106. Synthesis *via* a Carbohydrate-Derived *Münchnone* of Pyrrolopyridines (Indolizines) and Imidazopyridines, and Their Evaluation as Inhibitors of β-D-Glucosidases

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Dedicated to *Oscar Jeger* on the occasion of his 80th birthday

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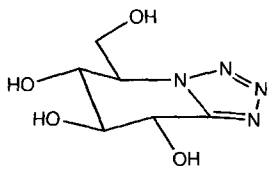
In the presence of activating agents, the *N*-acylglycine **8** reacts with electrophilic alkynes *via* the *münchnone* **9** to the pyrrolopyridines (= indolizines) **10**, **18**, and **19** (*Scheme 1*). Depending on the nature of the activating agent and the reaction temperature, the formation of the pyrroles was accompanied by partial epimerization to the *manno*-configurated epimers **16** and **17**. The *gluco*-configurated pyrrolopyridine **10** was deprotected to **12**. Silylation of **12**, followed by reduction and desilylation, gave the hexol **15**. Cycloaddition of **9** to 4-toluenesulfonyl cyanide yielded 53% of the imidazole **23**, while cycloaddition to phenyl cyanate gave the phenoxyimidazole **28** in low yields only (*Scheme 2*). As expected, the deprotected pyrroles **12**, **15**, **20**, and **21** are weak inhibitors of retaining β-glucosidases, while the deprotected imidazole **24** derived from **23** proved a good inhibitor of sweet-almond β-glucosidases and a powerful inhibitor of *Caldocellum saccharolyticum* β-glucosidase.

Introduction. – In 1991, we showed that the glucopyranose-related tetrazolopyridine **1** inhibits β-D-glucosidases [1], and *Streith* and co-workers described a D-arabinopyranose and an L-xylofuranose-related imidazopyridine as potential glycosidase inhibitors [2]. Soon afterwards, the groups of *Aoyagi*, *Takeuchi* and co-workers [3] [4] reported that *Nagstatin* (**2**), an *N*-acetylgalactosamine-related, substituted tetrahydroimidazopyridine from a *Streptomyces amakusaensis* strain, is a very strong inhibitor of an *N*-acetyl-β-glucosaminidase. Since then, a number of pyrrolopyridines [5] and azolopyridines [6–10] have been prepared, tested as glycosidase inhibitors, and used as probes for the mechanism of glycosidases [11–13]. The synthesis of these pyrrolopyridines and imidazopyridines, and of some of the triazolopyridines are based on an intramolecular *N*-alkylation of a pyrrole or azole.

General strategies for the construction of these and related heterocycles from an easily available, advanced, common intermediate should simplify their synthesis, and the gluconolactam **3** [13–15] appeared to qualify for this purpose. It has already proved useful in the synthesis of the triazole **4** and the imidazole **5** and its *manno*-configurated isomer. These heterocycles were prepared from **3** by annulation of hydrazinecarbaldehyde and aminoacetaldehyde dimethyl acetal [13]. Another general method for the synthesis of five-membered heterocycles is based on the 1,3-dipolar cycloaddition [16–19].

[1]) Taken in part from the Diploma Thesis of *F. G.*, ETH-Zürich, 1995.
[2]) Taken in part from the Diploma Thesis of *L. H.* ETH-Zürich, 1996.



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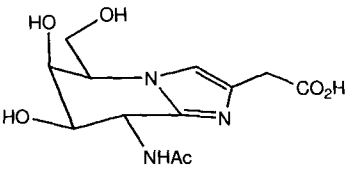

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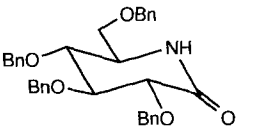

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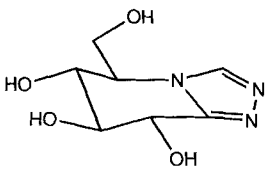

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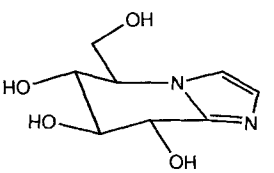

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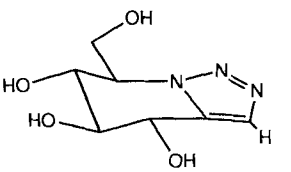

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Indeed, the intramolecular 1,3-dipolar cycloaddition of an azidonitrile [1][3]) and an azidoalkyne [11] has led to the tetrazole **1** and the triazole **6**, respectively. The intermolecular cycloaddition of 1,3-dipoles derived from the common intermediate **3** should lead to an advantageous synthesis of five-membered heterocycles.

We report the synthesis of the tetrahydroindolizines **12**, **15**, **20**, **21**, and of the tetrahydroimidazopyridine **24** by cycloaddition of the *münchnone* (oxazolium-5-olate) **9** to alkynes and nitriles[4]).

Synthesis. – The *münchnone* [23–25] **9** was generated from the *N*-acylglycine **8** in the presence of dimethyl acetylenedicarboxylate (DMAD) or methyl propiolate (*Scheme 1*). The *N*-acylglycine **8** was synthesized in a yield of 97% by *N*-alkylation of the lactam **3** with ethyl iodoacetate (DMF/NaH; → **7**), followed by hydrolysis.

The *N*-acylglycine **8** reacted with Ac_2O or methanesulfonyl chloride (MsCl)/Et_3N (*cf.* [26–29]) and 5 equiv. of DMAD to yield *ca.* 50% of the disubstituted pyrrole **10**, while treatment of a solution of **8** in DMAD and Ac_2O raised the yield to 95%.

Attempts to transform **10** into the fully deprotected indolizinetrimethanol **15** *via* **11** failed. Transfer hydrogenation of the indolizinedimethanol **11**, obtained by reduction of **10** with $LiAlH_4$, led to a complex mixture. However, the desired indolizine **15** was readily prepared from the tetrahydroxy diester **12** by silylation, (→ **13**) reduction with $LiAlH_4$, (→ **14**), and desilylation.

The result of the cycloaddition of **9** to methyl propiolate depended on the temperature and the nature of the condensing agent. Treating **8** at 80° with Ac_2O and methyl propiolate led to a mixture of the *gluco*-configurated regioisomeric pyrroles **18** and **19**, and of their *manno*-isomers **16** and **17** (1:1:1:1; 31%). Replacing Ac_2O by *N*-[3-(dimethylamino)propyl]-*N'*-ethylcarbodiimide hydrochloride (EDC)[5]) [28] [30] [31] and perform-

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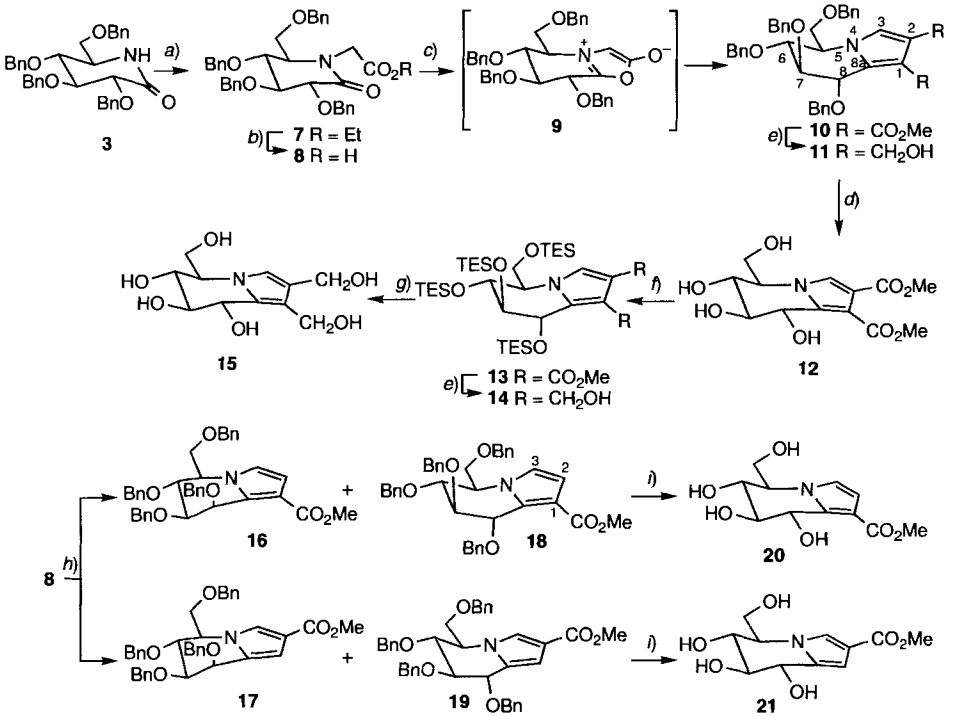
[3]) A shorter route to **1** involves the reaction of **3** with triflic anhydride and NaN_3 [20].

[4]) To the best of our knowledge, carbohydrate-derived *münchnones* have not been reported, while the cycloaddition of *münchnones* and the (diastereoselective) cycloaddition of a *thioisomünchnone* to carbohydrate derivatives have been studied [21] [22].

[5]) No cycloaddition products were formed when Ac_2O was replaced by MsCl/Et_3N.

Scheme 1



a) ICH_2CO_2Et, NaH, DMF; 97%. *b*) LiOH, THF, H_2O; > 99%. *c*) Dimethyl acetylenedicarboxylate (DMAD), Ac_2O; 95%. *d*) **10**, $Pd(OH)_2$, HCO_2NH_4, EtOH; 79%. *e*) $LiAlH_4$, THF; **11**: 56%, **14**: 79%. *f*) Triethylsilyl trifluoromethanesulfonate (CF_3SO_3TES), pyridine; 93%. *g*) $Bu_4NF \cdot 3\,H_2O$, THF; 83%. *h*) Methyl propiolate, Ac_2O; **16**/**17**/**18**/**19** 1:1:1:1 31%; *or* methyl propiolate, *N*-[3-(dimethylamino)propyl]-*N'*-ethylcarbodiimide hydrochloride (EDC); **18**/**19** 4:3 77%. *i*) $Pd(OH)_2$, HCO_2NH_4, EtOH; 75%

ing the reaction at 25° led exclusively to the *gluco*-configurated pyrroles **18** and **19** (4:3; 77%), while raising the temperature from 25 to 90° yielded a mixture of the *gluco*- and only traces of the *manno*-isomers **16**–**19** (2:2:48:48; 68%). As the *gluco*-pyrroles **18** and **19** were epimerized neither under the reaction conditions nor after the addition of AcOH, epimerization must have taken place at the stage of the intermediate *münchnone* **9**. Transfer hydrogenation ($Pd(OH)_2$, $HCOONH_4$, EtOH) [32] [33] of the diester **10** and of the regioisomeric monoesters **18** and **19** led in *ca.* 75% to the tetrahydroxy esters **12**, **20**, and **21**, respectively.

The pyrrole **10** is characterized in the UV spectrum by λ_{max} 258 nm ($\log \varepsilon = 3.9$) and in the ^{13}C-NMR spectrum by two $^{13}C{=}O$ *s* at 164.15 and 164.95 ppm. The structure of the regioisomeric *gluco*- and *manno*-configurated pairs of monoesters **18**/**19** and **16**/**17** was assigned on the basis of the difference of the J(H,H) and chemical-shift values for the H-atoms of the pyrrolo moiety (**16** and **18**: $J(2,3) = 3$ Hz, δ(H–C(2)) = 6.6 ppm, δ(H–C(3)) = 6.8 ppm; **17** and **19**: $J(1,3) = 1.7$ Hz, δ(H–C(1)) ≈ 6.6 ppm, δ(H–C(3)) ≈ 7.5 ppm; systematic numbering (see **10**)). The *gluco*-configuration of **18** and **19** was assigned on the basis of the X-ray analysis of the deprotected regioisomers **20** (*Fig. 1*) and – with a poorer resolution – **21** (*Fig. 2*)[6]). Comparison of the δ values for

[6]) Crystallographic data have been deposited at the *Cambridge Crystallographic Data Center*, 12 Union Road, Cambridge CB2 1EW, England.

