, *J* = 11.2), 4.72 (*d*, *J* = 11.1), 4.89 (*d*, *J* = 11.1, 5 PhC*H*); 5.44 (*s*, exchange with D_2O, NH); 7.11–7.35 (*m*, 35 arom. H). ^{13}C-NMR ($CDCl_3$, 125 MHz): 51.32 (*d*, C(5′)); 57.07 (*q*, MeO); 69.11, 69.56 (2*t*, C(6), C(6′)); 70.30, 71.53, 72.22, 73.11, 73.49 (5*t*, 5 Ph*C*H_2); 73.64 (*d*); 73.73 (*d*); 74.81, 75.01 (2*t*, 2 Ph*C*H_2); 80.37 (*d*); 80.40 (*d*); 80.62 (*d*); 81.92 (*d*); 82.39 (*d*); 104.61 (*d*, C(1)); 127.20–128.49 (several *d*); 137.45–139.17 (several *s*); 149.05 (*s*, C(1′)). FAB-MS (3-NOBA: 999 (35, $[M+H]^+$), 967 (17), 133 (60), 91 (100). Anal. calc. for $C_{62}H_{66}N_2O_{10}$ (999.21): C 74.53, H 6.66, N 2.80; found: C 74.27, H 6.74, N 3.09.

Methyl 2,3,6-Tri-O-*acetyl-4*-O-*[(*Z*)-(2,3,4,6-tetra*-O-*acetyl-5-amino-5-deoxy*-D-*glucopyranosylidene)amino]-β*-D-*glucopyranoside* (**22**). At −70°, a soln. of **21** (1.50 g, 1.50 mmol) in THF (6.5 ml) was added dropwise to a deep-blue soln. of Li (0.31 g, 44.3 mmol) in condensed $EtNH_2$ (*ca.* 50 ml). The mixture was stirred at −70° for 15 min and treated with NH_4Cl (2.0 g). After evaporation, the residue was dried, dissolved in pyridine (20 ml), and treated with Ac_2O (10 ml) at −15°. After 12 h at 22°, the mixture was taken to dryness and the residue was dissolved in CH_2Cl_2 (25 ml), and washed with brine (2 × 25 ml). Drying ($MgSO_4$), evaporation, and FC (hexane/AcOEt 6 : 4) afforded **22** (0.81 g, 80%), which was further purified by HPLC (hexane/AcOEt 2 : 1). Colourless oil. R_f (hexane/AcOEt 4 : 6) 0.50. IR (CH_2Cl_2): 3400*w*, 3068*m*, 2987*s*, 1756*s*, 1659*w*, 1550*w*, 1422*s*, 1369*m*, 1237*s*, 1160*w*, 1040*m*, 987*w*, 896*s*. ^{1}H-NMR ($CDCl_3$, 500 MHz): 2.03, 2.05, 2.08, 2.09, 2.10, 2.11, 2.14 (7*s*, 7 AcO); 3.50 (*s*, MeO); 3.67 (*dddd*, *J* = 9.3, 6.4, 2.9, 1.5, H–C(5′)); 3.83 (*ddd*, *J* = 9.9, 5.3, 2.2, H–C(5)); 4.03 (*dd*, *J* = 11.9, 6.4, H–C(6′)); 4.07 (*t*, *J* ≈ 9.7, H–C(4)); 4.26 (*dd*, *J* = 12.1, 5.3, H–C(6)); 4.29 (*dd*, *J* = 11.9, 2.9, H′–C(6′)); 4.36 (*dd*, *J* = 12.1, 2.2, H′–C(6)); 4.39 (*d*, *J* = 8.0, H–C(1)); 4.95 (*dd*, *J* = 9.7, 8.0, H–C(2)); 4.99 (*dd*, *J* = 9.3, 5.9, H–C(4′)); 5.20 (*t*, *J* ≈ 5.8, H–C(3′)); 5.32 (*d*, *J* = 5.8, H–C(2′)); 5.35 (*t*, *J* ≈ 9.5, H–C(3)); 5.35 (br. *s*, NH). ^{13}C-NMR ($CDCl_3$, 75 MHz): 20.60, 20.66, 20.74, 20.79, 20.82, 20.87 (6*q*, 7 Me); 52.24 (*d*, C(5′)); 57.06 (*q*, MeO); 62.86, 63.08 (2*t*, C(6), C(6′)); 67.64 (*d*); 69.99 (*d*); 71.79 (*d*); 71.87 (*d*); 72.04 (*d*); 72.27 (*d*); 78.35 (*d*, C(4)); 101.71 (*d*, C(1)); 147.85 (*s*, C(1′)); 169.00–171.28 (several *s*, 7 C=O). FAB-MS (3-NOBA): 663 (100, $[M+H]^+$), 631 (16), 360 (14).

Methyl 4-O-*[(*Z*)-(5-Amino-5-deoxy*-D-*glucopyranosylidene)amino]-β*-D-*glucopyranoside* (**5**). At 0°, a soln. of **22** (0.75 g, 1.13 mmol) in MeOH (15 ml) was treated dropwise with a sat. soln. of NH_3 in MeOH (1.0 ml), stirred at 5° for 6 h, and evaporated to give after reversed-phase HPLC (*RP-18* silica gel) **5** (320 mg, 77%). Colourless solid. R_f (AcOEt/MeOH/H_2O 4 : 2 : 1) 0.45. M.p. 115.5–116° (MeOH). $[\alpha]_D^{25} = -10.4$ (*c* = 1.16, MeOH). IR (KBr): 3425*s*, 3343*s*, 3292*s*, 2991*m*, 2942*m*, 1661*s*, 1643*s*, 1456*m*, 1417*m*, 1334*s*, 1097*s*, 1078*s*, 975*s*, 875*m*. ^{1}H-NMR (500 MHz, CD_3OD): 3.15 (*ddd*, *J* = 9.1, 6.8, 2.9, H–C(5′)); 3.23 (*dd*, *J* = 8.9, 8.0, H–C(2)); 3.39 (*dd*, *J* = 9.1, 8.6, H–C(4′)); 3.52–3.57 (*m*, H–C(5), H–C(6′)); 3.53 (*s*, MeO); 3.55 (*t*, *J* ≈ 8.6, H–C(3′)); 3.71 (*dd*, *J* = 12.3, 4.9, H–C(6)); 3.75 (*t*, *J* ≈ 9.2, H–C(3)); 3.79 (*t*, *J* ≈ 9.2, H–C(4)); 3.82 (*dd*, *J* = 12.3, 2.3, H′–C(6)); 3.88 (*dd*, *J* = 11.1, 2.9, H′–C(6′)); 3.99 (*d*, *J* = 8.4, H–C(2′)); 4.19 (*d*, *J* = 7.8, H–C(1)). ^{13}C-NMR (75 MHz, D_2O): 55.16 (*d*, C(5′)); 58.34 (*q*, MeO); 62.08, 63.35 (2*t*, C(6), C(6′)); 70.40 (*d*); 70.81 (*d*); 71.48 (*d*); 72.33 (*d*); 73.35 (*d*); 76.65 (*d*); 80.16 (*d*, C(4)); 100.71 (*d*, C(1)); 154.16 (*s*, C(1′)). FAB-MS (3-NOBA): 391 (49), 369 (100, $[M+H]^+$), 289 (20), 136 (35). Anal. calc. for $C_{13}H_{24}N_2O_{10} \cdot ½\ H_2O$ (377.33): C 41.38, H 6.68, N 7.42; found: C 41.18, H 6.53, N 7.72.

3. *Preparation of* **6**. *Methyl 2,3,6-Tri*-O-*benzyl-4*-O-*[(trifluoromethyl)sulfonyl]-α*-D-*galactopyranoside* (**16**) [16] [35]. At −20°, Tf_2O (4.7 g, 2.8 ml, 18.1 mmol) was added dropwise within 15 min to a stirred suspension of **15** [27] (4.2 g, 9.0 mmol), pyridine (1.5 ml, 18.1 mmol), and 3-Å molecular sieves (0.1 g) in CH_2Cl_2 (25 ml). The suspension was stirred at −10° for 8 h, poured into cold 1M aq. HCl soln. (50 ml), and the org. layer was washed with H_2O (3 × 40 ml). Evaporation and FC (hexane/AcOEt 4 : 1) gave **16** (4.8 g, 90%). Colourless oil. R_f (hexane/AcOEt 7 : 3) 0.60. IR (CH_2Cl_2): 3100*w*, 2880*w*, 1456*m*, 1412*s*, 1208*s*, 1136*s*, 1100*s*, 1076*s*, 935*s*. ^{1}H-NMR ($CDCl_3$, 300 MHz): 3.38 (*s*, MeO); 3.55–3.65 (*m*, 2 H–C(6)); 3.79 (*dd*, *J* = 10.0, 3.1, H–C(2)); 4.00 (*dd*, *J* = 10.0, 2.5, H–C(3)); 4.09 (*t*, *J* ≈ 6.9, H–C(5)); 4.47 (*d*, *J* = 11.2), 4.62 (*d*, *J* = 11.8, 2 PhC*H*); 4.64 (*d*, *J* = 3.1, H–C(1)); 4.66 (*d*, *J* = 12.1), 4.67 (*d*, *J* = 11.5), 4.85 (*d*, *J* = 12.5), 4.88 (*d*, *J* = 11.8, 4 PhC*H*); 5.42 (*d*, *J* = 2.5, H–C(4)); 7.27–7.44 (*m*, 15 arom. H). ^{13}C-NMR ($CDCl_3$, 75 MHz): 55.53 (*q*, MeO); 66.60 (*d*, C(4)); 67.29 (*t*, C(6)); 73.00, 73.52, 73.80 (3*t*, 3 PhCH_2); 74.65 (*d*); 74.86 (*d*); 83.71 (*d*, C(3)); 98.68 (*d*, C(1)); 118.51 (*q*, ^1J(C,F) = 319.8, CF_3); 127.75–128.46 (several *d*); 137.34, 137.39, 137.86 (3*s*). ^{19}F-NMR ($CDCl_3$, 282 MHz): −73.71.

