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Stereocontrolled synthesis of imidazolo[1,5]hexopiperidinoses and imidazol-4(5)-yl-*C*-glycosides

Andrzej Frankowski,[a,*] Dariusz Deredas,[a] Estelle Dubost,[b] François Gessier,[b] Stefan Jankowski,[a] Markus Neuburger,[c] Czesława Seliga,[a] Théophile Tschamber[b] and Kamil Weinberg[a]

[a]*Institute of Organic Chemistry, Technical University of Lodz, ul. Zwirki 36, 90924 Lodz, Poland*
[b]*Ecole Nationale Supérieure de Chimie, Université de Haute-Alsace, 3 rue Alfred Werner, 68093 Mulhouse, France*
[c]*Institut für anorganische Chemie, Universität Basel, Spitalstrasse 51, CH-4056 Basel, Switzerland*

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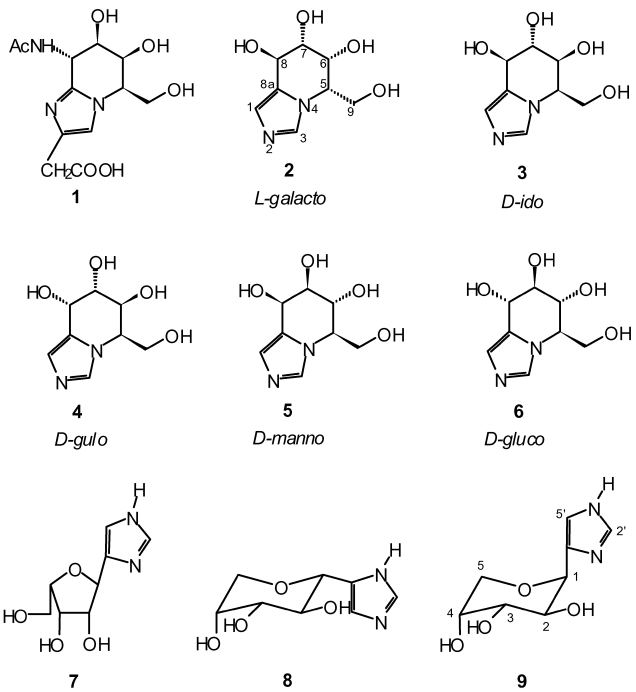
Dedicated to Professor Jacques Streith on the occasion of his 70th birthday

Abstract—The syntheses of imidazolo[1,5]hexopiperidinoses **2**–**6** and imidazol-4(5)-yl *C*-glycosides **7**–**9** are reported. The crucial step of this approach relies upon the S_N2-type cyclisation of selectively protected C(1), C(2), C(3) and C(5)-substituted 1-[imidazol-4(5)-yl]pentitols in which the imidazole nitrogen or the C(1)-connected oxygen are involved as the competitive nucleophilic centers, respectively. Six selected imidazolosugars were evaluated as potential inhibitors of glycosidases.

1. Introduction

The mechanism of oligo- and polysaccharide hydrolysis by glycosidases is thought to involve a cyclic oxocarbonium ion as an intermediate, in which the pyranose ring adopts a half-chair conformation.[1] Imidazolosugars are flattened azasugar analogues which mimic the transition state for glycosidic bond hydrolysis and are therefore potential glycosidase inhibitors. Only one imidazolosugar, nagstatine (**1**), has been isolated from natural sources so far, and this has proved to be a potent inhibitor of *N*-acetyl-β-D-glucosaminidase.[2,3]

Imidazolosugars can be considered as 1,2- or 1,5-disubstituted imidazole derivatives, depending on the mode of imidazole annelation to the azasugar ring. The synthesis of imidazolo[1,2]-azasugars has been the subject of interest of several research groups.[4–11] Some of these compounds have proven to be potent glycosidase inhibitors, mainly of β-glycosidases, in accordance with the postulated (and proved) mechanism of lateral protonation of imidazole nitrogen by retentive β-glycosidases.[12] Our previous research has been concerned with syntheses and transformations of imidazolo[1,5]azapentoses,[13–17] some of which are moderately active as inhibitors of α-glycosidases. In this paper we present syntheses of imidazolo[1,5] hexopiperidinoses **2**–**6** containing the *exo*-hydroxymethyl group, which are close analogues of the corresponding hexopyranoses, and imidazole *C*-glycosides **7**–**9** formed in competitive reactions (see our preliminary paper[23]).



Keywords: imidazolohexapiperidinoses; imidazolyl-*C*-glycosides; glycosidase inhibition.
* Corresponding author. Tel.: +48-426313144; fax: +48-426365530; e-mail: andfrank@ck-sg.p.lodz.pl

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2. Results and discussion

2.1. Synthesis of imidazolo[1,5]hexopiperidinoses and 1[imidazol-4(5)-yl]-*C*-glycosides

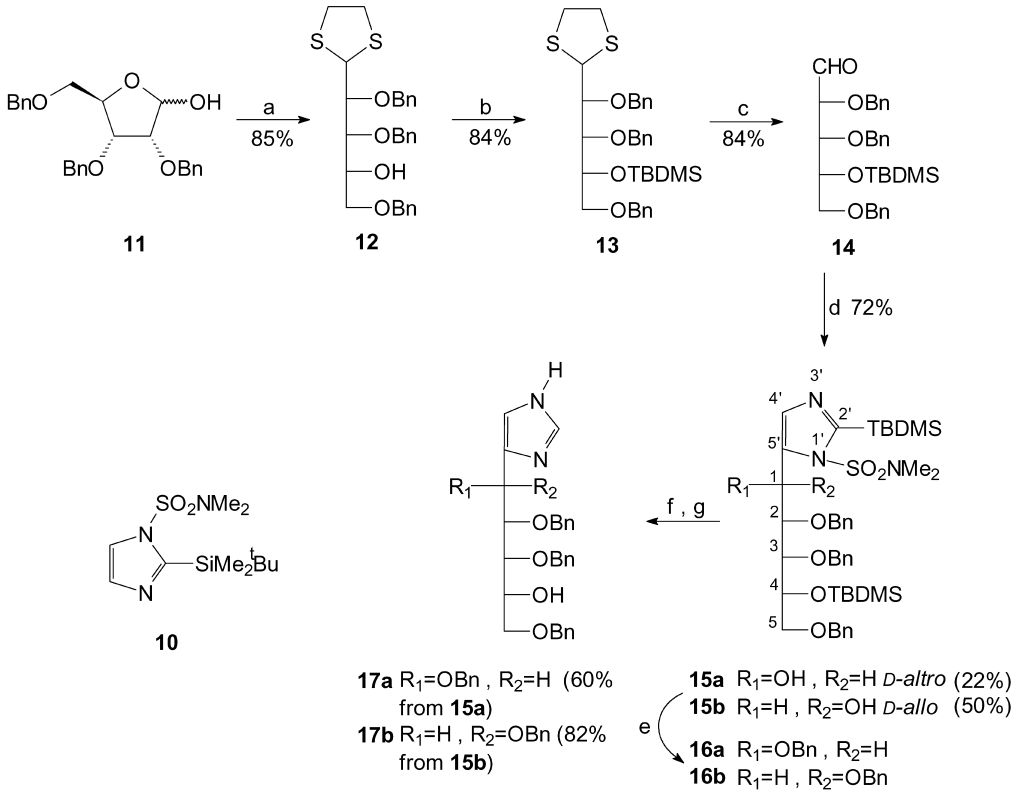
We present herein the syntheses of five imidazolo[1,5]hexopiperidinoses: **2**–**6**. These products have been obtained from 1-[4(5)-imidazolyl]pentitols, which have been activated towards intramolecular S_N2 attack at C(4) of the pentitol moiety. The N–cyclisation competes with a nucleophilic attack of O(1) at C(4). The latter reaction initiates the formation of imidazole *C*-glycosides **7**, **8** and **9**. We have observed this course of reaction in the L-*talo* series where only *C*-glycoside **7** was formed. In the D-*gluco* series, where two *C*-glycosides **8** and **9** were obtained, the imidazolopiperidinose **6** was isolated as a minor product.

The imidazolyl-pentitols were obtained by addition of the lithiated derivative of the 1,2-disubstituted imidazole **10**[18] to protected pentoses. Each of these reactions resulted in two epimeric imidazolyl-pentitols. Each pair of products was chromatographically separated and they were separately subjected to sequences of analogous reactions leading to the target structures.

2.1.1. L-*galacto* and L-*talo* series. Tri-*O*-benzyl-D-ribofuranose[19] **11**, used as a chiral precursor, and treated with 1,2-dithioethane in anhydrous HCl/dioxane, to give the 1,2-dithioacetal **12** in 85% yield. The remaining OH group on C-4 was protected with a TBDMS group under standard conditions to give compound **13** in 84% yield. The dithioacetal function in **13** was removed with mercury perchlorate and $CaCO_3$ to give the aldehyde **14** in 90% yield. A mixture of epimeric imidazolyl-pentitols **15a** (D-*altro*) and **15b** (D-*allo*) was prepared by nucleophilic addition of the 5-lithiated imidazole **10** to aldehyde **14**. The epimers were obtained in a 1:2 ratio, determined by comparison of integration of H–C(1) protons in ^{1}H NMR spectra. They were chromatographically separated and subjected to analogous reaction sequences. Thus, benzylation of **15a** under standard conditions (NaH, BnBr, Bu_4NI, THF) resulted in the formation of tetrabenzyl derivative **16a**. The silyl group on **16a** was removed by treatment with Bu_4NF and then the imidazole ring was deprotected under acidic conditions (HCl, THF, reflux) to give 1,2,3,5-tetra-*O*-benzyl-1[4(5)-imidazolyl]-D-*altro*-pentitol (**17a**) in 60% yield (2 steps). The same reaction sequence starting from imidazolyl-D-*allo*-pentitol (**15b**) led to the formation of 1,2,3,5-tetra-*O*-benzyl-1[4(5)-imidazolyl]-D-*allo*-pentitol (**17b**) in 82% overall yield (Scheme 1).

The compound **17a** was subsequently mesylated and immediately treated with acetic anhydride in pyridine at 80°C to give the cyclised product **18** in 67% yield. Its subsequent hydrogenolysis in the presence of $Pd(OH)_2$ (Pearlman's catalyst) yielded imidazolo[1,5]-L-*galacto*-piperidinose (**2**) in 78% yield.

The latter compound **17b**, treated with triflic anhydride and pyridine in CH_2Cl_2 at −20°C, was converted into the ditriflated derivative **19** which was gradually transformed into the *N*-triflated imidazolyl-*C*-glycoside **20**. It was immediately *N*-deprotected with NaOH in methanol to yield the tribenzylated derivative of imidazolyl-*C*-glycoside



Scheme 1. *Reagents and conditions*: (a) $HSCH_2CH_2SH$, dioxane/HCl, room temp., 12 h; (b) TBDMSCl, imidazole, DMF, room temp. 24 h; (c) $Hg(ClO_4)_2$, $CaCO_3$, THF/H_2O, room temp. 2 h; (d) **10**, *n*-BuLi, THF, −70°C; (e) NaH, BnBr, Bu_4NI cat., THF, room temp., 12 h; (f) Bu_4NF, room temp.; (g) 1.5 M HCl, reflux, 2 h.

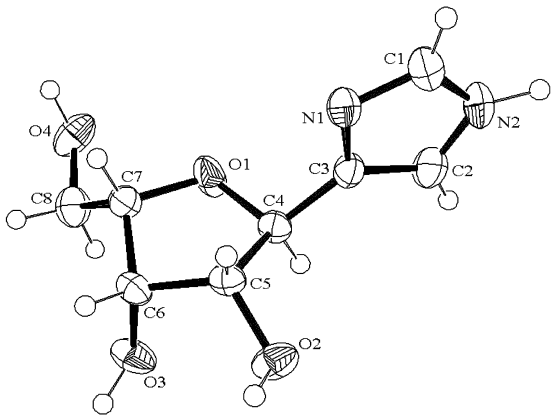
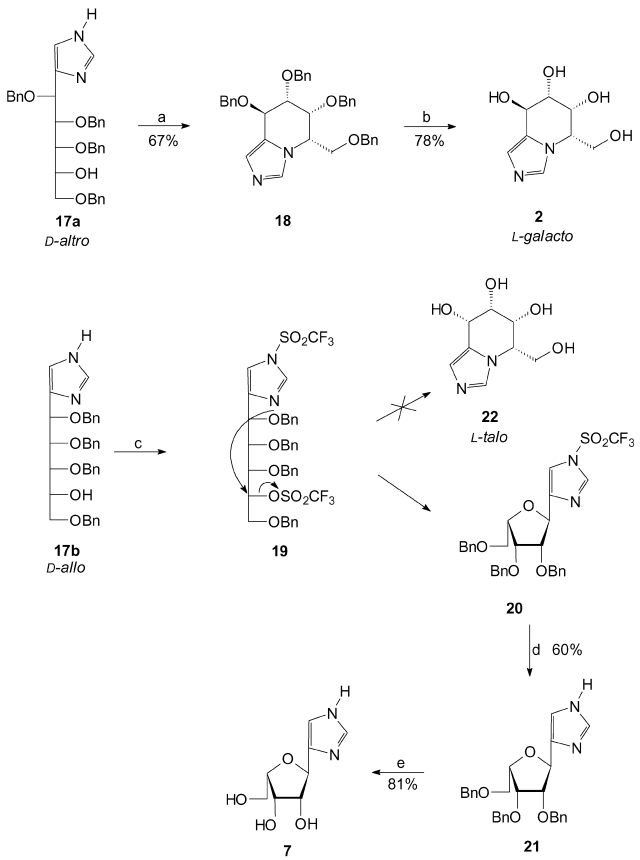
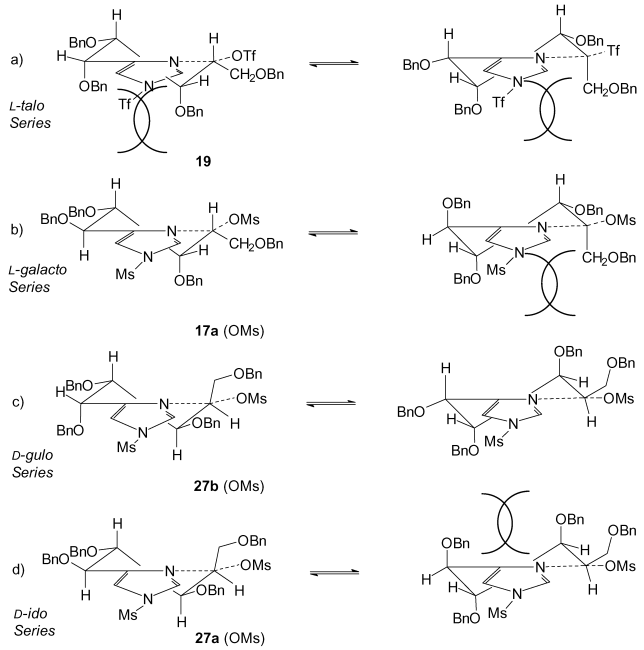


Figure 1. Molecular structure of **7** with the atom-numbering scheme (ORTEP plot. Displacement elipsoids are drown at the 50% probability level); Selected torsion angles [°]: O(1)–C(4)–C(5)–C(6)=29.5, O(1)–C(7)–C(6)–C(5)=30.1, C(4)–C(5)–C(6)–C(7)=−35.7.



Scheme 2. *Reagents and conditions*: (a) (1) MsCl, Py, room temp.; 1 h. (2) Ac_2O, Py, 80°C, 24 h (b) H_2, $Pd(OH)_2/C$, EtOH, AcOH; (c) Tf_2O, Py, CH_2Cl_2, −20°C then room temp., 5 h; (d) 4 M NaOH, MeOH, room temp.; (e) H_2, $Pd(OH)_2/C$, room temp., 48 h.

21, which was subsequently debenzylated by hydrogenolysis in the presence of palladium hydroxide to give 4,5-(α-L-lyxofuranosyl)-1*H*-imidazole **7** in 81% yield. Structure of the furanoside **7** was clearly demonstrated by the X-ray diffraction analysis as shown in Figure 1. The expected formation of imidazolo[1,5]-L-*talo*-piperidinose **22** was not observed at all (Scheme 2).

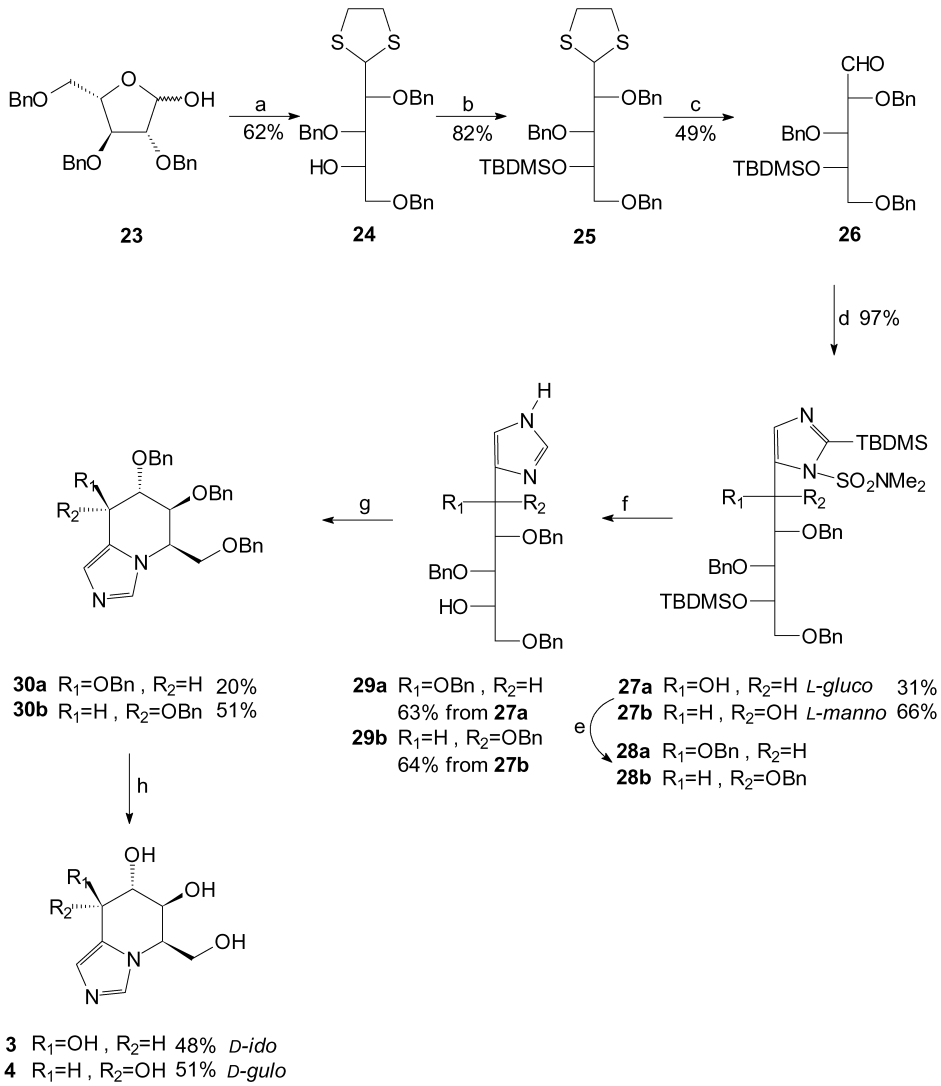


Scheme 3. Steric interactions in the transition states.

