

Synthesis of New *C*(2)-Substituted *gluco*-Configured Tetrahydroimidazopyridines and Their Evaluation as Glucosidase Inhibitors

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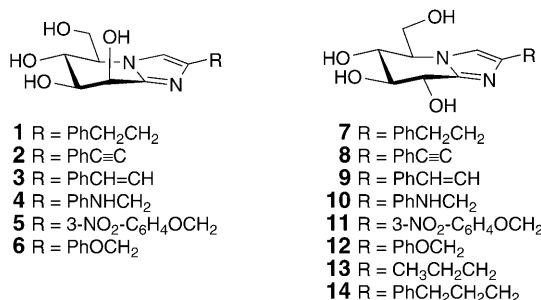
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Albert Eschenmoser zum 80. Geburtstag mit herzlichen Glückwünschen zugeeignet.

The *gluco*-configured *C*(2)-substituted tetrahydroimidazopyridines **8–14** were prepared and tested as inhibitors of the β -glucosidases from *Caldocellum saccharolyticum* and from sweet almonds, and of the α -glucosidase from brewer's yeast. All new imidazopyridines are nanomolar inhibitors of the β -glucosidases and micromolar inhibitors of the α -glucosidase. The 3-phenylpropyl derivative **14** proved the strongest inhibitor of the *Caldocellum* β -glucosidase ($K_i=0.9$ nM), only slightly weaker than the known 2-phenylethyl analogue **7**, and the propyl derivative **13** is the strongest inhibitor of the sweet almond β -glucosidases ($K_i=3.2$ nM), again slightly weaker than **7**. There is no strong dependence of the inhibition on the nature of the *C*(2)-substituent and no clear correlation between the inhibitory strength of the known *manno*-configured imidazopyridines **2–6** and the *gluco*-analogues **8–12**. While most *manno*-imidazopyridines are competitive inhibitors, the *gluco*-analogues proved non-competitive inhibitors of the *Caldocellum* β -glucosidase and mixed-type or partial mixed-type inhibitors of the sweet almond β -glucosidases.

Introduction. – A recent comparison of the inhibition of retaining β -glucosidases and snail β -mannosidase [1–3] by *C*(2)-substituted *manno*- and *gluco*-configured tetrahydroimidazopyridines [4–11] and by appropriately configured isoquinuclidines [12–14] strongly suggested that β -glucosidases and β -mannosidases use a different conformational itinerary to attain a similar transition state. In the course of this work, we noticed that the nature of the *C*(2)-substituent of the *gluco*-, *manno*-, and GlcNAc-derived tetrahydroimidazopyridines had an analogous effect on the strength of the inhibition of the β -glucosidases from *Caldocellum saccharolyticum* [15], β -mannosidase from snail [8], and *N*-acetyl β -glucosaminidase from bovine kidney [16], respectively. We also found that the *manno*-configured inhibitors **2–6** [17] for which there were no *gluco*-configured counterparts are particularly strong inhibitors of snail β -mannosidase, *ca.* 3–5 times stronger than **1** ($K_i=20$ nM) [17], the *manno*-analogue of the *gluco*-configured 2-phenylethyl imidazopyridine **7** that is so far the strongest known inhibitor of a retaining β -glucosidase ($K_i=0.1$ nM, *C. saccharolyticum*) [15]. The parallel effect of the *C*(2)-substituents on the strength of the inhibition suggested that the *gluco*-configured imidazopyridines **8–12** corresponding to **2–6** should be stronger inhibitors than **7**. However, a comparison of the *gluco*- and *manno*-configured *C*(2)-substituted imidazopyridines shows that the analogous effect of the *C*(2)-substituent on the strength of the inhibition is not reflected by a similarity of the type of inhibition (mixed, competitive, or non-competitive), casting some doubt on the validity of the above extrapolation. In view of these considerations and of our interest in very strong glucosidase inhibitors, we decided to prepare the *gluco*-analogues **8–12**. Considering the strong inhibition by the

2-phenylethyl derivative **7**, we also wished to synthesise the propyl derivative **13** and the 3-phenylpropyl derivative **14**.



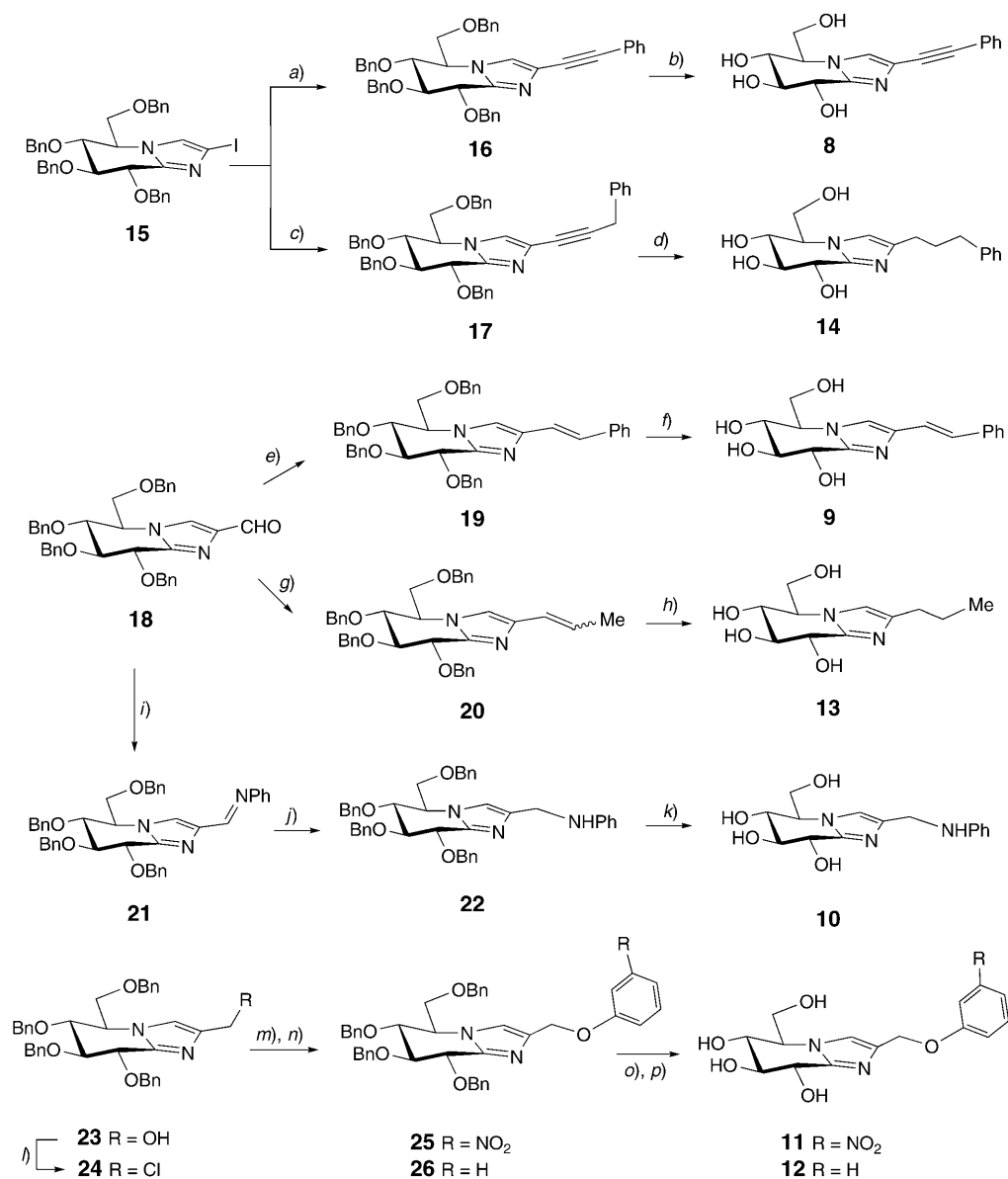
Synthesis. – We prepared the *gluco*-analogues **8–14** via the 2-iodo-imidazopyridine **15**, according to the established synthesis of the corresponding *manno*-imidazopyridines [17]. The compound **15** is available in five steps and in an overall yield of 50–53% from 5-amino-2,3,4,6-tetra-*O*-benzyl-5-deoxy-D-gluconolactam [18–20].

