127. Synthesis and Evaluation as Glycosidase Inhibitors of 1*H*-Imidazol-2-yl *C*-Glycopyranosides

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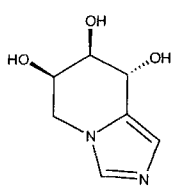
The (1*H*-imidazol-2-yl)ulose **8** and the 1*H*-imidazol-2-yl *C*-glycopyranosides **23** and **24** have been prepared from tetra-*O*-benzylgluconolactone **6** in two and six steps, respectively. The imidazoles **8** and **24** are moderate competitive inhibitors of sweet-almond β-glucosidase (pH 6.8, $K_i \approx 0.79$ and 0.64 mM, respectively), while **23** is a competitive inhibitor of yeast α-glucosidase (pH 6.8, $K_i \approx 0.26$ mM). Addition of 2-lithiated 1-[(dimethylamino)methyl]-1*H*-imidazole to **6** gave the ulose **7** (68%), which was deprotected to **8**. Reduction of **7** with $NaBH_4$ yielded a 12:88 mixture **10**/**11**. Attempts to selectively mesylate HO–C(1) of these diols failed, while dinitrobenzoylation led to **19**/**20**, which cyclized easily (NaH) to a 25:75 mixture of **21** and **22** which were separated and debenzylated to the *C*-glycosides **23** and **24**.

Introduction. – *Shinitzky et al.* [1] have reported the inhibition of lysozyme by imidazole derivatives[1]). *Field et al.* [2] and *Li* and *Byers* [3] have shown that derivatives of L-histidine, histamine (1*H*-imidazole-4-ethanamine), and 1*H*-imidazole are inhibitors of sweet-almond β-glucosidase and yeast α-glucosidase. Substitution of 1*H*-imidazole by a hydrophobic group enhanced the binding to glucosidases[2]). The inhibitory activity of 1*H*-imidazole derivatives was rationalized by postulating the formation of a proton-transfer complex between the 1*H*-imidazole and the two carboxylic groups in the active site of the enzyme [2]. Imidazoles possessing a saccharide-derived moiety and acting as (potential) glycosidase inhibitors have recently been described, such as the 6-epicastanospermine analogue **1** [4], the glucosidase I inhibitor **2** [5], the hexosaminidase inhibitor *Nagstatin* [6] [7] and its analogues **3** and **4** [8], the nucleoside-hydrolase inhibitor **5** [9], and an *N*-chitobiosylhistidinamide, active as an inhibitor of the *endo*- and *exo*-chitinase of the brine shrimp *Artemia salina* chitinase [10]. Protected (furanose-1-*C*-yl)-derived imidazoles have been prepared by addition of 2-lithiated 1-benzylimidazole to



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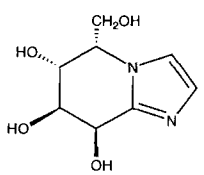

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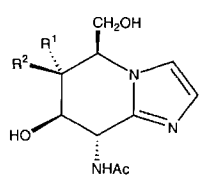
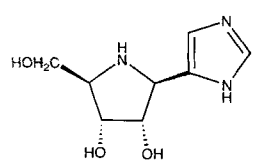


3 R^1 = OH, R^2 = H
4 R^1 = H, R^2 = OH



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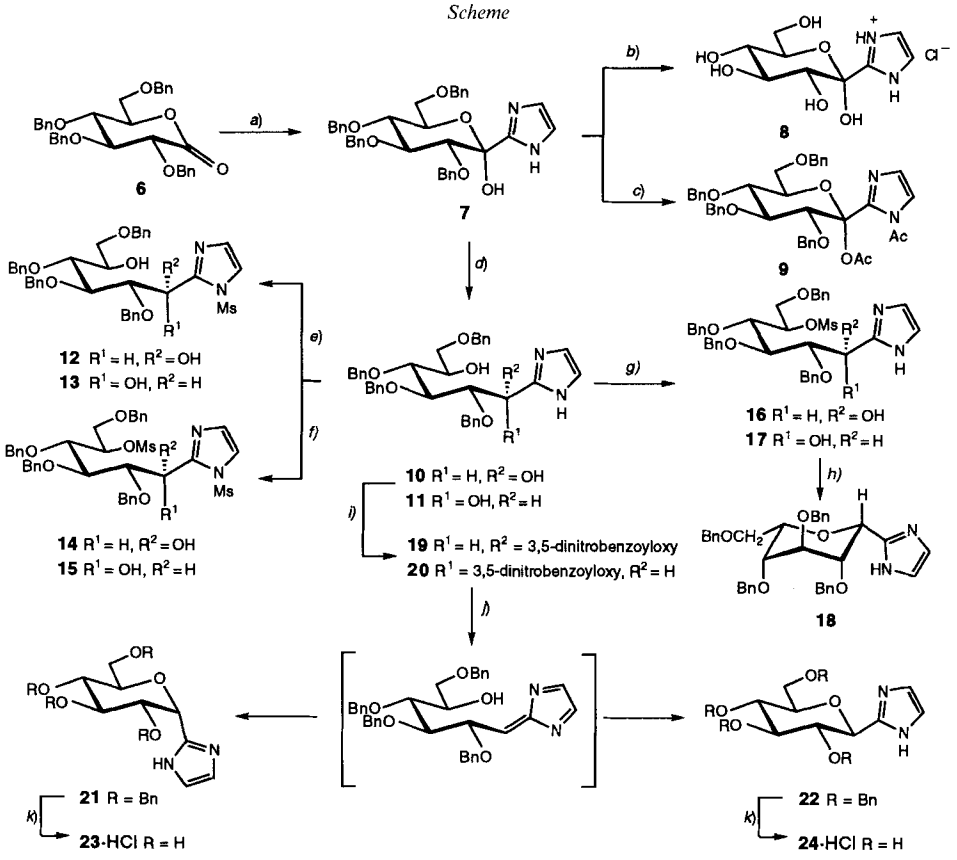
[1]) IC_{50}: 65 mM for 1*H*-imidazole, 16 mM for histamine.

[2]) K_i values [μM] against sweet almond β-glucosidase [2] [3]: 1*H*-imidazole, 530; N_ω-acetylhistamine, 35; L-histidine β-naphthylamide, 17; 4-phenyl-1*H*-imidazole, 0.8.

D-ribono- or L-gulono-1,4-lactones [11] [12] and of 4-lithiated *N*-sulfonylimidazoles to protected ribose- and 2-deoxyribose derivatives [13]. No (pyranos-*C*-yl)imidazoles appear to be known; the closest analogues are the anomeric *O*-benzylated (glucopyranos-1-*C*-yl)thiazoles derived from the corresponding gluconolactone [14]. (Glycopyranos-1-*C*-yl)imidazoles are of interest as potential glycosidase inhibitors. We describe the syntheses of the (glucos-1-*C*-yl)-1*H*-imidazoles **8**, **23**, and **24**, and their evaluation as inhibitors of α- and β-glucosidases.

Results. – Addition of 2-lithio 1-[(dimethylamino)methyl]-1*H*-imidazole [15] to the tetra-*O*-benzylgluconolactone **6** [16] followed by aqueous workup (where the imidazole moiety is deprotected [15]) afforded the crystalline α-D-glucopyranose **7** (68%; *Scheme*). No isomers were observed. Hydrogenolysis yielded the crystalline hydrochloride **8**.

Scheme



a) BuLi, 1-(Me_2NCH_2)Im, THF; 68%. *b*) H_2, 10% Pd/C, 1N HCl, AcOEt; 77%. *c*) Ac_2O, pyridine, 25°, 17 h; 65%. *d*) $NaBH_4$, dioxane, H_2O, AcOH; > 99% (**10**/**11** 12:88). *e*) 1.6 equiv. of MsCl, pyridine, 1.2 equiv. of 4-(dimethylamino)pyridine, 5°, 2.5 h; 39%. *f*) 2.4 equiv. of MsCl, pyridine, 1.2 equiv. of 4-(dimethylamino)pyridine, 25°, 5.5 h; 30%. *g*) 2.3 equiv. of MsCl, pyridine, CH_2Cl_2, 25°, 17 h; 50% of **16**/**17**, 46% of **10**/**11**. *h*) **17**, NaH, DMF; 58%. *i*) 3,5-Dinitrobenzoyl chloride, pyridine; 73% **19**/**20** (15:85). *j*) NaH, DMF; 80% **21**/**22** (25:75). *k*) H_2, 10% Pd/C, 1N HCl, MeOH; 70%.

