Synthesis of *C(2)*-Substituted *manno*-Configured Tetrahydroimidazopyridines and Their Evaluation as Inhibitors of Snail β-Mannosidase

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It was shown that retaining β-glucosidases and galactosidases of families 1–3 feature a strong interaction between C(2)OH of the substrate and the catalytic nucleophile. An analogous interaction can hardly take place for retaining β-mannosidases. A structure–activity comparison between the inhibition of the β-glucosidase from *Caldocellum saccharolyticum* (family 1) and β-glucosidase from sweet almonds by the *gluco*-imidazoles **1**–**6**, and the inhibition of snail β-mannosidase by the corresponding *manno*-imidazoles **8**–**13** does not show any significant difference, suggesting that also the mechanisms of action of these glycosidases do not differ significantly. For this comparison, we synthesized and tested the *manno*-imidazoles **9**–**13**, **28**, **29**, **32**, **35**, **40**, **41**, **43**, **46**, **47**, and **50**. Among these, the alkene **29** is the strongest known inhibitor of snail β-mannosidase (K_i = 6 nM, non-competitive); the aniline **35** is the strongest competitive inhibitor (K_i = 8 nM).

Introduction. – The strong inhibition of β-glucosidases by imidazoles of type **1** [1–3] has been rationalized by the similarity of shape of the inhibitor and of the putative reactive intermediate, an oxycarbenium cation, and by the cooperative interaction of the imidazole with the catalytic nucleophile and acid [4]. A correlation between the inhibition constant and the p*K* value of the *C(2)*- and *C(3)*-acetamido imidazoles **7** and **14**–**16**, and by related azoles has established that substituents at C(3) lower the inhibitory activity [5]. The structure–activity relation (SAR) resulting from varying the *C(2)*-substituents has been studied in detail [6]. It was shown that the $HOCH_2$ group at C(2) in **2**, and particularly the flexible hydrophobic $PhCH_2CH_2$ group in **3** lead to an improved inhibition, with K_i values as low as 0.1 nM (against *Caldocellum saccharolyticum* β-glucosidase)[1]. The *C(2)*-substituents affect both the strength and the type of the inhibition (competitive or mixed, with α varying between 2.5 and 15).

Legler and *Withers* evidenced that the C(2)OH group of β-glucosides and β-galactosides interacts with the catalytic nucleophile of the retaining β-glucosidases and β-galactosidases of families 1 [8], 2 [9], and 3 [10][11]. 2-Deoxy- and 2-deoxy-2-fluoro-β-D-glucosides and -galactosides are cleaved much less readily than the parent substrates, the rate-determining step being deglycosylation of the enzyme. The transition state for this reaction is considered very similar to that of the enzyme glycosylation [9], and the most important interaction in the transition state was considered with the C(2)OH[2]). That 2-deoxyglucosides are cleaved less readily than the parent substrates is surprising, as the OH group at C(2) is known to destabilize an

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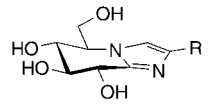
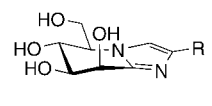
[1]) Similar effects of these substituents on the inhibition of *Escherichia coli* β-galactosidase and almonds β-glucosidase have recently been reported for L-arabinose-derived imidazoles [7].

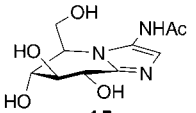
[2]) However, a crystal structure of the retaining β-glucosidase from maize (ZMGlu1) in complex with 4-nitrophenyl-β-D-thioglucoside showed only interactions of C(3)-, C(4)- and C(6)OH of the glucoside with the enzyme [12].



1 R = H
2 R = CH_2OH
3 R = CH_2CH_2Ph
4 R = CH_2CH_2COOMe
5 R = CH_2CH_2COOH
6 R = I
7 R = NHAc



8 R = H
9 R = CH_2OH
10 R = CH_2CH_2Ph
11 R = CH_2CH_2COOMe
12 R = CH_2CH_2COOH
13 R = I
14 R = NHAc



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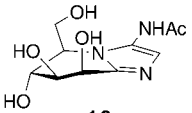

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oxycarbenium cation [13]. It appears improbable that the catalytic nucleophile of retaining β-mannosidases will similarly interact with C(2)OH located on the opposite side of the β-mannopyranoside ring. This prompts the question to which extent the mechanism of action of retaining β-glucosidases and β-mannosidases differ from each other. We wondered if a comparison of the SAR for the inhibition of retaining β-glucosidases with the SAR for the inhibition of retaining β-mannosidases by *C(2)*-substituted *gluco*- and *manno*-configured imidazoles, respectively, would suggest such a difference, or not.

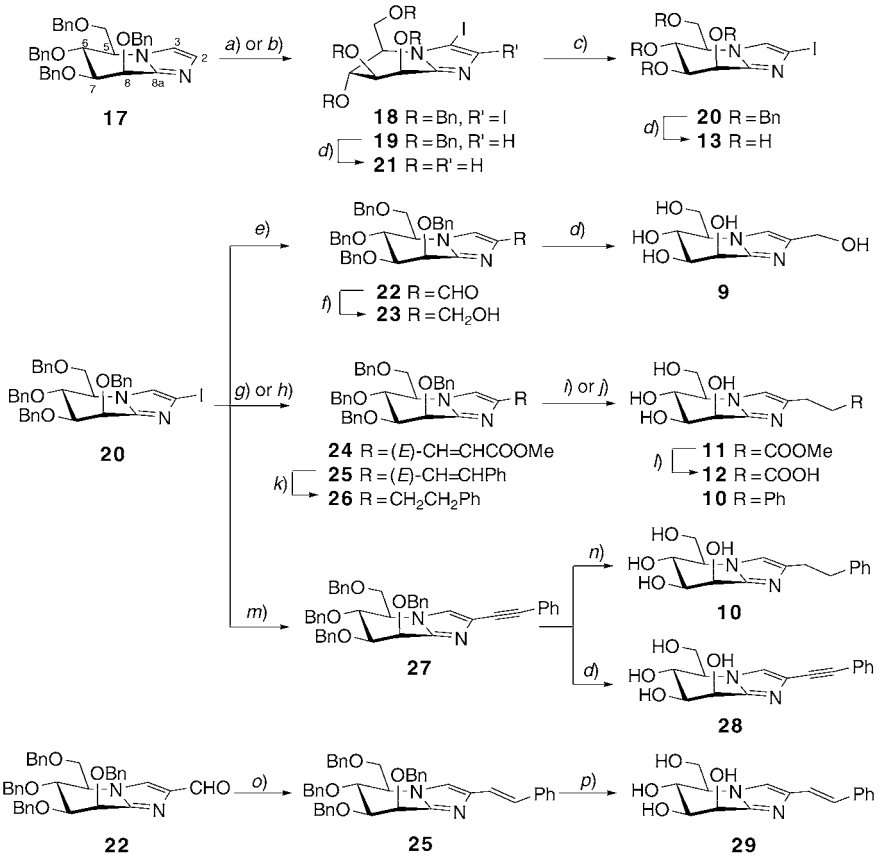
So far, the inhibitory activity of the 2- and 3-acetamido-D-*manno*-imidazopyridines **14** and **16** has been compared to that of the unsubstituted imidazopyridine **8**, and to the inhibition of β-glucosidases from *Caldocellum saccharolyticum* (family 1) and from sweet almonds by the corresponding *gluco*-imidazopyridines **7**, **15**, and **1**, respectively [5]. A similar effect of the substituent at C(3) was observed. We decided to further explore the inhibition of snail β-mannosidase by *manno*-imidazopyridines possessing further substituents at C(2), differing in polarity and flexibility, and to compare the inhibition of the relevant mannosidases and glucosidases by the *manno*- and *gluco*-imidazopyridines **9**–**13** and **2**–**6**, respectively.

We planned to prepare the *manno*-imidazopyridines by first iodinating the known imidazopyridine **17** (*Scheme 1*). The resulting *C(2)*-iodinated intermediate **20** should allow the straightforward synthesis of the desired *manno*-imidazopyridines (*Schemes 1–3*).

Synthesis. – The *manno*-imidazopyridine **17** is available from 5-amino-2,3,4,6-tetra-*O*-benzyl-5-deoxy-D-gluconolactam in three steps [2], leading to mixtures of **17** and its *gluco*-analogue in ratios of up to 3 : 1. We obtained **17** in an overall yield of 35–37% on a scale of 15–30 g[3]). The 2-iodoimidazopyridine **20** (*Scheme 1*) was prepared similarly as described for the corresponding 2-halo-*gluco*- and -*galacto*-imidazoles [6][15]. Treatment of **17** with excess NIS led to the 2,3-diiodo derivative **18** (80%), while milder conditions resulted in the formation of the 3-iodo derivative **19** (55%) besides **18** (22%). Mono-deiodination of **18** by sequential treatment with EtMgBr and H_2O

[3]) Similar results were obtained, on a scale of 100 mg, by starting from 5-amino-2,3,4,6-tetra-*O*-benzyl-5-deoxy-D-mannonolactam [14].

Scheme 1



a) *N*-Iodosuccinimide (NIS), DMF, 80°; 80% of **18**. *b*) NIS, DMF, 50°; 56% of **19**, 23% of **18**. *c*) EtMgBr, THF; 88%. *d*) BCl_3, CH_2Cl_2, $-78° \rightarrow 10°$; 97% of **9**, 64% of **13**, 56% of **21**, 85% of **28**. *e*) 1. EtMgBr, THF, 2. DMF, $-35° \rightarrow 23°$; 85%. *f*) $NaBH_4$, EtOH; 89%. *g*) Methyl acrylate, $Pd(OAc)_2[P(2\text{-tolyl})_3]_2$, K_2CO_3, DMF, 90°; 94% of **24**. *h*) Styrene, $Pd(OAc)_2[P(2\text{-tolyl})_3]_2$, K_2CO_3, DMF, 80°; 45% of **25**. *i*) H_2, Pd/C, AcOEt/MeOH/AcOH; 88% of **11**. *j*) H_2, $Pd(OH)_2$/C, AcOEt/MeOH/H_2O/AcOH; 46% of **10**. *k*) H_2, Pd/C, AcOEt/MeOH/AcOH; 48%. *l*) 1M aq. HCl, 60°; 85%. *m*) Phenylacetylene, $[Pd(PPh_3)_4]$, CuI, Et_3N, DMF, 80°; 83%. *n*) H_2, $Pd(OH)_2$/C, AcOEt/MeOH/H_2O/AcOH; 80%. *o*) Diethyl benzylphosphonate, *t*-BuOK, THF, 0°; 87%. *p*) *N*,*N*-Dimethylaniline, $AlCl_3$; 42%.

yielded 88% of the 2-iodo derivative **20**. The unprotected iodoimidazopyridines **21**[4]) and **13** were obtained by BCl_3-promoted debenzylation [16] of **19** (56%) and **20** (64%), respectively.

The 2-(hydroxymethyl)imidazopyridine **9** was synthesized similarly to the *gluco*-analogue **2** [6] by sequential formylation of **20** to the carbaldehyde **22** (85%), reduction of **22** to the alcohol **23** (89%), and debenzylation (BCl_3, 97%).

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[4]) Similarly to the *C(3)*-substituted *gluco*- and *manno*-imidazopyridines **15** and **16** [5], **21** possesses a distorted conformation (see below) and proved a poor inhibitor of the snail β-mannosidase ($K_i = 73$ μM).

To prepare the [2-(methoxycarbonyl)ethyl]-, the 2-(carboxyethyl)-, and the (2-phenylethyl)imidazopyridines **11**, **12**, and **10**, respectively, we again followed the synthesis of their *gluco*-analogues **4**, **5**, and **3** [6]. The reaction of **20** with methyl acrylate or styrene under standard *Heck* conditions ($Pd(OAc)_2$, Ph_3P, Et_3N or K_2CO_3, DMF, 80–90°) gave the coupling products **24** (54%) and **25** (25%), respectively, besides variable amounts of **17** and **20**. The yield of **24** and **25** was increased to 94 and 45%, respectively, by replacing $Pd(OAc)_2/PPh_3$ by *Herrmann*'s catalyst [17]. In contrast to the *gluco*-series [6], addition of H_2O (14% (*v*/*v*)) lowered the yield of **25** to 18–24%. Treating the benzylated acrylate **24** with H_2 in the presence of Pd/C (AcOH, 6 bar) afforded the unprotected methyl propanoate **11** (88%) that was hydrolyzed to the acid **12**. Hydrogenation of the 2-phenylethenyl derivative **25** under conditions that led to smooth debenzylation of **24** proceeded slowly and yielded mostly the benzylated 2-phenylethyl derivative **26**, while treatment with H_2 in the presence of $Pd(OH)_2/C$ gave the desired debenzylated **10** (46%). The overall yield of **10** from the iodoimidazopyridine **20** was significantly increased by proceeding *via* the alkyne **27**. It was obtained in 83% yield by *Sonogashira* coupling [18–20] of **20** with phenylacetylene, followed by hydrogenation (proceeding more rapidly than the one of **25**) to the imidazopyridine **10** (80%).

In addition to the *manno*-imidazopyridines **9**–**13** corresponding to known *gluco*-isomers, we prepared the unprotected phenylethynyl and phenylethenyl derivatives **28** and **29**, respectively, to learn about the influence of flexibility of the substituent at C(2). BCl_3-Promoted debenzylation of **27** yielded 85% of **28**, while the analogous debenzylation of **25** to **29** proceeded in only 34%. This yield was increased to 42% by using $AlCl_3$/*N*,*N*-dimethylaniline [21], providing **29** in an overall yield of 19% from **20**. The overall yield of **29** was increased to 31% by alkenylating **22** with diethyl benzylphosphonate [22][23], to provide 87% of **25**[5]).

Further analogues of the 2-phenylethyl derivative **10**, which were considered of interest, are the phenoxymethyl and anilinomethyl derivatives **32** and **35**, respectively (*Scheme 2*). We had observed [6] that the introduction of the $HOCH_2$ substituent of **2** led to a fourfold increase of the inhibition of the *C. saccharolyticum* β-glucosidase, while the introduction of the H_2NCH_2 group lowered the inhibition from $K_i = 20$ nM to $IC_{50} = 150$ nM. This was rationalized by postulating a binding interaction between the catalytic acid, and both the imidazole N(1) and the $HOCH_2$–C(2) group, and by the competing interaction of the H_3N^+CH–C(2) group and the catalytic acid with N(1). A combination of the hydrophobic Ph group with the H-bond accepting ether O-atom in **32**, or with the (weakly basic) NH in **35** should then lead to strong inhibition.

To prepare the phenoxymethyl derivative **32**, we treated the alcohol **23** with $SOCl_2$. The chloride **30** was obtained in 86% yield after chromatographic purification. Treating this chloride with phenol and *t*-BuOK in DMF [25] yielded 74% of **31**; other conditions [26–29] (*cf. Exper. Part*) resulted in lower yields. The overall yield of **31** from **23** was increased from 64 to 70% when **30** was not purified. Debenzylation of **31** ($Pd(OH)_2/C$, 1 atm.) yielded the [(phenoxy)methyl]imidazopyridine **32** (63%) and the cyclohexyloxymethyl analogue **33** (9%)[6]).

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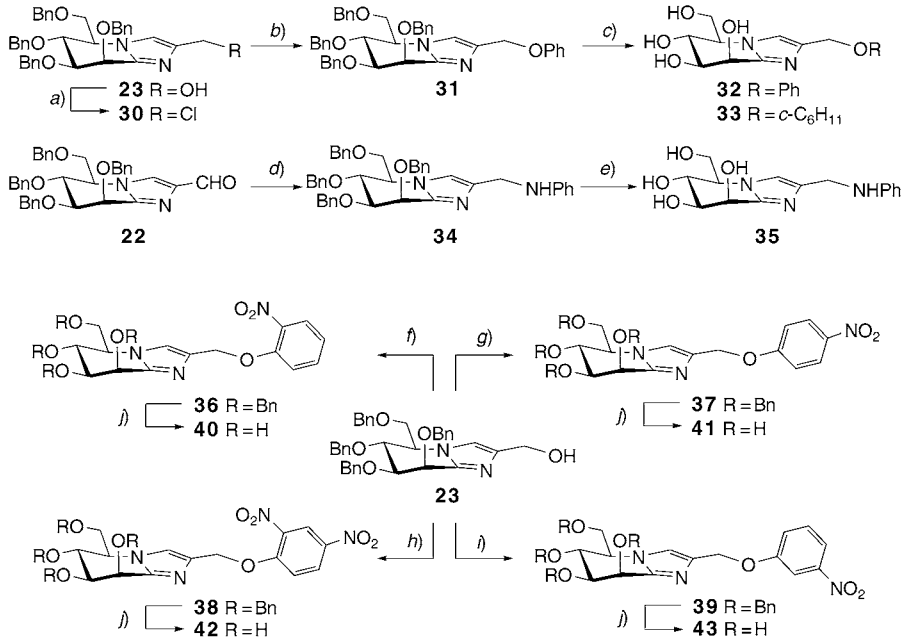
[5]) No reaction was observed when the aldehyde **22** was subjected to a Zn-promoted olefination with α,α-dichlorotoluene in the presence of Me_3SiCl [24].

Scheme 2



a) $SOCl_2$, CH_2Cl_2; 86%. *b*) PhOH, *t*-BuOK, DMF, 80°; 74%. *c*) H_2, $Pd(OH)_2$/C, AcOEt/MeOH/H_2O/AcOH; 63% of **32** and 9% of **33**. *d*) 1. Aniline, $MgSO_4$, CH_2Cl_2, 2. $NaBH_4$, EtOH; 75%. *e*) BCl_3, CH_2Cl_2, $-78° \rightarrow 15°$; 77%. *f*) 1-Fluoro-2-nitrobenzene, NaH, DMF, 80°; 94%. *g*) 1-Fluoro-4-nitrobenzene, NaH, DMF, 80°; 89%. *h*) 1-Fluoro-2,4-dinitrobenzene, NaH, DMF; 63%. *i*) 1-Fluoro-3-nitrobenzene, NaH, DMF, 140°; 56%. *j*) Anisole, $AlCl_3$, CH_2Cl_2; 75% of **40**, 72% of **41**, 75% of **42**, 54% of **43**.

To study the influence of substituents of the Ph ring of **32**, we prepared the mono- and dinitrophenyl-substituted imidazoles **40**–**43**. For this, the alcohol **23** was *O*-arylated with either 1-fluoro-2-nitro- and 1-fluoro-4-nitrobenzene (NaH, DMF, 80°) to give the imidazopyridines **36** (94%) and **37** (89%), respectively. Similarly, treatment of **23** with NaH and 1-fluoro-3-nitrobenzene at elevated temperature (140°) gave the (3-nitrophenyloxy)methyl derivative **39** (56%). The reaction of **23** with 1-fluoro-2,4-dinitrobenzene (DNP; NaH, DMF, 80°) did not lead to the (2,4-dinitrophenyloxy)-methyl derivative **38**, which was, however, obtained in 63% yield by performing the reaction at 23°. The imidazopyridines **36**–**39** were debenzylated with $AlCl_3$ in the presence of anisole [21] to provide **40** (75%), **41** (72%), **42** (75%), and **43** (54%)[7]). The compound **42** was not stable enough to be tested.

Reductive amination of the carbaldehyde **22** with aniline yielded 75% of the (phenylamino)methyl derivative **34**. Debenzylation with BCl_3 provided **35** (77%).

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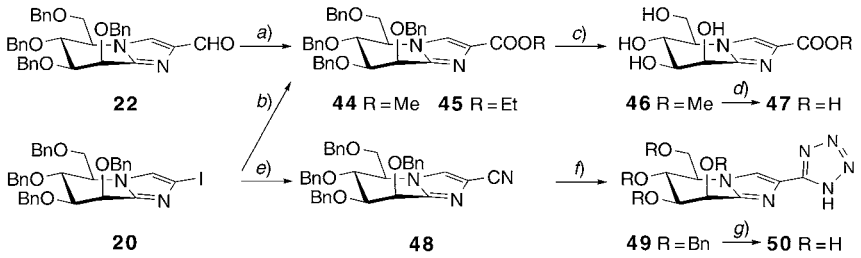
[6]) For examples of a Pd-catalyzed hydrogenation of phenols, *cf.* [30–34].

[7]) The 4-nitrophenyl ether **41** was also obtained (70%) by BCl_3-promoted debenzylation. Cleavage of the $C(2)CH_2-OC_6H_4NO_2$ bond was not observed, while the BCl_3-promoted debenzylation of **31** to **32** was accompanied by substantial cleavage of the $C(2)CH_2-OPh$ bond (*cf. Exper. Part*).

Considering the strong effects of the short $HOCH_2$ and H_2NCH_2 substituents, we also prepared the ester **46**, the corresponding acid **47**, and the tetrazolylimidazopyridine **50** (*Scheme 3*). The tetrazolyl group is an established mimic of the carboxy group [35][36]. The acid **47** and the tetrazolyl derivative **50** should, however, differ by their p*K* values.

Scheme 3



a) MnO_2, NaCN, AcOH/MeOH; 78% of **44** or 65% of **44** and 21% of **45** (*cf. Exper. Part*). *b*) 1. BuLi, THF, 2. ClCOOMe, $-78° \rightarrow 23°$; 43%. *c*) H_2, Pd/C, AcOEt/MeOH/AcOH; 88%. *d*) KOH, EtOH/H_2O, 50°; 83%. *e*) 1. EtMgBr, THF, 2. TsCN; 73%. *f*) Me_3Al, Me_3SiN_3, toluene, 80°; 76%. *g*) BCl_3, CH_2Cl_2, $-78° \rightarrow 10°$; 85% of **50**.

The methyl ester **44** was obtained by two routes. Oxidation of the carbaldehyde **22** (MnO_2, NaCN, MeOH) [37][38] provided **44** in a yield of 78%[8]). A shorter, but lower-yielding route, *viz.* lithiation of the iodoimidazopyridine **20** followed by methoxycarbonylation [40][41] also provided **44** (35–48%), besides the deiodonation product **17** (42–58%). Debenzylation of **44** (H_2, Pd/C, AcOH) yielded 88% of the ester **46** that was saponified to afford 83% of the desired acid **47**. The ester **46** was hydrolysed by treatment with 1M HCl at 50–90°.

To synthesize the tetrazolyl derivative **50**, we prepared the 2-carbonitrile **48**, similarly as described for its *gluco*-analogue [6], by treatment of the organomagnesium derivative of the 2-iodoimidazopyridine **20** with TsCN. Attempts to improve the yield of **48** (73%) by Pd-catalyzed coupling of **20** with various metal cyanides were not successful. Thus, treatment of **20** with $Zn(CN)_2$ in DMF at 150° in the presence of $[Pd(PPh_3)_4]$ [42–44] afforded **48** in only 40% yield, while almost no reaction was observed when **20** was heated with either NaCN, CuI, and $[Pd(PPh_3)_4]$ in DMF or MeCN [45], or with $Zn(CN)_2$ in DMF in the presence of $Pd(OAc)_2$ [46]. To form the tetrazole ring, the 2-carbonitrile **48** was subjected to a 1,3-dipolar cycloaddition with *in situ* prepared $Al(N_3)_3$ [47]. This yielded 76% of the tetrazolyl derivative **49**[9]), which was debenzylated (BCl_3) to afford the tetrazolylimidazopyridine **50** (85%).

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[8]) The methyl ester **44** was isolated by aqueous workup, followed by chromatography. If aqueous workup was omitted, chromatography (SiO_2; hexane/AcOEt) led to isolation of **44** (65%) and the corresponding ethyl ester **45** (21%); transesterification was presumably catalysed by residual AcOH (*cf.* [39]).

[9]) Similar results were obtained when **48** was treated with Me_3SiN_3 in toluene at 110° in the presence of Bu_2SnO [48], while no reaction was observed upon treating **48** with either NaN_3 and NH_4Cl in DMF [49–51], or with NaN_3 in DMSO [52].

The structure of the diiodoimidazopyridine **18** was established by X-ray analysis[10] (*Fig.*). Similarly to its *gluco*-analogue [6], it adopts a conformation between $^{6}H_{7}$[11]) and a sofa conformation with C(7) below the ring plane, as expected from the 1,5-interaction between the I-substituent at C(3) and the C(5)–CH_2OBn group (*cf.* [5][6]). This conformation is also observed in solution, as evidenced by the vicinal coupling constants (*cf. Table 4* in *Exper. Part*). As expected, a similar conformation is also adopted by the 3-iodoimidazopyridine **19**, while the 2-iodoimidazopyridine **20**, similarly to the parent **17** [2], is a 2:1 mixture of the $^{7}H_{6}$ and $^{6}H_{7}$ conformers.

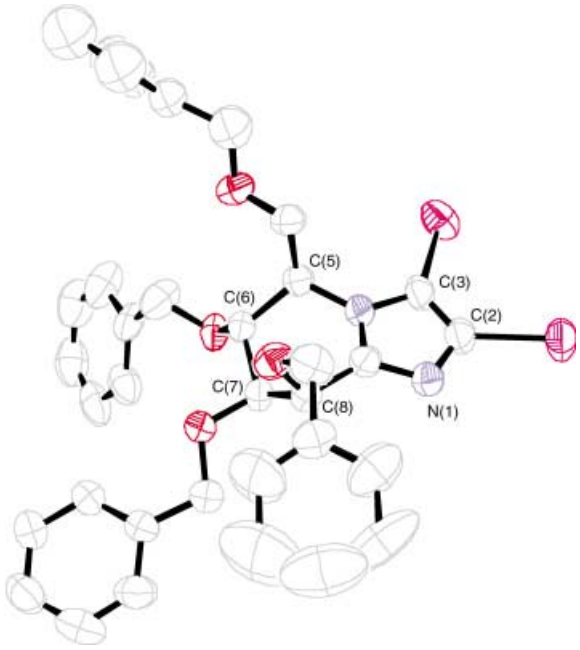


Figure. *ORTEP Representation of the crystal structure of the diiodoimidazole* **18**

With the exception of the additional signals of the substituents at C(2) and their influence on the chemical shifts of H–C(3), C(2), and C(3), the ^{1}H- and ^{13}C-NMR spectra of the protected and unprotected *C(2)*-functionalized imidazopyridines **9**–**12**, **22**–**48**, and **50** closely resemble those of the 2,3-unsubstituted imidazopyridines **17** and **8** [2]. The ^{13}C signals of C(5)–C(8) of the protected imidazoles **27**, **31**, and **34** (*cf. Table 5* in *Exper. Part*) were assigned on the basis of HSQC.GRASP spectra; those of the other imidazopyridines were assigned by analogy. The signals of C(5)–C(8) of the unprotected imidazopyridines (*cf. Table 6* in *Exper. Part*) differ from those of the *O*-Bn-

[10]) The crystallographic data have been deposited with the *Cambridge Crystallographic Data Centre* as deposition No. CCDC-213714. Copies of the data can be obtained, free of charge, on application to the CCDC, 12 Union Road, Cambridge CB21EZ, UK (fax: +44(1223)336033; e-mail: deposit@ccdc.cam.ac.uk).