Sonogashira coupling [21] of **15** (Scheme) with phenylacetylene yielded 76% of the known phenylethynyl derivative **16** [15] that was debenzylated (BCl₃) to the desired phenylethynyl imidazopyridine **8** (59%). Similarly, the *Sonogashira* coupling of **15** with 3-phenylprop-1-yne yielded **17** that was hydrogenated to the 3-phenylpropyl-imidazopyridine **14** (31% from **15**).

For the synthesis of the remaining inhibitors, we transformed **15** into the known carbaldehyde **18** and the known alcohol **23** [15]. *Wittig–Horner* reaction of **18** with diethyl benzylphosphonate gave the known 2-phenylethenyl derivative **19** [15] that was debenzylated with AlCl₃ in the presence of *N,N*-dimethylaniline to yield 60% of **9**. *Wittig* olefination of **18** with (ethyldiene)(triphenyl)phosphorane yielded 88% of **20** as 45 : 55 (*E*)/(*Z*) mixture that was hydrogenated to provide the propyl-imidazopyridine **13** (82%). The (phenylamino)methyl derivative **10** was obtained by reductive amination of **18** (77%). Treatment of **18** with aniline provided the (phenylimino)methyl derivative **21** that was reduced with NaBH₄ and then debenzylated with BCl₃ (61%). The (3-nitrophenoxy)methyl derivative **11** was obtained in a yield of 34% by treatment of the hydroxymethyl-imidazopyridine **23** with 1-fluoro-3-nitrobenzene and NaH, followed by debenzylation of the resulting **25** with AlCl₃ in the presence of anisole, while the phoxymethyl derivative **26** was prepared in a yield of 77% by alkylation of phenol with the (chloromethyl)-imidazopyridine **24**, followed by hydrogenolysis (63%). The compound **24** was readily obtained in a yield of 91% from **23** and SOCl₂.

Enzymatic Tests and Discussion. – The *gluco*-imidazopyridines **8–14** were tested as inhibitors of the β-glucosidase from *Caldocellum saccharolyticum* (0.08M phosphate buffer, pH 6.8, 55°), the β-glucosidases from sweet almonds (0.08M phosphate buffer, pH 6.8, 37°), and the α-glucosidase from brewer's yeast (0.08M phosphate buffer, pH 6.8, 37°). Table 1 summarises the results, listing the *manno*- and the corresponding *gluco*-configured imidazopyridines in order of decreasing inhibitory strength of the *manno*-isomers. Although all *gluco*-imidazopyridines are nanomolar inhibitors of the

Scheme



a) Phenylacetylene, [Pd(PPh₃)₄], CuI, Et₃N; 76%. b) BCl₃, CH₂Cl₂; 59%. c) 3-Phenylprop-1-yne, [Pd(PPh₃)₄], CuI, Et₃N; 58%. d) H₂, Pd/C, AcOH; 53%. e) Diethyl benzylphosphonate, *t*-BuOK, THF; 81%. f) AlCl₃, CH₂Cl₂, *N,N*-dimethylaniline; 75%. g) Ethyl(triphenyl)phosphonium bromide, BuLi, THF; 88%. h) Pd/C, 6 bar of H₂, AcOH, 82%. i) Aniline, 4-Å mol. sieves, CH₂Cl₂. j) NaBH₄, EtOH; 77% from **18**. k) BCl₃, CH₂Cl₂, -78° to 15°; 61%. l) SOCl₂, CH₂Cl₂; 91%. m) 1-Fluoro-3-nitrobenzene, NaH, DMF; 59% of **25**. n) PhOH, *t*-BuOK, DMF; 77% of **26**. o) AlCl₃, anisole, CH₂Cl₂; 58% of **11**. p) H₂, Pd(OH)₂/C, AcOEt/MeOH/H₂O/AcOH; 63% of **12**.

Table 1. Inhibition of the β -Glucosidases from *C. saccharolyticum* and Sweet Almonds, the α -Glucosidase from Brewer's Yeast, and the β -Mannosidase from Snail by the *C*(2)-Substituted gluco- and manno-Imidazoles: K_i and pK_{HA} Values

R	Inhibition of β -mannosidase ^{a)b)}			Inhibition of β -glucosidases				Inhibition of α -glucosidase
	<i>manno</i> - Imidazoles	pK_{HA}	K_i [nM] ^{c)}	<i>gluco</i> - Imidazoles	pK_{HA}	from <i>C. sacch.</i> ^{d)e)} K_i [nM]	from sweet almonds ^{f)g)} K_i [nM](α)	from brewer's yeast ^{f)h)} K_i [nM]
PhCH=CH	3	4.77	6	9	4.83	2.6	7.6 (1.3)	3230
PhC $\equiv$ C	2	ⁱ⁾	7	8	ⁱ⁾	7.4	2.4 (1.1)	7300
PhCH ₂ NH	4	5.09 ^{j)}	8	10	5.62/9.51	2.3	5.4 (4.4)	1920
3-NO ₂ -C ₆ H ₄ OCH ₂	5	4.36	12	11	4.46	2.2	6.6 (2.0)	1770
PhOCH ₂	6	4.39	12	12	4.69	2.4	9.7 (2.0)	3220
MeCH ₂ CH ₂				13	6.42	1.6	3.2 (1.1)	1890
PhCH ₂ CH ₂ CH ₂				14	6.63	0.9	8.5 (0.9)	450
PhCH ₂ CH ₂	1	6.04	20	7^{k)}	6.03	0.11 ^{l)}	1.2	500

^{a)} At 25° and pH 4.5. ^{b)} Data taken from [17]. ^{c)} Competitive-type inhibition except for **3**. ^{d)} At 55° and pH 6.8. ^{e)} Non-competitive-type inhibition. ^{f)} At 37° and pH 6.8. ^{g)} Mixed-type inhibition except for **14** (partial mixed type) [22]. ^{h)} IC_{50} . ⁱ⁾ No inflection of the titration curve was observed within pH 2.1–5.4. ^{j)} Second pK value not reported. ^{k)} Data taken from [15]. ^{l)} Mixed-type inhibition ($\alpha=15$).

β -glucosidases, none was stronger than the 2-phenylethyl derivative **7**. The strength of the inhibition of the *C. saccharolyticum* β -glucosidase does not vary widely, with K_i values of 0.9 and 7.4 nM for the strongest and weakest inhibitors **14** and **8**, respectively, that correspond to **2–6**.

This is also observed for the inhibition of the sweet almond β -glucosidases that were inhibited less strongly than the *Caldocellum* enzyme, as noticed earlier for related imidazopyridines [15]. The extreme K_i values for the *gluco*-analogues of the *manno*-imidazopyridines **2–6** are 24 nM for **8** and 5.4 nM for **10**. An even stronger inhibitor is the propyl derivative **13** with a K_i of 1.6 nM for the *Caldocellum* β -glucosidase and 3.2 nM for the sweet almond enzymes. The 3-phenylpropyl derivative **14** proved the strongest inhibitor of the *Caldocellum* β -glucosidase ($K_i=0.9$ nM). It is, however, a weaker inhibitor of the sweet almond enzyme than **13**. In contradistinction to the inhibition by the *manno*-configured imidazopyridines that is competitive (with an exception for **3**), the *gluco*-analogues showed a non-competitive-type inhibition of the *Caldocellum* and a mixed-type inhibition of the sweet almond β -glucosidases characterised by small α -values with the exception of **14** that proved a partial mixed-type inhibitor. With micromolar K_i values characterising the inhibition of brewer's yeast α -glucosidase the *gluco*-imidazopyridines **7–14** are rather selective inhibitors of β -glucosidases. There is no obvious correlation of the strength of the inhibition with basicity. In view of the narrow range of the strength of the inhibition, one may interpret the absence of a clear correspondence of the influence of the nature of the *C*(2)-substituent on the inhibition by the *manno*- and *gluco*-imidazopyridines as denoting the limits of the effect of these aglycon mimics on the strength of the inhibition rather than as indicating a different nature of the reactive intermediates.

We thank Dr. B. Bernet for checking the experimental part, M. Schneider and D. Manser for the pK_{HA} determination, and the Swiss National Science Foundation and F. Hoffmann-La Roche, Basel, for generous financial support.