We believe the different outcomes of both the above cyclisations result from different steric interactions in the transition states of those reactions (Scheme 3).

In the L-*talo* series the transition state leading to *N*-cyclisation of the D-*allo*-pentitol **19** (with formation of the piperidinose ring) in both possible conformations has unfavourable 1,3-interactions of the pseudoaxial C(1)–OBn with the axial C(3)–OBn and the axial C(2)–OBn with the pseudoaxial C(4)–CH_2OBn (Scheme 3a). The situation in the L-*galacto* series is the opposite. One of the two possible conformations of the transition state leading to the piperidine ring formation has no 1,3-diaxial interactions (Scheme 3b).

2.1.2. D-*gulo* and D-*ido* series. Following the reaction pathway shown in Scheme 4, dithioacetal **24** was obtained from tri-*O*-benzyl-L-*arabino*-furanose **23**[20] in 62% yield and was subsequently silylated to give its 4-*O*-TBDMS derivative **25** in 82% yield. The thioacetal function of **25** was cleaved in conditions described by Fetizon (CH_3I, Na_2CO_3, acetone/water, 60°C)[21] to give 2,3,5-tri-*O*-benzyl-4-*O*-t-butyldimethylsilyl-L-arabinose **26** in 49% yield. As a result of addition of the 5-lithiated imidazole **10** to aldehyde **26** a mixture of L-*gluco*-**27a** and L-*manno*-imidazolyl-pentitols **27b** was obtained in 97% yield. The epimers **27a** and **27b** were chromatographically separated and isolated in a 1:2 ratio (31 and 66% yields, respectively). They were subjected to analogous reaction sequences. Benzylation of the epimers **27a** and **27b** resulted in the tetrabenzyl derivatives **28a** and **28b**, respectively. They were subsequently deprotected from acid-labile groups (including TBDMS) with 1.5 M HCl in refluxing THF to give tetrabenzyl-imidazolyl-pentitols **29a** (63% yield from **27a**) and **29b** (64% yield from **27b**), respectively. Their mesylation and subsequent treatment with acetic anhydride in pyridine at 80°C resulted in cyclisation with formation of

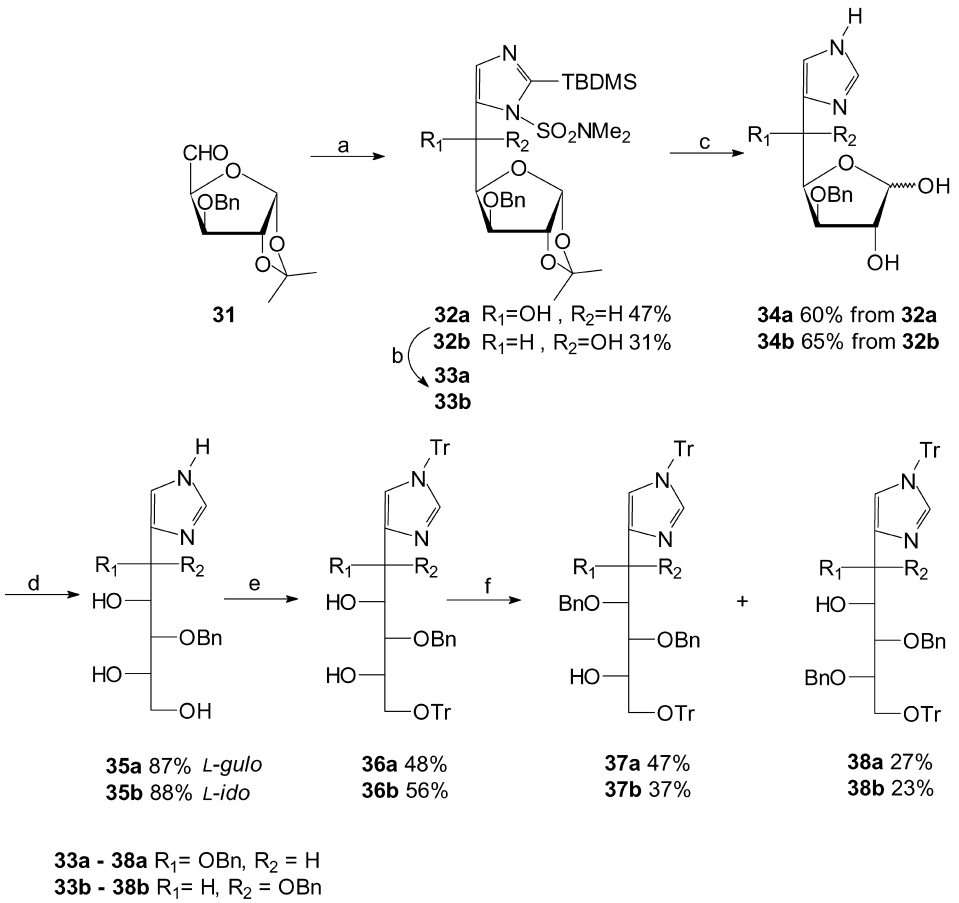


Scheme 4. *Reagents and conditions*: (a) $HSCH_2CH_2SH$, dioxane/HCl, room temp., 24 h; (b) TBDMSCl, imidazole, DMAP, DMF, room temp. 20 h; (c) CH_3I, acetone/H_2O, 60°C, 24 h; (d) 10, *n*-BuLi, THF, −70°C, 2.5 h; (e) NaH, BnBr, Bu_4NI cat., THF, room temp., 12 h; (f) 1.5 M HCl, reflux, 2 h; (g) (1) MsCl, Py, 0°C to room temp., 1 h. (2) Ac_2O, 80°C, 20 h; (h) H_2, Pd/C, room temp., 48 h.

tetrabenzyl-imidazolo[1,5]piperidinoses with D-*ido* (**30a**, 20% yield) and D-*gulo* (**30b**, 51% yield) configurations, respectively. They were both debenzylated by hydrogenolysis to produce the target compounds imidazolo[1,5]-D-*ido*-piperidinose **3** and imidazolo[1,5]-D-*gulo*-piperidinose **4** in 48 and 51% yields, respectively. In both cases the steric conditions do not disfavour *N*-cyclisation with formation of imidazolopiperidinoses **3** and **4**. In the D-*gulo* series both conformations of the transition state leading to *N*-cyclisation are free from 1,3-diaxial interactions (Scheme 3c). In the D-*ido* series one of the conformations of the transition state leading to *N*-cyclisation is free from such interactions (Scheme 3d).

2.1.3. D-*manno* and D-*gluco* series. Dialdofuranose **31**, readily available from D-glucose,[22] under treatment with lithiated imidazole **10** gave a mixture of the two epimeric imidazolyl-pentoses **32a** and **32b** in 78% yield. These two diastereomers were chromatographically separated and isolated in a 3:2 ratio. They were subiected to analogous reaction sequences. Thus, benzylation of **32a** and **32b** yielded compounds **33a** and **33b**, which were deprotected under acidic conditions without isolation to give imidazolyl-furanoses **34a** (60% yield from **32a**) and **34b** (65% yield from **32b**), respectively, both as mixtures of anomers. Reduction of **34a** and **34b** by $NaBH_4$ resulted in 1,3-di-*O*-benzyl-L-*gulo*- (**35a**) and 1,3-di-*O*-benzyl-L-*ido*-imidazolyl-pentitol (**35b**) in 87 and 88% yields, respectively. These were tritylated to form dityrityl derivatives **36a** (48%) and **36b** (56%). Their monobenzylation afforded mixtures of 1,2,3- and 1,3,4-tri-*O*-benzyl-pentitols: **37a** (47%) and **38a** (27%) in the L-*gulo* and **37b** (37%) and **38b** (23%) in the L-*ido* series, respectively. Compounds **37a** and **37b** were used in further reactions (Scheme 5).

Treatment of **37a** and **37b** with phenylmethanesulphonyl chloride gave epimeric sulphonates **39a** and **39b**, respectively. As a result of their heating in pyridine and subsequent acidic cleavage of the trityl groups, different ways of cyclisation in both series were observed. L-*gulo*-Pentitol **39a** afforded *N*-cyclisation with formation of tribenzyl-imidazolo-D-*manno*-piperidinose **40a**, which after hydrogenolytic cleavage of benzyl groups gave imidazolo[1,5]-D-*manno*-piperidinose (**5**) in 75% yield. L-*ido*-Pentitol **39b**



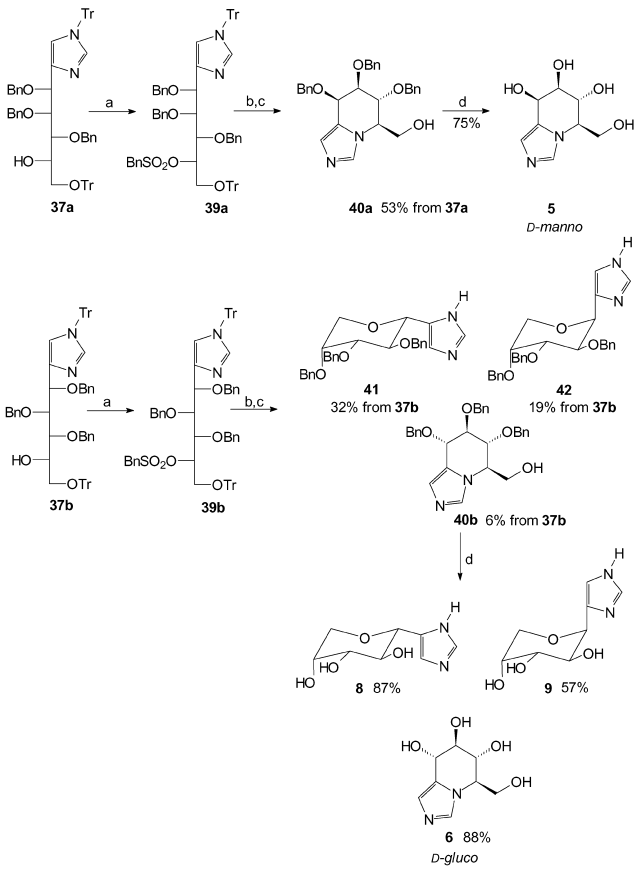
Scheme 5. *Reagents and conditions*: (a) **10**, *n*-BuLi, THF, −70°C; (b) BnBr, NaH, DMF, room temp.; (c) HCl aq, THF, reflux; (d) $NaBH_4$, MeOH, 0°C to room temp.; (e) TrCl, Py, DMAP, 80–90°C; (f) BnBr, NaH, Bu_4NI cat., THF, 0°C to room temp.

under the same experimental conditions gave mainly *O*-cyclisation products—4(5)(α-D-arabinopyranosyl)imidazole **41** and 4(5)(β-D-arabinopyranosyl)imidazole **42**. Tribenzylimidazolo-D-*gluco*-piperidinose **40b**, a result of *N*-cyclisation, was a minor product (**41**:**42**:**40b**=7:4:1). Hydrogenolytic cleavage of the benzyl groups in **41**, **42** and **40b** resulted in the *C*-pyranosides **8** and **9** and imidazolo[1,5]-D-*gluco*-piperidinose (**6**) in 87, 57 and 88%, respectively, (Scheme 6). Structures of both pyranosides **8** and **9** were deduced from their ^1H and ^{13}C NMR spectra (vide infra).

The formation of two anomeric pyranosides **41** and **42**, each with three benzyl groups, together with a transfer of one such group from C(1) to C(4) and a configuration change on C(4), may be tentatively explained in the following way: Firstly, the C(1) benzyloxyl group oxygen attacks at C(4) inducing phenylmethanesulphonoxyl anion departure, inversion of configuration on C(4) and formation of a furanose oxonium ion. The subsequent opening of this cation involves the departure of a benzyloxyl group and formation of a resonance-stabilised allyl-type cation. Then, nucleophilic attack of the C(5) oxygen on the C(1) atom of the cation results in the formation of two anomeric pyranosides as trityl oxonium ions. The departure of a stabilised trityl carbocation then affords the pyranosides **41** and **42** (Scheme 7).

In addition to spectroscopic analysis (vide infra) the configuration on the C-1 stereogenic centre in both epimeric series D-*manno* and D-*gluco* was also determined independently by chemical means according to our previously described results.[23]

Phenylmethanesulphonylation of both OH groups in imidazolyl-pentitol **36a** and subsequent acidic cleavage of the trityl groups afforded a mixture of the disulphonate derivative **43a** and imidazolo-D-*manno*-piperidinose **44** in a 2:1 ratio. Under treatment with $NaNH_2$, compound **44**, as a result of *trans*-elimination, afforded an unsaturated derivative **46**, which was catalytically hydrogenated to give the imidazolopiperidinose **48**. Pentitol **43a** under the same reaction conditions ($NaNH_2$) yielded an unsaturated azepanose **45**. Its hydrogenolytic debenzylation and reduction resulted in formation of imidazoloazepanose **47**. Both of the above reaction pathways involve *trans*-elimination and prove *R* configuration on C-1 in the epimer **32a** and L-*gulo* configuration in all imidazolyl-pentitols originating from it. Thus, the target imidazolopiperidinose **5** has the D-*manno* configuration. The epimeric imidazolyl-pentitol **36b** in a sequence of analogous reactions gave, via disulphonate **43b**, a tricyclic structure **49**, which was catalytically hydrogenated to afford imidazolopyrrolydinose **50** (Scheme 8). The stereochemical outcome of these reactions, involving a contraction of the intermediately formed piperidinose ring,[23] is only possible with an antiperiplanar position for the C(8)–C(8a) bond relative the sulphonyloxy leaving group, proving L-*ido* configuration in the epimer **32b** and all

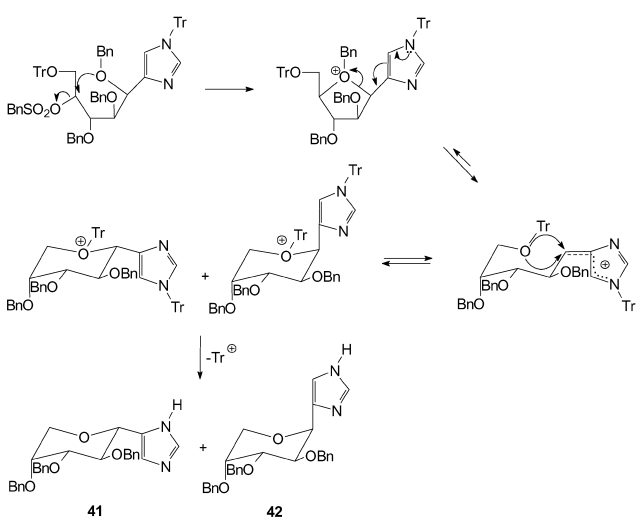


Scheme 6. *Reagents and conditions*: (a) $BnSO_2Cl$, Py, −30°C to room temp.; (b) Py, 60–80°C; (c) 6 M HCl aq, THF, reflux; (d) H_2, Pd/C, EtOH, room temp.

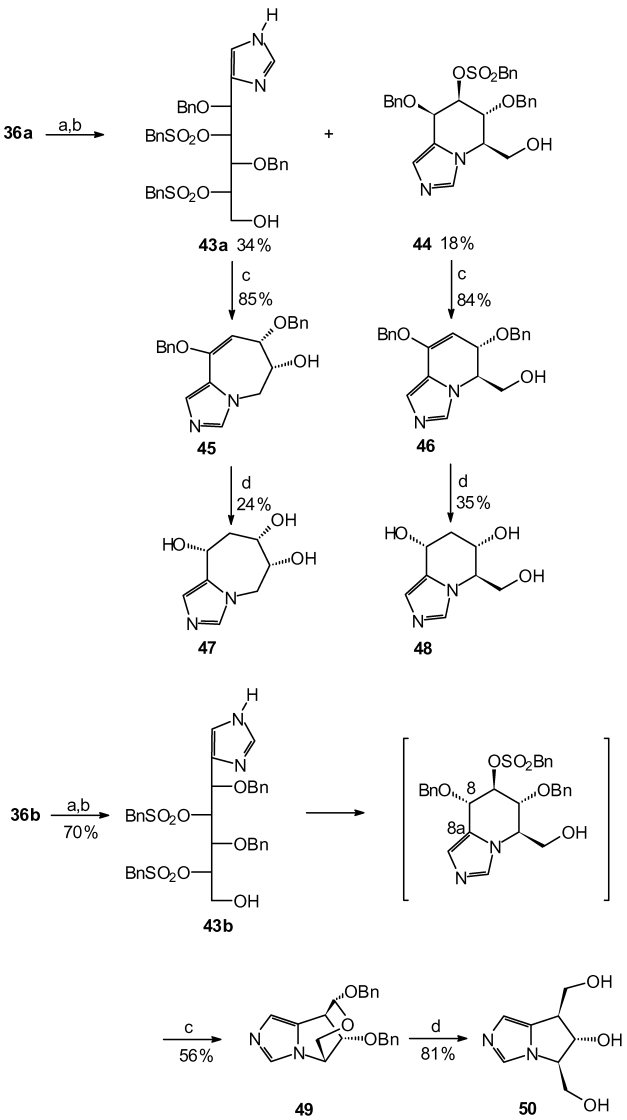
imidazolyl-pentitols originating from it. Thus, imidazolopiperidinose **6** has the D-*gluco* configuration.

2.2. Structure analysis

The structural and configurational assignments of imidazolo-hexopiperidinoses and imidazolyl-*C*-glycosides were determined from the ^1H and ^{13}C NMR spectroscopic data.



Scheme 7. Proposed reaction pathway to the pyranosides **41** and **42**.



Scheme 8. *Reagents and conditions*: (a) $BnSO_2Cl$, Py, −30°C to room temp.; (b) 6 M HCl aq, THF, reflux; (c) $NaNH_2$, DMF, room temp.; (d) H_2, Pd/C, EtOH, room temp.

The structures of imidazolopiperidinoses **2**–**6** were asigned from ^{13}C NMR data analysis. The chemical shifts of C-5 in imidazolopiperidinoses **2**–**6** and their benzyl derivatives are within the range of 55–58 ppm. This range is diagnostic for carbons bonded to the imidazole ring nitrogen. The D-*gulo* configuration of tetrabenzyl-imidazolo[1,5]piperidinose **30b** was confirmed by application of the nuclear Overhauser effect (NOE). Irradiation of H-8 generated NOE enhancement at H-7 (5.3%) and when H-7 was irradiated, the 9.0% NOE at H-8 was observed. The same configuration was confirmed in **4** after debenzylation: irradiation of H-8 generated nuclear Overhauser enhancement at H-7 (10.5%). The additional splitting observed for H-8 (0.9 Hz) in **4** can be explained by the allylic proton–proton coupling with H-1.