Methyl 2,3,6-Tri-O-*benzyl-4*-O-*phthalimido-α*-D-*glucopyranoside* (**17**). A soln. of **16** (5.2 g, 8.8 mmol) and *N*-hydroxyphthalimide (1.8 g, 11.0 mmol) in DMPU (20 ml) and Et(i-Pr)$_2$N (1.9 ml, 11.1 mmol) was stirred at 22°. After 24 h, the mixture was poured into H_2O (80 ml) and extracted with Et_2O (4 × 25 ml). The org. layer was washed with H_2O (2 × 25 ml), dried ($MgSO_4$), and evaporated to afford, after FC (hexane/AcOEt 4 : 1), **17** (4.0 g, 76%). Colourless oil. R_f (hexane/AcOEt 7 : 3) 0.35. IR (CH_2Cl_2): 3032*w*, 2912*w*, 1790*w*, 1733*s*, 1497*w*,

1468*w*, 1454*w*, 1375*m*, 1189*m*, 1156*m*, 1098*m*, 1082*m*, 1047*m*, 1027*m*, 1018*m*, 1002*m*, 878*w*. ^{1}H-NMR ($CDCl_3$, 300 MHz): 3.42 (*s*, MeO); 3.59 (*dd*, *J* = 9.4, 3.4 H–C(2)); 3.93 (*dd*, *J* = 11.2, 5.0, H–C(6)); 3.99–4.06 (*m*, H–C(5), H′–C(6)); 4.38 (*t*, *J* ≈ 8.7, H–C(4)); 4.53 (*t*, *J* ≈ 9.0, H–C(3)); 4.58 (*d*, *J* = 12.2), 4.62 (*d*, *J* = 11.8, 2 PhC*H*); 4.63 (*d*, *J* = 2.9, H–C(1)); 4.68 (*d*, *J* = 12.1, PhC*H*); 4.71 (*d*, *J* = 11.8, 2 PhC*H*); 5.12 (*d*, *J* = 11.5, PhC*H*); 7.03–7.11 (*m*, 4 arom. H); 7.22–7.37 (*m*, 12 arom. H); 7.55–7.60 (*m*, 3 arom. H). ^{13}C-NMR ($CDCl_3$, 75 MHz): 55.18 (*q*, MeO); 67.84 (*d*, C(5)); 69.21 (*t*, C(6)); 73.06, 73.54, 74.57 (3*t*, 3 Ph*C*H$_2$); 79.74 (*d*); 80.42 (*d*); 82.25 (*d*); 97.51 (*d*, C(1)); 123.17–128.52 (several *d*); 128.73 (2*s*); 134.05 (2*d*); 137.79, 138.24, 138.89 (3*s*); 163.16 (*s*, 2 C=O). FAB-MS (3-NOBA): 608 (4), 181 (45), 91 (100).

Methyl 4-O-*Amino-2,3,6-tri*-O-*benzyl-α*-D-*glucopyranoside* (**18**). A soln. of **17** (4.5 g, 7.6 mmol) in EtOH (100 ml) and hydrazine hydrate (80%, 10 ml) was kept under reflux for 2 h. Concentration to *ca.* 50 ml gave a colourless solid, which was removed by filtration. Further evaporation and FC of the residue (hexane/AcOEt 4:1) afforded **18** (2.9 g, 80%). Colourless oil. R_f (hexane/AcOEt 7:3) 0.20. $[\alpha]_D^{25} = +17.9$ (*c* = 1.45, $CHCl_3$). IR (CH_2Cl_2): 3591*w*, 3327*w*, 3089*m*, 3032*m*, 2912*m*, 2870*m*, 1721*w*, 1585*w*, 1496*m*, 1453*m*, 1361*m*, 1328*m*, 1194*m*, 1158*m*, 1097*s*, 1048*s*, 1028*s*, 910*m*. ^{1}H-NMR ($CDCl_3$, 300 MHz): 3.39 (*s*, MeO); 3.55 (*dd*, *J* = 9.7, 3.4, H–C(2)); 3.60 (*t*, *J* ≈ 9.4, H–C(3)); 3.66 (*dd*, *J* = 10.9, 4.7, H–C(6)); 3.72 (*dd*, *J* = 10.9, 2.5, H′–C(6)); 3.87 (*ddd*, *J* = 10.0, 4.4, 2.2, H–C(5)); 4.07 (*t*, *J* ≈ 9.4, H–C(4)); 4.56 (*d*, *J* = 12.1, PhC*H*); 4.61 (*d*, *J* = 4.0, H–C(1)); 4.62 (*d*, *J* = 12.1), 4.66 (*d*, *J* = 12.2, 2 PhC*H*); 4.80 (*d*, *J* = 12.4, 2 PhC*H*); 4.98 (*d*, *J* = 11.5, PhC*H*); 5.20 (br. *s*, NH_2); 7.20–7.45 (*m*, 15 arom. H). ^{13}C-NMR ($CDCl_3$, 75 MHz): 55.40 (*q*, MeO); 68.57 (*d*, C(5)); 69.36 (*t*, C(6)); 73.47, 73.61, 75.30 (3*t*, 3 Ph*C*H$_2$); 78.84 (*d*); 80.31 (*d*); 82.33 (*d*); 98.28 (*d*, C(1)); 127.86–128.72 (several *d*); 138.45 (2*s*); 139.30 (*s*). FAB-MS (3-NOBA): 610 (25), 520 (50), 488 (100), 448 (60, $[M - HNO]^+$), 91 (18). Anal. calc. for $C_{28}H_{33}NO_6$ (479.57): C 70.13, H 6.94, N 2.92; found: C 70.21, H 7.00, N 2.75.

Methyl 4-O-*[(Z)-(5-Amino-2,3,4,6-tetra*-O-*benzyl-5-deoxy*-D-*glucopyranosylidene)amino]-2,3,6-tri*-O-*benzyl-α*-D-*glucopyranoside* (**23**). At 22°, a soln. of **20** (2.8 g, 5.0 mmol) and **18** (2.4 g, 5.0 mmol) in THF (60 ml, freshly distilled) was treated with Et(i-Pr)$_2$N (3.0 ml, 17.5 mmol) and $Hg(OAc)_2$ (2.4 g, 7.5 mmol), and kept for 8 h at 22°. After filtration through *Celite* and evaporation, the residue was dissolved in CH_2Cl_2 (100 ml) and washed with sat. aq. $NaHCO_3$ soln. (2 × 25 ml). Drying of the org. phase ($MgSO_4$), evaporation, and FC (hexane/AcOEt 9:1) afforded **23** (3.5 g, 70%), which was sufficiently pure (^{1}H-NMR) to be used for the next step. Colourless oil. R_f (hexane/AcOEt 7:3) 0.50. IR (CH_2Cl_2): 3422*w*, 3088*m*, 3032*m*, 2912*m*, 2868*m*, 1651*m*, 1497*m*, 1454*s*, 1362*m*, 1323*m*, 1208*m*, 1162*m*, 1097*s*, 1052*s*, 1028*s*, 914*m*. ^{1}H-NMR ($CDCl_3$, 300 MHz): 3.42–3.50 (*m*, H–C(5), H–C(6′)); 3.46 (*s*, MeO); 3.61 (*m*, *J* = 12.5, 3.1, H′–C(6′)); 3.60–3.78 (*m*, H–C(2), H–C(6), H–C(4′), H–C(5′)); 3.90 (*t*, *J* ≈ 3.3, H–C(3′)); 4.06 (br. *s*, H–C(2′)); 4.12–4.17 (*m*, H–C(4), H′–C(6)); 4.33 (*t*, *J* ≈ 9.0, H–C(3)); 4.35 (*d*, *J* = 11.5), 4.36 (*d*, *J* = 11.7), 4.47 (*d*, *J* = 12.2, 3 PhC*H*); 4.49 (*s*, PhCH_2); 4.53 (*d*, *J* = 11.2, PhC*H*); 4.54 (*s*, PhCH_2); 4.56 (*d*, *J* = 11.2), 4.68 (*d*, *J* = 11.8, 2 PhC*H*); 4.69 (*d*, *J* = 3.7, H–C(1)); 4.71 (*d*, *J* = 12.2, PhC*H*); 4.78 (*s*, PhCH_2); 4.87 (*d*, *J* = 12.1, PhC*H*); 5.45 (*s*, NH); 7.16–7.40 (*m*, 35 arom. H). ^{13}C-NMR ($CDCl_3$, 75 MHz): 51.31 (*d*, C(5)); 55.15 (*q*, MeO); 69.06 (*d*); 68.93, 69.11 (2*t*, C(6), C(6′)); 70.28, 71.52, 72.25, 73.06, 73.38, 73.42, 75.23 (7*t*, 7 Ph*C*H$_2$); 78.61 (*d*); 79.55 (*d*); 80.26 (*d*); 80.50 (2*d*); 81.97 (*d*); 98.50 (*d*, C(1)); 127.54–128.80 (several *d*); 137.53–139.41 (several *s*); 148.93 (*s*, C(1′)). FAB-MS (3-NOBA): 999 (100, $[M + H]^+$), 967 (45), 91 (17).