Experimental Part

General. See [16].

(5R,6R,7S,8S)-5,6,7,8-Tetrahydro-5-(hydroxymethyl)-2-(2-phenylethynyl)imidazo[1,2-a]pyridine-6,7,8-triol (**8**). A soln. of **16** [15] (38 mg, 57.5 μmol) in CH_2Cl_2 (1.5 ml) was cooled to -78° , treated with 1M BCl_3 in CH_2Cl_2 (0.9 ml, 0.923 mmol), and stirred until the mixture had reached 5° (ca. 5 h). The mixture was cooled to -78° , treated with H_2O (1 ml), and neutralised with aq. NH_3 (1 ml). Evaporation and FC (AcOEt/MeOH/ H_2O 1:0:0 $\rightarrow$ 20:1:1 $\rightarrow$ 15:1:1) gave **8** (10 mg, 59%). White hygroscopic solid. R_f (AcOEt/MeOH/ H_2O 10:1:1) 0.15. $^1\text{H-NMR}$ (CD_3OD , 300 MHz): see Table 2; additionally, 7.32–7.36 (m, H–C(3), H–C(4), and H–C(5) of Ph); 7.45–7.48 (m, H–C(2) and H–C(6) of Ph). $^{13}\text{C-NMR}$ (CD_3OD , 75 MHz): see Table 3; additionally, 83.39 (s, $\text{C}\equiv\text{C-C}(2)$); 89.76 (s, $\text{C}\equiv\text{C-C}(2)$); 124.06 (d, C(4) of Ph); 124.60 (s, C(1) of Ph, C(2)); 129.06 (2d); 131.80 (2d). HR-MALDI-MS: 323.1000 (49, $[\text{M}+\text{Na}]^+$, $\text{C}_{16}\text{H}_{16}\text{N}_2\text{NaO}_4^+$; calc. 323.1008), 301.1183 (58, $[\text{M}+\text{H}]^+$, $\text{C}_{16}\text{H}_{17}\text{N}_2\text{O}_4^+$; calc. 301.1188), 283.1071 (100, $[\text{M}-\text{OH}]^+$, $\text{C}_{16}\text{H}_{15}\text{N}_2\text{O}_3^+$; calc. 283.1083). Anal. calc. for $\text{C}_{16}\text{H}_{16}\text{N}_2\text{O}_4 \cdot \text{H}_2\text{O}$ (318.12): C 60.37, H 5.70, N 8.80; found: C 60.24, H 5.64, N 8.78.

(5R,6R,7S,8S)-6,7,8-Tris(benzyloxy)-5-[(benzyloxy)methyl]-5,6,7,8-tetrahydro-2-[(3-phenylprop-1-ynyl)-imidazo[1,2-a]pyridine (**17**). A soln. of **15** (172 mg, 0.25 mmol), CuI (5 mg, 0.026 mmol), and Et_3N (174 μl , 1.25 mmol) in degassed DMF (7 ml) was treated with $\text{Pd}(\text{PPh}_3)_4$ (14 mg, 0.012 mmol), degassed with Ar, treated with $\text{PhCH}_2\text{C}\equiv\text{CH}$ (93 μl , 0.75 mmol), heated to 80° , stirred for 2 h, cooled to r.t., diluted with Et_2O , washed with sat. NH_4Cl soln. and H_2O , dried (Na_2SO_4), and evaporated. FC (hexane/AcOEt 3:2) gave **17** (98 mg, 58%). Pale brown oil. R_f (hexane/AcOEt 2:3) 0.52. $[\alpha]_{\text{D}}^{25} = +28.7$ ($c=0.88$, CHCl_3). UV (CHCl_3): 295 (3.3), 245 (4.2). IR (CHCl_3): 3067w, 3023s, 3015s, 2869m, 2123w, 1602m, 1496m, 1454s, 1361m, 1336m, 1095s, 1028s, 911w. $^1\text{H-NMR}$ (CDCl_3 , 300 MHz): see Table 4; additionally, 3.86 (br. s, $\text{PhCH}_2\text{C}\equiv\text{C}$); 4.44 (d, $J=12.1$, PhCH); 4.48 (d, $J=12.3$, PhCH); 4.50 (d, $J=11.8$, PhCH); 4.64 (d, $J=11.3$, PhCH); 4.80 (d, $J=11.3$, PhCH); 4.81 (d, $J=12.3$, PhCH); 4.87 (d, $J=12.1$, PhCH); 5.19 (d, $J=11.5$, PhCH); 7.16–7.18 (m, 3 arom. H); 7.25–7.37 (m, 18 arom. H); 7.43–7.45 (m, 4 arom. H). $^{13}\text{C-NMR}$ (CDCl_3 , 75 MHz): see Table 3; additionally, 26.00 (t, $\text{PhCH}_2\text{C}\equiv\text{C}$); 72.75, 73.28, 73.80, 73.98 (4t, 4 PhCH_2); 126.46 (2d); 127.49 (2d); 127.80–128.44 (several d); 136.54, 137.02, 137.32, 137.53, 137.97 (5s). HR-MALDI-MS: 697.2989 (23, $[\text{M}+\text{Na}]^+$, $\text{C}_{45}\text{H}_{42}\text{N}_2\text{NaO}_4^+$; calc. 697.3042), 676.3246 (20), 675.3209 (39, $[\text{M}+\text{H}]^+$, $\text{C}_{45}\text{H}_{43}\text{N}_2\text{O}_4^+$; calc. 675.3223), 568.2649 (42), 567.2614 (100, $[\text{M}-\text{BnO}]^+$, $\text{C}_{38}\text{H}_{35}\text{N}_2\text{O}_3^+$; calc. 567.2648).

Table 2. Selected $^1\text{H-NMR}$ Chemical Shifts [ppm] and Coupling Constants [Hz] of the Deprotected C(2)-Substituted gluco-Imidazoles **8–14** in CD_3OD ^{a)}

Compound	8	9	10	11	12	13	14
H–C(3)	7.59	7.38	7.16	7.43	7.37	7.12	6.99
H–C(5)	3.89–3.91	3.85–3.90	3.77–3.82	3.87–3.89	3.86–3.89	3.87–3.89	3.80–3.84
H–C(6)	3.82	3.81	3.78	3.81	3.81	3.81	3.78
H–C(7)	3.70	3.71	3.66	3.68	3.68	3.68	3.66
H–C(8)	4.49	4.52	4.47	4.49	4.49	4.52	4.46
CH–C(5)	3.96	3.95	3.91	3.94	3.93	3.94	3.92
CH'–C(5)	4.18	4.19	4.13	4.17	4.17	4.17	4.15
$J(5,6)$	8.7	8.4	8.4	8.6	8.7	8.4	8.1
$J(6,7)$	8.7	8.4	8.1	8.9	8.7	8.7	8.4
$J(7,8)$	8.1	7.8	7.8	8.0	7.8	7.5	7.8
$J(5,\text{CH})$	4.0	3.4	3.9	4.3	4.3	3.9	3.9
$J(5,\text{CH}')$	2.0	1.5	2.1	^{b)}	1.9	1.5	2.1
$J(\text{CH},\text{CH}')$	10.8	11.8	12.0	11.0	11.5	11.5	12.0

^{a)} Assignment based on homodecoupling experiments. ^{b)} Not assigned.