10, **18**, and **19** on the one hand, and for **16** and **17**, on the other hand, provide further evidence for the *gluco*-configuration of **10** and the *manno*-configuration of **16** and **17**, as the chemical shift of H–C(6) and H–C(7) reflect the influence of one, or two *cis*-oriented BnO groups. A more or less flattened $^{5,8}B$ conformation is adopted by the *gluco*-configurated **10**, **11**, **13**, **14**, and **18**, minimizing the 1,5 interaction between the substituents at O–C(8) and C(1), while the *manno*-configurated derivatives **16** and **17** adopt conformations between $B_{5,8}$ and ^{7}E [34]. The 2-substituted *gluco*-configurated protected monoester **19** possesses a E_6 conformation and the corresponding tetrahydroxy ester **21** a $^{7}H_6$ conformation both in the solid state and in D_2O. The 1-substituted analogues **12**, **15**, and **20** adopt conformations between $^{7}H_6$ and E_6. The tetrahydroxy ester **20** possesses a $^{7}H_6$ conformation in the solid state (*Fig. 1*); the destabilizing O–C(8)/COOMe 1,5-interaction in **18** is replaced by a H-bond between HO–C(8) and the COOMe group.

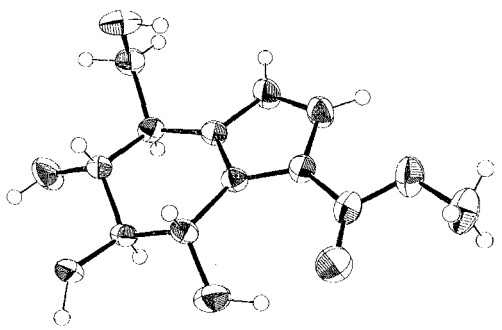


Fig. 1. *X-Ray analysis of the tetrahydroindolizine* **20**

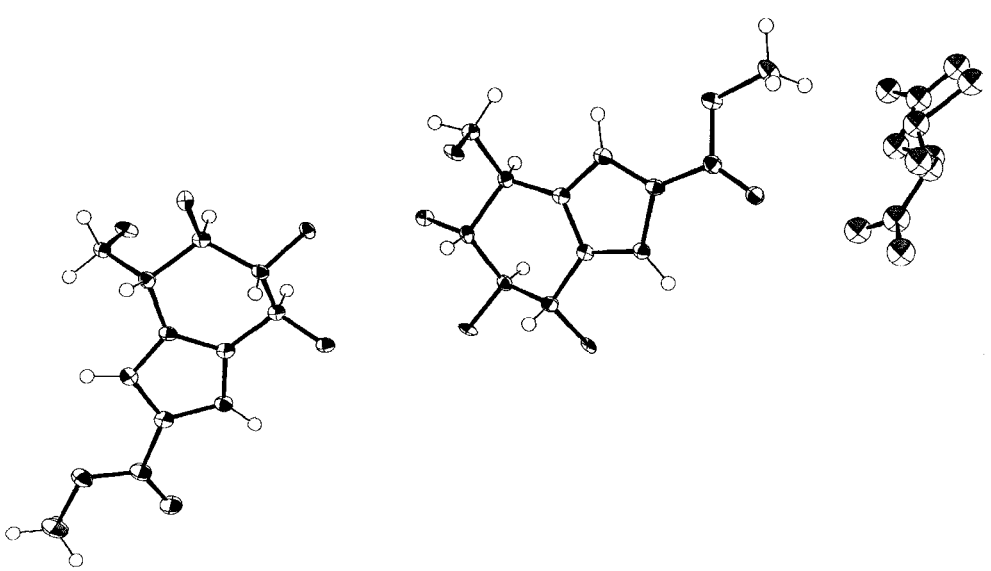
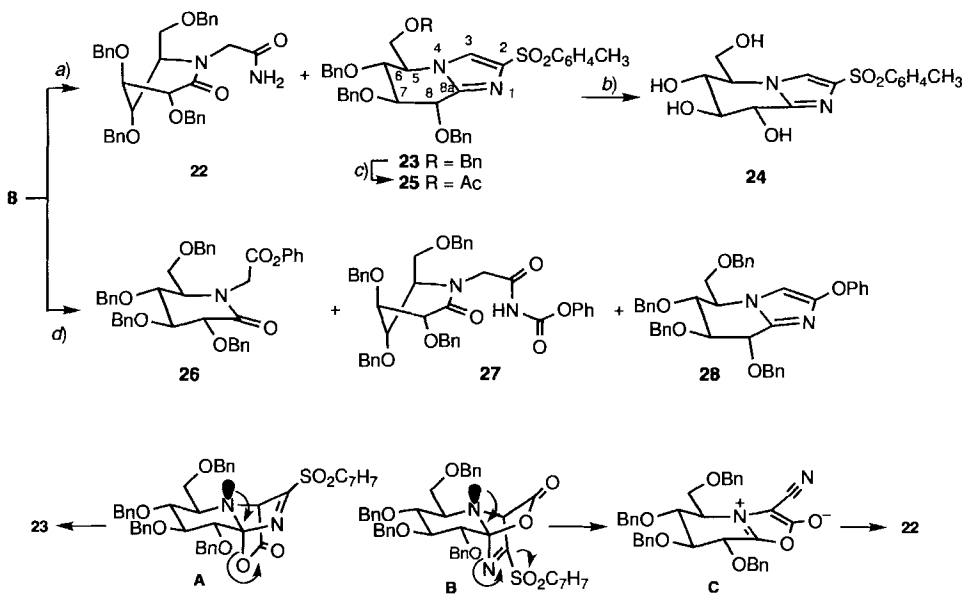


Fig. 2. *X-Ray analysis of the 2:1 complex between tetrahydroindolizine* **21** *and AcOEt*

For the synthesis of imidazopyridines, we treated the *N*-acylglycine **8** with 4-toluenesulfonyl cyanide [7]) in the presence of $MsCl/Et_3N$ at $-20°$ (*Scheme 2*). This led regioselectively in 38% yield to the sulfonylated imidazopyridine **23**. The yield was increased to 53% by using $(i\text{-}Pr)_2EtN$ instead of Et_3N.

We wondered if the unsatisfactory yield may reflect the formation of two diastereoisomeric cycloaddition products **A** and **B**, of which only **A** would decarboxylate and lead to the imidazopyridine **23**, while **B** would lead to the cyano-*münchnone* **C** [8]), expected to be less reactive in 1,3-dipolar cycloadditions [41]. Indeed, stirring the reaction mixture with aqueous hydrogen carbonate for *ca.* 3 h yielded 23% of the carboxamide **22** [42]; this amide was also prepared from the acid **8** (see *Exper. Part*). The formation of **22** is rationalized by postulating that **C** is hydrolyzed to a cyanomalonate, decarboxylation and neighboring-group-assisted nitrile hydration leading to **22**, independently of the sequence of these steps.

Scheme 2



a) TsCN, DCC, $(i\text{-}Pr)_2EtN$; **22** 23%, **23** 53%. *b*) $Pd(OH)_2$, 2N HCl, MeOH, H_2; 73%. *c*) Ac_2O, $BF_3 \cdot OEt_2$, CH_2Cl_2; 73%. *d*) PhOCN, Ac_2O; **26** 16%, **27** 16%, **28** 17%.

Harsh conditions were required for the debenzylation of the sulfonyl-imidazopyridine **23**. Hydrogenolysis (6 bar of H_2, $Pd(OH)_2$) in AcOEt/EtOH 2:1 containing AcOH (2%) failed, while hydrogenolysis in $AcOEt/MeOH/CH_2Cl_2$ 10:30:3 containing 2N HCl

[7]) Methyl carbonocyanidate (methyl cyanoformate) reacted with **8** in the presence of a range of cyclizing agents and in various solvents to give a mixture of the *gluco*/*manno*-configurated methyl imidazopyridine-3-carboxylates in low yield [35].

[8]) Conformationally biased cycloadducts where the N lone pair is not aligned with the C,O bond should not decarboxylate readily. Such tricyclic primary cycloadducts of *münchnones* [36–38] and *sydnones* [39] [40] have indeed been isolated, characterized, and shown to be stable.

(6%) yielded 73% of the tetrol **24**. Acetolysis for 14 h of **23** ($BF_3 \cdot OEt_2/Ac_2O$ in CH_2Cl_2) cleaved selectively the (benzyloxy)methyl group, leading to **25**. Longer reaction times gave a mixture of compounds, which were not isolated.

Finally, we briefly examined by cycloaddition of the *münchnone* **9** to phenyl cyanate [43]. The reaction of a *münchnone* with 2,4-dimethylphenyl cyanate has been reported to yield an (aryloxy)imidazole (41%) [44]. We obtained only 17% of the phenoxyimidazopyridine **28**, besides 16% of the phenyl ester **26** and 16% of the acylcarbamate **27**[9]).

The amide **22** and the *N*-(phenoxycarbonyl)amide **27** possess very similar conformations. Remarkably, they differ significantly from those of **26** and **7**. While **26** and **7** are a *ca.* 2:1 mixture of the $^4H_3$ and $^3H_4$ conformers, **22** and **27** are a mixture of the $^4H_3$ and $^5S_1$ conformers[10]). This difference must be due to an intramolecular weak H-bond of H–N to the C(1) carbonyl O-atom from either side of the π-plane, as suggested by the force-field calculations. The structure of sulfonyl-imidazopyridine **23** is evidenced by the characteristic C(8a) *s* at *ca.* 145 and the C(3) *d* at *ca.* 122 ppm (*ca.* 152 and 101 ppm for the phenoxy-imidazopyridine **28**). The configuration of the imidazopyridines was assigned by comparing their J(H,H) and chemical-shift values to those of the corresponding indolizines, and confirmed by an X-ray analysis of **24**[6]) possessing an ^7E conformation in the solid state (*Fig. 3*). The torsion angle C(5)–N(4)–C(8a)–C(8) is 1.4°. The J(H,H) values of **24** are in keeping with a $^7H_6$ conformation in D_2O.

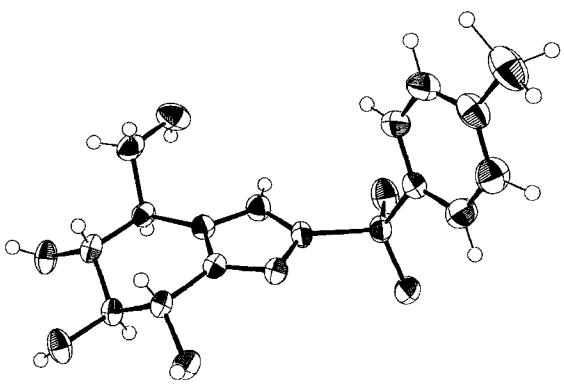


Fig. 3. *X-Ray analysis of the imidazopyridine* **24**

In keeping with the proposal that retaining β-glucosidases protonate their substrate in the plane of the pyranose ring [11] [13], the indolizine (pyrrolopyridine) derivatives are poor competitive inhibitors of the sweet almond β-glucosidases (**12**: $K_i = 25$ mM; **20**: $K_i = 0.3$ mM; **21**: $K_i = 6$ mM; **15**: $K_i = 14$ mM; pH 6.8, 37°), while the imidazopyridine **24** is a good competitive inhibitor of the sweet almond β-glucosidases ($K_i = 5$ μM, $K_i/K_m = 1.5 \cdot 10^{-3}$, pH 6.8, 37°). The β-glucosidase from *Caldocellum saccharolyticum* was strongly inhibited in a mixed fashion ($K_i = 0.04$ μM, $K_i/K_m = 8 \cdot 10^{-5}$, $\alpha = 2.2$, pH 6.8, 55°). In keeping with recently reported observations [12], brewer's yeast α-glucosidase was also inhibited ($K_i = 60$ μM, pH 6.8, 37°, noncompetitive inhibition).