Reductive dehydroxylation of the hemiacetal **7** or the corresponding *O*-acetyl derivative **9** with Et_3SiH and $BF_3 \cdot OEt_2$ failed, probably due to coordination of BF_3 with the imidazole group, preventing the formation of the glycosyl cation. Therefore, the hemiacetal was reduced with $NaBH_4$ to yield in over 99% a 12:88 mixture of the diols **10**/**11**. The diols were separated by HPLC. The major isomer possesses the (*R*)-configuration at C(1). For reasons which will become clear in sequel, the following reactions were performed with the mixture of the diastereoisomers.

Attempts to selectively mesylate HO–C(1) of **10**/**11** and to close the pyranosyl ring by an intramolecular S_N2-type reaction failed. The imidazoles were first *N*-sulfonylated (MsCl/py) to a mixture **12**/**13**, isolated by preparative TLC in 39%, followed by sulfonylation of HO–C(5), yielding 29% of **14**/**15**. Longer reaction times led to partial conversion to the *N*-desulfonylated monomesylates **16**/**17**. Migration of the *N*-sulfonyl group to HO–C(1), however, could not be induced. The mesylate **17** was cyclized to **18** (see below).

Acylation by 3,5-dinitrobenzoyl chloride of the diols **10**/**11** led regioselectively to the 1-(3,5-dinitrobenzoates) **19**/**20**, isolated in 72% yield, and easily cyclized by treatment with NaH in DMF at −10° to a mixture of the desired anomers **21** and **22** (80%, α-D/β-D 25:75), presumably through an elimination/addition mechanism (*cf.* [17] [13])[3]). The anomers were separated by flash chromatography. Cyclization of the pure dinitrobenzoates **19** and **20**, obtained from the pure diols, yielded similar mixtures of **21** and **22**.

Similarly to **7**, the *C*-glucosides **21** and **22** were deprotected to give the hydrochlorides of **23** and **24**, respectively. The imidazoles **8** and **24** are rather weak competitive inhibitors of sweet-almond β-glucosidases with K_i values of 0.79 and 0.64 mM, respectively, while **23** inhibited yeast (maltase) α-glucosidase with a K_i value of 0.26 mM.

The imidazole **7** is characterized by an OH band at 3500 cm^{-1}, an NH band at 3453 cm^{-1}, and the absence of a C=O absorption. The characteristic ^{13}C signal of the imidazole moiety is found at 147.6 and the one of the hemiacetal C at 94.8 ppm.

Reduction of **7** to the diols **10**/**11** is confirmed by the ^1H-NMR signals of H–C(1) at 5.14 (*d*, $J = 2.9$) and 5.05 ppm (*d*, $J = 4.0$), for the major and the minor isomers, respectively, and by the ^{13}C-NMR spectrum, which shows 5 *d* in addition to the signals of the aromatic C-atoms. The NMR spectra of the mixture **19**/**20** show only two C=O signals at 162.30 and 162.27 ppm, and an H–C(1) *d* at 6.45 and 6.38 ppm, for the major and the minor isomers, respectively, considerably downfield from the corresponding signals of **10** and **11**. The anomeric configuration of **21** and **22** is evidenced by the $J(1,2)$ values of 5.6 and 9.5 Hz, respectively.

Some information about the conformations of the diols **10**/**11** and of the esters **19**/**20** is derived from the values of the vicinal coupling constants. Qualitatively, the conformation of **10** and **11** appears to be quite similar to other open-chain glucose derivatives [18]. The $J(1,2)$ value of **11** ($J(1,2) = 2.9$ Hz) changes upon acylation of HO–C(1) to **20** ($J(1,2) = 8.4$) in agreement with the disappearance of a H-bond between HO–C(1) and BnO–C(3) and a preferred ${}_1G^+$ conformation of **20**. The analogous *O*-acylation of **10**, however, does not affect $J(1,2)$ but $J(2,3)$ which changes from 3.8 in **10** to 7.1 in **19**, evidencing a conformational change, leading to a ${}_2G^-$ sickle conformation.

A comparison of the CD spectra of **7**, **21**, and **22** shows similar negative *Cotton* effects at 220 nm for **7** and **22**, and a positive *Cotton* effect for **21**, further evidencing their configuration at C(1). To determine the C(1) configuration of the diols, a pure sample of **11** was mesylated to **17** and cyclized to the L-*ido*-derivative **18** which adopts a $^1C_4$ conformation. An NOE effect between H–C(1) and H–C(5) is a strong evidence for the (1*R*)-configuration of **18** and consequently also for **11**. The structure of **22** was estab-

[3]) A range of conditions (NaH in DMF, KH in DMF, KF in THF, BuLi in THF) did not lead to equilibration of either the α-D-anomer **21** or the β-D-anomer **22**.

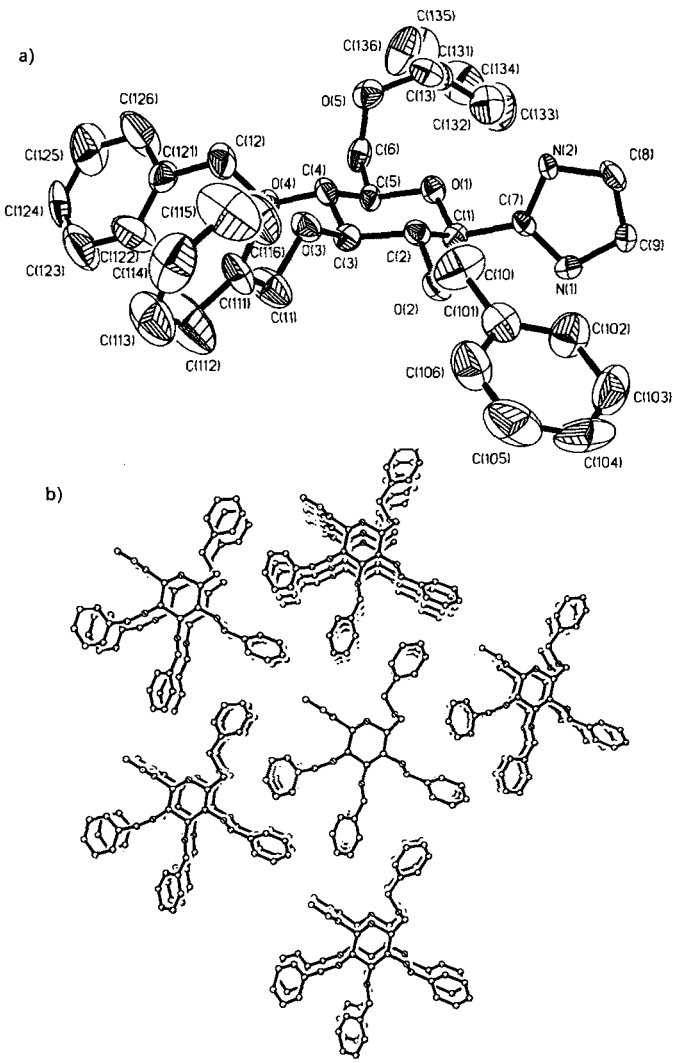


Figure. a) *ORTEP Representation and* b) *X-ray structure of* **22** (projection on the *x*-axis)

lished by X-ray analysis, which shows that the plane of the imidazole ring is perpendicular to the one of the pyranose ring. The torsional angle O(1)–C(1)–C(7)–N(1) (*cf. Fig.*) is –129° and the torsional angle C(2)–C(1)–C(7)–N(1) is 111°. The crystals are stabilized by intermolecular H-bonds between the imidazole rings (N–H···N: 1.69 A)[4]).

The ^{13}C-NMR spectrum of **8** shows the expected characteristic C(1) *s* at 96.93 ppm. The ^{1}H-NMR spectra of **23**·HCl and **24**·HCl exhibit the expected characteristic H–C(1) *d* (**24**·HCl in CD_3OD: 4.63 ppm, $J = 8.8$ Hz; **23**·HCl in D_2O: 5.47 ppm, $J = 6.2$ Hz).