Table 3. Selected ^{13}C -NMR Chemical Shifts [ppm] of the C(2)-Substituted gluco-Imidazoles **8–14**, **16**, **17**, **19**, **20**, **22**, **25**, and **26**

Compd.	Solvent	C(3)	C(5)	$\text{CH}_2\text{--C}(5)$	C(6)	C(7)	C(8)	C(8a)
16	CDCl_3	122.13	58.42	68.49	74.16	81.72	73.84	144.47
17	CDCl_3	121.12	58.34	68.28	75.78	81.27	73.99	143.53
19	CDCl_3	115.95	58.07	68.47	76.30	82.03	74.24	144.73
20 ^{a)}	C_6D_6	113.52/116.17	58.03/58.11	68.46	76.27	82.50	76.17	143.79/144.41
22 ^{b)}	CDCl_3	114.42	58.07	68.23	75.93	81.85	74.29	143.56
25 ^{b)}	CDCl_3	117.05	58.27	68.42	75.86	81.62	73.98	144.11
26 ^{b)}	CDCl_3	116.27	58.12	68.25	75.92	81.85	73.96	143.71
8	CD_3OD	122.45	62.79	61.02	69.37	76.06	68.79	148.02
9	CD_3OD	116.50	62.53	61.08	69.47	76.23	68.87	147.96
10	CD_3OD	115.38	62.44	61.09	69.48	76.21	69.05	147.09
11	CD_3OD	117.88	62.59	61.15	69.46	76.25	68.90	147.21
12	CD_3OD	116.57	61.70	60.28	68.63	75.44	68.09	146.88
13	CD_3OD	114.16	61.97	59.98	68.16	75.15	67.96	145.69
14	CD_3OD	113.67	61.60	60.17	68.50	75.44	68.07	145.79

a) (Z)/(E) 55 : 45. b) Assignment based on a HSQC spectrum.

Table 4. Selected ^1H -NMR Chemical Shifts [ppm] and Coupling Constants [Hz] of the Protected C(2)-Substituted gluco-Imidazoles **16**, **17**, **19**, **20**, **22**, **25**, and **26**

Compound	16 ^{a)}	17	19 ^{a)}	20 ^{b)}	22 ^{c)}	25 ^{c)}	26 ^{c)}
H–C(3)	^{d)}	7.19	7.06	6.82/6.94	6.93	7.15	7.11
H–C(5)	4.23	4.15–4.20	4.19	3.89–3.92	4.12–4.16	4.19	4.15–4.20
H–C(6)	3.88	3.80–3.84	3.86	3.66/3.67	3.88	3.85	3.86
H–C(7)	4.14	4.10	4.11	4.02/4.03	4.09	4.11	4.11
H–C(8)	4.76	4.74	4.78	4.77	4.74	4.75	4.76
CH–C(5)	3.76	3.72	3.75	3.40/3.41	3.72	3.74	3.74
CH'–C(5)	3.87	3.82	3.86	3.49	3.82	3.85	3.85
$J(5,6)$	6.9	^{e)}	7.8	^{e)}	7.6	7.2	7.8
$J(6,7)$	6.9	7.1	7.2	8.1	7.5	7.2	7.5
$J(7,8)$	5.0	5.2	5.3	5.9	5.6	5.3	5.3
$J(5,\text{CH})$	5.3	5.2	5.6	5.1	5.3	5.3	5.3
$J(5,\text{CH}')$	2.8	^{e)}	2.2	2.8	2.8	3.4	3.1
$J(\text{CH},\text{CH}')$	10.3	10.5	10.6	10.3	10.3	10.9	11.5

a) Data taken from [15]. b) (Z)/(E) 55 : 45 and in solvent C_6D_6 . c) Assignment based on a HSQC spectrum. d) Hidden by aromatic signals. e) Not assigned.

(5R,6R,7S,8S)-5,6,7,8-Tetrahydro-5-(hydroxymethyl)-2-(3-phenylpropyl)imidazo[1,2-a]pyridine-6,7,8-triol (**14**). A soln. of **17** (41 mg, 0.061 mmol) in AcOH (3 ml) was treated with 10% Pd/C (40 mg), hydrogenated for 72 h under 6 bar of H_2 , diluted with MeOH, and filtered over *Celite*. Evaporation, co-evaporation with toluene, and FC (AcOEt/MeOH/ H_2O 10:0:0 $\rightarrow$ 10:1:0 $\rightarrow$ 10:3:1) gave **14** (10 mg, 53%). White solid. A sample for microanalysis was dried for 4 d at 10^{-4} Torr. R_f (AcOEt/MeOH/ H_2O 10:1:1) 0.22. $[\alpha]_{25}^{+} = -28.4$ ($c = 0.53$, MeOH). UV (MeOH): 209 (4.0). IR (KBr): 3500–3180s (br.), 2922s, 2851m, 1631w, 1495w, 1452m, 1179w, 1104m, 1018m, 870w, 747w, 699m. ^1H -NMR (CD_3OD , 300 MHz): see Table 2; additionally, 1.12–1.28 (1 H), 1.61–1.71 (1 H), 1.88–1.98 (1 H), 2.48–2.67 (3 H) (4m, $\text{PhCH}_2\text{CH}_2\text{CH}_2$); 3.66 (t, $J \approx 8.4$, irrad. 4.15 $\rightarrow$ d, $J \approx 8.1$, H–C(7)); 4.46 (d, $J = 7.8$, irrad. 3.66 $\rightarrow$ s, H–C(8)); 7.12–7.26 (m, 5 arom. H). ^{13}C -NMR (CD_3OD , 75 MHz): see Table 3; additionally, 31.12, 33.36, 35.26 (3t, $\text{PhCH}_2\text{CH}_2\text{CH}_2$); 125.55 (d); 128.11 (2d); 128.30 (2d); 141.59, 142.35 (2s, C(2), C(1) of Ph). HR-MALDI-MS: 341.1474 (27, $[\text{M} + \text{Na}]^+$, $\text{C}_{17}\text{H}_{22}\text{N}_2\text{NaO}_4^+$; calc. 341.1477), 325.2114 (55), 320.1690 (25), 319.1649 (100, $[\text{M} + \text{H}]^+$, $\text{C}_{17}\text{H}_{23}\text{N}_2\text{O}_4^+$; calc. 319.1658), 301.1546 (15,

$[M - OH]^+$, $C_{17}H_{21}N_2O_4^+$; calc. 301.1552). Anal. calc. for $C_{17}H_{22}N_2O_4 \cdot H_2O$ (327.37): C 60.88, H 6.91, N 8.35; found: C 60.66, H 6.66, N 8.35.

(5R,6R,7S,8S)-5,6,7,8-Tetrahydro-5-(hydroxymethyl)-2-[(E)-2-phenylethenyl]imidazo[1,2-a]pyridine-6,7,8-triol (**9**). A soln. of **19** (29 mg, 43.6 μ mol) in CH_2Cl_2 (1 ml) was treated with $AlCl_3$ (93 mg, 0.69 mmol) and *N,N*-dimethylaniline (66 μ l, 0.52 mmol), stirred at 23° for 12 h, diluted with AcOEt, and extracted with H_2O . Evaporation of the aq. layer and FC (AcOEt/MeOH/ H_2O 1:0:0 $\rightarrow$ 20:1:1 $\rightarrow$ 15:1:1) gave **9** (10 mg, 75%). White hygroscopic solid. A sample for microanalysis was dried for 4 d at 10^{-4} Torr. R_f (AcOEt/MeOH/ H_2O 10:1:1) 0.25. 1H -NMR (CD_3OD , 300 MHz): see Table 2; additionally, 3.71 (br. t, $J \approx 8.4$, H-C(7)); 7.00 (d, $J = 17.1$, CH=CH); 7.14–7.21 (m, H-C(4) of Ph, CH=CH); 7.30 (dd, $J = 7.8$, 7.1, H-C(3) and H-C(5) of Ph); 7.45–7.48 (m, H-C(2) and H-C(6) of Ph). ^{13}C -NMR (CD_3OD , 75 MHz): see Table 3; additionally, 120.65 (d, PhCH=CH); 126.69 (d, C(3) and C(5) of Ph); 127.68, 127.72 (2d, PhCH=CH, C(4) of Ph); 129.13 (d, C(2) and C(6) of Ph); 138.58 (s, C(1) of Ph); 141.10 (s, C(2)). HR-MALDI-MS: 303.1336 (100, $[M + H]^+$, $C_{16}H_{19}N_2O_4^+$; calc. 303.1345), 285.1230 (24, $[M - OH]^+$, $C_{16}H_{17}N_2O_4^+$; calc. 285.1239). Anal. calc. for $C_{16}H_{18}N_2O_4 \cdot 0.5 MeOH$ (318.34): C 62.25, H 6.33, N 8.80; found: C 62.18, H 6.31, N 8.84.