We thank *T. Mäder* for the HPLC purifications, Dr. *B. Schweizer* for the X-ray analyses, and the *Swiss National Science Foundation* and *F. Hoffmann-La Roche AG*, Basel, for generous support.

[9]) The formation of esters [45–47] and acylcarbamates [48] from carboxylic acids and cyanates is known [49] [50].

[10]) In keeping both with the coupling constants and with force field calculations (Macromodel, MM3*, gas phase). We thank Dr. *Bruno Bernet* for the calculations.

Experimental Part

General. Sweet-almond β-glucosidases were purchased from *Fluka* and β-glucosidase from *Caldocellum saccharolyticum* and α-glucosidase from brewer's yeast from *Sigma Chemical Co.*; they were used without further purification. Solvents were distilled before use. Normal workup implies distribution of the crude product between CH_2Cl_2 and sat. aq. NH_4Cl soln. and ice, unless indicated otherwise, drying of the org. layer ($MgSO_4$), filtration, and evaporation of the filtrate. TLC: *Merck* silica gel *60F-254* plates; detection by heating with mostain (400 ml of 10% H_2SO_4 soln., 20 g of $(NH_4)_6Mo_7O_{24} \cdot 6H_2O$, 0.4 g of $Ce(SO_4)_2$). Flash chromatography (FC): silica gel *Merck 60* (0.04–0.063 mm). M.p.: uncorrected. Optical rotations: 1-dm cell. UV Spectra (λ_{max} in nm ($\log \varepsilon$)): 1-cm quartz cell. CD Spectra (λ_{max} in nm (molar ellipticity [θ] in deg · cm^2 · decimol^{-1})): *Jasco-J-710* spectropolarimeter. IR Spectra: KBr or 3% $CHCl_3$ soln. ^{1}H-NMR (300 MHz, if not indicated otherwise) and ^{13}C-NMR (75 MHz, if not indicated otherwise): chemical shifts δ in ppm and coupling constants J in Hz. FAB- and CI-MS: 3-nitrobenzyl alcohol and NH_3 as matrix, resp., unless indicated otherwise.

*2,3,4,6-Tetra-*O*-benzyl-5-deoxy-5-{[(ethoxycarbonyl)methyl]amino}-*D*-glucono-1,5-lactam* (**7**). At 25°, a soln. of **3** (1.24 g, 2.3 mmol) and ethyl iodoacetate (1.5 ml, 12.7 mmol) in DMF (20 ml) was treated with NaH (in oil, washed with hexane before use: 350 mg, 14.6 mmol) portionwise within 8 h. The mixture was stirred for further 30 min, diluted with Et_2O/AcOEt 4:1 (200 ml), and poured into sat. aq. NH_4Cl soln. and ice. The aq. phase was extracted with Et_2O (2 × 30 ml). Drying of the combined org. phases ($MgSO_4$), evaporation, and FC (hexane/Et_2O 1:1) gave **7** (1.39 g, 97%). Oil. R_f (hexane/Et_2O 1:3) 0.53. IR ($CHCl_3$): 3090*w*, 3067*w*, 3008*m*, 2909*m*, 2869*w*, 1744*s*, 1669*s*, 1497*w*, 1454*s*, 1398*m*, 1374*m*, 1300*m*, 1096*s*, 1072*s*, 1028*m*, 911*w*. ^{1}H-NMR ($CDCl_3$): 1.23 (*t*, J = 7.1, Me); 3.50–3.54 (*m*, irrad. at 3.64 → change, 2 H–C(6)); 3.60–3.66 (*m*, irrad. at 3.80 → change, H–C(5)); 3.80 (*dd*, J = 5.9, 7.2, irrad. at 3.94 → *d*, $J \approx$ 7.9, H–C(4)); 3.94 (*dd*, J = 7.2, 8.8, irrad. at 3.80 → change, H–C(3)); 4.02 (*d*, J = 17.4, NCHCO): 4.11 (*d*, $J \approx$ 9.0, irrad. at 3.94 → change, H–C(2)); 4.13 (*q*, J = 7.1, irrad. at 1.23 → *s*, CH_2O); 4.389 (*d*, J = 17.4, NCHCO); 4.395 (*s*, 2 PhC*H*); 4.50 (*d*, J = 11.6, PhC*H*); 4.68 (*d*, J = 11.1, PhC*H*); 4.69 (*d*, J = 11.4, PhC*H*); 4.78 (*d*, J = 11.6, PhC*H*); 4.88 (*d*, J = 11.1, PhC*H*); 5.15 (*d*, J = 11.3, PhC*H*); 7.20–7.45 (*m*, 20 arom. H). ^{13}C-NMR ($CDCl_3$): 14.16 (*q*, Me); 46.76 (*t*, NCH_2CO); 61.13 (*d*, C(5)); 61.26 (*t*, CH_2O); 68.54 (*t*, C(6)); 73.26 (*t*, $PhCH_2$); 73.53 (*t*, $PhCH_2$); 74.37 (*t*, $PhCH_2$); 74.44 (*t*, $PhCH_2$); 77.17, 78.23, 81.12 (3*d*, C(2), C(3), C(4)); 127.71–128.51 (several *d*); 137.40 (*s*); 137.85 (*s*); 138.08 (*s*); 138.15 (*s*); 169.00, 170.16 (2*s*, C(1), CO_2). FAB-MS: 625 (3, $[M + 1]^+$), 624 (6), 91 (100).

*2,3,4,6-Tetra-*O*-benzyl-5-[(carboxymethyl)amino]-5-deoxy-*D*-glucono-1,5-lactam* (**8**). At 25°, a soln. of **7** (1.2 g, 1.92 mmol) in THF/H_2O 7:3 (51 ml) was treated with LiOH · H_2O (204 mg, 4.9 mmol) and stirred 50 min. The soln. was diluted with Et_2O/ice and acidified with 2N HCl to pH 1. The aq. phase was extracted with Et_2O (3 × 100 ml). Drying of the combined org. phases ($MgSO_4$), evaporation, and drying *i.v.* gave **8** (1.15 g, > 99%; purity > 95% (^{1}H-NMR)). Oil. R_f (AcOEt/MeOH 4:1) 0.51. IR ($CHCl_3$): 3490*w*, 3450–3090*w*, 3090*w*, 3067*w*, 3008*m*, 2927*m*, 2909*m*, 2868*m*, 2868–2350*m*, 1728*s*, 1669*s*, 1497*w*, 1455*s*, 1401*m*, 1363*m*, 1261*m*, 1096*s*, 1028*m*, 911*w*. ^{1}H-NMR ($CDCl_3$): 3.50–3.53 (*m*, 2 H–C(6)); 3.59–3.63 (*m*, irrad. at 3.81 → *d*, $J \approx$ 4.8, H–C(5)); 3.81 (*dd*, J = 5.8, 6.7, irrad. at 3.93 → change, H–C(4)); 3.93 (*dd*, J = 6.8, 8.4, irrad. at 3.81 → change, irrad. at 4.1 → change, H–C(3)); 4.06 (*d*, J = 17.3, NCHCO); 4.10 (*d*, $J \approx$ 8.5, irrad. at 3.93 → change, H–C(2)); 4.36 (*d*, $J \approx$ 17.0, NCHCO); 4.37 (*d*, J = 11.8, PhC*H*); 4.41 (*d*, J = 11.8, PhC*H*); 4.48 (*d*, J = 11.8, PhC*H*); 4.62 (*d*, J = 11.3, PhC*H*); 4.66 (*d*, J = 11.2, PhC*H*); 4.73 (*d*, J = 11.8, PhC*H*); 4.84 (*d*, J = 11.2, PhC*H*); 5.13 (*d*, J = 11.2, PhC*H*); 7.18–7.44 (*m*, 20 arom. H). ^{13}C-NMR ($CDCl_3$): 46.76 (*t*, NCH_2CO); 61.60 (*d*, C(5)); 67.99 (*t*, C(6)); 73.31 (*t*, $PhCH_2$); 73.54 (*t*, $PhCH_2$); 74.30 (*t*, $PhCH_2$); 74.56 (*t*, $PhCH_2$); 76.53, 78.29, 80.97 (3*d*, C(2), C(3), C(4)); 127.82–128.52 (several *d*); 137.15 (*s*); 137.41 (*s*); 137.84 (*s*); 137.96 (*s*); 170.77, 172.34 (2*s*, C(1), CO_2H). FAB-MS: 618 (3, $[M + Na]^+$), 596 (3, $[M + 1]^+$), 91 (100).

Dimethyl (5R,6R,7S,8S)-6,7,8-Tris(benzyloxy)-5-[(benzyloxy)methyl]-5,6,7,8-tetrahydroindolizine-1,2-dicarboxylate (**10**). At 25°, a soln. of **8** (1.02 g, 1.7 mmol) and dimethyl acetylenedicarboxylate (DMAD; 3.60 ml, 32.5 mmol) in C_6H_6 (1.8 ml) was treated with Ac_2O (1.8 ml, 21.1 mmol) within 15 min and stirred for 2 h at 25° and for 30 min at 90°. Drying *i.v.* and FC (hexane/Et_2O 6:1 → 1:1) gave **10** (1.10 g, 95%). Oil. R_f (hexane/Et_2O 1:3) 0.53. $[\alpha]_D^{25} = +25.0$ (c = 0.25, $CHCl_3$). UV ($CHCl_3$): 258 (3.9). CD ($CHCl_3$): 259 (–9005). IR ($CHCl_3$): 3089*w*, 3066*w*, 3008*m*, 2962*m*, 2867*m*, 1717*s*, 1603*w*, 1558*w*, 1525*m*, 1496*m*, 1454*m*, 1389*m*, 1362*m*, 1286*s*, 1262*s*, 1097*s*, 1016*s*, 865*m*, 603*w*. ^{1}H-NMR ($CDCl_3$): 3.73 (*dd*, J = 4.0, 9.3, irrad. at 4.19 → *d*, J = 9.1, irrad. at 4.33 → change, H–C(6)); 3.77 (*s*, MeO); 3.84 (*s*, MeO); 3.87 (*dd*, J = 5.9, 10.8, HC–C(5)); 4.00 (*dd*, J = 2.2, 10.9, HC–C(5)); 4.19 (*dd*, J = 3.0, 3.9, H–C(7)); 4.33 (*ddd*, J = 2.2, 5.9, 9.3, H–C(5)); 4.44 (*d*, J = 11.8, PhC*H*); 4.52–4.57 (*m*, 5 PhC*H*); 4.65 (*d*, J = 11.5, PhC*H*); 4.67 (*d*, J = 11.8, PhC*H*); 5.27 (*d*, J = 2.8, irrad. at 4.19 → *s*, H–C(8)); 7.19–7.41 (*m*, 20 arom. H); 7.43 (*s*, H–C(3)). ^{13}C-NMR ($CDCl_3$): 51.46 (*q*, MeO); 51.58 (*q*, MeO); 56.98 (*d*, C(5)); 66.56 (*t*, CH_2–C(5)); 69.34 (*d*, C(8)); 70.61 (*t*, $PhCH_2$); 71.83 (*t*, $PhCH_2$); 72.69 (*t*, $PhCH_2$); 73.32

(*t*, $PhCH_2$); 78.69, 81.60 (2*d*, C(6), C(7)); 115.14, 115.70 (2*s*, C(1), C(2)); 125.29 (*d*, C(3)); 127.56–128.56 (several *d*); 132.75 (*s*, C(8a)); 137.18 (*s*); 137.40 (*s*); 137.46 (*s*); 138.06 (*s*); 164.15 (*s*, CO_2); 164.95 (*s*, CO_2). CI-MS (NH_3): 675 (2, M^+), 644 (2, $[M - OMe]^+$), 584 (2, $[M - Bn]^+$), 91 (100). Anal. calc. for $C_{41}H_{41}NO_8$ (675.8): C 72.87, H 6.12, N 2.07; found: C 72.93, H 6.32, N 2.00.