[11]) Since the direction of the atom numbering of imidazopyridines (*cf.* **17** in *Scheme 1*) is opposite to that of pyranosides, the sides above and below the plane of the imidazopyridines, as defined by the clockwise and counterclockwise numbering, are interchanged with those defined according to carbohydrate numbering.

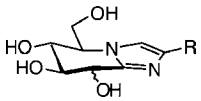
protected analogues by upfield shifts of *ca.* 5–9 ppm. A strong deshielding effect for H–C(5), H–C(7), and H–C(8) with $\Delta\delta$ values of 0.14, 0.20, and 0.64 ppm (as compared to **17**), respectively, is observed for the tetrazolyl derivative **49** (*cf. Table 7* in *Exper. Part*), while the coupling constants did not change significantly.

Enzymatic Tests and Discussion. – The *C(2)*-substituted imidazopyridines **9**–**13**, **28**, **29**, **32**, **35**, **40**, **41**, **43**, **46**, **47**, and **50**, and the 2,3-unsubstituted imidazopyridine **8** were tested as inhibitors of β-mannosidase from snail (acetate buffer, 25°, pH 4.5) and α-mannosidase from *Jack* beans (acetate buffer + $ZnCl_2$, 37°, pH 4.5), with the corresponding 4-nitrophenyl mannosides as substrates. The inhibition data for the β-mannosidase – K_i (in some cases IC_{50}) and K_i/K_M – and the pK values for those *manno*- and *gluco*-imidazopyridines that possess the same substituents at C(2) are compiled in *Table 1*, while the data for the inhibition of this β-mannosidase by the other *manno*-imidazopyridines are listed in *Table 2*. *Table 3* shows the inhibition data for the α-mannosidase from *Jack* beans, and the selectivity of the inhibition of the two mannosidases.

A comparison of the inhibition data in *Table 1* shows qualitatively the same dependence of the K_i and K_i/K_M values on the nature of the substituent at C(2) in the *gluco*- and *manno*-series. The difference between the inhibition of the two glucosidases is somewhat smaller than the difference between the inhibition of the glucosidases and the mannosidase. That the *manno*-imidazopyridines, overall, are weaker inhibitors than the *gluco*-imidazopyridines may reflect the different pH optima of the glycosidases, and the different extent to which the imidazopyridines are protonated at the pH of the assay. Considering this, the quantitative differences between the relative K_i values for imidazopyridines of the *gluco*- and *manno*-series are small. This may reflect, in part, the strong interaction of a protonated imidazopyridine with the catalytic nucleophile [4], meaning that only the interaction with the catalytic acid is impaired for the more strongly basic imidazopyridines. This comparison of the SAR in the *gluco*- and *manno*-series evidences that the mechanisms of action for β-glucosidases of family 1 and snail β-mannosidase do not differ significantly. A recent rationalization of the interaction of the catalytic nucleophile with HO–C(2) in β-glucosidases, but not in β-mannosidases [54], suggests that this factor should decrease rather than increase the mechanistic differences. It is, however, not clear how far this finding can be generalised to include retaining β-glucosidases and -mannosidases of other families.

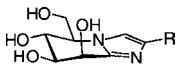
A comparison of the inhibition by the 2-phenylethyl derivative **10** and its analogues **32**, **35**, **40**, **41**, and **43** shows that the aniline **35** is the best inhibitor, in keeping with the rationalization of the effect of the C(2)CH_2OH and C(2)CH_2NH_2 substituents in the *gluco*-imidazopyridines. The phenoxy derivative **32** is only a slightly weaker (mixed-type) inhibitor, and the introduction of a NO_2 group weakens the inhibition, with the exception of the 3-nitro derivative **43**, where the effects of lowering the basic properties of the phenoxy group and of the modified interaction with the β-mannosidase appear to cancel out. Unexpectedly, the restriction of the flexibility of the 2-phenylethyl-imidazopyridine, and the concomitant lowering of the pK value, as realized in the phenylethynyl and 2-phenylethenyl derivatives **28** and **29**, respectively, resulted in very strong, albeit no longer competitive inhibition. The carboxylic acid **47** (essentially dissociated at the pH of the assay) is a weak, mixed-type inhibitor ($K_i = 1.21$ μM). The

Table 1. *The* C(2)-*Substituted* manno- *and* gluco-*Imidazoles* **8**–**13** *and* **1**–**6**: *p*K$_{HA}$ *Values and a Comparison of the Inhibition of the β-Mannosidase from Snail, and of the β-Glucosidases from* Caldocellum saccharolyticum *and from Sweet Almonds*

	*manno*-Imidazoles		Inhibition of β-mannosidase[a])		*gluco*-Imidazoles[b])		Inhibition of β-glucosidases[b])				Comparison of K_i values		
							from *Caldocellum saccharolyticum*		from sweet almonds		K_i (rel) β-Mannosidase (snail)	K_i (rel) β-Glucosidase (*C. saccharolyticum*)	K_i (rel) β-Glucosidase (almonds)
R	No.	pK_{HA}	K_i [nM]	K_i/K_M[c])	No.	pK_{HA}	K_i [nM]	K_i/K_M[d])	K_i [nM]	K_i/K_M[e])			
I	**13**	[f])	227	$3.72 \cdot 10^{-4}$	**6**	4.62	170	$3.33 \cdot 10^{-4}$	640[g])	$2.13 \cdot 10^{-4}$	1.974	8.50	6.40
H	**8**	5.7[h])	115[i])	$1.89 \cdot 10^{-4}$	**1**	6.12	20[j])	$3.92 \cdot 10^{-5}$	100	$3.33 \cdot 10^{-5}$	≡1	≡1	≡1
CH_2CH_2COOH	**12**	4.15[k])	100[l])	$1.64 \cdot 10^{-4}$	**5**	4.06/7.05	9[g])	$1.76 \cdot 10^{-5}$	27.5[g])	$9.17 \cdot 10^{-6}$	0.870	0.45	0.275
CH_2OH	**9**	5.08	67	$1.10 \cdot 10^{-4}$	**2**	5.22	5	$9.80 \cdot 10^{-6}$	11	$3.67 \cdot 10^{-6}$	0.583	0.25	0.11
CH_2CH_2COOMe	**11**	5.52	28	$4.59 \cdot 10^{-5}$	**4**	6.17	1.8[m])	$3.53 \cdot 10^{-6}$	9.9[n])	$3.30 \cdot 10^{-6}$	0.243	0.09	0.099
CH_2CH_2Ph	**10**	6.04	20	$3.28 \cdot 10^{-5}$	**3**	6.03	0.11[o])	$2.16 \cdot 10^{-7}$	1.2	$4.00 \cdot 10^{-7}$	0.174	0.0055	0.012

[a]) At 25° and pH 4.5. [b]) Data taken from [6]. [c]) $K_M = 0.61$ mM (mean value of all measurements; *cf. Exper. Part*). [d]) $K_M = 0.51$ mM [53]. [e]) $K_M = 3.0$ mM. [f]) No inflection of the titration curve was observed between pH values of 1.7 and 4.9. [g]) $IC_{50}/2$. [h]) Taken from [5]. [i]) $IC_{50} = 115$ nM [3]. [j]) Mixed-type inhibition ($\alpha = 3.2$). [k]) No second p*K* value was observed between pH 2.2 and 5.5. [l]) Mixed-type inhibition ($\alpha = 5.3$). [m]) Mixed-type inhibition ($\alpha = 2.5$). [n]) Non-competitive inhibition. [o]) Mixed-type inhibition ($\alpha = 15$).

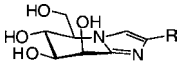
Table 2. *The* C(2)-*Substituted* manno-*Imidazoles* **8**, **28**, **29**, **32**, **35**, **40**, **41**, **43**, **46**, **47**, *and* **50**: pK_{HA} *Values and a Comparison of the Inhibition of the β-Mannosidase from Snail:* K_i, K_i/K_M, *and* K_i *(rel)*



	manno-Imidazoles		Inhibition of β-mannosidase[a])		
R	No.	pK_{HA}	K_i [nM]	K_i/K_M[b])	K_i (rel)
COOH	**47**	4.70/2.2–5.3[c])	1210 ($\alpha = 4.8$)	$1.98 \cdot 10^{-3}$	10.522
COOMe	**46**	2.2–5.3[d])	142 ($\alpha = 4.3$)	$2.33 \cdot 10^{-4}$	1.235
CHN_4	**50**	4.54/6.41	120 ($\alpha = 6.1$)	$1.97 \cdot 10^{-4}$	1.043
H	**8**	5.7[e])	115[f])	$1.89 \cdot 10^{-4}$	≡1
$CH_2OC_6H_4(2\text{-}NO_2)$	**40**	4.25	43	$7.05 \cdot 10^{-5}$	0.374
$CH_2OC_6H_4(4\text{-}NO_2)$	**41**	4.15	22 ($\alpha = 3.8$)	$3.61 \cdot 10^{-5}$	0.191
$CH_2OC_6H_4(3\text{-}NO_2)$	**43**	4.36	12	$1.97 \cdot 10^{-5}$	0.104
CH_2OPh	**32**	4.39	12 ($\alpha = 2.0$)	$1.97 \cdot 10^{-5}$	0.104
CH_2NHPh	**35**	5.09/2.3–7.4[c])	8	$1.31 \cdot 10^{-5}$	0.070
C≡CPh	**28**	2.1–5.4[d])	7 ($\alpha = 1.8$)	$1.15 \cdot 10^{-5}$	0.061
CH=CHPh	**29**	4.77	6[g])	$9.84 \cdot 10^{-6}$	0.052

[a]) At 25° and pH 4.5. [b]) $K_M = 0.61$ mM (mean value of all measurements; *cf. Exper. Part*). [c]) No second p*K* value was observed in the indicated pH range. [d]) No inflection of the titration curve was observed between indicated pH values. [e]) Taken from [5]. [f]) $IC_{50} = 115$ nM [3]. [g]) Non-competitive inhibition.

Table 3. *The* C(2)-*Substituted Imidazoles* **8**–**13**, **28**, **29**, **32**, **35**, **40**, **41**, **43**, **46**, **47**, *and* **50**: pK_{HA} *Values and a Comparison of the Inhibition of the α-Mannosidase from* Jack *Beans and of the β-Mannosidase from Snail:* K_i, K_i/K_M, *and* K_i *(rel)*



		manno-Imidazoles	Inhibition of α-mannosidase[a])		Inhibition of β-mannosidase[b])	Comparison of K_i values	
R	No.	pK_{HA}	K_i [μM]	K_i/K_M[c])	K_i [nM]	K_i (rel) α-mannosidase (*Jack* beans)	K_i (rel) (α-mannosidase/β-mannosidase)
COOMe	**46**	2.2–5.3[d])	12.5	$5.43 \cdot 10^{-3}$	142	16.667	88.0
CH_2OH	**9**	5.08	3.78	$1.64 \cdot 10^{-3}$	67	5.04	56.4
I	**13**	1.7–4.9[d])	3.50	$1.52 \cdot 10^{-3}$	227	4.667	15.4
C≡CPh	**28**	2.1–5.4[d])	2.41	$1.05 \cdot 10^{-3}$	7	3.213	344.3
COOH	**47**	4.70/2.2–5.3[e])	1.33	$5.78 \cdot 10^{-4}$	1210	1.773	1.1
CHN_4	**50**	4.54/6.41	0.78	$3.39 \cdot 10^{-4}$	120	1.04	6.5
CH_2CH_2COOH	**12**	4.15/2.2–5.5[e])	0.78	$3.39 \cdot 10^{-4}$	100	1.04	7.8
H	**8**	5.7[f])	0.75[g])	$3.26 \cdot 10^{-4}$	115	≡1	6.5
CH_2CH_2COOMe	**11**	5.52	0.60	$2.61 \cdot 10^{-4}$	28	0.8	21.4
CH_2OPh	**32**	4.39	0.273	$1.19 \cdot 10^{-4}$	12	0.364	22.8
CH_2CH_2Ph	**10**	6.04	0.23	$1.00 \cdot 10^{-4}$	20	0.307	11.5
CH=CHPh	**29**	4.77	0.15	$6.52 \cdot 10^{-5}$	6	0.2	25
$CH_2OC_6H_4(3\text{-}NO_2)$	**43**	4.36	0.125	$5.43 \cdot 10^{-5}$	12	0.167	10.4
$CH_2OC_6H_4(2\text{-}NO_2)$	**40**	4.25	0.094	$4.09 \cdot 10^{-5}$	43	0.125	2.2
CH_2NHPh	**35**	5.09/2.3–7.4[e])	0.068	$2.96 \cdot 10^{-5}$	8	0.091	8.5
$CH_2OC_6H_4(4\text{-}NO_2)$	**41**	4.15	0.041	$1.78 \cdot 10^{-5}$	22	0.055	1.9

[a]) At 37° and pH 4.5. [b]) Only K_i values shown (for the inhibition type see *Tables 1* and *2*). [c]) $K_M = 2.3$ mM (mean value of all measurements; *cf. Exper. Part*). [d]) No inflection of the titration curve was observed between indicated pH values. [e]) No second p*K* value was observed in the indicated pH range. [f]) Taken from [5]. [g]) $IC_{50} = 0.60$ μM [3].

corresponding methyl ester **46** proved a better inhibitor by *ca.* one order of magnitude. Also the tetrazolyl derivative **50** (essentially undissociated at the pH of the assay) is a better inhibitor than the acid, about equipotent to the ester, suggesting a disrupting influence of the negative charge of the carboxylate, perhaps diverting the protonation of the 'glycosidic heteroatom' by the catalytic acid.

To the best of our knowledge, the aniline **35** is the strongest competitive inhibitor of the β-mannosidase from snail, and the 2-phenylethenyl derivative **29** the most potent, albeit non-competitive, inhibitor of this enzyme.

Table 3 shows the data for the inhibition of the α-mannosidase from *Jack* beans. All imidazopyridines proved competitive inhibitors. The selectivity for the inhibition of the β- *vs.* α-mannosidase range from 1.1 for the carboxylate **47** to 344 for the 2-phenylethynyl derivative **28**. There is no clear correlation of the selectivity with the strength of the inhibition of the β-mannosidase; weaker inhibitors tend to be more selective. For the imidazoles **9**, **32**, **40**, **41**, and **43**, possessing an oxymethylene substituent at C(2), one finds a correlation between the selectivity and the pK value ($R = 0.96$), the more strongly basic imidazopyridines being more highly selective[12]). This correlation still holds ($R = 0.90$), when the 2-phenylethenyl derivative **29** is included in the comparison, but not when the aniline **35** is included ($R = 0.40$). The best inhibitor of the α-mannosidase is the (4-nitrophenoxy)methyl derivative **41** ($K_i =$ 41 nM).

We thank Dr. *B. Schweizer* for the determination of the X-ray structure of **18**, *M. Schneider* and *D. Manser* for the pK_{HA} determinations, Dr. *B. Bernet* for checking the experimental part, and the *Swiss National Science Foundation* and *Oxford Glycosciences Ltd.*, Abingdon (UK), for generous support.

Experimental Part

General. Solvents were distilled before use: THF and toluene from Na, benzophenone and CH_2Cl_2 from P_2O_5, and DMF from CaH_2. Reactions were carried out under Ar, unless stated otherwise. Qual. TLC: precoated silica-gel plates (*Merck* silica gel *60 F_{254}*); detection by heating with 'mostain' (400 ml of 10% H_2SO_4 soln., 20 g of $(NH_4)_6Mo_7O_{24} \cdot 6\,H_2O$, 0.4 g of $Ce(SO_4)_2$). Flash chromatography (FC): silica gel *Fluka 60* (0.04–0.063 mm). M.p.: uncorrected. Optical rotations: 1-dm cell at 25°, 589 nm. UV Spectra (*ca.* 0.2 mM solns.): in 1-cm cell at 25° in the range of 190 to 500 nm (log ε values in parenthesis). FT-IR spectra: KBr or *ca.* 2% soln. in $CHCl_3$, absorption in cm^{-1}. ^1H- and ^{13}C-NMR spectra: chemical shifts δ in ppm rel. to TMS as external standard, and coupling constants J in Hz. FAB-MS: in 3-nitrobenzyl alcohol (NOBA) matrix. MALDI- and HR-MALDI-MS: in gentisic acid (=2,5-dihydroxybenzoic acid, DHB) matrix. The pK_{HA} values were determined in H_2O by potentiometric titration with HCl at 25°. $[Pd(OAc)_2(P(2\text{-tolyl})_3)_2]$ was prepared according to [17]. The β-mannosidase from snail acetone powder (EC 3.2.1.25, as a suspension in 3.0M $(NH_4)_2SO_4$ containing 10 mM AcONa, pH *ca.* 4.0, *Sigma M-9400*), α-mannosidase from *Jack* beans (EC 3.2.1.24, as a suspension in 3.0M $(NH_4)_2SO_4$ and 0.1 mM zinc acetate, pH *ca.* 7.5, *Sigma M-7257*), 4-nitrophenyl β-D-mannopyranoside (*Sigma N-1268*), and 4-nitrophenyl α-D-mannopyranoside (*Sigma N-2127*) were used without further purification.

*(5*R*,6*R*,7*S*,8*R*)-6,7,8-Tris(benzyloxy)-5-[(benzyloxy)methyl]-5,6,7,8-tetrahydro-2,3-diiodoimidazo[1,2-*a*]pyridine* (**18**) *and (5*R*,6*R*,7*S*,8*R*)-6,7,8-Tris(benzyloxy)-5-[(benzyloxy)methyl]-5,6,7,8-tetrahydro-3-iodoimidazo[1,2-*a*]pyridine* (**19**). *a*) A soln. of **17** (5.34 g, 9.52 mmol) in DMF (60 ml) was treated with *N*-iodosuccinimide (NIS; 21.6 g, 96.0 mmol, 10 equiv.) and stirred under Ar at 80° for 14 h. The brown mixture was cooled, diluted with Et_2O (250 ml), and washed with $Na_2S_2O_3$ (10% aq. soln., 3×150 ml). The combined H_2O layers were extracted with Et_2O (2×100 ml). The combined org. layers were washed with H_2O (150 ml) and

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[12]) Among the lactone and lactame oxime-derived inhibitors, the more strongly basic ones proved less selective [55].

brine (150 ml), dried ($MgSO_4$), filtered, and concentrated *i.v.* FC (cyclohexane/AcOEt 1:0 → 5:1 → 1:3) gave **18** (6.17 g, 80%) as an oil, which crystallized *i.v.* Recrystallisation from AcOEt/hexane gave **18** as white crystals.

b) A soln. of **17** (100 mg, 0.178 mmol) in DMF (1.5 ml) was treated with NIS (136 mg, 0.604 mmol, 3.4 equiv.) and stirred under Ar at 50° for 8 h. After workup and FC (similarly as described in *a*), **19** (68 mg, 56%) and **18** (33 mg, 23%) were obtained.

Data of **18**: R_f (hexane/AcOEt 5:1) 0.32. M.p. 134.6–135.5°. $[\alpha]_D^{25} = -99.9$ ($c = 1.08$, $CHCl_3$). UV ($CHCl_3$): 268 (2.98). IR ($CHCl_3$): 3065*w*, 2870*m*, 1953*w*, 1878*w*, 1812*w*, 1603*w*, 1497*w*, 1451*m*, 1358*m*, 1178*w*, 1098*s*, 1026*m*, 978*w*, 911*w*. ^{1}H-NMR ($CDCl_3$, 300 MHz): see *Table 4*; additionally, 4.44 (*d*, *J* = 11.8, PhC*H*); 4.51 (*d*, *J* = 12.1, PhC*H*); 4.55 (*d*, *J* = 11.5, PhC*H*); 4.60 (br. *s*, PhCH_2); 4.62 (*d*, *J* = 12.1, PhC*H*); 4.74 (*d*, *J* = 11.8, PhC*H*); 4.78 (*d*, *J* = 12.5, PhC*H*); 7.23–7.39 (*m*, 20 arom. H). ^{13}C-NMR ($CDCl_3$, 75 MHz): see *Table 5*; additionally, 70.66, 70.91 (2*t*, CH_2–C(5), PhCH_2); 72.04 (*t*, PhCH_2); 73.33 (*t*, 2 PhCH_2); 127.78–128.52 (several *d*); 137.39, 137.52, 137.64, 138.08 (4*s*). FAB-MS: 1625 (5, $[2M+H]^+$), 813 (100, $[M+H]^+$), 721 (6, $[M-Bn]^+$), 705 (18, $[M-BnO]^+$), 685 (5, $[M-I]^+$), 579 (9), 493 (6), 91 (83). HR-MALDI-MS: 851.0275 (7, $C_{36}H_{34}I_2KN_2O_4$, $[M+K]^+$; calc. 851.0249), 835.0490 (100, $C_{36}H_{34}I_2N_2NaO_4$, $[M+Na]^+$; calc. 835.0509), 813.0681 (37, $C_{36}H_{35}I_2N_2O_4$, $[M+H]^+$; calc. 813.0690), 709.1560 (30), 705.0119 (92, $C_{29}H_{27}I_2N_2O_3$, $[M-BnO]^+$; calc. 705.0115), 687.1698 (44), 579.1132 (60), 561.2747 (9), 451.2002 (21). Anal. calc. for $C_{36}H_{34}I_2N_2O_4$ (812.48): C 53.22, H 4.22, N 3.45; found: C 53.45, H 4.37, N 3.63.

Table 4. *Selected ^{1}H-NMR Chemical Shifts* [ppm] *and Coupling Constants* [Hz] *of the Protected Imidazoles* **18**–**20**, **22**–**27**, *and* **30** *in $CDCl_3$*

	18	**19**	**20**	**22**	**23**	**24**	**25**	**26**	**27**	**30**
H–C(3)	–	–	[a])	7.86	7.11	[a])	7.20	6.82	7.41	7.19
H–C(5)	4.36	4.41	4.11	4.18	4.09	4.12	4.13	4.06	4.12	4.09
H–C(6)	4.47	4.51	4.26	4.25	4.29	4.24	4.30	4.31	4.26	4.26
H–C(7)	3.75	3.79	3.84	3.88	3.86	3.86	3.90	3.88	3.86	3.88
H–C(8)	4.75	4.79	4.77	4.81	4.79	4.80	4.87	4.80	4.761	4.79
CH–C(5)	3.62	3.68	3.57	3.60	3.60	3.59	3.63	3.59	3.60	3.58
CH′–C(5)	3.72	3.75	3.72	3.73	3.75	3.73	3.77	3.73	3.73	3.73
J(5,6)	2.5	2.2	7.2	6.8	7.5	7.2	7.2	7.2	7.2	7.2
J(6,7)	7.8	7.8	9.3	8.7	9.3	9.3	9.3	9.3	9.3	9.3
J(7,8)	3.1	3.1	3.1	3.1	3.1	3.1	2.8	3.1	3.1	2.8
J(5,CH)	5.0	5.0	7.2	7.2	6.9	7.2	7.2	6.9	7.2	7.2
J(5,CH′)	8.7	9.0	3.1	2.8	2.8	3.1	3.1	3.1	3.0	2.8
J(CH,CH′)	9.3	9.3	10.3	10.0	10.0	10.0	10.0	10.0	10.1	10.0

[a]) Hidden by signals of the Ph groups at 7.24–7.42 ppm.

X-Ray Analysis of **18**. Orthorhombic $P2_12_12_1$; $a = 11.9793(2)$, $b = 14.8025(3)$, $c = 19.5612(5)$; $V = 3468.66(13)$ Å^3, $D_{calc} = 1.556$ Mg/m^3, $Z = 4$. The reflexions were measured on a *Bruker Nonius-KappaCCD* difractometer (graphite monochromator, MoK_α radiation, $\lambda = 0.71073$) at 298 K. $R = 0.0535$, $R_w = 0.1541$. All calculations were performed using maXus [56]. The non-H-atoms were refined anisotropically with SHELXL-97 [57]. The H-atoms were calculated at idealized positions and included in the structure-factor calculation with fixed isotropic displacement parameters.