(5R,6R,7S,8S)-6,7,8-Tris(benzyloxy)-5-[(benzyloxy)methyl]-5,6,7,8-tetrahydro-2-[(E/Z)-2-prop-1-enyl]imidazo[1,2-a]pyridine (**20**). A suspension of EtPPh₃Br (137 mg, 0.36 mmol) in Et₂O (5 ml) was cooled to –40°, treated slowly with 1.5M BuLi in hexane (195 μ l, 0.29 mmol), stirred for 10 min, warmed to r.t., stirred for 15 min, cooled to –78°, treated with a soln. of **18** (144 mg, 0.25 mmol) in THF (5 ml), warmed to r.t. within 20 min, cooled to –78°, and treated with sat. NH_4Cl soln. Normal workup gave (Z)/(E)-**20** 55:45 (129 mg, 88%). R_f (hexane/AcOEt 3:2) 0.60. IR ($CHCl_3$): 3089m, 3066s, 3011s, 2918m, 2869m, 1951w, 1603s, 1504s, 1454s, 1430m, 1311m, 1179m, 1070s, 1028m, 911m. 1H -NMR (C_6D_6 , 300 MHz; (Z)/(E) 55:45): 1.81 (dd, $J = 1.5$, 6.7, 1.35 H), 2.23 (dd, $J = 1.7$, 7.0, 1.65 H) (Me); 3.40 (dd, $J = 5.3$, 10.0, 0.45 H), 3.41 (dd, $J = 5.1$, 10.2, 0.55 H) (CH–C(5)); 3.49 (dd, $J = 2.8$, 10.3, CH–C(5)); 3.66 (t, $J = 8.1$, 0.45 H), 3.67 (t, $J = 8.1$, 0.55 H) (H–C(6)); 3.85–3.92 (m, H–C(5)); 4.02, 4.03 (2dd, $J = 5.9$, 8.1, H–C(7)); 4.07, 4.12 (2d, $J = 11.5$, PhCH); 4.33, 4.35 (2d, $J = 11.5$, PhCH); 4.58 (d, $J = 11.5$, PhCH); 4.77 (d, $J = 5.9$, H–C(8)); 4.78, 4.80 (2d, $J = 11.2$, 2 PhCH); 5.12 (d, $J = 11.8$, PhCH); 5.48 (d, $J = 11.7$, 0.45 H), 5.51 (d, $J = 11.7$, 0.55 H) (PhCH); 5.75 (qd, $J = 7.8$, 11.5, 0.55 H), 6.77 (qd, $J = 7.8$, 15.5, 0.45 H) (CH=CHMe); 6.50 (qd, $J = 1.5$, 15.5, 0.45 H), 6.70 (qd, $J = 1.5$, 11.5, 0.55 H) (CH=CHMe); 6.82 (s, 0.45 H), 6.94 (s, 0.55 H) (H–C(3)); 7.06–7.26 (m, 16 arom. H); 7.24 (d, $J = 8.1$, 2 arom. H); 7.53 (d, $J = 7.8$, 2 arom. H). ^{13}C -NMR (C_6D_6 , 75 MHz; (Z)/(E) 55:45): 15.41, 18.31 (2q, Me); 58.03, 58.11 (2d, C(5)); 68.46 (t, CH_2 –C(5)); 72.56, 73.00, 74.01, 74.05 (4t, 4 PhCH₂); 76.17 (d, C(8)); 76.27 (d, C(6)); 82.50 (d, C(7)); 113.52, 116.17 (2d, C(3)); 123.43, 123.85, 124.05, 124.10 (4d, CH=CH); 127.58–128.77 (several d); 137.83, 137.88, 138.49, 138.71, 139.01 (5s); 141.08, 141.56 (2s); 143.79, 144.41 (2s, C(8a)). HR-MALDI-MS: 623.2881 (9, $[M + Na]^+$, $C_{39}H_{40}N_2NaO_4^+$; calc. 623.2886), 601.3058 (100, $[M + H]^+$, $C_{39}H_{41}N_2O_4^+$; calc. 601.3066), 509.2427 (10, $[M - Bn]^+$, $C_{32}H_{33}N_2O_4^+$; calc. 509.2440), 493.2483 (99, $[M - BnO]^+$, $C_{32}H_{33}N_2O_4^+$; calc. 493.2491), 387.2059 (11, $[M - 2 BnO + H]^+$, $C_{25}H_{27}N_2O_4^+$; calc. 387.2073).

(5R,6R,7S,8S)-5,6,7,8-Tetrahydro-5-(hydroxymethyl)-2-propylimidazo[1,2-a]pyridine-6,7,8-triol (**13**). A soln. of **20** (60 mg, 0.1 mmol) in AcOH (5 ml) was treated with 10% Pd/C (60 mg) and hydrogenated at 6 bar for 68 h, diluted with MeOH, and filtered over Celite. Evaporation of the filtrate, co-evaporation with toluene, and FC (AcOEt/MeOH/ H_2O 10:0:0 $\rightarrow$ 10:1:0 $\rightarrow$ 10:2:1) gave **13** (20 mg, 82%). White hygroscopic solid. A sample for microanalysis was dried for 4 d at 10^{-4} Torr. R_f (AcOEt/MeOH/ H_2O 10:1:1) 0.20. $[a]_D^{25} = -30.8$ ($c = 0.35$, MeOH). UV (MeOH): 224 (3.7). IR (ATR): 3500–3100s (br.), 2959s, 2926s, 2851s, 1505m, 1455s, 1318s, 1254m, 1198m, 1115s, 1026s, 867m. 1H -NMR (CD_3OD , 300 MHz): see Table 2; additionally, 0.96 (t, $J = 7.5$, Me); 1.65 (sext., $J = 7.5$, $MeCH_2CH_2$); 2.53 (t, $J = 7.5$, $MeCH_2CH_2$); 4.52 (d, $J = 8.0$, irradiated at 3.68 $\rightarrow$ s, H–C(8)). ^{13}C -NMR (CD_3OD , 75 MHz): see Table 3; additionally, 12.89 (q, Me); 22.30 (t, $MeCH_2CH_2$); 28.96 (t, $MeCH_2CH_2$); 140.38 (s, C(2)). HR-MALDI-MS: 265.1156 (5, $[M + Na]^+$, $C_{11}H_{18}N_2NaO_4^+$; calc. 265.1164), 243.1336 (100, $[M + H]^+$, $C_{11}H_{19}N_2O_4^+$; calc. 243.1345). Anal. calc. for $C_{11}H_{18}N_2O_4 \cdot 1/3 H_2O$ (248.27): C 53.21, H 7.58, N 11.28; found: C 53.12, H 7.28, N 11.28.

(5R,6R,7S,8S)-6,7,8-Tris(benzyloxy)-5-[(benzyloxy)methyl]-5,6,7,8-tetrahydro-2-[(phenylimino)methyl]imidazo[1,2-a]pyridine (**21**). A suspension of **18** (84 mg, 0.142 mmol) and 4-Å activated mol. sieves in CH_2Cl_2 (2 ml) was treated with freshly distilled aniline (16 μ l, 0.17 mmol), stirred at 23° for 5 h, and filtered. The filtrate was diluted with Et₂O, washed with sat. $NaHCO_3$ soln. and brine, dried (Na_2SO_4), and evaporated. The 1H -NMR spectrum of the residue (105 mg) evidenced **21**. 1H -NMR ($CDCl_3$, 300 MHz): 3.81 (dd, $J = 5.0$, 10.6, CH–C(5)); 3.88–3.93 (m, CH–C(5), H–C(6)); 4.16 (dd, $J = 5.0$, 6.8, H–C(7)); 4.25–4.30 (m, H–C(5)); 4.48 (d, $J = 12.0$, PhCH); 4.50 (s, PhCH₂); 4.67 (d, $J = 11.0$, PhCH); 4.81 (d, $J = 10.5$, PhCH); 4.82 (d, $J = 4.8$, H–C(8)); 4.83, 4.87 (d, $J = 11.7$, 2 PhCH); 5.15 (d, $J = 11.2$, PhCH); 7.14–7.45 (m, 25 arom. H); 7.72 (s, H–C(3)); 8.48 (s, CH=NPh).