The compound **30b** was assigned the D-*gulo* configuration, therefore the isomer **30a** should have the D-*ido* configuration. For both isomers **30a** and **30b** the vicinal coupling constants between H-8 and H-7 or H-7 and H-6 are similar (around 3.5 and 7 Hz, respectively). This can be

Table 1. Inhibition values of the compounds **2**, **4**, **5**, **47**, **48**, **50** against six commercially available glycosidases. The percentage of inhibition was measured at 1 mM. NI=no inhibition at [I]=1 mM

	2	**4**	**5**
α-D-Glucosidase (baker's yeast)	NI	NI	10%
β-D-Glucosidase (almonds)	NI	NI	K_i=230 μM
α-D-Galactosidase (green coffee beans)	NI	K_i=90 μM	NI
β-D-Galactosidase (*Escherichia coli*)	NI	K_i=100 μM	NI
α-D-Mannosidase (Jack beans)	NI	NI	17%
β-D-Mannosidase (acetone snail powder)	NI	NI	NI
	47	**48**	**50**
α-D-Glucosidase (baker's yeast)	NI	14%	16%
β-D-Glucosidase (almonds)	NI	NI	NI
α-D-Galactosidase (green coffee beans)	NI	NI	NI
β-D-Galactosidase (*Escherichia coli*)	NI	NI	NI
α-D-Mannosidase (Jack beans)	NI	NI	NI
β-D-Mannosidase (acetone snail powder)	22%	33%	13%

explained by the conformations of **30a** and **30b** in which benzyloxy groups attached to C-6 and C-7 are axial and *exo*-benzyloxymethyl group occupies the pseudo-equatorial position.

In the D-*gluco* series the two major products **41** and **42** are tribenzyl-*C*-pyranosides. As was proved by HMBC experiment, only the proton assigned as H-1 has the heteronuclear shift correlation with C-2′ and C-5′ atoms. The configuration at the C-1 atom can be deduced from the analysis of the vicinal coupling constants. Their significant difference between H-1 and H-2: 9.77 Hz (**8**) and 1.71 Hz (**9**) undoubtedly provides evidence for *equatorial* (**8**) and *axial* (**9**) position for the imidazole ring.

2.3. Enzymatic assays

The compounds **2**, **4**, **5**, **47**, **48**, **50** have been evaluated as potential inhibitors of six commercially available glycosidases, and the results compiled in Table 1. The imidazolo derivatives which do show some activity proved to be competitive inhitors, but only moderate inhibitions could be measured. The D-*gulo* **4** inhibits the α-D-galactosidase (green coffee beans) and the β-D-galactosidase (*Escherichia coli*) with K_i values of 90 and 100 μM, respectively. This stereoisomer **4** has an identical configuration with the D-galactose in the C(8), C(6), C(5) positions. The D-*manno* **5** inhibits the β-D-glucosidase (almonds) with a K_i of 230 μM. In the stereoisomer **5** the three configurations C(7), C(6) and C(5) are identical with those of the asymmetric centres of the D-glucose. Unexpectedly D-*manno* **5** inhibits very weakly α-D-mannosidase (Jack bean) neverthless that all stereogenic centers have the same configuration as D-mannose. The previously described[23] compounds **47**, **48**, **50** show a very weak inhibition when tested with a concentration of 1 mM. It appears therefore that these compounds are very poor inhibitors. The L-*galacto* **2** was inactive towards the pool of evaluated D-glycosidases.

3. Experimental

3.1. General

Flash chromatography: silica gel (Merck 60; 230–400 mesh). TLC: silica gel on plastic sheets (Merck 60 HF_{254}); the spots were viewed under UV or by heating with a termogun after spraying with a solution of $KMnO_4$ (20 g) and Na_2CO_3 (40 g) in H_2O (1 L) or a solution of phosphomolybdic acid (5 in 96% EtOH). Mp Kofler hot-bench or Büchi-SMP-30 aparatus; corrected values. Optical rotations were measured at 20°C: Schmidt–Haensch Polartronic Universal and Perkin–Elmer 241 polarimeters. ^1H and ^{13}C NMR spectra: Bruker ACF 250 and Avance DPX 250 spectrometers at 300 K. Internal references for ^1H NMR: $SiMe_4$ (δ=0.00), $CDCl_3$ (δ=7.26), CD_3OD (δ=3.30), [D_4]TSP for spectra in D_2O (δ=0.00); for ^{13}C NMR: $CDCl_3$ (δ=77.03), CD_3OD (δ=49.02); δ in ppm and J in Hz. HR-MS on Finnigan MAT 95 (Finnigan MAT GmbH, Germany) and ZabSpec TOF Micromass spectometers at 8Kv (source temp. 40°C). Elemental analysis were carried out by the Microanalysis Service of CNRS (Verneson, France).

3.2. X-Ray diffraction analysis

Single crystals of **7**, suitable for X-ray crystallography, were grown by crystallization from methanol. Data were collected at 293 K on a Bruker-Nonius KappaCCD area detector using Mo Kα radiation (λ=0.71073). The compound with the chemical formula of $C_8H_{12}N_2O_4$ crystallized in the orthorhombic space group $P2_12_12_1$.The dimensions of the unit-cell are: a=6.9605(3), b=8.0701(4), c=16.5064(7), $\alpha=\beta=\gamma=90°$. The usual corrections were applied. The structure was solved using the program SIR 92.[24] Anisotropic refinement on all non-hydrogen atoms was carried out using the program CRYSTALS.[25] Scattering factors were taken from the International Tables Vol. IV table 2.2B.. The plots were created using ORTEP-3 for Windows.[26]

3.3. Enzymatic assays

Glycosidases [α-mannosidase (EC 3.2.1.24) from Jack beans, β-mannosidase (EC 3.2.1.25) from snail acetone powder, α-glucosidase (EC 3.2.1.20) from baker's yeast, β-glucosidase (EC 3.2.1.21) from almonds, α-galactosidase (EC 3.2.1.22) from green coffee beans, β-galactosidase from *Escherichia coli* (EC 3.2.1.23)], and their corresponding substrates were purchased from Sigma Co. Spectrophotometric assays were performed at the optimum pH for each enzyme,[27] with *p*-nitrophenyl-α-D-mannopyranoside

as a substrate for α-mannosidase (K_m=2 mM, pH=4.5), *p*-nitrophenyl-β-D-mannopyranoside for β-mannosidase (K_m=1.33 mM, pH=4.0), *p*-nitrophenyl-α-D-glucopyranoside for α-glucosidase (K_m=0.3 mM, pH=7), *p*-nitrophenyl-β-D-glucopyranoside for β-glucosidase (K_m=1.3 mM, pH=5.0), *p*-nitrophenyl-α-D-galactopyranoside for α-D-galactosidase (K_m=0.25 mM, pH=6.5) and *p*-nitrophenyl-β-D-galactopyranoside for β-D-galactosidase (K_m=0.4 mM, pH=7). The release of *p*-nitrophenol was measured continuously at 405 nm to determine initial velocities. All kinetics were performed at 25°C and the reaction was started by the addition of enzyme in a 1 mL assay medium (acetate buffer 50 mM, or phosphate buffer 20 mM according to the desired pH value) using substrate concentrations around the K_m value of each enzyme. The K_i values were determined for the most potent inhibitors, by the Dixon graphical procedure.[28,29]

3.3.1. 2,3,5-Tri-*O*-benzyl-D-ribose ethylenedithioacetal (12). A solution of 2,3,5-tri-*O*-benzyl-D-ribofuranose **11**[19] (520 mg, 1.24 mmol) and ethanedithiol (0.16 mL, 1.8 mmol) in dioxane saturated with HCl (5 mL) was stirred at room temperature overnight. The mixture was treated with $CHCl_3$ (20 mL) and washed with a saturated aq. solution of $NaHCO_3$ and water. The organic layer was dried ($MgSO_4$), filtered and evaporated. The residue was purified by flash chromatography (AcOEt/cyclohexane 1:9 to 2:8) to give the title *compound* **12** (520 mg, 85%) as a pale yellow oil. [Found: C 67.5, H 6.4, S 12.9 $C_{28}H_{32}O_4S_2$ requires C 67.71, H 6.49, S 12.91%]; $[\alpha]_D^{20}$=+11 (*c*=3.0; $CHCl_3$); ν_{max} (film): 3030, 3018, 2920, 1485, 1436, 1186, 1092, 900, 736, 696, 620 cm^{-1}; δ_H (250 MHz, $CDCl_3$) 7.40– 7.25 (15H, m, 3Ph), 4.96 (1H, d, *J*=7.5 Hz, C(1)*H*), 4.84 and 4.77 (2H, AB, *J*=11.0 Hz, OCH_2Ph), 4.69 and 4.54 (2H, AB, *J*=11.4 Hz, OCH_2Ph), 4.52 and 4.45 (2H, AB, *J*=11.9 Hz, OCH_2Ph), 4.15 (1H, m, C(4)*H*), 3.81 (1H, dd, *J*=7.5, 3.1 Hz, C(2)*H*), 3.77 (1H, dd, *J*=7.0, 3.1 Hz, C(3)*H*), 3.65 (1H, dd, *J*=9.7, 3.0 Hz, C(5)H_aH_b), 3.56 (1H, dd, *J*=9.7, 6.3 Hz, C(5)H_aH_b), 3.12–3.23 (4H, m, S(CH_2)$_2$), 2.62 (1H, exhange with D_2O, d, *J*=4.7 Hz, C(4)O*H*); δ_C (60 MHz, $CDCl_3$) 138.0–138.2 (3 * *C* s-arom.), 128.4–127.7 (*C*H arom), 84.6 (*C*-2). 81.1 (*C*-3), 75.2 (O*C*H_2Ph), 73.4 (O*C*H_2Ph), 73.2 (O*C*H_2Ph), 71.3 (*C*-5), 70.7 (*C*-4), 54.7 (*C*-1), 38.7 and 38.1 (S(*C*H_2)$_2$); HRMS (Cl, NH_3) MH^+, 497.1818. $C_{28}H_{33}O_4S_2$ requires 497.1820.

3.3.2. 2,3,5-Tri-*O*-benzyl-4-*O*-*tert*-butyldimethylsilyl-D-ribose ethylenedithioacetal (13). A solution of thioacetal **12** (1.25 g, 2.5 mmol), anhydrous imidazole (514 mg, 7.5 mmol) and TBDMSCl (760 mg, 5.0 mmol) in anhydrous DMF (10 mL) was stirred at room temperature for 24 h. The mixture was treated with saturated aq. solution of NH_4Cl (80 mL) and extracted with cyclohexane. The extracts were dried ($MgSO_4$), filtered and evaporated. The residue was purified by flash chromatography (AcOEt/cyclohexane 5:95) to give the title *compound* **13** (1.29 g, 84%) as a colourless oil. $[\alpha]_D^{20}$=−5.0 (*c*=1.0; $CHCl_3$); ν_{max} (film): 3046, 2910, 2856, 1498, 1456, 1360, 1252, 1100, 838, 776, 736, 696 cm^{-1}; δ_H (250 MHz, $CDCl_3$) 7.33–7.25 (15H, m, 3Ph), 4.97 (1H, d, *J*=4.1 Hz, C(1)*H*), 4.88 and 4.76 (2H, AB, *J*=10.9 Hz, OCH_2Ph), 4.76 and 4.59 (2H, AB, *J*=11.2 Hz, OCH_2Ph),4.47 (2H, s, OCH_2Ph), 4.24 (1H, ddd, *J*=6.0, 4.4, 3.0 Hz, C(4)*H*), 3.88 (1H, dd, *J*=6.9, 4.1 Hz, C(2)*H*), 3.74 (1H, dd, *J*=6.9, 3.0 Hz, C(3)*H*), 3.68 (1H, dd, *J*=9.8, 4.4 Hz, C(5)H_aH_b), 3.54 (1H, dd, *J*=9.8, 6.0 Hz, C(5)H_aH_b), 3.31–3.11 (4H, m, S(CH_2)$_2$), 0.92 (9H, s, SiC(CH_3)$_3$), 0.09 and 0.07 (6H, 2 * s, Si(CH_3)$_2$); δ_C (60 MHz, $CDCl_3$) 138.5, 138.4, 138.2 (*C* s-arom.), 128.3, 127.4 (*C*H arom.), 83.1 (*C*-3), 83.0 (*C*-2), 75.1 (O*C*H_2Ph), 73.7 (O*C*H_2Ph), 73.2 (O*C*H_2Ph), 72.6 (*C*-4), 72.3 (*C*-5), 54.9 (*C*-1), 38.8, 38.4, (S(*C*H_2)$_2$), 25.9 ((*C*H_3)$_3$CSi), 18.1 ((CH$_3$)$_3$*C*Si), −4.55,-4.66 ((*C*H_3)$_2$Si); HRMS (Cl, NH_3) MH^+, 611.2685. $C_{34}H_{47}O_4S_2Si$ requires 611.2685.

3.3.3. 2,3,5-Tri-*O*-benzyl-4-*O*-*tert*-butyldimethylsilyl-D-ribose (14). To a stirred mixture of compound **13** (1.29 g, 2.1 mmol), $CaCO_3$ (630 mg, 6.3 mmol) and water (4 mL) in THF (15 mL) was added dropwise a solution of $Hg(ClO_4)_2$. H_2O (2.26 g, 4.6 mmol) in water (4 mL) at room temperature. The mixture was vigorously stirred at room temperature for 2 h and filtered. The filtrate was diluted with Et_2O (100 mL) and washed with brine (2×60 mL). The organic layer was dried ($MgSO_4$), filtered and evaporated. The residue was purified by flash chromatography (AcOEt/cyclohexane 1:9) to yield the title *compound* **14** (1.01 g, 90%) as a colourless oil. $[\alpha]_D^{20}$=+4.0 (*c*=3.0; $CHCl_3$); δ_H (250 MHz, $CDCl_3$) 9.67 (1H, d, *J*=0.9 Hz, C(1)*H*), 7.33–7.21 (15H, m, 3Ph), 4.64 and 4.57 (2H, AB, *J*=11.9 Hz, OCH_2Ph), 4.68 and 4.56 (2H, AB, *J*=11.9 Hz, OCH_2Ph), 4.46 and 4.41 (2H, AB *J*=12.1 Hz, OCH_2Ph), 4.13 (2H, m, C(2)H, C(4)H), 3.95 (1H, dd, C(3)*H*), 3.54 (2H, d, *J*=4.4 Hz, C(5)H_aH_b), 0.86 (9H, s, SiC(CH_3)$_3$), 0.06 and 0.05 (6H, 2 * s Si(CH_3)$_2$); δ_C (60 MHz, $CDCl_3$) 201.8 (*C*-1), 138.1, 137.8, 137.4 (*C* s-arom.), 128.4–127.6 (*C*H arom.), 82.5 (*C*-2), 81.4 (*C*-3), 73.3 (O*C*H_2Ph), 73.2 (O*C*H_2Ph), 72.8 (O*C*H_2Ph), 71.4 (*C*-5), 71.3 (*C*-4), 25.9 ((*C*H_3)$_3$CSi), 18.1 ((CH$_3$)$_3$*C*Si), −4.5 ((*C*H_3)$_2$Si); HRMS (Cl, NH_3) MH^+, 535.2880. $C_{32}H_{43}O_5Si$ requires 535.2879.

3.3.4. Coupling reaction between the C(5)-lithio derivative of imidazole 10 and 14: synthesis of D-*altro* (15a) and D-*allo* (15b) epimers. A solution of *n*-BuLi in hexanes (2.5 M, 4.5 mL, 11.2 mmol) was added under argon at −78°C to a stirred solution of imidazole derivative **10** (1.80 g, 10.3 mmol) in anhydrous THF (50 mL). After 30 min the TBDMSCl (1.85 g, 12.2 mmol) was added at once and the mixture was stirred at room temperature for 2 h, then cooled again to −78°C and treated with *n*-BuLi in hexane (2.5 M, 4.9 mL, 12.2 mmol). After 30 min, a solution of ribose derivative **14** (3.65 g, 6.8 mmol) in anhydrous THF (5 mL) was added dropwise and the stirring was continued at −78°C for 30 min and then at room temperature for 12 h. The reaction mixture was quenched with water (1 mL) and concentrated under reduced pressure. The residue was diluted with Et_2O (100 mL) and washed with brine (80 mL). The organic layer was dried ($MgSO_4$), filtered and evaporated. The two epimers were separated by careful chromatography (AcOEt/cyclohexane 1:9, 2:8, then 1:1) to give the D-*altro* epimer **15a** (1.24 g, 22%) as an orange-coloured oil and the D-*allo* epimer **15b** (2.84 g, 50%) as a yellow oil. **15a** δ_H (250 MHz, $CDCl_3$) 7.37–7.14 (16H, m, C(4′)*H*, 3Ph), 5.33 (1H, d, *J*=1.2 Hz, C(1)*H*), 4.88 and 4.58 (2H, AB, *J*=11.0 Hz, OCH_2Ph), 4.47 (2H, s, OCH_2Ph), 4.42 and 3.80 (2H, AB, *J*=10.4 Hz, OCH_2Ph), 4.24 (1H, ddd, *J*=6.1, 5.2, 1.8 Hz, C(4)*H*), 4.07 (1H, dd,

J=8.5, 1.2 Hz, C(2)H), 3.84 (1H, dd, J=8.5, 1.2 Hz, C(3)H), 3.74 (1H, dd, J=9.8, 5.2 Hz, C(5)H_aH_b), 3.56 (1H, dd, J=9.8, 6.1 Hz, C(5)H$_a$$H_b$), 2.59 (6H, s, N(C$H_3$)$_2$), 0.98 (9H, s, SiC(C$H_3$)$_3$), 0.90 (9H, s, SiC(C$H_3$)$_3$), 0.40 (6H, s, Si(C$H_3$)$_2$) 0.08 (6H, s, Si(C$H_3$)$_2$); HRMS (Cl, NH$_3$) MH$^+$, found 824.4178. $C_{43}H_{66}N_3O_7Si_2S$ requires 824.4160.**15b** δ_H (250 MHz, CDCl$_3$) 7.49 (1H, s, C(4′)H), 7.33–7.11 (15H, m, 3Ph), 5.28 (1H, dd, J=6.1, 4.3 Hz, C(1)H), 4.69 and 4.51 (2H, AB, J=11.3 Hz, OCH_2Ph), 4.61 and 4.42 (2H, AB, J=1.3 Hz, OCH_2Ph), 4.51 and 4.45 (2H, AB, J=11.9 Hz, OCH_2Ph), 4.26 (1H, ddd, J=5.8, 4.9, 3.7 Hz, C(4)H), 4.05 (1H, t, J=5.5 Hz, C(2)H), 3.81 (1H, dd, J=5.5, 3.7 Hz, C(3)H), 3.67 (1H, dd, J=9.8, 4.9 Hz, C(5)H_aH_b), 3.56 (1H, dd, J=9.8, 5.8 Hz, C(5)H$_a$$H_b$), 3.84 (1H, dd, J=8.5, 1.2 Hz, C(3)H), 3.49 (1H exchange with D$_2$O, d, J=4.3 Hz, C(1)OH), 2.60 (6H, s, N(CH_3)$_2$), 0.98 (9H, s, SiC(CH_3)$_3$), 0.90 (9H, s, SiC(CH_3)$_3$), 0.37 (6H, s, Si(CH_3)$_2$) 0.09 (6H, s, Si(CH_3)$_2$); HRMS (Cl, NH$_3$) MH$^+$, found 824.4179. $C_{43}H_{66}N_3O_7Si_2S$ requires 824.4160.