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

The chemical shift of H–C(3) and H–C(5) of **23**·HCl, possessing an axial imidazolium substituent, changes upon deprotonation of the imidazolium moiety. Neutralization of **23**·HCl in D_2O by Et_3N induces a downfield shift of 0.5 ppm for H–C(3) and 0.3 ppm for H–C(5). At the same time, the signal of H–C(1) is shifted upfield ($\Delta\delta = 0.3$ ppm). The values of the coupling constants do not change noticeably. The pyranose ring thus remains in a flattened $^4C_1$ conformation. The chemical-shift differences, however, indicate a change of the torsion angle between the imidazole and the pyranose rings. In the neutral compound, the torsional angles O(1)–C(1)–C(7)–N(1) and C(2)–C(1)–C(7)–N(1) appears to be close to 120°, similarly to solid **22** (*Fig.*), exposing H–C(3) and H–C(5) to the shielding effect of the imidazole ring, while the protonated imidazole ring appears to rotate by *ca.* 90° around the C(1)–C(7) bond, exposing H–C(3) and H–C(5) to its deshielding effect. Neutralization of **24**·HCl, possessing an equatorial imidazolium substituent, does not lead to any similar change of the chemical shift of the pyranose ring protons, except for H–C(1), which is shifted upfield ($\Delta\delta \approx 0.2$ ppm).

We thank *A. Martelletti* for determining the X-ray structure, and the *Swiss National Science Foundation* and *F. Hoffmann-La Roche AG*, Basel, for generous support.

Experimental Part

General. See [19]. Prep. HPLC: *Merck LiChrosorb NH2* (7 μm) 250 × 25 mm column. UV Spectra (λ_{max} in nm (log ε)): 1-cm quartz cell. CD Spectra (λ_{max} in nm (molar ellipticity [θ] in deg·cm^2·decimol^{-1})): *JASCO-J-710* spectropolarimeter. IR Spectra: KBr or 3% $CHCl_3$ soln. K_i Determinations were performed at pH 6.8, 37° with 4-nitrophenyl β-D-glucopyranoside (*Fluka Biochemica*) as substrate for **8** and **24**, and 4-nitrophenyl α-D-glucopyranoside (*Fluka Biochemica*) as substrate for **23** [20].

*2,3,4,6-Tetra-*O*-benzyl-1-*C*-(1*H*-imidazol-2-yl)-α-*D*-glucopyranose* (**7**). At −78°, a soln. of 1-[(dimethylamino)methyl]-1*H*-imidazole (764 mg, 6.87 mmol) in THF (40 ml) was treated dropwise with BuLi (1.6M in hexane, 4.24 ml) and stirred at −78° for 1 h. A soln. of **6** (3.320 g, 6.15 mmol) in THF (30 ml) was added dropwise within 35 min at −78°. The yellow soln. was then stirred at −78° for 5 h and neutralized with a sat. soln. of NH_4Cl. Normal workup afforded 3.8 g of a white foam which was crystallized from $CHCl_3/Et_2O$ 15:85 (82 ml) to give 2.52 g of **7** (67.5%). White, slightly hygroscopic crystals. M.p. 141°. R_f (AcOEt/hexane 4:1) 0.39. $[\alpha]_D^{25} = +31.3$ ($c = 0.93$, $CHCl_3$). UV (MeOH): 208 (4.6). CD (MeOH): 220 (−15400). IR ($CHCl_3$): 3500*w*, 3453*m*, 3191*w*, 3090*w*, 3067*w*, 3043*w*, 3008*m*, 2928*m*, 2870*m*, 1603*w*, 1497*m*, 1454*s*, 1403*m*, 1361*m*, 1263*m*, 1152*s*, 1067*s*, 1028*s*, 949*m*, 913*w*, 823*w*, 646*w*, 608*w*, 532*w*. ^{1}H-NMR ($CDCl_3$): 3.59 (*dd*, $J = 2.1$, 10.2, H–C(6)); 3.68 (*dd*, $J = 4.2$, 10.5, H′–C(6)); 3.74 (*t*, $J \approx 9.9$, H–C(4)); 3.99 (*d*, $J = 9.3$, H–C(2)); 4.13 (*t*, $J = 9.1$, H–C(3)); 4.12–4.20 (*m*, H–C(5)); 4.22 (*d*, $J = 10.3$, PhC*H*); 4.36 (*s*, PhCH_2); 4.47 (*d*, $J = 10.2$, PhC*H*); 4.52 (*d*, $J = 10.4$, PhC*H*); 4.84 (*d*, $J = 11.1$, PhC*H*); 4.85 (*d*, $J = 11.0$, PhC*H*); 4.95 (*d*, $J = 11.1$, PhC*H*); 6.91 (*s*, NCH=CHN); 7.36–7.00 (*m*, 20 arom. H). ^{1}H-NMR (C_6D_6): 3.58 (*dd*, $J = 1.3$, 10.0, irrad. at 3.71 → br. *s*, irrad. at 4.47 → *d*, $J \approx 10.0$, H–C(6)); 3.71 (*dd*, $J = 3.9$, 10.6, irrad. at 4.47 → *d*, $J \approx 10.0$, H′–C(6)); 4.00 (*t*, $J = 9.4$, H–C(4)); 4.23–4.33 (*m*, H–C(2), PhCH_2); 4.36 (*d*, $J = 10.3$, PhC*H*); 4.43 (*t*, $J = 9.3$, H–C(3)); 4.45–4.50 (*m*, irrad. at 3.71 → br. *d*, $J \approx 10.5$, irrad. at 4.00 → br. *s*, H–C(5)); 4.57–4.62 (*m*, PhCH_2); 4.84 (*d*, $J = 11.4$, PhC*H*); 4.96 (*d*, $J = 11.5$, PhC*H*); 5.00 (*d*, $J = 11.5$, PhC*H*); 6.5 (br. *s*, OH); 6.9–7.4 (*m*, 22 arom. H); 10.5 (br. *s*, NH). ^{13}C-NMR ($CDCl_3$): 68.79 (*t*); 71.23 (*d*); 73.67 (*t*); 74.80 (*t*); 74.94 (*t*); 75.74 (*t*); 77.49 (*d*); 82.80 (*d*); 83.44 (*d*); 94.77 (*s*); 127.6–128.6 (several *d*); 136.96 (*s*); 137.68 (*s*); 138.25 (*s*); 138.65 (*s*); 147.62 (*s*). FAB-MS: 607 (100, $[M + 1]^+$), 589 (36, $[M - H_2O]^+$). Anal. calc. for $C_{37}H_{38}N_2O_6$ (606.72): C 73.25, H 6.31, N 4.62; found: C 72.99, H 6.58, N 4.60.

*1-*C*-(1*H*-Imidazol-2-yl)-α-*D*-glucopyranose Hydrochloride* (**8**). At 25°, a suspension of Pd/C (10%, 70 mg) in 1N HCl (5 ml) was activated for 2 h under H_2 (7 bar). After the addition of a soln. of **7** (69 mg, 0.114 mmol) in AcOEt (2 ml), the suspension was stirred at 7 bar and 25° for 24 h, diluted with MeOH, and filtered through *Celite*. The filtrate was concentrated to *ca.* 0.5 ml. Crystallization was induced by addition of acetone (15 ml) affording 25 mg of **8** (77%). White crystals. M.p. 205°. R_f (AcOEt/MeOH/AcOH 7:5:1) 0.125. $[\alpha]_D^{25} = +51.4$ ($c = 0.52$, H_2O). UV (H_2O): 214 (3.7). IR (KBr): 3487*s*, 3349*s*, 3290*s*, 3160*s*, 3092*s*, 3003*s*, 2964*m*, 2910*m*, 1618*m*, 1567*w*, 1518*w*, 1423*m*, 1384*m*, 1356*m*, 1332*m*, 1276*s*, 1259*m*, 1195*m*, 1169*m*, 1151*m*, 1111*s*, 1092*m*, 1068*s*, 1051*s*, 1032*s*, 1018*s*, 938*m*, 912*m*, 894*m*, 878*w*, 851*w*, 814*m*, 785*s*, 622*m*, 574*m*, 553*m*, 530*m*. ^{1}H-NMR (D_2O): 3.50 (*d*, $J = 9.3$, H–C(2)); 3.63 (*t*, $J = 9.0$, H–C(4)); 3.83–4.05 (*m*, irrad. at 3.50 → change, H–C(5), 2 H–C(6), H–C(3)); 7.50 (*s*, NCH=CHN). ^{13}C-NMR (D_2O): 62.87 (*t*); 71.72 (*d*); 75.56 (*d*); 75.91 (*d*); 77.15 (*d*); 96.93 (*s*); 122.11 (*d*); 122.25 (*d*); 148.18 (*s*). FAB-MS: 247 (100, $[M - Cl]^+$), 229 (13, $[M - H_2O - Cl]^+$). Anal. calc. for $C_9H_{15}ClN_2O_6$ (282.68): C 38.24, H 5.35, Cl 12.54, N 9.91; found: C 38.42, H 5.15, Cl 12.57, N 9.79.