(5R,6R,7S,8S)-6,7,8-Tris(benzyloxy)-5-[(benzyloxy)methyl]-5,6,7,8-tetrahydro-2-[(phenylamino)methyl]imidazo[1,2-a]pyridine (**22**). A soln. of crude **21** (105 mg) in EtOH (10 ml) was treated with NaBH₄ (18 mg, 0.5 mmol), stirred at 23° for 3 h, and evaporated. The residue was treated with sat. NH₄Cl soln. and extracted with Et₂O. The org. layer was dried (Na₂SO₄) and evaporated. FC (hexane/AcOEt 1:1) gave **22** (80 mg, 84% from **18**). White solid. M.p. 94°. *R*_f (hexane/AcOEt 2:3) 0.40. $[\alpha]_D^{25} = +45.9$ (*c* = 0.96, CHCl₃). UV (CHCl₃): 295 (3.3), 245 (4.2). IR (CHCl₃): 3319*m*, 3059*m*, 3030*s*, 2870*s*, 1954*w*, 1819*w*, 1602*s*, 1508*s*, 1497*m*, 1454*m*, 1435*m*, 1309*s*, 1256*m*, 1069*s*, 989*m*. ¹H-NMR (CDCl₃, 300 MHz; assignment based on a HSQC spectrum): see Table 4; additionally, 4.21 (br. *s*, NH); 4.28 (*s*, CH₂–C(2)); 4.41 (*d*, *J* = 12.1, PhCH); 4.46 (*d*, *J* = 12.1, PhCH); 4.50 (*d*, *J* = 11.2, PhCH); 4.70 (*d*, *J* = 11.2, PhCH); 4.81 (*d*, *J* = 11.2, PhCH); 4.83 (*d*, *J* = 11.2, PhCH); 4.84 (*d*, *J* = 11.2, PhCH); 5.16 (*d*, *J* = 11.5, PhCH); 6.70–6.75 (*m*, 3 arom. H); 7.17–7.34 (*m*, 20 arom. H); 7.43 (*dd*, *J* = 1.5, 7.6, 2 arom. H). ¹³C-NMR (CDCl₃, 75 MHz; assignment based on a HSQC spectrum): see Table 3; additionally, 42.52 (*t*, CH₂–C(2)); 72.69, 73.25, 74.01, 74.18 (4*t*, 4 PhCH₂); 113.05 (2*d*); 117.31 (*d*); 127.48–129.03 (several *d*); 137.17, 137.48, 137.71, 138.11 (4*s*); 140.18 (*s*, C(2)); 148.23 (*s*, C(1) of NHPh). HR-MALDI-MS: 688.3123 (26, [M + Na]⁺, C₄₃H₄₃N₃NaO₄⁺; calc. 688.3151), 666.3319 (29, [M + H]⁺, C₄₃H₄₄N₃O₄⁺; calc. 666.3332), 574.2773 (39), 573.2733 (100, [M – PhNH]⁺, C₃₇H₃₇N₂O₄⁺; calc. 573.2753). Anal. calc. for C₄₃H₄₃N₃O₄ (665.83): C 77.57, H 6.51, N 6.31; found: C 77.53, H 6.73, N 6.24.

(5R,6R,7S,8S)-5,6,7,8-Tetrahydro-5-(hydroxymethyl)-2-[(phenylamino)methyl]imidazo[1,2-a]pyridine-6,7,8-triol (**10**). A soln. of **22** (38 mg, 57.1 μmol) in CH₂Cl₂ (3 ml) was cooled to –78°, treated with 1*M* BCl₃ in CH₂Cl₂ (0.68 ml, 0.685 mmol), stirred until the mixture had reached a temp. of 10°, cooled to –78°, diluted with H₂O, and washed with AcOEt. The aq. layer was evaporated. The residue was dissolved in H₂O and applied to ion-exchange chromatography (Amberlite CG-120, H⁺ form, elution with 0.1*M* NH₃). Evaporation, lyophilisation, and drying gave **10** (15 mg, 86%). Hygroscopic white solid. A sample for microanalysis was dried for 4 d at 10^{–4} Torr. *R*_f (AcOEt/MeOH/H₂O 10:1:1) 0.12. $[\alpha]_D^{25} = -25.7$ (*c* = 0.44, MeOH). UV (MeOH): 293 (3.2), 245 (4.1), 205 (4.3). IR (ATR): 3300–3200*s* (br.), 3026*m*, 2882*m*, 1600*s*, 1496*s*, 1318*m*, 1256*m*, 1177*m*, 1087*s*, 1025*s*, 907*m*. ¹H-NMR (CD₃OD, 300 MHz): see Table 2; additionally, 4.19 (*s*, CH₂–C(2)); 4.47 (*d*, *J* = 7.8, irr. at 3.66 → *s*, H–C(8)); 6.60 (*tt*, *J* = 7.3, 0.9, H–C(4) of Ph); 6.67 (*dt*, *J* = 7.5, 0.9, H–C(2) and H–C(6) of Ph); 7.05–7.11 (*m*, H–C(3) and H–C(5) of Ph). ¹³C-NMR (CD₃OD, 75 MHz): see Table 3; additionally, 42.45 (*t*, CH₂–C(2)); 113.90 (2*d*); 117.84 (*d*); 129.48 (2*d*); 141.03 (*s*, C(2)); 149.41 (*s*, C(1) of Ph). HR-MALDI-MS: 328.1273 (33, [M + Na]⁺, C₁₅H₁₉N₃NaO₄⁺; calc. 328.1273), 306.1450 (100, [M + H]⁺, C₁₅H₂₀N₃O₄⁺; calc. 306.1454), 213.0871 (43, [M – PhNH]⁺, C₉H₁₃N₂O₄⁺; calc. 213.0875). Anal. calc. for C₁₅H₁₉N₃O₄ · 1/2 H₂O (314.33): C 57.31, H 6.31, N 13.37; found: C 57.01, H 6.06, N 13.19.

(5R,6R,7S,8S)-6,7,8-Tris(benzyloxy)-5-[(benzyloxy)methyl]-2-(chloromethyl)-5,6,7,8-tetrahydroimidazo[1,2-a]pyridine (**24**). A soln. of **23** [15] (170 mg, 0.288 mmol) in CH₂Cl₂ (7 ml) was treated with SOCl₂ (42 μl, 0.58 mmol), stirred at 22° for 25 min, treated with sat. NaHCO₃ soln., and extracted with Et₂O. The organic layer was washed with sat. NaHCO₃ soln. and brine, dried (Na₂SO₄), and evaporated affording crude **24** (161 mg, sufficiently pure for the next reaction). FC (hexane/AcOEt 1:1) gave pure **24** (136 mg, 77%). White solid. *R*_f (hexane/AcOEt 3:2) 0.52. M.p. 80.9°. $[\alpha]_D^{25} = +50.4$ (*c* = 0.94, CHCl₃). UV (CHCl₃): 240 (3.6). IR (CHCl₃): 3067*w*, 3032*m*, 3020*s*, 3013*s*, 2869*m*, 1497*m*, 1454*s*, 1362*m*, 1259*m*, 1216*m*, 1094*s*, 1028*m*. ¹H-NMR (CDCl₃, 300 MHz): 3.76 (*dd*, *J* = 5.3, 10.4, CH–C(5)); 3.86 (*dd*, *J* = 3.1, 10.1, CH'–C(5)); 3.88 (*t*, *J* = 7.5, H–C(6)); 4.14 (*dd*, *J* = 5.6, 7.3, H–C(7)); 4.18–4.21 (*m*, H–C(5)); 4.47 (*d*, *J* = 12.1, PhCH); 4.53 (*d*, *J* = 12.1, PhCH); 4.63 (*d*, *J* = 12.1, PhCH); 4.65 (*s*, CH₂–C(2)); 4.71 (*d*, *J* = 11.5, PhCH); 4.78 (*d*, *J* = 5.4, H–C(8)); 4.84 (*d*, *J* = 10.9, PhCH); 4.86 (*d*, *J* = 11.5, PhCH); 4.88 (*d*, *J* = 11.2, PhCH); 5.20 (*d*, *J* = 11.5, PhCH); 7.09 (*s*, H–C(3)); 7.22–7.24 (*m*, 2 arom. H); 7.30–7.37 (*m*, 16 arom. H); 7.39–7.47 (*m*, 2 arom. H). ¹³C-NMR (CDCl₃, 75 MHz): 40.36 (*t*, CH₂–C(2)); 58.35 (*d*, C(5)); 68.45 (*t*, CH₂–C(5)); 72.81, 73.46, 74.10 (3*t*, 3 PhCH₂); 74.18 (*d*, C(8)); 74.30 (*t*, PhCH₂); 76.09 (*d*, C(6)); 81.85 (*d*, C(7)); 116.78 (*d*, C(3)); 127.82–128.79 (several *d*); 137.57, 137.75, 137.97, 138.39, 138.84 (5*s*); 144.33 (*s*, C(8a)). HR-MALDI-MS: 631.2337 (31, [M + Na]⁺, C₃₇H₃₇ClN₂NaO₄⁺; calc. 631.2340), 609.2509 (90, [M + H]⁺, C₃₇H₃₈ClN₂O₄⁺; calc. 609.2520), 575.2901 (36, [M – Cl + 2 H]⁺, C₃₇H₃₉N₂O₄⁺; calc. 575.2910), 501.1942 (100, [M – BnO]⁺, C₃₀H₃₀ClN₂O₃⁺; calc. 501.1945). Anal. calc. for C₃₇H₃₇ClN₂O₄ (609.16): C 72.95, H 6.12, N 4.60; found: C 73.07, H 6.32, N 4.62.