3.3.5. 1,2,3,5-Tetra-*O*-benzyl-1-[1*H*-imidazol-4(5)yl]-D-*altro*-pentitol (17a). To a stirred solution of epimer **15a** (1.20 g 1.46 mmol) and Bu$_4$NI (catalytic amount) in anhydrous THF (50 mL) was added portionwise 50% NaH in oil (210 mg, ca. 4.4 mmol) at room temperature. When the evolution of H$_2$ ceased, BnBr (0.3 mL, 2.50 mmol) was added at room temperature. Stirring was continued at room temperature for 12 h. The mixture was quenched with MeOH (10 mL) and the solvents were evaporated. The residue was diluted with Et$_2$O (100 mL), washed with water (50 mL) and brine (50 mL). The organic layer was dried (MgSO$_4$), filtered and evaporated. The residue was purified by flash chromatography (AcOEt/cyclohexane 1:9) to obtain the benzylated product **16a** (1.07 g, 1.17 mmol 80%) as a yellow oil. This compound **16a** was dissolved in anhydrous THF (16 mL) and treated with the solution of TBAF in THF (1 M, 4 mL, 4.0 mmol, 3 equiv.). The mixture was stirred at room temperature for 12 h and concentrated in vacuo. The residue was diluted with Et$_2$O (60 mL), washed with a saturated aq. solution of NH$_4$Cl (30 mL) and the organic layer was evaporated without drying. The residue was dissolved in aq. HCl (1.5 M, 30 mL) and the solution was refluxed for 2 h. The reaction mixture was neutralised with NH$_4$OH and extracted with CHCl$_3$ (2×30 mL). The organic layers were dried (MgSO$_4$), filtered and evaporated. The residue was purified by flash chromatography (CH$_2$Cl$_2$/MeOH-NH$_3$ 96:4) to give the title *compound* **17a** (507 mg, 60% from **15a**) as a light yellow resin. $[\alpha]_D^{20}$=−3 (c=1.0; CHCl$_3$); δ_H (250 MHz, CDCl$_3$) 7.44 (1H, s, C(2′)H), 7.36–7.08 (20H, m, 4Ph), 6.97 (1H, s, C(5′)H), 5.87 (1H, d, J=7.3 Hz, C(1)H), 4.75 and 4.66 (2H, AB, J=11.4 Hz, OCH_2Ph), 4.50 and 4.38 (2H, AB, J=11.6 Hz, OCH_2Ph), 4.47 and 4.42 (2H, AB, J=11.9 Hz, OCH_2Ph), 4.52 and 4.34 (2H, AB, J=11.3 Hz, OCH_2Ph), 4.10 (1H, dd, J=7.3, 2.4 Hz, C(2)H), 3.89 (1H, ddd, J=7.6, 5.8, 2.4 Hz, C(4)H), 3.63 (1H, dd, J=9.8, 2.4 Hz, C(5)H_aH_b), 3.61 (1H, dd, J=7.6, 2.4 Hz, C(3)H), 3.51 (1H, dd, J=9.8, 5.8 Hz, C(5)H$_a$$H_b$); δ_C (60 MHz, CDCl$_3$): 138.0–138.6 (*C* s-arom.), 135.5 (*C*-2′), 128.3–127.5 (*C*H arom.), 82.7 (*C*-4), 79.3 (*C*-3), 75.9 (*C*-1), 75.0 (OCH$_2$Ph), 73.3 (OCH$_2$Ph), 72.7 (OCH$_2$Ph), 71.7 (OCH$_2$Ph), 71.0 (*C*-5), 70.3 (*C*-2); HRMS (Cl, NH$_3$) MH$^+$, found 579.2863. $C_{36}H_{39}N_2O_5$ requires 579.2859.

3.3.6. 5,6,7,8-Tetra-*O*-benzyl-imidazolo[1,5]-L-*galacto*-piperidinose (18). To a stirred solution of compound **17a** (230 mg, 0.4 mmol) in dry pyridine (5 mL) at 0°C was added MsCl (0.125 mL, 1.6 mmol). After stirring for 1 h at room temperature, followed by addition of Ac$_2$O (0.25 mL), the mixture was heated at 80°C for 20 h, and neutralised at room temperature with EtOH (1 mL). The reaction mixture was diluted with AcOEt (25 mL) and washed with brine (3×20 mL). The organic layer was dried (MgSO$_4$), filtered and evaporated. The residue was purified by flash chromatography (Et$_2$O/MeOH-NH$_3$ 98:2) to yield the title *compound* **18** (150 mg, 67%) as a yellow oil. $[\alpha]_D^{20}$=−56 (c=1.0; CHCl$_3$), δ_H (250 MHz, CDCl$_3$) 8.06 (1H, s, C(1)H), 7.42–7.06 (20H, m, 4Ph), 7.42 (1H, s, C(3)H), 4.75 (1H, d, J=4.5 Hz, C(8)H), 4.53 and 4.31 (2H, AB, J=11.8 Hz, OCH_2Ph), 4.42 (2H, s, OCH_2Ph),4.24 (1H, ddd, J=8.4, 2.3, 1.8 Hz, C(5)H), 4.19 (1H, dd, J=6.3, 1.8 Hz, C(6)H), 4.12 and 4.03 (2H, AB, J=11.8 Hz, OCH_2Ph), 3.98 (1H, dd, J=9.9, 2.3 Hz, C(9) H_aH_b), 3.97 (1H, dd, J=6.3, 4.5 Hz, C(7)H), 3.77 (1H, dd, J=9.9, 8.4 Hz, C(9)H$_a$$H_b$); δ_C (60 MHz, CDCl$_3$) 137.7–137.4 (*C* s-arom.), 136.8 (*C*-3), 127.4–128.4 (*C*H arom., *C*-1), 124.9 (*C*-8a), 77.3 (*C*-7), 73.5 (*C*-6), 73.3 (OCH$_2$Ph), 72.6 (OCH$_2$Ph), 72.3 (OCH$_2$Ph), 70.8 (*C*-9), 70.7 (OCH$_2$Ph), 69.6 (*C*-8), 56.3 (*C*-5); HRMS (Cl, NH$_3$) MH$^+$, found 561.2754. $C_{36}H_{37}N_2O_4$ requires 561.2753.

3.3.7. Imidazolo[1,5]-L-*galacto*-piperidinose (2). A suspension of piperidinose **18** (130 mg, 0.23 mmol) and 10% Pd(OH)$_2$/C (Pearlman's catalyst) (250 mg) in EtOH/AcOH (4 mL, 1:1) was vigorously stirred under H$_2$ (ca. 2 atm.) at room temperature for 24 h. The suspension was centrifuged and the catalyst was washed several times with MeOH. The solution was evaporated to dryness in vacuo and the residue was dissolved in MeOH and passed over an Amberlyst IRA 400 (OH$^-$) column (elution with MeOH). The combined fractions were evaporated and the residue was purified by flash chromatography (CHCl$_3$/MeOH/NH$_4$OH 5:4:1) to give the title *compound* **2** (36 mg, 78%) as a pale yellow powder. $[\alpha]_D^{20}$=+12 (c=0.5; H$_2$O); δ_H (400 MHz; D$_2$O) 7.83 (1H, s, C(3)H), 6.98 (1H, s, C(1)H), 4.80 (1H, d, J=8.6 Hz, C(8)H), 4.33 (1H, t, J=2.5 Hz, C(6)H), 4.25 (1H, ddd, J=6.7, 5.3, 2.5 Hz, C(5)H), 4.08 (1H, dd, J=11.7, 6.7 Hz, C(9)H_aH_b), 3.99 (1H, dd, J=11.7, 5.3 Hz, C(9)H$_a$$H_b$), 3.81 (1H, dd, J=8.6, 2.2 Hz, C(7)H); δ_C (100.6 MHz; D$_2$O): 135.5 (*C*-3), 130.5 (*C*-8a), 124.6 (*C*-1), 73.4 (*C*-7), 69.6 (*C*-6), 65.2 (*C*-8), 61.1 (*C*H$_2$OH), δ=58.1 (*C*-5); HRMS (Cl, NH$_3$) MH$^+$, found 201.0877. $C_8H_{13}N_2O_4$ requires 201.0875.

3.3.8. 1,2,3,5-Tetra-*O*-benzyl-[1*H*-imidazol-4(5)-yl]-D-*allo*-pentitol (17b). The same procedure as described for the preparation of **17a** (see above) was used, starting from **15b** (2.68 g, 3.25 mmol) in THF (40 mL), Bu$_4$NI (catalytic amount) and a 50% suspension of NaH in oil (468 mg, ca.10 mmol) and BnBr (0.5 mL, 4.19 mmol) to give after workup **16b**, which without purification was treated with a solution of TBAF in THF (1 M, 10 mL, 10.0 mmol) and after workup as above, was refluxed in aq. HCl (1.5 M, 40 mL). After workup and chromatography (CH$_2$Cl$_2$/MeOH-NH$_3$ 96:4) the title *compound* **17b** was given (1.54 g, 82%) as a yellow resin. $[\alpha]_D^{20}$=+46 (c=1.0; CHCl$_3$); δ_H (400 MHz, CDCl$_3$) 7.48 (1H, s, C(2′)H),

7.34–7.13 (20H, m, 4Ph), 6.92 (1H, s, C(4′,5′)*H*), 4.85 (1H, d, *J*=4.3 Hz, C(1)*H*), 4.75 and 4.63 (2H, AB, *J*=11.0 Hz, OC*H*$_2$Ph), 4.48 (2H, s, OC*H*$_2$Ph), 4.54 and 4.44 (2H, AB, *J*=11.1, OC*H*$_2$Ph), 4.48 and 4.33 (2H, AB, *J*=11.8, OC*H*$_2$Ph), 4.15 (1H, dd, *J*=5.9, 4.3 Hz, C(2)*H*), 4.14 (1H, ddd, *J*=6.6, 4.9, 3.2 Hz, C(4)*H*), 3.60 (1H, dd, *J*=9.8, 6.6 Hz, C(5)*H*$_a$H$_b$), 3.57 (1H, dd, *J*=9.8, 3.2 Hz, C(5)H$_a$*H*$_b$), 3.55 (1H, t, *J*=4.9 Hz, C(3)*H*); δ_C (100.6 MHz; $CDCl_3$) 138.0–137.9 (*C* s-arom.), 135.7 (*C*-2′), 128.5–127.6 (*C*H arom.), 81.3 (*C*-4), 79.1 (*C*-3), 74.6 (O*C*H$_2$Ph), 73.7 (*C*-1), 73.4 (O*C*H$_2$Ph), 73.3 (O*C*H$_2$Ph), 71.1 (*C*-2), 71.0 (*C*-5), 70.4 (O*C*H$_2$Ph); HRMS (Cl, NH_3) MH^+, found 579.2860. $C_{36}H_{39}N_2O_5$ requires 579.2859.

3.3.9. 2,3,5-Tri-*O*-benzyl-1[1*H*-imidazol-4(5)-yl]α-L-*lyxo*-furanoside (21). To a stirred solution of **17b** (480 mg, 0.83 mmol) and dry pyridine (0.27 mL, 3.32 mmol) in dry CH_2Cl_2 (40 mL) Tf_2O (0.42 mL, 2.5 mmol) was added dropwise at −20°C. Stirring was continued at −20°C for 2 h and for another 3 h at room temperature. The reaction mixture was washed with saturated aq. $NaHCO_3$ solution. The organic layer was evaporated without drying. The residue was dissolved in MeOH (20 mL) and NaOH aq. solution (4 M, 10 mL) was added. The mixture was stirred at room temperature for 30 min and concentrated under reduced pressure. The residue was diluted with CH_2Cl_2 (50 mL), washed with H_2O (40 mL) and extracted with CH_2Cl_2 (2×20 mL). The organic layers were dried ($MgSO_4$), evaporated and the residue purified by flash chromatography (CH_2Cl_2/MeOH-NH_3 95:5) to give the title *compound* **21** (233 mg, 60%) as a colourless resin. $[\alpha]_D^{20}=-29$ (*c*=1.0; $CHCl_3$); δ_H (400 MHz, $CDCl_3$) 7.34–7.16 (16H, m, C*H* arom. and C(2′)*H*), 6.67 (1H, s, C(4′, 5′)*H*), 5.03 (1H, d, *J*=7.1 Hz, C(1)*H*), 4.76 and 4.54 (2H, AB, *J*=11.7, OC*H*$_2$Ph), 4.54 and 4.47 (2H, AB, *J*=12.1, OC*H*$_2$Ph), 4.45 (2H, s, OC*H*$_2$Ph), 4.44 (1H, m, C(4)*H*), 4.38 (1H, dd, *J*=7.1, 4.2 Hz, C(2)*H*), 4.19 (1H, t, *J*=4.3 Hz, C(3)*H*), 3.78 (1H, dd, *J*=9.9, 6.8 Hz, C(5)*H*$_a$H$_b$), 3.75 (1H, dd, *J*=9.9, 5.4 Hz, C(5)H$_a$*H*$_b$); δ_C (100.6 MHz, $CDCl_3$) 138.2–137.8 (3 * *C* s-arom.), 137.6 (*C*-5′), 135.8 (*C*-2′), 127.5–128.4 (*C*H arom.), 116.5 (*C*-4′), 83.0 (*C*-2), 78.6 (*C*-4), 77.7 (*C*-3), 75.6 (*C*-1), 73.4 (2 * O*C*H$_2$Ph), 72.4 (O*C*H$_2$Ph), 69.4 (*C*-5); HRMS (Cl, NH_3) MH^+, found 471.2282. $C_{29}H_{31}N_2O_4$ requires 471.2284.

3.3.10. 4,5-(α-L-Lyxofuranosyl)-*H*-imidazole (7). A mixture of furanoside **21** (297 mg, 0.63 mmol), 10% $Pd(OH)_2$/C (350 mg) and PdO (50 mg) in EtOH (10 mL) was vigorously stirred under H_2 (ca. 2 atm) at room temperature for 48 h. The suspension was centrifuged and the catalyst was washed several times with EtOH. The combined organic solutions were evaporated and the residue was purified by flash chromatography ($CHCl_3$/MeOH/H_2O) 5:4.5:0.5) to give the title *compound* **7** (102 mg, 81%) as a colourless oil which was crystallised (MeOH) mp 197–198°C (dec.). [Found: C 48.1, H 6.2, N 13.7 $C_8H_{12}N_2O_4$ requires C 48.00, H 6.04, N 13.99%]. $[\alpha]_D^{20}=-57$ (*c*=1.0; D_2O); δ_H (250 MHz, CD_3OD) 8.04 (1H, s, C(2′)*H*), 7.22 (1H, s, C(4′, 5′)*H*), 4.87 (1H, d, *J*=6.9 Hz, C(1)*H*), 4.36–4.24 (3H, m, C(2)*H*, C(3)*H* and C(4)*H*), 3.84 (1H, dd, *J*=11.6, 4.6 Hz, C(5)*H*$_a$H$_b$), 3.77 (1H, dd, *J*=11.6, 5.8 Hz, C(5)H$_a$*H*$_b$); δ_C (60 MHz, CD_3OD) 137.7 (*C*-4′), 136.8 (*C*-2′), 118.0 (*C*-5′), 82.2 (*C*-2), 78.0 (*C*-4), 77.7 (*C*-3), 73.2 (*C*-1), 62.1 (*C*-5); HRMS (Cl, NH_3) MH^+, found 201.0878. $C_8H_{13}N_2O_4$ requires 201.0875.

3.3.11. 2,3,5-Tri-*O*-benzyl-L-arabinose ethylenedithioacetal (24). The same procedure as for the preparation of **12** was used, starting from 2,3,5-tri-*O*-benzyl-L-arabinofuranose **23**[20] (5.65 g, 13.4 mmol) and ethanedithiol (1.9 g, 20 mmol) in dioxane saturated with HCl (60 mL). After workup as for **12**, the crude product was purified by flash chromatography (AcOEt/hexane 1:3) to give the title *compound* **24** (4.1 g, 61.5%) as a pale yellow oil. $[\alpha]_D^{20}=-23.1$ (*c*=1.4; $CHCl_3$); ν_{max} (film): 3030, 3016, 2920, 1484, 1436, 1188, 1092, 900, 736, 696, 620; δ_H (250 MHz, $CDCl_3$) 7.40–7.25 (15H, m, 3Ph), 4.91 (1H, d, *J*=8.1 Hz, C(1)*H*), 4.96 and 4.74 (2H, AB, *J*=11.6 Hz, OC*H*$_2$Ph), 4.65 and 4.53 (2H, AB, *J*=11.0 Hz, OC*H*$_2$Ph), 4.54 and 4.49 (2H, AB, *J*=11.9 Hz, OC*H*$_2$Ph), 3.98 (1H, m, C(4)*H*), 3.85 (1H, dd, *J*=8.1, 2.4 Hz, C(2)*H*), 3.78 (1H, dd, *J*=8.8, 2.4 Hz, C(3)*H*), 3.67 (1H, dd, *J*=9.5, 3.3 Hz, C(5)*H*$_a$H$_b$), 3.59 (1H, dd, *J*=9.7, 4.9 Hz, C(5)H$_a$*H*$_b$), 3.30–3.14 (4H, m, S(C*H*$_2$)$_2$), 2.59 (1H, exhange with D_2O, d, *J*=4.7 Hz, C(4)O*H*); δ_C (60 MHz, $CDCl_3$) 138.2–137.7 (3 * *C* s-arom.), 128.4–127.5 (*C*H arom), 83.7 (*C*-2), 79.8 (*C*-3), 75.3 (O*C*H$_2$Ph), 74.2 (O*C*H$_2$Ph), 73.4 (O*C*H$_2$Ph), 71.0 (*C*-5), 70.1 (*C*-4), 54.4 (*C*-1), 38.7 and 37.8 (S(*C*H$_2$)$_2$); HRMS (Cl, NH_3) MH^+, 497.1817. $C_{28}H_{33}O_4S_2$ requires 497.1820.