Dimethyl (5R,6R,7S,8S)-5,6,7,8-Tetrahydro-6,7,8-trihydroxy-5-(hydroxymethyl)indolizine-1,2-dicarboxylate (**12**). A soln. of **10** (130 mg, 0.19 mmol) in EtOH (6 ml) was treated with ammonium formate (270 mg) and 20% $Pd(OH)_2/C$ (229 mg) and heated at 70° for 6 h. The mixture was filtered through *Celite* and evaporated. FC (AcOEt → AcOEt/MeOH 100:3) gave **12** (48 mg, 79%). Samples for elemental analysis and enzymatic tests were purified by HPLC (H_2O/MeCN 9:1, *Merck LiChrosorb RP-18* (7 µm) 250 × 25 mm). R_f (AcOEt/MeOH 10:1): 0.35. UV (H_2O): 255 (4.2). ^{1}H-NMR (D_2O): 3.75 (*dd*, J = 7.8, 9.7, irrad. at 4.77 → *d*, $J \approx 9.7$, H–C(7)); 3.81 (*s*, MeO); 3.87 (*s*, MeO); 3.88 (*t*, $J \approx 9.5$, H–C(6)); 4.03 (*td*, $J \approx 2.0$, 10.0, H–C(5)); 4.11 (*dd*, J = 1.8, 13.1, HC–C(5)); 4.24 (*dd*, J = 1.8, 12.8, HC–C(5)); 4.77 (*d*, $J \approx 7.8$, H–C(8)); 7.61 (*s*, H–C(3)). ^{13}C-NMR (D_2O): 54.94 (*q*, MeO); 55.72 (*q*, MeO); 61.45 (*t*, CH_2–C(5)); 64.46 (*d*, C(5)); 69.84, 70.51, 77.51 (3, C(6), C(7), C(8)); 115.76, 117.60 (2*s*, C(1), C(2)); 127.99 (*d*, C(3)); 138.39 (*s*, C(8a)); 169.11 (*s*, CO_2); 171.50 (*s*, CO_2). FAB-MS: 626 (*18*), 625 (*76*), 611 (*13*), 610 (*32*), 609 (*100*), 565 (*11*), 558 (*10*), 557 (*34*), 525 (*20*), 523 (*10*), 338 (*14*, $[M + Na]^+$), 323 (14), 322 (85), 321 (12), 316 (7, $[M + 1]^+$), 314 (4), 284 (12), 266 (12), 160 (19). Anal. calc. for $C_{13}H_{17}NO_8 \cdot 0.5\ H_2O$ (324.3): C 48.15, H 5.59, N 4.32; found: C 48.02, H 5.65, N 4.24.

Reaction of **8** *with Methyl Propiolate. a*) A soln. of **8** (3.5 g, 5.88 mmol) and methyl propiolate (5 ml, 59.8 mmol) in C_6H_6 (10 ml) was treated with *N*-[3-(dimethylamino)propyl]-*N'*-ethylcarbodiimide hydrochloride (EDC; 2 g, 10.4 mmol) and stirred for 5 h at r.t. Normal workup and FC (AcOEt/hexane 1:5) gave **18** (1.6 g, 44%) and **19** (1.2 g, 33%).

b) A soln. of **8** (643 mg, 1.079 mmol) and methyl propiolate (1.71 ml, 20.5 mmol) in C_6H_6 (1.3 ml) was treated with ECD (310 mg, 1.619 mmol) and stirred 30 min at 90°. The mixture was diluted with Et_2O and poured into aq. sat. $NaHCO_3$ soln. The layers were separated, and the aq. phase was extracted with CH_2Cl_2. Drying of the combined org. phases ($MgSO_4$) and evaporation gave **16**/**17**/**18**/**19** 2:2:48:48 (^{1}H-NMR). Several FC (hexane/Et_2O 6:1 → 3:1 and CH_2Cl_2/hexane 2:1 → 5:1) gave **16** (14 mg, 2%), **18** (246 mg, 37%), **17** (14 mg, 2%), and **19** (177 mg, 27%).

c) A soln. of **8** (36.8 mg, 0.062 mmol) and methyl propiolate (0.098 ml, 1.17 mmol) in C_6H_6 (0.07 ml) was treated with Ac_2O (0.07 ml, 0.76 mmol) and stirred at 80° for 2.5 h. FC (hexane/Et_2O 2:1) of the crude **16**/**17**/**18**/**19** 1:1:1:1 (^{1}H-NMR) gave **16**/**18** 1:1 (6.2 mg, 16%) and **17**/**19** 1:1 (5.6 mg, 15%).

Methyl (5R,6R,7S,8R)-6,7,8-Tris(benzyloxy)-5-[(benzyloxy)methyl]-5,6,7,8-tetrahydroindolizine-1-carboxylate (**16**): R_f (hexane/CH_2Cl_2 1:3) 0.27. UV ($CHCl_3$): 243 (3.8). CD ($CHCl_3$): 260 (3000). IR ($CHCl_3$): 3089*w*, 3066*w*, 2950*m*, 2866*m*, 1952*w*, 1876*w*, 1810*w*, 1698*s*, 1686*w*, 1559*m*, 1497*s*, 1454*m*, 1439*m*, 1362*m*, 1311*m*, 1261*s*, 1156*m*, 1097*s*, 1027*s*, 929*w*, 912*w*, 606*w*. ^{1}H-NMR (500 MHz, $CDCl_3$): 3.62 (*dd*, J = 7.2, 9.9, CH–C(5)); 3.70 (*dd*, J = 4.0, 9.9, CH–C(5)); 3.75 (*s*, MeO); 3.79 (*dd*, J = 2.7, 8.6, H–C(7)); 4.23 (*dd*, J = 5.0, 8.6, H–C(6)); 4.24 (*td*, $J \approx 5.0$, 7.2, H–C(5)); 4.38 (*d*, J = 12.0, PhC*H*); 4.42 (*d*, J = 12.0, PhC*H*); 4.58 (*d*, J = 12.1, PhC*H*); 4.66 (*d*, J = 11.3, PhC*H*); 4.67 (*d*, J = 12.1, PhC*H*); 4.68 (*d*, J = 11.8, PhC*H*); 4.79 (*d*, J = 11.9, PhC*H*); 4.90 (*d*, J = 11.3, PhC*H*); 5.56 (*d*, J = 2.7, H–C(8)); 6.59 (*d*, J = 3.0, H–C(2)); 6.80 (*d*, J = 3.0, H–C(3)); 7.21–7.39 (*m*, 20 arom. H). ^{13}C-NMR (100 MHz, $CDCl_3$): 50.90 (*q*, MeO); 61.87 (*d*, C(5)); 67.10 (*d*, C(8)); 70.92 (*t*, CH_2–C(5)); 71.80 (*t*, $PhCH_2$); 72.24 (*t*, $PhCH_2$); 73.21 (*t*, $PhCH_2$); 74.18 (*t*, $PhCH_2$); 75.56, 81.41 (2*d*, C(6), C(7)); 110.69 (*d*, C(2)); 113.23 (*s*, C(1)); 121.58 (*d*, C(3)); 127.19–128.44 (several *d*); 132.67 (*s*, C(8a)); 137.71 (*s*); 138.18 (*s*); 138.27 (*s*); 139.02 (*s*); 165.33 (*s*, CO_2). CI-MS (NH_3): 618 (1, $[M + 1]^+$), 617 (3), 526 (5, $[M - Bn]^+$), 510 (100, $[M - OBn]^+$).

Methyl (5R,6R,7S,8R)-6,7,8-Tris(benzyloxy)-5-[(benzyloxy)methyl]-5,6,7,8-tetrahydroindolizine-2-carboxylate (**17**): R_f (hexane/Et_2O 1:1) 0.31. UV ($CHCl_3$): 243 (3.8). CD ($CHCl_3$): 239 (–2000). IR ($CHCl_3$): 3089*w*, 3066*m*, 2926*m*, 2867*m*, 1703*s*, 1952*w*, 1876*w*, 1603*w*, 1564*w*, 1518*w*, 1496*w*, 1454*m*, 1393*m*, 1361*m*, 1298*m*, 1261*m*, 1170*m*, 1094*s*, 1027*m*, 1006*m*, 930*m*, 910*w*, 600*w*. ^{1}H-NMR (500 MHz, $CDCl_3$): 3.65 (*dd*, J = 7.1, 10.0, HC–C(5)); 3.74 (*dd*, J = 4.2, 10.0, HC–C(5)); 3.79 (*dd*, J = 2.1, 8.6, H–C(7)); 3.81 (*s*, MeO); 4.21 (*ddd*, J = 4.2, 5.6, 7.0, H–C(5)); 4.25 (*dd*, J = 5.7, 8.6, H–C(6)); 4.38 (*d*, J = 12.5, PhC*H*), 4.43 (*d*, J = 12.1, PhC*H*); 4.48 (*d*, J = 12.1, PhC*H*); 4.56 (*d*, J = 12.3, PhC*H*); 4.59 (*d*, J = 11.1, PhC*H*); 4.60 (*d*, J = 2.9, H–C(8)); 4.64 (*d*, J = 11.3, PhC*H*); 4.65 (*d*, J = 11.8, PhC*H*); 4.91 (*d*, J = 11.3, PhC*H*); 6.51 (*d*, J = 1.7, H–C(1)); 7.23–7.35 (*m*, 20 arom. H); 7.51 (*d*, J = 1.7, H–C(3)). ^{13}C-NMR (100 MHz, $CDCl_3$): 51.07 (*q*, MeO); 61.51 (*d*, C(5)); 67.57 (*d*, C(8)); 69.25 (*t*, CH_2–C(5)); 71.61 (*t*, $PhCH_2$); 71.82 (*t*, $PhCH_2$); 73.25 (*t*, $PhCH_2$); 74.32 (*t*, $PhCH_2$); 75.45, 80.77 (2*d*, C(6), C(7)); 109.89 (*d*, C(1)); 115.92 (*s*, C(2)); 115.92 (*d*, C(3)); 127.64–128.45 (several *d* and 1*s* for C(8a)); 137.66 (*s*); 137.99 (*s*); 138.03 (*s*); 138.21 (*s*); 165.15 (*s*, CO_2). CI-MS (NH_3): 618 (9, $[M + 1]^+$), 617 (6), 526 (8, $[M - Bn]^+$), 91 (100).