(5R,6R,7S,8S)-6,7,8-Tris(benzyloxy)-5-[(benzyloxy)methyl]-5,6,7,8-tetrahydro-2-[(3-nitrophenoxy)methyl]imidazo[1,2-a]pyridine (**25**). A suspension of **23** (190 mg, 0.32 mmol) and NaH (60% washed with dry hexane, 23 mg, 0.96 mmol) in degassed DMF (3 ml) was treated with 1-fluoro-3-nitrobenzene (68 μl, 0.64 mmol), stirred for 5 h at 65°, cooled to r.t., diluted with Et₂O (50 ml), and washed with sat. NH₄Cl soln. The combined org. layers were washed with brine, dried (Na₂SO₄), filtered, and evaporated. FC (hexane/AcOEt 1:0 → 3:1 → 2:1 → 1:1) gave **25** (130 mg, 57%) and **23** (27 mg, 14%).

Data of 25: Pale yellow solid. R_f (hexane/AcOEt 2:3) 0.71. M.p. 98.5°. $[\alpha]_D^{25} = +39.4$ ($c = 1.04$, CHCl_3). UV (CHCl_3): 329 (3.3), 269 (3.8), 240 (3.9). IR (CHCl_3): 3019s, 2976w, 2895w, 1884m, 1728w, 1618w, 1580w, 1529s, 1477m, 1423m, 1391m, 1351m, 1335m, 1046s, 928s, 877m, 849m. $^1\text{H-NMR}$ (CDCl_3 , 300 MHz; assignment based on a HSQC spectrum): see Table 4; additionally, 4.43 (d , $J = 12.1$, PhCH); 4.49 (d , $J = 11.8$, PhCH); 4.50 (d , $J = 11.2$, PhCH); 4.68 (d , $J = 11.5$, PhCH); 4.82 (d , $J = 11.5$, PhCH); 4.83 (d , $J = 11.2$, PhCH); 4.86 (d , $J = 11.8$, PhCH); 5.08 (d , $J = 11.7$, $\text{CH}-\text{C}(2)$); 5.13 (d , $J = 11.5$, $\text{CH}'-\text{C}(2)$); 5.17 (d , $J = 11.5$, PhCH); 7.17–7.21 (m , 2 arom. H); 7.26–7.43 (m , 18 arom. H, H–C(6) of PhNO_2 , H–C(5) of PhNO_2); 7.82 (dt , $J = 7.8$, 1.8, H–C(4) of PhNO_2); 7.95 (t , $J = 2.1$, H–C(2) of PhNO_2). $^{13}\text{C-NMR}$ (CDCl_3 , 75 MHz; assignment based on a HSQC spectrum): see Table 3; additionally, 65.14 (t , $\text{CH}_2-\text{C}(2)$); 72.69, 73.29 ($2t$, 2 PhCH_2); 74.15 (t , 2 PhCH_2); 109.48 (d , C(2) of PhNO_2); 115.69 (d , C(4) of PhNO_2); 121.95 (d , C(6) of PhNO_2); 127.54–128.46 (several d); 129.73 (d , C(5) of PhNO_2); 136.95, 137.11, 137.38, 137.63, 138.01 (5s); 149.02 (s , C(3) of PhNO_2); 159.21 (s , C(1) of PhNO_2). HR-MALDI-MS: 712.3008 (9, $[M+H]^+$, $\text{C}_{43}\text{H}_{42}\text{N}_3\text{O}_7^+$; calc. 712.3023), 605.2461 (40), 604.2432 (100, $[M-\text{BnO}]^+$, $\text{C}_{36}\text{H}_{34}\text{N}_3\text{O}_6^+$; calc. 604.2448), 573.2727 (5, $[M-\text{C}_6\text{H}_4\text{NO}_3]^+$, $\text{C}_{37}\text{H}_{37}\text{N}_2\text{O}_4^+$; calc. 573.2753), 465.2158 (20, $[M-\text{C}_6\text{H}_4\text{NO}_3-\text{BnOH}]^+$, $\text{C}_{30}\text{H}_{29}\text{N}_2\text{O}_3^+$; calc. 465.2178), 375.1695 (21, $\text{C}_{23}\text{H}_{23}\text{N}_2\text{O}_3^+$, $[M-\text{C}_6\text{H}_4\text{NO}_3-\text{BnO}-\text{Bn}]^+$; calc. 375.1709), 359.1745 (20, $[M-\text{C}_6\text{H}_4\text{NO}_3-2\text{BnO}]^+$, $\text{C}_{23}\text{H}_{23}\text{N}_2\text{O}_2^+$; calc. 359.1760). Anal. calc. for $\text{C}_{43}\text{H}_{41}\text{N}_3\text{O}_7$ (711.81): C 72.56, H 5.81, N 5.90; found: C 72.61, H 5.54, N 6.04.

(5R,6R,7S,8S)-6,7,8-Tris(benzyloxy)-5-[(benzyloxy)methyl]-5,6,7,8-tetrahydro-2-(phenoxymethyl)imidazo[1,2-a]pyridine (**26**). A soln. of **24** (49 mg, 0.081 mmol) in DMF (2 ml) was treated with $t\text{-BuOK}$ (13 mg, 0.12 mmol) and PhOH (11.0 mg, 0.12 mmol), stirred for 3.5 h at 80°, cooled to r.t., diluted with H_2O , and extracted with Et_2O . The org. layer was washed with 0.5M NaOH and brine, dried (Na_2SO_4), and evaporated. FC (hexane/AcOEt 1:1) yielded **26** (41 mg, 77%). Colourless oil. R_f (hexane/AcOEt 3:2) 0.52. $[\alpha]_D^{25} = +37.2$ ($c = 0.865$, CHCl_3). UV (CHCl_3): 271 (3.3), 240 (3.5). $^1\text{H-NMR}$ (CDCl_3 , 300 MHz; assignment based on a HSQC spectrum): see Table 4; additionally, 4.43 (d , $J = 12.1$, PhCH); 4.48 (d , $J = 11.8$, PhCH); 4.51 (d , $J = 11.8$, PhCH); 4.69 (d , $J = 11.5$, PhCH); 4.82 (d , $J = 11.8$, PhCH); 4.84 (d , $J = 12.1$, PhCH); 4.86 (d , $J = 11.8$, PhCH); 5.04 (d , $J = 11.8$, $\text{CH}-\text{C}(2)$); 5.09 (d , $J = 11.8$, $\text{CH}'-\text{C}(2)$); 5.19 (d , $J = 11.8$, PhCH); 6.96 (tt , $J = 7.2$, 0.9, H–C(4) of PhO); 7.05 (dt , $J = 1.2$, 8.9, H–C(3) and H–C(5) of PhO); 7.17–7.24 (m , 2 arom. H); 7.25–7.36 (m , 18 arom. H); 7.43 (dd , $J = 1.5$, 7.8, H–C(2) and H–C(6) of PhO). $^{13}\text{C-NMR}$ (CDCl_3 , 75 MHz; assignment based on a HSQC spectrum): see Table 3; additionally, 64.63 (t , $\text{CH}_2-\text{C}(2)$); 72.61, 73.24, 73.94, 74.15 ($4t$, 4 PhCH_2); 114.79 (d , C(2) and C(6) of PhO); 120.59 (d , C(4) of PhO); 127.73–129.23 (several d); 137.11, 137.43, 137.67, 138.09, 138.20 (5s); 158.69 (s , C(1) of PhO). HR-MALDI-MS: 689.2943 (34, $[M+\text{Na}]^+$, $\text{C}_{43}\text{H}_{42}\text{N}_3\text{NaO}_5^+$; calc. 689.2991), 667.3159 (100, $[M+H]^+$, $\text{C}_{43}\text{H}_{43}\text{N}_3\text{O}_5^+$; calc. 667.3172), 573.2732 (18, $[M-\text{PhO}]^+$, $\text{C}_{37}\text{H}_{37}\text{N}_2\text{O}_4^+$; calc. 573.2753), 559.2589 (27, $[M-\text{BnO}]^+$, $\text{C}_{36}\text{H}_{35}\text{N}_2\text{O}_4^+$; calc. 559.2597), 375.1701 (24). Anal. calc. for $\text{C}_{43}\text{H}_{42}\text{N}_3\text{O}_5$ (666.82): C 77.45, H 6.35, N 4.20; found: C 77.51, H 6.46, N 4.07.