3.3.12. 2,3,5-Tri-*O*-benzyl-4-*O*-*tert*-butyldimethylsilyl-L-arabinose ethylenedithioacetal (25). To a stirred solution of compound **24** (4.65 g, 9.4 mmol) in anhydrous DMF was added anhydrous imidazole (1.92 g, 28 mmol) and TBDMSCl (4.23 g, 28 mmol) and stirring was continued at 80°C for 20 h. The reaction mixture was poured into ice-water (150 mL) and extracted with cyclohexane. The extracts were dried ($MgSO_4$), filtered and evaporated. The residue was purified by flash chromatography (AcOEt/hexane 4:1) to gove the title *compound* **25** (4.7 g, 82%) as a pale yellow oil. $[\alpha]_D^{20}=+1.5$ (*c*=1.0; $CHCl_3$); ν_{max} (film): 3048, 2912, 2856, 1496, 1456, 1360, 1252, 1100, 836, 776, 736, 696; δ_H (250 MHz, $CDCl_3$) 7.33–7.25 (15H, m, 3Ph), 4.86 (1H, d, *J*=5.5 Hz, C(1)*H*), 4.83 and 4.74 (2H, AB, *J*=11.6 Hz, OC*H*$_2$Ph), 4.77 and 4.66 (2H, AB, *J*=11.1 Hz, OC*H*$_2$Ph), 4.47 (2H, s, OC*H*$_2$Ph), 4.09 (1H, ddd, *J*=5.4, 4.7, 3.7 Hz, C(4)*H*), 3.83 (1H, dd, *J*=5.5, 3.7 Hz, C(3)*H*), 3.79 (1H, dd, *J*=9.7, 4.7 Hz, C(5)*H*$_a$H$_b$), 3.76 (1H, t, *J*=5.5 Hz, C(2)*H*), 3.52 (1H, dd, *J*=9.7, 5.4 Hz, C(5)H$_a$*H*$_b$), 3.31–3.10 (4H, m, S(C*H*$_2$)$_2$), 0.91 (9H, s, SiC(C*H*$_3$)$_3$), 0.11 and 0.10 (6H, 2 * s, Si(C*H*$_3$)$_2$); δ_C (60 MHz, $CDCl_3$) 138.8, 138.6, 138.1 (*C* s-arom.), 128.3–127.3 (*C*H arom.), 84.3 (*C*-3), 84.1 (*C*-2), 75.8 (O*C*H$_2$Ph), 75.0 (O*C*H$_2$Ph), 73.3 (O*C*H$_2$Ph), 73.1 (*C*-4), 71.5 (*C*-5), 54.6 (*C*-1), 38.8, 38.7, (S(*C*H$_2$)$_2$), 25.9 ((*C*H$_3$)$_3$CSi), 18.1 ((CH$_3$)$_3$*C*Si), −4.33, −4.63 ((*C*H$_3$)$_2$Si); HRMS (Cl, NH_3) MH^+, 611.2684. $C_{34}H_{47}O_4S_2Si$ requires 611.2685.

3.3.13. 2,3,5-Tri-*O*-benzyl-4-*O*-*tert*-butyldimethylsilyl-L-arabinose (26). To a stirred solution of thioacetal **25** (4 g, 6.5 mmol) in a mixture of acetone and water (100 mL, 4:1) were added Na_2CO_3 (4.8 g, 45 mmol) and MeI (10 mL) and the mixture was stirred at reflux under argon atmosphere for 16 h. Additional portions (2×2.5 mL) of MeI were added during heating. After evaporation of the acetone, residue

was diluted with H_2O and extracted with cyclohexane. The organic layer was dried ($MgSO_4$), filtered and evaporated. The residue was purified by flash chromatography (AcOEt/hexane 1:10) to give the title *compound* **26** (1.7 g, 48.6%) as a pale yellow thick oil; δ_H (250 MHz, $CDCl_3$) 9.78 (1H, d, J=1.1 Hz, C(1)*H*), 7.39–7.28 (15H, m, 3Ph), 4.79 and 4.63 (2H, AB, J=11.8 Hz, OCH_2Ph), 4.66 and 4.58 (2H, AB, J=11.9, OCH_2Ph), 4.54 (2H, s, OCH_2Ph), 4.23 (1H, ddd, J=5.1, 4.7, 4.6 Hz C(4)*H*), 4.13 (2H, dd, J=4.4, 1.1 Hz, C(2)*H*), 4.07 (1H, dd, J=4.4, 4.6 Hz, C(3)*H*), 3.80 (2H, dd, J=9.9, 4.7 Hz, C(5)H_aH_b),), 3.66 (2H, dd, J=9.9, 5.1 Hz, C(5)H_aH_b), 0.95 (9H, s, SiC(CH_3)$_3$), 0.13 and 0.12 (6H, 2 * s Si(CH_3)$_2$); δ_C (60 MHz, $CDCl_3$) 201.7 (*C*-1), 138.1, 137.8, 137.4 (*C* s-arom.), 128.4–127.5 (*C*H arom.), 83.3 (*C*-2), 80.3 (*C*-3), 73.5 (O*C*H$_2$Ph), 73.2 (O*C*H$_2$Ph), 73.1 (O*C*H$_2$Ph), 72.0 (*C*-4), 71.3 (*C*-5), 25.8 ((*C*H$_3$)$_3$CSi), 18.1 ((CH$_3$)$_3$*C*Si), −4.4 ((*C*H$_3$)$_2$Si); HRMS (Cl, NH_3) MH^+, 535.2881. $C_{32}H_{43}O_5Si$ requires 535.2879.

3.3.14. Coupling reaction between the C(5)-lithio derivative of imidazole 10 and 26: synthesis of L-*gluco* (27a) and L-*manno* (27b) epimers. To a stirred solution of imidazole **10** (1.23 g, 4.26 mmol) in anhydrous THF (15 mL) was added dropwise a solution of BuLi in hexane (1.6 M, 2.9 mL, 4.65 mmol) under Ar at −70°C and the stirring was continued at −50°C for 20 min. To the mixture cooled again to −70°C was added dropwise a solution of **26** (1.32 g, 2.46 mmol) in anhydrous THF (15 mL) and the stirring was continued at −70°C for 30 min and then at room temperature for 2.5 h. The reaction mixture was diluted with H_2O, THF was evaporated under reduced pressure and the residue was extracted with CH_2Cl_2. The organic layer was dried ($MgSO_4$), filtered and evaporated. The two epimers were separated by careful chromatography (AcOEt/hexane 1:2) to give the L-*gluco* epimer **27a** (0.63 g, 31%, R_f=0.5) and the L-*manno* epimer **27b** (1.35 g, 66.5%, R_f=0.7) both as a pale yellow oils. **27a** $[\alpha]_D^{20}$=−19.7 (c=1.2 $CHCl_3$); δ_H (250 MHz, $CDCl_3$) 7.47 (1H, s, C(4′)*H*), 7.41–7.18 (15H, m, 3Ph), 5.25 (1H, d, J=5.8 Hz, C(1)*H*), 4.71 (2H, s, OCH_2Ph), 4.53 (2H, s, OCH_2Ph), 4.52 and 4.24 (2H, AB, J=10.8 Hz, OCH_2Ph), 4.07 (1H, ddd, J=7.0, 6.5, 5.8 Hz, C(4)*H*), 3.98 (1H, dd, J=5.8, 1.5 Hz, C(2)*H*), 3.84 (1H, dd, J=6.5, 1.5 Hz, C(3)*H*), 3.86 (1H, dd, J=10.1, 5.8 Hz, C(5)H_aH_b), 3.85 (1H, dd, J=6.5, 1.5 Hz, C(3)*H*), 3.71 (1H, dd, J=10.1, 7.0 Hz, C(5)H_aH_b), 2.78 (6H, s, N(CH_3)$_2$), 1.01 (9H, s, SiC(CH_3)$_3$), 0.90 (9H, s, SiC(CH_3)$_3$), 0.47 (3H, s, Si(CH_3)$_2$), 0.46 (3H, s, Si(CH_3)$_2$), 0.16 (3H, s, Si(CH_3)$_2$), 0.15 (3H, s, Si(CH_3)$_2$), δ_C (60 MHz, $CDCl_3$) 155.7 (*C*-2′), 138.3, 137.6, 135.0, (*C* s-arom.), 132.2 (*C*-5′), 128.3–127.4 (*C*H arom.), 81.6 (*C*-3), 80.1 (*C*-2), 77.2 (*C*-4), 74.9 (O*C*H$_2$Ph), 74.1 (O*C*H$_2$Ph), 73.1 (O*C*H$_2$Ph), 72.0 (*C*-5), 64.9 (*C*-1), 37.6 (*C*H$_3$)$_2$N, 27.4 ((*C*H$_3$)$_3$CSi), 25.9 ((*C*H$_3$)$_3$CSi), 18.32 ((CH$_3$)$_3$*C*Si), 18.21 ((CH$_3$)$_3$*C*Si), −3.22, −3.43, −4.49, −4.76, ((*C*H$_3$)$_2$Si); HRMS (Cl, NH_3) MH^+, found 824.4179. $C_{43}H_{66}N_3O_7Si_2S$ requires 824.4160. **27b** $[\alpha]_D^{20}$=+20.3 (c=0.8 $CHCl_3$); δ_H (250 MHz, $CDCl_3$) 7.65 (1H, s, C(4′)*H*), 7.39–7.16 (15H, m, 3Ph), 5.08 (1H, dd, J=10.3, 4.5 Hz, C(1)*H*), 4.56 and 4.48 (2H, AB, J=11.8 Hz, OCH_2Ph), 4.19 (1H, dd, J=7.5, 4.5 Hz, C(2)*H*), 3.93 (1H, dd, J=12.6, 4.8 Hz, C(5)H_aH_b), 3.91 (1H, ddd, J=8.2, 4.8, 0.8 Hz, C(4)*H*), 3.85 (1H, dd, J=7.5, 0.8 Hz, C(3)*H*), 3.48 (1H, dd, J=12.6, 8.2 Hz, C(5)H_aH_b), 2.70 (6H, s, N(CH_3)$_2$), 2.57 (1H, d, J=10.3 Hz, C(1)O*H*), 1.06 (9H, s, SiC(CH_3)$_3$), 0.81 (9H, s, SiC(CH_3)$_3$), 0.36 (3H, s, Si(CH_3)$_2$), −0.06 (3H, s, Si(CH_3)$_2$), −0.24 (6H, s, Si(CH_3)$_2$)); δ_C (60 MHz, $CDCl_3$) 155.7 (*C*-2′), 138.9, 138.7, 138.2 (*C* s-arom.), 133.1 (C-4′), 132.3 (*C*-5′), 128.4–127.4 (*C*H arom.), 85.7 (*C*-3), 83.7 (*C*-2), 77.2 (*C*-4), 75.9 (O*C*H$_2$Ph), 75.6 (O*C*H$_2$Ph), 73.4 (O*C*H$_2$Ph), 70.8 (*C*-5), 62.9 (*C*-1), 36.9 (*C*H$_3$)$_2$N, 27.1 ((*C*H$_3$)$_3$CSi), 25.7 ((*C*H$_3$)$_3$CSi), 18.5 ((CH$_3$)$_3$*C*Si), 17.8 ((CH$_3$)$_3$*C*Si), −3.7, −3.9, −5.2, ((*C*H$_3$)$_2$Si); HRMS (Cl, NH_3) MH^+, found 824.4179. $C_{43}H_{66}N_3O_7Si_2S$ requires 824.4160.

3.3.15. 1,2,3,5-Tetra-*O*-benzyl-1-[1*H*-imidazol-4(5)-yl]-L-*manno*-pentitol (29b). To a stirred solution of compound **27b** (0.68 g, 0.826 mmol) in anhydrous DMF (7.5 mL) was added portionwise 50% NaH in oil (80 mg, ca. 3.3 mmol) at 10°C. When the evolution of H_2 ceased, BnBr (0.24 mL, 1.98 mmol) was added at 0°C. Stirring was continued at room temperature overnight. The mixture was neutralised with a saturated aq. $NaHCO_3$ solution (5 mL) and extracted with AcOEt. The organic layer was dried ($MgSO_4$), filtered and evaporated. The crude product **28b** was dissolved in the mixture of THF (24 mL)/aq. HCl solution (1.5 M, 12 mL) and refluxed for 2 h, then stirred at room temperature overnight. The reaction mixture was neutralised with saturated aq. K_2CO_3 solution, extracted with $CHCl_3$, dried ($MgSO_4$) and evaporated. The residue was purified by flash chromatography ($CHCl_3$/EtOH 10:1) to give the title *compound* **29b** (306 mg, 64% from **27b**) as a pale yellow oil. $[\alpha]_D^{20}$=+6.4 (c=0.55; $CHCl_3$).); δ_H (400 MHz, $CDCl_3$) 7.57 (1H, s, C(2′)*H*), 7.34–7.13 (20H, m, 4Ph), 7.11 (1H, s, C(4′,5′)*H*), 4.74 (1H, d, J=5.7 Hz, C(1)*H*), 4.44 (2H, s, OCH_2Ph), 4.48 (2H, s, OCH_2Ph), 4.57 and 4.41 (2H, AB, J=10.7, OCH_2Ph), 4.46 and 4.25 (2H, AB, J=11.7, OCH_2Ph), 4.22 (1H, dd, J=5.7, 4.7 Hz, C(2)*H*), 3.94 (1H, ddd, J=7.5, 5.5, 3.7 Hz, C(4)*H*), 3.71 (1H, dd, J=7.5, 4.7 Hz, C(3)*H*), 3.66 (1H, dd, J=9.6, 3.7 Hz, C(5)H_aH_b), 3.57 (1H, dd, J=9.6, 5.5 Hz, C(5)H_aH_b); δ_C (100.6 MHz; $CDCl_3$), 138.2, 138.1, 138.0, 137.8 (4 * *C* s-arom.), 135.5 (*C*-2′), 133.7 (C-4′), 128.4–127.6 (*C*H arom.), 124.5 (C-5′), 82.0 (*C*-2), 79.2 (*C*-3), 75.1 (O*C*H$_2$Ph), 74.4 (O*C*H$_2$Ph), 73.5 (*C*-1), 73.4 (O*C*H$_2$Ph), 71.1 (*C*-5), 71.0 (*C*-4), 70.1 (O*C*H$_2$Ph); HRMS (Cl, NH_3) MH^+, found 579.2861. $C_{36}H_{39}N_2O_5$ requires 579.2859.

3.3.16. 1,2,3,5-Tetra-*O*-benzyl-1-[1*H*-imidazol-4(5)-yl]-L-*gluco*-pentitol (29a). The same procedure as for the preparation of **29b** was used, starting from **27a** (0.68 g, 0.826 mmol) in anhydrous DMF (7.5 mL), 50% NaH in oil (80 mg, ca. 3.3 mmol) and BnBr (0.24 mL, 1.98 mmol). Acid hydrolysis of the crude **28a** and workup followed by chromatography gave the title *compound* **29a** (300 mg, 63% from **27a**) as a pale yellow oil. $[\alpha]_D^{20}$=−26.0 (c=0.45; $CHCl_3$); δ_H (400 MHz, $CDCl_3$) 7.43 (1H, s, C(2′)*H*), 7.39–7.08 (20H, m, 4Ph), 6.90 (1H, s, C(4′,5′)*H*), 4.84 (1H, d, J=5.7 Hz, C(1)*H*), 4.56 and 4.50 (2H, AB, J=10.9 Hz OCH_2Ph), 4.71 and 4.48 (2H, AB, J=10.3, OCH_2Ph), 4.46 (2H, s, OCH_2Ph), 4.53 and 4.29 (2H, AB, J=11.8, OCH_2Ph), 4.08–3.98 (2H, m, C(2)*H* and C(4)*H*), 3.75 (1H, dd, J=6.3, 4.2 Hz, C(3)*H*), 3.63 (1H, dd, J=9.4, 3.8 Hz, C(5)H_aH_b), 3.61 (1H, dd, J=9.4, 6.4 Hz, C(5)H_aH_b); δ_C (100.6 MHz; $CDCl_3$) 138.1, 138.0, 137.9, 137.7 (4 * *C* s-arom.), 132.4 (*C*-2′), 128.8–126.7 (*C*H arom.), 121.5 (C-5′), 81.4 (*C*-2), 78.2 (*C*-3), 74.8 (O*C*H$_2$Ph), 74.5

(O*C*H$_2$Ph), 73.6 (*C*-1), 73.2 (O*C*H$_2$Ph), 71.1 (*C*-2), 73.6 (*C*-5), 70.8 (O*C*H$_2$Ph), 70.7 (*C*-4); HRMS (Cl, NH$_3$) MH$^+$, found 579.2864. $C_{36}H_{39}N_2O_5$ requires 579.2859.

3.3.17. 5,6,7,8-Tetra-*O*-benzyl-imidazolo[1,5]-L-*ido*-piperidinose (30a). The same procedure as for the preparation of **18** was used, starting from **29a** (200 mg, 0.346 mmol), in anhydrous pyridine (4.5 mL), MsCl (0.11 mL, 1.385 mmol) and Ac$_2$O (0.22 mL) to give after workup and chromatography (CH$_2$Cl$_2$/acetone 2.5:1) the title *compound* **30a** (39 mg, 20%) as an yellow oil. $[\alpha]_D^{20}$=+36.0 (*c*=0.95; CHCl$_3$); δ_H (250 MHz, CDCl$_3$) 7.69 (1H, s, C(3)*H*), 7.39–7.15 (20H, m, 4Ph), 7.10 (1H, s, C(1)*H*), 4.80 and 4.70 (2H, AB, *J*=11.8 Hz, OC*H*$_2$Ph), 4.59 and 4.53 (2H, AB, *J*=11.9 Hz, OC*H*$_2$Ph), 4.69 (1H, d, *J*=3.5 Hz, C(8)*H*), 4.67 (s, 2H, OC*H*$_2$Ph), 4.52–4.45 (1H, bd, from COSY obscured by OCH$_2$Ph, C(5)*H*), 4.47 (2H, s, OC*H*$_2$Ph), 4.12 (1H, dd, *J*=7.5, 3.5 Hz, C(7)*H*), 3.92 (1H, dd, *J*=10.1, 3.4 Hz, C(9) *H*$_a$H$_b$), 3.86 (1H, dd, *J*=7.5, 5.0 Hz, C(6)*H*), 3.84 (1H, dd, *J*=10.1, 4.2 Hz, C(9)H$_a$*H*$_b$); δ_C (60 MHz, CDCl$_3$) 137.8 (*C*-8a), 137.5–137.4 (*C* s-arom.), 136.3 (*C*-3), 128.2–127.6 (*C*H arom.), 125.5 (*C*-1), 78.8 (*C*-7), 76.8 (*C*-6), 73.5 (O*C*H$_2$Ph), 73.3 (O*C*H$_2$Ph), 73.2 (O*C*H$_2$Ph), 71.7 (*C*-9), 70.9 (O*C*H$_2$Ph), 69.5 (*C*-8), 55.0 (*C*-5); HRMS (Cl, NH$_3$) MH$^+$, found 561.2754. $C_{36}H_{37}N_2O_4$ requires 561.2753.