Methyl 2,3,6-Tri-O-*acetyl-4*-O-*[(Z)-(2,3,4,6-tetra*-O-*acetyl-5-amino-5-deoxy*-D-*glucopyranosylidene)amino]-α*-D-*glucopyranoside* (**24**). A soln. of **23** (0.31 g, 0.31 mmol) in THF (1.5 ml) was added to a deep-blue soln. of Li (50 mg, 7.1 mmol) in condensed $EtNH_2$ (*ca.* 15 ml) at −60° within 4 min. The mixture was stirred at −60° for 15 min and treated with NH_4Cl (50 mg). After evaporation, the residue was dried, dissolved in pyridine (10 ml), and treated with Ac_2O (5 ml) at 0°. After 16 h at 21°, the mixture was taken to dryness, and the residue was dissolved in CH_2Cl_2 (25 ml) and washed with sat. aq. $NaHCO_3$ soln. (2 × 25 ml). Drying of the org. phase ($MgSO_4$), evaporation, and FC (hexane/AcOEt 6:4) afforded **24** (0.15 g, 73%). Colourless oil. R_f (hexane/AcOEt 1:1) 0.15. IR (CH_2Cl_2): 3392*w* (br.), 2999*w*, 2941*m*, 2843*w*, 1732*s*, 1657*s*, 1434*s*, 1372*s*, 1330*m*, 1206*s*, 1170*m*, 1129*m*, 1036*s*, 904*m*. ^{1}H-NMR ($CDCl_3$, 300 MHz): 2.02, 2.06, 2.07, 2.08, 2.09, 2.12, 2.13 (7*s*, 7 AcO); 3.38 (*s*, MeO); 3.59–3.64 (*m*, H–C(5′)); 3.96–4.10 (*m*, H–C(4), H–C(5), H–C(6′)); 4.23–4.32 (*m*, 2 H–C(6), H′–C(6′)); 4.82 (*dd*, *J* = 8.7, 3.4, H–C(2)); 4.89 (*d*, *J* = 3.0, H–C(1)); 4.98 (*dd*, *J* = 8.4, 6.2, H–C(4′)); 5.19 (*t*, *J* ≈ 6.2, H–C(3′)); 5.29 (*d*, *J* = 6.2, H–C(2′)); 5.32 (br. *s*, NH); 5.48 (*t*, *J* ≈ 8.7, H–C(3)). ^{13}C-NMR ($CDCl_3$, 75 MHz): 20.58, 20.63, 20.68, 20.73, 20.78, 20.84, 20.91 (7*q*, 7 Me); 52.31 (*d*, C(5)); 55.35 (*q*, MeO); 62.90, 63.07 (2*t*, C(6), C(6′)); 67.60 (*d*); 67.69 (*d*); 69.81 (*d*); 69.92 (*d*); 71.09 (*d*); 71.75 (*d*); 78.94 (*d*); 96.81 (*d*, C(1)); 147.74 (*s*, C(1′)); 169.03, 169.73, 169.76, 170.33, 170.57, 170.96, 171.25 (7*s*, 7 C=O). FAB-MS (3-NOBA): 663 (100, $[M + H]^+$), 631 (20).

Methyl 4-[(Z)-(5-Amino-5-deoxy-D-*glucopyranosylidene)amino]-α*-D-*glucopyranoside* (**6**). At 0°, a soln. of **24** (0.14 g, 0.21 mmol) in MeOH (5 ml) was treated dropwise with a freshly prepared 1N soln. of NaOMe in

MeOH (*ca.* 0.2 ml). The mixture was stirred at 5° for 8 h, neutralized by treatment with *Amberlite IR-120* (H^+ form), filtered, and evaporated. The crude product was purified by reversed-phase HPLC (*RP-18* silica gel, MeOH/H_2O 1:9 → 9:1) to give, after crystallization from MeOH, **6** (68 mg, 88%). Colourless crystals. R_f (AcOEt/MeOH/H_2O 4:2:1) 0.40. M.p. 128–129° (dec., MeOH/H_2O). $[\alpha]_D^{25} = +110.9$ ($c = 0.71$, MeOH). IR (KBr): 3425*s*, 3343*s*, 3310*s*, 2928*m*, 1662*s*, 1450*m*, 1405*w*, 1332*s*, 1109*s*, 935*s*, 906*m*. ^{1}H-NMR (CD_3OD, 500 MHz): 3.15 (*ddd*, $J = 9.2, 6.9, 2.9$, H–C(5′)); 3.38 (*dd*, 9.1, 8.5, H–C(4′)); 3.40 (*s*, MeO); 3.46 (*dd*, $J = 9.6$, 3.8, H–C(2)); 3.53 (*dd*, $J = 11.1, 7.1$, H–C(6′)); 3.55 (*t*, $J \approx 8.5$, H–C(3′)); 3.69–3.80 (*m*, H–C(3), H–C(5), 2 H–C(6)); 3.88 (*dd*, $J = 11.1, 2.9$, H′–C(6′)); 3.92 (*t*, $J \approx 9.2$, H–C(4)); 3.99 (*d*, $J = 8.4$, H–C(2′)); 4.67 (*d*, $J =$ 3.8, H–C(1)). ^{13}C-NMR (50 MHz, CD_3OD): 55.16 (*d*, C(5)); 58.34 (*q*, MeO); 62.08, 63.35 (2*t*, C(6), C(6′)); 70.40 (*d*); 70.81 (*d*); 71.48 (*d*); 72.33 (*d*); 73.35 (*d*); 76.65 (*d*); 80.16 (*d*); 100.71 (*d*, C(1)); 154.16 (*s*, C(1′)). FAB-MS (3-NOBA): 737 (4, $[2M + H]^+$), 391 (30), 369 (100, $[M + H]^+$), 337 (32). Anal. calc. for $C_{13}H_{24}N_2O_{10} \cdot$ ½ H_2O (377.33): C 41.38, H 6.68, N 7.42; found: C 41.20, H 6.51, N 7.63.

4. *Preparation of* **7**. *5-Amino-2,3,4,6-tetra*-O-*benzyl-5-deoxy-1-thio*-D-*galactono-1,5-lactam* (**26**). A soln. of **25** [37] (1.5 g, 2.8 mmol) in toluene (20 ml) was treated with *Lawesson*'s reagent (1.0 g, 2.5 mmol), heated at 80° for 20 min, and evaporated. FC (hexane/Et_2O 1:2) of the residue gave **26** (1.4 g, 88%). Colourless oil. R_f (hexane/AcOEt 4:1) 0.50. $[\alpha]_D^{25} = +106.5$ ($c = 1.0$, $CHCl_3$). IR ($CHCl_3$): 3356*w*, 3006*w*, 2870*w*, 1514*m*, 1454*m*, 1361*w*, 1316*m*, 1135*m*, 1102*s*, 1069*s*, 1028*m*. ^{1}H-NMR ($CDCl_3$, 200 MHz): 3.48–3.76 (*m*, H–C(5), 2 H–C(6)); 3.82 (*dd*, $J = 7.9, 2.1$, H–C(3)); 4.06 (*m*, H–C(4)); 4.44 (*d*, $J = 12.0$, PhC*H*); 4.48 (*d*, $J = 7.5$, H–C(2)); 4.50 (*d*, $J =$ 12.0), 4.56 (*d*, $J = 12.0$), 4.63 (*d*, $J = 12.4$), 4.76 (*d*, $J = 12.0$), 4.84 (*d*, $J = 11.6$), 4.87 (*d*, $J = 10.8$), 5.37 (*d*, $J = 10.4$, 7 PhC*H*); 7.23–7.49 (*m*, 20 arom. H); 8.17 (br. *s*, NH). ^{13}C-NMR ($CDCl_3$, 50 MHz): 57.25 (*d*, C(5)); 69.15 (*t*, C(6)); 72.07 (*d*); 72.67, 73.28, 73.39, 73.56 (4*t*, 4 Ph*C*H_2); 78.86 (*d*); 80.93 (*d*); 125.46–128.92 (several *d*); 137.20, 137.60, 137.84, 137.97 (4*s*); 201.61 (*s*, C(1)). FAB-MS (3-NOBA): 1105 (2, $[2M - H]^+$), 554 (100, $[M + H]^+$), 91 (21). Anal. calc. for $C_{34}H_{35}NO_4S$ (553.72): C 73.75, H 6.37, N 2.53; found: C 73.74, H 6.38, N 2.52.