Data of **19**: R_f (hexane/Et_2O 5:1) 0.38. $[\alpha]_D^{25} = -90.2$ ($c = 1.00$, $CHCl_3$). UV ($CHCl_3$): 285 (2.74), 258 (3.11), 242 (3.80). IR ($CHCl_3$): 3065*w*, 2936*m*, 2870*m*, 1953*w*, 1878*w*, 1812*w*, 1744*w*, 1638*w*, 1603*w*, 1497*m*, 1450*s*, 1357*m*, 1096*s*, 1026*s*, 911*m*, 833*m*. ^{1}H-NMR ($CDCl_3$, 300 MHz): see *Table 4*; additionally, 4.49 (*d*, *J* = 11.8, PhC*H*); 4.53 (*d*, *J* = 12.1, PhC*H*); 4.55 (*d*, *J* = 11.8, PhC*H*); 4.57 (*d*, *J* = 11.2, PhC*H*); 4.61 (*d*, *J* = 11.2, PhC*H*); 4.65 (*d*, *J* = 12.1, PhC*H*); 4.78 (*d*, *J* = 12.1, PhC*H*); 4.82 (*d*, *J* = 12.1, PhC*H*); 7.15 (*s*, H–C(2)); 7.26–7.43 (*m*, 20 arom. H). ^{13}C-NMR ($CDCl_3$, 75 MHz): see *Table 5*; additionally, 70.73, 71.16 (2*t*, CH_2–C(5), PhCH_2); 72.07, 73.40, 73.46 (3*t*, 3 PhCH_2); 127.94–128.65 (several *d*); 137.77, 137.92, 138.03, 138.45 (4*s*). HR-MALDI-MS: 725.1251 (4, $C_{36}H_{35}IKN_2O_4$, $[M+K]^+$; calc. 725.1280), 709.1534 (83, $C_{36}H_{35}IN_2NaO_4$, $[M+Na]^+$; calc. 709.1541), 687.1715 (62, $C_{36}H_{36}IN_2O_4$, $[M+H]^+$; calc. 687.1721), 579.1141 (87, $C_{29}H_{28}IN_2O_3$, $[M-BnO]^+$; calc. 579.1146), 561.2756

Table 5. *Selected ^{13}C-NMR Chemical Shifts* [ppm] *of the Protected Imidazoles* **18**–**20**, **22**–**27**, **30**, **31**, **34**, **36**–**39**, **44**, **45**, **48**, *and* **49** *in $CDCl_3$*

Compound	C(2)	C(3)	C(5)	CH_2–C(5)	C(6)	C(7)	C(8)	C(8a)
18	96.30	82.51	62.60	[a])	77.61	80.39	68.69	148.71
19	136.98	69.93	60.99	[a])	77.99	80.92	68.74	146.80
20	82.17	125.04	60.10	[a])	73.75	79.79	68.22	145.08
22	142.00	125.95	60.47	[a])	73.67	79.47	68.55	145.04
23	142.11	116.65	59.80	70.80	73.92	80.06	68.63	143.05
24	127.95–128.93	122.33	60.14	[a])	74.03	79.83	68.19	144.72
25	140.48	[b])	59.89	[a])	74.03	80.03	68.46	143.34
26	[b])	115.38	59.68	[a])	74.14	80.29	68.79	[b])
27[c])	124.30	123.48	60.09	70.78	73.82	79.87	68.33	143.20
30	137.67–138.80	118.54	59.99	[a])	74.00	80.18	68.76	143.57
31[c])	138.17	118.33	59.84	70.74	73.93	80.06	68.63	142.99
34[c])	140.29	116.39	59.81	70.77	74.04	80.13	68.79	142.78
36	137.01	118.43	59.92	[a])	73.89	79.91	68.43	142.76
37	136.86	119.23	60.10	70.99	73.99	80.05	68.83	143.61
38	135.61	119.48	59.89	[a])	73.68	79.58	68.39	143.23
39	136.78	118.71	59.92	[a])	73.84	79.89	68.56	143.26
44	133.35	125.78	60.42	[a])	73.76	79.97	68.45	143.99
45	133.77	125.71	60.34	[a])	73.79	79.99	68.75	144.05
48	114.11–114.76	127.72–128.52	60.48	[a])	73.41	78.95	67.81	144.65
49	126.85	121.31	60.78	[a])	73.20	78.86	67.50	145.63

[a]) Two *t* for CH_2–C(5) and a PhCH_2 at 70.07–71.45 ppm. [b]) Not assigned. [c]) Assignments based on HSQC-GRASP spectrum.

(100), 453.2174 (57). Anal. calc. for $C_{36}H_{35}IN_2O_4$ (686.58): C 62.98, H 5.14, N 4.08; found: C 63.04, H 5.25, N 4.09.

*(5*R*,6*R*,7*S*,8*R*)-6,7,8-Tris(benzyloxy)-5-[(benzyloxy)methyl]-5,6,7,8-tetrahydro-2-iodoimidazo[1,2-*a*]pyridine* (**20**). EtMgBr soln. in THF (1M, 7.5 ml, 7.50 mmol) was added dropwise to a stirred soln. of **18** (5.11 g, 6.29 mmol) in freshly distilled THF (60 ml) at 23° for 10 min. After 25 min, the mixture was treated with sat. NH_4Cl soln. (50 ml) and diluted with Et_2O (100 ml). The layers were separated, and the org. layer was washed with sat. NH_4Cl soln. (2 × 50 ml). The combined H_2O layers were extracted with Et_2O (2 × 40 ml). The combined org. layers were washed with H_2O (70 ml) and brine (70 ml), dried ($MgSO_4$), filtered, and evaporated. FC (hexane/AcOEt 1:0 → 8:1 → 5:1 → 1:1) gave **20** (3.82 g, 88%) and **17** (0.36 g, 10%) as oils.

Data of **20**: R_f (hexane/AcOEt 1:1) 0.62. $[\alpha]_D^{25} = -37.5$ ($c = 0.98$, $CHCl_3$). IR ($CHCl_3$): 3065*w*, 2869*m*, 1954*w*, 1879*w*, 1813*w*, 1728*w*, 1602*w*, 1495*m*, 1454*m*, 1427*w*, 1363*m*, 1256*w*, 1112*s*, 1026*s*, 946*w*, 914*w*. ^{1}H-NMR ($CDCl_3$, 300 MHz): see *Table 4*; additionally, 4.46 (br. *s*, PhCH_2); 4.60 (*d*, *J* = 12.1, PhCH); 4.61 (*d*, *J* = 11.2, PhCH); 4.66 (*d*, *J* = 12.1, PhCH); 4.67 (*d*, *J* = 11.8, PhCH); 4.75 (*d*, *J* ≈ 12.8, PhCH); 4.99 (*d*, *J* = 11.2, PhCH); 7.24–7.42 (*m*, 20 arom. H, H–C(3)). ^{13}C-NMR ($CDCl_3$, 75 MHz): see *Table 5*; additionally, 70.63, 70.79, (2*t*, CH_2–C(5), PhCH_2); 71.86, 73.23 (2*t*, 2 PhCH_2); 75.00 (*t*, PhCH_2); 127.61–128.58 (several *d*); 137.33, 137.69, 137.87, 137.98 (4*s*). FAB-MS: 1373 (5, $[2M+1]^+$), 687 (100, $[M+1]^+$), 579 (14), 473 (6), 367 (5), 91 (51). HR-MALDI-MS: 709.1563 (48, $C_{36}H_{35}IN_2NaO_4$, $[M+Na]^+$; calc. 709.1541), 687.1705 (100, $C_{36}H_{36}IN_2O_4$, $[M+H]^+$; calc. 687.1721), 579.1149 (73, $C_{29}H_{28}IN_2O_3$, $[M-BnO]^+$; calc. 579.1146), 561.2750 (27), 453.2167 (16). Anal. calc. for $C_{36}H_{35}IN_2O_4$ (686.58): C 62.98, H 5.14, N 4.08; found: C 62.89, H 5.27, N 3.97.

*(5*R*,6*R*,7*S*,8*R*)-5-(Hydroxymethyl)-5,6,7,8-tetrahydro-3-iodoimidazo[1,2-*a*]pyridine-6,7,8-triol* (**21**). A soln. of **19** (35 mg, 51.0 μmol) in CH_2Cl_2 (1.5 ml) was treated at −78° with 1M BCl_3 soln. in CH_2Cl_2 (0.9 ml, 0.90 mmol), stirred until the mixture had reached a temp. of 15° (*ca.* 5 h), cooled to −78°, and treated with H_2O (2 ml). After evaporation, FC (AcOEt/MeOH 10:1 → 5:1) and lyophilisation gave **21** (9.3 mg, 56%) as a colourless hygroscopic resin. R_f (AcOEt/MeOH 5:1) 0.11. $[\alpha]_D^{25} = -39.0$ ($c = 0.70$, MeOH). UV (MeOH): 223 (3.63). IR (KBr): 3600–2400*s* (br.), 2921*m*, 1632*w*, 1523*w*, 1443*m*, 1340*w*, 1273*w*, 1177*m*, 1130*w*, 1077*s*, 979*w*, 937*w*, 899*w*. ^{1}H-NMR (CD_3OD, 300 MHz): 3.90 (*dd*, *J* = 6.5, 14.3, CH–C(5)); 3.91 (*dd*, *J* = 4.1, 6.2, irrad. at

Table 6. *Selected ^{13}C-NMR Chemical Shifts* [ppm] *of the Deprotected Imidazoles* **9**–**13**, **21**, **28**, **29**, **32**, **35**, **40**, **41**, **43**, **46**, **47**, *and* **50** *in CD_3OD*

Compound	C(2)	C(3)	C(5)	CH_2–C(5)	C(6)	C(7)	C(8)	C(8a)
9[a])	143.65	118.80	63.63	62.11	67.34	73.63	66.55	147.91
10	[c])	115.62	63.44	62.95	67.06	73.15	65.69	145.79
11	141.78	115.96	63.61	62.94	67.15	73.17	65.71	146.32
12[a])	136.30	115.72	61.83[b])	59.32	65.08	69.29	62.26[b])	142.71
13	81.61	125.38	64.07	62.90	67.31	72.66	66.35	149.18
21	136.95	69.86	64.83	63.26	70.43	72.79	66.05	150.51
28	[c])	123.61	64.04	62.95	67.09	72.81	65.55	147.23
29	141.09	[c])	63.80	62.94	67.08	73.00	65.75	147.20
32	138.71	118.62	63.76	63.00	67.10	73.01	65.68	146.83
35[a])	139.70	115.36	60.77	59.22	64.48[b])	70.81	63.71[b])	147.31
40	141.75	[c])	63.22[b])	62.15	69.11[b])	70.13[b])	64.04[b])	147.47
41	137.68	119.47	63.86	63.07	67.16	73.01	65.72	147.37
43	137.72	119.17	63.82	63.05	67.12	72.98	65.69	147.13
46	133.49	126.01	64.25	62.98	67.05	72.70	65.62	148.42
47[a])	137.70	121.84	61.55	59.56	64.74[b])	70.79	63.90[b])	145.42
50[a])	131.48	116.70	61.14	59.30	64.51[b])	70.76	63.81[b])	145.92

[a]) Measured in D_2O. [b]) Assignment may be interchanged. [c]) Not assigned.

4.45 → *d*, *J* = 4.1, irrad. at 4.80 → *d*, *J* = 6.2, H–C(7)); 4.14 (*dd*, *J* = 7.2, 14.3, CH′–C(5)); 4.11–4.17 (*m*, irrad. at 4.45 → change, H–C(5)); 4.45 (*dd*, *J* = 2.2, 6.2, H–C(6)); 4.80 (*d*, *J* = 3.7, H–C(8)); 7.10 (*s*, H–C(2)). ^{13}C-NMR (CD_3OD, 75 MHz): see *Table 6*. HR-MALDI-MS: 326.9830 (100, $C_8H_{12}IN_2O_4$, $[M+H]^+$; calc. 326.9844).

*(5*R*,6*R*,7*S*,8*R*)-5,6,7,8-Tetrahydro-5-(hydroxymethyl)-2-iodoimidazo[1,2-*a*]pyridine-6,7,8-triol* (**13**). A soln. of **20** (100 mg, 0.146 mmol) in CH_2Cl_2 (4 ml) was treated at −78° with 1M BCl_3 soln. in CH_2Cl_2 (2.5 ml, 2.50 mmol), stirred until the mixture had reached a temp. of 15° (*ca.* 5 h), cooled to −78°, and treated with H_2O (3 ml). After evaporation, FC (AcOEt/MeOH 10:1), ion-exchange chromatography (*Amberlite CG-120*, H^+ form, elution with 0.1M aq. NH_3), and lyophilisation gave **13** (30.6 mg, 64%). Colourless hygroscopic resin. R_f (AcOEt/MeOH 5:1) 0.20. $[\alpha]_D^{25} = -16.5$ (*c* = 0.47, MeOH). UV (MeOH): 226 (3.56), 206 (3.76). IR (KBr): 3600–2400*s* (br.), 2925*m*, 2852*w*, 1695*w*, 1632*m*, 1485*w*, 1432*m*, 1382*m*, 1337*m*, 1259*w*, 1223*m*, 1176*w*, 1098*m*, 1004*w*, 957*w*, 903*w*, 635*w*. ^{1}H-NMR (CD_3OD, 300 MHz): 3.80 (*dd*, *J* = 3.7, 9.0, irrad. at 4.09 → br. *d*, *J* ≈ 3.4, irrad. at 4.79 → *d*, *J* = 9.0, H–C(7)); 3.87 (*dd*, *J* = 5.6, 13.4, CH–C(5)); 3.85–3.92 (*m*, irrad. at 4.09 → change, H–C(5)); 4.09 (*dd*, *J* = 7.2, 9.3, irrad. at 3.80 → br. *d*, *J* ≈ 6.2, H–C(6)); 4.13 (*dd*, *J* = 5.3, 13.4, CH′–C(5)); 4.79 (*d*, *J* = 3.7, irrad. at 3.80 → *s*, H–C(8)); 7.44 (*s*, H–C(3)). ^{13}C-NMR (CD_3OD, 75 MHz): see *Table 6*. HR-MALDI-MS: 326.9838 (100, $C_8H_{12}IN_2O_4$, $[M+H]^+$; calc. 326.9844).

*(5*R*,6*R*,7*S*,8*R*)-6,7,8-Tris(benzyloxy)-5-[(benzyloxy)methyl]-5,6,7,8-tetrahydroimidazo[1,2-*a*]pyridine-2-carbaldehyde* (**22**). A soln. of **20** (320 mg, 0.466 mmol, dried for 1 week *i.v.* over P_2O_5[13]) in THF (6.5 ml) was treated at −35° with 1M EtMgBr soln. in THF (940 µl, 0.940 mmol), stirred under Ar at −35° for 10 min and at 23° for 10 min. The mixture was cooled to −35°, treated with DMF (600 µl, 7.80 mmol), and stirred at −35° to 23° for 3 h. The mixture was treated with H_2O (10 ml), diluted with Et_2O (60 ml), and washed with sat. NH_4Cl soln. (3 × 30 ml). The combined aq. layers were extracted with Et_2O (2 × 30 ml). The combined org. layers were washed with H_2O (40 ml) and brine (40 ml), dried ($MgSO_4$), filtered, and evaporated. FC (hexane/AcOEt 2:1 → 1:1) gave **22** (234 mg, 85%) as an oil, which crystallized *i.v.*, and **17** (18 mg, 7%) as an oil.

Data of **22**: R_f (hexane/AcOEt 1:1) 0.29. $[\alpha]_D^{25} = -48.6$ (*c* = 1.17, $CHCl_3$). UV ($CHCl_3$): 278 (3.34). IR ($CHCl_3$): 3150*w*, 3065*w*, 3008*m*, 2868*m*, 1954*w*, 1878*w*, 1812*w*, 1689*s*, 1604*w*, 1537*m*, 1497*w*, 1454*m*, 1364*m*, 1257*w*, 1106*s*, 1025*m*, 914*w*. ^{1}H-NMR ($CDCl_3$, 300 MHz): see *Table 4*; additionally, 4.44 (*d*, *J* = 12.1, PhC*H*); 4.48 (*d*, *J* = 12.1, PhC*H*); 4.61 (*d*, *J* = 11.8, PhC*H*); 4.62 (*d*, *J* = 11.2, PhC*H*); 4.68 (*d*, *J* = 12.5, 2 PhC*H*); 4.78 (*d*, *J* = 12.5, PhC*H*); 4.96 (*d*, *J* = 11.5, PhC*H*); 7.23–7.28 (*m*, 4 arom. H); 7.29–7.38 (*m*, 14 arom. H); 7.39–7.43 (*m*, 2 arom. H); 9.88 (*s*, CHO). ^{13}C-NMR ($CDCl_3$, 75 MHz): see *Table 5*; additionally, 70.48, 71.03 (2*t*, Ph*C*H$_2$,

[13]) Required to secure reproducible yields of **22** (80–90%).

*C*H$_2$–C(5)); 72.06 (*t*, Ph*C*H$_2$); 73.33 (*t*, Ph*C*H$_2$); 74.83 (*t*, Ph*C*H$_2$); 127.76–128.60 (several *d*); 137.10, 137.55, 137.66, 137.68 (4*s*); 185.79 (*d*, CHO). HR-MALDI-MS: 611.2509 (65, $C_{37}H_{36}N_2NaO_5$, $[M+Na]^+$; calc. 611.2522), 589.2688 (100, $C_{37}H_{37}N_2O_5$, $[M+H]^+$; calc. 589.2702), 481.2132 (53, $C_{30}H_{29}N_2O_4$, $[M-BnO]^+$; calc. 481.2127), 453.2179 (17, $C_{29}H_{29}N_2O_3$, $[M-BnO-CO]^+$; calc. 453.2178). Anal. calc. for $C_{37}H_{36}N_2O_5$ (588.70): C 75.49, H 6.16, N 4.76; found: C 75.53, H 6.35, N 4.68.

*(5*R*,6*R*,7*S*,8*R*)-6,7,8-Tris(benzyloxy)-5-[(benzyloxy)methyl]-5,6,7,8-tetrahydroimidazo[1,2-*a*]pyridine-2-methanol* (**23**). *a*) A soln. of **22** (100 mg, 0.170 mmol) in THF (6 ml) was treated at 23° with $LiAlH_4$ (65 mg, 1.71 mmol) and stirred for 30 min. The mixture was treated with MeOH/H_2O (4:1, 5 ml). The suspension was filtered through *Celite*, and the residue was washed with Et_2O (80 ml). The filtrate was washed with sat. NH_4Cl soln. (3 × 30 ml), and the combined aq. layers were extracted with Et_2O (2 × 20 ml). The combined org. layers were washed with H_2O (60 ml) and brine (60 ml), dried ($MgSO_4$), filtered, and evaporated. FC (hexane/AcOEt 1:1 → 0:1) gave **23** (85 mg, 85%). Colourless oil.

b) At 23°, a soln. of **22** (95 mg, 0.161 mmol) in EtOH (6 ml) was treated with $NaBH_4$ (12 mg, 0.317 mmol), stirred for 30 min, and evaporated. Workup and FC (as described in *a*) gave **23** (85 mg, 89%).

Data of **23**: R_f (AcOEt) 0.15. $[\alpha]_D^{25} = -33.7$ ($c = 0.96$, $CHCl_3$). UV ($CHCl_3$): 266 (3.21). IR ($CHCl_3$): 3400*w*, 3160*w*, 3066*w*, 3008*m*, 2929*m*, 2870*m*, 1954*w*, 1878*w*, 1812*w*, 1729*w*, 1603*w*, 1498*m*, 1454*m*, 1364*m*, 1258*m*, 1101*s*, 1025*s*, 913*w*. ^{1}H-NMR ($CDCl_3$, 300 MHz): see *Table 4*; additionally, 3.30–3.47 (br. *s*, exchange with CD_3OD, OH); 4.45 (br. *s*, PhC*H*$_2$); 4.58–4.62 (*m*, irrad. at 3.38 → change, C*H*$_2$OH); 4.59 (*d*, *J* = 11.8, PhC*H*); 4.60 (*d*, *J* = 11.2, PhC*H*); 4.67 (*d*, *J* = 11.8, PhC*H*); 4.68 (*d*, *J* = 12.1, PhC*H*); 4.75 (*d*, *J* = 12.1, PhC*H*); 5.00 (*d*, *J* = 11.2, PhC*H*); 7.23–7.35 (*m*, 18 arom. H); 7.36–7.41 (*m*, 2 arom. H). ^{13}C-NMR ($CDCl_3$, 75 MHz): see *Table 5*; additionally, 58.49 (*t*, *C*H$_2$–C(2)); 70.80 (2*t*, Ph*C*H$_2$, *C*H$_2$–C(5)); 71.76 (*t*, Ph*C*H$_2$); 73.18 (*t*, PhCH$_2$); 74.94 (*t*, Ph*C*H$_2$); 127.49–128.51 (several *d*); 137.48, 137.81, 137.97, 138.21 (4*s*). HR-MALDI-MS: 613.2673 (37, $C_{37}H_{38}N_2NaO_5$, $[M+Na]^+$; calc. 613.2678), 591.2848 (100, $C_{37}H_{39}N_2O_5$, $[M+H]^+$; calc. 591.2859), 483.2296 (32, $C_{30}H_{31}N_2O_2$, $[M-BnO]^+$; calc. 483.2284), 453.2183 (14, $C_{29}H_{29}N_2O_3$, $[M-BnO-CH_2O]^+$; calc. 453.2178), 375.1714 (11), 359.1761 (11). Anal. calc. for $C_{37}H_{38}N_2O_5$ (590.72): C 75.23, H 6.48, N 4.74; found: C 75.16, H 6.58, N 4.70.

*(5*R*,6*R*,7*S*,8*R*)-5,6,7,8-Tetrahydro-2,5-bis(hydroxymethyl)imidazo[1,2-*a*]pyridine-6,7,8-triol* (**9**). A soln. of **23** (70 mg, 0.119 mmol) in CH_2Cl_2 (3 ml) was treated at −78° with 1M BCl_3 in CH_2Cl_2 (1.5 ml, 1.5 mmol), stirred until the mixture had reached a temp. of 10° (*ca.* 4 h), cooled to −78°, treated with H_2O (3 ml), neutralised with sat. $NaHCO_3$ soln. (10 ml), and evaporated. The residue was taken up in H_2O (3 ml) and applied to ion-exchange column (*Amberlite CG-120*, H^+ form, elution with 0.1M aq. NH_3). Lyophilisation gave **9** (26.5 mg, 97%). Colourless hygroscopic resin. R_f (AcOEt/MeOH 2:1) 0.13. $[\alpha]_D^{25} = -41.1$ ($c = 1.00$, H_2O). UV (MeOH): 220 (3.74). IR (KBr): 3600–2400*s* (br.), 2926*m*, 2879*m*, 1642*m*, 1572*w*, 1512*m*, 1456*m*, 1412*m*, 1381*m*, 1320*m*, 1213*m*, 1178*m*, 1095*s*, 1062*s*, 1029*m*, 995*s*, 901*m*. ^{1}H-NMR (D_2O, 300 MHz): 3.91 (*dt*, *J* = 3.1, 7.8, irrad. at 4.00 → change, H–C(5)); 3.93 (*dd*, *J* = 4.0, 10.0, irrad. at 4.87 → *d*, *J* = 10.3, H–C(7)); 4.00 (*dd*, *J* = 3.1, 12.8, CH–C(5)); 4.18 (*dd*, *J* = 8.1, 10.3, irrad. at 3.93 → change, H–C(6)); 4.19 (*dd*, *J* ≈ 3.1, 13.4, irrad. at 4.00 → br. *d*, *J* ≈ 4.4, CH′–C(5)); 4.48 (br. *s*, CH$_2$–C(2)); 4.87 (*d*, *J* = 3.7, irrad. at 3.93 → *s*, H–C(8)); 7.24 (*s*, H–C(3)). ^{13}C-NMR (D_2O, 75 MHz): see *Table 6*; additionally, 59.59 (*t*, *C*H$_2$–C(2)). HR-MALDI-MS: 253.0802 (56, $C_9H_{14}N_2NaO_5$, $[M+Na]^+$; calc. 253.0802), 231.0979 (100, $C_9H_{15}N_2O_5$, $[M+H]^+$; calc. 231.0981), 213.0876 (59, $C_9H_{13}N_2O_4$, $[M-OH]^+$; calc. 213.0876).

*Methyl (*E*)-3-[(5*R*,6*R*,7*S*,8*R*)-6,7,8-Tris(benzyloxy)-5-[(benzyloxy)methyl]-5,6,7,8-tetrahydroimidazo[1,2-*a*]pyridin-2-yl]-prop-2-enoate* (**24**). *a*) At 23°, a suspension of **20** (50.9 mg, 74.1 μmol), $Pd(OAc)_2$ (5.9 mg, 26.3 μmol), PPh_3 (7.5 mg, 28.6 μmol), and Et_3N (16 μl, 0.115 mmol) in freshly distilled and degassed DMF (1 ml) was treated with methyl acrylate (10 μl, 0.111 mmol) and heated to 90° for 15 h. The mixture was diluted with Et_2O (10 ml) and washed with sat. $NaHCO_3$ soln. (3 × 10 ml). The combined aq. layers were extracted with Et_2O (2 × 10 ml). The combined org. layers were washed with H_2O (15 ml) and brine (15 ml), dried ($MgSO_4$), filtered, and evaporated. FC (hexane/AcOEt 1:0 → 9:1 → 7:3 → 1:1) gave **24** (25.8 mg, 54%) and **17** (4.5 mg, 11%). Oils.

b) A suspension of **20** (115 mg, 0.168 mmol), $[Pd(OAc)_2(P(2\text{-tolyl})_3)_2]$ (11.6 mg, 11.9 μmol) and K_2CO_3 (65 mg, 0.656 mmol) in freshly distilled and degassed DMF (2 ml) was treated with methyl acrylate (0.2 ml, 2.22 mmol) and heated to 90° for 165 min. Workup and FC, as described in *a*, gave **24** (101.6 mg, 94%).