3.3.18. 5,6,7,8-Tetra-*O*-benzyl-imidazolo[1,5]-D-*gulo*-piperidinose (30b). The same procedure as for the preparation of **30a** was used, starting from **29b** (200 mg, 0.346 mmol), in anhydrous pyridine (4.5 mL), MsCl (0.11 mL, 1.385 mmol) and Ac$_2$O (0.22 mL). Workup followed by chromatography (CH$_2$Cl$_2$/acetone 2.5:1) gave the title *compound* **30b** (99 mg, 51%) as a yellow oil. $[\alpha]_D^{20}$=+4.3 (*c*=0.7; CHCl$_3$); δ_H (250 MHz, CDCl$_3$) 7.73 (1H, s, C(3)*H*), 7.41–7.11 (20H, m, 4Ph), 7.01 (1H, s, C(1)*H*), 4.79 (1H, d, *J*=3.3 Hz, C(8)*H*), 4.71 and 4.58 (2H, AB, *J*=12.0 Hz, OC*H*$_2$Ph), 4.67 and 4.54 (2H, AB, *J*=12.4 Hz, OC*H*$_2$Ph), 4.64–4.56 (1H, bd, from COSY obscured by OCH$_2$Ph, C(5)*H*), 4.62–4.50 (2H, AB, *J*=11.7 Hz, OC*H*$_2$Ph), 4.54–4.48 (2H, AB, *J*=11.8 Hz, OC*H*$_2$Ph), 4.23 (1H, dd, *J*=6.9, 4.8 Hz, C(6)*H*), 3.98 (1H, dd, *J*=6.9, 3.3 Hz, C(7)*H*), 3.81 (2H, d, *J*=5.9 Hz, C(9)*H*$_a$H$_b$); δ_C (60 MHz, CDCl$_3$) 138.0 (*C*-8a), 137.9–137.5 (*C* s-arom.), 136.3 (*C*-3), 129.8–127.7 (*C*H arom.), 126.9 (*C*-1), 77.2 (*C*-7), 75.1 (O*C*H$_2$Ph), 74.7 (*C*-6), 73.5 (O*C*H$_2$Ph), 73.4 (O*C*H$_2$Ph), 72.6 (*C*-9), 70.8 (O*C*H$_2$Ph), 68.6 (*C*-8), 54.9 (*C*-5); HRMS (Cl, NH$_3$) MH$^+$, found 561.2755. $C_{36}H_{37}N_2O_4$ requires 561.2753.

3.3.19. Imidazolo[1,5]-D-*ido*-piperidinose (3). A suspension of piperidinose **30a** (65 mg, 0.115 mmol) and 10% Pd(OH)$_2$/C (Pearlman's catalyst) (150 mg) in EtOH/AcOH (4 mL, 1:1) was vigorously stirred under H$_2$ (ca. 2 atm) at room temperature for 24 h. The suspension was centrifuged and the catalyst was washed several times with MeOH. The solution was evaporated under reduced pressure and the residue was dissolved in MeOH and passed over an Amberlyst IRA 400 (OH$^-$) column (elution with MeOH). The combined fractions were evaporated and the residue was purified by flash chromatography (CHCl$_3$/MeOH/NH$_4$OH 5:4:1) to yield the title *compound* **3** (11 mg, 48%) as a pale yellow powder. $[\alpha]_D^{20}$=+8.0 (*c*=0.25; CH$_3$OH); δ_H (400 MHz; CD$_3$OD) 7.76 (1H, s, C(3)*H*), 7.01 (1H, s, C(1)*H*), 4.70 (1H, overlaps with HDO signal, C(8)H), 4.50–4.40 (1H, m, C(5)H), 4.20 (1H, dd, *J*=5.5, 2.5 Hz, C(6)H), 4.10 (1H, dd, *J*=9.6, 5.5 Hz, C(7)*H*), 4.00 (1H, dd, *J*=12.2, 3.7 Hz, C(9)*H*$_a$H$_b$), 3.79 (1H, dd, *J*=12.2, 6.8 Hz, C(9)H$_a$*H*$_b$); δ_C (100.6 MHz; D$_2$O): 131.9 (*C*-3), 129.0 (*C*-8a), 123.7 (*C*-1), 72.7 (*C*-7), 69.2 (*C*-6), 67.6 (*C*-9), 61.1 (*C*-8), 58.9 (*C*-5); HRMS (Cl, NH$_3$) MH$^+$, found 201.0878. $C_8H_{13}N_2O_4$ requires 201.0875.

3.3.20. Imidazolo[1,5]-D-*gulo*-piperidinose (4). The same procedure as for the preparation of **3** was used staring from **30b** (170 mg, 0.43 mmol) to give after workup **4** (31 mg, 51%) as a pale yellow powder. $[\alpha]_D^{20}$=−46.9 (*c*=1.15; CH$_3$OH); δ_H (400 MHz; CD$_3$OD) 8.20 (1H, s, C(3)*H*), 7.15 (1H, s, C(1)*H*), 4.98 (1H, dd, *J*=4.0, 0.9 Hz, C(8)H), 4.45–4.39 (1H, m, C(5)H), 4.37 (1H, dd, *J*=7.1, 6.3 Hz, C(6)H), 4.17 (1H, dd, *J*=6.3, 4.0 Hz, C(7)*H*), 4.03 (1H, dd, *J*=12.1, 4.1 Hz, C(9)*H*$_a$H$_b$), 3.95 (1H, dd, *J*=12.1, 6.4 Hz, C(9)H$_a$*H*$_b$); δ_C (100.6 MHz; D$_2$O): 133.5 (*C*-3), 128.5 (*C*-8a), 120.6 (*C*-1), 66.5 (*C*-7), 65.8 (*C*-6), 60.1 (*C*-9), 59.2 (*C*-8), 54.3 (*C*-5); HRMS (Cl, NH$_3$) MH$^+$, found 201.0878. $C_8H_{13}N_2O_4$ requires 201.0875.

3.3.21. Coupling reaction between the C(5)-lithio derivative of imidazole 10 and 3-*O*-benzyl-1,2-*O*-isopropylidene-1,5-D-xylo-dialdofuranose 31: synthesis of L-*gulo* (32a) and L-*ido* (32b) epimers. To a stirred solution of imidazole **10** (8.8 g, 30.4 mmol) in anhydrous THF (65 mL) was added dropwise a solution of *n*-BuLi in hexane (1.6 M, 19 mL, 30.4 mmol) under argon at −70°C. After 15 min a solution of **31** (4.7 g, 16.9 mmol) in anhydrous THF (70 mL) was added dropwise at −60°C. After another 15 min the acetone-dry ice bath was removed and the mixture was stirred for 2.5 h at room temperature. The reaction was quenched with cold water, evaporated under reduced pressure and the residue was diluted with water, extracted with CH$_2$Cl$_2$, dried (MgSO$_4$), filtered and evaporated. The two epimers were separated by careful chromatography (CH$_2$Cl$_2$/acetone 12:1) to give the L-*gulo* epimer **32a** (4.5 g, 7.9 mmol, 47%, R_F=0.48) and the L-*ido* epimer **32b** (3.0 g, 5.3 mmol, 31%, R_f=0.3) both as a yellow foams. **32a** $[\alpha]_D^{20}$=−34 (*c*=1.4; CHCl$_3$); ν_{max} (film): 3384, 2928, 2856, 1460, 1380, 1252, 1160, 1076, 1028, 844, 832, 780, 728, 700 cm^{-1}; δ_H (250 MHz, CDCl$_3$) 7.37–7.27 (5H, m, Ph), 7.26 (1H, s, C(4′)*H*), 5.89 (1H, d, *J*=3.6 Hz, C(5)*H*), 5.25 (1H, dd, *J*=8.5, 4.8 Hz, C(1)*H*), 4.64 (1H, d, *J*=3.6 Hz, C(4)H), 4.74 and 4.62 (2H, AB, *J*=11.2 Hz, OC*H*$_2$Ph), 4.52 (1H, dd, *J*=8.5, 3.0 Hz, C(2)*H*), 4.22 (1H, d, *J*=3.0 Hz, C(3)*H*), 3.15 (1H, d, *J*=4.8 Hz, O*H*), 2.75 (6H, s, N(C*H*$_3$)$_2$), 1.51 and 1.33 (6H, 2s, C(C*H*$_3$)$_2$), 1.01 (9H, s, SiC(C*H*$_3$)$_3$), 0.38 (6H, s, Si(C*H*$_3$)$_2$); δ_C (60 MHz, CDCl$_3$) 153.3 (*C*-2′), 136.6 (*C* s-arom.), 129.5 (*C*-4′), 128.5–126.9 (*C*H arom., *C*-5′), 112.6 (*C*(CH$_3$)$_2$), 105.1 (*C*-5), 82.2 (*C*-3), 81.4 (*C*-4), 79.5 (*C*-2), 72.4 (O*C*H$_2$Ph), 63.7 (*C*-1), 38.1 (N(*C*H$_3$)$_2$), 27.0 (Si(*C*(CH$_3$)$_3$), 26.4 and 25.7 (C(*C*H$_3$)$_2$), 14.5 (C(*C*H$_3$)$_3$), −3.7 (Si(*C*H$_3$)$_2$); FAB-MS: 568 (MH$^+$); HRMS (Cl, NH$_3$) MH$^+$, found 568.2512. $C_{26}H_{42}N_3O_7SSi$ requires 568.2513. **32b** $[\alpha]_D^{20}$=−35 (*c*=1.1; CHCl$_3$); ν_{max} (film): 3472, 2936, 2856, 1460, 1376, 1252, 1160, 1076, 1020, 844, 832, 784, 728, 696 cm^{-1}; δ_H (250 MHz, CDCl$_3$) 7.37–7.16 (5H, m, Ph), 7.21 (1H, s, C(4′)*H*), 6.04 (1H, d, *J*=3.8 Hz, C(5)*H*), 5.26 (1H, dd, *J*=5.7, 2.6 Hz, C(1)*H*),

4.57 (1H, d, J=3.8 Hz, C(4)H),4.57 (1H, dd, J=5.7, 3.7 Hz, C(2)*H*), 4.54 and 4.38 (2H, AB, J=11.8 Hz, OCH_2Ph), 4.03 (1H, d, J=3.7 Hz, C(3)*H*), 3.20 (1H, d, J=2.6 Hz, O*H*), 2.77 (6H, s, N(CH_3)$_2$), 1.49 and 1.33 (6H, 2s, C(CH_3)$_2$), 1.00 (9H, s, SiC(CH_3)$_3$), 0.40 and 0.39 (6H, 2s, Si(CH_3)$_2$); δ_C (60 MHz, $CDCl_3$) 156.1 (*C*-2′), 137.0 (*C* s-arom.), 130.9 (*C*-4′), 128.5–127.6 (*C*H arom., *C*-5′), 111.6 (*C*(CH$_3$)$_2$), 104.9 (*C*-5), 82.5 (*C*-3), 82.3 (*C*-4), 80.1 (*C*-2), 71.8 (O*C*H$_2$Ph), 62.7 (*C*-1), 37.3 (N(*C*H$_3$)$_2$), 27.2 (Si(*C*(CH$_3$)$_3$), 26.7 and 26.2 (C(*C*H$_3$)$_2$), 18.3 (C(*C*H$_3$)$_3$), −3.6 and −3.7 (Si(*C*H$_3$)$_2$); HRMS (Cl, NH_3) MH^+, found 568.2512. $C_{26}H_{42}N_3O_7SSi$ requires 568.2513.

3.3.22. (5*R*)-3,5-Di-*O*-benzyl-5-[1*H*-imidazol-4(5)-yl]-D-xylofuranose (34a). To a stirred solution of compound **32a** (2.54 g, 4.47 mmol) in anhydrous DMF (40 mL) was added portionwise 50% NaH in oil (0.44 g, ca 9.1 mmol) at room temperature. After 30 min the mixture was cooled to 0°C and BnBr (1.3 mL, 10.8 mmol) was added dropwise. Stirring was continued at room temperature overnight. The mixture was neutralised with saturated aq. $NaHCO_3$ solution (50 mL) and extracted with AcOEt. The organic layer was dried ($MgSO_4$), filtered and evaporated. The crude product **33a** was dissolved in THF (12.5 mL) and aq. HCI solution (1.5 M, 20 mL) was added. The mixture was refluxed for 1.5 h, neutralised with saturated aq. K_2CO_3 solution, evaporated under reduced pressure and coevaporated several times with dry ethanol to remove water. Residue was extracted a few times with dry ethanol and chromatographed after evaporation ($CHCl_3$/EtOH 5:1) to give the title *compound* **34a** (1.06 g, 2.67 mmol, 60% from **32a**) as a yellow oil containing mixture of anomers (two pairs of imidazole signals on ^{1}H NMR spectrum); HRMS (Cl, NH_3) MH^+, found 397.1764. $C_{22}H_{25}N_2O_5$ requires 397.1763.

3.3.23. (5*S*)-3,5-Di-*O*-benzyl-5-[1*H*-imidazol-4(5)-yl]-D-xylofuranose (34b). The same procedure as for the preparation of **34a** was used starting from **32b** (5.58 g, 9.815 mmol) to give after workup the title *compound* **34b** (2.53 g, 6.38 mmol, 65% from **32b**) as a yellow oil containing mixture of anomers (two pairs of imidazole signals on ^{1}H NMR spectrum); HRMS (Cl, NH_3) MH^+, found 397.1764. $C_{22}H_{25}N_2O_5$ requires 397.1763.

3.3.24. 1,3-Di-*O*-benzyl-1-[1*H*-imidazol-4(5)-yl]-L-*gulo*-pentitol (35a). To a stirred solution of compound **34a** (0.33 g, 0.83 mmol) in anhydrous methanol (5 mL) was added portionwise $NaBH_4$ (0.16 g, 4.2 mmol) at 0°C. The mixture was stirred at 0°C for 30 min and stirring was continued at room temperature overnight. The reaction was quenched with saturated aq. NH_4Cl solution, evaporated to dryness and purified by chromatography ($CHCl_3$/EtOH 1:1) to give the title *compound* **35a** (0.29 g, 0.73 mmol, 87%) as a yellow foam. $[\alpha]_D^{20}$=−49 (c=0.8; MeOH); ν_{max} (film): 3288, 2872, 1496, 1456, 1228, 1064, 756, 700 cm^{-1}; δ_H (60 MHz, acetone-d$_6$) 7.78 (1H, bs, C(2′)*H*), 7.40–7.20 (10H, m, 2Ph), 7.19 (1H, bs, C(5′)*H*), 4.77 and 4.62 (2H, AB, J=11.5 Hz, OCH_2Ph), 4.69 (1H, d, J=7.3 Hz, C(1)*H*), 4.47 and 4.33 (2H, AB, J=11.5 Hz, OCH_2Ph), 4.24 (1H, dd, J=7.3, 2.0 Hz, C(2)H), 3.95–3.85 (2H, m, C(3)*H*, C(4)*H*), 3.66 (2H, bd, J=4.8 Hz, C(5)H_aH_b); δ_C (60 MHz, acetone-d$_6$) 140.1, 139.3 (*C* s-arom.), 136.7 (*C*-2′), 135.9 (*C*-4′), 129.0–128.0 (*C*H arom.), 120.6 (*C*-5′), 79.5 (*C*-3), 75.3 (*C*-1), 74.9 (O*C*H$_2$Ph), 73.7 (*C*-4), 73.5 (*C*-2), 70.6 (O*C*H$_2$Ph), 63.6 (*C*-5); HRMS (Cl, NH_3) MH^+, found 399.1919. $C_{22}H_{27}N_2O_5$ requires 399.1920.

3.3.25. 1,3-Di-*O*-benzyl-1-[1*H*-imidazol-4(5)-yl]-L-*ido*-pentitol (35b). The same procedure as for the preparation of **35a** was used starting from **34b** (0.34 g, 0.86 mmol) to give after workup the title *compound* **35b** (0.30 g, 0.75 mmol, 88%) as a yellow foam. $[\alpha]_D^{20}$=+28° (c=0.9; MeOH); ν_{max} (film): 3240, 2872, 1496, 1456, 1224, 1088, 788, 700 cm^{-1}; δ_H (60 MHz, acetone-d$_6$) 7.79 (1H, bs, C(2′)*H*), 7.40–7.20 (10H, m, 2Ph), 7.15 (1H, bs, C(5′)*H*), 4.79 (1H, d, J=6.5 Hz, C(1)*H*), 4.69 and 4.61 (2H, AB, J=11.8 Hz, OCH_2Ph), 4.50 and 4.41 (2H, AB, J=11.8 Hz, OCH_2Ph), 4.28 (1H, dd, J=6.5, 3.8 Hz, C(2)H), 3.94 (1H, dt, J=5.5, 4.5 Hz, C(4)*H*), 3.66 (2H, bd, J=5.5 Hz, C(5)H_aH_b), 3.59 (1H, dd, J=4.5, 3.8 Hz, C(3)*H*); δ_C (60 MHz, acetone-d$_6$) 140.2, 139.5 (*C* s-arom.), 136.6 (*C*-4′), 136.1 (*C*-2′), 128.9–128.0 (*C*H arom.), 119.5 (*C*-5′), 80.2 (*C*-3), 76.1 (*C*-1), 74.6 (O*C*H$_2$Ph), 74.4 (*C*-2), 73.2 (*C*-4), 70.8 (O*C*H$_2$Ph), 63.7 (*C*-5); HRMS (Cl, NH_3) MH^+, found 399.1919. $C_{22}H_{27}N_2O_5$ requires 399.1920.