*(*Z*)-5-Amino-2,3,4,6-tetra*-O-*benzyl-5-deoxy*-D-*galactonohydroximo-1,5-lactam* (**27**). A soln. of **26** (1.10 g, 2.0 mmol) in dry MeOH (20 ml) was treated with $NH_2OH \cdot HCl$ (0.45 g, 6.5 mmol) and $NaHCO_3$ (0.55 g, 6.5 mmol), and kept under reflux for 2 h. Evaporation and FC (hexane/AcOEt 3:1) gave **27** (0.98 g, 89%). Colourless oil. R_f (hexane/AcOEt 1:1) 0.45. $[\alpha]_D^{25} = +32.2$ ($c = 1.14$, $CHCl_3$). IR ($CHCl_3$): 3597*w*, 3397*w* (br.), 3006*w*, 2869*w*, 1731*w*, 1648*m*, 1496*w*, 1454*m*, 1368*w*, 1308*w*, 1252*w*, 1094*s*, 1027*m*. ^{1}H-NMR ($CDCl_3$, 300 MHz): 3.77 (*s*, H–C(5), 2 H–C(6)); 3.92 (*dd*, $J = 5.3$, 2.2, H–C(3)); 4.19 (*d*, $J = 5.3$, H–C(2)); 4.22–4.25 (*m*, H–C(4)); 4.49 (*d*, $J = 11.9$), 4.54 (*d*, $J = 11.8$), 4.56 (*d*, $J = 11.9$), 4.57 (*d*, $J = 11.8$), 4.59 (*d*, $J = 12.1$), 4.67 (*d*, $J = 12.1$), 4.68 (*d*, $J = 11.8$), 4.82 (*d*, $J = 11.5$, 8 PhC*H*); 5.80 (br. *s*, NH); 7.23–7.38 (*m*, 20 arom. H); 8.09 (br. *s*. OH). ^{13}C-NMR ($CDCl_3$, 75 MHz): 53.66 (*d*, C(5)); 71.46 (*t*, C(6)); 72.06, 72.38, 72.59 (3*t*, 3 Ph*C*H_2); 73.29 (*d*); 73.35 (*t*, Ph*C*H_2); 74.00 (*d*); 77.49 (*d*); 127.56–128.49 (several *d*); 138.11, 138.21, 138.32 (3*s*, 4 C); 150.10 (*s*, C(1)). FAB-MS (3-NOBA): 1105 (3, $[2M + H]^+$), 553 (100, $[M + H]^+$), 91 (27). Anal. calc. for $C_{34}H_{36}N_2O_5$ (552.67): C 73.89, H 6.57, N 5.07; found: C 73.85, H 6.56, N 4.86.

*(*Z*)-N*^{1}*,2,3,4,6-Penta*-O-*acetyl-5-amino-5-deoxy*-D-*galactonohydroximo-1,5-lactam* (**28**). At −60°, a soln. of **27** (0.75 g, 1.4 mmol) in THF (2 ml) was added to a deep-blue soln. of Li (0.10 g, 14.3 mmol) in condensed $EtNH_2$ (*ca.* 10 ml) within 2 min. The mixture was stirred at −60° for 10 min and treated with NH_4Cl (0.10 g). After evaporation, the residue was dried, dissolved in pyridine (10 ml), and treated with Ac_2O (5 ml) at 0°. After 1 h at 20°, the mixture was taken to dryness, and the residue was dissolved in CH_2Cl_2 (25 ml) and washed with sat. aq. NaHCO soln. (2 × 25 ml). Drying of the org. phase ($MgSO_4$), evaporation, and FC (hexane/AcOEt 1:2), followed by HPLC (hexane/AcOEt 2:3), afforded **28** (0.39 g, 69%). Colourless oil. R_f (hexane/AcOEt 1:2) 0.22. $[\alpha]_D^{25} = +31.0$ ($c = 1.0$, $CHCl_3$). IR (CH_2Cl_2): 3408*w*, 3068*w*, 2960*w*, 1753*s*, 1640*m*, 1438*m*, 1370*m*, 1218*s*, 1078*m*, 1047*m*, 1002*m*, 941*m*, 596*w*. ^{1}H-NMR ($CDCl_3$, 300 MHz): 1.98, 2.03, 2.06, 2.08, 2.11 (5*s*, 5 AcO); 3.83 (*m*, H–C(5)); 3.99 (*dd*, $J = 11.2$, 7.5, H–C(6)); 4.15 (*dd*, $J = 11.2$, 5.9, H′–C(6)); 5.26 (*dd*, $J = 9.3$, 2.8, H–C(3)); 5.55 (*m*, H–C(4)); 5.65 (*d*, $J = 9.3$, H–C(2)); 5.66 (*s*, NH). ^{13}C-NMR ($CDCl_3$, 75 MHz): 19.43, 20.27, 20.35, 20.43 (4*q*, 5 Me); 51.66 (*d*, C(5)); 62.97 (*t*, C(6)); 65.13 (*d*); 66.01 (*d*); 69.87 (*d*); 151.36 (*s*, C(1)); 169.00, 169.71, 169.81, 170.53 (4*s*, 5 C=O). FAB-MS (3-NOBA): 1207 (4, $[3M + H]^+$), 805 (40, $[2M + H]^+$), 747 (5), 403 (100, $[M + H]^+$), 360 (9). Anal. calc. for $C_{16}H_{22}N_2O_{10} \cdot$ ½ H_2O (411.34): C 46.72, H 5.64, N 6.81; found: C 46.74, H 5.40, N 6.71.

*(*Z*)-5-Amino-5-deoxy*-D-*galactonohydroximo-1,5-lactam* (**7**) [36]. At 5°, a soln. of **28** (160 mg, 0.4 mmol) in MeOH (5 ml) was treated with a sat. soln. of NH_3 in MeOH (2 ml), stirred at 5° for 4 h, and evaporated to give, after crystallization from MeOH, **7** (70 mg, 91%). Colourless crystals. R_f (AcOEt/MeOH/H_2O 4:2:1) 0.15. M.p. 149–151° (dec., MeOH/H_2O). IR (KBr): 3418*s*, 3344*s*, 3290*s*, 2993*m*, 2942*m*, 1663*s*, 1643*s*, 1456*m*, 1419*m*, 1338*s*, 1159*m*, 1096*s*, 1078*s*, 974*s*, 875*m*. ^{1}H-NMR (D_2O, 300 MHz): 3.33–3.37 (*m*, H–C(5)); 3.58 (*dd*, $J = 11.2$, 7.1, H–C(6)); 3.66 (*dd*, $J = 11.2$, 5.9, H′–C(6)); 3.70 (br. *d*, $J = 8.1$, H–C(3)); 4.04 (br. *s*, H–C(4)); 4.27

(br. *d*, *J* = 9.3, H–C(2)). ^{13}C-NMR (D_2O, 75 MHz): 53.58 (*d*, C(5)); 60.02 (*t*, C(6)); 65.00 (*d*); 66.37 (*d*); 71.58 (*d*); 156.80 (*s*, C(1)). Anal. calc. for $C_6H_{12}N_2O_5 \cdot ¼\ H_2O$ (196.66): C 36.64, H 6.36, N 14.24; found: C 36.89, H 6.41, N 14.05.

5. *Preparation of* **8**. *Methyl 4*-O-*[(*Z*)-(5-Amino-2,3,4,6-tetra*-O-*benzyl-5-deoxy*-D-*galactopyranosylidene)-amino]-2,3,6-tri*-O-*benzyl-β*-D-*glucopyranoside* (**29**). At 22°, a soln. of **26** (0.25 g, 0.45 mmol) and **14** (0.23 g, 0.48 mmol) in THF (10 ml, freshly distilled) was treated with Et(i-Pr)$_2$N (1 ml, 5.8 mmol) and Hg(OAc)$_2$ (0.23 g, 0.72 mmol), and kept for 8 h at 22°. After filtration through *Celite* and evaporation, the residue was dissolved in CH_2Cl_2 (25 ml) and washed with sat. aq. $NaHCO_3$ soln. (2 × 25 ml). Drying of the org. phase ($MgSO_4$), evaporation, and FC (hexane/AcOEt 9 : 1) afforded **29** (0.38 g), which was sufficiently pure (^{1}H-NMR) to be used for the next step. Colourless oil. R_f (hexane/AcOEt 4 : 1) 0.50. IR (CH_2Cl_2): 3089*w*, 3033*m*, 2910*m*, 2868*m*, 1654*m*, 1497*m*, 1454*m*, 1421*w*, 1390*m*, 1361*m*, 1310*m*, 1211*m*, 1070*s*, 1028*s*, 896*m*. ^{1}H-NMR ($CDCl_3$, 200 MHz): 3.45–3.47 (*m*, H–C(5)); 3.60 (*s*, MeO); 3.66–3.72 (*m*, H–C(2), H–C(5′), 2 H–C(6′)); 3.78–3.80 (*m*, H–C(3)); 3.81–3.91 (*m*, H–C(4), H–C(6), H–C(3′)); 4.07 (*d*, *J* = 8.3, H–C(2′)); 4.05–4.12 (*m*, H′–C(6)); 4.19 (*m*, H–C(4′)); 4.28 (*d*, *J* = 12.4, PhC*H*); 4.34 (*d*, *J* = 7.0, H–C(1)); 4.38 (*d*, *J* = 11.2), 4.46 (*d*, *J* = 11.7), 4.47 (*d*, *J* = 12.0, 3 PhC*H*); 4.54 (*s*, PhCH_2); 4.57 (*d*, *J* = 12.4, 2 PhC*H*); 4.59 (*d*, *J* = 11.6, 2 PhC*H*); 4.72 (*d*, *J* = 11.6, 2 PhC*H*); 4.79 (*d*, *J* = 11.6), 4.89 (*d*, *J* = 11.2, 2 PhC*H*); 5.63 (*s*, NH); 7.11–7.36 (*m*, 35 arom. H). ^{13}C-NMR ($CDCl_3$, 75 MHz): 53.84 (*d*, C(5′)); 57.17 (*q*, MeO); 69.55, 71.81 (2*t*, C(6), C(6′)); 71.85, 72.56, 72.83 (3*t*, 3 PhCH_2); 73.30 (*d*); 73.40, 73.58, 73.68, 73.74 (4*t*, 4 PhCH_2); 73.92 (*d*); 74.34 (*d*); 77.74 (*d*); 80.27 (*d*); 80.66 (*d*); 82.46 (*d*); 104.80 (*d*, C(1)); 127.45–128.81 (several *d*); 138.31–139.44 (several *s*); 149.55 (*s*, C(1′)). FAB-MS (3-NOBA): 999 (65, $[M+H]^+$), 967 (12), 91 (100).