1-O-Acetyl-1-C-(1-acetyl-1H-imidazol-2-yl)-2,3,4,6-tetra-O-benzyl-α-D-glucopyranose (**9**). A soln. of **7** (110 mg, 0.18 mmol) in pyridine (2 ml) and Ac_2O (1 ml) was stirred at 25° for 14 h. Normal workup and FC (AcOEt/hexane 1:1) afforded 82 mg (65%) of **9**. R_f (AcOEt) 0.57. IR ($CHCl_3$): 3066*w*, 3043*w*, 3008*m*, 2927*m*, 2867*m*, 1758*s*, 1604*w*, 1497*m*, 1454*m*, 1389*m*, 1366*m*, 1265*s*, 1156*s*, 1085*s*, 1028*m*, 1013*m*, 948*m*. ^{1}H-NMR ($CDCl_3$): 2.21 (*s*, Ac); 2.39 (*s*, Ac); 3.69 (*dd*, J = 1.0, 10.8, irrad. at 3.87 → *d*, $J \approx 10.6$, H–C(6)); 3.77 (*dd*, J = 3.2, 10.8, irrad. at 3.87 → *d*, $J \approx 10.0$, H′–C(6)); 3.83–3.92 (*m*, H–C(5)); 3.92 (*t*, J = 9.9, H–C(4)); 4.12 (*t*, J = 9.1, 10.0, irrad. at 4.54 → *d*, $J \approx 8.7$, H–C(3)); 4.43–4.51 (*m*, 2 PhC*H*); 4.54 (*d*, J = 9.3, H–C(2)); 4.55–4.64 (*m*, 3 PhC*H*); 4.88 (*d*, J = 10.8, PhC*H*); 4.90 (*d*, J = 10.7, PhC*H*); 4.98 (*d*, J = 11.1, PhC*H*); 7.00 (*d*, J = 1.7, NCH=C); 7.11 (*d*, J = 1.7, NCH=C); 7.14–7.37 (*m*, 20 arom. H). ^{13}C-NMR ($CDCl_3$, 50 MHz): 22.17 (*q*); 25.28 (*q*); 68.71 (*t*); 73.35 (*t*); 73.93 (*d*); 74.88 (*t*); 75.60 (*t*); 75.93 (*t*); 77.49 (*d*); 79.86 (*d*); 83.87 (*d*); 100.55 (*s*); 120.14 (*d*); 127.69–129.04 (several *d*); 138.35 (*s*); 138.43 (*s*); 138.68 (*s*); 139.07 (*s*); 144.93 (*s*); 167.33 (*s*); 168.68 (*s*).

(1S)- and (1R)-2,3,4,6-Tetra-O-benzyl-1-C-(1H-imidazol-2-yl)-D-glucitol (**10** and **11**, resp.). A soln. of **7** (1.2 g, 1.98 mmol) in dioxane/H_2O 4:1 (90 ml) and AcOH (0.3 ml) was treated at 0° within 3 min with $NaBH_4$ (1.2 g). The suspension was stirred at 0° for 40 min and at 25° for 1 h. Neutralization by addition of a sat. NH_4Cl soln. (200 ml) and normal workup afforded 1.2 g (99%) of **10**/**11** 12:88 (^{1}H-NMR). White foam. FC (AcOEt) and HPLC (THF/hexane 1:10) of the crude material from a different batch provided pure samples of **10** and **11**.

Data of **10**/**11** 12:88: R_f (AcOEt) 0.13. UV (MeOH): 258 (2.9), 219 (3.9). CD (MeOH): 220 (−1800). IR ($CHCl_3$): 3456*m*, 3090*w*, 3067*w*, 3043*w*, 3007*m*, 2926*m*, 2869*m*, 1603*w*, 1545*w*, 1497*w*, 1454*s*, 1401*m*, 1358*m*, 1257*m*, 1075*s*, 1028*s*, 920*w*, 850*w*, 648*w*, 604*w*, 534*w*. FAB-MS: 609 (100, $[M + 1]^+$).

Data of **10**: UV (MeOH): 258 (3.0), 218 (4.1). CD (MeOH): 223 (−10200). IR (CH_2Cl_2): 3546*w*, 3446*m*, 3089*w*, 3033*m*, 2927*m*, 2860*m*, 1616*w*, 1576*w*, 1540*w*, 1497*m*, 1456*m*, 1395*m*, 1362*w*, 1210*w*, 1098*s*, 1028*s*, 920*w*. ^{1}H-NMR ($CDCl_3$): 3.60–3.64 (*m*, irrad. at 3.95 → change, 2 H–C(6)); 3.78 (*dd*, J = 3.8, 4.4, H–C(3)); 3.86 (*dd*, J = 4.9, 7.1, irrad. at 3.78 → *d*, $J \approx 7.1$, H–C(4)); 3.90–4.00 (*m*, irrad. at 3.86 → change, H–C(5)); 4.22 (*t*, J = 3.9, irrad. at 5.05 → *d*, $J \approx 3.8$, irrad. at 3.78 → *d*, $J \approx 4.0$, H–C(2)); 4.38 (*d*, J = 11.2, PhC*H*); 4.49 (*d*, J = 11.9, PhC*H*); 4.51 (*d*, J = 11.9, PhC*H*); 4.54 (*d*, J = 11.3, PhC*H*); 4.55 (*d*, J = 10.9, PhC*H*); 4.59 (*d*, J = 11.8, PhC*H*); 4.62 (*s*, 2 PhC*H*); 4.66 (*d*, J = 11.2, PhC*H*); 5.05 (*d*, J = 4.0, irrad. at 4.36 → *s*, H–C(1)); 6.93 (*s*, NCH=CHN); 7.17–7.36 (*m*, 20 arom. H). ^{13}C-NMR ($CDCl_3$): 68.32 (*d*); 71.19 (*d*); 71.30 (*t*); 73.45 (*t*); 73.62 (*t*); 74.03 (*t*); 74.44 (*t*); 77.25 (*d*); 79.06 (*d*); 80.73 (*d*); 127.69–128.55 (several *d*); 137.60 (*s*); 137.75 (*s*); 138.03 (*s*); 138.08; 147.83 (*s*).

Data of **11**: UV (MeOH): 258 (3.0), 215 (4.4). CD (MeOH): 228 (−1800). IR (CH_2Cl_2): 3554*w*, 3447*m*, 3089*w*, 3033*m*, 2914*m*, 2869*m*, 1605*w*, 1586*w*, 1543*w*, 1497*m*, 1454*m*, 1399*m*, 1358*m*, 1213*m*, 1074*s*, 1028*s*, 920*w*. ^{1}H-NMR ($CDCl_3$): 3.62 (*dd*, J = 5.0, 9.9, H–C(6)); 3.66 (*dd*, J = 3.5, 9.9, H′–C(6)); 3.87 (*dd*, J = 4.0, 7.2, irrad. at 4.10 → *s*, H–C(4)); 4.04–4.17 (*m*, irrad. at 3.6 or 3.87 → change, H–C(3), H–C(5)); 4.22 (*d*, J = 11.0, PhC*H*); 4.36 (*dd*, J = 2.9, 6.1, irrad. at 4.10 → *d*, $J \approx 2.7$, H–C(2)); 4.49 (*d*, J = 11.9, PhC*H*); 4.51 (*d*, J = 11.3, PhC*H*); 4.55 (*d*, J = 12.0, PhC*H*); 4.56 (*d*, J = 11.4, PhC*H*); 4.57–4.63 (*m*, 2 PhC*H*); 5.14 (*d*, J = 2.9, irrad. at 4.36 → *s*, H–C(1)); 6.92 (*s*, NCH=CHN); 7.10–7.50 (*m*, 20 arom. H). ^{13}C-NMR ($CDCl_3$): 68.21 (*d*); 71.12 (*d*); 71.36 (*t*); 73.46 (*t*, 2 C); 74.39 (*t*); 74.80 (*t*); 77.19 (*d*); 79.59 (*d*); 80.85 (*d*); 127.00–129.00 (several *d*); 137.67 (*s*); 137.79 (*s*); 137.92 (*s*); 138.09 (*s*); 148.64 (*s*).