3.3.26. 1,3-Di-*O*-benzyl-1-(1-triphenylmethyl-1*H*-imidazol-4-yl)-5-*O*-triphenylmethyl-L-*gulo*-pentitol (36a). The solution of compound **35a** (0.42 g, 1.05 mmol), TrCl (0.88 g, 3.14 mmol) and DMAP (18 mg) in dry pyridine (6 mL) was stirred under argon atmosphere at 80–90°C for 48 h. The mixture was evaporated under reduced pressure, coevaporated several times with toluene to remove pyridine and purified by chromatography (AcOEt/hexane 2:1) to yield the title *compound* **36a** (0.45 g, 0.51 mmol, 48%) as a white foam. $[\alpha]_D^{20}$=−32 (c=0.85; $CHCl_3$); ν_{max} (film): 3064, 3048, 3032, 2984, 2880, 1596, 1492, 1448, 1216, 1072, 788, 704 cm^{-1}; δ_H (250 MHz, $CDCl_3$) 7.49 (1H, d, J=1.3 Hz, C(2′)*H*), 7.45–7.00 (40H, m, 8Ph), 6.86 (1H, d, J=1.3 Hz, C(5′)*H*), 4.50 (1H, d, J=8 Hz, C(1)*H*), 4.44 and 4.22 (2H, AB, J=12.0 Hz, OCH_2Ph), 4.42 (2H, s, OCH_2Ph), 4.20–4.12 (3H, m, C(2)*H*, C(3)*H*, C(4)*H*), 3.36 (1H, dd, J=8.0, 5.0 Hz, C(5)H_aH_b), 3.19 (1H, dd, J=8.0, 6.0 Hz, C(5)H_aH_b); δ_C (60 MHz, $CDCl_3$) 139.1 (*C*-2′), 130.0–127.0 (m, *C*H arom., *C*-4′), 121.4 (*C*-5′), 77.1 (*C*-3), 75.5 (*C*-1), 75.3 (*C*-2), 74.8 (O*C*H$_2$Ph), 72.9 (*C*-4), 70.4 (O*C*H$_2$Ph), 64.5 (*C*-5); HRMS (Cl, NH_3) MH^+, found 883.4110. $C_{60}H_{55}N_2O_5$ requires 883.4111.

3.3.27. 1,3-Di-*O*-benzyl-1-(1-triphenylmethyl-1*H*-imidazol-4-yl)-5-*O*-triphenylmethyl-L-*ido*-pentitol (36b). The same procedure as for the preparation of **36a** was used starting from **35b** (0.39 g, 0.98 mmol) to give after workup the title *compound* **36b** (0.48 g, 0.54 mmol, 56%) as white foam. $[\alpha]_D$=+18 (c=0.8; $CHCl_3$); ν_{max} (film): 3064, 3048, 3032, 2984, 2880, 1596, 1492, 1448, 1216, 1072, 788, 704 cm^{-1}; δ_H (250 MHz, $CDCl_3$) 7.40 (1H, d, J=1.3 Hz, C(2′)*H*), 7.35–7.00 (40H, m, 8Ph), 6.73 (1H, d, J=1.3 Hz, C(5′)*H*), 4.58 (1H, d, J=6.0 Hz, C(1)*H*), 4.55 and 4.31 (2H, AB, J=11.5 Hz, OCH_2Ph), 4.53 and 4.35 (2H, AB, J=11.0 Hz, OCH_2Ph), 4.22 (1H, dd, J=6.0, 4.0 Hz, C(2)*H*,), 4.08 (1H, ddd, J=7.0, 6.0, 2.5 Hz, C(4)*H*), 3.84 (1H, dd, J=4.0, 2.5 Hz, C(3)*H*), 3.34 (1H, dd, J=9.0, 6.0 Hz, C(5)H_aH_b), 3.18 (1H, dd, J=9.0, 7.0 Hz, C(5)H_aH_b);

δ_C (60 MHz, $CDCl_3$) 139.1 (*C*-2′), 130.0–127.0 (m, *C* arom., *C*-4′), 121.4 (*C*-5′), 77.1 (*C*-3), 75.5 (*C*-1), 75.3 (*C*-2), 74.8 (O*C*H_2Ph), 72.9 (*C*-4), 70.4 (O*C*H_2Ph), 64.5 (*C*-5); HRMS (Cl, NH_3) MH^+, found 883.4110. $C_{60}H_{55}N_2O_5$ requires 883.4111.

3.3.28. 1,2,3-Tri-*O*-benzyl-1-(1-triphenylmethyl-1*H*-imidazol-4-yl)-5-*O*-triphenylmethyl-L-*gulo*-pentitol (37a) and 1,3,4-Tri-*O*-benzyl-1-(1-triphenylmethyl-1*H*-imidazol-4-yl)-5-*O*-triphenylmethyl-L-*gulo*-pentitol (38a). To a stirred solution of **36a** (120 mg, 0.14 mmol) in anhydrous THF (2 mL) was added portionwise 50% NaH in oil (10 mg, ca. 0.2 mmol) at 0°C. After 30 min a catalytic amount of Bu_4NI was added and then BnBr (0.025 mL, 0.21 mmol) was added dropwise. The reaction mixture was stirred overnight at room temperature, quenched with MeOH and evaporated to dryness. Residue was diluted with water and extacted with $CHCl_3$. The organic layer was dried ($MgSO_4$), filtered and evaporated. The residue was purified by flash chromatography (AcOEt/hexane 3:2) to give title *compounds* **37a** (62 mg, 0.064 mmol, 47%, R_f=0.55) and **38a** (36 mg, 0.037 mmol, 27%, R_f=0.48) both as a white foams. **37a** $[\alpha]_D^{20}=-9$ (c=1.1; CH_2Cl_2); ν_{max} (film): 3064, 3048, 3032, 2984, 2872, 1600, 1496, 1448, 1212, 1068, 788, 700 cm^{-1}; δ_H (250 MHz, $CDCl_3$) 7.40 (1H, d, J=1.3 Hz, C(2′)*H*), 7.38–6.80 (45H, m, 9Ph), 6.77 (1H, d, J=1.3 Hz, C(5′)*H*), 4.77 (1H, d, J=5.5 Hz, C(1)*H*), 4.52 and 4.30 (2H, AB, J=11.0 Hz, OCH_2Ph), 4.47 and 4.33 (2H, AB, J=11.5 Hz, OCH_2Ph), 4.46 (2H, s, OCH_2Ph), 4.22 (1H, ddd, J=7.5, 6.0, 2.0 Hz, C(4)*H*), 4.17 (1H, t, J=2.0 Hz, C(3)*H*), 4.02 (1H, dd, J=5.5, 2.0 Hz, C(2)*H*), 3.33 (1H, dd, J=9.0, 6.0 Hz, C(5)H_aH_b), 3.12 (1H, dd, J=9.0, 7.5 Hz, C(5)H_aH_b); δ_C (60 MHz, $CDCl_3$) 143.0, 141.3 (*C*Ph_3), 137.7–137.3 (m, *C*-2′, *C*-4′, *C* s-arom.), 128.7–125.8 (m, *C*-arom.), 120.6 (*C*-5′), 81.2 (*C*-2), 77.9 (*C*-3), 74.4 (*C*-1), 73.7 (O*C*H_2Ph), 73.0 (O*C*H_2Ph), 69.4 (O*C*H_2Ph), 69.1 (*C*-4), 62.5 (*C*-5); HRMS (Cl, NH_3) MH^+, found 973.4580. $C_{67}H_{61}N_2O_5$ requires 973.4580. **38a** $[\alpha]_D^{20}=-15$ (c=1.8; CH_2Cl_2); ν_{max} (film): 3064, 3048, 3032, 2984, 2872, 1600, 1492, 1448, 1240, 1068, 756, 700 cm^{-1}; δ_H (250 MHz, $CDCl_3$) 7.58–6.90 (46H, m, 9Ph, C(2′)*H*), 6.78 (1H, d, J=1.3 Hz, C(5′)*H*), 4.69 and 4.36 (2H, AB, J=11.3 Hz, OCH_2Ph), 4.68 and 4.60 (2H, AB, J=11.8 Hz, OCH_2Ph), 4.44 (1H, d, J=3.3 Hz, C(1)*H*), 4.42 and 4.13 (2H, AB, J=12.5 Hz, OCH_2Ph), 4.16 (1H, dd, J=6.3, 65.3 Hz, C(3)*H*), 4.00 (1H, dd, J=6.3, 3.3 Hz, C(2)*H*), 3.94 (1H, dt, J=5.3, 3.3 Hz, C(4)*H*), 3.45 (1H, dd, J=10.5, 3.3 Hz, C(5)H_aH_b), 3.29 (1H, dd, J=10.5, 5.3 Hz, C(5)H_aH_b); δ_C (60 MHz, $CDCl_3$) 144.0, 142.3 (*C*Ph_3), 139.8–138.3 (m, *C*-2′, *C*-4′, *C* s-arom.), 129.7–126.7 (m, *C*-arom.), 120.8 (*C*-5′), 80.2 (*C*-4), 77.9 (*C*-3), 75.8 (*C*-1), 74.3 (O*C*H_2Ph), 73.0 (*C*-2), 72.9 (O*C*H_2Ph), 70.0 (O*C*H_2Ph), 63.5 (*C*-5); HRMS (Cl, NH_3) MH^+, found 973.4581. $C_{67}H_{61}N_2O_5$ requires 973.4580.

3.3.29. 1,3,4-Tri-*O*-benzyl-1-(1-triphenylmethyl-1*H*-imidazol-4-yl)-5-*O*-triphenylmethyl-L-*ido*-pentitol (37b) and 1,3,4-tri-*O*-benzyl-1-(1-triphenylmethyl-1*H*-imidazol-4-yl)-5-*O*-triphenylmethyl-L-*ido*-pentitol (38b). The same procedure as for the preparation of **37a** and **38a** was used starting from **36b** (120 mg, 0.14 mmol) to give after workup title *compounds* **37b** (49 mg, 0.05 mmol, 37%, R_f=0.50) and **38b** (31 mg, 0.032 mmol, 23%, R_f=0.58) as a white foams. **37b** $[\alpha]_D^{20}=-1$ (c=1.4; CH_2Cl_2); ν_{max} (film): 3064, 3048, 3032, 2984, 1600, 1492, 1448, 1216, 1072, 908, 788, 700 cm^{-1}; δ_H (250 MHz, $CDCl_3$) 7.45 (1H, d, J=1.3 Hz, C(2′)*H*), 7.42–6.88 (45H, m, 9Ph), 6.86 (1H, d, J=1.3 Hz, C(5′)*H*), 4.81 (1H, d, J=5.3 Hz, C(1)*H*), 4.60 and 4.53 (2H, AB, J=11.3 Hz, OCH_2Ph), 4.53 and 4.41 (2H, AB, J=11.5 Hz, OCH_2Ph), 4.45 and 4.25 (2H, AB, J=11.0 Hz, OCH_2Ph), 4.14 (1H, dd, J=6.3, 5.3 Hz, C(2)*H*), 4.05 (1H, ddd, J=8.0, 6.0, 1.8 Hz, C(4)*H*), 3.95 (1H, dd, J=6.3, 1.8 Hz, C(3)*H*),3.31 (1H, dd, J=9.0, 6.0 Hz, C(5)H_aH_b), 3.04 (1H, dd, J=9.0, 8.0 Hz, C(5)H_aH_b); δ_C (60 MHz, $CDCl_3$) 143.8, 142.3 (*C*Ph_3), 139.1–138.0 (m, *C*-2′, *C*-4′, *C* s-arom.), 129.6–126.8 (m, *C*H arom.), 120.7 (*C*-5′), 82.1 (*C*-2), 78.5 (*C*-3), 76.7 (*C*-1), 75.1 (O*C*H_2Ph), 74.2 (O*C*H_2Ph), 71.1 (O*C*H_2Ph), 70.1 (*C*-4), 64.4 (*C*-5); HRMS (Cl, NH_3) MH^+, found 973.4579. $C_{67}H_{61}N_2O_5$ requires 973.4580. **38b** $[\alpha]_D^{20}=+13$ (c=0.9; CH_2Cl_2). IR (film): 3064, 3048, 3032, 2984, 2872, 1600, 1492, 1448, 1216, 1068, 908, 740, 700 cm^{-1}; δ_H (250 MHz, $CDCl_3$) 7.50–7.00 (46H, m, 9Ph, C(2′)*H*), 6.51 (1H, d, J=1.3 Hz, C(5′)*H*), 4.65 and 4.43 (2H, AB, J=11.3 Hz, OCH_2Ph), 4.62 and 4.43 (2H, AB, J=11.0 Hz, OCH_2Ph), 4.49 and 4.20 (2H, AB, J=12.0 Hz, OCH_2Ph), 4.36 (1H, d, J=6.8 Hz, C(1)*H*), 4.06 (1H, dd, J=6.8, 3.5 Hz, C(2)*H*), 3.90 (1H, ddd, J=5.8, 5.5, 3.5 Hz, C(4)*H*), 3.73 (1H, dd, J=5.5, 3.5 Hz, C(3)*H*), 3.44 (1H, dd, J=10.3, 3.5 Hz, C(5)H_aH_b), 3.30 (1H, dd, J=10.3, 5.8 Hz, C(5)H_aH_b); δ_C (60 MHz, $CDCl_3$) 144.1, 142.2 (*C*Ph_3), 138.8–138.0 (m, *C*-2′, *C*-4′, *C* s-arom.), 129.6–126.7 (m, *C*H arom.), 121.3 (*C*-5′), 79.7 (*C*-4), 78.4 (*C*-3), 74.9 (*C*-1), 74.5 (O*C*H_2Ph), 73.5 (*C*-2), 72.7 (O*C*H_2Ph), 70.0 (O*C*H_2Ph), 63.5 (*C*-5); HRMS (Cl, NH_3) MH^+, found 973.4581. $C_{67}H_{61}N_2O_5$ requires 973.4580.

3.3.30. 6,7,8-Tri-*O*-benzyl-imidazolo[1,5]-D-*manno*-piperidinose (40a). To a stirred solution of $BnSO_2Cl$ (53 mg, 0.27 mmol) in dry pyridine (1.25 mL) was added dropwise under argon atmosphere a solution of **37a** (86 mg, 0.088 mmol) in dry pyridine (1.25 mL) at −30°C. After 30 min the acetone-dry ice bath was removed and the reaction was stirred overnight at room temperature. The mixture was evaporated under reduced pressure, coevaporated several times with toluene to remove pyridine and purified by flash chromatography (hexane/AcOEt 2:1) to give the title *compound* **39a** (R_f=0.50) which was dried, dissolved in dry pyridine (7.5 mL) and stirred at 60–80°C for 3 days, until **39a** disappeared (TLC). The mixture was evaporated under reduced pressure and the residue was dissolved in THF (7.5 mL). To this solution aq. HCl (6 M, 2.5 mL) was added and the mixture was refluxed for 1.5 h. THF was evaporated under reduced pressure and the residue was neutralised with saturated aq. solution of K_2CO_3 and extracted with $CHCl_3$. The organic layer was dried ($MgSO_4$), filtered, evaporated and the residue was purified by flash chromatography ($CHCl_3$/MeOH 9:1) to give **40a** (22 mg, 0.047 mmol, 53% from **37a**) as a white foam. $[\alpha]_D^{20}=-62$ (c=0.9; $CHCl_3$); ν_{max} (film): 3064, 3048, 3032, 2928, 2864, 1496, 1456, 1360, 1228, 1112, 936, 788, 696, 664 cm^{-1}; δ_H (250 MHz, $CDCl_3$): 7.69 (1H, bs, C(3)*H*), 7.37–7.27 (15H, m, 3Ph), 6.96 (1H, bs, C(1)*H*), 4.97 and 4.73 (2H, AB, J=11.3 Hz, OCH_2Ph), 4.70 (1H, d, J=3.0 Hz, C(8)*H*), 4.68 and 4.60 (2H, AB, J=12.0, OCH_2Ph), 4.63 and 4.32 (2H, AB, J=12.3 Hz, OCH_2Ph), 4.27 (1H, dd, J=8.5, 5.8 Hz, C(6)*H*), 4.19 (1H, ddd, J=6.5,

5.8, 3.5 Hz, C(5)*H*), 3.93 (1H, dd, *J*=11.5, 3.5 Hz,), 3.80 (1H, dd, *J*=11.5, 6.5 Hz, C(5)H_aH_b), 3.80 (1H, dd, *J*=8.5, 3.0 Hz, C(7)*H*); δ_H (60 MHz, $CDCl_3$) 137.8, 137.6 and 137.4 (*C* s-arom.), 136.9 (*C*-3), 135.8 (*C*-8a), 125.6 (*C*-1), 80.3 (*C*-7), 74.8 (*C*-6), 74.2 (O*C*H_2Ph), 71.8 (O*C*H_2Ph), 69.5 (O*C*H_2Ph), 65.7 (*C*-8), 63.7 (*C*-9), 61.5 (*C*-5); HRMS (Cl, NH_3) MH^+, found 471.2281. $C_{29}H_{31}N_2O_4$ requires 471.2283.

3.3.31. Imidazolo[1,5]-D-*manno*-piperidinose (5). To a solution of piperidinose **40a** (22 mg, 0.047 mmol) in 95% ethanol (2 mL) was added 10% Pd/C catalyst (50 mg) and the mixture was stirred at room temperature overnight under H_2 atmosphere. The presence of substrate was still monitored (TLC). Addition of a new portion of the catalyst (50 mg) and additional time (24 h) was necessary for substrate disappearance. Then mixture was filtered through celite pad, evaporated and purified by flash chromatography (EtOH/NH_3aq. 6:1) to give the title *compound* **5** (7 mg, 0.035 mmol, 75%) as a brown foam. $[\alpha]_D^{20}=-25$ (*c*=0.35; MeOH); δ_H (250 MHz, D_2O) 8.22 (1H, bs, C(3)*H*), 7.27 (1H, bs, C(1)*H*), 5.14 (1H, d, *J*=3.5 Hz, C(8)*H*), 4.35 (1H, dd, *J*=12.3, 2.5 Hz, C(9)H_aH_b), 4.30 (1H, dd, *J*=9.5, 8.0 Hz, C(6)*H*), 4.18 (1H, ddd, *J*=8.0, 4.3, 2.5 Hz, C(5)*H*), 4.12 (1H, dd, *J*=12.3, 4.3 Hz, C(9)H_aH_b), 4.02 (1H, dd, *J*=9.5, 3.5 Hz, C(7)*H*); δ_C (60 MHz, D_2O) 133.8 (*C*-8a), 128.2 (*C*-3), 122.4 (*C*-1), 69.0 (*C*-7), 63.2 (*C*-6), 59.9 (*C*-8), 59.4 (*C*-5), 58.3 (*C*-9); HRMS (Cl, NH_3) MH^+, found 201.0878. $C_8H_{13}N_2O_4$ requires 201.0875.