Data of **24**: R_f (hexane/AcOEt 3:1) 0.16. $[\alpha]_D^{25} = -42.2$ ($c = 0.90$, $CHCl_3$). UV ($CHCl_3$): 328 (2.73). IR ($CHCl_3$): 3148*w*, 3065*w*, 2950*m*, 2869*m*, 1953*w*, 1878*w*, 1812*w*, 1705*s*, 1643*s*, 1497*w*, 1447*m*, 1364*m*, 1301*m*, 1271*s*, 1168*s*, 1109*s*, 1025*s*, 981*m*, 914*w*. ^{1}H-NMR ($CDCl_3$, 300 MHz): see *Table 4*; additionally, 3.79 (*s*, MeO); 4.46 (br. *s*, PhC*H*$_2$); 4.57 (*d*, *J* = 12.1, PhC*H*); 4.62 (*d*, *J* = 12.1, PhC*H*); 4.66 (*d*, *J* = 12.1, PhC*H*); 4.69 (*d*, *J* = 12.1, PhC*H*); 4.77 (*d*, *J* = 11.2, PhC*H*); 4.99 (*d*, *J* = 11.2, PhC*H*); 6.60 (*d*, *J* = 15.6, C*H*=CH–C(2)); 7.25–7.38 (*m*, 18 arom. H,

H–C(3)); 7.42–7.45 (*m*, 2 arom. H); 7.56 (*d*, *J* = 15.6, CH=C*H*–C(2)). ^{13}C-NMR ($CDCl_3$, 75 MHz): see *Table 5*; additionally, 51.61 (*q*, MeO); 70.77, 70.98 (2*t*, Ph*C*H$_2$, *C*H$_2$–C(5)); 71.92 (*t*, Ph*C*H$_2$); 73.42 (*t*, Ph*C*H$_2$); 75.02 (*t*, Ph*C*H$_2$); 115.94 (*d*, *C*H=CH–C(2)); 127.95–128.83 (several *d*, including C(2)); 136.72 (*d*, CH=*C*H–C(2)); 137.56, 137.90, 138.08, 138.37 (4*s*); 168.43 (*s*, C=O). FAB-MS: 1289 (3, $[2M+1]^+$), 645 (100, $[M+1]^+$), 537 (11), 431 (9), 220 (7), 91 (77). Anal. calc. for $C_{40}H_{40}N_2O_6$ (644.77): C 74.51, H 6.25, N 4.34; found: C 74.69, H 6.30, N 4.28.

*(5*R*,6*R*,7*S*,8*R*)-6,7,8-Tris(benzyloxy)-5-[(benzyloxy)methyl]-5,6,7,8-tetrahydro-2-[(*E*)-2-phenylethenyl]-imidazo[1,2-*a*]pyridine* (**25**). *a*) A suspension of **20** (31 mg, 45.2 μmol), $Pd(OAc)_2$ (1.5 mg, 6.68 μmol), PPh_3 (3.0 mg, 11.4 μmol), and K_2CO_3 (9.5 mg, 68.7 μmol) in degassed DMF (0.7 ml) was treated with styrene (0.1 ml, 0.87 mmol), and stirred at 80° for 16 h, cooled to r.t., diluted with Et_2O (15 ml), and washed with sat. NH_4Cl soln. (3 × 10 ml). The combined aq. layers were extracted with Et_2O (2 × 5 ml). The combined org. layers were washed with H_2O (10 ml) and brine (10 ml), dried ($MgSO_4$), filtered, and evaporated. FC (hexane/AcOEt 1:0 → 7:1 → 1:1 → 1:2) gave **17** (5.0 mg, 20%) as an oil, and **25**/**20** (17 mg, *ca.* 3:2). HPLC (hexane/Et_2O 3:1) of this mixture gave **25** (7.6 mg, 25%) and **20** (5.6 mg, 18%) as yellowish oils.

b) As described in *a*, but with $[Pd(OAc)_2(P(2\text{-tolyl})_3)_2]$ instead of $Pd(OAc)_2$ and PPh_3. Compounds **17** (2%), **25** (45%), and **20** (23%) were isolated as oils.

c) As described in *a*, but in DMF/H_2O 6:1 instead of DMF. After workup, FC and HPLC gave **17** (5%), **25** (24%), and **20** (25%).

d) As described in *c*, but with $[Pd(OAc)_2(P(2\text{-tolyl})_3)_2]$ instead of $Pd(OAc)_2$ and PPh_3: workup gave **17** (13%), **25** (18%), and **20** (30%).

e) A soln. of **22** (40 mg, 67.947 μmol) and diethyl benzylphosphonate (43 μl, 0.2063 mmol) in THF (1.3 ml) was treated at 0° with 1M soln. of *t*-BuOK in THF (0.20 ml, 0.20 mmol) and stirred at 0° for 5 min. The mixture was treated with sat. NH_4Cl soln. (3 ml). The mixture was diluted with CH_2Cl_2 (25 ml) and washed with sat. NH_4Cl soln. (25 ml). The aq. layer was extracted with CH_2Cl_2 (2 × 25 ml). The combined org. extracts were washed with brine (40 ml), dried ($MgSO_4$), filtered, and evaporated. FC (hexane/AcOEt 5:1) gave **25** (39.3 mg, 87%). Colourless oil.

Data of **25**: R_f (hexane/AcOEt 4:1) 0.26. $[\alpha]_D^{25} = -32.8$ (*c* = 1.00, $CHCl_3$). UV ($CHCl_3$): 311 (4.37), 302 (4.37), 239 (3.99). IR ($CHCl_3$): 3150*w*, 3067*w*, 3033*m*, 3013*m*, 2929*m*, 2869*m*, 1950*w*, 1877*w*, 1812*w*, 1644*w*, 1599*w*, 1535*w*, 1497*m*, 1455*m*, 1364*m*, 1343*m*, 1266*w*, 1113*s*, 1028*m*, 963*m*, 910*m*. ^{1}H-NMR ($CDCl_3$, 300 MHz): see *Table 4*; additionally, 4.48 (br. *s*, Ph*C*H$_2$); 4.62 (*d*, *J* = 12.1, Ph*C*H); 4.63 (*d*, *J* = 11.2, Ph*C*H); 4.71 (*d*, *J* = 12.1, Ph*C*H); 4.74 (*d*, *J* = 11.8, Ph*C*H); 4.81 (*d*, *J* = 12.1, Ph*C*H); 5.02 (*d*, *J* = 11.2, Ph*C*H); 6.99 (*d*, *J* = 16.2, C(2)–CH=C*H*); 7.22–7.38 (*m*, 21 arom. H, C(2)–C*H*=CH); 7.41–7.45 (*m*, 2 arom. H); 7.49–7.52 (*m*, 2 arom. H). ^{13}C-NMR ($CDCl_3$, 75 MHz): see *Table 5*; additionally, 70.62, 70.92 (2*t*, *C*H$_2$–C(5), Ph*C*H$_2$); 71.67 (*t*, Ph*C*H$_2$); 73.18 (*t*, Ph*C*H$_2$); 74.89 (*t*, Ph*C*H$_2$); 117.61 (*d*); 120.23 (*d*); 126.21 (2*d*); 127.06 (2*d*); 127.51 (*d*); 127.73–128.55 (several *d*); 137.45, 137.66, 137.74, 137.96, 138.10 (5*s*). MALDI-MS: 1327 ($[2M+H]^+$), 663 ($[M+H]^+$). HR-MALDI-MS: 685.3043 (14, $C_{44}H_{42}N_2NaO_4$, $[M+Na]^+$; calc. 685.3042), 663.3209 (100, $C_{44}H_{43}N_2O_4$, $[M+H]^+$; calc. 663.3223), 555.2633 (40, $C_{37}H_{35}N_2O_3$, $[M-BnO]^+$; calc. 555.2647). Anal. calc. for $C_{44}H_{42}N_2O_4$ (662.83): C 79.73, H 6.39, N 4.23; found: C 79.85, H 6.55, N 4.29.

*(5*R*,6*R*,7*S*,8*R*)-6,7,8-Tris(benzyloxy)-5-[(benzyloxy)methyl]-5,6,7,8-tetrahydro-2-(2-phenylethyl)imidazo[1,2-*a*]pyridine* (**26**). *a*) A soln. of **25** (25 mg, 37.7 μmol) in AcOEt/MeOH/AcOH 1:1:1 (1.5 ml) was treated with 10% Pd/C (12 mg) and hydrogenated for 96 h at 6 bar. Filtration over *Celite*, evaporation and FC (hexane/AcOEt 2:1) gave **26** (12 mg, 48%). Colourless oil.

b) A soln. of **25** (22 mg, 33.2 μmol) in AcOEt (1 ml) was treated with 10% Pd/C (10 mg) and hydrogenated for 6 h at 6 bar. Workup and FC as described in *a* gave **26** (16.5 mg, 75%). R_f (hexane/AcOEt 2:1) 0.18. $[\alpha]_D^{25} = -32.3$ (*c* = 1.03, $CHCl_3$). UV ($CHCl_3$): 241 (3.69). IR ($CHCl_3$): 3088*w*, 3066*w*, 3031*m*, 3012*m*, 2928*m*, 2865*m*, 1951*w*, 1875*w*, 1810*w*, 1726*w*, 1603*w*, 1585*w*, 1559*w*, 1497*m*, 1454*s*, 1363*m*, 1315*w*, 1267*w*, 1207*w*, 1171*w*, 1099*s*, 1027*s*, 913*m*. ^{1}H-NMR ($CDCl_3$, 300 MHz): see *Table 4*; additionally, 2.83–2.99 (*m*, CH_2CH_2); 4.41 (*d*, *J* = 12.1, Ph*C*H); 4.46 (*d*, *J* = 12.1, Ph*C*H); 4.62 (*d*, *J* = 11.2, Ph*C*H); 4.64 (*d*, *J* = 11.8, Ph*C*H); 4.68 (*d*, *J* = 11.5, Ph*C*H); 4.71 (*d*, *J* = 11.8, Ph*C*H); 4.76 (*d*, *J* = 12.1, Ph*C*H); 5.01 (*d*, *J* = 11.2, Ph*C*H); 7.13–7.21 (*m*, 2 arom. H); 7.22–7.40 (*m*, 23 arom. H). ^{13}C-NMR ($CDCl_3$, 75 MHz): see *Table 5*; additionally, 30.46, 35.90 (2*t*, CH_2CH_2); 70.53, 70.83 (2*t*, *C*H$_2$–C(5), Ph*C*H$_2$); 71.65 (*t*, Ph*C*H$_2$); 73.12 (*t*, Ph*C*H$_2$); 74.92 (*t*, Ph*C*H$_2$); 125.67 (*d*, C(4) of Ph); 127.26 (*d*); 127.58–128.32 (several *d*); 137.45, 137.76, 137.94, 138.23 (4*s*); 141.90, 141.93, 142.18 (3*s*, C(2), C(8a), C(1) of Ph). HR-MALDI-MS: 687.3209 (13, $C_{44}H_{44}N_2NaO_4$, $[M+Na]^+$; calc. 687.3199), 665.3381 (100, $C_{44}H_{45}N_2O_4$, $[M+H]^+$; calc. 665.3379), 557.2803 (24, $C_{37}H_{37}N_2O_3$, $[M-BnO]^+$; calc. 557.2804), 537.2750 (76).

*Methyl 3-[(5*R*,6*R*,7*S*,8*R*)-5,6,7,8-Tetrahydro-6,7,8-trihydroxy-5-(hydroxymethyl)imidazo[1,2-*a*]pyridin-2-yl]-propanoate* (**11**). A soln. of **24** (117 mg, 0.181 mmol) in AcOEt/MeOH/AcOH 1:1:1 (2.4 ml) was treated

with 10% Pd/C (100 mg), hydrogenated for 41 h at 6 bar, and filtered over *Celite* (washing with 25 ml of MeOH/H_2O 9:1). Evaporation, FC (AcOEt/MeOH/H_2O 15:1:1 → 7:1:1), and drying gave **11** (45.7 mg, *ca.* 88%) as a colourless solid containing substantial amounts of H_2O. The sample for microanalysis was dried for 4 d at 10^{-4} Torr. R_f (AcOEt/MeOH/H_2O 7:1:1) 0.11. $[\alpha]_D^{25} = -22.1$ ($c = 1.01$, MeOH). UV (MeOH): 224 (3.71). IR (KBr): 3600–2400*s* (br.), 2946*m*, 2926*m*, 2851*m*, 1738*s*, 1717*s*, 1635*w*, 1565*w*, 1505*w*, 1442*s*, 1370*m*, 1330*m*, 1260*m*, 1202*m*, 1176*s*, 1098*s*, 1059*s*, 1008*m*, 904*m*, 837*w*, 792*m*. ^{1}H-NMR (CD_3OD, 300 MHz): 2.61–2.68 (*m*, 2 H), 2.79–2.86 (*m*, 2 H) (CH_2CH_2); 3.65 (*s*, MeO); 3.77 (*dd*, $J = 3.7$, 9.3, irrad. at 4.79 → *d*, $J = 9.3$, H–C(7)); 3.80 (*ddd*, $J = 2.8$, 5.3, 7.8, irrad. at 4.15 → change, H–C(5)); 3.88 (*dd*, $J = 5.3$, 11.8, irrad. at 4.15 → br. *d*, $J \approx 4.7$, CH–C(5)); 4.09 (*dd*, $J = 7.8$, 9.3, irrad. at 3.77 → br. *d*, $J \approx 6.9$, H–C(6)); 4.15 (*dd*, $J = 2.8$, 11.8, irrad. at 3.88 → br. *d*, $J \approx 3.7$, CH′–C(5)); 4.79 (*d*, $J = 3.7$, irrad. at 3.77 → *s*, H–C(8)); 7.09 (*s*, H–C(3)). ^{13}C-NMR (CD_3OD, 75 MHz): see *Table 6*; additionally, 24.43, 34.65 (2*t*, CH_2CH_2); 52.14 (*q*, MeO); 175.17 (*s*, C=O). HR-MALDI-MS: 325.0795 (2, $C_{12}H_{18}KN_2O_6$, $[M+K]^+$; calc. 325.0802), 309.1052 (77, $C_{12}H_{18}N_2NaO_6$, $[M+Na]^+$; calc. 309.1062), 287.1233 (100, $C_{12}H_{19}N_2O_6$, $[M+H]^+$; calc. 287.1243), 269.1133 (14, $C_{12}H_{17}N_2O_5$, $[M-OH]^+$; calc. 269.1137), 255.0973 (3, $C_{11}H_{15}N_2O_5$, $[M-MeO]^+$; calc. 255.0981), 237.0868 (11, $C_{11}H_{13}N_2O_4$, $[M-OH-MeOH]^+$; calc. 237.0875). Anal. calc. for $C_{12}H_{18}N_2O_6 \cdot 0.6\ H_2O$ (297.09): C 48.51, H 6.51, N 9.43; found: C 48.40, H 6.22, N 9.12.

*3-[(5*R*,6*R*,7*S*,8*R*)-5,6,7,8-Tetrahydro-6,7,8-trihydroxy-5-(hydroxymethyl)imidazo[1,2-*a*]pyridin-2-yl]propanoic Acid* (**12**). A soln. of **11** (15 mg, 52.4 μmol) in 1M aq. HCl (1 ml) was stirred at 60° for 1 h and applied to ion-exchange chromatography (*Amberlite CG-120*, H^+ form, elution with 0.1M aq. NH_3). Evaporation, dissolving in H_2O (3 ml), and lyophilisation yielded **12** (12.2 mg, 85%) as a colourless hygroscopic resin. R_f (AcOEt/MeOH/H_2O 3:1:1) 0.14. $[\alpha]_D^{25} = -11.5$ ($c = 0.26$, MeOH). UV (MeOH): 225 (3.63). IR (KBr): 3600–2400*s* (br.), 2925*s*, 1944*w*, 1633*m*, 1568*s*, 1405*s*, 1309*m*, 1211*m*, 1166*m*, 1099*s*, 1071*s*, 1019*m*, 904*m*, 828*m*. ^{1}H-NMR (D_2O, 300 MHz): 2.51 (*t*, $J = 7.2$, 2 H), 2.88 (*t*, $J = 7.2$, 2 H) (CH_2CH_2); 4.03 (*dd*, $J = 3.7$, 12.5, CH–C(5)); 4.05 (*dd*, $J = 4.1$, 9.0, H–C(7)); 4.10 (*td*, $J \approx 3.1$, 6.5, H–C(5)); 4.18 (*dd*, $J = 2.8$, 12.5, CH′–C(5)); 4.27 (*dd*, $J = 6.5$, 9.0, H–C(6)); 5.07 (*d*, $J = 4.1$, H–C(8)); 7.28 (*s*, H–C(3)). ^{13}C-NMR (D_2O, 75 MHz): see *Table 6*; additionally, 21.80, 35.78 (2*t*, CH_2CH_2); 180.57 (*s*, C=O). HR-MALDI-MS: 295.0896 (98, $C_{11}H_{16}N_2NaO_6$, $[M+Na]^+$; calc. 295.0906), 273.1075 (100, $C_{11}H_{17}N_2O_6$, $[M+H]^+$; calc. 273.1086).

*(5*R*,6*R*,7*S*,8*R*)-5,6,7,8-Tetrahydro-5-(hydroxymethyl)-2-(2-phenylethyl)imidazo[1,2-*a*]pyridine-6,7,8-triol* (**10**). A soln. of **25** (50 mg, 75.4 μmol) in AcOEt/MeOH/H_2O 1:1:1 (1.5 ml) was treated with AcOH (1.5 ml) and 20% $Pd(OH)_2$/C (50 mg), hydrogenated at 6 bar for 120 h, and filtered through *Celite* (washing with MeOH/H_2O (9:1, 25 ml)). Evaporation of the combined filtrates, co-evaporation with toluene (3 × 5 ml), FC (AcOEt/MeOH/H_2O 15:1:1), FC (*RP-C18* SiO_2; MeOH/H_2O 7:3), and drying gave **10** (10.6 mg, *ca.* 46%) as a white solid containing substantial amounts of H_2O. The sample for microanalysis was dried for 4 d at 10^{-4} Torr. R_f (AcOEt/MeOH/H_2O 10:1:1) 0.17. $[\alpha]_D^{25} = -19.4$ ($c = 0.98$, MeOH). UV (MeOH): 211 (3.98). IR (KBr): 3600–2400*s* (br.), 3026*m*, 2925*m*, 2858*m*, 1938*w*, 1869*w*, 1801*w*, 1633*w*, 1604*w*, 1560*w*, 1497*m*, 1454*m*, 1401*w*, 1365*w*, 1331*m*, 1309*m*, 1263*w*, 1206*w*, 1182*w*, 1107*s*, 1060*m*, 1005*m*, 903*m*. ^{1}H-NMR (CD_3OD, 300 MHz): 2.77–2.82 (*m*, 2 H); 2.88–2.93 (*m*, 2 H) (CH_2CH_2); 3.77 (*dd*, $J = 3.7$, 9.3, H–C(7)); 3.78 (*ddd*, $J = 2.5$, 5.6, 7.5, H–C(5)); 3.87 (*dd*, $J = 5.3$, 11.8, CH–C(5)); 4.09 (*dd*, $J = 7.8$, 9.3, H–C(6)); 4.13 (*dd*, $J = 2.5$, 11.8, CH′–C(5)); 4.80 (*d*, $J = 3.7$, H–C(8)); 7.02 (*s*, H–C(3)); 7.10–7.27 (*m*, 5 arom. H). ^{13}C-NMR (CD_3OD, 75 MHz): see *Table 6*; additionally, 31.29, 36.88 (2*t*); 126.73 (*d*, C(4) of Ph); 129.16 (2*d*); 129.24 (2*d*); 142.70, 142.98 (2*s*, C(1) of Ph, C(2)). HR-MALDI-MS: 327.1315 (13, $C_{16}H_{20}N_2NaO_4$, $[M+Na]^+$; calc. 327.1321), 305.1491 (100, $C_{16}H_{21}N_2O_4$, $[M+H]^+$; calc. 305.1501), 287.1387 (11, $C_{16}H_{19}N_2O_3$, $[M-OH]^+$; calc. 287.1396). Anal. calc. for $C_{16}H_{20}N_2O_4 \cdot 0.5\ H_2O$ (313.36): C 61.33, H 6.75, N 8.94; found: C 61.55, H 6.78, N 8.75.

*(5*R*,6*R*,7*S*,8*R*)-5,6,7,8-Tetrahydro-6,7,8-tris(benzyloxy)-5-[(benzyloxy)methyl]-2-(2-phenylethynyl)imidazo[1,2-*a*]pyridine* (**27**). At 23°, a suspension of **20** (305 mg, 0.444 mmol), $Pd(PPh_3)_4$ (25 mg, 21.6 μmol), CuI (9 mg, 47.3 μmol), and Et_3N (300 μl, 2.15 mmol) in degassed DMF (7.5 ml) was treated with phenylacetylene (150 μl, 1.37 mmol), stirred at 80° for 3 h, cooled to r.t., diluted with Et_2O (50 ml), and washed with sat. NH_4Cl soln. (3 × 20 ml). The combined aq. layers were extracted with Et_2O (3 × 15 ml). The combined org. layers were washed with H_2O (25 ml) and brine (25 ml), dried ($MgSO_4$), filtered, and evaporated. FC (hexane/AcOEt 1:0 → 7:1 → 4:1 → 1:2) gave **27** (245 mg, 83%) and **17** (24 mg, 10%). Oils.

Data of **27**: R_f (hexane/AcOEt 4:1) 0.27. $[\alpha]_D^{25} = -27.8$ ($c = 0.99$, $CHCl_3$). UV ($CHCl_3$): 299 (4.2), 283 (4.2), 252 (4.0), 241 (4.0). IR ($CHCl_3$): 3157*w*, 3089*w*, 3066*w*, 2941*m*, 2868*m*, 2100*w*, 1952*w*, 1876*w*, 1811*w*, 1731*w*, 1599*s*, 1586*m*, 1496*s*, 1454*s*, 1364*m*, 1301*m*, 1174*m*, 1112*s*, 1050*s*, 1028*s*, 913*w*. ^{1}H-NMR ($CDCl_3$, 400 MHz): see *Table 4*; additionally, 4.46 (br. *s*, PhCH_2); 4.59 (*d*, $J = 12.0$, PhC*H*); 4.61 (*d*, $J = 11.2$, PhC*H*); 4.659 (*d*, $J = 12.0$, PhC*H*); 4.664 (*d*, $J = 12.2$, PhC*H*); 4.760 (*d*, $J = 12.1$, PhC*H*); 4.99 (*d*, $J = 11.2$, PhC*H*); 7.23–7.36 (*m*, 21 arom. H); 7.40–7.42 (*m*, 2 arom. H); 7.52–7.54 (*m*, H–C(2) and H–C(6) of Ph). ^{13}C-NMR ($CDCl_3$, 100 MHz): see *Table 5*;

additionally, 70.68 (*t*, Ph*C*H$_2$); 71.77 (*t*, Ph*C*H$_2$); 73.20 (*t*, Ph*C*H$_2$); 74.90 (*t*, Ph*C*H$_2$); 82.98 (*s*, *C*≡C–C(2)); 89.31 (*s*, C≡*C*–C(2)); 123.23 (*s*, C(1) of Ph); 127.53–128.49 (several *d*); 131.48 (2*d*, C(2) and C(6) of Ph); 137.32, 137.66, 137.86, 137.93 (4*s*). HR-MALDI-MS: 683.2916 (26, $C_{44}H_{40}N_2NaO_4$, $[M+Na]^+$; calc. 683.2886), 661.3069 (100, $C_{44}H_{41}N_2O_4$, $[M+H]^+$; calc. 661.3066), 553.2499 (63, $C_{37}H_{33}N_2O_3$, $[M-BnO]^+$; calc. 553.2491). Anal. calc. for $C_{44}H_{40}N_2O_4$ (660.81): C 79.98, H 6.10, N 4.24; found: C 79.91, H 6.11, N 4.09.

Hydrogenation of **27**. A soln. of **27** (91 mg, 0.1377 mmol) in AcOEt/MeOH/H$_2$O 3:1:1 (2.5 ml) was treated with AcOH (2.5 ml), 20% Pd(OH)$_2$/C (90 mg), hydrogenated at 6 bar for 41 h, and filtered through *Celite* (washing with MeOH/H$_2$O (9:1, 25 ml)). Evaporation of combined filtrates, co-evaporation with toluene (3 × 5 ml), FC (AcOEt/MeOH/H$_2$O 15:1:1), and FC (RP-C18 SiO$_2$; MeOH/H$_2$O 7:3) afforded **10** (33.4 mg, 80%).

*(5*R*,6*R*,7*S*,8*R*)-5,6,7,8-Tetrahydro-5-(hydroxymethyl)-2-(phenylethynyl)imidazo[1,2-*a*]pyridine-6,7,8-triol* (**28**). A soln. of **27** (90 mg, 0.136 mmol) in CH_2Cl_2 (3.6 ml) was treated at −78° with 1M BCl_3 in CH_2Cl_2 (2.25 ml, 2.25 mmol), stirred until the mixture had reached a temp. of 10° (*ca.* 5 h), cooled to −78°, treated with H$_2$O (3 ml), neutralised with aq. NH_3 (1 ml), and evaporated. FC (AcOEt/MeOH/H$_2$O 1:0:0 → 20:1:1), lyophilisation, and drying afforded **28** (34.7 mg, ca. 85%) as a yellowish hygroscopic resin containing substantial amounts of H$_2$O. The sample for microanalysis was dried for 4 d at 10^{-4} Torr. R_f (AcOEt/MeOH/H$_2$O 10:1:1) 0.16. $[\alpha]_D^{25} = -16.0$ ($c = 0.80$, MeOH). UV (MeOH): 265 (4.02), 249 (4.02), 238 (4.05), 220 (4.12). IR (KBr): 3600–2400*s* (br.), 2925*m*, 2851*m*, 2219*w*, 2072*w*, 1958*w*, 1893*w*, 1721*w*, 1656*m*, 1630*m*, 1598*m*, 1550*m*, 1513*w*, 1487*m*, 1442*m*, 1406*m*, 1384*m*, 1314*m*, 1261*m*, 1210*m*, 1181*m*, 1094*s*, 1068*s*, 1008*m*, 902*m*, 841*w*, 805*w*. ^{1}H-NMR (CD$_3$OD, 300 MHz): 3.84 (*dd*, $J = 3.7$, 9.0, irrad. at 4.13 → *d*, $J = 3.7$, irrad. at 4.82 → *d*, $J \approx 8.7$, H–C(7)); 3.87–3.93 (*m*, H–C(5)); 3.91 (*dd*, $J = 5.9$, 13.7, CH–C(5)); 4.13 (*dd*, $J \approx 6.9$, 9.3, irrad. at 3.84 → *d*, $J \approx 5.0$, H–C(6)); 4.17 (*dd*, $J = 5.0$, 14.0, CH′–C(5)); 4.82 (*d*, $J = 3.7$, irrad. at 3.84 → *s*, H–C(8)); 7.31–7.38 (*m*, H–C(3), H–C(4), and H–C(5) of Ph); 7.43–7.49 (*m*, H–C(2) and H–C(6) of Ph); 7.60 (*s*, H–C(3)). ^{13}C-NMR (CD$_3$OD, 75 MHz): see *Table 6*; additionally, 83.54 (*s*, *C*≡C–C(2)); 90.07 (*s*, C≡*C*–C(2)); 124.30, 124.70 (2*s*, C(1) of Ph, C(2)); 129.20 (*d*, C(4) of Ph); 129.37 (2*d*, C(3) and C(5) of Ph); 132.11 (2*d*, C(2) and C(6) of Ph). HR-MALDI-MS: 323.0995 (5, $C_{16}H_{16}N_2NaO_4$, $[M+Na]^+$; calc. 323.1008); 301.1178 (100, $C_{16}H_{17}N_2O_4$, $[M+H]^+$; calc. 301.1188); 283.1070 (8, $C_{16}H_{15}N_2O_3$, $[M-OH]^+$; calc. 283.1083). Anal. calc. for $C_{16}H_{16}N_2O_4 \cdot 0.6\ H_2O$ (311.12): C 61.77, H 5.57, N 9.00; found: C 61.73, H 5.54, N 8.90.