(1S)- and (1R)-2,3,4,6-Tetra-O-benzyl-1-C-[1-(methylsulfonyl)-1H-imidazol-2-yl]-D-glucitol (**12** and **13**, resp.). At 5°, a soln. of **10**/**11** 12:88 (100 mg, 0.16 mmol) in pyridine (2 ml, freshly distilled) was treated with 4-(dimethylamino)pyridine (23 mg, 0.19 mmol) and methanesulfonyl chloride (MsCl, 20 µl, 0.26 mmol), and kept for 2.5 h at 5°. After the addition of ice/sat. NH_4Cl soln., normal workup and prep. TLC (AcOEt) afforded 44 mg (39%) of **12**/**13** 1:5 (^{1}H-NMR), 6 mg (5%) of **14**/**15**, 3 mg (3%) of **10**/**11**. R_f (AcOEt) 0.54. IR ($CHCl_3$): 3350*m*, 3090*w*, 3067*w*, 3043*w*, 3008*w*, 2927*m*, 2866*m*, 1604*w*, 1536*w*, 1498*m*, 1454*m*, 1375*s*, 1330*w*, 1262*m*, 1178*m*, 1167*m*, 1151*s*, 1091*s*, 1028*m*, 970*m*. ^{1}H-NMR ($CDCl_3$, 200 MHz, **12**/**13** 1:5): signals of **13**: 3.08 (*s*, Me); 3.65 (*dd*, J = 5.0, 9.9, irrad. at 4.06 → *m*, H–C(6)); 3.71 (*dd*, J = 3.3, 9.9, irrad. at 4.06 → *d*, $J \approx 9.6$, H′–C(6)); 3.89 (*dd*, J = 4.2, 7.5, irrad. at 4.06 → *s*, H–C(4)); 4.08 (*t*, J = 4.4, H–C(3)); 4.04–4.12 (*m*, irrad. at 3.68 → *d*, $J \approx 8.0$, H–C(5)); 4.38 (*d*, J = 10.8, PhC*H*); 4.49–4.71 (*m*, 5 PhC*H*, H–C(2)); 4.82 (*d*, J = 10.8, PhC*H*); 4.94 (*d*, J = 10.8, PhC*H*); 5.40 (*d*, J = 4.3, H–C(1)); 6.99 (*d*, J = 1.7, NCH=C); 7.01–7.50 (*m*, 21 arom. H); signals of **12**: 3.03 (*s*, 0.6 H, Me); 5.50 (*d*, J = 8.7, 0.2 H, H–C(1)). ^{13}C-NMR ($CDCl_3$, 50 MHz, **12**/**13** 1:5, only signals of **13** listed): 43.29 (*q*); 65.49 (*d*); 71.25 (*t*); 71.49 (*d*); 73.43 (*t*); 73.49 (*t*); 73.85 (*t*); 74.73 (*t*); 76.40 (*d*); 77.65 (*d*); 79.21 (*d*); 120.38 (*d*); 127.32 (*d*); 127.70–128.61 (several *d*); 137.49 (*s*); 137.88 (*s*, 2 C); 138.20 (*s*); 148.61 (*s*).

(1S)- and (1R)-2,3,4,6-Tetra-O-benzyl-5-O-(methylsulfonyl)-1-C-[1-(methylsulfonyl)-1H-imidazol-2-yl]-D-glucitol (**14** and **15**, resp.). At 5°, a soln. of **10**/**11** 12:88 (100 mg, 0.16 mmol) in pyridine (2 ml, freshly distilled) was treated with 4-(dimethylamino)pyridine (23 mg, 0.19 mmol) and MsCl (20 µl, 0.26 mmol), and allowed to warm up to 25° within 1 h. After stirring for 2 h at 25°, a second fraction of MsCl (10 µl, 0.13 mmol) was added and stirring continued for a further 3.5 h. After the addition of ice/sat. NH_4Cl soln., normal workup and prep. TLC

(AcOEt) afforded 33 mg (29.5%) of **14**/**15** 15:85. R_f (AcOEt) 0.64. IR ($CHCl_3$): 3600–3300*w*, 3090*w*, 3067*w*, 3043*w*, 3008*w*, 2928*m*, 2870*m*, 1604*w*, 1537*w*, 1497*m*, 1454*m*, 1408*m*, 1375*s*, 1262*m*, 1175*s*, 1152*s*, 1098*s*, 1043*s*, 1028*s*, 969*s*. ^{1}H-NMR ($CDCl_3$, 200 MHz, **14**/**15** 15:85): signals of **15**: 2.94 (*s*, Me); 3.25 (*s*, Me); 3.45 (*d*, J = 6.7, OH–C(1)); 3.80 (*dd*, J = 5.0, 6.2, irrad. at 4.28 → *d*, $J \approx 4.5$, H–C(3)); 3.85–3.90 (*m*, irrad. at 5.20 → *s*, 2 H–C(6)); 4.28 (*dd*, J = 2.5, 6.2, irrad. at 5.20 → *d*, $J \approx 6.2$, H–C(4)); 4.42–4.62 (*m*, 4 PhC*H*, H–C(2)); 4.70–4.85 (*m*, 4 PhC*H*); 5.16–5.23 (*m*, H–C(5)); 5.38 (*dd*, J = 4.1, 7.0, irrad. at 3.45 → *d*, $J \approx 4.1$, H–C(1)); 6.96 (*d*, J = 1.7, NCH=C); 7.15–7.45 (21 arom. H); signals of **14**: 2.90 (*s*, 0.6 H, Me); 3.09 (*s*, 0.6 H, Me). ^{13}C-NMR ($CDCl_3$, 200 MHz, **14**/**15** 15:85, only signals of **15** listed): 38.50 (*q*); 43.50 (*q*); 67.40 (*d*); 69.05 (*t*); 73.38 (*t*); 74.49 (*t*); 74.59 (*t*); 74.95 (*t*); 78.08 (*d*); 78.41 (*d*); 80.03 (*d*); 83.19 (*d*); 120.35 (*d*); 127.50–128.80 (several *d*); 137.60 (*s*); 137.66 (*s*); 137.80 (*s*); 137.89 (*s*); 148.10 (*s*).

(1S)- and (1R)-2,3,4,6-Tetra-O-benzyl-5-O-(methylsulfonyl)-1-C-(1H-imidazol-2-yl)-D-glucitol (**16** and **17**, resp.). a) At 5°, a soln. of crude **10**/**11** 12:88 (50 mg, 0.08 mmol) in CH_2Cl_2/pyridine 1:10 (2.2 ml) was treated with MsCl (14 µl, 0.18 mmol), and kept for 17 h at 25°. After addition of ice/sat.NH_4Cl soln., normal workup and FC (AcOEt/hexane 2:1) afforded 28 mg (50%) of **16**/**17** 1:5 (^{1}H-NMR) and 23 mg (46%) of **10**/**11**. Selected ^{1}H-NMR ($CDCl_3$, 200 MHz) signal of **16**: 5.11 (*d*, J = 4.5, 0.2 H, H–C(1)).

b) Similarly, a pure sample of **11** (15 mg, 0.005 mmol) gave 8 mg (47%) of **17** and 5 mg (33%) of **11**.

Data of **17**: R_f (AcOEt) 0.41. IR ($CHCl_3$): 3550–3460*w*, 3455*m*, 3450–3200*w*, 3090*w*, 3067*w*, 3043*w*, 3007*w*, 2929*m*, 2872*m*, 1605*w*, 1545*w*, 1497*m*, 1454*s*, 1401*w*, 1355*s*, 1174*s*, 1094*s*, 1028*s*, 970*w*. ^{1}H-NMR ($CDCl_3$, 200 MHz): 2.94 (*s*, Me); 3.73–3.95 (*m*, H–C(3), 2 H–C(6)); 4.19 (*dd*, J = 2.3, 5.7, irrad. at 5.15 → *d*, $J \approx 5.5$, H–C(4)); 4.26 (*d*, J = 11.5, PhC*H*); 4.32 (*dd*, J = 2.5, 5.6, irrad. at 5.11 → *d*, $J \approx 5.6$, H–C(2)); 4.40–4.50 (*m*, 3 PhC*H*); 4.54 (*d*, J = 11.0, PhC*H*); 4.62 (*d*, J = 11.0, PhC*H*); 4.68 (*d*, J = 11.1, PhC*H*); 4.76 (*d*, J = 11.0, PhC*H*); 5.11 (*d*, J = 2.5, irrad. at 4.32 → *s*, H–C(1)); 5.15 (*m*, irrad. at 3.90 → *d*, $J \approx 2.0$, H–C(5)); 6.95 (*s*, 2 NCH=C); 7.20–7.40 (*m*, 20 arom. H).

