Synthesis of Glucuronic, Mannuronic, and Galacturonic Acid-Derived Imidazoles as Inhibitors of Bovine Liver β-Glucuronidase

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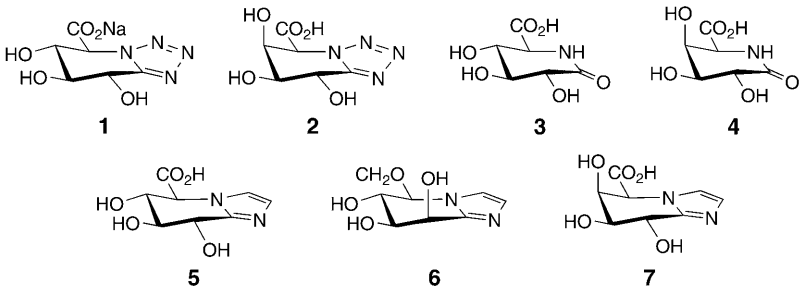
The *gluco*-, *manno*-, and *galacto*-configured imidazopyridine-5-carboxylates **5**–**7**, respectively, were synthesized and evaluated as inhibitors of bovine liver β-glucuronidase. The gluconolactam **15** was transformed into the *gluco*- and *manno*-imidazoles **5** and **6** in nine steps and in an overall yield of 9 and 12%, respectively. Oxidation and esterification of the selectively protected *gluco*- and *manno*-configured hydroxymethyl-imidazopyridines **23** and **25**, respectively (both obtained from gluconolactam **15**), provided the benzhydryl esters **24** and **26**, respectively. Hydrogenolysis afforded the *gluco*-imidazopyridine-carboxylic acid **5** and the *manno*-isomer **6**. Similarly, the hydroxymethyl-imidazopyridine **33**, obtained from galactonolactam **27**, was subjected to oxidation, esterification, and deprotection to afford the *galacto*-configured imidazopyridine-carboxylate **7** in ten steps from the galactonolactam **27** and in an overall yield of 13%. The *gluco*-configured imidazole **5** is the strongest known inhibitor of β-glucuronidases ($K_i = 12$ nM), while the *manno*- and *galacto*-configured imidazoles **6** and **7** are micromolar inhibitors of bovine β-glucuronidase. The small difference between the inhibitory strength of the imidazopyridine-carboxylic acid **5** and the tetrazolopyridine-carboxylic acid **1**, and the difference between the configurational selectivity of **5**–**7** as compared to the unselectivity of the corresponding lactams **3** and **4** are discussed.

Introduction. – Lactone-type inhibitors of retaining β-glycosidases possessing an annulated imidazole ring with a N-atom correctly located to mimic the glycosidic O-atom are stronger inhibitors[1]) than the corresponding tetrazoles and triazoles[2]); they are also stronger inhibitors than the corresponding glyconolactams and hydroximolactams [3][6–14]. The strength of the inhibition by such N-heterocycles correlates with their basic properties and with the extent of their interaction with the catalytic acid of the glycosidases [2][10][11]. This correlation should also be valid for the inhibition of β-glucuronidases[3]), and imidazopyridine-5-carboxylates are expected to be stronger glycuronidase inhibitors than the corresponding known glycarolactam and tetrazolopyridine-5-carboxylates [17][18]. This expectation is also in agreement with the obser-

[1]) For reviews on glycosidase inhibitors, see [1][2].
[2]) 1,2,3-Triazoles and imidazoles with an incorrectly located glycosidic heteroatom [3–5] are weak inhibitors of retaining β-glycosidases.
[3]) For other inhibitors of β-glucuronidases, see [15–17].

vation that β-glucuronidases, β-galactosidases, and β-mannosidases belong to the same family 2[4]) of glycosidases.

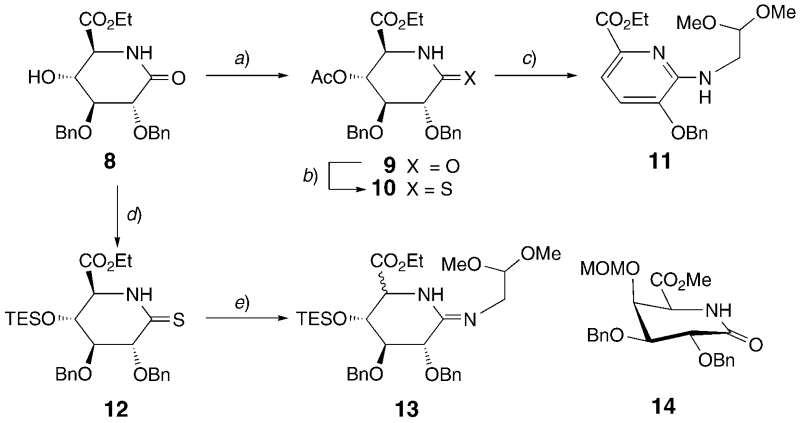
We have recently reported the synthesis and evaluation of glycarolactams and tetrazolopyridine-5-carboxylates as inhibitors of bovine liver β-glucuronidase [17][18]. The tetrazolopyridine-5-carboxylate **1**, glucaro-1,5-lactam **3**, and galactaro-1,5-lactam **4** inhibit bovine liver β-glucuronidase to the same extent ($K_i = 25-32$ nM), while the *galacto*-configured tetrazole **2** ($K_i = 6.3$ μM) is a *ca.* 200-fold weaker inhibitor of this enzyme than galactaro-1,5-lactam **4** [15][17]. We were, therefore, interested in the imidazopyridine-5-carboxylate **5**, and in the *manno*- and *galacto*-configured analogues **6** and **7** to test the effect of the imidazole ring and of the configuration on the inhibition of bovine liver β-glucuronidase. We planned to prepare the *gluco*-configured imidazole **5** [17][18] either by annulating the imidazole ring to the glucaro-1,5-lactam **8** according to a known method [4][10], or by oxidising the selectively protected imidazole **23** that should be readily obtained from the gluconolactam **15** [4]. We expected the *manno*-configured isomer **6** as by-product of the synthesis of **5**, while the *galacto*-configured imidazole **7** should be readily prepared from either the galactarolactam **14** or the galactonolactam **27** [17].



Results and Discussion. – We first attempted to synthesize the imidazopyridine-carboxylic acids **5**–**7** by annulating the imidazole ring to the glucaro-1,5-lactam **8** [17] and galactaro-1,5-lactam **14**. Acetylation of **8** to **9**, followed by thionation, yielded 79% of the thionolactam **10** (*Scheme 1*). However, treatment of **10** with aminoacetaldehyde dimethyl acetal in the presence of $Hg(OAc)_2$ [4][10] led only to the 2,3,6-trisubstituted pyridine **11** by β-elimination of the AcO and of the BnO group; the desired amidine was not observed. Similar β-eliminations of uronic acid derivatives were first reported by *Kiss* [20]. They are also catalysed by lyases in the course of the degradation of some polysaccharides and glycosaminoglycans [21]. To suppress the facile elimination of the AcO group at C(4), we replaced it by a Et_3SiO (TESO) group. The silyl ether **12** indeed reacted with aminoacetaldehyde dimethyl acetal to provide a mixture of amidines **13**. This mixture, however, decomposed upon mild treatment with $TsOH \cdot H_2O$ or $BF_3 \cdot Et_2O$. The known galacturonic acid-derived methoxymethyl acetal **14** [17] decomposed already upon treatment with *Lawesson*'s reagent; not surprisingly, β-elimination

[4]) Glycosidases are classified into families based on their sequence similarities [19]. A regularly updated database is available on the internet (http://afmb.cnrs-mrs.fr/CAZY/index.html).

Scheme 1



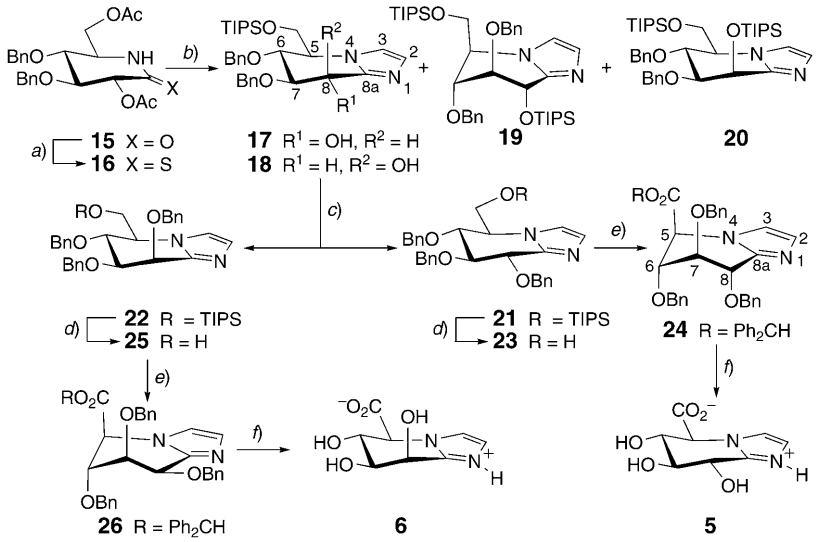
a) Ac_2O, pyridine. *b*) *Lawesson*'s reagent, toluene, 80°; 79% (from **8**). *c*) $NH_2CH_2CH(OMe)_2$, $Hg(OAc)_2$, THF, 0°; 56%. *d*) 1. Et_3SiCl, pyridine, 60°; 2. *Lawesson*'s reagent, toluene, 80°; 48%. *e*) $NH_2CH_2CH(OMe)_2$, $Hg(OAc)_2$, THF, 0°.

of this galacturonate, possessing an axial leaving group at C(4), occurred particularly readily. It is known that aminoacetaldehyde dimethyl acetals substituted with an electron-withdrawing group are less reactive towards thionolactams than the unsubstituted analogue [22][23]. The scope of this method for the formation of imidazopyridines from thionolactams and aminoacetaldehyde dimethyl acetals thus depends sensibly on the nucleophilicity of the acetal and of the intermediate amidine.