Methyl (5R,6R,7S,8S)-6,7,8-Tris(benzyloxy)-5-[(benzyloxy)methyl]-5,6,7,8-tetrahydroindolizine-1-carboxylate (**18**): R_f (hexane/CH_2Cl_2 1:3) 0.23. $[\alpha]_D^{25} = +49.0$ ($c = 0.47$, $CHCl_3$). UV ($CHCl_3$): 242 (3.8). CD ($CHCl_3$): 263 (−1000). IR ($CHCl_3$): 3089*w*, 3066*m*, 3007*m*, 2951*m*, 2866*m*, 1952*w*, 1876*w*, 1811*w*, 1698*s*, 1603*m*, 1563*m*, 1496*s*, 1454*s*, 1439*m*, 1363*m*, 1312*m*, 1261*s*, 1155*m*, 1095*s*, 1027*s*, 931*m*, 912*m*, 605*w*. ^{1}H-NMR (500 MHz, $CDCl_3$): 3.70 (*dd*, $J = 3.1, 8.9$, H−C(6)); 3.76 (*s*, MeO); 3.88 (*dd*, $J = 5.9, 10.8$, HC−C(5)); 4.00 (*dd*, $J = 2.6, 10.7$, HC−C(5)); 4.20 (*dd*, $J = 2.0, 3.5$, H−C(7)); 4.34 (*ddd*, $J = 2.6, 5.9, 8.9$, H−C(5)); 4.41 (*d*, $J = 11.6$, PhC*H*); 4.48 (*d*, $J = 11.8$, PhC*H*); 4.52 (*d*, $J = 11.1$, PhC*H*); 4.51–4.53 (*m*, 2 PhC*H*); 4.54 (*d*, $J = 11.9$, PhC*H*); 4.60 (*d*, $J = 11.6$, PhC*H*); 4.65 (*d*, $J = 11.7$, PhC*H*); 5.53 (*d*, $J = 1.8$, H−C(8)); 6.57 (*d*, $J = 3.1$, H−C(2)); 6.81 (*d*, $J = 3.1$, H−C(3)); 7.16–7.35 (*m*, 20 arom. H). ^{13}C-NMR ($CDCl_3$): 50.91 (*q*, MeO); 56.51 (*d*, C(5)); 67.37 (*t*, CH_2−C(5)); 69.00 (*d*, C(8)); 70.28 (*t*, PhCH_2); 71.42 (*t*, PhCH_2); 72.35 (*t*, PhCH_2); 73.28 (*t*, PhCH_2); 79.15, 81.56 (2*d*, C(6), C(7)); 109.90 (*d*, C(2)); 115.03 (*s*, C(1)); 119.24 (*d*, C(3)); 127.42–128.51 (several *d*); 132.27 (*s*, C(8a)); 137.50 (*s*); 137.61 (*s*); 137.74 (*s*); 138.61 (*s*); 165.50 (*s*, CO_2). CI-MS (NH_3): 618 (1, $[M + 1]^+$), 617 (3), 526 (4, $[M - Bn]^+$), 510 (62, $[M - OBn]^+$), 91 (100). Anal. calc. for $C_{39}H_{39}NO_6$ (617.7): C 75.83, H 6.36, N 2.27; found: C 75.62, H 6.66, N 2.24.

Methyl (5R,6R,7S,8S)-6,7,8-Tris(benzyloxy)-5-[(benzyloxy)methyl]-5,6,7,8-tetrahydroindolizine-2-carboxylate (**19**): R_f (hexane/Et_2O 1:1) 0.35. $[\alpha]_D^{25} = +58.0$ ($c = 0.44$, $CHCl_3$). UV ($CHCl_3$). 242 (3.8). CD ($CHCl_3$): 244 (+800). IR ($CHCl_3$): 3089*w*, 3066*m*, 2951*m*, 2923*m*, 2868*m*, 1952*w*, 1876*w*, 1703*s*, 1603*m*, 1562*m*, 1518*m*, 1469*m*, 1454*s*, 1441*m*, 1387*m*, 1362*m*, 1329*m*, 1264*s*, 1152*m*, 1092*s*, 1027*s*, 1004*m*, 934*m*, 910*m*, 606*w*. ^{1}H-NMR (500 MHz, $CDCl_3$): 3.79 (*dd*, $J = 6.3, 8.9$, H−C(6)); 3.80 (*s*, MeO); 3.82 (*dd*, $J = 5.1, 10.7$, HC−C(5)); 3.94 (*dd*, $J = 2.6, 10.6$, HC−C(5)); 4.06 (*dd*, $J = 4.7, 6.3$, H−C(7)); 4.19 (*ddd*, $J = 2.7, 5.0, 8.4$, H−C(5)); 4.47 (*d*, $J = 11.4$, PhC*H*); 4.48 (*d*, $J = 12.5$, PhC*H*); 4.51 (*d*, $J = 12.6$, PhC*H*); 4.56 (*d*, $J = 11.8$, PhC*H*); 4.60 (br. *d*, $J = 4.7$, H−C(8)); 4.65 (*d*, $J = 11.5$, PhC*H*); 4.66 (*d*, $J = 11.8$, PhC*H*); 4.71 (*d*, $J = 11.6$, PhC*H*); 4.74 (*d*, $J = 11.4$, PhC*H*); 6.64 (*dd*, $J = 0.6, 1.6$, H−C(1)); 7.12–7.37 (*m*, 20 arom. H); 7.45 (*d*, $J = 1.6$, H−C(3)). ^{13}C-NMR (75 MHz, $CDCl_3$): 50.06 (*q*, MeO); 58.05 (*d*, C(5)); 67.33 (*t*, CH_2−C(5)); 71.05 (*t*, PhCH_2); 73.09 (*t*, PhCH_2); 73.09 (*d*, C(8)); 73.33 (*t*, PhCH_2); 73.69 (*t*, PhCH_2); 77.98, 83.17 (2*d*, C(6), C(7)); 109.47 (*d*, C(1)); 115.88 (*s*, C(2)); 124.31 (*d*, C(3)); 127.74–128.53 (several *d*); 128.84 (*s*, C(8a)); 137.35 (*s*); 137.72 (*s*); 137.84 (*s*); 138.00 (*s*); 165.28 (*s*, CO_2). CI-MS (NH_3): 618 (13, $[M + 1]^+$), 617 (4), 526 (7, $[M - Bn]^+$), 91 (100). Anal. calc. for $C_{39}H_{39}NO_6$ (617.7): C 75.83, H 6.36, N 2.27; found: C 75.90, H 6.42, N 2.16.

Methyl (5R,6R,7S,8S)-5,6,7,8-Tetrahydro-6,7,8-trihydroxy-5-(hydroxymethyl)indolizine-1-carboxylate (**20**): A soln. of **18** (128 mg, 0.21 mmol) in EtOH (10 ml) was treated with ammonium formate (400 mg) and 20% $Pd(OH)_2$/C (300 mg) and heated at 55° for 6 h. The mixture was filtered through *Celite* and evaporated. FC (AcOEt → AcOEt/MeOH 100:3) gave **20** (40 mg, 75%). Recrystallization from AcOEt/MeOH gave crystals suitable for X-ray analysis. A sample for enzymatic tests was purified by HPLC (H_2O/MeOH 8:2 → 6:4; *Merck LiChrosorb RP-18* (7 μm) 250 × 25 mm). White solid. M.p. 180°. R_f (AcOEt/MeOH 10:1): 0.45. UV (H_2O): 237 (4.3), 220 (4.2). ^{1}H-NMR (D_2O): 3.81 (*s*, MeO); 3.80–3.86 (*m*, irrad. at 4.91 → change, H−C(7)); 3.86 (*t*, $J \approx 9.7$, irrad. at 4.00 → change, H−C(6)); 3.95–4.05 (*m*, H−C(5)); 4.06 (*dd*, $J = 2.2, 12.6$, irrrad. at 4.00 → *d*, $J \approx 12.0$, HC−C(5)); 4.22 (*dd*, $J = 2.4, 12.7$, irrad. at 4.00 → *d*, $J \approx 12.0$, HC−C(5)); 4.91 (*d*, $J = 6.7$, H−C(8)); 6.69 (*d*, $J = 3.3$, H−C(2)); 6.91 (*d*, $J = 3.3$, H−C(3)). ^{13}C-NMR (D_2O): 54.89 (*q*, MeO); 61.20 (*t*, CH_2−C(5)); 64.40 (*d*, C5)); 70.05 (*d*); 70.76 (*d*); 76.96 (*d*); 108.90 (*s*, C(1)); 114.59 (*d*, C(2)); 121.85 (*d*, C(3)); 138.89 (*s*, C(8a)); 171.32 (*s*, CO_2). FAB-MS: 280 (31, $[M + Na]^+$), 264 (85), 258 (34, $[M + 1]^+$), 257 (13, M^+), 256 (12), 245 (20), 240 (100), 176 (38), 165 (16).

X-Ray Analysis of **20**: Monoclinic *C*2; $a = 14.902(3)$, $b = 5.0816(6)$, $c = 15.564(5)$; $\beta = 105.90(2)°$; $V = 1133.5(4)$ Å^3; $D_{calc} = 1.507$ Mg/m^3; $Z = 4$. The reflexion were measured on an *Enraf-Nonius-CAD4* diffractometer (graphite monochromator, MoK_α, $\lambda = 0.71073$) at 293 K. $R = 0.0429$, $R_w = 0.1199$. The structures were solved with the direct-methods routine of SHELX-86 and the refinement performed with SHELXL-92 [51] [52].

Methyl (5R,6R,7S,8S)-5,6,7,8-Tetrahydro-6,7,8-trihydroxy-5-(hydroxymethyl)indolizine-2-carboxylate (**21**). As described for **20**, with **19** (58 mg, 0.094 mmol). FC (AcOEt → AcOEt/MeOH 100:5) gave **21** (18 mg, 75%). Recrystallization from AcOEt/EtOH gave crystals suitable for X-ray analysis. A sample for enzymatic tests was purified by HPLC (H_2O/MeOH 8:2; *Merck LiChrosorb RP-18* (7 μm 250 × 25 mm). M.p. 90°. R_f (AcOEt/MeOH 10:1): 0.23. ^{1}H-NMR (D_2O): 3.60 (*dd*, $J = 8.9, 9.7$, irrad. at 4.52 → *d*, $J \approx 9.9$, H−C(7)); 3.75 (*s*, MeO); 3.82 (*dd*, $J = 9.2, 9.7$, irrad. at 3.94 → *d*, $J \approx 8.7$, H−C(6)); 3.94 (*td*, $J = 2.2, 9.1$, H−C(5)); 4.02 (*dd*, $J = 2.5, 12.7$, irrad. at 3.94 → *d*, $J \approx 12.3$, HC−C(5)); 4.19 (*dd*, $J = 2.4, 12.7$, irrad. at 3.94 → *d*, $J \approx 12.9$, HC−C(5)); 4.52 (*dd*, $J = 1.1, 9.0$, irrad. at 6.52 → *d*, $J \approx 8.8$, H−C(8)); 6.52 (*t*, $J \approx 1.6$, irrad. at 4.52 → *d*, $J \approx 1.6$, H−C(1)); 7.54 (*d*, $J = 1.8$, irrad. at 6.52 → *s*, H−C(3)). ^{13}C-NMR (D_2O): 54.59 (*q*, MeO); 61.77 (*t*, CH_2−C(5)); 64.31 (*d*, C(5)); 70.54 (*d*); 70.99 (*d*); 77.75 (*d*); 109.11 (*d*, C(1)); 118.55 (*s*, C(2)); 127.21 (*d*, C(3)); 136.50 (*s*, C(8a)); 170.74 (*s*, CO_2).