*(5*R*,6*R*,7*S*,8*R*)-5,6,7,8-Tetrahydro-5-(hydroxymethyl)-2-[(*E*)-phenylethenyl]imidazo[1,2-*a*]pyridine-6,7,8-triol* (**29**). *a*) A soln. of **25** (40 mg, 60.3 μmol) in CH_2Cl_2 (1.5 ml) was treated at −78° with 1M BCl_3 in CH_2Cl_2 (1.05 ml, 1.05 mmol), stirred until the mixture had reached a temp. of 15° (*ca.* 5 h), cooled to −78°, treated with H$_2$O (3 ml), neutralised with aq. NH_3 (1 ml), and evaporated. FC (AcOEt/MeOH/H$_2$O 1:0:0 → 15:1:1), lyophilisation, and drying yielded **29** (6.2 mg, ca. 34%) as a yellowish hygroscopic resin containing substantial amounts of AcOEt and H$_2$O. The sample for microanalysis was dried for 4 d at 10^{-4} Torr.

b) A soln. of **25** (30 mg, 45.3 μmol) in CH_2Cl_2 (1 ml) was treated with $AlCl_3$ (97 mg, 0.727 mmol) and *N*,*N*-dimethylaniline (70 μl, 0.552 mmol), stirred for 18 h at 22°, and treated with H$_2$O (15 ml). The mixture was diluted with AcOEt (15 ml) and extracted with H$_2$O. Evaporation of the aq. layer, FC (as described in *a*), lyophilisation, and drying yielded **29** (5.7 mg, *ca.* 42%) containing substantial amounts of AcOEt and H$_2$O.

Data of **29**: R_f (AcOEt/MeOH/H$_2$O 10:1:1) 0.13. $[\alpha]_D^{25} = +2.5$ ($c = 0.25$, MeOH). UV (MeOH): 295 (4.19), 226 (4.04), 203 (4.22). IR (KBr): 3600–2400*s* (br.), 2925*m*, 2851*w*, 1633*w*, 1597*w*, 1535*w*, 1513*w*, 1490*w*, 1443*w*, 1381*w*, 1323*w*, 1261*w*, 1208*w*, 1180*w*, 1152*w*, 1095*m*, 1068*m*, 963*w*, 902*w*, 833*w*, 762*w*, 693*m*. ^{1}H-NMR (CD$_3$OD, 300 MHz): 3.83 (*dd*, $J = 3.7$, 9.3, H–C(7)); 3.85–3.91 (*m*, H–C(5)); 3.93 (*dd*, $J = 5.6$, 11.5, CH–C(5)); 4.13 (*dd*, $J = 7.2$, 9.3, H–C(6)); 4.19 (*dd*, $J = 2.5$, 11.5, CH′–C(5)); 4.86 (*d*, $J = 3.7$, H–C(8)); 7.01 (*d*, $J = 16.2$, C(2)–CH=C*H*); 7.15 (*d*, $J = 16.5$, C(2)–C*H*=CH); 7.16–7.23 (*m*, H–C(4) of Ph); 7.27–7.34 (*m*, H–C(3) and H–C(5) of Ph); 7.44 (*s*, H–C(3)); 7.45–7.50 (*m*, H–C(2) and H–C(6) of Ph). ^{13}C-NMR (CD$_3$OD, 75 MHz): see *Table 6*; additionally, 117.85 (*d*); 120.68 (*d*); 127.03 (*d*, C(2) and C(6) of Ph); 128.11 (*d*); 128.22 (*d*); 129.49 (*d*, C(3) and C(5) of Ph); 138.78 (*s*, C(1) of Ph). HR-MALDI-MS: 325.1160 (16, $C_{16}H_{18}N_2NaO_4$, $[M+Na]^+$; calc. 325.1164); 303.1342 (100, $C_{16}H_{19}N_2O_4$, $[M+H]^+$; calc. 303.1345); 285.1230 (16, $C_{16}H_{17}N_2O_3$, $[M-OH]^+$, calc. 285.1239). Anal. calc. for $C_{16}H_{18}N_2O_4 \cdot 0.5$ AcOEt $\cdot 0.5\ H_2O$ (355.39): C 60.83, H 6.52, N 7.88; found: C 60.67, H 6.28, N 7.88.

*(5*R*,6*R*,7*S*,8*R*)-6,7,8-Tris(benzyloxy)-5-[(benzyloxy)methyl]-2-(chloromethyl)-5,6,7,8-tetrahydroimidazo[1,2-*a*]pyridine* (**30**). A soln. of **23** (85 mg, 0.144 mmol) in CH_2Cl_2 (3 ml) was treated with $SOCl_2$ (20 μl, 0.275 mmol), stirred at 23° for 40 min, and treated with sat. $NaHCO_3$ soln. (10 ml). The mixture was diluted with Et_2O (15 ml) and washed with sat. $NaHCO_3$ soln. (2 × 10 ml). The combined aq. layers were extracted with Et_2O (2 × 10 ml). The org. layers were combined, washed with H$_2$O (15 ml) and brine (15 ml), dried ($MgSO_4$), filtered, and evaporated. FC (hexane/AcOEt 3:1) gave **30** (76 mg, 86%). Colourless oil. R_f (hexane/AcOEt 3:1) 0.12. $[\alpha]_D^{25} = -17.7$ ($c = 1.02$, $CHCl_3$). UV ($CHCl_3$): 258 (3.04), 240 (3.57). IR ($CHCl_3$): 3067*w*, 3007*m*,

2868*w*, 1959*w*, 1879*w*, 1813*w*, 1497*m*, 1454*m*, 1363*m*, 1260*m*, 1097*s*, 1028*s*, 914*w*. ^{1}H-NMR ($CDCl_3$, 300 MHz): see *Table 4*; additionally, 4.44 (*d*, *J* = 12.5, PhC*H*); 4.48 (*d*, *J* = 12.5, PhC*H*); 4.55 (*d*, *J* = 12.1, PhC*H*); 4.58 (*s*, CH_2Cl); 4.61 (*d*, *J* ≈ 10.9, PhC*H*); 4.66 (*d*, *J* = 12.1, PhC*H*); 4.69 (*d*, *J* = 12.1, PhC*H*); 4.74 (*d*, *J* = 12.1, PhC*H*); 5.00 (*d*, *J* = 11.2, PhC*H*); 7.24–7.34 (*m*, 18 arom. H); 7.37–7.40 (*m*, 2 arom. H). ^{13}C-NMR ($CDCl_3$, 75 MHz): see *Table 5*; additionally, 39.91 (*t*, *C*H_2–C(2)); 70.83, 70.86 (2*t*, Ph*C*H_2, *C*H_2–C(5)); 71.91 (*t*, Ph*C*H_2); 73.29 (*t*, Ph*C*H_2); 75.05 (*t*, Ph*C*H_2); 127.73–128.75 (several *d*); 137.67, 138.02, 138.18, 138.36, 138.80 (5*s*). HR-MALDI-MS: 1145.5028 (43), 631.2339 (18, $C_{37}H_{37}ClN_2NaO_4$, $[M+Na]^+$; calc. 631.2339), 609.2519 (91, $C_{37}H_{38}ClN_2O_4$, $[M+H]^+$; calc. 609.2520), 573.2754 (59, $C_{37}H_{37}N_2O_4$, $[M-Cl]^+$; calc. 573.2753), 501.1963 (100, $C_{30}H_{30}ClN_2O_3$, $[M-BnO]^+$; calc. 501.1945), 467.2372 (50). Anal. calc. for $C_{37}H_{37}ClN_4$ (609.16): C 72.95, H 6.12, N 4.60; found: C 73.04, H 6.42, N 4.33.

*(5*R*,6*R*,7*S*,8*R*)-6,7,8-Tris(benzyloxy)-5-[(benzyloxy)methyl]-5,6,7,8-tetrahydro-2-(phenoxymethyl)imidazo[1,2-*a*]pyridine* (**31**). *a*) A suspension of **30** (14.5 mg, 23.8 μmol), phenol (3.4 mg, 36.1 μmol), and K_2CO_3 (4.9 mg, 35.5 μmol) in THF (1 ml) was stirred for 13 h at 55–60°, diluted with Et_2O (15 ml), and washed with sat. NH_4Cl soln. (3 × 8 ml). The combined aq. layers were extracted with Et_2O (2 × 8 ml). The combined org. layers were washed with H_2O (10 ml) and brine (10 ml), dried ($MgSO_4$), filtered, and evaporated. FC (hexane/AcOEt 3:1) gave **31** (7.9 mg, 50%). Colourless oil.

b) A suspension of **30** (24 mg, 39.4 μmol), phenol (8 mg, 85.0 μmol), and *t*-BuOK (7.5 mg, 66.8 μmol) in DMF (1 ml) was stirred for 4 h at 80°. Workup and FC as described in *a* gave **31** (16.2 mg, 74%).

c) As described in *b*, but with K_2CO_3 instead of *t*-BuOK, yielding 60% of **31**.

d) A soln. of **30** (16 mg, 26.3 μmol) in DMF (1 ml) was treated with 0.26M soln. of NaOPh (141 μl, 36.7 μmol, prepared by the addition of Na (18 mg, 0.783 mmol) to a soln. of PhOH (76 mg, 0.808 mmol) in DMF (3 ml) at 23°) and stirred for 4 h at 80°. Workup and FC as described in *a* gave **31** (6.6 mg, 38%).

e) A soln. of **23** (100 mg, 0.169 mmol) in CH_2Cl_2 (4 ml) was treated with $SOCl_2$ (25 μl, 0.344 mmol), stirred at 23° for 3 h, and treated with sat. $NaHCO_3$ soln. (5 ml). The mixture was diluted with Et_2O (25 ml) and washed with sat. $NaHCO_3$ soln. (3 × 15 ml). The combined aq. layers were extracted with Et_2O (2 × 15 ml). The combined org. layers were washed with H_2O (25 ml) and brine (25 ml), dried ($MgSO_4$), and filtered. After evaporation, crude **30** (96 mg of a yellowish oil) was dissolved in DMF (4 ml), treated with *t*-BuOK (27 mg, 0.241 mmol) and PhOH (29 mg, 0.308 mmol), and stirred for 3.5 h at 80°. Workup and FC as described in *a* gave **31** (79.1 mg, 70% from **23**).

Data of **31**: R_f (hexane/AcOEt 2:1) 0.28. $[\alpha]_D^{25} = -22.5$ (*c* = 1.00, $CHCl_3$). UV ($CHCl_3$): 271 (3.3), 265 (3.2), 240 (3.4). IR ($CHCl_3$): 3157*w*, 3089*w*, 3066*m*, 2941*m*, 2868*m*, 1952*w*, 1876*w*, 1811*w*, 1731*w*, 1599*m*, 1586*m*, 1496*s*, 1454*s*, 1364*m*, 1301*m*, 1174*m*, 1112*s*, 1050*s*, 1028*s*, 913*w*. ^{1}H-NMR ($CDCl_3$, 400 MHz): see *Table 7*; additionally, 4.43 (br. *s*, PhCH_2); 4.60 (*d*, *J* = 11.2, PhC*H*); 4.61 (*d*, *J* = 12.1, PhC*H*); 4.67 (*d*, *J* = 12.0, 2 PhC*H*); 4.76 (*d*, *J* = 12.2, PhC*H*); 4.98 (*d*, *J* = 11.5, CH–C(2)); 4.99 (*d*, *J* = 11.1, PhC*H*); 5.02 (*d*, *J* = 11.7, CH′–C(2)); 6.94 (*tt*, *J* = 1.0, 7.3, H–C(4) of Ph); 6.99–7.02 (*m*, H–C(2) and H–C(6) of Ph); 7.23–7.34 (*m*, 18 arom. H, H–C(3) and H–C(5) of Ph, H–C(3)); 7.38–7.41 (*m*, 2 arom. H). ^{13}C-NMR ($CDCl_3$, 100 MHz): see *Table 5*; additionally, 64.32 (*t*, *C*H_2–C(2)); 70.65 (*t*, Ph*C*H_2); 71.77 (*t*, Ph*C*H_2); 73.16 (*t*, Ph*C*H_2); 74.92 (*t*, Ph*C*H_2); 114.83 (*d*, C(2) and C(6) of Ph); 120.78 (*d*, C(4) of Ph); 127.46–128.48 (several *d*); 129.35 (*d*, C(3) and C(5) of Ph); 137.45, 137.79, 137.97 (3*s*), 138.17 (2*s*, including C(2)); 158.76 (*s*, C(1) of Ph). HR-MALDI-MS: 689.2968 (26, $C_{43}H_{42}N_2O_5$, $[M+Na]^+$; calc. 689.2991), 667.3172 (100, $C_{43}H_{43}N_2O_5$, $[M+H]^+$; calc. 667.3171), 573.2733 (18, $C_{37}H_{37}N_2O_4$, $[M-PhO]^+$; calc. 573.2753), 559.2594 (21, $C_{36}H_{35}N_2O_4$, $[M-BnO]^+$; calc. 559.2597), 465.2172 (11, $C_{30}H_{29}N_2O_3$, $[M-BnO-PhOH]^+$; calc. 465.2178), 375.1705 (24), 359.1751 (14). Anal. calc. for $C_{43}H_{42}N_2O_5$ (666.82): C 77.45, H 6.35, N 4.20; found: C 77.39, H 6.50, N 4.18.

*(5*R*,6*R*,7*S*,8*R*)-5,6,7,8-Tetrahydro-5-(hydroxymethyl)-2-(phenoxymethyl)imidazo[1,2-*a*]pyridine-6,7,8-triol* (**32**) *and (5*R*,6*R*,7*S*,8*R*)-2-[(Cyclohexyloxy)methyl]-5,6,7,8-tetrahydro-5-(hydroxymethyl)imidazo[1,2-*a*]pyridine-6,7,8-triol* (**33**). A soln. of **31** (39 mg, 58.5 μmol) in AcOEt/MeOH/H_2O 3:1:1 (2 ml) was treated with AcOH (2 ml) and 20% $Pd(OH)_2$/C (40 mg), and hydrogenated at atmospheric pressure for 44 h. The suspension was filtered through *Celite*, and the residue was washed with MeOH/H_2O 9:1 (30 ml). Evaporation of the combined filtrates, co-evaporation with toluene (3 × 5 ml), FC (AcOEt/MeOH/H_2O 1:0:0 → 15:1:1 → 10:1:1), and drying afforded **32** (11.3 mg, *ca.* 63%) containing substantial amounts of H_2O, and **33** (1.7 mg, 9%). Colourless oils. The sample of **32** for microanalysis was dried for 4 d at 10^{-4} Torr.

Data of **32**: R_f (AcOEt/MeOH/H_2O 10:1:1) 0.20. $[\alpha]_D^{25} = -18.8$ (*c* = 0.64, MeOH). UV (MeOH): 277 (3.10), 271 (3.19), 219 (4.12). IR (KBr): 3600–2400*s* (br.), 2925*m*, 2857*m*, 1631*w*, 1599*s*, 1586*m*, 1496*s*, 1461*m*, 1384*m*, 1300*m*, 1239*s*, 1176*m*, 1094*s*, 1080*s*, 1030*m*, 1006*m*, 989*m*, 902*m*, 859*m*. ^{1}H-NMR (CD_3OD, 300 MHz): 3.81 (*dd*, *J* = 3.7, 9.3, irrad. at 4.83 → *d*, *J* = 9.3, H–C(7)); 3.83–3.94 (*m*, H–C(5), CH–C(5)); 4.07–4.21 (*m*, H–C(6), CH′–C(5)); 4.83 (*d*, *J* = 3.7, irrad. at 3.81 → *s*, H–C(8)); 4.95 (br. *s*, CH_2–C(2)); 6.91 (*tt*, *J* = 0.9,

Table 7. *Selected ^{1}H-NMR Chemical Shifts* [ppm] *and Coupling Constants* [Hz] *of the Protected Imidazoles* **31**, **34**, **36**–**39**, **44**, **45**, **48**, *and* **49** *in* $CDCl_3$

	31	**34**	**36**	**37**	**38**	**39**	**44**	**45**	**48**	**49**
H–C(3)	[a])	7.04	[a])	[a])	[a])	[a])	7.85	7.80	7.71	8.11
H–C(5)	4.10	4.07	4.12	4.13	4.10	4.14	4.16	4.12	4.14	4.29
H–C(6)	4.28	4.28	4.30	4.28	4.24	4.28	4.28	4.25	4.18	4.34
H–C(7)	3.88	3.87	3.88	3.90	3.87	3.90	3.86	3.82	3.84	4.07
H–C(8)	4.80	4.77	4.77	4.80	4.75	4.81	4.82	4.80	4.74	5.45
CH–C(5)	3.60	3.59	3.62	3.62	3.59	3.62	3.57	3.54	3.56	3.71
CH′–C(5)	3.74	3.73	3.76	3.76	3.73	3.76	3.72	3.69	3.69	3.79
J(5,6)	7.4	7.2	7.2	7.2	7.2	7.2	7.2	7.2	6.9	6.5
J(6,7)	9.4	9.3	9.3	9.3	9.0	9.3	9.3	9.3	8.4	8.4
J(7,8)	3.1	3.0	3.1	3.1	3.4	3.1	2.8	2.8	3.1	2.8
J(5,CH)	7.0	6.8	6.8	7.2	7.2	7.2	7.2	7.2	7.5	6.5
J(5,CH′)	3.0	3.1	3.1	2.8	3.1	3.1	3.1	3.1	2.5	3.4
J(CH,CH′)	10.1	10.1	10.0	10.0	10.0	10.0	10.0	10.0	10.3	10.0

[a]) Hidden by signals of the Ph groups at 7.21–7.41 ppm.

7.2, H–C(4) of Ph); 6.94–6.99 (*m*, H–C(2) and H–C(6) of Ph); 7.21–7.28 (*m*, H–C(3) and H–C(5) of Ph); 7.43 (*s*, H–C(3)). ^{13}C-NMR (CD_3OD, 75 MHz): see *Table 6*; additionally, 64.55 (*t*, *C*H_2–C(2)); 115.61 (*d*, C(2) and C(6) of Ph); 121.71 (*d*, C(4) of Ph); 130.27 (*d*, C(3) and C(5) of Ph); 159.90 (*s*, C(1) of Ph). HR-MALDI-MS: 329.1109 (62, $C_{15}H_{18}N_2NaO_5$, $[M+Na]^+$; calc. 329.1113); 307.1290 (82, $C_{15}H_{19}N_2O_5$, $[M+H]^+$; calc. 307.1294); 213.0867 (100, $C_9H_{13}N_2O_4$, $[M-PhO]^+$; calc. 213.0875). Anal. calc. for $C_{15}H_{18}N_2O_5 \cdot 0.5\ H_2O$ (315.33): C 57.14, H 6.07, N 8.88; found: C 57.14, H 5.98, N 8.64.

Data of **33**: R_f (AcOEt/MeOH/H_2O 10:1:1) 0.11. ^{1}H-NMR (CD_3OD, 300 MHz): 1.20–1.38 (*m*, 3 CH_2 of C_6H_{11}); 1.70–1.80 (*m*, CH_2 of C_6H_{11}); 1.89–2.00 (*m*, CH_2 of C_6H_{11}); 3.36–3.48 (*m*, H–C(1) of C_6H_{11}); 3.79 (*dd*, *J* = 3.7, 9.3, H–C(7)); 3.85 (*ddd*, *J* ≈ 2.5, 5.6, 8.1, H–C(5)); 3.89 (*dd*, *J* = 5.6, 11.5, CH–C(5)); 4.10 (*dd*, *J* = 7.5, 9.3, H–C(6)); 4.16 (*dd*, *J* = 2.5, 11.5, CH′–C(5)); 4.44 (br. *s*, CH_2–C(2)); 4.80 (*d*, *J* = 3.7, H–C(8)); 7.30 (*s*, H–C(3)). HR-MALDI-MS: 335.1576 (61, $C_{15}H_{24}N_2NaO_5$, $[M+Na]^+$; calc. 335.1583); 313.1754 (41, $C_{15}H_{25}N_2O_5$, $[M+H]^+$; calc. 313.1763); 213.0870 (100, $C_9H_{13}N_2O_4$, $[M-c\text{-}C_6H_{11}O]^+$; calc. 213.0875).

BCl_3-Promoted Debenzylation of **31**. *a*) A soln. of **31** (10 mg, 15.0 μmol) in CH_2Cl_2 (0.4 ml) was treated at −78° with 1M BCl_3 in CH_2Cl_2 (0.25 ml, 0.25 mmol), stirred until the mixture had reached a temp. of 15° (*ca.* 4.5 h), cooled to −78°, treated with H_2O (1 ml), and evaporated. The residue was taken up in H_2O (2 ml) and applied to ion-exchange chromatography (*Amberlite CG-120*, H^+ form, elution with 0.1M aq. NH_3). Evaporation and lyophilisation gave a 1:5 mixture of **35** and a product missing the PhO group (2.7 mg).

b) As described in *a*, but the mixture was neutralised with *Amberlite IRA-68* after the addition of H_2O. Filtration, evaporation, and ion-exchange chromatography (*Amberlite CG-120*, H^+ form, elution with 0.1M aq. NH_3) gave a 1:1 mixture of **35** and a product missing the PhO group (3.1 mg).

*(5*R*,6*R*,7*S*,8*R*)-6,7,8-Tris(benzyloxy)-5-[(benzyloxy)methyl]-5,6,7,8-tetrahydro-2-[(phenylamino)methyl]-imidazo[1,2-a]pyridine* (**34**). A suspension of **22** (50.0 mg, 84.9 μmol) and $MgSO_4$ (12 mg, 99.7 μmol) in CH_2Cl_2 (1 ml) was treated with freshly distilled $PhNH_2$ (9 μl, 98.7 μmol) and stirred for 4 h at 23°. The mixture was diluted with Et_2O (15 ml) and washed with sat. $NaHCO_3$ soln. (3 × 10 ml). The combined aq. layers were extracted with Et_2O (2 × 10 ml). The combined org. layers were washed with H_2O (15 ml) and brine (15 ml), dried ($MgSO_4$), filtered, and evaporated. The ^{1}H-NMR spectrum of the crude product (57 mg) showed a mixture of the corresponding imine and starting material in a ratio *ca.* 91:9. This mixture was diluted with EtOH (2 ml), treated with $NaBH_4$ (10 mg, 0.264 mmol), stirred for 3 h at 23°, treated with H_2O (0.3 ml), evaporated, diluted with Et_2O (20 ml), and washed with sat. NH_4Cl soln. (3 × 15 ml). The combined aq. layers were extracted with Et_2O (2 × 15 ml). The combined org. layers were washed with H_2O (25 ml) and brine (25 ml), dried ($MgSO_4$), filtered, and evaporated. FC (hexane/AcOEt 2:1 → 1:1 → 1:2) gave **34** (42.6 mg, 75%) and **23** (1.8 mg, 4%). Oils.

Data of **34**: R_f (hexane/AcOEt 1:1) 0.19. $[\alpha]_D^{25} = -27.1$ ($c = 1.00$, $CHCl_3$). UV ($CHCl_3$): 295 (3.3), 244 (4.1). IR ($CHCl_3$): 3416*w*, 3089*w*, 3065*w*, 3032*w*, 2938*m*, 2868*m*, 1952*w*, 1876*w*, 1812*w*, 1731*w*, 1603*s*, 1504*s*, 1454*s*,

1430*w*, 1364*m*, 1311*m*, 1260*m*, 1180*w*, 1099*s*, 1028*s*, 913*w*. ^{1}H-NMR ($CDCl_3$, 400 MHz): see *Table 7*; additionally, 4.11–4.19 (br. *s*, NH); 4.23 (br. *s*, CH_2–C(2)); 4.42 (br. *s*, PhCH_2); 4.60 (*d*, *J* = 11.2, PhC*H*); 4.62 (*d*, *J* = 12.0, PhC*H*); 4.68 (br. *d*, *J* ≈ 10.9, 2 PhC*H*); 4.76 (*d*, *J* = 11.3, PhC*H*); 4.98 (*d*, *J* = 11.2, PhC*H*); 6.65–6.72 (*m*, H–C(2), H–C(4), and H–C(6) of Ph); 7.14–7.19 (*m*, H–C(3) and H–C(5) of Ph); 7.21–7.34 (*m*, 18 arom. H); 7.36–7.39 (*m*, 2 arom. H). ^{13}C-NMR ($CDCl_3$, 100 MHz): see *Table 5*; additionally, 42.29 (*t*, *C*H_2–C(2)); 70.77 (*t*, Ph*C*H_2, *C*H_2–C(5)); 71.80 (*t*, Ph*C*H_2); 73.21 (*t*, Ph*C*H_2); 74.88 (*t*, Ph*C*H_2); 113.15 (*d*, C(2) and C(6) of Ph); 117.50 (*d*, C(4) of Ph); 127.46–128.48 (several *d*); 129.13 (*d*, C(3) and C(5) of Ph); 137.52, 137.85, 138.03, 138.28 (4*s*); 148.26 (*s*, C(1) of Ph). HR-MALDI-MS: 704.2906 (1, $C_{43}H_{43}KN_3O_4$, $[M+K]^+$; calc. 704.2890), 688.3140 (24, $C_{43}H_{43}N_3NaO_4$, $[M+Na]^+$; calc. 688.3151), 666.3329 (24, $C_{43}H_{44}N_3O_4$, $[M+H]^+$; calc. 666.3332), 573.2739 (100, $C_{37}H_{37}N_2O_4$, $[M-PhNH]^+$; calc. 573.2753), 558.2759 (2, $C_{36}H_{36}N_3O_3$, $[M-BnO]^+$; calc. 558.2756), 467.2322 (16). Anal. calc. for $C_{43}H_{43}N_3O_4$ (665.83): C 77.57, H 6.51, N 6.31; found: C 77.69, H 6.47, N 6.19.