In view of these results we planned to prepare the glycarolactam-derived imidazopyridine-carboxylic acids **5**–**7** by oxidation of the $HOCH_2$ group of the partially protected imidazoles **23**, **25**, and **33**. Thionation of the gluconolactam-derived diacetate **15** [4] (*Scheme 2*) gave the thionolactam **16** (99%) that was condensed with aminoacetaldehyde dimethyl acetal in the presence of $Hg(OAc)_2$ [4][10] to the corresponding amidines. Their cyclisation in the presence of $TsOH \cdot H_2O$ in wet toluene was accompanied by deacetylation. Silylation of the crude with $^iPr_3SiOTf$ gave a 1:1 mixture (52%) of the monosilylated *gluco*- and *manno*-imidazopyridines **17** and **18**[5]), besides minor amounts of the disilyl ethers **19** (14%) and **20** (13%). The mixture **17**/**18** was *O*-benzylated, and the epimeric benzyl ethers were separated by chromatography to provide the *gluco*-configured tribenzyl ether **21** (37%) and its *manno*-isomer **22** (37%). Desilylation of **21** gave the primary alcohol **23** (91%). It was oxidised with *Jones*' reagent, and the crude product was esterified by treatment with diphenyl diazomethane (Ph_2CN_2) to yield 70% of the benzhydryl ester **24**. Hydrogenolytic deprotection of **24** provided the *gluco*-configured imidazopyridine-carboxylate **5** (80%). Similarly, the *manno*-configured imidazole **22** was desilylated to the alcohol **25** (94%), which was oxi-

[5]) The direction of numbering of imidazopyridines (*cf.* **17**/**18** in *Scheme 2*) is opposite to that of pyranosides. Thus, the sides above and below the plane of the imidazoles, as defined by clockwise and counterclockwise numbering, are interchanged relative to those defined by carbohydrate nomenclature.

Scheme 2



a) *Lawesson*'s reagent, toluene, 80°; 99%. *b*) 1. $NH_2CH_2CH(OMe)_2$, $Hg(OAc)_2$, THF; 2. $TsOH \cdot H_2O$, toluene/H_2O 10:1, 64°; 3. $^iPr_3SiOTf$, 1*H*-imidazole, DMF; 52% of **17**/**18** (1:1), 14% of **19**, and 13% of **20**. *c*) BnBr, NaH, DMF; 37% of **21** and 37% of **22**. *d*) $Bu_4NF \cdot 3\,H_2O$, THF; 91% of **23**; 94% of **25**. *e*) 1. *Jones*' oxidation; 2. Ph_2CN_2, acetone; 70% of **24**; 73% of **26**. *f*) H_2, 10% Pd/C, EtOH; 80% of **5**; 99% of **6**.

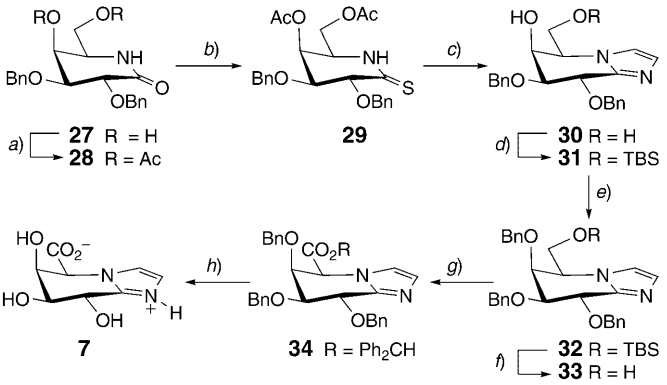
dised and transformed into the benzyhydryl ester **26** in 73% yield. Catalytic hydrogenolysis of **26** provided the *manno*-configured imidazopyridine-carboxylate **6** (99%).

The *galacto*-configured selectively *O*-benzylated imidazopyridine **33** was prepared from the partially benzylated galactono-1,5-lactam **27** [17] (*Scheme 3*). Acetylation of **27** to the diacetate **28** (99%), treatment with *Lawesson*'s reagent to afford the thionolactam **29** (85%), and annulation of the imidazole ring as described for **16** provided the dihydroxyimidazopyridine **30**. Regioselective silylation of **30** to **31** (84%), followed by *O*-benzylation, provided the tribenzyl ether **32** (66%) that was desilylated to yield 85% of the desired primary alcohol **33**. It was similarly oxidized as described for **23** and **25**, and the resulting acid was transformed into the benzhydryl ester **34** that was obtained in 34% yield besides unreacted alcohol **33**[6]) (18%). Hydrogenolysis of **34** gave the fully deprotected D-*galacto*-imidazopyridine-carboxylate **7** (98%).

The structure of the 2,3,6-trisubstituted pyridine **11** was deduced from ^{1}H-NMR *d*s at 6.89 (H–C(4)) and 7.42 (H–C(5)) ppm with a $J(4,5) = 8.0$ Hz. Formation of the benzhydryl esters **24**, **26**, and **34** is evidenced by the ^{13}C *s* (C=O) at 166.90 (**24**), 167.12 (**26**), and 166.35 ppm (**34**), the ^{13}C-NMR *d* (Ph_2CH) at 75.25 (**24**), 77.91 (**26**), and 78.39 ppm (**34**), the ^{1}H-NMR *s* (Ph_2CH) at 6.74 (**24**), 6.79 (**26**), and 6.98 ppm (**34**), the disappearance of H_2C–C(5) ^{1}H-signals, and a strong C=O IR band (see *Exper. Part*). The *gluco*-

[6]) Longer duration of the oxidation led to unidentified side products.

Scheme 3



a) Ac_2O, pyridine; 99%. *b*) *Lawesson*'s reagent, toluene, 80°; 85%. *c*) 1. $NH_2CH_2CH(OMe)_2$, $Hg(OAc)_2$, THF, 0°; 2. $TsOH \cdot H_2O$, toluene/H_2O 12:3, 75°. *d*) ^{t}Bu$(Me)_2$SiCl, Et_3N, 4-(dimethylamino)pyridine (DMAP), DMF; 84% from **29**. *e*) BnBr, NaH, DMF; 66%. *f*) $Bu_4NF \cdot 3\,H_2O$, THF, 0°; 85%. *g*) 1. CrO_3, 1M H_2SO_4, acetone; 2. Ph_2CN_2, acetone; 34% of **34**, and 18% of **33**. *h*) H_2 (6 bar), 10% Pd/C, MeOH/H_2O 2:1; 98%.

configured imidazopyridine **24** adopts predominantly the $^7H_6$ conformation in $CDCl_3$ as evidenced by $J(5,6) = 3.0$, $J(6,7) = 5.1$, and $J(7,8) = 3.3$ Hz. The $^6H_7$ conformer of **24** is destabilised by the steric interaction between the substituents at C(5) and C(6). The coupling constants of the *manno*-imidazopyridine **26** could not be determined due to signal overlap, and we tentatively assigned the $^7H_6$ conformation to **26** by analogy to the *gluco*-configured **24**. The *galacto*-configured imidazopyridine **34** exists as a *ca.* 1:3 mixture of $^7H_6$ and $^6H_7$ conformers as evidenced by $J(5,6) = 4.7$, $J(6,7) = 1.9$, and $J(7,8) = 8.1$ Hz (*Table 3* in *Exper. Part* and modelling with MM3*). Similar to their tetrazolopyridine analogues [17], the deprotected imidazopyridine-carboxylic acids **5**–**7** adopt the $^6H_7$ conformation in D_2O (for J(H,H) see *Table 3* in *Exper. Part*).

Enzymatic Tests and Discussion. – The imidazopyridine-carboxylic acids **5**–**7** were tested as inhibitors of bovine liver β-glucuronidase (acetate buffer, 30°, pH 5.0) with 4-nitrophenyl β-D-glucuronide as substrate. The inhibition data (K_i) and the pK values of the inhibitors are summarized in *Table 1*.

Table 1. *Comparison of the* K_i *Values* [μM] *of the Inhibition of β-Glucuronidase from Bovine Liver by the Imidazoles* **5**, **6**, *and* **7**, *and the Tetrazoles* **1** *and* **2** *at pH 5.0 and 5.7*

	pH	Imidazoles			Tetrazoles	
		5	**6**	**7**	**1**	**2**
pK_{HA}		6.5	6.6	6.6	2.53[a])	2.52[a])
K_i	5.0	0.012	14.0	6.7	0.025[a])	6.3[a])
		($\alpha = 2.4$)	(non-competitive)	($\alpha = 1.3$)	($\alpha = 1.9$)	($\alpha = 5.4$)
	5.7	0.007[b])	5.85[b])	3.25[b])		

[a]) Data taken from [17]. [b]) $IC_{50}/2$ in μM.

The *gluco*-imidazopyridine-carboxylic acid **5** ($K_i = 12$ nM) inhibits β-glucuronidase from bovine liver only two times more strongly than the corresponding tetrazole **1**. The *galacto*-isomer **7** ($K_i = 6.7$ μM) is a much weaker inhibitor of this glucuronidase. However, there is again only a small difference between the inhibition by the (*galacto*) imidazopyridine **7** and the corresponding tetrazolopyridine **2** (6.3 μM). The configurational selectivity of the inhibition by the *gluco*-imidazopyridine **5** is further demonstrated by a K_i value of 14 μM for the *manno*-imidazopyridine **6** that is three orders of magnitude weaker than **5**, similarly as the *galacto*-isomer **7**.

Increasing the pH of the assay from 5.0 and 5.7[7]) improves the inhibition by each one of the imidazopyridines **5**–**7** *ca.* twofold (*Table 1*). This rather slight increase of the inhibition suggests that **5**–**7** exist largely as zwitterions at these pH values (*Schemes 2* and *3*). This is in keeping with the pK_{HA} values[8]) for **5** (6.5), **6** (6.6), and **7** (6.6). Although only somewhat stronger than the corresponding tetrazolopyridine **1**, the *gluco*-imidazopyridine **5** is the strongest known inhibitor of β-glucuronidases.

The strong configurational dependence of the inhibition of bovine liver β-glucuronidase by the imidazopyridines **5**–**7** and by the tetrazolopyridines **1** and **2** contrasts surprisingly with the absence of a dependence on the configuration at C(4) of the inhibition by the glucaro-1,5-lactam **3**[9]) and galactaro-1,5-lactam **4** ($K_i \approx 30$ nM) [17]; it is rationalised by the higher flexibility of the lactams. Such a difference between the configurational selectivity of azoles and lactams is not observed for family-1 glucosidases [4][9][10][25][26], while the configurational selectivity of these types of inhibitors for glycosidases belonging to other families is not known. The different configurational selectivities for lactams and azoles suggest that the restriction of flexibility may increase the selectivity both of inhibitors mimicking the reactive intermediate and those mimicking the reactive conformation of the substrate [27].