(5R,6R,7S,8S)-5,6,7,8-Tetrahydro-5-(hydroxymethyl)-2-[(3-nitrophenoxy)methyl]imidazo[1,2-a]pyridine-6,7,8-triol (**11**). A soln. of **25** (21.8 mg, 28.1 μmol) in CH_2Cl_2 (1.5 ml) was treated with AlCl_3 (49 mg, 0.33 mmol) and anisole (53 μl , 0.49 mmol), stirred for 10 h at 23°, and treated with H_2O (20 ml) and AcOEt (15 ml). After separation of the layers, the org. layer was extracted with H_2O . The combined aq. layers were evaporated. FC (AcOEt/MeOH/ H_2O 1:0:0 $\rightarrow$ 20:1:1 $\rightarrow$ 15:1:1) yielded **11** (6.3 mg, 58%). White solid. R_f (AcOEt/MeOH/ H_2O 10:1:1) 0.25. $[\alpha]_D^{25} = -23.7$ ($c = 0.435$, MeOH). UV (MeOH): 325 (3.2), 268 (3.7), 213 (4.3). IR (KBr): 3675–2800s (br.), 2925m, 2853m, 1618m, 1580m, 1528s, 1481m, 1460m, 1350s, 1285m, 1250m, 1177m, 1103m, 1025m, 1008m, 871m, 829m, 801m, 738s. $^1\text{H-NMR}$ (CD_3OD , 300 MHz): see Table 2; additionally, 4.49 (d , $J = 8.1$, irradiat. at 3.68 $\rightarrow$ s , H–C(8)); 5.08 (br. s , $\text{CH}_2-\text{C}(2)$); 7.37–7.41 (m , H–C(6) of PhNO_2); 7.47–7.53 (m , H–C(5) of PhNO_2); 7.81 (m , H–C(2) and H–C(4) of PhNO_2). $^{13}\text{C-NMR}$ (CD_3OD , 75 MHz): see Table 3; additionally, 65.08 (t , $\text{CH}_2-\text{C}(2)$); 109.97 (d , C(2) of PhNO_2); 116.13 (d , C(4) of PhNO_2); 122.24 (d , C(6) of PhNO_2); 130.87 (d , C(5) of PhNO_2); 136.87 (s , C(2)); 149.42 (s , C(3) of PhNO_2); 159.55 (s , C(1) of PhNO_2). HR-MALDI-MS: 374.0956 (15, $[M+\text{Na}]^+$, $\text{C}_{15}\text{H}_{17}\text{N}_3\text{NaO}_7^+$; calc. 374.0964), 358.1011 (27, $[M+\text{Na}-\text{O}]^+$, $\text{C}_{15}\text{H}_{17}\text{N}_3\text{NaO}_6^+$; calc. 358.1015), 352.1139 (28, $[M+H]^+$, $\text{C}_{15}\text{H}_{18}\text{N}_3\text{O}_7^+$; calc. 352.1145), 336.1190 (35), 320.1240 (31), 213.0871 (100, $[M-\text{C}_6\text{H}_4\text{NO}_3]^+$, $\text{C}_9\text{H}_{13}\text{N}_2\text{O}_4^+$; calc. 213.0875), 195.0763 (39, $[M-\text{C}_6\text{H}_4\text{NO}_3-\text{H}_2\text{O}]^+$, $\text{C}_9\text{H}_{11}\text{N}_2\text{O}_3^+$; calc. 195.077). Anal. calc. for $\text{C}_{15}\text{H}_{17}\text{N}_3\text{O}_7$ (351.32): C 51.30, H 5.05, N 11.69; found: C 51.28, H 4.88, N 11.96.

(5R,6R,7S,8S)-5,6,7,8-Tetrahydro-5-(hydroxymethyl)-2-(phenoxymethyl)imidazo[1,2-a]pyridine-6,7,8-triol (**12**). A soln. of **26** (40 mg, 60.1 μmol) in AcOEt/MeOH/ H_2O 3:1:1 (2 ml) was treated with 20% Pd/C (20 mg), hydrogenated at amb. pressure for 46 h, and filtered through *Celite* (washing with MeOH). Evaporation of the combined filtrates, FC (AcOEt/MeOH/ H_2O 1:0:0 $\rightarrow$ 20:1:1 $\rightarrow$ 15:1:1), and drying afforded **12** (11.5 mg, 63%). White hygroscopic solid. R_f (AcOEt/MeOH/ H_2O 10:1:1) 0.10. $[\alpha]_D^{25} = +29.2$ ($c = 0.605$, MeOH). UV (MeOH): 277 (3.1), 271 (3.2), 220 (4.1). IR (KBr): 3600–3000s (br.), 2926m, 1598m, 1586m, 1458m, 1383w, 1299w, 1240s, 1175m, 1103m, 1028s, 874w, 754m, 691m. $^1\text{H-NMR}$ (CD_3OD , 300 MHz): see Table 2; additionally,

4.95 (s, CH₂–C(2)); 6.90 (tt, $J = 0.9$, 7.3, H–C(4) of PhO); 6.94–6.97 (m, H–C(2) and H–C(6) of PhO); 7.21–7.27 (m, H–C(3) and H–C(5) of PhO). ¹³C-NMR (CD₃OD, 75 MHz): see Table 3; additionally, 63.51 (t, CH₂–C(2)); 114.56 (d, C(2) and C(6) of PhO); 120.65 (d, C(4) of PhO); 129.25 (d, C(3) and C(5) of PhO); 137.87 (s, C(2)); 158.96 (s, C(1) of PhO). HR-MALDI-MS: 329.1109 (35, [M + Na]⁺, C₁₅H₁₈N₂NaO₅⁺; calc. 329.1113), 307.1290 (88, [M + H]⁺, C₁₅H₁₉N₂O₅⁺; calc. 307.1294), 213.0870 (100, [M – PhO]⁺, C₉H₁₃N₂O₄⁺; calc. 213.0875). Anal. calc. for C₁₅H₁₈N₂O₅ · 0.5 H₂O (315.32): C 57.14, H 6.07, N 8.88; found: C 56.90, H 6.43, N 8.73.

Inhibition Studies. See [23]. The β-glucosidase from *Caldocellum saccharolyticum* (EC 3.2.1.21, as lyophilised powder, *Sigma G-6906*), β-glucosidase from almonds (as lyophilised powder, *Fluka 49290*), α-glucosidase from yeast (as lyophilised powder, *Fluka 63412*), 4-nitrophenyl β-D-glucopyranoside (*Fluka 73676*), and 4-nitrophenyl α-D-glucopyranoside (*Fluka 73673*) were used without further purification. The inhibition studies were carried out for β-glucosidases from *C. saccharolyticum* and sweet almonds, and α-glucosidase from brewer's yeast. The results of the inhibition studies are summarised in Table 1.

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