(1R)-1,5-Anhydro-2,3,4,6-tetra-O-benzyl-1-C-(1H-imidazol-2-yl)-L-iditol (**18**). At 25°, a soln. of **17** (4 mg, 0.006 mmol) in DMF (1 ml) was treated with NaH (5 mg, 0.21 mmol) and stirred for 3 h at 100°. Normal workup and FC (AcOEt/hexane 1:1) gave 2.1 mg (59%) of **18**. R_f (AcOEt) 0.49. UV (MeOH): 258 (3.1), 211 (4.4.). CD (MeOH): 223 (−12000). IR ($CHCl_3$): 3448*m*, 3222*w*, 3088*w*, 3066*w*, 3008*w*, 2960*m*, 2927*m*, 2860*w*, 1558*m*, 1540*m*, 1456*m*, 1362*w*, 1262*s*, 1015*s*, 918*m*. ^{1}H-NMR ($CDCl_3$): 3.37–3.40 (*m*, irrad. at 3.62 → br. *s*, irrad. at 4.12 → *dd*, $J \approx 0.9$, 2.1, H–C(4)); 3.57 (*dd*, J = 5.7, 9.8, irrad. at 4.12 → *d*, $J \approx 10.2$, H–C(6)); 3.62 (*dd*, J = 2.1, 2.6, irrad. at 3.39 → *d*, $J \approx 2.6$, H–C(3)); 3.77 (*dd*, J = 6.6, 10.1, irrad. at 4.12 → *d*, J = 9.8, H′–C(6)); 3.79–3.82 (br. *s*, irrad. at 3.39 → change, irrad. at 3.62 → *d*, $J \approx 1.7$, irrad. at 5.10 → change, H–C(2)); 4.12 (*ddd*, J = 1.8, 5.8, 6.6, H–C(5)); 4.15 (*d*, J = 11.8, PhC*H*); 4.24 (*d*, J = 12.1, PhC*H*); 4.25 (*d*, J = 12.1, PhC*H*); 4.34 (*d*, J = 12.1, PhC*H*); 4.39 (*d*, J = 12.4, PhC*H*); 4.48 (*d*, J = 12.3, PhC*H*); 4.53 (*d*, J = 12.2, PhC*H*); 4.56 (*d*, J = 12.1, PhC*H*); 5.1 (*d*, J = 1.6, H–C(2)); 6.96–7.40 (*m*, 22 arom. H); 9.76 (br. *s*, exchange with D_2O, NH). ^{13}C-NMR ($CDCl_3$, 75 MHz): 69.64 (*t*); 70.37 (*d*); 71.93 (*t*); 72.22 (*t*); 72.39 (*d*); 73.33 (*t*); 73.41 (*t*); 73.53 (*d*); 74.61 (*d*); 75.60 (*d*); 115.20 (*d*); 127.70–128.76 (several *d*); 137.53 (*s*); 137.68 (*s*); 137.78 (*s*); 138.06 (*s*); 145.88 (*s*). FAB-MS: 592 (35, $[M + 2]^+$), 591 (100, $[M + 1]^+$).

(1S)- and (1R)-2,3,4,6-Tetra-O-benzyl-1-O-(3,5-dinitrobenzoyl)-1-C-(1H-imidazol-2-yl)-D-glucitol (**19** and **20**, resp.). a) *From Crude* **10**/**11**: At 25°, a soln. of **10**/**11** 12:88 (500 mg, 0.82 mmol) in pyridine (20 ml, freshly distilled) was treated with 3,5-dinitrobenzoyl chloride (228 mg, 0.99 mmol) and kept for 2 h at 0° and for 18 h at 25°. After the addition of ice/H_2O (20 ml), normal workup afforded a yellow foam. FC (AcOEt/hexane 10:15) gave 478.5 mg (72.5%) of **19**/**20** 15:85 (^{1}H-NMR). Foam.

b) Similarly, a pure sample of **10** (2.8 mg, 0.005 mmol) gave 2.4 mg of **19** (65%).

c) Similarly, a pure sample of **11** (80 mg, 0.13 mmol) gave 72 mg of **20** (68%).

Data of **19**/**20** 12:88: R_f (AcOEt) 0.75. UV (MeOH): 209 (4.7). IR ($CHCl_3$): 3570*w*, 3407*w*, 3102*w*, 3067*w*, 3043*w*, 3007*w*, 2962*w*, 2870*w*, 1954*w*, 1736*m*, 1629*w*, 1599*w*, 1599*w*, 1548*s*, 1497*w*, 1455*w*, 1345*s*, 1263*s*, 1166*m*, 1092*s*, 1028*w*, 922*w*, 823*w*. FAB-MS: 804 (52, $[M + 2]^+$), 803 (100, $[M + 1]^+$), 591 (28, $[M + 1 - C_7H_4N_2O_6]^+$).

Data of **19**: UV (MeOH): 214 (4.8). CD (MeOH): 222 (−340000). IR (CH_2Cl_2): 3562*w*, 3438*m*, 3102*m*, 3033*m*, 2962*w*, 2927*w*, 1737*s*, 1630*m*, 1548*s*, 1497*w*, 1454*m*, 1345*s*, 1288*m*, 1209*w*, 1163*w*, 1096*s*, 1027*s*. ^{1}H-NMR ($CDCl_3$): 2.91 (br. *s*, OH); 3.64 (*dd*, J = 4.5, 9.8, irrad. at 4.09 → *d*, $J \approx 9.5$, H–C(6)); 3.70 (*dd*, J = 3.3, 9.7, irrad. at 4.09 → *d*, $J \approx 9.8$, H′–C(6)); 3.71 (*dd*, J = 3.5, 7.1, irrad. at 3.81 → *d*, $J \approx 7.0$, irrad. at 4.60 → *d*, $J \approx 3.6$, H–C(3)); 3.81 (*dd*, J = 3.5, 7.8, irrad. at 4.09 → *d*, $J \approx 3.5$, H–C(4)); 4.04–4.13 (*m*, H–C(5)); 4.51 (*d*, J = 11.8, PhC*H*); 4.54 (*d*, J = 12.0, PhC*H*); 4.55 (*d*, J = 10.6, PhC*H*); 4.56 (*d*, J = 10.9, 2 PhC*H*); 4.58 (*d*, J = 11.7, PhC*H*); 4.60 (*dd*, J = 3.4, 7.1, irrad. at 6.38 → *d*, $J \approx 7.3$, H–C(2)); 4.67 (*d*, J = 11.5, PhC*H*); 4.78 (*d*, J = 11.1, PhC*H*); 6.38 (*d*, J = 3.8, irrad. at 4.60 → *s*, H–C(1)); 7.05–7.38 (*m*, 22 arom. H); 8.93 (*d*, J = 2.1, 2 arom. H); 9.18 (*t*, J = 2.1, 1

arom. H); 9.98 (br. *s*, NH). ^{1}H-NMR ($CDCl_3$ + 5% CD_3OD): 3.65 (*dd*, *J* = 4.4, 9.7, H–C(6)); 3.70 (*dd*, *J* = 2.9, 9.8, H′–C(6)); 3.75 (*dd*, *J* = 4.2, 6.4, irrad. at 4.48 → *d*, *J* ≈ 4.0, H–C(3)); 3.82 (*dd*, *J* = 4.1, 7.8, irrad. at 3.75 → *d*, *J* ≈ 7.6, H–C(4)); 4.01 (*ddd*, *J* = 2.9, 4.4, 7.6, H–C(5)); 4.34 (*d*, *J* = 11.2, PhC*H*); 4.48 (*dd*, *J* = 5.0, 6.4, irrad. at 3.75 → *d*, *J* ≈ 5.1, H–C(2)); 4.50 (*d*, *J* = 11.2, PhC*H*); 4.51 (*d*, *J* = 11.8, PhC*H*); 4.56 (*d*, *J* = 11.5, PhC*H*); 4.58 (*dd*, *J* = 11.8, PhC*H*); 4.59 (*d*, *J* = 11.5, PhC*H*); 4.67 (*d*, *J* = 11.2, 2 PhC*H*); 6.24 (*d*, *J* = 4.9, irrad. at 4.48 → *s*, H–C(1)); 7.05–7.41 (*m*, 22 arom. H); 8.95 (*d*, *J* = 2.1, 2 arom. H); 9.16 (*t*, *J* = 2.1, 1 arom. H). ^{13}C-NMR ($CDCl_3$): 70.79 (*t*); 70.94 (*d*); 71.63 (*d*); 73.50 (*t*); 73.61 (*t*); 74.67 (*t*); 75.65 (*t*); 77.23 (*d*); 78.69 (*d*); 79.20 (*d*); 122.40 (*d*); 127.83–129.50 (several *d*); 133.17 (*s*); 137.41 (*s*, 2 C); 137.88 (*s*, 2 C); 142.28 (*s*); 148.42 (2*s*); 161.27 (*s*).