Both bovine liver β-glucuronidase and *E. coli* β-galactosidase belong to family 2. Similar to the inhibition of bovine liver β-glucuronidase, the inhibition of *E. coli* β-galactosidase is sensitive to the configuration at C(4). The *galacto*-imidazopyridine **36** is a very strong inhibitor of *E. coli* β-galactosidase, while the *gluco*-isomer **35** is inactive (*Fig.*) [9]; this configurational selectivity appears to be a characteristic feature of glycosidases of family 2.

The above mentioned small difference between the inhibition of bovine liver β-glucuronidase by the tetrazolopyridine **1** and the imidazopyridine **5** contrasts with the large difference between the inhibition of glucosidases of family 1 by analogous imidazo- and tetrazolopyridines. Thus, the β-glucosidases from sweet almonds and from *Caldocellum saccharolyticum* are inhibited *ca*. 1500- and 3000-fold more strongly by the *gluco*-configured imidazopyridine **35** [10] (*Fig.*) than by the tetrazolopyridine **37** [4]. This difference was explained by the much stronger interaction of the imidazole with the catalytic acid of the enzyme. The similar inhibition of bovine liver β-glucuronidase by the tetrazolopyridine **1** and the imidazopyridine **5** suggests that the interaction of **5** with the catalytic acid of the enzyme is impaired by the protonation of the imi-

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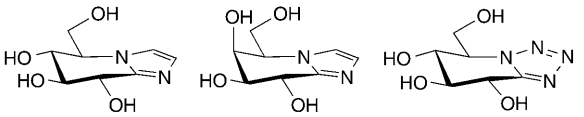
[7]) The pH optimum of the related rat liver β-glucuronidase is 5.1 [24]; hydrolysis of the substrate was very slow above pH 5.7.

[8]) A single inflection of the titration curve was observed between pH values 2.0 and 7.0.

[9]) The inhibition by mannaro-1,5-lactams and the corresponding tetrazoles is not known.



	35	**36**	**37**
β-Galactosidase (*E. coli*)	> 100 μM	0.004 μM	–
β-Glucosidase (Sweet almonds)	0.1 μM	–	150 μM
β-Glucosidase (*C. saccharolyticum*)	0.02 μM	–	60 μM

Figure. *Inhibition* (K_i in μM) *of β-Galactosidase from E. coli by the Imidazoles* **35** *and* **36** [9][28] *and of β-Glucosidases from Sweet Almonds and Caldocellum saccharolyticum by the Imidazole* **35** *and the Tetrazole* **37** [4][10]

dazole in its zwitterionic form. We assume that **1** interacts with both the catalytic acid and the catalytic nucleophile, while the zwitterionic form of **5** does not interact with the catalytic acid, but particularly strongly with the catalytic nucleophile. In agreement with this rationalisation, the interaction of the tetrazolopyridine **37** with the catalytic acid and the catalytic nucleophile of a β-glucosidase was indeed estimated as *ca*. 2 kcal/mol each, cooperativity increasing the effect, while the interaction of the protonated imidazopyridine **35** with the catalytic nucleophile was estimated as *ca*. 6 kcal/mol [2].

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Experimental Part

General. See [17].

*6-Ethyl 4-*O*-Acetyl-5-amino-2,3-di-*O*-benzyl-5-deoxy-*D*-glucarate-1,5-thiolactam* (**10**). A soln. of **8** (20 mg, 0.05 mmol) in pyridine (2 ml) and Ac_2O (1 ml) was kept for 2 h and evaporated. A soln. of the residue (*i.e.*, **9**) and *Lawesson*'s reagent (20 mg, 0.05 mmol) in toluene (2 ml) was heated to 80°, and stirred for 30 min. Normal workup (AcOEt/H_2O) and FC (AcOEt/hexane 1:4) gave **10** (18 mg, 79%). R_f (AcOEt/cyclohexane 1:4) 0.46. ^{1}H-NMR (300 MHz, $CDCl_3$): 8.34 (br. *s*, NH); 7.38–7.26 (*m*, 10 arom. H); 5.33 (*dd*, *J* = 8.1, 3.0, H–C(4)); 4.90 (*d*, *J* = 11.5, PhC*H*); 4.68 (*d*, *J* = 11.8, PhC*H*); 4.60 (*d*, *J* = 12.4, PhC*H*); 4.55 (*d*, *J* = 11.8, PhC*H*); 4.48 (*d*, *J* ≈ 3.0, H–C(2)); 4.43 (*dd*, *J* = 8.1, 2.1, H–C(5)); 4.21 (*q*, *J* = 7.2, MeCH_2O); 3.84 (*t*, *J* = 3.1, H–C(3)); 2.05 (*s*, AcO); 1.25 (*t*, *J* = 7.2, *Me*CH_2O).

Ethyl 5-(Benzyloxy)-6-[(2,2-dimethoxyethyl)amino]pyridine-2-carboxylate (**11**). A soln. of **10** (18 mg, 0.04 mmol) in THF (3 ml) was cooled to 0°, treated with $Hg(OAc)_2$ (64 mg, 0.04 mmol) and $H_2NCH_2CH(OMe)_2$ (22 μl, 0.2 mmol), stirred for 2 h, diluted with Et_2O (5 ml), filtered through *Celite*, and evaporated. FC (AcOEt/cyclohexane 1:4) gave **11** (8 mg, 56%). R_f (AcOEt/cyclohexane 1:1) 0.50. ^{1}H-NMR (300 MHz, $CDCl_3$): 7.42 (*d*, *J* = 8.0, H–C(5)); 7.39–7.37 (*m*, 5 arom. H); 6.89 (*d*, *J* = 8.0, H–C(4)); 5.29 (*t*, *J* = 5.8, NH); 5.12 (*s*, PhCH_2); 4.56 (*t*, *J* = 5.4, OCHO); 4.35 (*q*, *J* = 7.2, MeCH_2O); 3.71 (*t*, *J* = 5.4, NHCH_2); 3.44 (*s*, 2 MeO); 1.38 (*t*, *J* = 7.2, *Me*CH_2O).

*6-Ethyl 5-Amino-2,3-di-*O*-benzyl-5-deoxy-4-*O*-(triethylsilyl)-*D*-glucarate-1,5-thiolactam* (**12**). A soln. of **8** (35 mg, 0.09 mmol) and Et_3SiCl (75 μl, 0.44 mmol) in pyridine (2 ml) was heated to 60°, stirred for 2 h, cooled to 25°, and evaporated. A soln. of the crude (45 mg) in toluene (2 ml) was treated with *Lawesson*'s reagent (35 mg, 0.09 mmol), heated to 80°, and stirred for 30 min. Normal workup (AcOEt/H_2O)

and FC (AcOEt/hexane 1:4) gave **12**[10]) (22 mg, 48%). R_f (AcOEt/cyclohexane 1:4) 0.62. ^{1}H-NMR (300 MHz, $CDCl_3$): 8.24 (br. *s*, NH); 7.41–7.23 (*m*, 10 arom. H); 4.93 (*d*, *J* = 11.5, PhC*H*); 4.71 (*d*, *J* = 11.8, PhC*H*); 4.57 (*d*, *J* = 11.2, PhC*H*); 4.51 (br. *d*, *J* ≈ 2.8, H–C(2)); 4.39 (*d*, *J* = 11.2, PhC*H*); 4.36–4.29 (hidden signal, H–C(5)); 4.29 (*q*, *J* = 7.2, MeCH_2O); 4.13 (*dd*, *J* = 7.5, 3.1, H–C(4)); 3.75 (*t*, *J* = 3.1, H–C(3)); 1.30 (*t*, *J* = 7.2, *Me*CH_2O); 0.91 (*t*, *J* = 8.1, $(MeCH_2)_3Si$); 0.57 (*q*, *J* = 7.8, $(MeCH_2)_3Si$).

2,6-Di-O*-acetyl-5-amino-3,4-di*-O*-benzyl-5-deoxy*-D*-glucono-1,5-thiolactam* (**16**). A soln. of **15** (988 mg, 2.24 mmol) and *Lawesson*'s reagent (580 mg, 1.43 mmol) in toluene (6 ml) was heated to 80°, and stirred for 45 min. Normal workup (AcOEt/H_2O/brine) and FC (AcOEt/hexane 3:7) gave **16** (1.1 g, 99%). Light-yellow solid. R_f (AcOEt/hexane 3:7) 0.12. M.p.: 123–124°. $[\alpha]_D^{25} = +133.7$ (*c* = 0.44, $CHCl_3$). IR ($CHCl_3$): 3361*w*, 2962*w*, 2914*w*, 1742*s*, 1513*s*, 1455*w*, 1371*m*, 1311*w*, 1263*m*, 1241*s*, 1070*s*, 1044*m*, 1026*m*, 808*w*. ^{1}H-NMR (300 MHz, $CDCl_3$): 8.06 (br. *d*, *J* = 12.6, NH); 7.38–7.24 (*m*, 10 arom. H); 5.60 (*d*, *J* = 8.1, H–C(2)); 4.80 (*d*, *J* = 11.4, PhC*H*); 4.77 (br. *s*, PhCH_2); 4.56 (*d*, *J* = 11.1, PhC*H*); 4.36 (*dd*, *J* = 12.0, 4.5, H–C(6)); 3.95 (*t*, *J* = 7.8, H–C(3)); 3.93 (*dd*, *J* = 12.0, 3.0, H′–C(6)); 3.73 (*t*, *J* = 8.1, H–C(4)); 3.69–3.67 (*m*, H–C(5)); 2.11, 2.06 (2*s*, 2 AcO). ^{13}C-NMR (75 MHz, $CDCl_3$): 198.55 (*s*, C=S); 170.00, 169.93 (2*s*, 2 C=O); 137.43, 136.89 (2*s*); 128.68 (2*d*); 128.58 (2*d*); 128.51 (2*d*); 128.38 (*d*); 128.09 (3*d*); 79.67 (*d*, C(3)); 75.99, 75.89 (2*d*, C(2), C(4)); 74.36 (*t*, 2 PhCH_2); 62.77 (*t*, C(6)); 57.72 (*d*, C(5)); 21.13, 20.79 (2*q*, 2 Me). HR-MALDI-MS: 480.1443 ($[M+Na]^+$, $C_{24}H_{27}NNaO_6S^+$; calc. 480.1451). Anal. calc. for $C_{24}H_{27}N_2O_6S$ (457.55): C 63.00, H 5.95, N 3.06; found: C 62.81, H 6.01, N 3.06.