Methyl 2,3,6-Tri-O-*acetyl-4*-O-*[(*Z*)-(2,3,4,6-tetra*-O-*acetyl-5-amino-5-deoxy*-D-*galactopyranosylidene)amino]-β*-D-*glucopyranoside* (**30**). At −60°, a soln. of **29** (0.31 g, 0.31 mmol) in THF (1 ml) was added to a deep-blue soln. of Li (50 mg, 7.1 mmol) in condensed $EtNH_2$ (*ca.* 15 ml) within 2 min. The mixture was stirred at −60° for 15 min and treated with NH_4Cl (50 mg). After evaporation, the residue was dried, dissolved in pyridine (10 ml), and treated with Ac_2O (5 ml) at 0°. After 3 h at 21°, the mixture was taken to dryness, and the residue was dissolved in CH_2Cl_2 (25 ml) and washed with sat. aq. $NaHCO_3$ soln. (2 × 25 ml). Drying of the org. phase ($MgSO_4$), evaporation, FC (hexane/AcOEt 2 : 1), and HPLC (hexane/AcOEt 1 : 1) afforded pure **30** (0.18 g, 88%). Colourless oil. R_f (hexane/AcOEt 1 : 1) 0.15. $[\alpha]_D^{25} = +7.7$ (*c* = 0.53, $CHCl_3$). IR (CH_2Cl_2): 3068*w*, 2960*w*, 1753*s*, 1647*m*, 1437*m*, 1370*s*, 1227*s*, 1172*m*, 1045*s*, 906*m*. ^{1}H-NMR ($CDCl_3$, 300 MHz): 2.03, 2.04, 2.05, 2.08, 2.10, 2.12, 2.15 (7*s*, 7 AcO); 3.49 (*s*, MeO); 3.71–3.79 (*m*, H–C(5), H–C(5′)); 3.95 (*dd*, 10.9, 7.8, H–C(6′)); 4.04 (*t*, *J* ≈ 9.7, H–C(4)); 4.18 (*dd*, *J* = 10.9, 5.3, H′–C(6′)); 4.24 (*dd*, *J* = 12.1, 5.6, H–C(6)); 4.38 (*d*, *J* = 8.1, H–C(1)); 4.43 (*dd*, *J* = 12.1, 2.2 H′–C(6)); 4.95 (*dd*, *J* = 10.0, 8.1, H–C(2)); 5.19 (*dd*, *J* = 9.3, 2.5, H–C(3′)); 5.28 (*t*, *J* ≈ 9.3, H–C(3)); 5.28 (*s*, NH); 5.56 (*m*, H–C(4′)); 5.65 (*d*, *J* = 9.3, H–C(2′)). ^{13}C-NMR ($CDCl_3$, 50 MHz): 20.59, 20.75 (2*q*, 7 Me); 51.66 (*d*, C(5′)); 56.84 (*q*, MeO); 62.90, 63.47 (2*t*, C(6), C(6′)); 65.09 (*d*); 66.26 (*d*); 70.20 (*d*); 71.44 (*d*); 72.26 (*d*); 72.36 (*d*); 78.74 (*d*); 101.53 (*d*, C(1)); 147.31 (*s*, C(1′)); 169.45–170.82 (several *s*, 7 C=O). FAB-MS (3-NOBA): 1347 (3, $[2M+H]^+$), 685 (22), 663 (100, $[M+H]^+$), 631 (12). Anal. calc. for $C_{27}H_{38}N_2O_{17}$ (662.60): C 48.94, H 5.78, N 4.23; found: C 48.96, H 5.90, N 4.20.

Methyl 4-O-*[(*Z*)-(5-Amino-5-deoxy*-D-*galactopyranosylidene)amino]-β*-D-*glucopyranoside* (**8**). At 0°, a soln. of **30** (0.11 g, 0.17 mmol) in MeOH (5 ml) was treated with a sat. soln. of NH_3 in MeOH (2 ml), stirred at 5° for 8 h, and evaporated to give, after crystallization from MeOH, **8** (59 mg, 94%). Colourless crystals. R_f (AcOEt/MeOH/H_2O 4 : 2 : 1) 0.10. M.p. 166–168° (dec., MeOH/H_2O). ^{1}H-NMR (CD_3OD, 500 MHz): 3.23 (*dd*, *J* = 8.7, 7.9, H–C(2)); 3.35 (*ddd*, *J* = 7.2, 5.3, 2.9, H–C(5′)); 3.52 (*s*, MeO); 3.54 (*ddd*, *J* = 9.4, 4.9, 2.3, H–C(5)); 3.67 (*dd*, *J* = 8.8, 2.6, H–C(3′)); 3.69–3.73 (*m*, 2 H–C(6′)); 3.74 (*t*, *J* ≈ 8.9, H–C(3)); 3.75 (*dd*, *J* = 12.5, 4.0, H–C(6)); 3.78 (*t*, *J* ≈ 9.3, H–C(4)); 3.82 (*dd*, *J* = 12.3, 2.2, H′–C(6)); 4.05 (*t*, *J* ≈ 2.7, H–C(4′)); 4.19 (*d*, *J* = 7.8, H–C(1)); 4.30 (*d*, *J* = 8.9, H–C(2′)). ^{13}C-NMR (CD_3OD, 75 MHz): 57.08 (*d*, C(5′)); 57.34 (*q*, MeO); 62.77, 63.73 (2*t*, C(6), C(6′)); 69.03 (*d*); 69.58 (*d*); 75.20 (*d*); 75.62 (2*d*); 76.51 (*d*); 81.48 (*d*); 105.68 (*d*, C(1)); 155.52 (*s*, C(1′)). FAB-MS (3-NOBA): 391 (44), 369 (100, $[M+H]^+$), 307 (22), 154 (25), 136 (22).

6. *Preparation of* **9**. *(*Z*)-5-Amino-2,3,4,6-tetra*-O-*benzyl-5-deoxy-1*-N-*(dodecyloxy)*-D-*gluconimido-1,5-lactam* (**33**). a) *From* **19** *and* **31**. A vigorously stirred mixture of **19** (0.43 g, 0.78 mmol), dodecyl bromide (**31**) (0.19 ml, 0.78 mmol), Et_4NBr (20 mg), in toluene (20 ml), and an aq. soln. of NaOH (1.3 g in 10 ml) was heated to reflux for 16 h. The layers were separated and the aq. layer was extracted with CH_2Cl_2 (2 × 15 ml). Drying of the combined org. layers ($MgSO_4$), evaporation, and FC (hexane/AcOEt 4 : 1) afforded **33** (0.38 g, 67%).

b) *From* **20** *and* **32**·HCl. A mixture of **20** (1.58 g, 2.85 mmol), **32**·HCl [38] (1.21 g, 5.10 mmol), and $NaHCO_3$ (0.80 g, 10.0 mmol) in MeOH (30 ml) was heated to reflux for 6 h. Evaporation and FC (hexane/

AcOEt 6:1) afforded **33** (1.50 g, 73%). Colourless oil. R_f (hexane/AcOEt 4:1) 0.80. IR (CH_2Cl_2): 3400*w*, 3088*m*, 3032*m*, 2930*s*, 2850*s*, 1650*m*, 1505*m*, 1453*s*, 1361*m*, 1326*m*, 1213*m*, 1158*m*, 1098*s*, 1050*s*, 1030*s*, 912*m*. ^{1}H-NMR ($CDCl_3$, 300 MHz): 0.90 (*t*, *J* = 6.9, Me); 1.27 (br. *s*, 18 H); 1.61–1.72 (*m*, 2 H); 3.51 (*dd*, *J* = 9.7, 6.8, H–C(6)); 3.53 (*dd*, *J* = 9.9, 4.3, H′–C(6)); 3.69–3.77 (*m*, H–C(4), H–C(5)); 3.94 (*dd*, *J* = 4.4, 2.5, H–C(3)); 4.03 (*t*, *J* = 6.8, CH_2O); 4.09 (br. *s*, H–C(2)); 4.37 (*d*, *J* = 11.5), 4.40 (*d*, *J* = 11.9), 4.50 (*d*, *J* ≈ 11.5), 4.52 (*d*, *J* ≈ 11.5), 4.55 (*d*, *J* = 12.1), 4.57 (*d*, *J* = 11.9), 4.66 (*d*, *J* = 11.5), 4.77 (*d*, *J* = 12.2, 8 PhC*H*); 5.47 (*s*, NH); 7.16–7.20 (*m*, 2 arom. H); 7.26–7.41 (*m*, 18 arom. H). ^{13}C-NMR ($CDCl_3$, 75 MHz): 14.03 (*q*, Me); 22.62, 26.00, 29.09 (3*t*); 29.30 (2*t*); 29.54 (2*t*); 29.60 (2*t*); 31.85 (*t*); 51.24 (*d*, C(5)); 69.26 (*t*, C(6)); 70.42, 71.70, 72.36, 73.06 (4*t*, 4 Ph*C*H$_2$); 73.58 (*t*, CH_2O); 74.34 (*d*); 80.60 (*d*); 82.26 (*d*); 127.72–128.57 (several *d*); 137.72, 137.98, 138.01, 138.08 (4*s*); 148.90 (*s*, C(1)).