Data of **20**: UV (MeOH): 210 (5.7). CD (MeOH): 211 (−210000). IR (CH_2Cl_2): 3566*w*, 3426*m*, 3101*m*, 3033*m*, 2921*m*, 2872*m*, 1734*s*, 1630*m*, 1599*w*, 1549*s*, 1497*w*, 1454*m*, 1345*s*, 1497*w*, 1454*m*, 1345*s*, 1288*m*, 1209*w*, 1166*m*, 1076*s*, 1028*m*, 984*w*. ^{1}H-NMR ($CDCl_3$): 3.63 (*d*, *J* = 4.6, 2 H–C(6)); 3.84 (*t*, *J* = 4.2, irrad. at 4.71 → *d*, *J* ≈ 4.2, H–C(3)); 3.96 (*dd*, *J* = 4.7, 6.5, H–C(4)); 4.07–4.11 (*m*, irrad. at 3.63 → *d*, *J* ≈ 7.0, H–C(5)); 4.29 (*d*, *J* = 11.5, PhC*H*); 4.53 (*d*, *J* = 11.7, 2 PhC*H*); 4.58 (*d*, *J* = 11.8, PhC*H*); 4.61 (*d*, *J* = 10.9, PhC*H*); 4.67 (*d*, *J* = 10.7, PhC*H*); 4.71 (*dd*, *J* = 3.7, 8.5, H–C(2)); 4.74 (*d*, *J* = 12.2, PhC*H*); 4.90 (*d*, *J* = 11.8, PhC*H*); 6.45 (*d*, *J* = 8.4, irrad. at 4.70 → *s*, H–C(1)); 6.69 (br. *s*, NCH=CHN); 6.98 (br. *s*, NCH=CHN); 7.20–7.50 (*m*, 20 arom. H); 8.97 (*d*, *J* = 2.1, 2 arom. H); 9.10 (*t*, *J* = 2.1, 1 arom. H); 9.16 (br. *s*, NH). ^{1}H-NMR ($CDCl_3$ + 5% CD_3OD): 3.62 (*d*, *J* = 4.4, 2 H–C(6)); 3.84 (*t*, *J* = 4.4, H–C(3)); 3.91 (*dd*, *J* = 4.2, 6.7, H–C(4)); 4.04–4.09 (*m*, H–C(5)); 4.28 (*d*, *J* = 11.3, PhC*H*); 4.47–4.60 (*m*, 6 PhC*H*); 4.65 (*dd*, *J* = 4.6, 7.5, H–C(2)); 4.84 (*d*, *J* = 11.8, PhC*H*); 6.50 (*d*, *J* = 7.5, H–C(1)); 6.86 (br. *s*, NCH=CHN); 7.06–7.30 (*m*, 20 arom. H); 8.90 (*d*, *J* = 2.1, 2 arom. H); 9.08 (*t*, *J* = 2.1, 1 arom. H). ^{13}C-NMR ($CDCl_3$): 71.14 (*t*); 71.25 (*d*); 72.14 (*d*); 73.53 (*t*, 3 C); 75.21 (*t*); 76.96 (*d*); 77.72 (*d*); 78.51 (*d*); 122.32 (*d*); 128.05–129.77 (several *d*); 133.23 (*s*); 137.46 (*s*); 137.53 (*s*); 137.82 (*s*); 137.93 (*s*); 142.43 (*s*); 148.38 (2*s*); 162.30 (*s*).

*(1R)- and (1S)-1,5-Anhydro-2,3,4,6-tetra-*O*-benzyl-1-*C*-(1H-imidazol-2-yl)-*D*-glucitol* (**21** and **22**, resp.). a) *From* **19**/**20**: At −10°, a soln. of **19**/**20** 15:85 (478 mg, 0.60 mmol) in DMF (25 ml) was treated with NaH (37 mg, 1.54 mmol) and stirred for 45 min, while turning slowly violet. After addition of a cold sat. NH_4Cl soln., normal workup gave 353 mg of a violet oil (^{1}H-NMR: **21**/**22** 25:75). FC (AcOEt/hexane) gave 208 mg (59%) of **22** and 81 mg (23%) of **21**. Both compounds were contaminated by traces (< 3%) of the other isomer. Pure **22** was obtained by recrystallization in THF/hexane 1:1. Isomer **21** did not crystallize and was used as such for the next step.

b) *From Pure* **19**: Similarly, a pure sample of **19** (2.4 mg, 0.002 mmol) gave 1.4 mg (79%) of **21**/**22** 20:88 (^{1}H-NMR).

c) *From Pure* **20**: Similarly, a pure sample of **20** (59 mg, 0.073 mmol) gave 40 mg (92%) of **21**/**22** 17:83 (^{1}H-NMR).

Data of **21**: R_f (AcOEt) 0.53. UV (MeOH): 230 (3.4). CD (MeOH): 226 (+3360). IR ($CHCl_3$): 3454*w*, 3212*w*, 3090*w*, 3067*w*, 3043*w*, 3008*w*, 2961*m*, 2927*m*, 2857*m*, 1672*w*, 1603*w*, 1497*w*, 1454*m*, 1400*w*, 1361*w*, 1262*s*, 1095*s*, 1028*s*, 909*m*, 804*w*, 823*m*, 658*w*, 598*w*. ^{1}H-NMR (C_6D_6): 3.73 (*d*, *J* = 3.1, irrad. at 4.4 → *s*, 2 H–C(6)); 3.92 (*dd*, *J* = 8.2, 9.5, irrad. at 4.0 → *d*, *J* ≈ 8.5, H–C(3)); 3.99 (*dd*, *J* = 5.6, 8.7, irrad. at 5.32 → *d*, *J* ≈ 8.7, H–C(2)); 4.27 (*d*, *J* = 12.1, PhC*H*); 4.30–4.55 (*m*, 3 PhC*H*, H–C(5), H–C(4)); 4.63 (*d*, *J* = 11.3, PhC*H*); 4.76 (*d*, *J* = 11.5, PhC*H*); 4.87 (*d*, *J* = 11.5, PhC*H*); 4.88 (*d*, *J* = 11.5, PhC*H*); 5.32 (*d*, *J* = 5.6, H–C(1)); 6.8–7.4 (*m*, 22 arom. H). ^{13}C-NMR ($CDCl_3$, 50 MHz): 68.51 (*t*); 69.97 (*d*); 73.59 (*t*); 73.72 (*d*); 74.30 (*t*); 74.59 (*t*); 75.00 (*t*); 77.52 (*d*); 79.41 (*d*); 81.70 (*d*); 127.77–128.69 (several *d*); 137.37 (*s*); 137.97 (*s*); 138.02 (*s*); 138.35 (*s*); 144.67 (*s*). FAB-MS: 592 (42, $[M + 2]^+$), 591 (100, $[M + 1]^+$).