Preparation of the Imidazopyridines **17**–**20**. A soln. of **16** (944 mg, 2.06 mmol) in THF (4 ml) was treated with $Hg(OAc)_2$ (1.26 g, 3.97 mmol) and $NH_2CH_2CH(OMe)_2$ (1.1 ml, 10.2 mmol), and stirred for 45 min. The mixture was treated with H_2O (5 ml), extracted with AcOEt (3 × 50 ml), washed with H_2O (25 ml), sat. aq. $NaHCO_3$ soln. (10 ml), dried (Na_2SO_4), and evaporated. A soln. of the residue (942 mg) in toluene/H_2O 10:1 (20.2 ml) was treated with $TsOH \cdot H_2O$ (880 mg, 4.58 mmol), stirred at 64° for 19 h, treated with sat. aq. $NaHCO_3$ soln. (5 ml), and extracted with AcOEt (2 × 50 ml). The combined org. layers were washed with brine, dried (Na_2SO_4), and evaporated. A soln. of the residue (320 mg, 0.86 mmol) in DMF (2 ml) was cooled to 3°, treated with 1*H*-imidazole (168 mg, 0.1 mmol) and ^{i}Pr$_3$SiOTf (0.197 ml, 0.105 mmol), warmed to 25°, and stirred for 18 h. Normal workup (AcOEt/H_2O/brine) and FC (AcOEt/hexane 1:4 → 1:1) gave **19** (81 mg, 14%), **20** (74 mg, 13%) and an inseparable 1:1 mixture of **17** and **18** (234 mg, 52%).

*Data of (5*R*,6*R*,7*S*,8*S*)-6,7-Bis(benzyloxy)-5,6,7,8-tetrahydro-8-(triisopropylsilyloxy)-5-[(triisopropylsilyloxy)methyl]imidazo[1,2-*a*]pyridine* (**19**). Colourless oil. R_f (AcOEt/hexane 1:4) 0.29. $[\alpha]_D^{25} = +46.9$ (*c* = 1.25, $CHCl_3$). IR ($CHCl_3$): 3160*w*, 3090*w*, 3067*w*, 2945*s*, 2892*s*, 2867*s*, 1682*w*, 1534*w*, 1496*w*, 1463*m*, 1384*w*, 1365*w*, 1319*w*, 1290*w*, 1262*w*, 1094*s*, 1067*s*, 1028*w*, 1014*m*, 996*m*, 909*m*, 883*m*, 843*s*. ^{1}H-NMR (300 MHz, $CDCl_3$): see *Table 2*; additionally, 7.41–7.27 (*m*, 10 arom. H); 7.22 (*d*, *J* = 0.9), 7.01 (*d*, *J* = 1.5) (H–C(2), H–C(3)); 4.74 (*d*, *J* = 11.7, PhC*H*); 4.65 (*d*, *J* = 11.4, PhC*H*); 4.58 (*d*, *J* = 12.0, PhC*H*); 4.44 (*d*, *J* = 11.7, PhC*H*); 1.17–0.97 (*m*, 2 $(Me_2CH)_3Si$). ^{13}C-NMR (75 MHz, $CDCl_3$): see *Table 2*; additionally, 137.68, 137.62 (2*s*); 128.38 (2*d*); 128.56 (2*d*); 127.92 (3*d*); 127.84 (*d*); 127.72 (2*d*); 127.67 (*d*, C(2)); 117.54 (*d*, C(3)); 72.14, 72.09 (2*t*, 2 PhCH_2); 18.26, 18.12, 18.05 (3*q*, 2 $(Me_2CH)_3Si$); 12.58, 12.5 (2*d*, 2 $(Me_2CH)_3Si$). HR-MALDI-MS: 693.4464 ($[M+H]^+$, $C_{40}H_{65}N_2O_4Si_2^+$; calc. 693.4477).

*Data of (5*R*,6*R*,7*S*,8*R*)-6,7-Bis(benzyloxy)-5,6,7,8-tetrahydro-8-(triisopropylsilyloxy)-5-[(triisopropylsilyloxy)methyl]imidazo[1,2-*a*]pyridine* (**20**). Colourless oil. R_f (AcOEt/hexane 1:4) 0.19. $[\alpha]_D^{25} = -21.5$ (*c* = 0.62, $CHCl_3$). IR ($CHCl_3$): 3158*w*, 2945*s*, 2892*s*, 2867*s*, 1496*w*, 1463*m*, 1384*w*, 1367*w*, 1316*w*, 1273*w*, 1134*m*, 1099*s*, 1072*m*, 1051*w*, 1014*m*, 997*m*, 910*s*, 884*m*, 836*s*. ^{1}H-NMR (300 MHz, $CDCl_3$): see *Table 2*; additionally, 7.41–7.27 (*m*, 10 arom. H); 7.19, 6.98 (2*d*, *J* = 1.2, H–C(2), H–C(3)); 4.97 (*d*, *J* = 11.4, PhC*H*); 4.85 (*d*, *J* = 11.7, PhC*H*); 4.73 (*d*, *J* = 11.1, PhC*H*); 4.67 (*d*, *J* = 11.4, PhC*H*); 1.21–0.96 (*m*, 2 $(Me_2CH)_3Si$)). ^{13}C-NMR (75 MHz, $CDCl_3$): see *Table 2*; additionally, 137.96,

[10]) The thionolactam **12** was transformed to the amidine **13** by treating with $H_2NCH_2CH(OMe)_2$ and $Hg(OAc)_2$.

Table 2. *Selected ^{1}H-NMR Chemical Shifts* [ppm] *and Coupling Constants* [Hz], *and ^{13}C-NMR Chemical Shifts* [ppm] *of the Protected Imidazoles* **19**–**23**, **25**, *and* **31**–**33** *in $CDCl_3$*

	19	**20**	**21**	**22**	**23**	**25**	**31**	**32**	**33**
H–C(5)	4.32	4.00	4.18–4.10	4.09–4.01	4.09	4.05	4.15	4.34	4.42
HC–C(5)	4.18	3.85	4.18–4.10	4.09–4.01	4.05	3.98	4.19	4.13	4.14–4.06
H'C–C(5)	3.98	3.70	3.96	3.89	3.93	3.79	4.02	3.95	4.03
H–C(6)	3.64	4.19	4.18–4.10	4.30	3.87	4.35	4.51	4.38	4.45
H–C(7)	4.11	3.80	3.84	3.88	4.12	3.96	3.97	4.08	4.12
H–C(8)	5.11	5.24	4.74	4.81	4.75	4.81	4.84	4.80	4.76
J(5,CH)	2.7	2.7	[a])	[a])	3.0	3.6	4.4	2.8	4.1
J(5,CH′)	7.5	8.4	6.0	7.2	7.2	6.0	6.5	8.1	10.7
J(CH,CH′)	10.8	10.2	10.5	10.5	12.0	11.7	10.0	10.9	11.8
J(5,6)	8.1	7.2	[a])	7.2	7.2	6.9	4.4	5.6	6.3
J(6,7)	2.7	9.3	7.5	9.3	7.5	9.3	2.2	1.6	1.9
J(7,8)	3.3	2.4	5.7	3.3	5.7	3.0	5.6	4.4	3.9
C(5)	59.37	62.18	60.09	62.10	59.39	61.68	58.66	59.70	58.04
CH_2–C(5)	63.34	65.84	63.66	64.99	60.85	63.35	64.24	64.15	62.18
C(6)	78.40	73.29	74.22[b])	74.01	74.13[b])	74.11	67.67	71.64	70.96
C(7)	82.36	82.03	81.71	80.34	81.49	80.03	80.57	77.73	76.46
C(8)	66.31	64.28	75.65[b])	67.92	75.70[b])	68.23	72.80	73.67	73.54
C(8a)	145.24	144.87	143.86	142.84	144.01	143.15	143.31	141.86	142.51

[a]) Not assigned. [b]) Assignments may be interchanged

137.85 (2*s*); 128.56 (2*d*), 128.49 (*d*); 128.39 (2*d*); 128.27 (2*d*); 127.87 (*d*); 127.70 (2*d*); 127.58 (*d*, C(2)); 119.55 (*d*, C(3)); 74.72, 72.04 (2*t*, 2 PhCH_2); 18.32, 18.13, 18.12 (3*q*, 2 (*Me*$_2$CH)$_3$Si); 12.64, 11.89 (2*d*, 2 (Me$_2$*C*H)$_3$Si). HR-MALDI-MS: 693.4464 ([*M*+H]$^+$, $C_{40}H_{65}N_2O_4Si_2^+$; calc. 693.4477).

*Data of (5*R*,6*R*,7*S*,8*S*)- and (5*R*,6*R*,7*S*,8*R*)-6,7-Bis(benzyloxy)-5,6,7,8-tetrahydro-5-[(triisopropylsilyloxy)methyl]imidazo[1,2-*a*]pyridin-8-ol* (**17** and **18**, resp.). Colourless oil. R_f (AcOEt/hexane 1:1) 0.48. IR ($CHCl_3$): 3067*w*, 3031*w*, 3012*w*, 2945*s*, 2892*s*, 2868*s*, 1603*w*, 1496*w*, 1455*m*, 1363*w*, 1309*w*, 1268*w*, 1166*w*, 1110*s*, 1066*w*, 1028*m*, 882*m*. ^{1}H-NMR (300 MHz, $CDCl_3$; **17**/**18** 1:1): 7.41–7.27 (*m*, 20 arom. H); 7.18, 7.13, 7.03 (2 H) (3*d*, *J*=1.2, H–C(2), H–C(3)); 5.36 (*d*, *J*=3.3, H–C(8) of **18**); 5.18 (*d*, *J*=11.4), 5.12 (*d*, *J*=11.7), 5.04 (*d*, *J*=11.4), 4.97 (*d*, *J*=11.4) (2 PhCH_2); 4.85 (*d*, *J*=6.9, H–C(8) of **17**); 4.87 (*d*, *J*=11.4), 4.77 (*d*, *J*=11.4), 4.74 (*d*, *J*=11.4), 4.67 (*d*, *J*=11.7) (2 PhCH_2); 4.26 (*dd*, *J*=11.7, 4.5), 4.17–4.04 (*m*), 4.01–3.84 (*m*) (H–C(5), H–C(6), H–C(7), H_2C–C(5)); 1.14–0.90 (*m*, (Me$_2$CH)$_3$Si). ^{13}C-NMR (75 MHz, $CDCl_3$; **17**/**18** 1:1): 147.58, 146.55 (2*s*, C=N); 138.88, 138.42, 138.35, 138.16 (4*s*); 129.19–128.05 (several *d*, including C(2)); 118.86, 117.55 (2*d*, C(3)); 83.38, 79.99 (2*d*, C(7)); 75.42, 75.34, 75.13, 75.01 (4*t*, 2 PhCH_2); 73.85, 72.00 (2*d*, C(6)); 67.56, 62.40 (2*d*, C(8)); 65.49, 63.99 (2*t*, CH_2–C(5)); 61.60, 61.19 (2*d*, C(5)); 18.30 (*q*, (*Me*$_2$CH)$_3$Si); 12.14, 12.09 (2*d*, (Me$_2$*C*H)$_3$Si).