(Z)-2,3,4,6-Tetra-O-*acetyl-5-amino-5-deoxy-1*-N-*(dodecyloxy)*-D-*gluconimido-1,5-lactam* (**34**). A soln. of **33** (0.22 g, 0.31 mmol) in THF (3.5 ml) was added to a deep-blue soln. of Li (50 mg, 7.1 mmol) in condensed $EtNH_2$ (*ca.* 35 ml) at −60° within 8 min. The mixture was stirred at −60° for 15 min and treated with NH_4Cl (50 mg). After evaporation, the residue was dried, dissolved in pyridine (10 ml), and treated with Ac_2O (5 ml) at 0°. After 8 h at 23°, the mixture was taken to dryness, and the residue was dissolved in CH_2Cl_2 (25 ml) and washed with sat. aq. $NaHCO_3$ soln. (2 × 25 ml). Drying of the org. phase ($MgSO_4$), evaporation, and FC (hexane/AcOEt 1:1) afforded **34** (0.13 g, 79%). Colourless oil. R_f (hexane/AcOEt 1:1) 0.80. IR (CH_2Cl_2): 3398*w*, 2928*m*, 2855*m*, 1752*s*, 1656*m*, 1466*w*, 1431*w*, 1370*m*, 1222*s*, 1044*m*, 907*w*. ^{1}H-NMR ($CDCl_3$, 300 MHz): 0.86 (*t*, *J* = 6.9, Me); 1.24 (br. *s*, 18 H); 1.57–1.75 (*m*, 2 H); 2.05, 2.06, 2.09, 2.10 (4*s*, 4 AcO); 3.68 (*dddd*, *J* = 9.3, 6.2, 3.1, 1.9, H–C(5)); 3.96 (*t*, *J* = 6.8, CH_2O); 4.40 (*dd*, *J* = 11.8, 6.2, H–C(6)); 4.28 (*dd*, *J* = 11.8, 2.8, H′–C(6)); 4.99 (*dd*, *J* = 9.6, 5.9, H–C(4)); 5.22 (*t*, *J* ≈ 5.6, H–C(3)); 5.36 (*d*, *J* = 5.3, H–C(2)); 5.39 (br. *s*, NH). ^{13}C-NMR ($CDCl_3$, 75 MHz): 14.13 (*q*, Me); 20.70 (*q*, 2 Me); 20.76, 20.84 (2*q*, 2 Me); 22.72, 26.02, 29.00 (3*t*); 29.40 (2*t*); 29.56 (*t*); 29.67 (2*t*); 29.72, 31.97 (2*t*); 51.95 (*d*, C(5)); 63.05 (*t*, C(6)); 68.26 (*d*); 70.41 (*d*); 72.45 (*d*); 74.20 (*t*, CH_2O); 146.20 (*s*, C(1)); 169.26, 169.65, 169.82, 171.10 (4*s*, 4 C=O). FAB-MS (3-NOBA): 1055 (6, $[2M-H]^+$), 529 (100, $[M+H]^+$).

(Z)-5-Amino-5-deoxy-1-N-*(dodecyloxy)*-D-*gluconimido-1,5-lactam* (**9**). At 0°, a soln. of **34** (0.12 g, 0.23 mmol) in MeOH (5 ml) was treated dropwise with a freshly prepared 1N soln. of NaOMe in MeOH (*ca.* 0.2 ml). The mixture was stirred at 22° for 8 h, neutralized by treatment with *Amberlite IR-120* (H^+-form), filtered, and evaporated to afford, after FC (AcOEt), **9** (80 mg, 97%). Colourless crystals. R_f (AcOEt/MeOH/H_2O 7:2:1) 0.75. M.p. 107.5–108° (dec., AcOEt/MeOH). $[\alpha]_D^{25} = +24.4$ (*c* = 0.66, MeOH). IR (KBr): 3425*s*, 3312*s*, 2990*m*, 2965*m*, 1663*s*, 1575*m*, 1453*m*, 1410*w*, 1322*s*, 1125*s*, 970*s*, 896*m*. ^{1}H-NMR (500 MHz, CD_3OD): 0.90 (*t*, *J* = 6.9, Me); 1.29 (br. *s*, 18 H); 1.61–1.66 (*m*, 2 H); 3.14 (*ddd*, *J* = 9.2, 7.5, 2.9, H–C(5)); 3.34 (*dd*, *J* = 9.2, 8.4, H–C(4)); 3.48 (*dd*, *J* = 11.0, 7.6, H–C(6)); 3.54 (*t*, *J* ≈ 8.3, H–C(3)); 3.91 (*dd*, *J* = 11.1, 2.9, H′–C(6)); 3.93 (10 lines, *J* = 6.7, CH_2O); 3.99 (*d*, *J* = 8.3, H–C(2)). ^{13}C-NMR (75 MHz, CD_3OD): 14.54 (*q*, Me); 23.85, 27.31, 30.22, 30.61, 30.79 (5*t*); 30.89 (3*t*); 30.94, 33.22 (2*t*); 58.81 (*d*, C(5)); 64.31 (*t*, C(6)); 71.12 (*d*); 71.83 (*d*); 74.49 (*t*, CH_2O); 77.69 (*d*); 154.26 (*s*, C(1)). FAB-MS (3-NOBA): 743 (18), 383 (71), 361 (100, $[M+H]^+$). Anal. calc. for $C_{18}H_{36}N_2O_5 \cdot \frac{1}{2}\,CH_3OH$ (376.49): C 59.02, H 10.17, N 7.44; found: C 58.83, H 10.17, N 7.53.

7. *Preparation of* **10**. cis-*2-Phenyl-5-[(trifluoromethyl)sulfonyloxy]-1,3-dioxane* (**36**). At −15°, Tf_2O (10.0 g, 5.8 ml, 38 mmol) was added dropwise within 25 min to a stirred suspension of cis-*2-phenyl-1,3-dioxan-5-ol* (**35**) [39] (3.4 g, 19 mmol), pyridine (3.0 ml, 36 mmol), and 3-Å molecular sieves (0.1 g) in CH_2Cl_2 (25 ml). The suspension was stirred at −15° for 2 h, poured into a cold 1M aq. HCl soln. (50 ml), and the org. layer was washed with H_2O (3 × 40 ml). Evaporation and FC (hexane/AcOEt 2:1) gave **36** (5.2 g, 88%), which was of sufficient purity for the next step. Colourless solid. R_f (hexane/AcOEt 1:1) 0.80. M.p. 35–36° (hexane/AcOEt). IR (CH_2Cl_2): 3030*w*, 2880*w*, 1520*w*, 1451*m*, 1408*s*, 1212*s*, 1145*s*, 1108*s*, 1079*s*, 1029*m*, 960*s*. ^{1}H-NMR ($CDCl_3$, 300 MHz): 4.23 (*dd*, *J* = 13.7, < 1.0, 2 H); 4.45 (*dd*, *J* = 13.7, 1.3, 2 H); 4.86 (br. *s*, H–C(5)); 5.57 (*s*, H–C(2)); 7.27–7.54 (*m*, 5 arom. H). ^{13}C-NMR ($CDCl_3$, 75 MHz): 68.95 (*t*, C(4), C(6)); 79.86 (*d*, C(5)); 101.67 (*d*, C(2)); 118.70 (*q*, ^1J(C,F) = 321, CF_3); 128.67 (2*d*); 129.75 (2*d*); 130.04 (*d*); 137.26 (*s*). ^{19}F-NMR ($CDCl_3$, 282 MHz): −74.99. FAB-MS (3-NOBA): 179 (70, $[M-CF_3SO_2]^+$), 105 (90), 91 (100).

trans-*2-Phenyl-5-(phthalimidooxy)-1,3-dioxane* (= *2-[(*trans-*2-Phenyl-1,3-dioxan-5-yl)oxy]-1*H-*isoindole-1,3-(2*H*)-dione*; **37**). A soln. of **36** (0.4 g, 1.2 mmol) and *N*-hydroxyphthalimide (0.24 g, 1.48 mmol) in DMPU (2 ml), and Et_3N (0.26 ml, 1.48 mmol) was stirred at 22°. After 20 h, the mixture was poured into H_2O (20 ml), and extracted with CH_2Cl_2 (4 × 25 ml). The org. layer was washed with a sat. aq. soln. of $NaHCO_3$ (3 × 15 ml), dried ($MgSO_4$), and evaporated to afford, after trituration with Et_2O, **37** (0.3 g, 77%). Colourless solid. R_f (hexane/AcOEt 1:1) 0.30. M.p. 172.5–173° (EtOH). IR (CH_2Cl_2): 3068*w*, 2952*w*, 2869*w*, 1792*m*, 1736*s*, 1469*m*, 1456*m*, 1394*m*, 1374*m*, 1222*m*, 1188*s*, 1158*m*, 1118*m*, 1100*s*, 1082*m*, 1026*s*, 1010*m*, 978*m*, 879*m*. ^{1}H-NMR ($CDCl_3$, 300 MHz): 3.97 (*t*, *J* ≈ 10.9, 2 H); 4.45–4.49 (*m*, H–C(5)); 4.58–4.60 (*m*, 2 H); 5.48 (*s*, H–C(2));

7.35–7.41 (*m*, 3 arom. H); 7.45–7.49 (*m*, 2 arom. H); 7.75–7.81 (*m*, 2 arom. H); 7.84–7.90 (*m*, 2 arom. H). ^{13}C-NMR ($CDCl_3$, 75 MHz): 68.47 (*t*, C(4), C(6)); 75.89 (*d*, C(5)); 101.50 (*d*, C(2)); 124.07 (2*d*); 126.40 (2*d*); 128.59 (2*d*); 128.97 (2*s*); 129.40 (*d*); 135.06 (2*d*); 137.39 (*s*); 163.93 (*s*, 2 C=O). FAB-MS (3-NOBA): 651 (4, $[2M+1]^+$), 326 (100, $[M+1]^+$), 220 (35). Anal. calc. for $C_{18}H_{15}NO_5$ (325.32): C 66.46, H 4.65, N 4.31; found: C 66.22, H 4.77, N 4.31.