X-Ray Analysis of **21**: The asymmetric unit contains two molecules of **21** and a disordered molecule of AcOEt. Monoclinic $P21$; $a = 8.319(4)$, $b = 7.715(8)$, $c = 22.17(2)$; $\beta = 97.43(6)°$; $V = 1411(2)$ Å^3; $D_{calc} = 1.419$ Mg/m^3; $Z = 4$. The reflexions were measured on an *Enraf-Nonius-CAD4* diffractometer (graphite monochromator, MoK_α, $\lambda = 0.71073$) at 293 K. $R = 0.0810$, $R_w = 0.2012$. The structures were solved with the direct-methods routine of SHELX-86 and the refinement performed with SHELXL-92 [51] [52].

(5R,6R,7S,8S)-6,7,8-Tris(benzyloxy)-5-[(benzyloxy)methyl]-5,6,7,8-tetrahydroindolizine-1,2-dimethanol (**11**). At 25°, a soln. of **10** (47 mg, 70 mmol) in THF (3 ml) was treated with $LiAlH_4$ (28 mg, 700 mmol) and stirred for 7 h. The mixture was diluted with CH_2Cl_2 and poured into sat. aq. NH_4Cl soln. The aq. phase was extracted with CH_2Cl_2. Drying of the combined org. phases ($MgSO_4$), evaporation, and FC (hexane/AcOEt 1:3) gave **11** (24 mg, 56%): Oil. R_f (hexane/Et_2O 1:3) 0.06. IR ($CHCl_3$): 3597*w*, 3444*w* (br.), 3089*w*, 3066*m*, 3007*m*, 2925*m*, 2873*w*, 2869*m*, 1952*w*, 1812*w*, 1729*w*, 1586*w*, 1529*m*, 1496*m*, 1454*m*, 1364*m*, 1332*m*, 1177*m*, 1094*s*, 1027*m*, 994*m*, 910*w*, 839*w*, 606*w*. ^{1}H-NMR ($CDCl_3$): 2.34 (br. *s*, OH); 2.43 (br. *s*, OH); 3.78 (*dd*, $J = 5.5$, 8.7, irrad. at 4.22 → change, irrad. at 4.15 → *d*, $J \approx 8.7$, H–C(6)); 3.83 (*dd*, $J = 5.4$, 8.6, irrad. at 4.22 → *d*, $J \approx 8.6$, HC–C(5)); 3.95 (*dd*, $J = 3.0$, 10.5, irrad. at 4.22 → change, HC–C(5)); 4.15 (*dd*, $J = 3.8$, 5.6, irrad. at 4.76 → *d*, $J \approx 5.6$, H–C(7)); 4.22 (*ddd*, $J = 3.0$, 5.4, 8.5, H–C(5)); 4.46–4.56 (*m*, 9 H); 4.64–4.66 (*m*, 2 H); 4.72 (*d*, $J = 11.5$, PhC*H*); 4.76 (*d*, $J = 3.7$, irrad. at. 4.15 → *s*, H–C(8)); 6.78 (*s*, H–C(3)); 7.25–7.40 (*m*, 20 arom. H). ^{13}C-NMR ($CDCl_3$): 55.55 (*t*, CH_2O); 57.05 (*d*, C(5)); 57.34 (*t*, CH_2O); 61.67 (*t*, CH_2–C(5)); 70.28 (*t*, PhCH_2); 71.33 (*d*, C(8)); 72.73 (*t*, PhCH_2); 73.28 (*t*, 2 PhCH_2); 77.96, 82.41 (2*d*, C(6), C(7)); 117.80 (*d*, C(3)); 121.93, 122.71 (2*s*, C(1), C(2)); 125.26 (*s*, C(8a)); 127.56–128.75 (several *d*); 137.48 (*s*); 137.72 (*s*); 137.78 (*s*); 138.06 (*s*). CI-MS (NH_3): 620 (5, $[M + 1]^+$), 619 (27), 602 (12, $[M - H_2O + 1]^+$), 512 (16, $[M - BnO]^+$), 480 (11), 420 (16), 108 (25, $[BnOH]^+$), 91 (100).

Dimethyl (5R,6R,7S,8S)-5,6,7,8-Tetrahydro-6,7,8-tris(triethylsilyloxy)-5-[(triethylsilyloxy)methyl]indolizine-1,2-dicarboxylate (**13**). At 25°, a soln. of **12** (121 mg, 0.38 mmol) in pyridine (3.5 ml) was treated with triethylsilyl trifluoromethanesulfonate (1 ml, 4.4 mmol) and stirred at 40° for 3 h. Evaporation and FC (hexane/CH_2Cl_2 1:1 → 1:3) gave **13** (276 mg, 93%). Oil. R_f (CH_2Cl_2/hexane 2:1) 0.1. UV ($CHCl_3$): 259 (4.2). IR ($CHCl_3$): 2958*s*, 2913*s*, 2878*s*, 1713*s*, 1601*w*, 1528*m*, 1458*m*, 1445*m*, 1414*m*, 1379*m*, 1339*w*, 1285*m*. ^{1}H-NMR ($CDCl_3$): 0.50–0.70 (*m*, 12 CH_2Si); 0.75–1.00 (*m*, 12 Me); 3.62 (*dd*, $J = 1.0$, 7.2, irrad. at 4.06 → *d*, $J \approx 4.2$, H–C(6)); 3.79 (*s*, MeO); 4.01 (*dd*, $J = 8.2$, 11.8, HC–C(5)); 4.06 (*dd*, $J \approx 1.2$, 3.4, irrad. at 3.62 → *d*, $J \approx 3.4$, H–C(7)); 4.11–4.17 (*m*, irrad. at 3.62 → change, H–C(5)); 4.17 (*dd*, $J = 2.5$, 11.8, CH–C(5)); 5.21 (*d*, $J = 3.1$, irrad. at 4.06 → *s*, H–C(8)); 7.56 (*s*, H–C(3)). ^{13}C-NMR ($CDCl_3$): 4.40 (*t*, (MeCH_2)$_3$Si); 4.61 (*t*, (MeCH_2)$_3$Si); 4.96 (*t*, (MeCH_2)$_3$Si); 5.07 (*t*, (MeCH_2)$_3$Si); 6.67 (*q*, 2 (*Me*CH_2)$_3$Si); 6.77 (*q*, (*Me*CH_2)$_3$Si); 6.86 (*q*, (*Me*CH_2)$_3$Si); 51.20 (*q*, MeO); 61.49 (*q*, MeO); 62.03 (*d*, C(5)); 66.20 (*t*, CH_2–C(5)); 69.34 (*d*, C(8)); 75.21, 77.55 (2*d*, C(6), C(7)); 113.13, 114.54 (2*s*, C(1), C2)); 125.75 (*d*, C(3)); 136.75 (*s*, C(8a)); 164.61 (*s*, 2 CO_2). FAB-MS: 777 (13), 776 (13), 775 (23), 774 (3), 773 (4), 772 (4), 771 (4, $[M + 1]^+$), 770 (5), 742 (100), 741 (13), 740 (16, $[M - OMe + 1]^+$), 611 (15), 610 (41), 608 (97), 115 (39, Et_3Si^+), 87 (60).

(5R,6R,7S,8S)-5,6,7,8-Tetrahydro-6,7,8-tris(triethylsilyloxy)-5-[(triethylsilyloxy)methyl]indolizine-1,2-dimethanol (**14**). At 25°, a soln. of **13** (41 mg, 0.053 mmol) in THF (2 ml) was treated with $LiAlH_4$ (20 mg, 0.53 mmol) and stirred for 2 h. Normal workup and FC (CH_2Cl_2 → CH_2Cl_2/AcOEt 3:1) gave **14** (30 mg, 79%). Oil. R_f (CH_2Cl_2/AcOEt 8:2) 0.49. UV ($CHCl_3$): 241 (3.8). IR ($CHCl_3$): 3407*m*, 3004*w*, 2958*s*, 2913*s*, 2878*s*, 1531*w*, 1459*m*, 1415*m*, 1364*m*, 1261*w*, 1102*s*, 1006*s*. ^{1}H-NMR ($CDCl_3$): 0.52–0.68 (*m*, 12 CH_2Si); 0.87–1.00 (*m*, 12 Me); 3.43 (br. *s*, 2 OH); 3.77 (*dd*, $J = 1.7$, 5.8, irrad. at 4.1 → *s*, H–C(6)); 3.91 (*dd*, $J = 7.3$, 10.4, irrad. at 4.05 → *d*, $J \approx 5.6$, CH–C(5)); 4.05 (*dd*, $J = 4.4$, 10.5, CH–C(5)); 4.06–4.12 (*m*, irrad. at 3.77 → change, irrad. at 3.91 → change, irrad. at 4.05 → change, H–C(7), H–C(5)); 4.55–4.63 (*m*, CH_2O); 4.72 (*d*, $J = 2.2$, irrad. at 4.1 → *s*, H–C(8)); 6.89 (*s*, H–C(3)). ^{13}C-NMR ($CDCl_3$): 4.44 (*t*, (MeCH_2)$_3$Si); 4.99 (*t*, 2 (MeCH_2)$_3$Si); 5.12 (*t*, (MeCH_2)$_3$Si); 6.78 (*q*, (*Me*CH_2)$_3$Si); 6.85 (*q*, (*Me*CH_2)$_3$Si); 6.90 (*q*, 2 (*Me*CH_2)$_3$Si); 56.14 (*t*, CH_2O); 57.74 (*t*, CH_2O); 61.48 (*d*, C(5)); 63.68 (*t*, CH_2–C(5)); 66.45 (*d*, C(8)); 74.15, 77.66 (2*d*, C(6), C(7)); 118.54 (*d*, C(3)); 119.80 (*s*), 121.94 (*s*, C(1), C(2)); 127.92 (*s*, C(8a)). FAB-MS: 716 (12, $[M + 1]^+$), 715 (21), 701 (20), 700 (41), 699 (74), 698 (100, $[M - H_2O + 1]^+$), 697 (16, $[M - H_2O]^+$), 696 (25), 687 (14), 686 (25), 685 (23), 684 (37), 683 (10), 682 (16), 670 (10), 669 (11), 668 (17), 584 (24, $[M - OSiEt_3]^+$), 566 (14), 115 (5, Et_3Si^+).

(5R,6R,7S,8S)-5,6,7,8-Tetrahydro-6,7,8-trihydroxyindolizine-1,2,5-trimethanol (**15**). A soln. of **14** (163 mg, 0.23 mmol) in THF (12 ml) was treated with $Bu_4NF \cdot 3\,H_2O$ (90 mg, 0.28 mmol) and stirred for 12 h. Evaporation and FC (silicic acid, AcOEt → AcOEt/MeOH 10:2) gave **15** (60 mg, 83%) as an oil which crystallized in EtOH/H_2O. M.p. 160°. UV (H_2O): 230 (3.8). ^{1}H-NMR (D_2O): 3.70 (*dd*, $J = 7.9$, 9.2, irrad. at 4.73 → *d*, $J \approx 9.3$, H–C(7)); 3.81 (*t*, $J = 9.2$, H–C(6)); 3.88 (*td*, $J \approx 2.5$, 9.0, H–C(5)); 4.05 (*dd*, $J = 2.2$, 12.8, irrad. at 3.88 → *d*, $J \approx 12.1$, HC–C(5)); 4.22 (*dd*, $J = 2.2$, 12.8, irrad. at 3.88 → *d*, $J \approx 12.1$, HC–C(5)); 4.53 (*s*, CH_2O); 4.61 (*d*, $J = 12.5$), 4.72 (*d*, $J = 12.5$, CH_2O); 4.73 (*d*, $J = 7.8$, irrad. at 3.70 → *s*, H–C(8)); 6.92 (*s*, H–C(3)).