Benzylation of **17**/**18**. A soln. of **17**/**18** 1:1 (282 mg, 0.53 mmol) in DMF (5 ml) was cooled to 0°, treated with NaH (50% suspension in oil, 100 mg, 8.33 mmol) and BnBr (0.1 ml), stirred for 16 h, treated with MeOH (1 ml), and evaporated. Normal workup (AcOEt/H_2O/brine) and FC (AcOEt/hexane 1:4) gave **21** (123 mg, 37%) and **22** (125 mg, 37%).

*Data of (5*R*,6*R*,7*S*,8*S*)-6,7,8-Tris(benzyloxy)-5,6,7,8-tetrahydro-5-[(triisopropylsilyloxy)methyl]-imidazo[1,2-*a*]pyridine* (**21**). Light-yellow oil. R_f (AcOEt/hexane 1:1) 0.64. $[\alpha]_D^{25} = +63.6$ (*c*=1.35, $CHCl_3$). IR ($CHCl_3$): 3067*w*, 3032*w*, 3010*w*, 2946*s*, 2868*s*, 1603*w*, 1496*w*, 1455*m*, 1363*m*, 1332*w*, 1220*w*, 1091*s*, 1028*m*, 882*w*. ^{1}H-NMR (300 MHz, $CDCl_3$): see *Table 2*; additionally, 7.47–7.26 (*m*, 15 arom. H); 7.21 (*d*, *J*=1.2), 7.13 (*d*, *J*=1.5) (H–C(2), H–C(3)); 5.26 (*d*, *J*=11.8, PhC*H*); 4.93 (*d*, *J*=11.7, 2 PhC*H*); 4.85 (*d*, *J*=11.1, PhCH); 4.60 (*d*, *J*=11.1, 2 PhC*H*); 1.10–0.99 (*m*, (Me$_2$CH)$_3$Si). ^{13}C-NMR (75 MHz, $CDCl_3$): see *Table 2*; additionally, 138.26, 137.80, 137.62 (3*s*); 129.23 (*d*, C(2));

128.40–127.49 (several *d*); 117.68 (*d*, C(3)); 74.28, 74.18 (3*t*, 3 PhCH$_2$); 18.12 (*q*, (*Me*$_2$CH)$_3$Si); 12.01 (*d*, (Me$_2$*C*H)$_3$Si). HR-MALDI-MS: 627.3602 ([*M*+Na]$^+$, $C_{38}H_{51}N_2O_4Si^+$; calc. 627.3613). Anal. calc. for $C_{38}H_{50}N_2O_4Si$ (626.34): C 72.93, H 8.00, N 4.53; found: C 72.80, H 8.04, N 4.47.

*Data of (5*R*,6*R*,7*S*,8*R*)-6,7,8-Tris(benzyloxy)-5,6,7,8-tetrahydro-5-[(triisopropylsilyloxy)methyl]-imidazo[1,2-*a*]pyridine* (**22**). Colourless oil. R_f (AcOEt/hexane 1:1) 0.39. $[\alpha]_D^{25} = -40.1$ (*c* = 1.35, $CHCl_3$). IR ($CHCl_3$): 3068*w*, 2945*s*, 2868*s*, 1604*w*, 1496*w*, 1455*m*, 1366*w*, 1269*w*, 1108*s*, 1027*m*, 915*w*, 882*m*. ^{1}H-NMR (300 MHz, $CDCl_3$): see *Table 2*; additionally, 7.47–7.27 (*m*, 15 arom. H); 7.24 (*d*, *J* = 1.2), 7.08 (*d*, *J* = 1.5) (H–C(2), H–C(3)); 5.07 (*d*, *J* = 11.8, PhC*H*); 4.76 (*d*, *J* = 11.4, PhC*H*); 4.73 (*d*, *J* = 11.1, PhC*H*); 4.69 (*d*, *J* = 12.0, PhC*H*); 4.67 (*d*, *J* = 12.0, PhC*H*); 4.57 (*d*, *J* = 12.0, PhC*H*); 1.06–0.97 (*m*, (Me$_2$CH)$_3$Si). ^{13}C-NMR (75 MHz, $CDCl_3$): see *Table 2*; additionally, 138.16, 138.10, 137.89 (3*s*); 128.47 (*d*, C(2)); 128.43–127.56 (several *d*); 119.52 (*d*, C(3)); 75.00, 71.59, 70.32 (3*t*, 3 PhCH$_2$); 17.94 (*q*, (*Me*$_2$CH)$_3$Si); 11.79 (*d*, (Me$_2$CH)$_3$Si). HR-MALDI-MS: 627.3622 ([*M*+H]$^+$, $C_{38}H_{51}N_2O_4Si^+$; calc. 627.3613). Anal. calc. for $C_{38}H_{50}N_2O_4Si$ (626.91): C 73.29, H 8.05, N 4.62; found: C 72.80, H 8.04, N 4.47.

*(5*R*,6*R*,7*S*,8*S*)-6,7,8-Tris(benzyloxy)-5,6,7,8-tetrahydroimidazo[1,2-*a*]pyridine-5-methanol* (**23**). A soln. of **21** (123 mg, 0.196 mmol) in THF (2 ml) was cooled to 0°, treated with $Bu_4NF \cdot 3\,H_2O$ (89 mg, 0.28 mmol), and stirred for 1.5 h. Evaporation and FC (AcOEt/hexane 1:1 → AcOEt → MeOH/AcOEt 1:9) gave **23** (84 mg, 91%). Colourless solid. R_f (AcOEt/hexane 4:1) 0.17. M.p. 144–146°. $[\alpha]_D^{25} = +68.2$ (*c* = 0.72, $CHCl_3$). IR ($CHCl_3$): 3410*w*, 3067*w*, 2963*m*, 2892*w*, 2867*s*, 1604*w*, 1496*w*, 1483*m*, 1454*m*, 1362*w*, 1262*m*, 1090*s*, 1070*s*, 1028*w*. ^{1}H-NMR (300 MHz, $CDCl_3$): see *Table 2*; additionally, 7.42–7.27 (*m*, 15 arom. H); 7.14 (*d*, *J* = 1.8), 7.05 (*d*, *J* = 1.5) (H–C(2), H–C(3)); 5.17 (*d*, *J* = 11.4, PhC*H*); 4.89 (*d*, *J* = 11.7, 2 PhC*H*); 4.83 (*d*, *J* = 11.4, PhC*H*); 4.70 (*d*, *J* = 11.1, PhC*H*); 4.62 (*d*, *J* = 11.4, PhC*H*); 2.05 (br. *s*, OH). ^{13}C-NMR (75 MHz, $CDCl_3$): see *Table 2*; additionally, 138.04, 137.61, 137.52 (3*s*); 129.25 (*d*, C(2); 128.45–127.55 (several *d*); 116.98 (*d*, C(3)); 74.12, 74.06, 72.79 (3*t*, 3 PhCH$_2$). HR-MALDI-MS: 471.2287 ([*M*+H]$^+$, $C_{29}H_{31}N_2O_4^+$; calc. 471.2278). Anal. calc. for $C_{29}H_{30}N_2O_4$ (470.55): C 74.02, H 6.43, N 5.95; found: C 74.04, H 6.55, N 5.90.

*Diphenylmethyl (5*R*,6*R*,7*S*,8*S*)-6,7,8-Tris(benzyloxy)-5,6,7,8-tetrahydroimidazo[1,2-*a*]pyridine-5-carboxylate* (**24**). A soln. of **23** (65 mg, 0.138 mmol) in acetone (10 ml) was treated with *Jones*' reagent (0.25 ml, 0.7M aq. soln.), stirred for 1 h, treated with ^{i}PrOH, and evaporated. A soln. of the residue in H_2O (5 ml) was extracted with AcOEt (3 × 50 ml). The combined org. layers were washed with brine (5 ml), dried (Na_2SO_4), and evaporated. A soln. of the residue in acetone (5 ml) was treated with Ph_2CN_2 (85 mg, 0.44 mmol) and stirred for 1 h. Evaporation and FC (AcOEt/hexane 1:4) gave **24** (63 mg, 70%). Colourless oil. R_f (AcOEt/hexane 2:3) 0.42. $[\alpha]_D^{25} = +49.3$ (*c* = 2.2, $CHCl_3$). IR ($CHCl_3$): 3063*w*, 3032*m*, 3013*w*, 2966*w*, 2866*w*, 1738*s*, 1602*m*, 1496*m*, 1454*w*, 1265*s*, 1213*s*, 1087*s*, 1003*m*, 909*w*, 821*w*. ^{1}H-NMR (300 MHz, $CDCl_3$): see *Table 3*; additionally, 7.38–7.18 (*m*, 24 arom. H, H–C(3)); 6.96 (br. *dd*, *J* = 7.8, 1.5, 1 arom. H); 6.84 (*d*, *J* = 1.2, H–C(2)); 6.74 (*s*, Ph$_2$C*H*); 5.12 (*d*, *J* = 12.0, PhC*H*); 4.97 (irrad. at 4.50 → *s*); 4.84 (*d*, *J* = 12.0, PhC*H*); 4.72 (*d*, *J* = 12.0, PhC*H*); 4.52 (*d*, *J* = 12.0, PhC*H*); 4.50 (irrad. at 4.97 → *d*, *J* = 5.1); 4.19 (*d*, *J* = 12.3, PhC*H*); 4.10 (*d*, *J* = 12.3, PhC*H*); 4.07 (irrad. at 4.50 → *d*, *J* = 3.3). ^{13}C-NMR (75 MHz, $CDCl_3$): see *Table 3*; additionally, 139.43, 139.28, 138.28, 137.10, 135.03 (5*s*); 129.22 (*d*, C(2)); 128.57–126.98 (several *d*); 119.79 (*d*, C(3)); 75.25 (*d*, Ph$_2$*C*H); 72.47 (*t*, PhCH$_2$); 72.26 (*t*, 2 PhCH$_2$). HR-MALDI-MS: 651.3 ([*M*+H]$^+$, $C_{42}H_{39}N_2NaO_5^+$; calc. 651.2853).