*(5*R*,6*R*,7*S*,8*R*)-5,6,7,8-Tetrahydro-5-(hydroxymethyl)-2-[(phenylamino)methyl]imidazo[1,2-*a*]pyridine-6,7,8-triol* (**35**). A soln. of **34** (64 mg, 96.1 μmol) in CH_2Cl_2 (4.9 ml) was treated at −78° with 1M BCl_3 in CH_2Cl_2 (1.2 ml, 1.20 mmol), stirred until the mixture had reached a temp. of 15° (*ca.* 4.5 h), cooled to −78°, treated with H_2O (2 ml), and evaporated. The residue was taken up in H_2O (2 ml) and applied to ion-exchange chromatography (*Amberlite CG-120*, H^+ form, elution with 0.1M aq. NH_3). Evaporation, lyophilisation, and drying gave **35** (22.6 mg, *ca.* 77%) as a colourless hygroscopic resin containing substantial amounts of H_2O. The sample for microanalysis was dried for 4 d at 10^{-4} Torr. R_f (AcOEt/MeOH/H_2O 10:1:1) 0.18. $[\alpha]_D^{25} = -23.3$ (*c* = 0.96, MeOH). UV (MeOH): 294 (3.28), 242 (4.02), 210 (4.02). IR (KBr): 3600–2400*s* (br.), 3053*m*, 2925*m*, 2852*m*, 1603*s*, 1506*s*, 1463*m*, 1432*m*, 1382*w*, 1312*m*, 1253*m*, 1180*m*, 1096*s*, 1066*m*, 1007*w*, 902*w*, 752*m*, 694*m*. ^{1}H-NMR (D_2O, 300 MHz): 3.80 (br. *td*, *J* ≈ 2.8, 8.7, irrad. at 3.96 → change, irrad. at 4.15 → change, H–C(5)); 3.84 (*dd*, *J* = 3.7, 10.0, irrad. at 4.15 → change, irrad. at 4.83 → *d*, *J* = 10.3, H–C(7)); 3.96 (*dd*, *J* = 3.4, 12.8, CH–C(5)); 4.12 (*dd*, *J* ≈ 2.5, 13.1, irrad. at 3.96 → change, CH′–C(5)); 4.15 (*dd*, *J* = 8.7, 10.3, irrad. at 3.84 → change, H–C(6)); 4.17 (*d*, *J* = 15.9, CH–C(2)); 4.23 (*d*, *J* = 15.9, CH′–C(2)); 4.83 (*d*, *J* = 3.7, irrad. at 3.84 → *s*, H–C(8)); 6.77–6.82 (*m*, H–C(2), H–C(4), and H–C(6) of Ph); 7.12 (*s*, H–C(3)); 7.18–7.23 (*m*, H–C(3) and H–C(5) of Ph). ^{13}C-NMR (D_2O, 75 MHz): see *Table 6*; additionally, 41.22 (*t*, *C*H_2–C(2)); 114.80 (*d*, C(2) and C(6) of Ph); 119.03 (*d*, C(4) of Ph); 129.23 (*d*, C(3) and C(5) of Ph); 144.62 (*s*, C(1) of Ph). HR-MALDI-MS: 328.1271 (56, $C_{15}H_{19}N_3NaO_4$, $[M+Na]^+$; calc. 328.1273), 306.1449 (100, $C_{15}H_{20}N_3O_4$, $[M+H]^+$; calc. 306.1454), 213.0866 (49, $C_9H_{13}N_2O_4$, $[M-PhNH]^+$; calc. 213.0875). Anal. calc. for $C_{15}H_{19}N_3O_4 \cdot 0.5\ H_2O$ (314.34): C 57.32, H 6.41, N 13.37; found: C 57.10, H 6.31, N 13.03.

*(5*R*,6*R*,7*S*,8*R*)-6,7,8-Tris(benzyloxy)-5-[(benzyloxy)methyl]-5,6,7,8-tetrahydro-2-[(2-nitrophenoxy)methyl]imidazo[1,2-*a*]pyridine* (**36**). A suspension of **23** (42 mg, 71.1 μmol) and NaH (8 mg, 0.183 mmol) in degassed DMF (1 ml) was treated with 1-fluoro-2-nitrobenzene (16 μl, 0.151 mmol), stirred for 1 h at 80°, cooled to r.t., diluted with Et_2O (20 ml), and washed with sat. NH_4Cl soln. (3 × 10 ml). The combined aq. layers were extracted with Et_2O (2 × 15 ml). The combined org. layers were washed with H_2O (30 ml) and brine (30 ml), dried ($MgSO_4$), filtered, and evaporated. FC (hexane/AcOEt 1:0 → 2:1 → 1:1) gave **36** (47.7 mg, 94%). Yellow oil. R_f (hexane/AcOEt 1:1) 0.26. $[\alpha]_D^{25} = -33.1$ (*c* = 1.00, $CHCl_3$). UV ($CHCl_3$): 326 (3.4), 259 (3.7), 240 (3.8). IR ($CHCl_3$): 3089*w*, 3067*w*, 2960*m*, 2869*m*, 1952*w*, 1890*w*, 1811*w*, 1731*m*, 1608*s*, 1584*m*, 1526*s*, 1496*m*, 1454*s*, 1356*s*, 1309*m*, 1276*s*, 1254*s*, 1166*m*, 1093*s*, 1047*s*, 1028*s*, 913*w*. ^{1}H-NMR ($CDCl_3$, 300 MHz): see *Table 7*; additionally, 4.45 (br. *s*, PhCH_2); 4.608 (*d*, *J* = 11.2, PhC*H*); 4.614 (*d*, *J* = 11.8, PhC*H*); 4.65 (*d*, *J* = 11.8, PhC*H*); 4.69 (*d*, *J* = 11.8, PhC*H*); 4.75 (*d*, *J* = 12.5, PhC*H*); 4.99 (*d*, *J* = 11.2, PhC*H*); 5.19 (br. *s*, CH_2–C(2)); 7.01 (*ddd*, *J* = 1.2, 7.5, 8.1, irrad. at 7.50 → br. *dd*, *J* ≈ 1.9, 7.8, irrad. at 7.83 → br. *dd*, *J* ≈ 0.9, 7.8, H–C(4) of $C_6H_4NO_2$); 7.22–7.41 (*m*, 20 arom. H, H–C(3), H–C(6) of $C_6H_4NO_2$); 7.50 (*ddd*, *J* = 1.9, 7.5, 9.3, irrad. at 7.01 → br. *dd*, *J* ≈ 2.8, 8.7, irrad. at 7.83 → br. *dd*, *J* ≈ 6.9, 8.4, H–C(5) of $C_6H_4NO_2$); 7.83 (*dd*, *J* = 1.9, 8.1, irrad. at 7.01 → br. *d*, *J* ≈ 2.5, irrad. at 7.50 → br. *d*, *J* ≈ 7.5, H–C(3) of $C_6H_4NO_2$). ^{13}C-NMR ($CDCl_3$, 75 MHz): see *Table 5*; additionally, 66.42 (*t*, *C*H_2–C(2)); 70.53, 70.59 (2*t*, Ph*C*H_2, *C*H_2–C(5)); 71.81 (*t*, Ph*C*H_2); 73.21 (*t*, Ph*C*H_2); 74.86 (*t*, Ph*C*H_2); 115.65 (*d*, C(6) of $C_6H_4NO_2$); 120.42 (*d*, C(4) of $C_6H_4NO_2$); 125.46 (*d*, C(3) of $C_6H_4NO_2$); 127.43–128.38 (several *d*); 133.87 (*d*, C(5) of $C_6H_4NO_2$); 137.01, 137.30, 137.65, 137.81, 137.93 (5*s* including C(2)); 140.10 (*s*, C(2) of $C_6H_4NO_2$); 142.76 (*s*, C(8a)); 152.01 (*s*, C(1) of $C_6H_4NO_2$). HR-MALDI-MS: 734.2771 (18, $C_{43}H_{41}N_3NaO_7$, $[M+Na]^+$; calc. 734.2842), 718.2896 (17, $C_{43}H_{41}N_3NaO_6$, $[M+Na-O]^+$; calc. 718.2893), 712.3025 (43, $C_{43}H_{42}N_3O_7$, $[M+H]^+$; calc. 712.3023), 702.2916 (10, $C_{43}H_{41}N_3NaO_5$, $[M+Na-O_2]^+$; calc. 702.2944), 604.2491 (10, $C_{36}H_{34}N_3O_6$, $[M-BnO]^+$; calc. 604.2447), 573.2767 (100, $C_{37}H_{37}N_2O_4$, $[M-C_6H_4NO_3]^+$; calc. 573.2753), 467.2384 (42), 465.2240 (10, $C_{30}H_{29}N_2O_3$, $[M-C_6H_4NO_3-BnOH]^+$; calc. 465.2178), 359.1824 (16). Anal. calc. for $C_{43}H_{41}N_3O_7$ (711.81): C 72.56, H 5.81, N 5.90; found: C 72.29, H 6.00, N 5.98.

*(5*R*,6*R*,7*S*,8*R*)-6,7,8-Tris(benzyloxy)-5-[(benzyloxy)methyl]-5,6,7,8-tetrahydro-2-[(4-nitrophenoxy)methyl]imidazo[1,2-*a*]pyridine* (**37**). A susp. of **23** (92 mg, 0.156 mmol) and NaH (15 mg, 0.344 mmol) in degassed DMF (3 ml) was treated with 1-fluoro-4-nitrobenzene (35 µl, 0.330 mmol), stirred for 1 h at 80°, cooled to r.t., diluted with Et_2O (20 ml), and washed with sat. NH_4Cl soln. (3 × 10 ml). The combined aq. layers were extracted with Et_2O (2 × 15 ml). The combined org. layers were washed with H_2O (30 ml) and brine (30 ml), dried ($MgSO_4$), filtered, and evaporated. FC (hexane/AcOEt 1:0 → 2:1 → 1:1) gave **37** (99 mg, 89%). Yellow oil. R_f (hexane/AcOEt 1:1) 0.30. $[\alpha]_D^{25} = -13.8$ ($c = 1.00$, $CHCl_3$). UV ($CHCl_3$): 312 (4.1), 240 (3.7). IR ($CHCl_3$): 3089*w*, 3066*w*, 2938*w*, 2870*w*, 1953*w*, 1890*w*, 1812*w*, 1731*m*, 1608*m*, 1593*s*, 1515*s*, 1497*s*, 1454*m*, 1374*m*, 1343*s*, 1298*m*, 1254*s*, 1174*m*, 1112*s*, 1046*m*, 1028*m*, 990*m*, 914*w*. ^{1}H-NMR ($CDCl_3$, 300 MHz): see *Table 7*; additionally, 4.44 (*d*, *J* = 12.1, PhC*H*); 4.48 (*d*, *J* = 12.8, PhC*H*); 4.62 (*d*, *J* = 11.2, PhC*H*); 4.63 (*d*, *J* = 11.8, PhC*H*); 4.68 (*d*, *J* = 12.1, PhC*H*); 4.70 (*d*, *J* = 12.1, PhC*H*); 4.78 (*d*, *J* = 12.8, PhC*H*); 5.01 (*d*, *J* = 11.2, PhC*H*); 5.07 (*d*, *J* = 11.5, CH−C(2)); 5.07 (*d*, *J* = 11.5, CH′−C(2)); 7.05–7.12 (*m*, J_{vic} = 9.3, irrad. at 8.19 → *s*, H−C(2) and H−C(6) of $C_6H_4NO_2$); 7.24–7.40 (*m*, 20 arom. H, H−C(3)); 8.16–8.22 (*m*, J_{vic} = 9.3, irrad. at 7.09 → *s*, H−C(3) and H−C(5) of $C_6H_4NO_2$). ^{13}C-NMR ($CDCl_3$, 75 MHz): see *Table 5*; additionally, 65.18 (*t*, *C*H_2−C(2)); 70.99 (*t*, Ph*C*H_2, *C*H_2−C(5)); 72.05 (*t*, Ph*C*H_2); 73.37 (*t*, Ph*C*H_2); 75.13 (*t*, Ph*C*H_2); 115.06 (*d*, C(2) and C(6) of $C_6H_4NO_2$); 126.02 (*d*, C(3) and C(5) of $C_6H_4NO_2$); 127.77–128.70 (several *d*); 137.58, 137.91, 138.04, 138.21 (4*s*); 141.72 (*s*, C(4) of $C_6H_4NO_2$); 163.96 (*s*, C(1) of $C_6H_4NO_2$). HR-MALDI-MS: 734.2789 (50, $C_{43}H_{41}N_3NaO_7$, $[M+Na]^+$; calc. 734.2842), 718.2898 (66, $C_{43}H_{41}N_3NaO_6$, $[M+Na-O]^+$; calc. 718.2893), 712.3026 (52, $C_{43}H_{42}N_3O_7$, $[M+H]^+$; calc. 712.3023), 698.3189 (55, $C_{43}H_{44}N_3O_6$, $[M+H-O_2+H_2O]^+$; calc. 698.3230), 696.3040 (55, $C_{43}H_{42}N_3O_6$, $[M+H-O]^+$; calc. 696.3073), 604.2490 (57, $C_{36}H_{34}N_3O_6$, $[M-BnO]^+$; calc. 604.2447), 596.2674 (30), 588.2529 (31, $C_{36}H_{34}N_3O_5$, $[M-O-BnO]^+$; calc. 588.2498), 574.2835 (100, $C_{37}H_{38}N_2O_4$, $[M+H-C_6H_4NO_3]^+$; calc. 574.2831), 573.2774 (78, $C_{37}H_{37}N_2O_4$, $[M-C_6H_4NO_3]^+$; calc. 573.2753), 467.2386 (48), 465.2244 (41, $C_{30}H_{29}N_2O_3$, $[M-C_6H_4NO_3-BnOH]^+$; calc. 465.2178), 375.1776 (74), 359.1827 (43). Anal. calc. for $C_{43}H_{41}N_3O_7$ (711.80): C 72.56, H 5.81, N 5.90; found: C 72.43, H 5.63, N 5.83.

*(5*R*,6*R*,7*S*,8*R*)-6,7,8-Tris(benzyloxy)-5-[(benzyloxy)methyl]-2-[(2,4-dinitrophenoxy)methyl]-5,6,7,8-tetrahydroimidazo[1,2-*a*]pyridine* (**38**). A suspension of **23** (50 mg, 84.6 µmol) and NaH (8 mg, 0.183 mmol) in degassed DMF (2 ml) was treated with 1-fluoro-2,4-dinitrobenzene (22 µl, 0.180 mmol) and stirred for 5 h at 80°. No reaction was observed at this moment (TLC). The mixture was left to stand at 23° for 3 weeks, diluted with Et_2O (20 ml), and washed with sat. NH_4Cl soln. (3 × 10 ml). The combined aq. layers were extracted with Et_2O (2 × 15 ml). The combined org. layers were washed with H_2O (30 ml) and brine (30 ml), dried ($MgSO_4$), filtered, and evaporated. FC (hexane/AcOEt 1:0 → 2:1 → 1:1) gave **38** (40.0 mg, 63%) and **23** (2.8 mg, 6%) as yellow oils.

Data of **38**: R_f (hexane/AcOEt 1:1) 0.23. $[\alpha]_D^{25} = -19.0$ ($c = 1.00$, $CHCl_3$). UV ($CHCl_3$): 296 (4.0), 258 (3.9), 240 (3.9). IR ($CHCl_3$): 3090*w*, 3067*w*, 2961*w*, 2870*m*, 1952*w*, 1872*w*, 1810*w*, 1731*s*, 1608*s*, 1538*s*, 1496*m*, 1454*m*, 1420*w*, 1345*s*, 1314*m*, 1274*s*, 1152*m*, 1098*s*, 1071*s*, 1046*s*, 1028*m*, 970*m*, 914*w*. ^{1}H-NMR ($CDCl_3$, 300 MHz): see *Table 7*; additionally, 4.43 (br. *s*, PhCH_2); 4.59 (*d*, *J* = 11.2, PhC*H*); 4.60 (*d*, *J* = 12.1, PhC*H*); 4.65 (*d*, *J* = 12.5, PhC*H*); 4.67 (*d*, *J* = 11.8, PhC*H*); 4.74 (*d*, *J* = 12.1, PhC*H*); 4.96 (*d*, *J* = 11.2, PhC*H*); 5.29 (br. *s*, CH_2−C(2)); 7.21–7.36 (*m*, 20 arom. H, H−C(3)); 7.62 (*d*, *J* = 9.3, irrad. at 8.33 → *s*, H−C(6) of $C_6H_3N_2O_4$); 8.33 (*dd*, *J* = 2.8, 9.3, irrad. at 7.62 → br. *d*, *J* ≈ 2.5, irrad. at 8.68 → *d*, *J* = 9.3, H−C(5) of $C_6H_3N_2O_4$); 8.68 (*d*, *J* = 2.8, irrad. at 8.33 → *s*, H−C(3) of $C_6H_3N_2O_4$). ^{13}C-NMR ($CDCl_3$, 75 MHz): see *Table 5*; additionally, 66.86 (*t*, *C*H_2−C(2)); 70.54, 70.73 (2*t*, *C*H_2−C(5), Ph*C*H_2); 71.88 (*t*, Ph*C*H_2); 73.18 (*t*, Ph*C*H_2); 74.80 (*t*, Ph*C*H_2); 115.81 (*d*, C(6) of $C_6H_3N_2O_4$); 121.69 (*d*, C(3) of $C_6H_3N_2O_4$); 127.65–128.48 (several *d*); 128.71 (*d*, C(5) of $C_6H_3N_2O_4$); 137.26, 137.64, 137.73, 137.84 (4*s*); 139.06, 139.97 (2*s*, C(2) and C(4) of $C_6H_3N_2O_4$); 156.58 (*s*, C(1) of $C_6H_3N_2O_4$). HR-MALDI-MS: 779.2660 (1, $C_{43}H_{40}N_4NaO_9$, $[M+Na]^+$; calc. 779.2693), 757.2862 (12, $C_{43}H_{41}N_4O_9$, $[M+H]^+$; calc. 757.2873), 743.3071 (17), 741.2910 (13, $C_{43}H_{41}N_4O_8$, $[M+H-O]^+$; calc. 741.2924), 649.2294 (8, $C_{36}H_{33}N_4O_8$, $[M-BnO]^+$; calc. 649.2298), 573.2732 (100, $C_{37}H_{37}N_2O_4$, $[M-C_6H_3N_2O_5]^+$; calc. 573.2732), 467.232 (28), 465.2167 (9, $C_{30}H_{29}N_2O_3$, $[M-C_6H_3N_2O_5-BnOH]^+$; calc. 465.2167), 359.1751 (12). Anal. calc. for $C_{43}H_{40}N_4O_9$ (756.81): C 68.24, H 5.33, N 7.40; found: C 68.25, H 5.45, N 7.27.

*(5*R*,6*R*,7*S*,8*R*)-6,7,8-Tris(benzyloxy)-5-[(benzyloxy)methyl]-5,6,7,8-tetrahydro-2-[(3-nitrophenoxy)methyl]imidazo[1,2-*a*]pyridine* (**39**). A suspension of **23** (33 mg, 55.9 µmol) and NaH (7 mg, 0.160 mmol) in degassed DMF (1 ml) was treated with 1-fluoro-3-nitrobenzene (12 µl, 0.112 mmol), stirred for 1 h at 80° (no reaction) and then for 20 h at 140°, cooled to r.t., diluted with Et_2O (20 ml), and washed with sat. NH_4Cl soln. (3 × 10 ml). The combined aq. layers were extracted with Et_2O (2 × 15 ml). The combined org. layers were washed with H_2O (30 ml) and brine (30 ml), dried ($MgSO_4$), filtered, and evaporated. FC (hexane/AcOEt 1:0 → 2:1 → 1:1 → 0:1) gave **39** (22.2 mg, 56%) and **23** (8.8 mg, 27%). Yellow oils.

Data of **39**: R_f (hexane/AcOEt 1:1) 0.43. $[\alpha]_D^{25} = -16.6$ ($c = 0.89$, $CHCl_3$). UV ($CHCl_3$): 328 (3.3), 269 (3.8), 240 (3.9). IR ($CHCl_3$): 3089*w*, 3067*w*, 2932*w*, 2869*w*, 1951*w*, 1870*w*, 1811*w*, 1731*w*, 1619*w*, 1582*w*, 1530*s*, 1497*m*, 1482*w*, 1454*m*, 1352*s*, 1319*m*, 1284*m*, 1097*s*, 1027*m*, 990*w*, 912*w*. ^{1}H-NMR ($CDCl_3$, 300 MHz): see *Table 7*; additionally, 4.47 (br. *s*, PhC*H*$_2$); 4.62 (*d*, *J* = 11.5, 2 PhC*H*); 4.688 (*d*, *J* = 12.1, PhC*H*); 4.693 (*d*, *J* = 11.8, PhC*H*); 4.77 (*d*, *J* = 12.1, PhC*H*); 5.01 (*d*, *J* = 11.2, PhC*H*); 5.05 (*d*, *J* = 11.8, CH–C(2)); 5.10 (*d*, *J* = 11.8, CH′–C(2)); 7.25–7.36 (*m*, 18 arom. H, H–C(3), H–C(6) of $C_6H_4NO_2$); 7.37–7.42 (*m*, 2 arom. H); 7.42 (*t*, *J* = 8.1, H–C(5) of $C_6H_4NO_2$); 7.83 (*ddd*, *J* = 0.9, 2.2, 8.1, H–C(4) of $C_6H_4NO_2$); 7.91 (*t*, *J* = 2.2, H–C(2) of $C_6H_4NO_2$). ^{13}C-NMR ($CDCl_3$, 75 MHz): see *Table 5*; additionally, 64.89 (*t*, *C*H$_2$–C(2)); 70.73, 70.81 (2*t*, PhCH$_2$, *C*H$_2$–C(5)); 71.81 (*t*, PhCH$_2$); 73.18 (*t*, PhCH$_2$); 74.94 (*t*, PhCH$_2$); 109.23 (*d*, C(2) of $C_6H_4NO_2$); 115.76 (*d*, C(4) of $C_6H_4NO_2$); 121.92 (*d*, C(6) of $C_6H_4NO_2$); 127.43–128.40 (several *d*); 129.71 (*d*, C(5) of $C_6H_4NO_2$); 137.27, 137.60, 137.75, 137.93 (4*s*); 148.97 (*s*, C(3) of $C_6H_4NO_2$); 159.07 (*s*, C(1) of $C_6H_4NO_2$). HR-MALDI-MS: 734.2799 (73, $C_{43}H_{41}N_3NaO_7$, $[M+Na]^+$; calc. 734.2842), 718.290 (92, $C_{43}H_{41}N_3NaO_6$, $[M + Na - O]^+$; calc. 718.2893), 712.3022 (71, $C_{43}H_{42}N_3O_7$, $[M+H]^+$; calc. 712.3023), 698.3188 (100, $C_{43}H_{44}N_3O_6$, $[M+H-O_2+H_2O]^+$; calc. 698.3230), 696.3047 (87, $C_{43}H_{42}N_3O_6$, $[M+H-O]^+$; calc. 696.3073), 604.2490 (98, $C_{36}H_{34}N_3O_6$, $[M-BnO]^+$; calc. 604.2447), 588.2529 (89, $C_{36}H_{34}N_3O_5$, $[M-O-BnO]^+$; calc. 588.2498), 573.2782 (81, $C_{37}H_{37}N_2O_4$, $[M-C_6H_4NO_3]^+$; calc. 573.2753), 465.2247 (63, $C_{30}H_{29}N_2O_3$, $[M-C_6H_4NO_3-BnOH]^+$; calc. 465.2178), 375.1777 (70), 359.1828 (61). Anal. calc. for $C_{43}H_{41}N_3O_7$ (711.81): C 72.56, H 5.81, N 5.90; found: C 72.59, H 5.90, N 5.83.