^{13}C-NMR (D_2O): 56.95 (*t*, CH_2O); 57.98 (*t*, CH_2O); 61.38 (*t*, CH_2–C(5)); 63.44 (*d*, C(5)); 70.28 (*d*); 71.51 (*d*); 78.76 (*d*); 120.06 (*d*, C(3)); 121.32, 125.82 (2*s*, C(1), C(3)); 131.74 (*s*, C(8a)). FAB-MS: 282 (14, $[M + Na]^+$), 259 (11), 242 (100, $[M - OH]^+$), 184 (13), 176 (16).

*(5*R*,6*R*,7*S*,8*S*)-6,7,8-Tris(benzyloxy)-5-[(benzyloxy)methyl]-5,6,7,8-tetrahydro-2-(4-tolylsulfonyl)imidazo-[1,2-a]pyridine* (**23**) *and 2,3,4,6-Tetra-*O*-benzyl-5-[(carbamoylmethyl)amino]-5-deoxy-*D*-glucono-1,5-lactam* (**22**). At −20°, a mixture of **8** (105 mg, 0.176 mmol) and 4-toluenesulfonyl cyanide (319 mg, 1.76 mmol) in CH_2Cl_2 (0.7 ml) was treated with MsCl (68 µl, 0.875 mmol) and ethyldiisopropylamine (181 µl, 1.06 mmol), stirred overnight, treated with H_2O/sat. aq. $NaHCO_3$ soln. 1:1 (10 ml), and stirred for further 3 h. The aq. phase was extracted with CH_2Cl_2 (3 × 20 ml). Drying of the combined org. phases ($MgSO_4$), evaporation, and FC (AcOEt/hexane 1:3 → 1:2) gave **23** (66 mg, 53%). Elution of the column with MeOH and FC (AcOEt) of the residue gave **22** (23.9 mg, 23%). A sample of **23** was recrystallized in CH_2Cl_2/Et_2O 1:5.

Data of **23**: White solid. M.p. 132–133°. R_f (AcOEt/hexane 1:2) 0.37. $[\alpha]_D^{25} = 26.7$ ($c = 0.43$, $CHCl_3$). UV ($CHCl_3$): 243 (4.2). IR ($CHCl_3$): 3158*w*, 3090*w*, 3067*w*, 3007*m*, 2924*w*, 2869*m*, 1952*w*, 1878*w*, 1810*w*, 1598*m*, 1497*m*, 1454*m*, 1362*m*, 1320*s*, 1304*s*, 1153*s*, 1110 (sh), 1100 (sh), 1084*s*, 1028*m*, 912*w*, 600*s*, 535*m*. ^{1}H-NMR ($CDCl_3$): 2.41 (*s*, Me); 3.72 (*dd*, $J = 5.6$, 10.6, HC–C(5)); 3.83 (*t*, $J = 7.3$, H–C(6)); 3.84 (*dd*, $J = 2.8$, 10.6, HC–C(5)); 4.07 (*dd*, $J \approx 5.0$, 7.0, H–C(7)); 4.21 (*ddd*, $J = 2.8$, 5.6, 7.5, H–C(5)); 4.46 (*d*, $J = 11.8$, PhC*H*); 4.48 (*d*, $J = 11.2$, PhC*H*); 4.51 (*d*, $J = 12.1$, PhC*H*); 4.64 (*d*, $J = 11.5$, PhC*H*); 4.72 (*d*, $J = 5.0$, H–C(8)); 4.73 (*d*, $J = 10.9$, PhC*H*); 4.77 (*d*, $J = 11.2$, PhC*H*); 4.81 (*d*, $J = 11.5$, PhC*H*); 5.09 (*d*, $J = 11.2$, PhC*H*); 7.16–7.20 (*m*, 2 arom. H); 7.24–7.44 (*m*, 20 arom. H); 7.80 (*s*, H–C(3)); 8.01 (*d*, $J = 8.4$, 2 arom. H). ^{13}C-NMR ($CDCl_3$): 21.70 (*q*, Me); 59.00 (*d*, C(5)); 68.03 (*t*, CH_2–C(5)); 72.77 (*t*, PhCH_2); 73.29 (*d*, C(8)); 73.56 (*t*, PhCH_2); 74.01 (*t*, PhCH_2); 74.22 (*t*, PhCH_2); 75.57, 80.94 (2*d*, C(6), C(7)); 122.48 (*d*, C(3)); 128.11–128.97 (several *d*); 129.88 (2*d*); 137.22 (*s*); 137.53 (*s*); 137.77 (*s*); 138.01 (*s*); 138.61 (*s*); 142.24 (*s*); 144.18, 146.38 (2*s*, C(8a), C(2)). FAB-MS: 715 (55, $[M + 1]^+$), 607 (7), 395 (5), 91 (100). Anal. calc. for $C_{43}H_{42}N_2O_6S$ (714.88): C 72.25, H 5.92, N 3.92; found: C 72.31, H 5.91, N 3.94.

Data of **22**: R_f (AcOEt) 0.41. IR ($CHCl_3$): 3482*w*, 3350*w*, 3090*w*, 3067*w*, 3008*m*, 2926*w*, 2869*w*, 1683*s*, 1601*m*, 1496*w*, 1455*m*, 1365*w*, 1329*w*, 1093*s*, 1073*s*, 912*w*, 603*w*. ^{1}H-NMR ($CDCl_3$): 3.56 (*dd*, $J = 6.0$, 10.0, H–C(6)); 3.64 (*dd*, $J = 5.6$, 10.0, H′–C(6)); 3.71–3.75 (*m*, H–C(5)); 3.78 (*d*, $J = 16.8$, NCHCO); 3.89 (*dd*, $J = 3.4$, 3.7, H–C(4)); 3.94 (*ddd*, $J = 1.25$, 3.4, 6.5, H–C(3)); 4.11 (*d*, $J = 6.5$, H–C(2)); 4.35 (*d*, $J = 16.8$, NCHCO); 4.40 (*d*, $J = 12.4$, PhC*H*); 4.42 (*d*, $J = 11.2$, PhC*H*); 4.47 (*d*, $J = 11.8$, PhC*H*); 4.59 (*d*, $J = 11.5$, PhC*H*); 4.60 (*d*, $J = 11.2$, PhC*H*); 4.66 (*d*, $J = 11.2$, PhC*H*); 4.69 (*d*, $J = 11.5$, PhC*H*); 5.12 (*d*, $J = 11.5$, PhC*H*); 5.13 (br. *s*, exchange with CD_3OD, NH); 6.97 (br. *s*, exchange with CD_3OD, NH); 7.18–7.65 (*m*, 20 arom. H). ^{13}C-NMR ($CDCl_3$): 50.54 (*t*, CH_2N); 62.29 (*d*, C(5)); 67.98 (*t*, C(6)); 72.57 (*t*, PhCH_2); 73.24 (*t*, PhCH_2); 73.55 (*t*, PhCH_2); 74.61 (*t*, PhCH_2); 75.79, 78.71, 81.41 (3*d*, C(2), C(3), C(4)); 128.05–128.91 (several *d*); 136.80 (*s*); 137.46 (*s*); 137.82 (*s*); 138.03 (*s*); 170.22, 171.31 (2*s*, C(1), $CONH_2$). FAB-MS: 617 (65, $[M + Na]^+$), 595 (31, $[M + 1]^+$), 594 (5, M^+), 578 (35), 91 (100).

Alternative Preparation of **22**. At r.t., a mixture of **8** (40 mg, 68 µmol) and DCC (40 mg, 194 µmol) in THF (2 ml) was stirred for 1 h, treated with 25% aq. NH_3 soln. (0.75 ml), and stirred for further 10 min. Evaporation and FC (AcOEt/hexane 3:1) gave **22** (17 mg, 42%) as an oil.

*(5*R*,6*R*,7*S*,8*S*)-5,6,7,8-Tetrahydro-5-(hydroxymethyl)-2-(4-tolylsulfonyl)imidazo[1,2-a]pyridine-6,7,8-triol* (**24**). A soln. of **23** (82.5 mg, 0.60 mmol) in AcOEt/MeOH/CH_2Cl_2 10:30:3 (4.3 ml) was treated with 2N HCl (0.3 ml) and 20% $Pd(OH)_2$/C (100 mg) and hydrogenated at atmospheric pressure for 45 min. The suspension was filtered through *Celite*. Evaporation of the filtrate and crystallization from EtOH gave **24** (30 mg, 73%). White crystals suitable for X-ray analysis. M.p. 150°. R_f (AcOEt/MeOH 4:1) 0.2. ^{1}H-NMR (D_2O): 2.41 (*s*, Me); 3.76 (*dd*, $J = 8.7$, 10.0, irrad. at 4.56 → change, irrad. at 3.91 → change, H–C(7)); 3.91 (*dd*, $J = 9.0$, 10.0, H–C(6)); 4.04 (*dd*, $J = 3.1$, 8.7, HC–C(5)); 4.07–4.10 (*m*, irrad. at 3.91 → change, H–C(5)); 4.20–4.27 (*m*, HC–C(5)); 4.56 (*d*, $J = 8.7$, irrad. at 3.76 → *s*, H–C(8)); 7.45 (*d*, $J = 8.1$, 2 arom. H); 7.86 (*d*, $J = 8.4$, 2 arom. H); 8.11 (*s*, H–C(3)). FAB-MS: 377 (100, $[M + Na]^+$), 355 (94, $[M + 1]^+$).

X-Ray Analysis of **24** · 0.5 AcOEt: Monoclinic *P*21; $a = 8.164(2)$, $b = 6.8394(1)$, $c = 14.164(7)$; $\beta = 90.77(3)°$; $V = 790.8(4)$ Å^3; $D_{calc} = 1.488$ Mg/m^3; $Z = 2$. The reflexions were measured on an *Enraf-Nonius-CAD4* diffractometer (graphite monochromator, MoK_α, $\lambda = 0.71073$) at 293 K. $R = 0.0297$, $R_w = 0.0830$. The structures were solved with the direct-methods routine of SHELX-86 and the refinement performed with SHELXL-92 [51] [52].