*(5*R*,6*R*,7*S*,8*S*)-5,6,7,8-Tetrahydro-6,7,8-trihydroxyimidazo[1,2-*a*]pyridine-5-carboxylic Acid* (**5**). A soln. of **24** (48 mg, 0.74 mmol) in EtOH (5 ml) was treated with 10% Pd/C (30 mg), stirred under H_2 for 48 h, and filtered through *Celite* (washing with 5 ml of EtOH). After evaporation, the solid residue was washed several times with hot AcOEt. A soln. of the solid in H_2O was lyophilised to give **5** (13 mg, 80%). Colourless powder. R_f (AcOEt/MeOH/AcOH 7:2.8:2) 0.45. M.p. 238–244° (dec.). pK_{HA} = 6.5. $[\alpha]_D^{25} = -13.9$ (*c* = 0.1, MeOH). IR (ATR): 3211*m*, 3148*m*, 2921*w*, 1617*s*, 1599*s*, 1530*w*, 1387*m*, 1297*m*, 1167*m*, 1083*s*, 1057*s*, 1011*m*, 879*m*. ^{1}H-NMR (300 MHz, D_2O): see *Table 3*; additionally, 7.41 (*d*, *J* = 2.1), 7.25 (*d*, *J* = 2.4) (H–C(2), H–C(3)). ^{13}C-NMR (75 MHz, D_2O): see *Table 3*; additionally, 121.97, 120.31 (2*d*, C(2), C(3)).

*(5*R*,6*R*,7*S*,8*R*)-6,7,8-Tris(benzyloxy)-5,6,7,8-tetrahydroimidazo[1,2-*a*]pyridine-5-methanol* (**25**). A soln. of **22** (125 mg, 0.199 mmol) in THF (2.5 ml) was cooled to 0°, treated with $Bu_4NF \cdot 3\,H_2O$ (95 mg,

Table 3. *Selected ^{1}H-NMR Chemical Shifts* [ppm] *and Coupling Constants* [Hz], *and ^{13}C-NMR Chemical Shifts* [ppm] *of the Protected Imidazoles* **24**, **26**, *and* **34** *in $CDCl_3$ and of the Deprotected Imidazoles* **5**, **6**, *and* **7** *in D_2O*

	24	**26**	**34**	**5**	**6**	**7**
H–C(5)	4.69	4.83–4.81	4.75	4.61	5.08	4.88
H–C(6)	4.07	4.83–4.81	4.02	3.89[a])	4.20	4.65
H–C(7)	4.50	3.89–3.85	4.59	4.21[a])	4.78	4.00
H–C(8)	4.97	4.83–4.81	4.97	4.80	4.80	5.01
J(5,6)	3.0	[b])	4.7	6.6	4.2	3.1
J(6,7)	5.1	[b])	1.9	7.8	5.1	2.3
J(7,8)	3.3	[b])	8.1	6.6	1.5	9.0
C=O	166.90	167.12	166.35	171.93	170.20	171.39
C(5)	60.40	61.49	58.45	62.04	62.25	63.69
C(6)	74.88[c])	76.67[c])	72.59	69.84	67.70	64.44
C(7)	78.54	78.88	78.48[c])	72.20	69.96	72.00
C(8)	70.01	68.88	75.52	65.65	62.62	69.30
C(8a)	142.64	143.52	143.95	144.05	144.13	144.65

[a]) Assignments may be interchanged. [b]) Not assigned. [c]) Assignments may be interchanged with the *d* of Ph_2CH (**24**: 75.25, **26**: 77.91, **34**: 78.39 ppm).

0.30 mmol), and stirred for 1 h. Evaporation and FC (AcOEt/hexane 1:1 → AcOEt → MeOH/AcOEt 1:9) gave **25** (88 mg, 94%). Colourless solid. R_f (AcOEt/hexane 4:1) 0.08. $[\alpha]_D^{25} = -80.6$ ($c = 0.48$, $CHCl_3$). IR ($CHCl_3$): 3397*w*, 3067*w*, 2941*m*, 2877*w*, 1603*w*, 1496*m*, 1454*m*, 1365*m*, 1263*m*, 1126*s*, 1090*s*, 1070*s*, 1027*m*, 912*w*. ^{1}H-NMR (300 MHz, $CDCl_3$): see *Table 2*; additionally, 7.42–7.27 (*m*, 15 arom. H); 7.12 (*d*, $J = 1.5$), 7.01 (*d*, $J = 1.5$) (H–C(2), H–C(3)); 5.02 (*d*, $J = 11.4$, PhC*H*); 4.75 (*d*, $J = 11.7$, PhC*H*); 4.71 (*d*, $J = 10.8$, PhC*H*); 4.68 (*d*, $J = 12.0$, PhC*H*); 4.66 (*d*, $J = 12.0$, PhC*H*); 4.56 (*d*, $J = 11.7$, PhC*H*); 3.35 (br. *s*, OH). ^{13}C-NMR (75 MHz, $CDCl_3$): see *Table 2*; additionally, 137.95, 137.83, 137.67 (3*s*); 129.15 (*d*, C(2); 128.38–127.55 (several *d*); 118.73 (*d*, C(3)); 74.84, 71.76, 70.76 (3*t*, 3 Ph*C*H_2). HR-MALDI-MS: 471.2287 ($[M+H]^+$, $C_{29}H_{31}N_2O_4^+$; calc. 471.2278). Anal. calc. for $C_{29}H_{30}N_2O_4 \cdot 0.25\ H_2O$ (475.06): C 73.32, H 6.47, N 5.90; found: C 74.04, H 6.26, N 5.85.

*Diphenylmethyl (5*R*,6*R*,7*S*,8*R*)-6,7,8-Tris(benzyloxy)-5,6,7,8-tetrahydroimidazo[1,2-a]pyridine-5-carboxylate* (**26**). A soln. of **25** (61 mg, 0.129 mmol) in acetone (10 ml) was treated with *Jones*' reagent (0.15 ml, 0.7M aq. soln.), stirred for 1 h, treated with ^{i}PrOH, and evaporated. A soln. of the residue in H_2O (5 ml) was extracted with AcOEt (3 × 50 ml). The combined org. layers were washed with brine (5 ml), dried, and evaporated. A soln. of the residue in acetone (5 ml) was treated with Ph_2CN_2 (100 mg, 0.51 mmol) and stirred for 1 h. Evaporation and FC (AcOEt/hexane 1:4) gave **26** (61 mg, 73%). Light-yellow oil. R_f (AcOEt/hexane 1:1) 0.55. $[\alpha]_D^{25} = -56.7$ ($c = 2.35$, $CHCl_3$). IR ($CHCl_3$): 3066*w*, 3033*w*, 3012*w*, 2947*w*, 2873*w*, 1746*s*, 1602*w*, 1496*m*, 1454*m*, 1360*m*, 1264*s*, 1110*s*, 1090*s*, 1003*m*, 975*m*, 909*s*. ^{1}H-NMR (300 MHz, $CDCl_3$): see *Table 3*; additionally, 7.39–7.18 (*m*, 25 arom. H); 7.15 (*d*, $J = 1.2$), 6.89 (*d*, $J = 1.5$) (H–C(2), H–C(3)); 6.79 (*s*, Ph_2CH); 4.78 (*d*, $J = 11.4$, PhC*H*); 4.72 (*d*, $J = 12.6$, PhC*H*); 4.60 (*d*, $J = 12.0$, PhC*H*); 4.59 (*d*, $J = 11.4$, PhC*H*); 4.50 (*d*, $J = 12.3$, PhC*H*); 4.45 (*d*, $J = 12.3$, PhC*H*). ^{13}C-NMR (75 MHz, $CDCl_3$): see *Table 3*; additionally, 139.24, 139.02, 137.85, 137.49, 135.30 (5*s*); 129.22 (*d*, C(2)); 128.51–126.94 (several *d*); 119.75 (*d*, C(3)); 77.91 (*d*, Ph_2CH); 73.78, 72.06, 71.11 (3*t*, 3 Ph*C*H_2). HR-MALDI-MS: 651.2854 ($[M+H]^+$, $C_{42}H_{39}N_2NaO_5^+$; calc. 651.2853).

*(5*R*,6*R*,7*S*,8*R*)-5,6,7,8-Tetrahydro-6,7,8-trihydroxyimidazo[1,2-a]pyridine-5-carboxylic Acid* (**6**). A soln. of **26** (44 mg, 0.61 mmol) in EtOH (5 ml) was treated with 10% Pd/C (28 mg), stirred under H_2 for 48 h, and filtered through *Celite* (washing with 5 ml of EtOH). After evaporation, the solid residue was washed several times with hot AcOEt. A soln. of the solid in H_2O was lyophilised to give **6** (16 mg, 99%). Colourless powder. R_f (AcOEt/MeOH/AcOH 7:2.8:2) 0.10. $pK_{HA} = 6.6$. $[\alpha]_D^{25} = -20.6$ ($c = 0.85$, MeOH). IR (ATR): 3219*m*, 3149*m*, 2933*m*, 1728*w*, 1612*m*, 1594*s*, 1527*m*, 1386*m*, 1297*m*,

1169*s*, 1056*s*, 966*m*, 874*m*. ^{1}H-NMR (300 MHz, D_2O): see *Table 3*; additionally, 7.38 (*d*, *J* = 1.8), 7.31 (*d*, *J* = 1.8) (H–C(2), H–C(3)). ^{13}C-NMR (75 MHz, $CDCl_3$): see *Table 3*; additionally, 123.03, 119.27 (2*d*, C(2), C(3)).