trans-*5-Aminooxy-2-phenyl-1,3-dioxane* (= O-*(*trans-*2-Phenyl-1,3-dioxan-5-yl)hydroxylamine*; **38**). A soln. of **37** (0.2 g, 0.6 mmol) in EtOH (5 ml) and hydrazine hydrate (80%, 1 ml) was kept under reflux for 2 h. Concentration to *ca.* 50 ml gave a colourless solid, which was removed by filtration. After evaporation to dryness the residue was purified by FC (CH_2Cl_2) to afford **38** (0.18 g, 75%). Colourless oil. R_f (hexane/AcOEt 1:4) 0.80. IR (CH_2Cl_2): 3331*w*, 3038*m*, 2982*m*, 2924*m*, 2862*m*, 2763*m*, 1674*w*, 1606*w*, 1589*w*, 1470*m*, 1456*m*, 1388*m*, 1316*m*, 1214*m*, 1156*m*, 1098*s*, 1077*s*, 1037*s*, 977*m*, 905*m*. ^{1}H-NMR ($CDCl_3$, 300 MHz): 3.63 (*t*, $J\approx10.4$, 2 H); 3.95–3.99 (*m*, H–C(5)); 4.46 (*dd*, $J=10.5, 5.0$, 2 H); 5.41 (*s*, H–C(2), NH_2); 7.36–7.42 (*m*, 3 arom. H); 7.49–7.52 (*m*, 2 arom. H). ^{13}C-NMR ($CDCl_3$, 75 MHz): 69.29 (*t*, C(4), C(6)); 72.06 (*d*, C(5)); 101.41 (*d*, C(2)); 126.42 (2*d*); 128.57 (2*d*); 129.23 (*d*); 137.99 (*s*). FAB-MS (3-NOBA): 236 (100), 196 (85, $[M+H]^+$), 130 (80, $[M-HNO]^+$), 105 (47), 91 (40).

*(*Z*)-5-Amino-2,3,4,6-tetra-*O*-benzyl-5-deoxy-1-*N*-[(*trans*-2-phenyl-1,3-dioxan-5-yl)oxy]-*D*-gluconimido-1,5-lactam* (**39**). At 21°, a soln. of **20** (0.97 g, 1.8 mmol) and **38** (0.34 g, 1.75 mmol) in THF (5 ml, freshly distilled) was treated with $Et(i\text{-}Pr)_2N$ (0.90 ml, 5.30 mmol) and $Hg(OAc)_2$ (0.84 g, 2.64 mmol), and stirred for 16 h at 21°. After filtration through *Celite* and evaporation, the residue was dissolved in CH_2Cl_2 (100 ml) and washed with sat. aq. $NaHCO_3$ soln. (2 × 25 ml). Drying of the org. phase ($MgSO_4$), evaporation, and FC (hexane/AcOEt 9:1) afforded **39** (1.01 g, 81%), which was sufficiently pure (^{1}H-NMR) to be used for the next step. Colourless oil. R_f (hexane/AcOEt 1:1) 0.75. IR (CH_2Cl_2): 3420*w*, 3085*w*, 3053*m*, 2912*m*, 2886*m*, 1650*w*, 1450*s*, 1362*m*, 1210*m*, 1155*m*, 1088*s*, 1050*s*, 914*m*. ^{1}H-NMR ($CDCl_3$, 300 MHz): 3.48 (*dd*, $J=10.2, 7.1$, H–C(6)); 3.49 (*dd*, $J=10.3, 3.7$, H′–C(6)); 3.69–3.79 (*m*, H–C(4), H–C(5), H–C(4′), H–C(6′)); 3.92 (*dd*, $J=4.4, 2.8$, H–C(3)); 4.04 (br. *s*, H–C(2)); 4.38–4.59 (*m*, 9 H); 4.62 (*d*, $J=11.9$), 4.75 (*d*, $J=11.8$, 2 PhC*H*); 5.36 (*s*, NH); 5.45 (*s*, H–C(2′)); 7.17–7.22 (*m*, 2 arom. H); 7.24–7.43 (*m*, 21 arom. H); 7.50–7.55 (*m*, 2 arom. H). ^{13}C-NMR ($CDCl_3$, 50 MHz): 50.58 (*d*, C(5)); 69.57, 69.92, 70.18 (3*t*, C(6), C(4′), C(6′)); 70.21 (*d*, C(5′)); 70.87, 72.08, 72.62, 73.32 (4*t*, 4 Ph*C*H$_2$); 74.02 (*d*); 80.52 (*d*); 82.11 (*d*); 101.63 (*d*, C(2′)); 126.49–129.28 (several *d*); 137.79 (*s*); 137.91 (2*s*); 138.07 (2*s*); 150.10 (*s*, C(1)). FAB-MS (3-NOBA): 715 (100, $[M+H]^+$), 91 (45).

*(*Z*)-2,3,4,6-Tetra-*O*-acetyl-5-amino-5-deoxy-1-*N*-[2-acetoxy-1-(acetoxymethyl)ethoxy]-*D*-gluconimido-1,5-lactam* (**40**). A soln. of **39** (0.20 g, 0.28 mmol) in THF (1.5 ml) was added to a deep-blue soln. of Li (50 mg, 7.1 mmol) in condensed $EtNH_2$ (*ca.* 15 ml) at −78° within 4 min. The mixture was stirred at −78° for 15 min and treated with NH_4Cl (50 mg). After evaporation, the residue was dried, dissolved in pyridine (10 ml), and treated with Ac_2O (5 ml) at 0°. After 16 h at 23°, the mixture was taken to dryness, and the residue was dissolved in CH_2Cl_2 (25 ml) and washed with sat. aq. $NaHCO_3$ soln. (2 × 25 ml). Drying of the org. phase ($MgSO_4$), evaporation FC (hexane/AcOEt 1:1), and HPLC (hexane/AcOEt 1:1) afforded **40** (0.11 g, 79%). Colourless oil. R_f (hexane/AcOEt 1:1) 0.10. IR (CH_2Cl_2): 3380*w* (br.), 3008*w*, 2940*m*, 2866*w*, 1730*s*, 1657*s*, 1430*s*, 1369*m*, 1207*s*, 1153*m*, 1129*m*, 1037*s*, 912*m*. ^{1}H-NMR ($CDCl_3$, 300 MHz): 2.05, 2.06, 2.07, 2.10, 2.11, 2.12 (6*s*, 6 AcO); 3.67 (*dddd*, $J=9.6, 6.2, 2.8, 1.6$, H–C(5)); 4.04 (*dd*, $J=12.2, 6.3$, H–C(6)); 4.19–4.29 (*m*, H–C(6′), 2 AcOC*H*$_2$); 4.33–4.39 (*m*, H–C(1′)); 5.02 (*dd*, $J=9.6, 6.5$, H–C(4)); 5.24 (*t*, $J\approx6.2$, H–C(3)); 5.37 (*d*, $J=5.9$, H–C(2)); 5.41 (br. *s*, NH). ^{13}C-NMR ($CDCl_3$, 75 MHz): 20.72, 20.75, 20.76, 20.82, 20.91, 20.98 (6*q*, 6 Me); 52.31 (*d*, C(5)); 62.53 (*t*, 2 AcO*C*H$_2$); 63.01 (*t*, C(6)); 67.92 (*d*); 70.11 (*d*); 72.24 (*d*); 78.50 (*d*, C(1′)); 147.78 (*s*, C(1)); 169.27, 169.69, 169.81, 171.02, 171.10, 171.15 (6*s*, 6 C=O). FAB-MS (3-NOBA): 519 (100, $[M+H]^+$).

*(*Z*)-5-Amino-5-deoxy-1-*N*-[2-hydroxy-1-(hydroxymethyl)ethoxy]-*D*-gluconimido-1,5-lactam* (**10**). At 0°, a soln. of **40** (0.10 g, 0.19 mmol) in MeOH (5 ml) was treated dropwise with a freshly prepared 1N soln. of NaOMe in MeOH (*ca.* 0.1 ml). The mixture was stirred at 23° for 1 h, neutralized by treatment with *Amberlite IR-120* (H^+ form), filtered, and evaporated. The crude product was purified by reversed-phase HPLC (*RP-18* silica gel, MeOH/H_2O 1:9 → 9:1) to afford, after lyophilization, **10** (50 mg, 97%). Colourless solid. R_f (AcOEt/MeOH/H_2O 4:2:1) 0.65. IR (KBr): 3423*s*, 3330*s*, 3295*s*, 2997*m*, 2951*m*, 1663*s*, 1453*m*, 1384*s*, 1093*s*, 966*s*. ^{1}H-NMR (CD_3OD, 500 MHz): 3.15 (*ddd*, $J=9.1, 6.4, 2.9$, H–C(5)); 3.42 (*t*, $J\approx8.5$, H–C(4)); 3.55 (*t*, $J\approx8.4$, H–C(3)); 3.57 (*dd*, $J=11.2, 6.3$, H–C(6)); 3.73 (*d*, $J=5.0$, CH_2O); 3.74 (*d*, $J=5.0$, CH_2O); 3.86 (*dd*, $J=11.2, 2.9$, H′–C(6)); 4.00 (*d*, $J=8.3$, H–C(2)); 4.01 (*quint.*, $J\approx5.0$, $(HOCH_2)_2CH$). ^{13}C-NMR (50 MHz, CD_3OD): 56.11 (*d*, C(5)); 59.32 (*t*, 2 CH_2O); 60.85 (*t*, C(6)); 68.05 (*d*); 68.50 (*d*); 74.24 (*d*); 81.45 (*d*, $(HOCH_2)_2CH$); 151.91 (*s*, C(1)). FAB-MS (3-NOBA): 329 (45), 307 (95), 289 (100), 267 (98, $[M+H]^+$), 176 (30), 154 (75), 137 (60).