*(5*R*,6*R*,7*S*,8*S*)-5-(Acetoxymethyl)-6,7,8-tris(benzyloxy)-5,6,7,8-tetrahydro-2-(4-tolylsulfonyl)imidazo[1,2-a]-pyridine* (**25**). At −15°, a soln. of **23** (19 mg, 0.027 mmol) in Ac_2O/CH_2Cl_2 8:2 (1 ml) was treated with $BF_3 \cdot OEt_2$ (0.1 ml, 0.56 mmol), stirred 2 h at −15°, and 12 h at 5°. The soln. was treated at 5° with sat. aq. $NaHCO_3$ soln. (10 ml). The aq. phase was extracted with $CHCl_3$ (3 × 10 ml). Drying of the combined org. phases ($MgSO_4$), evaporation, and FC (AcOEt/hexane 1:2) gave **25** (13 mg, 73%). R_f (AcOEt/hexane 2:3) 0.31. IR ($CHCl_3$): 2979*s*,

2928*s*, 2873*s*, 1747*m*, 1603*w*, 1496*m*, 1456*m*, 1383*m*, 1321*w*, 1262*m*, 1154*s*, 1110*s*, 1019*m*, 909*s*. ^{1}H-NMR ($CDCl_3$): 2.02 (*s*, Ac); 2.41 (*s*, Me); 3.75 (*dd*, J = 6.2, 6.5, irrad. at 4.07 → change, irrad. at 4.25 → *d*, $J \approx 6.0$, H–C(6)); 4.07 (*dd*, J = 4.4, 6.2, irrad. at 4.69 → *d*, J = 6.2, H–C(7)); 4.21–4.28 (*m*, irrad. at 3.75 → change, irrad. at 4.50 → change, H–C(5)); 4.28 (*dd*, J = 5.9, 9.3, irrad. at 4.50 → change, HC–C(5)); 4.49 (*d*, 11.2, PhC*H*); 4.50 (*dd*, J = 6.0, 9.3, irrad. at 4.25 → change, HC–C(5)); 4.56 (*d*, J = 11.5, PhC*H*); 4.69 (*d*, J = 4.4, irrad. at 4.07 → *s*, H–C(8)); 4.71 (*d*, J = 11.8, PhC*H*); 4.71 (*d*, J = 11.2, PhC*H*); 4.76 (*d*, J = 11.5, PhC*H*); 4.98 (*d*, J = 11.5, PhC*H*); 7.18–7.34 (*m*, 17 arom. H); 7.62 (*s*, H–C(3)); 7.98 (*d*, J = 8.4, 2 arom. H). ^{13}C-NMR ($CDCl_3$): 21.64 (*q*, Me); 22.18 (*q*, Me); 57.89 (*d*, C(5)); 62.34 (*t*, CH_2–C(5)); 72.18 (*d*, C(8)); 72.46 (*t*, PhCH_2); 73.54 (*t*, 2 PhCH_2); 74.65, 79.64 (2*d*, C(6), C(7)); 121.57 (*d*, C(3)); 128.15–128.84 (several *d*); 129.88 (2*d*); 137.00 (*s*); 137.20 (*s*); 137.54 (*s*); 138.00 (*s*); 144.08 (*s*); 145.86, 149.67 (2*s*, C(8a), C(2)); 166.46 (*s*, C=O). FAB-MS: 667 (100, $[M + 1]^+$), 559 (13), 505 (15), 393 (16), 322 (14), 91 (31).

Reaction of **8** *with Phenyl Cyanate.* A mixture of **8** (54 mg, 0.091 mmol) and phenyl cyanate (200 mg, 5.7 mmol) [43] was treated with Ac_2O (0.04 mol, 0.4 mmol), and heated for 2 h at 100°. Evaporation and FC (hexane/Et_2O 1:0 → 1:2) gave **28** (10 mg, 16.9), **26** (10 mg, 16.4%), and **27** (10 mg, 15.5%).

*(5*R*,6*R*,7*S*,8*S*)-6,7,8-Tris(benzyloxy)-5-[(benzyloxy)methyl]-5,6,7,8-tetrahydro-2-phenoxyimidazo[1,2-a]-pyridine* (**28**): R_f (AcOEt/hexane 1:1) 0.45. UV ($CHCl_3$): 242 (4.0). IR ($CHCl_3$): 3090*w*, 3066*m*, 3008*w*, 2934*w*, 2863*w*, 1596*w*, 1556*s*, 1491*s*, 1456*m*, 1359*s*, 1262*s*, 1175*m*, 1096*m*. ^{1}H-NMR ($CDCl_3$): 3.71 (*dd*, J = 4.9, 10.3, HC–C(5)); 3.86 (*dd*, J = 3.0, 10.4, HC–C(5)); 3.87 (*t*, J = 7.7, H–C(6)); 4.08 (*dd*, J = 5.7, 7.8, irrad. at. 4.70 → *d*, $J \approx 7.9$, H–C(7)); 4.08–4.17 (*m*, H–C(5)); 4.38 (*d*, J = 12.0, PhC*H*); 4.46 (*d*, J = 12.0, PhC*H*); 4.52 (*d*, J = 11.3, PhC*H*); 4.70 (*d*, J = 5.7, H–C(7)); 4.71 (*d*, J = 10.1, PhC*H*); 4.85 (*d*, J = 11.5, 2 PhC*H*); 4.86 (*d*, J = 11.2, PhC*H*); 5.19 (*d*, J = 11.4, PhC*H*); 6.54 (*s*, H–C(3)); 7.05–7.50 (*m*, 25 arom. H). ^{13}C-NMR ($CDCl_3$): 58.37 (*d*, C(4)); 68.12 (*t*, CH_2–C(5)); 72.83 (*t*, PhCH_2); 73.29 (*t*, PhCH_2); 74.22 (*t*, PhCH_2); 74.30 (*d*, C(8)); 74.42 (*t*, PhCH_2); 75.60, 81.87 (2*d*, C(6), C(7)); 101.10 (*d*, C(3)); 117.60 (2*d*); 121.47 (*d*); 127.50–129.50 (several *d*); 137.20 (*s*); 137.58 (*s*); 137.89 (*s*); 138.15 (*s*); 139.57 (*s*); 151.65, 152.93 (2*s*, C(2), C(8a)); 157.67 (*s*). FAB-MS: 1305 (32, $[2\ M + 1]^+$), 653 (100, $[M + 1]^+$), 652 (11, M^+), 561 (14), 545 (27, $[M - \text{BnOH} + 1]^+$), 439 (14), 91 (90).

*2,3,4,6-Tetra-*O*-benzyl-5-deoxy-5-{[(phenoxycarbonyl)methyl]amino}-*D*-glucono-1,5-lactam* (**26**): R_f (hexane/Et_2O 1:1) 0.33. IR ($CHCl_3$): 3067*m*, 3008*m*, 2868*m*, 1713*s*, 1672*s*, 1593*m*, 1563*m*, 1492*s*, 1474*s*, 1456*s*, 1373*s*, 1289*m*, 1173*s*, 1095*m*. ^{1}H-NMR ($CDCl_3$): 3.55–3.62 (*m*, 2 H–C(6)); 3.71–3.77 (*m*, H–C(5)); 3.80 (*t*, J = 6.4, H–C(4)); 3.96 (*dd*, J = 6.9, 8.5, H–C(3)); 4.11 (*d*, J = 8.5, H–C(2)); 4.30 (*d*, J = 17.2, NCHCO); 4.42 (*s*, 2 PhC*H*); 4.51 (*d*, J = 11.5, PhC*H*); 4.62 (*d*, J = 17.0, NCHCO); 4.66 (*d*, J = 11.2, PhC*H*); 4.70 (*d*, J = 11.8, PhC*H*); 4.77 (*d*, J = 11.6, PhC*H*); 4.86 (*d*, J = 11.3, PhC*H*); 5.15 (*d*, J = 11.6, PhC*H*); 7.00–7.50 (*m*, 25 arom. H). ^{13}C-NMR ($CDCl_3$): 47.03 (*t*, NCH_2CO); 61.19 (*d*, C(5)); 68.83 (*t*, C(6)); 73.33 (*t*, PhCH_2); 73.47 (*t*, PhCH_2); 74.32 (*t*, 2 PhCH_2); 77.10, 78.12, 81.02 (3*d*, C(2), C(3), C(4)); 121.40 (2*d*); 125.95 (*d*); 126.00–130.00 (several *d*); 137.28 (*s*); 137.73 (*s*); 137.95 (*s*); 138.04 (*s*); 150.43 (*s*); 167.70, 170.20 (2*s*, C(1), CO_2). FAB-MS: 1345 (10), 1343 (22, $[2M + 1]^+$), 673 (39), 672 (100, $[M + 1]^+$), 670 (20), 358 (10), 181 (31).

*2,3,4,6-Tetra-*O*-benzyl-5-deoxy-5-{{[(phenoxycarbonyl)carbamoyl]methyl}amino}-*D*-glucono-1,5-lactam* (**27**): R_f (hexane/Et_2O 1:1) 0.13. IR ($CHCl_3$): 3393*w*, 3268*w*, 3067*w*, 3008*m*, 2869*m*, 1801*s*, 1730*s*, 1677*s*, 1597*m*, 1561*s*, 1519*s*, 1491*m*, 1456*m*, 1373*s*, 1173*s*, 1088*m*. ^{1}H-NMR (200 MHz, $CDCl_3$): 3.50–3.60 (*m*, 2 H–C(6)); 3.62–3.69 (*m*, H–C(5)); 3.78 (*t*, J = 4.4, H–C(4)); 3.93 (*dd*, J = 4.6, 6.7, H–C(3)); 4.10 (*d*, J = 7.1, H–C(2)); 4.24 (*d*, J = 17.6,NCHCO); 4.36 (*d*, J = 12.3, PhC*H*); 4.45 (*d*, J = 11.6, PhC*H*); 4.48 (*d*, J = 10.1, PhC*H*); 4.56 (*d*, J = 17.4, NCHCO); 4.57 (*d*, J = 11.5, PhC*H*); 4.67 (*d*, J = 11.0, PhC*H*); 4.70 (*d*, J = 11.6, PhC*H*); 4.77 (*d*, J = 12.3, PhC*H*); 5.13 (*d*, J = 11.3, PhC*H*); 7.00–7.50 (*m*, 25 arom. H, NH). ^{13}C-NMR (50 MHz, $CDCl_3$): 51.54 (*t*, NCH_2CO); 62.66 (*d*, C(5)); 68.50 (*t*, C(6)); 72.79 (*t*, PhCH_2); 73.58 (*t*, PhCH_2); 73.70 (*t*, PhCH_2); 74.78 (*t*, PhCH_2); 75.30, 78.91, 81.13 (3*d*, C(2), C(3), C(4)); 121.72 (2*d*); 126.38 (*d*); 126.00–130.00 (several *d*); 137.34 (*s*); 137.56 (*s*); 138.00 (*s*); 138.07 (*s*); 149.69 (*s*, NCO_2); 151.97 (*s*); 168.62, 170.84 (2*s*, C(1), CON). FAB-MS: 1430 (3, $[2M + 1]^+$), 715 (100, $[M + 1]^+$), 578 (19), 358 (16), 154 (43).

Inhibition of Glucosidases. Determinations of the inhibition constants (K_i) were performed at different concentrations of the inhibitor (usually 4–6 concentrations) which bracket the K_i value.

a) Inhibition of sweet-almond β-glucosidases: Inhibition constants (K_i) were determined at 37°, using a 0.08M KH_2PO_4/K_2HPO_4 buffer (pH 6.8), and 4-nitrophenyl β-D-glucopyranoside as substrate. Measurements were started by addition of the substrate. 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). K_i were determined by taking the slopes from the *Lineweaver-Burk* plots [53] and plotting them against the inhibitor concentration [54]. After fitting the data to a straight line, the negative [*I*] intercept of this plot gave the appropriate K_i.

b) Inhibition of *Caldocellum saccharolyticum* β-glucosidase: Similarly as *a*). The inhibition constants were determined at 55°.

c) Inhibition of brewers yeast α-glucosidase: Similarly as *a*). The inhibition constants were determined at 37° using 0.025M KH_2PO_4/K_2HPO_4/NaCl buffer (pH 6.8), and 4-nitrophenyl α-D-glucopyranoside as substrate.

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