4,6-Di-O-*acetyl-5-amino-2,3-di*-O-*benzyl-5-deoxy*-D-*galactono-1,5-lactam* (**28**). A soln. of **27** (1.0 g, 2.79 mmol) in pyridine (10 ml) was cooled to 0°, treated with Ac_2O (4 ml), stirred for 6 h, and evaporated to afford **28** (1.23 g, 99%). Colourless oil. A small sample was purified by FC (AcOEt/cyclohexane 1:4). R_f (AcOEt/cyclohexane 2:1) 0.21. $[\alpha]_D^{25} = +112.3$ (*c* = 1.05, $CHCl_3$). IR (ATR): 3208*w*, 3106*w*, 3063*w*, 3029*w*, 2981*w*, 2933*w*, 2873*w*, 1736*s*, 1707*w*, 1677*s*, 1496*w*, 1454*w*, 1418*w*, 1364*m*, 1310*w*, 1228*s*, 1174*w*, 1119*m*, 1099*s*, 1064*m*, 1045*m*, 1028*m*, 955*w*, 913*w*, 826*w*. ^{1}H-NMR (300 MHz, $CDCl_3$): 7.42–7.26 (*m*, 10 arom. H); 6.90 (br. *s*, NH); 5.69 (*dt*, *J* = 2.8, 1.2, H–C(4)); 5.16 (*d*, *J* = 10.9, PhC*H*); 4.79 (*d*, *J* = 11.2, PhC*H*); 4.72 (*d*, *J* = 11.5, PhC*H*); 4.55 (*d*, *J* = 11.5, PhC*H*); 4.23 (*dd*, *J* = 11.2, 5.0, H–C(6)); 4.14 (*d*, *J* = 9.0, H–C(2)); 3.97 (*dd*, *J* = 10.9, 8.4, H′–C(6)); 3.87 (*dd*, *J* = 9.3, 2.5, H–C(3)); 3.81 (*ddd*, *J* = 11.2, 5.0, 2.8 H–C(5)); 2.12, 2.09 (2*s*, 2 AcO). ^{13}C-NMR (75 MHz, $CDCl_3$): 171.04, 170.27, 169.73 (3*s*, 3 C=O); 137.82, 137.13 (2*s*); 128.31 (2*d*); 128.18 (2*d*); 128.09 (2*d*); 127.90 (2*d*); 127 81 (*d*); 127.65 (*d*); 77.70 (*d*, C(3)); 76.47 (*d*, C(2)); 75.63, 72.02 (2*t*, 2 PhCH_2); 65.61 (*d*, C(4)); 63.45 (*t*, C(6)); 51.24 (*d*, C(5)); 20.83, 20.78 (2*q*, 2 Me). HR-MALDI-MS: 464.1674 (100, $[M+Na]^+$, $C_{24}H_{27}NNaO_7^+$; calc. 464.1680).

2,6-Di-O-*acetyl-5-amino-2,3-di*-O-*benzyl-5-deoxy*-D-*galactono-1,5-thiolactam* (**29**). A soln. of **28** (660 mg, 1.49 mmol) in toluene (12 ml) was treated with *Lawesson*'s reagent (605 mg, 1.49 mmol), heated to 80° for 30 min, cooled to 25°, and treated with $NaHCO_3$ (125 mg, 1.29 mmol). FC (AcOEt/cyclohexane 1:4) gave **29** (580 mg, 85%). Yellow foam. R_f (AcOEt/cyclohexane 1:1) 0.55. $[\alpha]_D^{25} = +172.9$ (*c* = 1.03, $CHCl_3$). IR (KBr): 3468*w*, 3170*w*, 3031*m*, 2929*w*, 2870*w*, 1956*w*, 1877*w*, 1749*s*, 1555*m*, 1530*m*, 1497*m*, 1370*m*, 1324*m*, 1226*s*, 1178*w*, 1102*s*, 1078*m*, 1056*m*, 1018*m*, 945*w*, 917*w*. ^{1}H-NMR (300 MHz, $CDCl_3$): 8.14 (br. *s*, NH); 7.45–7.23 (*m*, 10 arom. H); 5.62 (br. *s*, H–C(4)); 5.25 (*d*, *J* = 10.6, PhC*H*); 4.81 (*d*, *J* = 10.6, PhC*H*); 4.57 (*d*, *J* = 11.8, PhC*H*); 4.51 (*d*, *J* = 11.8, PhC*H*); 4.32 (*dd*, *J* = 11.2, 3.7, H–C(6)); 4.28 (*d*, *J* = 7.5, irrad. at 3.82 → *s*, H–C(2)); 4.05 (*dd*, *J* = 11.2, 9.0, H′–C(6)); 3.87 (*ddd*, *J* ≈ 9.0, 4.0, 2.5 H–C(5)); 3.82 (*dd*, *J* = 7.2, 2.5, H–C(3)); 2.12, 2.11 (2*s*, 2 AcO). ^{13}C-NMR (75 MHz, $CDCl_3$): 202.04 (*s*, C=S); 170.58, 170.07 (2*s*, 2 C=O); 137.83, 137.31 (2*s*); 128.89 (2*d*); 128.70 (2*d*); 128.60 (2*d*); 128.22 (4*d*); 80.33 (*d*, C(2)); 76.82 (*d*, C(3)); 75.98, 72.46 (2*t*, 2 PhCH_2); 65.92 (*d*, C(4)); 63.81 (*t*, C(6)); 55.16 (*d*, C(5)); 20.99 (*q*, 2 Me). HR-MALDI-MS: 458.1634 (100, $[M+H]^+$, $C_{24}H_{28}NO_6S^+$; calc. 458.1632). Anal. calc. for $C_{24}H_{27}NO_6S$ (457.16): C 63.00, H 5.95, N 3.06; found: C 62.79, H 5.96, N 3.08.

*(5*R*,6*S*,7*S*,8*S*)-7,8-Bis(benzyloxy)-5-{[(*tert*-butyl)dimethylsilyloxy]methyl}-5,6,7,8-tetrahydroimidazo[1,2-*a*]pyridin-6-ol* (**31**). A soln. of **29** (580 mg, 1.27 mmol) in THF (12 ml) was cooled to 0°, treated with $Hg(OAc)_2$ (444 mg, 1.39 mmol) and $H_2NCH_2CH(OMe)_2$ (0.75 ml, 6.34 mmol), stirred for 2 h, diluted with Et_2O (50 ml), filtered through *Celite*, and evaporated. A soln. of the residue in toluene/H_2O 12:3 (15 ml) was treated with $TsOH \cdot H_2O$ (1.45 g, 7.6 mmol) and stirred at 75° for 24 h. The mixture was diluted with AcOEt (50 ml) and washed with sat. K_2CO_3 soln. The aq. layer was extracted with AcOEt (2 × 50 ml). The combined org. layers were dried (Na_2SO_4), filtered, and evaporated. A soln. of the residue (*i.e.*, **30**) in DMF (10 ml) was treated with Et_3N (0.73 ml, 2.53 mmol). DMAP (31 mg, 0.253 mmol), and ^{t}Bu(Me)$_2$SiCl (190 mg, 1.27 mmol), and stirred for 16 h. Normal workup (AcOEt/H_2O) and FC (AcOEt/cyclohexane 1:2) afforded **31** (300 mg, 84%). R_f (AcOEt/cyclohexane 1:1) 0.39. $[\alpha]_D^{25} = +55.3$ (*c* = 1.04, $CHCl_3$). IR (ATR): 3513–3164*w* (br.), 3087*w*, 3032*w*, 2928*w*, 2856*w*, 1470*w*, 1454*w*, 1389*w*, 1360*w*, 1305*w*, 1252*m*, 1210*w*, 1131*w*, 1075*s*, 1027*m*, 1005*m*, 936*w*, 834*s*. ^{1}H-NMR (300 MHz, $CDCl_3$): see *Table 2*; additionally, 7.43–7.25 (*m*, 10 arom. H); 7.12, 7.10 (2*d*, *J* = 1.2, H–C(2), H–C(3)); 5.15 (*d*, *J* = 11.5, PhC*H*); 4.87 (*d*, *J* = 10.9, PhC*H*); 4.84 (irrad. at 3.97 → *s*); 4.75 (*d*, *J* = 11.8, PhC*H*); 4.66 (*d*, *J* = 11.5, PhC*H*); 4.51 (irrad. at 3.97 → br. *d*, *J* = 3.7, addition of CD_3OD → *dd*, *J* = 4.0, 2.2); 3.97 (irrad. at 4.84 → *d*, *J* = 2.2); 3.47 (br. *s*, exchange with CD_3OD, HO–C(6)); 0.91 (*s*, *t*-Bu); 0.08, 0.05 (2*s*, Me_2Si). ^{13}C-NMR (75 MHz, $CDCl_3$): see *Table 2*; additionally, 138.18, 137.57 (2*s*); 129.07 (*d*, C(2)); 128.40 (2*d*); 128.23 (2*d*); 127.99 (2*d*); 127.86 (*d*); 127.72 (2*d*); 127.50 (*d*); 117.87 (*d*, C(3)); 72.89, 72.56 (2*t*, 2 PhCH_2); 25.94 (*q*, *Me*$_3$C); 18.28 (*s*, Me$_3$*C*); –5.31, –5.41 (2*q*, Me_2Si). HR-MALDI-MS: 495.2666 (100, $[M+H]^+$, $C_{28}H_{39}N_2O_4Si^+$; calc. 495.2674). Anal. calc. for $C_{28}H_{38}N_2O_4Si$ (494.26): C 67.98, H 7.74, N 5.66; found: C 67.94, H 7.72, N 5.66.