Data of **22**: R_f (AcOEt) 0.49. M.p. 152.5°. $[\alpha]_D^{25} = 21.9$ (*c* = 0.48, $CHCl_3$). UV (MeOH): 209 (4.5). CD (MeOH): 220 (−44000). IR ($CHCl_3$): 3454*w*, 3207*w*, 3090*w*, 3067*w*, 3043*w*, 3008*w*, 2924*m*, 2871*m*, 1606*w*, 1572*w*, 1497*m*, 1454*m*, 1398*w*, 1361*m*, 1282*w*, 1262*m*, 1069*s*, 1028*m*, 1004*m*, 915*w*, 856*w*, 822*w*, 635*w*. ^{1}H-NMR ($CDCl_3$, 200 MHz): 3.51 (*m*, *J* = 2.6, 6.1, 9.4, H–C(5)); 3.60–3.75 (*m*, H–C(4), 2 H–C(6)); 3.82 (*t*, *J* = 8.5, H–C(3)); 3.92 (*t*, *J* = 8.8, irrad. at 4.50 → *d*, *J* ≈ 8.5, H–C(2)); 4.13 (*d*, *J* = 10.4, PhC*H*); 4.39–4.58 (*m*, 2 PhCH_2, H–C(1)); 4.85 (*d*, *J* = 10.9, PhC*H*); 4.86 (*d*, *J* = 11.2, PhC*H*); 4.97 (*d*, *J* = 11.2, PhC*H*); 7.00 (*m*, 4 arom. H); 7.10–7.36 (*m*, 18 arom. H). ^{1}H-NMR (C_6D_6, 200 MHz): 3.29–3.37 (*m*, irrad. at 3.92 → br. *s*, H–C(5)); 3.50 (*dd*, *J* = 1.0, 11.0, H–C(6)); 3.60 (*dd*, *J* = 3.7, 11.0, H′–C(6)); 3.86–3.96 (*m*, H–C(3), H–C(4)); 4.08–4.10 (*m*, irrad. at 3.92 → change, H–C(2)); 4.20–4.40 (*m*, 3 PhC*H*); 4.53 (*d*, *J* = 10.5, PhC*H*); 4.59 (*d*, *J* = 11.1, PhC*H*); 4.79 (*d*, *J* = 9.5, H–C(1)); 4.88 (*d*, *J* = 11.1, PhC*H*); 4.90 (*d*, *J* = 11.1, PhC*H*); 5.07 (*d*, *J* = 11.2, PhC*H*); 6.90–7.40 (*m*, 22 arom. H). ^{13}C-NMR ($CDCl_3$): 69.25 (*t*); 73.64 (*t*); 75.06 (*t*); 75.26 (*t*); 75.49 (*d*); 75.88 (*t*); 78.16 (*d*); 79.26 (*d*); 82.44 (*d*); 86.73 (*d*); 127.90–129.7 (several *d*); 138.12 (*s*); 138.31 (*s*); 138.54 (*s*); 139.00 (*s*); 145.36 (*s*). FAB-MS: 591 (100, $[M + 1]^+$). Anal. calc. for $C_{37}H_{38}N_2O_5$ (590.72): C 75.23, H 6.48, N 4.79; found: C 74.94, H 6.39, N 4.79.

(1R)-1,5-Anhydro-1-C-(1H-imidazol-2-yl)-D-glucitol Hydrochloride (**23**·HCl). A suspension of Pd/C (10%, 80 mg) in 1N HCl (6 ml) was activated for 3 h under H_2 (7 bar) at 25°. After addition of a soln. of **21** (62 mg, 0.11 mmol) in MeOH (2 ml), the suspension was hydrogenated for 10 h at 9.5 bar and 25°, diluted with MeOH, and filtered through *Celite*. Evaporation of the filtrate and crystallization from MeOH/acetone gave 14 mg (50%) of **23**. White crystals. Crystallization of the filtrate afforded a second crop of 6 mg (21%) of **23**. M.p. 239°. R_f (AcOEt/MeOH/AcOH 7:5:1) 0.25. $[\alpha]_D^{20} = +131.6$ ($c = 0.53$, H_2O). UV (H_2O): 217 (3.8). CD (H_2O): 215.5 (+10000). IR (KBr): 3600–3138*s*, 2968*m*, 1600*w*, 1384*w*, 1341*w*, 1131*m*, 1111*m*, 1068*m*, 1052*m*, 1020*m*, 916*w*, 876*w*, 814*w*, 769*w*, 661*w*, 522*w*. ^{1}H-NMR (D_2O): 3.29–3.34 (*m*, H–C(5)); 3.48–3.57 (*m*, irrad. at 3.33 → change, H–C(3), H–C(4)); 3.77 (*dd*, $J = 4.7$, 12.5, irrad. at 3.33 → *d*, $J \approx 12.0$, H–C(6)); 3.87 (*dd*, $J = 2.4$, 12.6, irrad. at 3.33 → *d*, $J \approx 12.0$, H′–C(6)); 4.07 (*dd*, $J = 6.3$, 9.7, irrad. at 5.47 → *d*, $J \approx 9.5$, irrad. at 3.50 → *m*, H–C(2)); 5.47 (*d*, $J = 6.2$, irrad. at 4.07 → *d*, $J \approx 2.5$, H–C(1)); 7.43 (*s*, NCH=CHN). ^{13}C-NMR (CD_3OD): 62.35 (*t*); 70.85 (*d*); 71.47 (*d*); 72.09 (*d*); 75.05 (*d*); 79.69 (*d*); 120.98 (*d*, 2 C); 146.93 (*s*). FAB-MS: 231 (100, $[M + 1 - Cl]^+$), 230 (9, $[M - Cl]^+$). Anal. calc. for $C_9H_{15}ClN_2O_5$ (266.68): C 40.53, H 5.67, Cl 13.29, N 10.50; found: C 40.52, H 5.51, Cl 13.35, N 10.21.

(1S)-1,5-Anhydro-1-C-(1H-imidazol-2-yl)-D-glucitol Hydrochloride (**24**·HCl). A suspension of Pd/C (10%, 125 mg) in 1N HCl (5 ml) was activated for 2.5 h under H_2 (7 bar) at 25°. After addition of a soln. of **22** (120 mg, 0.20 mmol) in MeOH (4 ml), the suspension was hydrogenated for 24 h at 7.5 bar and 25°, diluted with MeOH, and filtered through *Celite*. Evaporation of the filtrate and crystallization from H_2O/acetone 1:10 (22 ml) gave 38 mg (70%) of **24**. White crystals. M.p. 227°. R_f (AcOEt/MeOH/AcOH 7:5:1) 0.25. $[\alpha]_D^{25} = 30.0$ ($c = 0.37$, H_2O). UV (H_2O): 214 (3.9). CD (H_2O): 216 (−14100). IR (KBr): 3600–3100*s*, 3170*s*, 3152*s*, 3062*m*, 2976*m*, 2898*m*, 2835*m*, 2807*m*, 2706*w*, 1611*m*, 1466*m*, 1421*m*, 1376*m*, 1350*m*, 1336*m*, 1318*m*, 1303*m*, 1256*m*, 1184*m*, 1136*m*, 1128*m*, 1115*m*, 1110*m*, 1081*m*, 1056*s*, 1006*m*, 994*m*, 920*m*, 896*w*, 760*m*, 725*w*, 668*m*. ^{1}H-NMR (D_2O): 3.48 (*t*, $J = 9.5$), 3.51 (*t*, $J = 9.3$, H–C(3), H–C(4)); 3.55–3.70 (*m*, irrad. at 4.70 → change at 3.65, H–C(2), H–C(5)); 3.76 (*dd*, $J = 5.2$, 12.4, irrad. at 3.6 → *d*, $J \approx 12.4$, H–C(6)); 3.90 (*dd*, $J = 1.5$, 12.4, irrad. at 3.6 → *d*, $J \approx 12.4$, H′–C(6)); 4.68–4.74 (covered by H_2O signal, H–C(1)); 7.41 (*s*, NCH=CHN). ^{1}H-NMR (CD_3OD): 3.20–3.59 (*m*, H–C(2), H–C(3), H–C(4), H–C(5)); 3.78 (*dd*, $J = 4.8$, 11.0, H–C(6)); 3.93 (*dd*, $J = 2.2$, 10.5, H′–C(6)); 4.63 (*d*, $J = 8.8$, H–C(1)); 7.53 (*s*, NCH=CHN). ^{13}C-NMR (D_2O): 63.34 (*t*); 71.75 (*d*); 74.84 (*d*); 75.34 (*d*); 79.10 (*d*); 82.75 (*d*); 121.85 (*d*); 121.95 (*d*); 146.15 (*s*). FAB-MS: 231 (100, $[M + 1 - Cl]^+$), 230 (12, $[M - Cl]^+$). Anal. calc. for $C_9H_{15}ClN_2O_5$ (266.68): C 40.53, H 5.67, Cl 13.29, N 10.50; found: C 40.28, H 5.76, Cl 13.23, N 10.39.

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