*(5*R*,6*R*,7*S*,8*R*)-5,6,7,8-Tetrahydro-5-(hydroxymethyl)-2-[(2-nitrophenoxy)methyl]imidazo[1,2-*a*]pyridine-6,7,8-triol* (**40**). A soln. of **36** (16.5 mg, 23.2 μmol) in CH_2Cl_2 (1 ml) was treated with $AlCl_3$ (38 mg, 0.285 mmol) and anisole (41 μl, 0.375 mmol), stirred for 13 h at 22°, and treated with H_2O (15 ml). The mixture was diluted with AcOEt (15 ml). After extraction with H_2O, the aq. layer was evaporated. FC (AcOEt/MeOH/H_2O 1:0:0 → 15:1:1 → 10:1:1) yielded **40** (6.1 mg, 75%). White solid. R_f (AcOEt/MeOH/H_2O 15:1:1) 0.10. $[\alpha]_D^{25} = -17.8$ ($c = 0.30$, MeOH). UV (MeOH): 320 (3.22), 254 (3.27), 214 (4.23). IR (KBr): 3600–2400*s* (br.), 2924*w*, 2857*w*, 1630*m*, 1608*s*, 1584*m*, 1525*s*, 1487*w*, 1459*m*, 1446*m*, 1398*w*, 1381*w*, 1352*m*, 1286*m*, 1260*m*, 1177*w*, 1165*m*, 1149*w*, 1121*m*, 1087*m*, 1040*m*, 910*w*, 861*w*. ^{1}H-NMR (CD_3OD, 300 MHz): 3.81 (*dd*, *J* = 3.7, 9.3, H–C(7)); 3.84–3.94 (*m*, H–C(5), CH–C(5)); 4.06–4.20 (*m*, H–C(6), CH′–C(5)); 4.82 (*d*, *J* = 3.7, H–C(8)); 5.12 (br. *s*, CH$_2$–C(2)); 7.06 (*ddd*, *J* = 1.2, 7.5, 8.1, H–C(4) of $C_6H_4NO_2$); 7.41 (*dd*, *J* = 1.2, 8.4, H–C(6) of $C_6H_4NO_2$); 7.48 (*s*, H–C(3)); 7.57 (*ddd*, *J* = 1.9, 7.5, 8.4, H–C(5) of $C_6H_4NO_2$); 7.75 (*dd*, *J* = 1.9, 8.1, H–C(3) of $C_6H_4NO_2$). ^{1}H-NMR (CD_3OD/D_2O 4:1, 300 MHz): 3.87 (*dd*, *J* = 3.7, 10.0, H–C(7)); 3.89 (*ddd*, *J* = 2.5, 4.7, 7.8, H–C(5)); 3.96 (*dd*, *J* = 4.7, 11.8, CH–C(5)); 4.17 (*dd*, *J* = 7.8, 9.7, H–C(6)); 4.19 (*dd*, *J* = 2.5, 12.1, CH′–C(5)); 4.87 (*d*, *J* = 3.7, H–C(8)); 5.16 (br. *s*, CH$_2$–C(2)); 7.12 (*ddd*, *J* = 1.2, 7.2, 8.4, H–C(4) of $C_6H_4NO_2$); 7.42 (*dd*, *J* = 0.9, 8.7, H–C(6) of $C_6H_4NO_2$); 7.44 (*s*, H–C(3)); 7.65 (*ddd*, *J* = 1.6, 7.5, 8.7, H–C(5) of $C_6H_4NO_2$); 7.83 (*dd*, *J* = 1.6, 8.1, H–C(3) of $C_6H_4NO_2$). ^{13}C-NMR (CD_3OD, 75 MHz): see *Table 6*; additionally, 66.57 (*t*, *C*H$_2$–C(2)); 116.52 (*d*, C(6) of $C_6H_4NO_2$); 122.32, 122.69 (2*d*, C(4) of $C_6H_4NO_2$, C(3)); 126.21 (*d*, C(3) of $C_6H_4NO_2$); 135.27 (*d*, C(5) of $C_6H_4NO_2$); 141.75 (*s*, C(2) of $C_6H_4NO_2$); 151.66 (*s*, C(1) of $C_6H_4NO_2$). HR-MALDI-MS: 374.0959 (100, $C_{15}H_{17}N_3NaO_7$, $[M+Na]^+$; calc. 374.0964), 360.1166 (54, $C_{15}H_{19}N_3NaO_6$, $[M+Na-O_2+H_2O]^+$; calc. 360.1171), 358.1012 (85, $C_{15}H_{17}N_3NaO_6$, $[M+Na-O]^+$; calc. 358.1015), 352.1137 (46, $C_{15}H_{18}N_3O_7$, $[M+H]^+$; calc. 352.1145), 342.1061 (31, $C_{15}H_{17}N_3NaO_5$, $[M+Na-O_2]^+$; calc. 342.1066), 336.1186 (30, $C_{15}H_{18}N_3O_6$, $[M+H-O]^+$; calc. 336.1195), 320.1238 (83, $C_{15}H_{18}N_3O_5$, $[M+H-O_2]^+$; calc. 320.1246), 213.0868 (88, $C_9H_{13}N_2O_4$, $[M-C_6H_4NO_3]^+$; calc. 213.0875).

*(5*R*,6*R*,7*S*,8*R*)-5,6,7,8-Tetrahydro-5-(hydroxymethyl)-2-[(4-nitrophenoxy)methyl]-imidazo[1,2-*a*]pyridine-6,7,8-triol* (**41**). *a*) A soln. of **37** (16.7 mg, 23.5 μmol) in CH_2Cl_2 (1 ml) was treated with $AlCl_3$ (38 mg, 0.285 mmol) and anisole (41 μl, 0.375 mmol), stirred for 17 h at 22°, and treated with H_2O (15 ml). The mixture was diluted with AcOEt (15 ml). After extraction with H_2O, the aq. layer was evaporated. FC (AcOEt/MeOH/H_2O 1:0:0 → 20:1:1) and drying yielded **41** (5.9 mg, *ca.* 72%) as a white foam containing substantial amounts of MeOH and H_2O. The sample for microanalysis was dried for 4 d at 10^{-4} Torr.

b) A soln. of **37** (30.7 mg, 43.1 μmol) in CH_2Cl_2 (1.1 ml) was treated at −78° with 1M BCl_3 in CH_2Cl_2 (0.8 ml, 0.80 mmol), stirred until the mixture had reached a temp. of 20° (*ca.* 5.5 h), cooled to −78°, treated with H_2O (2 ml), and evaporated. FC (AcOEt/MeOH/H_2O 1:0:0 → 20:1:1) gave **41** (10.7 mg, *ca.* 70%) containing substantial amounts of MeOH and H_2O.

Data of **41**: R_f (AcOEt/MeOH/H_2O 10:1:1) 0.17. $[\alpha]_D^{25}$ −24.3 ($c = 0.48$, MeOH). UV (MeOH): 307 (3.99), 219 (4.09), 204 (4.15). IR (KBr): 3600–2400*s* (br.), 2928*m*, 1631*w*, 1606*m*, 1593*s*, 1510*s*, 1459*m*, 1383*m*, 1344*s*, 1299*m*, 1259*s*, 1177*m*, 1112*s*, 986*m*, 902*w*, 870*m*, 846*m*. ^{1}H-NMR (CD_3OD, 300 MHz): 3.82 (*dd*, *J* = 3.7, 9.0, H–C(7)); 3.84–3.94 (*m*, H–C(5), CH–C(5)); 4.06–4.22 (*m*, H–C(6), CH′–C(5)); 4.83 (*d*, *J* = 3.7, H–C(8)); 5.10 (br. *s*, CH$_2$–C(2)); 7.11–7.18 (*m*, J_{vic} = 9.3, H–C(2) and H–C(6) of $C_6H_4NO_2$); 7.50 (*s*, H–C(3)); 8.16–

8.23 (*m*, J_{vic} = 9.3, H–C(3) and H–C(5) of $C_6H_4NO_2$). ^{13}C-NMR (CD_3OD, 75 MHz): see *Table 6*; additionally, 65.41 (*t*, CH_2–C(2)); 116.06 (*d*, C(2) and C(6) of $C_6H_4NO_2$); 126.78 (*d*, C(3) and C(5) of $C_6H_4NO_2$); 142.83 (*s*, C(4) of $C_6H_4NO_2$); 165.26 (*s*, C(1) of $C_6H_4NO_2$). HR-MALDI-MS: 374.0957 (5, $C_{15}H_{17}N_3NaO_7$, $[M+Na]^+$; calc. 374.0964), 360.1163 (6, $C_{15}H_{19}N_3NaO_6$, $[M+Na-O_2+H_2O]^+$; calc. 360.1171), 358.0997 (7, $C_{15}H_{17}N_3NaO_6$, $[M+Na-O]^+$; calc. 358.1015), 352.1138 (27, $C_{15}H_{18}N_3O_7$, $[M+H]^+$; calc. 352.1145), 338.1350 (38, $C_{15}H_{20}N_3O_6$, $[M+H-O_2+H_2O]^+$; calc. 338.1350), 336.1191 (28, $C_{15}H_{18}N_3O_6$, $[M+H-O]^+$; calc. 336.1195), 320.1237 (16, $C_{15}H_{18}N_3O_5$, $[M+H-O_2]^+$; calc. 320.1246), 302.1130 (5, $C_{15}H_{16}N_3O_4$, $[M-O_2-OH]^+$; calc. 302.1141), 235.0681 (10, $C_9H_{12}N_2NaO_4$, $[M+Na-C_6H_5NO_3]^+$; calc. 235.0695), 213.0866 (100, $C_9H_{13}N_2O_4$, $[M-C_6H_4NO_3]^+$; calc. 213.0875). Anal. calc. for $C_{15}H_{17}N_3O_7 \cdot 0.5\ MeOH \cdot 0.5\ H_2O$ (376.34): C 49.47, H 5.36, N 11.17; found: C 49.57, H 5.25, N 10.95.

*(5*R*,6*R*,7*S*,8*R*)-2-[(2,4-Dinitrophenoxy)methyl]-5,6,7,8-tetrahydro-5-(hydroxymethyl)imidazo[1,2-*a*]pyridine-6,7,8-triol* (**42**). A soln. of **38** (27 mg, 35.7 μmol) in CH_2Cl_2 (1.6 ml) was treated with $AlCl_3$ (60 mg, 0.450 mmol) and anisole (63 μl, 0.577 mmol), stirred for 17 h at 22°, and treated with H_2O (20 ml). The mixture was diluted with AcOEt (25 ml). After extraction with H_2O, the aq. layer was evaporated. FC (AcOEt/MeOH/H_2O 1:0:0 → 15:1:1) yielded pure **42** (7.6 mg, 75%; colourless solid) which partially decomposed before the NMR measurement. R_f (AcOEt/MeOH/H_2O 15:1:1) 0.13. IR (KBr): 3600–2400*s* (br.), 2930*m*, 1955*w*, 1837*w*, 1603*s*, 1564*s*, 1525*s*, 1478*m*, 1432*m*, 1373*m*, 1330*s*, 1265*s*, 1169*m*, 1133*s*, 1096*m*, 1060*m*, 998*m*, 925*m*, 834*m*, 751*m*, 714*m*. ^{1}H-NMR (CD_3OD, 300 MHz, 3:1 mixture of **42** and a product missing the dinitrophenoxy group): 3.83 (*dd*, *J* = 3.7, 9.0, H–C(7)); 3.86–3.95 (*m*, H–C(5), CH–C(5)); 4.07–4.20 (*m*, H–C(6), CH′–C(5)); 4.83 (*d*, *J* = 3.7, H–C(8)); 5.29 (br. *s*, CH_2–C(2)); 7.56 (*s*, H–C(3)); 7.67 (*d*, *J* = 9.3, H–C(6) of $C_6H_3N_2O_4$); 8.47 (*dd*, *J* = 2.8, 9.3, H–C(5) of $C_6H_3N_2O_4$); 8.69 (*d*, *J* = 2.8, H–C(3) of $C_6H_3N_2O_4$). HR-MALDI-MS: 396.9894 (24, $C_{15}H_{17}N_4O_9$, $[M+H]^+$; calc. 397.0995), 213.0865 (100, $C_9H_{13}N_2O_4$, $[M-C_6H_3N_2O_5]^+$; calc. 213.0875).

*(5*R*,6*R*,7*S*,8*R*)-5,6,7,8-Tetrahydro-5-(hydroxymethyl)-2-[(3-nitrophenoxy)methyl]imidazo[1,2-*a*]pyridine-6,7,8-triol* (**43**). A soln. of **39** (9.7 mg, 13.6 μmol) in CH_2Cl_2 (0.6 ml) was treated with $AlCl_3$ (22 mg, 0.165 mmol) and anisole (24 μl, 0.220 mmol), stirred for 13 h at 22°, and treated with H_2O (10 ml). The mixture was diluted with AcOEt (10 ml). After extraction with H_2O, the aq. layer was evaporated. FC (AcOEt/MeOH/H_2O 1:0:0 → 20:1:1 → 15:1:1) yielded **43** (2.6 mg, *ca.* 54%) as a white solid containing substantial amounts of MeOH. The sample for microanalysis was dried for 4 d at 10^{-4} Torr. R_f (AcOEt/MeOH/H_2O 10:1:1) 0.23. $[\alpha]_D^{25} = -14.2$ (*c* = 0.29, MeOH). UV (MeOH): 267 (3.68), 214 (4.25). IR (KBr): 3600–2400*s* (br.), 2925*m*, 2851*m*, 1616*m*, 1528*s*, 1482*m*, 1460*m*, 1384*m*, 1351*s*, 1323*m*, 1285*m*, 1244*m*, 1181*w*, 1095*m*, 1029*w*, 1007*m*, 903*w*, 843*w*, 825*w*, 796*w*, 737*m*. ^{1}H-NMR (CD_3OD, 300 MHz): 3.81 (*dd*, *J* = 3.7, 9.3, irrad. at 4.11 → *d*, *J* ≈ 4.0, irrad. at 4.83 → *d*, *J* = 9.3, H–C(7)); 3.84–3.90 (*m*, H–C(5)); 3.90 (*dd*, *J* = 5.6, 10.9, CH–C(5)); 4.06–4.22 (*m*, H–C(6), CH′–C(5)); 4.83 (*d*, *J* = 3.7, irrad. at 3.81 → *s*, H–C(8)); 5.08 (br. *s*, CH_2–C(2)); 7.39 (*ddd*, *J* = 0.9, 2.5, 8.4, H–C(6) of $C_6H_4NO_2$); 7.49 (*s*, H–C(3)); 7.50 (*t*, *J* = 8.4, H–C(5) of $C_6H_4NO_2$); 7.81 (*ddd*, *J* = 0.9, 2.2, 8.7, H–C(4) of $C_6H_4NO_2$); 7.82 (*t*, *J* ≈ 1.9, H–C(2) of $C_6H_4NO_2$). ^{13}C-NMR (CD_3OD, 75 MHz): see *Table 6*; additionally, 65.30 (*t*, CH_2–C(2)); 110.27 (*d*, C(2) of $C_6H_4NO_2$); 116.48 (*d*, C(4) of $C_6H_4NO_2$); 122.56 (*d*, C(6) of $C_6H_4NO_2$); 131.19 (*d*, C(5) of $C_6H_4NO_2$); 150.39 (*s*, C(3) of $C_6H_4NO_2$); 160.47 (*s*, C(1) of $C_6H_4NO_2$). HR-MALDI-MS: 374.0952 (39, $C_{15}H_{17}N_3NaO_7$, $[M+Na]^+$; calc. 374.0964), 360.1168 (65, $C_{15}H_{19}N_3NaO_6$, $[M+Na-O_2+H_2O]^+$; calc. 360.1171), 358.1018 (67, $C_{15}H_{17}N_3NaO_6$, $[M+Na-O]^+$; calc. 358.1015), 352.1143 (70, $C_{15}H_{18}N_3O_7$, $[M+H]^+$; calc. 352.1145), 338.1347 (100, $C_{15}H_{20}N_3O_6$, $[M+H-O_2+H_2O]^+$; calc. 338.1352), 336.1191 (96, $C_{15}H_{18}N_3O_6$, $[M+H-O]^+$; calc. 336.1195), 320.1234 (82, $C_{15}H_{18}N_3O_5$, $[M+H-O_2]^+$; calc. 320.1246), 213.0868 (90, $C_9H_{13}N_2O_4$, $[M-C_6H_4NO_3]^+$; calc. 213.0875), 195.0758 (61, $C_9H_{11}N_2O_3$, $[M-C_6H_4NO_3-H_2O]^+$; calc. 195.0770). Anal. calc. for $C_{15}H_{17}N_3O_7 \cdot MeOH$ (383.36): C 50.13, H 5.52, N 10.96; found: C 50.34, H 5.36, N 10.94.

*Methyl and Ethyl (5*R*,6*R*,7*S*,8*R*)-6,7,8-Tris(benzyloxy)-5-[(benzyloxy)methyl]-5,6,7,8-tetrahydroimidazo[1,2-*a*]pyridine-2-carboxylate* (**44** and **45**, resp.). *a*) A soln. of **20** (210 mg, 0.306 mmol) in THF (10 ml) was cooled to −78°, treated with a 1.44M soln. of BuLi[14]) in hexane (0.48 ml, 0.691 mmol), stirred for 1 h, treated with ClCOOMe (0.20 ml, 2.60 mmol), stirred for 1 h at −78°, and for another 17 h at 22°. The mixture was treated with sat. NH_4Cl soln. (10 ml) and diluted with Et_2O (40 ml). The layers were separated, and the Et_2O layer was washed with sat. NH_4Cl soln. (2 × 20 ml). The combined aq. layers were extracted with Et_2O (2 × 15 ml). The combined org. layers were washed with H_2O (40 ml), brine (40 ml), and dried ($MgSO_4$). Evaporation and FC (hexane/AcOEt 1:0 → 7:3 → 1:1) yielded **44** (82 mg, 43%) and **17** (41 mg, 24%). Oils.

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[14]) The molar concentration of BuLi was determined by titration of $Ph_2CHCOOH$ as described by *Kofron* and *Baclawski* [58].

b) A suspension of **22** (75 mg, 0.127 mmol), MnO_2 (285 mg, 3.28 mmol, *Aldrich 21,764-6*) and NaCN (35 mg, 0.714 mmol) in MeOH (4 ml) was treated with AcOH (20 µl, 0.350 mmol), stirred at 22° for 12 h, filtered through *Celite* (washing with 20 ml of MeOH and 20 ml of AcOEt). Evaporation of the filtrate and FC (hexane/AcOEt 1:0 → 2:1 → 1:1) gave **45** (17.1 mg, 21%) and **44** (51.6 mg, 65%). Colourless oils.

c) As described in *b*. After evaporation of the filtrate, the crude product was diluted with AcOEt (60 ml) and washed with sat. $NaHCO_3$ soln. (3 × 30 ml). The combined aq. layers were extracted with AcOEt (2 × 40 ml). The combined org. layers were washed with H_2O (70 ml) and brine (70 ml), dried ($MgSO_4$), filtered, and evaporated. FC (cyclohexane/AcOEt 1:0 → 1:1) afforded **44** (78%) as a single product.

Data of **44**: R_f (hexane/AcOEt 1:1) 0.35. $[\alpha]_D^{25} = -37.1$ ($c = 1.00$, $CHCl_3$). UV ($CHCl_3$): 243 (3.98). IR ($CHCl_3$): 3090*w*, 3068*w*, 3024*m*, 3018*m*, 2953*m*, 2928*w*, 2869*w*, 1952*w*, 1876*w*, 1811*w*, 1718*s*, 1603*w*, 1552*m*, 1497*m*, 1455*m*, 1428*w*, 1363*m*, 1343*m*, 1327*m*, 1262*m*, 1217*s*, 1146*m*, 1097*s*, 1028*s*, 1010*s*, 943*w*, 913*w*. ^{1}H-NMR ($CDCl_3$, 300 MHz): see *Table 7*; additionally, 3.91 (*s*, MeO); 4.45 (br. *s*, PhCH_2); 4.62 (*d*, $J = 11.2$, PhC*H*); 4.64 (*d*, $J = 12.1$, PhC*H*); 4.66 (*d*, $J = 11.5$, PhC*H*); 4.70 (*d*, $J = 12.1$, PhC*H*); 4.74 (*d*, $J = 11.8$, PhC*H*); 4.99 (*d*, $J = 11.2$, PhC*H*); 7.23–7.38 (*m*, 20 arom. H). ^{13}C-NMR ($CDCl_3$, 75 MHz): see *Table 5*; additionally, 51.80 (*q*, MeO); 70.45, 70.93 (2*t*, Ph*C*H$_2$, *C*H$_2$–C(5)); 71.95 (*t*, Ph*C*H$_2$); 73.23 (*t*, Ph*C*H$_2$); 74.92 (*t*, Ph*C*H$_2$); 127.44–128.44 (several *d*); 137.07, 137.49, 137.65, 137.80 (4*s*); 163.12 (*s*, C=O). HR-MALDI-MS: 657.2380 (4, $C_{38}H_{38}KN_2O_6$, $[M+K]^+$; calc. 657.2367), 641.2586 (77, $C_{38}H_{38}N_2NaO_6$, $[M+Na]^+$; calc. 641.2627), 619.2809 (100, $C_{38}H_{39}N_2O_6$, $[M+H]^+$; calc. 619.2808), 587.2574 (3, $C_{37}H_{35}N_2O_5$, $[M-MeO]^+$; calc. 587.2546), 511.2265 (31, $C_{31}H_{31}N_2O_5$, $[M-BnO]^+$; calc. 511.2232), 479.2002 (15, $C_{30}H_{27}N_2O_4$, $[M-BnO-MeOH]^+$; calc. 479.1970). Anal. calc. for $C_{38}H_{38}N_2O_6$ (618.73): C 73.77, H 6.19, N 4.53; found: C 73.79, H 6.33, N 4.64.

Data of **45**: R_f (hexane/AcOEt 1:1) 0.53. $[\alpha]_D^{25} = -35.6$ ($c = 0.58$, $CHCl_3$). UV ($CHCl_3$): 242 (4.01). IR ($CHCl_3$): 3159*w*, 3090*w*, 3068*w*, 3019*m*, 2963*m*, 2929*w*, 2870*w*, 1953*w*, 1878*w*, 1811*w*, 1717*m*, 1603*w*, 1550*w*, 1497*w*, 1455*m*, 1393*w*, 1367*m*, 1338*w*, 1323*m*, 1262*m*, 1217*s*, 1146*m*, 1096*s*, 1027*s*, 930*w*, 913*w*. ^{1}H-NMR ($CDCl_3$, 300 MHz): see *Table 7*; additionally, 1.36 (*t*, $J = 7.2$, *Me*CH$_2$); 4.34 (*q*, $J = 7.2$, MeC*H*$_2$); 4.42 (br. *s*, PhC*H*$_2$); 4.58 (*d*, $J = 11.2$, PhC*H*); 4.60 (*d*, $J = 12.1$, PhC*H*); 4.62 (*d*, $J = 11.5$, PhC*H*); 4.66 (*d*, $J = 11.2$, PhC*H*); 4.70 (*d*, $J = 12.1$, PhC*H*); 4.95 (*d*, $J = 11.2$, PhC*H*); 7.20–7.35 (*m*, 20 arom. H). ^{13}C-NMR ($CDCl_3$, 75 MHz): see *Table 5*; additionally, 14.46 (*q*, *Me*CH$_2$); 60.53 (*t*, MeCH$_2$); 70.48, 70.86 (2*t*, Ph*C*H$_2$, *C*H$_2$–C(5)); 71.89 (*t*, Ph*C*H$_2$); 73.22 (*t*, Ph*C*H$_2$); 74.90 (*t*, Ph*C*H$_2$); 127.51–128.50 (several *d*); 137.19, 137.58, 137.77, 137.93 (4*s*); 162.87 (*s*, C=O). MALDI-MS: 655 ($[M+Na]^+$), 633 ($[M+H]^+$). HR-MALDI-MS: 671.2537 (9, $C_{39}H_{40}KN_2O_6$, $[M+K]^+$; calc. 671.2523), 655.2787 (100, $C_{39}H_{40}N_2NaO_6$, $[M+Na]^+$; calc. 655.2784), 633.2966 (54, $C_{39}H_{41}N_2O_6$, $[M+H]^+$; calc. 633.2964), 587.2550 (7, $C_{37}H_{35}N_2O_5$, $[M-EtO]^+$; calc. 587.2546), 525.2393 (26, $C_{32}H_{33}N_2O_5$, $[M-BnO]^+$; calc. 525.2389), 479.1981 (19, $C_{30}H_{27}N_2O_4$, $[M-BnO-EtOH]^+$; calc. 479.1971). Anal. calc. for $C_{39}H_{40}N_2O_6$ (632.75): C 74.03, H 6.37, N 4.43; found: C 74.18, H 6.50, N 4.23.

*Methyl (5*R*,6*R*,7*S*,8*R*)-5,6,7,8-Te trahydro-6,7,8-trihydroxy-5-(hydroxymethyl)imidazo[1,2-*a*]pyridine-2-carboxylate* (**46**). A soln. of **44** (105 mg, 0.170 mmol) in AcOEt/MeOH 1:1 (1.8 ml) was treated with AcOH (0.9 ml) and 10% Pd/C (50 mg), hydrogenated at 6 bar for 48 h, and filtered through *Celite* (washing with MeOH/H_2O 9:1 (20 ml)). Evaporation of the combined filtrates, FC (AcOEt/MeOH/H_2O 1:0:0 → 10:1:1), lyophilisation, and drying gave **46** (38.5 mg, ca. 88%) as a colourless hygroscopic resin containing substantial amounts of MeOH and H_2O. The sample for microanalysis was dried for 4 d at 10^{-4} Torr. R_f (AcOEt/MeOH/H_2O 10:1:1) 0.12. $[\alpha]_D^{25}$ −21.6 ($c = 1.02$, MeOH). UV (MeOH): 238 (3.95), 200 (3.67). IR (KBr): 3600–2400*s* (br.), 2952*m*, 2924*m*, 1716*s*, 1636*w*, 1553*m*, 1442*m*, 1356*m*, 1334*m*, 1219*s*, 1138*m*, 1095*s*, 1011*m*, 945*w*, 902*w*, 834*w*, 805*w*, 769*m*. ^{1}H-NMR (CD_3OD, 300 MHz): 3.83 (*s*, MeO); 3.84 (*dd*, $J \approx 3.7, 8.7$, irrad. at 4.11 → change, irrad. at 4.84 → *d*, $J = 9.0$, H–C(7)); 3.89 (*dd*, $J = 5.9, 11.2$, irrad. at 4.17 → change, CH–C(5)); 3.90–3.97 (*m*, irrad. at 4.11 → change, irrad. at 4.17 → change, H–C(5)); 4.11 (*dd*, $J = 7.2, 9.0$, irrad. at 3.84 → *d* $J \approx 6.5$, H–C(6)); 4.17 (*dd*, $J = 2.2, 11.2$, CH′–C(5)); 4.84 (*d*, $J = 3.7$, irrad. at 3.84 → *s*, H–C(8)); 8.01 (*s*, H–C(3)). ^{13}C-NMR (CD_3OD, 75 MHz): see *Table 6*; additionally, 51.95 (*q*, MeO); 164.34 (*s*, C=O). HR-MALDI-MS: 281.0742 (100, $C_{10}H_{14}N_2NaO_6$, $[M+Na]^+$; calc. 281.0749), 259.0928 (60, $C_{10}H_{15}N_2O_6$, $[M+H]^+$; calc. 259.0930), 227.0658 (21, $C_9H_{11}N_2O_5$, $[M-MeO]^+$; calc. 227.0668). Anal. calc. for $C_{10}H_{14}N_2O_6 \cdot 0.6\,MeOH \cdot 0.1\,H_2O$ (279.26): C 45.59, H 5.99, N 10.03; found: C 45.45, H 5.70, N 9.77.