8. *Inhibition Studies.* a) *Inhibition of Sweet-Almond β-Glucosidases.* The IC_{50} value was determined at 37°, using commercial sweet-almond-β-glucosidases, a 0.08M KH_2PO_4/K_2HPO_4 buffer (pH 6.8), and 4-nitrophenyl β-

D-glucopyranoside (1.2 mM) as substrate. Measurements were started by addition of the enzyme. The increase of absorption per min at 400 nm was taken as velocity for the hydrolysis of the substrate. The increase was linear during all measurements (3 min).

b) *Inhibition of* Caldocellum saccharolyticum *β-Glucosidase*. Similarly as described in *a*, using commercial *Caldocellum saccharolyticum* β-glucosidase. The IC_{50} value was determined at 55°.

c) *Inhibition of Brewer's Yeast α-Glucosidase*. Similarly as described in *a* using commercial brewer's yeast α-glucosidase and 4-nitrophenyl α-D-glucopyranoside (1.2 mM) as substrate.

d) *Inhibition of Bovine β-Galactosidase*. Similarly as described in *a* using commercial bovine β-galactosidase, a 0.05M NaH_2PO_4/Na_2HPO_4 buffer (pH 7.0), 0.1% BSA (bovine serum albumin), 1 mM $MgCl_2$, and 4-nitrophenyl β-D-galactopyranoside (0.24 mM) as substrate.

e) *Inhibition of* E. coli *β-Galactosidase*. The K_i value was determined at 30°, using commercial *E. coli* β-D-galactosidase, a 0.2M KH_2PO_4/K_2HPO_4 buffer (pH 6.8), 1 mM $MgCl_2$, and 4-nitrophenyl β-D-galactopyranoside (0.1 – 1.0 mM) as substrate. Rates were measured at a series of substrate concentrations (typically 7 concentrations) which bracket the K_M value in the presence of a range of inhibitor concentrations (typically 5 concentrations) which bracket the K_i value ultimately determined.

f) *Inhibition of Coffee Beans α-Galactosidase*. Similarly as described in *e* using commercial coffee beans α-galactosidase, a 0.1M NaH_2PO_4/Na_2HPO_4 buffer (pH 6.0), and 4-nitrophenyl α-D-galactopyranoside (0.1 – 1.2 mM) as substrate.

REFERENCES

[1] B. Ganem, G. Papandreou, *J. Am. Chem. Soc.* **1991**, *113*, 8984.
[2] R. Hoos, A. B. Naughton, W. Thiel, A. Vasella, W. Weber, K. Rupitz, S. G. Withers, *Helv. Chim. Acta* **1993**, *76*, 2666.
[3] G. A. Levvy, S. M. Snaith, *Adv. Enzymol. Relat. Areas Mol. Biol*. **1972**, *36*, 151.
[4] M. P. Dale, H. E. Ensley, K. Kern, K. A. R. Sastry, L. D. Byers, *Biochemistry* **1985**, *24*, 3530.
[5] P. Ermert, A. Vasella, *Helv. Chim. Acta* **1991**, *74*, 2043.
[6] S. G. Whithers, K. Rupitz, D. Trimbur, R. A. J. Warren, *Biochemistry* **1992**, *31*, 9979.
[7] R. Hoos, A. Vasella, K. Rupitz, S. G. Withers, *Carbohydr. Res.* **1997**, *298*, 291.
[8] D. Beer, A. Vasella, *Helv. Chim. Acta* **1986**, *69*, 267.
[9] M. Therisod, H. Therisod, A. Lubineau, *Biorg. Med. Chem. Lett*. **1995**, *5*, 2055.
[10] S. Knapp, A. Purandare, K. Rupitz, S. G. Withers, *J. Am. Chem. Soc*. **1994**, *116*, 7461.
[11] Y. Bleriot, T. Dintinger, N. Guillo, C. Tellier, *Tetrahedron Lett*. **1995**, *36*, 5175.
[12] W. Dong, T. Jespersen, M. Bols, T. Skrydstrup, M. R. Sierks, *Biochemistry* **1996**, *35*, 2788.
[13] K. Krähenbühl, S. Picasso, P. Vogel, *Bioorg. Med. Chem. Lett.* **1997**, *7*, 893.
[14] B. A. Johns, Y. T. Pan, A. D. Elbein, C. R. Johnson, *J. Am. Chem. Soc*. **1997**, *119*, 4856.
[15] S. Cottaz, J. S. Brimacombe, M. A. J. Ferguson, *Carbohydr. Res.* **1993**, *247*, 341.
[16] S. Knapp, Y. H. Choe, E. Reilly, *Tetrahedron Lett*. **1993**, *34*, 4443.
[17] P. S. Liu, *J. Org. Chem.* **1987**, *52*, 4717.
[18] C. R. Johnson, M. W. Miller, A. Golebiowski, H. Sundram, M. B. Ksebati, *Tetrahedron Lett*. **1994**, *35*, 8991.
[19] O. M. Saavedra, O. R. Martin, *J. Org. Chem.* **1996**, *61*, 6987.
[20] K. Suzuki, H. Hashimoto, *Tetrahedron Lett*. **1994**, *35*, 4119.
[21] J. Lehmann, B. Rob, H.-A. Wagenknecht, *Carbohydr. Res.* **1995**, *278*, 167.
[22] K. Suzuki, T. Fujii, K. Sato, H. Hashimoto, *Tetrahedron Lett*. **1996**, *37*, 5921.
[23] A. Baudat, P. Vogel, *J. Org. Chem.* **1997**, *62*, 6252.
[24] E. C. Rodriguez, K. A. Winans, D. S. King, C. R. Bertozzi, *J. Am. Chem. Soc.* **1997**, *119*, 9905.
[25] S. E. Cervigni, P. Dumy, M. Mutter, *Angew. Chem.* **1996**, *108*, 1325.
[26] T. Granier, N. Panday, A. Vasella, *Helv. Chim. Acta* **1997**, *80*, 979.
[27] P. J. Garegg, H. Hultberg, S. Wallin, *Carbohydr. Res.* **1982**, *108*, 97.
[28] C. Grandjean, G. Lukacs, *J. Carbohydr. Chem.* **1996**, *15*, 831.
[29] H. Shinozuki, N. Yoshida, M. Tajima, *Chem. Lett*. **1980**, 869.
[30] E. E. v. Tamelen, P. McCurry, U. Huber, *Proc. Natl. Acad. Sci. U.S.A.* **1971**, *68*, 1294.
[31] E. J. Reist, V. J. Bartuska, L. Goodman, *J. Org. Chem.* **1964**, *29*, 3725.
[32] J. M. J. Tronchet, D. Schwarzenbach, E. Winter-Mihaly, C. Diamantides, U. Likic, G. Galland-Barrera, C. Jorand, K. D. Pallie, J. Ojha-Poncet, J. Rupp, G. Moret, M. Geoffrey, *Helv. Chim. Acta* **1982**, *65*, 1404.
[33] E. M. Nashed, E. Grochowski, E. Czyzewska, *Carbohydr. Res.* **1990**, *196*, 184.

[34] E. L. Schumann, R. V. Heinzelman, M. E. Greig, W. Veldkamp. *J. Med. Chem.* **1964**, *7*, 329.
[35] L. A. Reed III, J. T. Huang, M. McGregor, L. Goodman, *Carbohydr. Res.* **1994**, *254*, 133.
[36] G. Papandreou, M. K. Tong, B. Ganem, *J. Am. Chem. Soc.* **1993**, *115*, 11682.
[37] H. S. Overkleeft, J. v. Wiltenburg, U. K. Pandit, *Tetrahedron* **1994**, *50*, 4215.
[38] R. G. Laughlin, *J. Am. Chem. Soc.* **1973**, *95*, 3295.
[39] P. H. J. Carlsen, K. Sørbye, T. Ulven, K. Aasbø, *Acta Chem. Scand.* **1996**, *50*, 185.
[40] R. Aneja, A. P. Davies, *J. Chem. Soc., Perkin Trans. 1* **1974**, 141.
[41] D. Barford, J. W. R. Schwabe, N. G. Oikonomakos, K. R. Acharya, J. Hajdu, A. C. Papageorgiou, J. L. Martin, J. C. A. Knott, A. Vasella, L. N. Johnson, *Biochemistry* **1988**, *27*, 6733.
[42] A. C. Papageorgiou, N. G. Oikonomakos, D. L. Leonidas, B. Bernet, D. Beer, A. Vasella, *Biochem. J.* **1991**, *274*, 329.
[43] S. He, S. G. Wither, *J. Biol. Chem.* **1997**, *272*, 24864.
[44] T. Barrett, C. G. Suresh, S. P. Tolley, E. J. Dodson, M. A. Hughes, *Structure* **1995**, *3*, 951.
[45] D. R. Love, R. Fisher, P. L. Bergquist, *Mol. Gen. Genet*. **1988**, *213*, 84.
[46] P. Greenberg, A. H. Merril, D. C. Liotta, G. A. Grabowski, *Biochim. Biophys. Acta* **1990**, *1039*, 12.
[47] G. Legler, M.-T. Finken, S. Felsch, *Carbohydr. Res.* **1996**, *292*, 91.
[48] G. Legler, M.-T. Finken, *Carbohydr. Res.* **1996**, *292*, 103.

Received July 2, 1998