*(5*R*,6*S*,7*S*,8*S*)-6,7,8-Tris(benzyloxy)-5-{[(*tert*-butyl)dimethylsilyloxy]methyl}-5,6,7,8-tetrahydroimidazo[1,2-*a*]pyridine* (**32**). A soln. of **31** (422 mg, 0.85 mmol) in DMF (6 ml) was cooled to 0°, treated with

NaH (60% suspension in oil, 68 mg, 1.71 mmol), stirred for 10 min, treated with BnBr (0.11 ml, 0.935 mmol), stirred for 4 h, treated with MeOH (1 ml), and stirred for 30 min. Normal workup (AcOEt/$NaHCO_3$ soln.) and FC (AcOEt/cyclohexane 1:2) afforded **32** (330 mg, 66%). R_f (AcOEt/cyclohexane 1:2) 0.39. $[\alpha]_D^{25} = +73.7$ ($c = 1.24$, $CHCl_3$). IR (ATR): 3059*w*, 3030*w*, 2951*w*, 2927*w*, 2884*w*, 2855*w*, 1949*w*, 1872*w*, 1808*w*, 1605*w*, 1496*w*, 1470*m*, 1454*m*, 1389*w*, 1359*w*, 1307*w*, 1255*m*, 1207*w*, 1076*s*, 1066*s*, 1027*m*, 1005*m*, 919*w*, 835*s*. ^{1}H-NMR (300 MHz, $CDCl_3$): see *Table 2*; additionally, 7.37–7.26 (*m*, 15 arom. H); 7.17, 7.08 (2*d*, $J = 1.5$, H–C(2), H–C(3)); 4.99 (*d*, $J = 11.8$, PhC*H*); 4.80 (irrad. at 4.08 → *s*); 4.78 (*d*, $J = 11.8$, PhC*H*); 4.72 (*d*, $J = 12.1$, PhC*H*); 4.71 (*d*, $J = 12.1$, PhC*H*); 4.65 (*d*, $J = 11.8$, PhC*H*); 4.63 (*d*, $J = 11.8$, PhC*H*); 4.38 (irrad. at 4.08 → *d*, $J = 5.6$); 4.34 (irrad. at 3.95 → *dd*, $J = 5.6$, 3.1); 4.13 (irrad. at 3.95 → *d*, $J = 5.6$); 4.08 (irrad. at 4.80 → *d*, $J = 1.6$); 0.91 (*s*, *t*-Bu); 0.02, 0.01 (2*s*, Me_2Si). ^{13}C-NMR (75 MHz, $CDCl_3$): see *Table 2*; additionally, 138.20, 137.81, 137.63 (3*s*); 128.69 (*d*, C(2)); 128.41–127.50 (several *d*); 119.41 (*d*, C(3)); 72.85, 72.38, 71.87 (3*t*, 3 Ph*C*H_2); 26.07 (*q*, *Me*$_3$C); 18.38 (*s*, Me$_3$*C*); −5.19, −5.34 (2*q*, Me_2Si). HR-MALDI-MS: 585.3135 (100, $[M+H]^+$, $C_{35}H_{45}N_2O_4Si^+$; calc. 585.3143). Anal. calc. for $C_{35}H_{44}N_2O_4Si$ (584.31): C 71.88, H 7.58, N 4.79; found: C 71.78, H 7.60, N 4.79.

*(5*R*,6*S*,7*S*,8*S*)-6,7,8-Tris(benzyloxy)-5,6,7,8-tetrahydroimidazo[1,2-*a*]pyridine-5-methanol* (**33**). A soln. of **32** (330 mg, 0.56 mmol) in THF (6 ml) was cooled to 0°, treated with 1M $Bu_4NF \cdot 3\,H_2O$ in THF (0.62 ml) and stirred for 1 h. Normal workup (AcOEt/$NaHCO_3$ soln.) and FC (AcOEt/cyclohexane 2:1 → AcOEt) afforded **33** (225 mg, 85%). R_f (AcOEt/cyclohexane 2:1) 0.15. $[\alpha]_D^{25} = +45.5$ ($c = 1.01$, $CHCl_3$). IR (KBr): 3412*m* (br.), 3159*m*, 3085*m*, 3059*m*, 3030*m*, 2922*m*, 2866*m*, 1953*w*, 1875*w*, 1810*w*, 1732*w*, 1606*w*, 1521*w*, 1496*m*, 1482*m*, 1453*s*, 1356*m*, 1306*m*, 1260*m*, 1208*m*, 1130*s*, 1094*s*, 1054*s*, 1027*s*, 914*w*, 844*w*, 820*w*. ^{1}H-NMR (300 MHz, $CDCl_3$): see *Table 2*; additionally, 7.38–7.25 (*m*, 15 arom. H); 7.10 (*d*, $J = 1.1$, H–C(2)); 7.06 (*d*, $J = 1.4$, H–C(3)); 4.88 (*d*, $J = 11.8$, PhC*H*); 4.76 (irrad. at 4.12 → *s*); 4.71 (*d*, $J = 12.1$, PhC*H*); 4.70 (*d*, $J = 12.1$, PhC*H*); 4.64 (*d*, $J = 11.8$, PhC*H*); 4.59 (*d*, $J = 12.1$, PhC*H*); 4.56 (*d*, $J = 11.8$, PhC*H*); 4.45 (irrad. at 4.12 → *d*, $J = 6.3$); 4.12 (irrad. at 4.76 → *d*, $J = 1.9$); 3.41 (br. *s*, exchange with CD_3OD, *H*OCH_2–C(5)). ^{13}C-NMR (75 MHz, $CDCl_3$): see *Table 2*; additionally, 138.28, 137.58, 137.30 (3*s*); 129.79 (*d*, C(2)); 128.81–127.88 (several *d*); 118.90 (*d*, C(3)); 73.24, 72.41, 71.85 (3*t*, 3 Ph*C*H_2). HR-MALDI-MS: 471.2271 (100, $[M+H]^+$, $C_{29}H_{31}N_2O_4^+$; calc. 471.2278). Anal. calc. for $C_{29}H_{30}N_2O_4$ (470.22): C 74.02, H 6.43, N 5.95; found: C 73.76, H 6.60, N 5.99.

*Diphenylmethyl (5*R*,6*S*,7*S*,8*S*)-6,7,8-Tris(benzyloxy)-5,6,7,8-tetrahydroimidazo[1,2-*a*]pyridine-5-carboxylate* (**34**). A soln. of **33** (95 mg, 0.2 mmol) in acetone (5 ml) was treated with a soln. of CrO_3 (101 mg, 1.01 mmol) in 1M H_2SO_4 (0.9 ml) and stirred for 24 h. The mixture was diluted with AcOEt (20 ml) and washed with H_2O. The aq. layer was extracted with AcOEt (2×20 ml), and the combined org. layers were dried (Na_2SO_4), filtered, and evaporated. A soln. of the crude in acetone (5 ml) was treated with Ph_2CN_2 (59 mg, 0.3 mmol), stirred for 2 h, and evaporated at 35°. FC (AcOEt/cyclohexane 1:2 → AcOEt) gave **34** (45 mg, 34%) and **33** (17 mg, 18%). R_f (AcOEt/cyclohexane 1:2) 0.34. $[\alpha]_D^{25} = +51.2$ ($c = 0.80$, $CHCl_3$). IR (KBr): 3062*w*, 3030*w*, 2924*w*, 2869*w*, 1953*w*, 1883*w*, 1808*w*, 1746*s*, 1603*w*, 1586*w*, 1495*m*, 1453*m*, 1355*w*, 1310*w*, 1276*m*, 1247*m*, 1193*m*, 1172*s*, 1079*s*, 1027*m*, 977*s*, 911*w*, 847*w*. ^{1}H-NMR (300 MHz, $CDCl_3$): see *Table 3*; additionally, 7.33–7.24 (*m*, 21 arom. H); 7.21–7.18 (*m*, 2 arom. H); 7.13 (*dd*, $J = 5.3$, 1.9, 2 arom. H); 7.08 (*d*, $J = 1.6$, H–C(2)); 6.98 (*s*, Ph_2CH); 6.69 (*d*, $J = 1.2$, H–C(3)); 4.88 (*d*, $J = 11.8$, PhC*H*); 4.67 (*d*, $J = 11.8$, PhC*H*); 4.59 (irrad. at 4.02 → *d*, $J = 8.1$); 4.57 (*d*, $J = 12.1$, PhC*H*); 4.51 (*d*, $J = 12.1$, PhC*H*); 4.41 (*d*, $J = 11.5$, PhC*H*); 4.36 (*d*, $J = 11.8$, PhC*H*); 4.02 (irrad. at 4.75 → *d*, $J = 1.9$, irrad. at 4.59 → *d*, $J = 4.4$). ^{13}C-NMR (75 MHz, $CDCl_3$): see *Table 3*; additionally, 139.40, 139.31, 138.04, 137.66, 137.29 (5*s*); 129.42 (*d*, C(2)); 128.40–126.75 (several *d*); 119.86 (*d*, C(3)); 78.39 (*d*, Ph_2CH); 73.40, 73.02, 72.89 (3*t*, 3 Ph*C*H_2). HR-MALDI-MS: 651.2865(100, $[M+H]^+$, $C_{42}H_{39}N_2O_5^+$; calc. 651.2854). Anal. calc. for $C_{42}H_{38}N_2O_5$ (650.76): C 77.52, H 5.89, N 4.30; found: C 77.70, H 5.93, N 4.32.

*(5*R*,6*S*,7*S*,8*S*)-6,7,8-Trihydroxy-5,6,7,8-tetrahydroimidazo[1,2-*a*]pyridine-5-carboxylic Acid* (**7**). A suspension of **34** (40 mg, 0.06 mmol) and 10% Pd/C in MeOH/H_2O 2:1 was hydrogenated (6 bar) for 2 days, filtered through *Celite*, evaporated, dissolved in H_2O (5 ml), and washed with AcOEt (4×). The aq. layer was lyophillised and dried (P_2O_5) to yield **7** (13 mg, 98%). $pK_{HA} = 6.6$. $[\alpha]_D^{25} = -79.7$ ($c = 0.71$, H_2O). IR (KBr): 3410*s* (br.), 2923*m*, 2857*m*, 2778*w*, 1631*s*, 1524*w*, 1491*w*, 1390*m*, 1313*m*, 1267*w*, 1235*w*, 1171*w*, 1102*m*, 907*w*, 860*w*, 831*w*. ^{1}H-NMR (300 MHz, D_2O): see *Table 3*; additionally,

7.37, 7.34 (2 br. *s*, H–C(2), H–C(3)). ^{13}C-NMR (75 MHz, D_2O): see *Table 3*; additionally, 122.39, 121.02 (2*d*, C(2), C(3)). ESI-MS (neg. mode): 213.3 (100, $[M-H]^-$). Anal. calc. for $C_8H_{10}N_2O_5 \cdot 1.05\ H_2O$ (232.97): C 41.22, H 5.23, N 12.02; found: C 41.05, H 4.76, N 11.60.

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