*(5*R*,6*R*,7*S*,8*R*)-5,6,7,8-Tetrahydro-6,7,8-trihydroxy-5-(hydroxymethyl)imidazo[1,2-*a*]pyridine-2-carboxylic Acid* (**47**). A soln. of **46** (25 mg, 96.8 µmol) in 0.4M soln. of KOH in EtOH/H_2O 4:1 (1 ml) was heated at 50° for 3 h, evaporated, taken up in H_2O (3 ml), and applied to ion-exchange chromatography (*Amberlite CG-120*, H^+ form, elution with 0.1M aq. NH_3). Lyophilisation gave **47** (19.5 mg, 83%) as a colourless hygroscopic resin. R_f (AcOEt/MeOH/H_2O 3:1:1) 0.13. $[\alpha]_D^{25} = -51.3$ ($c = 0.74$, H_2O). UV (H_2O): 226 (3.96), 193 (3.99). IR (KBr): 3600–2400*s* (br.), 2918*m*, 2857*m*, 1619*s*, 1575*s*, 1544*s*, 1434*m*, 1398*s*, 1337*m*, 1265*m*, 1183*m*, 1094*s*, 1065*s*, 1000*m*, 902*m*, 835*m*, 775*m*, 724*m*. ^{1}H-NMR (D_2O, 300 MHz): 3.84 (*dd*, $J = 3.4, 9.7$, H–C(7)); 3.82–3.89 (*m*, H–C(5));

3.89 (*dd*, *J* = 3.4, 12.1, CH–C(5)); 4.04–4.14 (*m*, H–C(6), CH′–C(5)); 4.79 (*d*, *J* = 3.4, H–C(8)); 7.53 (*s*, H–C(3)). ^{13}C-NMR (D_2O, 75 MHz): see *Table 6*; additionally, 169.88 (*s*, C=O). HR-MALDI-MS: 289.0405 (12, $C_9H_{11}N_2Na_2O_6$, $[M-H+2\,Na]^+$; calc. 289.0412); 267.0584 (51, $C_9H_{12}N_2NaO_6$, $[M+Na]^+$; calc. 267.0593); 245.0768 (100, $C_9H_{13}N_2O_6$, $[M+H]^+$; calc. 245.0774), 227.0657 (23, $C_9H_{11}N_2O_5$, $[M-OH]^+$; calc. 227.0668).

*(5*R*,6*R*,7*S*,8*R*)-6,7,8-Tris(benzyloxy)-5-[(benzyloxy)methyl]-5,6,7,8-tetrahydroimidazo[1,2-*a*]pyridine-2-carbonitrile* (**48**). *a*) A soln. of **20** (235 mg, 0.342 mmol) in THF (2.3 ml) was treated at 0° with 1M EtMgBr soln. in THF (1.18 ml, 1.18 mmol), stirred under Ar for 15 min, treated with a suspension of TsCN (620 mg, 3.42 mmol) in THF (4.7 ml), and stirred at 0° → 23° for 4 h. The mixture was cooled to 0°, treated with sat. NH_4Cl soln. (10 ml), diluted with Et_2O (50 ml), and washed with sat. NH_4Cl soln. (3 × 30 ml). The combined aq. layers were extracted with Et_2O (2 × 20 ml). The combined org. layers were washed with H_2O (50 ml) and brine (50 ml), dried ($MgSO_4$), filtered, and evaporated. FC (hexane/AcOEt 5:1 → 3:1) gave **48** (147 mg, 73%). Colourless oil.

b) A suspension of **20** (50 mg, 72.8 μmol), $Zn(CN)_2$ (17 mg, 0.145 mmol) and $[Pd(PPh_3)_4]$ (25 mg, 21.6 μmol) in degassed DMF (0.2 ml) was stirred at 150° for 1 h. The mixture was cooled to r.t., diluted with AcOEt (15 ml), and washed with sat. NH_4Cl soln. (3 × 10 ml). The combined aq. layers were extracted with AcOEt (2 × 15 ml). The combined org. layers were washed with H_2O (20 ml) and brine (20 ml), dried ($MgSO_4$), filtered, and evaporated. FC (hexane/AcOEt 2:1 → 1:1 → 0:1) gave **48** (17 mg, 40%) and **17** (11 mg, 27%).

Data of **48**: R_f (hexane/AcOEt 2:1) 0.60. $[\alpha]_D^{25} = -43.1$ (*c* = 1.02, $CHCl_3$). UV ($CHCl_3$): 259 (3.02), 240 (3.55). IR ($CHCl_3$): 3157*w*, 3090*w*, 3068*w*, 3024*m*, 3016*m*, 2927*w*, 2870*m*, 2238*m*, 1952*w*, 1879*w*, 1811*w*, 1730*w*, 1603*w*, 1531*w*, 1497*w*, 1455*m*, 1364*m*, 1266*m*, 1098*s*, 1028*s*, 913*w*. ^{1}H-NMR ($CDCl_3$, 300 MHz): see *Table 7*; additionally, 4.43 (*d*, *J* = 12.5, PhC*H*); 4.47 (*d*, *J* = 12.8, PhC*H*); 4.56 (*d*, *J* = 12.1, PhC*H*); 4.60 (*d*, *J* = 12.8, PhC*H*); 4.65 (*d*, *J* = 12.1, PhC*H*); 4.68 (*d*, *J* = 11.5, PhC*H*); 4.76 (*d*, *J* = 12.8, PhC*H*); 4.94 (*d*, *J* = 11.2, PhC*H*); 7.22–7.44 (*m*, 20 arom. H). ^{13}C-NMR ($CDCl_3$, 75 MHz): see *Table 5*; additionally, 70.49, 71.00 (2*t*, Ph*C*H_2, *C*H_2–C(5)); 72.06 (*t*, Ph*C*H_2); 73.34 (*t*, Ph*C*H_2); 74.78 (*t*, Ph*C*H_2); 114.11, 114.76 (2*s*, C(2), C≡N); 127.72–128.52 (several *d* incl. C(3)); 136.77 (*s*), 137.22 (2*s*), 137.34 (*s*). HR-MALDI-MS: 624.2254 (4, $C_{37}H_{35}KN_3O_4$, $[M+K]^+$; calc. 624.2264); 608.2527 (100, $C_{37}H_{35}N_3NaO_4$, $[M+Na]^+$; calc. 608.2525); 586.2707 (62, $C_{37}H_{36}N_3O_4$, $[M+H]^+$; calc. 586.2706); 478.2111 (53, $C_{30}H_{28}N_3O_3$, $[M-BnO]^+$; calc. 478.2131). Anal. calc. for $C_{37}H_{35}N_3O_4$ (585.71): C 75.88, H 6.02, N 7.17; found: C 75.90, H 6.12, N 7.24.

*(5*R*,6*R*,7*S*,8*R*)-6,7,8-Tris(benzyloxy)-5-[(benzyloxy)methyl]-5,6,7,8-tetrahydro-2-(1*H*-tetrazol-5-yl)imidazo[1,2-*a*]pyridine* (**49**). At 0°, a soln. of 2M Me_3Al in toluene (0.34 ml, 0.68 mmol) in toluene (1 ml) was treated with Me_3SiN_3 (90 μl, 0.684 mmol), stirred for 10 min, and treated dropwise with a soln. of **48** (81 mg, 0.138 mmol) in toluene (1 ml). The mixture was stirred at 80° for 1.5 h, cooled to 0°, treated with sat. NH_4Cl soln. (5 ml), diluted with AcOEt (40 ml), and washed with sat. NH_4Cl soln. (3 × 30 ml). The combined aq. layers were extracted with AcOEt (2 × 25 ml). The combined org. layers were washed with H_2O (50 ml) and brine (50 ml), dried (Na_2SO_4), filtered, and evaporated. The crude product (77 mg, a single compound according to the ^{1}H-NMR spectrum) was precipitated from hexane/AcOEt 3:1 (4 ml) at −50° to afford after drying **49** (66 mg, ca. 76%) as a colourless solid containing substantial amounts of H_2O. The sample for microanalysis was dried for 4 d at 10^{-4} Torr. R_f (AcOEt/MeOH 5:1) 0.21. R_f ($CHCl_3$/MeOH/AcOH 16:1:1) 0.61. M.p. 116.2–118.1°. $[\alpha]_D^{25} = +7.9$ (*c* = 0.79, $CHCl_3$). UV ($CHCl_3$): 248 (4.21). IR ($CHCl_3$): 3200–2400*m* (br.), 3163*w*, 3089*m*, 3067*m*, 3033*m*, 3011*m*, 2959*m*, 2905*m*, 2867*m*, 1952*w*, 1878*w*, 1812*w*, 1629*m*, 1527*w*, 1496*m*, 1454*m*, 1421*w*, 1364*m*, 1337*m*, 1262*s*, 1097*s*, 1026*s*, 963*m*, 912*w*. ^{1}H-NMR ($CDCl_3$, 300 MHz): see *Table 7*; additionally, 4.51 (br. *s*, PhCH_2); 4.52 (*d*, *J* = 12.1, PhC*H*); 4.63 (*d*, *J* = 12.1, PhC*H*); 4.64 (*d*, *J* = 11.2, PhC*H*); 4.71 (*d*, *J* = 12.1, PhC*H*); 4.84 (*d*, *J* = 11.8, PhC*H*); 4.98 (*d*, *J* = 11.5, PhC*H*); 7.01–7.03 (*m*, 3 arom. H); 7.07–7.10 (*m*, 2 arom. H); 7.24–7.36 (*m*, 13 arom. H); 7.39–7.42 (*m*, 2 arom. H). ^{13}C-NMR ($CDCl_3$, 75 MHz): see *Table 5*; additionally, 70.07, 71.45 (2*t*, Ph*C*H_2, *C*H_2–C(5)); 72.04 (*t*, Ph*C*H_2); 73.39 (*t*, Ph*C*H_2); 74.73 (*t*, Ph*C*H_2); 127.37–128.50 (several *d*); 136.89 (2*s*); 137.14, 137.44 (2*s*); 149.32 (*s*, C(5) of CHN_4). HR-MALDI-MS: 673.2530 (6, $C_{37}H_{35}N_6Na_2O_4$, $[M-H+2\,Na]^+$; calc. 673.2515), 651.2730 (93, $C_{37}H_{36}N_6NaO_4$, $[M+Na]^+$; calc. 651.2696), 629.2878 (100, $C_{37}H_{37}N_6O_4$, $[M+H]^+$; calc. 629.2876), 623.2647 (48, $C_{37}H_{36}N_4NaO_4$, $[M-N_2+Na]^+$; calc. 623.2634), 601.2822 (62, $C_{37}H_{37}N_4O_4$, $[M+H-N_2]^+$; calc. 601.2815), 572.2656 (10, $C_{37}H_{36}N_2O_4$, $[M-2\,N_2]^+$; calc. 572.2675), 521.2292 (6, $C_{30}H_{29}N_6O_3$, $[M-BnO]^+$; calc. 521.2301), 493.2235 (58, $C_{30}H_{29}N_4O_3$, $[M-BnO-N_2]^+$; calc. 493.2239), 464.2089 (14, $C_{30}H_{28}N_2O_3$, $[M-BnOH-2\,N_2]^+$; calc. 464.2100). Anal. calc. for $C_{37}H_{35}N_3O_4 \cdot 1.5\,H_2O$ (655.76): C 67.77, H 5.99, N 12.82; found: C 68.03, H 6.04, N 12.82.

*(5*R*,6*R*,7*S*,8*R*)-5,6,7,8-Tetrahydro-5-(hydroxymethyl)-2-(1*H*-tetrazol-5-yl)imidazo[1,2-*a*]pyridine-6,7,8-triol* (**50**). A soln. of **49** (35 mg, 55.7 μmol) in CH_2Cl_2 (1.4 ml) was treated at −78° with 1M BCl_3 in CH_2Cl_2 (0.88 ml, 0.88 mmol), stirred until the mixture had reached a temp. of 10° (*ca.* 5 h), cooled to −78°, treated with H_2O (2 ml), and evaporated. The residue was taken up in H_2O (3 ml) and applied to ion-exchange column

(*Amberlite CG-120*, H^+ form, elution with 0.1M aq. NH_3). Lyophilisation gave **50** (12.7 mg, 85%). Colourless hygroscopic resin. R_f (AcOEt/MeOH/AcOH 7:5:1) 0.10. $[\alpha]_D^{25} = -33.8$ ($c = 0.57$, MeOH). UV (MeOH): 233 (3.91). IR (KBr): 3600–2400*s* (br.), 2930*m*, 1630*m*, 1519*w*, 1452*m*, 1401*m*, 1333*m*, 1246*m*, 1200*m*, 1097*s*, 965*w*, 904*m*, 873*w*. ^{1}H-NMR (D_2O, 300 MHz): 3.98–4.06 (*m*, irrad. at 5.00 → change, H–C(7), H–C(5)); 4.08 (*dd*, $J = 3.1, 13.7$, CH–C(5)); 4.23–4.33 (*m*, H–C(6), CH′–C(5)); 5.00 (*d*, $J = 3.4$, H–C(8)); 7.74 (*s*, H–C(3)). ^{13}C-NMR (D_2O, 75 MHz): see *Table 6*; *s* for CHN_4 hidden by the noise. HR-MALDI-MS: 313.0307 (15, $C_9H_{11}N_6Na_2O_4$, $[M - H + 2\,Na]^+$; calc. 313.0637), 291.0807 (38, $C_9H_{12}N_6NaO_4$, $[M + Na]^+$; calc. 291.0818), 269.0991 (100, $C_9H_{13}N_6O_4$, $[M + H]^+$; calc. 269.0998), 241.0933 (21, $C_9H_{13}N_4O_4$, $[M + H - N_2]^+$; calc. 241.0937), 212.1441 (90, $C_9H_{12}N_2O_4$, $[M - 2\,N_2]^+$; calc. 212.0797), 198.9984 (53, $C_8H_{11}N_2O_4$, $[M - CHN_4]^+$; calc. 199.0719).

Inhibition Studies. Determination of the inhibition constants (K_i) or the IC_{50} values was performed with a range of inhibitor concentrations (typically 4–7 concentrations), which bracket the K_i or IC_{50} value, and substrate concentrations, which bracket the K_M value of each enzyme (for K_i, typically 5–7 concentrations), or correspond to it (for IC_{50}).

a) *Inhibition of Snail β-Mannosidase.* $K_M = 0.42–0.80$. Inhibition constants (K_i) and IC_{50} values were determined at 25° at an enzyme concentration of 0.048 units/ml, with a 0.05M acetate buffer (pH 4.5) and 4-nitrophenyl β-D-mannopyranoside as the substrate. The enzymatic reaction was started after incubation of the enzyme (100 µl) in presence of the inhibitor (50 µl) during 1 h at 25°, by the addition of the substrate (50 µl). The enzyme reaction was quenched by addition of 0.2M borate buffer (pH 9.2, 100 µl) after 5 min, and the absorption at 405 nm was taken as rate for the hydrolysis of the substrate. IC_{50} Values were determined by plotting the reciprocal value of the rate of substrate hydrolysis *vs.* the inhibitor concentration. After fitting a straight line to the data by linear regression, the negative [*I*] intercept of this plot provided the appropriate IC_{50} value. K_i Values were determined by taking the slopes from the *Lineweaver–Burk* plots [59] and plotting them *vs.* the inhibitor concentrations [60]. After fitting a straight line to the data by linear regression, the negative [*I*] intercept of this plot provided the appropriate K_i value.

b) *Inhibition of* Jack *Beans α-Mannosidase.* $K_M = 1.8–2.8$ ([61]: 2.5 mM). As described in *a*, inhibition studies were carried out at 37° at an enzyme concentration of 0.086 units/ml, with a 0.05M acetate buffer (pH 4.5), containing 2 mmol of $ZnCl_2$ and 4-nitrophenyl α-D-mannopyranoside as the substrate. The enzymatic reaction was started after the incubation at 37° for 1 h.

REFERENCES

[1] T. Aoyagi, H. Suda, K. Uotani, F. Kojima, T. Aoyama, K. Horiguchi, M. Hamada, T. Takeuchi, *J. Antibiot.* **1992**, *45*, 1404.
[2] T. Granier, N. Panday, A. Vasella, *Helv. Chim. Acta* **1997**, *80*, 979.
[3] K. Tatsuta, S. Miura, S. Ohta, H. Gunji, *J. Antibiot.* **1995**, *48*, 286.
[4] T. D. Heightman, A. Vasella, K. E. Tsitsanou, S. E. Zographos, V. T. Skamnaki, N. G. Oikonomakos, *Helv. Chim. Acta* **1998**, *81*, 853.
[5] N. Panday, A. Vasella, *Synthesis* **1999**, 1459.
[6] N. Panday, Y. Canac, A. Vasella, *Helv. Chim. Acta* **2000**, *83*, 58.
[7] E. Dubost, T. Tschamber, J. Streith, *Tetrahedron Lett.* **2003**, *44*, 3667.
[8] M. N. Namchuk, S. G. Withers, *Biochemistry* **1995**, *34*, 16194.
[9] J. D. McCarter, M. J. Adam, S. G. Withers, *Biochem. J.* **1992**, *286*, 721.
[10] K.-R. Roeser, G. Legler, *Hoppe-Seyler's Z. Physiol. Chem.* **1980**, *361*, 321.
[11] K.-R. Roeser, G. Legler, *Biochim. Biophys. Acta* **1981**, *657*, 321.
[12] M. Czjzek, M. Cicek, V. Zamboni, W. P. Burmeister, D. R. Bevan, B. Henrissat, A. Esen, *Biochem. J.* **2001**, *354*, 37.
[13] S. G. Withers, *Carbohydr. Polym.* **2001**, *44*, 325.
[14] H. S. Overkleeft, J. van Wiltenburg, U. K. Pandit, *Tetrahedron* **1994**, *50*, 4215.
[15] K. Tatsuta, S. Miura, H. Gunji, *Bull. Chem. Soc. Jpn.* **1997**, *70*, 427.
[16] D. R. Williams, D. L. Brown, J. W. Benbow, *J. Am. Chem. Soc.* **1989**, *111*, 1923.
[17] W. A. Herrmann, C. Brossmer, K. Öfele, C. P. Reisinger, T. Priermeier, M. Beller, H. Fischer, *Angew. Chem., Int. Ed.* **1995**, *34*, 1844.
[18] K. Sonogashira, Y. Tohda, N. Hagihara, *Tetrahedron Lett.* **1975**, *16*, 4467.
[19] T. Sakamoto, H. Nagata, Y. Kondo, M. Shiraiwa, H. Yamanaka, *Chem. Pharm. Bull.* **1987**, *35*, 823.
[20] M. D. Cliff, S. G. Pyne, *Tetrahedron* **1996**, *52*, 13703.

[21] T. Akiyama, H. Hirofuji, S. Ozaki, *Bull. Chem. Soc. Jpn.* **1992**, *65*, 1932.
[22] W. S. Wadsworth, W. D. Emmons, *J. Am. Chem. Soc.* **1961**, *83*, 1733.
[23] M. Larsen, F. C. Krebs, M. Jørgensen, N. Harrit, *J. Org. Chem.* **1998**, *63*, 4420.
[24] Y. Ishino, M. Mihara, S. Nishihama, I. Nishiguchi, *Bull. Chem. Soc. Jpn.* **1998**, *71*, 2669.
[25] L. G. Fröhlich, P. Kotsonis, H. Traub, S. Taghavi-Moghadam, N. Al-Masoudi, H. Hofmann, H. Strobel, H. Matter, W. Pfleiderer, H. H. H. W. Schmidt, *J. Med. Chem.* **1999**, *42*, 4108.
[26] P. M. Ruoff, R. C. Scott, *J. Am. Chem. Soc.* **1950**, *72*, 4950.
[27] H. Tagawa, S. Kubo, F. Ishikawa, *Chem. Pharm. Bull.* **1981**, *29*, 3515.
[28] J. M. Lehn, F. Schmidt, J. P. Vigneron, *J. Heterocycl. Chem.* **1990**, *27*, 1633.
[29] R. D. Youssefyeh, E. Magnien, T. D. Y. Lee, W. K. Chan, C. J. Lin, R. A. Galemmo, W. H. Johnson, J. Tan, H. F. Campbell, F. C. Huang, G. W. Nuss, G. W. Carnathan, C. A. Sutherland, R. G. Van Inwegen, *J. Med. Chem.* **1990**, *33*, 1186.
[30] R. H. Martin, R. Robinson, *J. Chem. Soc.* **1949**, 1866.
[31] M. Farina, G. Audisio, *Tetrahedron* **1970**, *26*, 1827.
[32] D. A. Frost, G. A. Morrison, *J. Chem. Soc., Perkin Trans. 1* **1973**, 2159.
[33] H. Alper, G. Vasapollo, *Tetrahedron Lett.* **1992**, *33*, 7477.
[34] I. Columbus, M. Haj-Zaroubi, J. S. Siegel, S. E. Biali, *J. Org. Chem.* **1998**, *63*, 9148.
[35] H. Singh, A. S. Chawla, V. K. Kapoor, D. Paul, R. K. Malhotra, *Prog. Med. Chem.* **1980**, *17*, 151.
[36] R. J. Herr, *Bioorg. Med. Chem.* **2002**, *10*, 3379.
[37] E. J. Corey, N. W. Gilman, B. E. Ganem, *J. Am. Chem. Soc.* **1968**, *90*, 5616.
[38] P. Karuso, W. C. Taylor, *Aust. J. Chem.* **1984**, *37*, 1271.
[39] W. Kinzy, R. R. Schmidt, *Liebigs Ann. Chem.* **1987**, 407.
[40] B. Iddon, N. Khan, *J. Chem. Soc., Perkin Trans. 1* **1987**, 1445.
[41] M. P. Groziak, L. Wei, *J. Org. Chem.* **1992**, *57*, 3776.
[42] M. W. Holladay, H. Bai, Y. Li, N. H. Lin, J. F. Daanen, K. B. Ryther, J. T. Wasicak, J. F. Kincaid, Y. He, A. M. Hettinger, P. Huang, D. J. Anderson, A. W. Bannon, M. J. Buckley, J. E. Campbell, D. L. Donnelly-Roberts, K. L. Gunther, D. J. B. Kim, T. A. Kuntzweiler, J. P. Sullivan, M. W. Decker, S. P. Arneric, *Bioorg. Med. Chem. Lett.* **1998**, *8*, 2797.
[43] P. E. Maligres, M. S. Waters, F. Fleitz, D. Askin, *Tetrahedron Lett.* **1999**, *40*, 8193.
[44] M. Alterman, A. Hallberg, *J. Org. Chem.* **2000**, *65*, 7984.
[45] B. A. Anderson, E. C. Bell, F. O. Ginah, N. K. Harn, L. M. Pagh, J. P. Wepsiec, *J. Org. Chem.* **1998**, *63*, 8224.
[46] A. S. Bell, S. F. Campbell, D. S. Morris, D. A. Roberts, M. H. Stefaniak, *J. Med. Chem.* **1989**, *32*, 1552.
[47] B. E. Huff, M. A. Staszak, *Tetrahedron Lett.* **1993**, *34*, 8011.
[48] S. J. Wittenberger, B. G. Donner, *J. Org. Chem.* **1993**, *58*, 4139.
[49] G. W. Danswan, P. W. Hairsine, D. A. Rowlands, J. B. Taylor, R. Westwood, *J. Chem. Soc., Perkin Trans. 1* **1982**, 1049.
[50] I. R. Ager, A. C. Barnes, G. W. Danswan, P. W. Hairsine, D. P. Kay, P. D. Kennewell, S. S. Matharu, P. Miller, P. Robson, D. A. Rowlands, W. R. Tully, R. Westwood, *J. Med. Chem.* **1988**, *31*, 1098.
[51] D. P. Matthews, J. R. McCarthy, J. P. Whitten, P. R. Kastner, C. L. Barney, F. N. Marshall, M. A. Ertel, T. Burkhard, P. J. Shea, T. Kariya, *J. Med. Chem.* **1990**, *33*, 317.
[52] T. D. Heightman, P. Ermert, D. Klein, A. Vasella, *Helv. Chim. Acta* **1995**, *78*, 514.
[53] A. R. Plant, J. E. Oliver, M. L. Patchett, R. M. Daniel, H. W. Morgan, *Arch. Biochem. Biophys.* **1988**, *262*, 181.
[54] A. Vasella, G. J. Davies, M. Böhm, *Curr. Opin. Chem. Biol.* **2002**, *6*, 619.
[55] R. Hoos, A. Vasella, K. Rupitz, S. G. Withers, *Carbohydr. Res.* **1997**, *298*, 291.
[56] S. Mackay, C. J. Gilmore, C. Edwards, N. Stewart, K. Shankland, 'maXus Computer Program for the Solution and Refinement of Crystal Structures', Bruker Nonius, The Netherlands, MacScience, Japan & The University of Glasgow, 1999.
[57] G. M. Sheldrick, 'SHELXL97. Program for the Refinement of Crystal Structures', University of Göttingen, Germany, 1997.
[58] W. G. Kofron, L. M. Baclawski, *J. Org. Chem.* **1976**, *41*, 1879.
[59] H. Lineweaver, D. Burk, *J. Am. Chem. Soc.* **1934**, *56*, 658.
[60] I. H. Segel, 'Enzyme Kinetics', Wiley, New York, 1975.
[61] Y. T. Li, *J. Biol. Chem.* **1967**, *242*, 5474.

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