3.3.32. 6,7,8-Tri-*O*-benzyl-imidazolo[1,5]-D-*gluco*-piperidinose (40b), 4,5-(2,3,4-tri-*O*-benzyl-α-D-arabinopyranosyl)-1*H*-imidazole (41) and 4,5-(2,3,4-tri-*O*-benzyl-β-D-arabinopyranosyl)1*H*-imidazole (42). The same procedure as for the preparation of **40a** was used starting from **37b** (230 mg, 0.24 mmol) to give first after flash chromatography (hexane/AcOEt 2:1) **39b**. According to farther procedure the ditrityl derivative **39b** was stirred in pyridine at 60–80°C until substrate disappeared (TLC) and subsequently after evaporation of pyridine the residue was refluxed in the mixture THF/aq. HCl (6 M). After workup as for **40a**, as a result of three subsequent chromatographies ($CHCl_3$/MeOH 9:1; acetone/CH_2Cl_2 3:1; AcOEt/$CHCl_3$/EtOH 6:3:1) three products were isolated: **41** (36 mg, 0.076 mmol, 32% from **37b**, R_f=0.29), **42** (21 mg, 0.044 mmol, 19% from **37b** R_f=0.20) and **40b** (7 mg, 0.015 mmol, 6% from **37b**, R_f=0.15) as a white foams. (R_f values in AcOEt/$CHCl_3$/EtOH 6:3:1). **40b** $[\alpha]_D^{20}=+9$ (*c*=0.25; $CHCl_3$); ν_{max} (film): 3064, 3048, 3032, 2928, 2864, 1496, 1456, 1364, 1264, 1152, 1200, 1108, 944, 784, 696, 648 cm^{-1}; δ_H (250 MHz, $CDCl_3$) 7.66 (1H, bs, C(3)*H*), 7.37–7.26 (15H, m, 3Ph), 7.05 (1H, bs, C(1)*H*), 4.84 and 4.62 (2H, AB, *J*=11.5 Hz, OCH_2Ph), 4.78 and 4.71 (2H, AB, *J*=11.5 Hz, OCH_2Ph), 4.70 (1H, d, *J*=5.0 Hz, C(8)*H*), 4.69 and 4.60 (2H, AB, *J*=11.8 Hz, OCH_2Ph), 4.15 (1H, ddd, *J*=7.8, 5.3, 3.0 Hz, C(5)*H*), 4.13 (1H, dd, *J*=12.8, 3.0 Hz, C(9)H_aH_b), 4.10 (1H, dd, *J*=6.8, 5.0 Hz, C(7)*H*), 3.98 (1H, dd, *J*=12.8, 5.3 Hz, C(9)H_aH_b), 3.81 (1H, dd, *J*=7.8, 6.8 Hz, C(6)*H*); δ_C (60 MHz, $CDCl_3$) 136.0–135.6 (m, *C* s-arom.), 132.6 (*C*-3), 129.8 (*C*-8a), 127.5–126.0 (m, *C*H arom., *C*-1), 82.7 (*C*-7), 77.3 (*C*-6), 73.8 (O*C*H_2Ph), 73.5 (O*C*H_2Ph), 72.0 (*C*-8), 71.4 (O*C*H_2Ph), 60.5 (*C*-9), 60.5 (*C*-5); HRMS (Cl, NH_3) MH^+, found 471.2280. $C_{29}H_{31}N_2O_4$ requires 471.2283. **41** $[\alpha]_D^{20}=-37$ (*c*=0.4; $CHCl_3$); ν_{max} (film): 3064, 3048, 3032, 2928, 2864, 1496, 1456, 1356, 1312, 1208, 1088, 912, 788, 740, 696 cm^{-1}; δ_H (250 MHz, $CDCl_3$) 7.61 (1H, s, C(2′)*H*), 7.45–7.08 (15H, m, 3Ph), 7.08 (1H, s, C(5′)*H*), 4.81 and 4.72 (2H, AB, *J*=12.5 Hz, OCH_2Ph), 4.73 and 4.25 (2H, AB, *J*=11.5 Hz, OCH_2Ph), 4.69 and 4.64 (2H, AB, *J*=12.0 Hz, OCH_2Ph), 4.30 (1H, d, *J*=9.3 Hz, C(1)*H*), 4.14 (1H, dd, *J*=12.5, 2.3 Hz, C(5)H_aH_b), 4.09 (1H, t, *J*=9.3 Hz, C(2)*H*), 3.83 (1H, ddd, *J*=3.3, 2.3, 1.0 Hz, C(4)*H*), 3.66 (1H, dd, *J*=9.3, 3.3 Hz, C(3)*H*), 3.43 (1H, dd, *J*=12.5, 1.0 Hz, C(5)H_aH_b); δ_C (60 MHz, $CDCl_3$) 138.3, 138.2 (*C* s-arom.), 135.1 (*C*-3′), 129.0–127.6 (m, *C*H arom.), 127.6 (*C*-1′), 118.5 (*C*-5′), 82.4 (*C*-3), 78.5 (*C*-2), 75.3 (*C*-1), 75.1 (O*C*H_2Ph), 73.0 (*C*-4), 72.0 (O*C*H_2Ph), 71.5 (O*C*H_2Ph), 67.3 (*C*-5); HRMS (Cl, NH_3) MH^+, found 471.2281. $C_{29}H_{31}N_2O_4$ requires 471.2283. **42** $[\alpha]_D^{20}=-6$ (*c*=0.7; $CHCl_3$); ν_{max} (film): 3064, 3048, 3032, 2928, 2864, 1496, 1456, 1352, 1304, 1208, 1092, 912, 752, 700 cm^{-1}; δ_H (250 MHz, acetone-d_6): 7.57 (1H, s, C(2′)*H*), 7.44–7.10 (15H, m, 3Ph), 6.96 (1H, s, C(5′)*H*), 4.89 (1H, d, *J*=1.5 Hz, C(1)*H*), 4.81 and 4.73 (2H, AB, *J*=11.8 Hz, OCH_2Ph), 4.61 (2H, s, OCH_2Ph), 4.37 and 4.29 (2H, AB, *J*=11.5 Hz, OCH_2Ph), 4.14 (1H, dd, *J*=4.0, 2.5 Hz, C(3)*H*), 3.96 (1H, dt, *J*=4.8, 2.5 Hz, C(4)*H*), 3.92 (1H, dd, *J*=4.0, 1.5 Hz, C(2)*H*), 3.84 (1H, dd, *J*=10.3, 4.8 Hz, C(5)H_aH_b), 3.78 (1H, dd, *J*=10.3, 2.5 Hz, C(5)H_aH_b); δ_C (60 MHz, $CDCl_3$) 138.3, 138.2, 137.6 (*C* s-arom.), 134.6 (*C*-3′), 129.8 (*C*-1′), 128.5–127.6 (m, *C*H arom.), 119.5 (*C*-5′), 77.9 (*C*-2), 73.3 (*C*-4), 73.0 (O*C*H_2Ph), 72.6 (O*C*H_2Ph), 72.4 (*C*-3), 71.3 (O*C*H_2Ph), 70.4 (*C*-1), 64.6 (*C*-5); HRMS (Cl, NH_3) MH^+, found 471.2281. $C_{29}H_{31}N_2O_4$ requires 471.2283.

3.3.33. 4,5-(α-D-Arabinopyranosyl)1*H*-imidazole (8). To a solution of compound **41** (66 mg, 0.098 mmol) in 95% EtOH (4 mL) was added 10% Pd/C catalyst 105 mg) and the mixture was stirred overnight in H_2 atmosphere at room temperature. The new portion of catalyst (120 mg) was added and the stirring was continued for the next 24 h until substrate disappeared (TLC). The mixture was filtered through celite, evaporated and purified by flash chromatography (EtOH/NH_3 aq. 6:1) to give the title *compound* **8** (17 mg, 0.085 mmol, 87%, R_f=0.35) as a colourless film. $[\alpha]_D^{20}=-42$ (*c*=0.26; CH_3OH); δ_H (250 MHz, CD_3OD) 7.88 (1H, br s, C(2′)*H*), 7.16 (1H, br s, C(5′)*H*), 4.19 (1H, d, *J*=9.8 Hz, C(1)*H*), 3.98 (1H, dd, *J*=3.5, 1.8 Hz, C(4)*H*), 3.95 (1H, dd, *J*=9.8, 9.6 Hz, C(2)*H*), 3.89 (1H, dd, *J*=12.8, 1.8 Hz, C(5)H_aH_b), 3.72 (1H, dd, *J*=12.8, 1.8 Hz, C(5)H_aH_b), 3.68 (1H, dd, *J*=9.6, 3.5 Hz, C(3)*H*); δ_C (60 MHz, CD_3OD) 135.5 (br, *C*-3′), 129.2 (*C*-1′), 118.3 (br, *C*-5′), 76.2 (*C*-2), 73.9 (*C*-4), 70.5 (*C*-6), 70.19 (*C*-3), 69.5 (*C*-5); HRMS (Cl, NH_3) MH^+, found 201.0878. $C_8H_{13}N_2O_4$ requires 201.0875.

3.3.34. 4,5-(β-D-Arabinopyranosyl)1*H*-imidazole (9). The same procedure as for the preparation of **8** was used starting from **42** (29 mg, 0.062 mmol) to give after workup the title *compound* **9** (7 mg, 0.035 mmol, 57%, R_f=0.15 in EtOH/NH_3 aq. 6:1) as a colourless film. $[\alpha]_D^{20}=+5.4$ (*c*=0.21; CH_3OH); δ_H (250 MHz, CD_3OD) 7.75 (1H, br s, C(2′)*H*), 7.15 (1H, br s, C(5′)*H*), 4.90 (1H, d, *J*=1.7 Hz, C(1)*H*), 4.14 (1H, dd, *J*=4.4, 3.3 Hz, C(3)*H*), 4.09 (1H, dd, *J*=5.1, 3.3 Hz, C(4)*H*), 4.04 (1H, dd, *J*=4.4, 1.7 Hz,

C(2)*H*), 3.84 (1H, dd, *J*=10.3, 5.1 Hz, C(5)H_aH_b), 3.73 (1H, dd, *J*=10.3, 5.1 Hz, C(5)H_aH_b); δ_C (60 MHz, CD_3OD) 133.6 (*C*-3′), 131.8 (*C*-1′), 115.1 (*C*-5′), 70.5 (*C*-6), 69.0 (*C*-2), 68.8 (*C*-1), 67.6 (*C*-3), 63.6 (*C*-5), 62.2 (*C*-4); HRMS (Cl, NH_3) MH^+, found 201.0878. $C_8H_{13}N_2O_4$ requires 201.0875.

3.3.35. Imidazolo[1,5]-D-*gluco*-piperidinose (6). The same procedure as for the preparation of **8** was used starting from **40b** (8 mg, 0.017 mmol) to give after workup the title *compound* **6** (3 mg, 0.015 mmol, 88%, R_f=0.30 in EtOH/NH_3 aq. 6:1) as a colourless film. $[\alpha]_D^{20}=-6.5$ (*c*=0.13; CH_3OH); δ_H (400 MHz, D_2O) 7.93 (1H, s, C(3)*H*), 6.76 (1H, s, C(1)*H*), 4.86 (1H, d, *J*=6.2 Hz, C(8)*H*), 4.47–4.38 (1H, m, C(5)*H*), 4.31 (1H, dd, *J*=9.2, 7.8 Hz, C(6)*H*), 4.07 (1H, dd, *J*=12.2, 4.5 Hz, C(9)H_aH_b), 3.96 (1H, dd, *J*=12.2, 3.1 Hz, C(9)H_aH_b), 3.89 (1H, dd, *J*=9.2, 6.2 Hz, C(7)*H*); δ_C (100.6 MHz, D_2O) 131.5 (*C*-8a), 130.9 (*C*-3), 121.6 (*C*-1), 70.3 (*C*-7), 60.9 (*C*-9), 60.3 (*C*-8), 58.8 (*C*-5); HRMS (Cl, NH_3) MH^+, found 201.0877. $C_8H_{13}N_2O_4$ requires 201.0875.

3.3.36. 1,3-Di-*O*-benzyl-2,4-di-*O*-phenylmethanesulphonyl-1-[1*H*-imidazol-4(5)yl]-L-*gulo*-pentitol (43a) and 6,8-di-*O*-benzyl-7-*O*-phenylmethanesulphonyl-imidazolo[1,5]-D-*manno*-piperidinose (44). To a stirred solution of $BnSO_2Cl$ (225 mg, 1.18 mmol) in anhydrous pyridine (2.5 mL) was added portionwise a solution of **36a** (250 mg, 0.28 mmol) in anhydrous pyridine (3.75 mL) at −30°C. After 30 min the dry ice-acetone bath was removed and the mixture was stirred at room temperature overnight then evaporated under reduced pressure and co-evaporated several times with toluene to remove pyridine. The residue was dissolved in THF (11.25 mL)/aq. HCl (6 M, 3.75 mL) mixture and refluxed for 75 min THF was evaporated and the remaining mixture was neutralised with saturated aq. K_2CO_3 solution and extracted with $CHCl_3$. The organic layer was dried ($MgSO_4$), filtered and evaporated. The residue was twofold flash-chromatographed ($CHCl_3$/MeOH 9:1; CH_2Cl_2/acetone 1:1) to give title *compounds* **43a** (69 mg, 0.10 mmol, 34%, R_f=0.35 in CH_2Cl_2/acetone 1:1) and **44** (28 mg, 0.05 mmol, 18%, R_f=0.15 in CH_2Cl_2/acetone 1:1) as a white foams. **43a** $[\alpha]_D^{20}=-35$ (*c*=0.5; CH_2Cl_2); ν_{max} (film): 3328, 2928, 1496, 1448, 1356, 1172, 1072, 788, 696, 644 cm^{-1}; δ_H(250 MHz, $CDCl_3$) 7.69 (1H, s, C(2′)*H*), 7.45–7.15 (20H, m, 4Ph), 6.97 (1H, s, C(5′)*H*), 5.35 (1H, dd, *J*=5.0, 4.5 Hz, C(2)*H*), 4.96–4.81 (2H, m, C(1)*H*, C(4)*H*), 4.64 and 4.48 (2H, AB, *J*=10.5 Hz, OCH_2Ph), 4.44 and 4.36 (2H, AB, *J*=10.8 Hz, OCH_2Ph), 4.38 and 4.31 (2H, AB, *J*=13.5 Hz, OSO_2CH_2Ph), 4.22 and 4.13 (2H, AB, *J*=14.1 Hz, OSO_2CH_2Ph), 4.04 (1H, t, *J*=5.0 Hz, C(3)*H*), 3.80 (1H, dd, *J*=12.5, 5.0 Hz, C(5)H_aH_b), 3.70 (1H, dd, *J*=12.5, 3.8 Hz, C(5)H_aH_b); δ_C (60 MHz, $CDCl_3$) 138.0–136.5 (m, *C* s-arom.), 135.9 (*C*-4′), 133.3 (*C*-2′), 131.5–126.0 (m, *C*H arom.), 119.3 (*C*-5′), 82.4 (*C*-4), 81.1 (*C*-2), 75.6 (*C*-3), 74.3 (O*C*H_2Ph), 71.9 (O*C*H_2Ph), 73.0 (*C*-1), 60.8 (*C*-5), 57.9 (OSO_2CH_2Ph), 57.5 (OSO_2CH_2Ph); HRMS (Cl, NH_3) MH^+, found 706.1938. $C_{36}H_{38}N_2O_9S_2$ requires 706.1940. **44** $[\alpha]_D^{20}=-32$ (*c*=1.25; $CHCl_3$); ν_{max} (film): 3064, 3048, 3032, 2992, 2864, 1528, 1496, 1456, 1356, 1172, 1084, 984, 788, 696 cm^{-1}; δ_H (250 MHz, $CDCl_3$) 7.60 (1H, s, C(3)*H*), 7.35–7.15 (15H, m, 3Ph), 6.80 (1H, s, C(1)*H*), 4.85 (1H, dd, *J*=8.7, 3.0 Hz, C(7)*H*), 4.73 and 4.63 (2H, AB, *J*=11.5 Hz, OCH_2Ph), 4.61 (1H, d, *J*=3.0 Hz, C(8)*H*), 4.48 and 4.33 (2H, AB, *J*=11.8 Hz, OCH_2Ph), 4.31 and 4.20 (2H, AB, *J*=14.0 Hz, OSO_2CH_2Ph), 4.29 (1H, dd, *J*=8.7, 3.5 Hz, C(6)*H*), 4.18 (1H, ddd, *J*=6.2, 4.6, 3.5 Hz, C(5)*H*), 3.86 (1H, dd, *J*=11.9, 4.6 Hz, C(9)H_aH_b), 3.72 (1H, dd, *J*=11.9, 6.2 Hz, C(9)H_aH_b); δ_C (60 MHz, $CDCl_3$) 137.0 (*C*-3), 129.0–127.5 (m, *C*H arom.), 127.2 (*C*-1), 124.7 (*C*-8a), 80.4 (*C*-7), 74.3 (O*C*H_2Ph), 73.2 (*C*-6), 70.3 (O*C*H_2Ph), 68.1 (*C*-8), 63.0 (*C*-9), 61.4 (*C*-5), 57.4 (OSO_2CH_2Ph); HRMS (Cl, NH_3) MH^+, found 535.1904. $C_{29}H_{31}N_2O_6S$ requires 535.1902.

3.3.37. 1,3-Di-*O*-benzyl-2,4-di-*O*-phenylmethanesulphonyl-1-[1*H*-imidazol-4(5)-yl]-L-*ido*-pentitol (43b). The same procedure as for the preparation of **43a** and **44** was used starting from **36b** (100 mg, 0.11 mmol) to give after workup the title *compound* **43b** (56 mg, 0.08 mmol, 70%, R_f=0.35 in CH_2Cl_2/acetone 1:1) as a white foam. $[\alpha]_D^{20}=+4$ (*c*=0.6; $CHCl_3$); ν_{max} (film): 3328, 2944, 1496, 1448, 1352, 1172, 1064, 788, 696, 652 cm^{-1}; δ_H (250 MHz, $CDCl_3$) 7.72 (1H, s, C(2′)*H*), 7.35–7.15 (20H, m, 4Ph), 6.81 (1H, s, C(5′)*H*), 5.27 (1H, dd, *J*=6.7, 3.9 Hz, C(2)*H*), 4.92 (1H, d, *J*=6.7 Hz, C(1)*H*), 4.80 (1H, ddd, *J*=7.8, 4.3, 2.8 Hz, C(4)*H*), 4.58 and 4.41 (2H, AB, *J*=11.3 Hz, OCH_2Ph), 4.44 and 4.29 (2H, AB, *J*=11.5 Hz, OCH_2Ph), 4.36 and 4.23 (2H, AB, *J*=14.0 Hz, OSO_2CH_2Ph), 4.26 (2H, s, OSO_2CH_2Ph), 3.94 (1H, dd, *J*=13.3, 4.3 Hz, C(5)H_aH_b), 3.88 (1H, dd, *J*=7.8, 3.9 Hz, C(3)*H*), 3.75 (1H, dd, *J*=13.3, 2.8 Hz, C(5)H_aH_b); δ_C (60 MHz, $CDCl_3$) 137.5–137.0 (m, *C* s-arom.), 136.5 (*C*-4′), 133.0 (*C*-2′), 129.0–127.0 (m, *C*H arom), 118.6 (*C*-5′), 83.2 (*C*-4), 82.0 (*C*-2), 75.5 (*C*-3), 74.9 (O*C*H_2Ph), 70.5 (O*C*H_2Ph), 73.1 (*C*-1), 60.7 (*C*-5), 57.3 (OSO_2CH_2Ph), 57.0 (OSO_2CH_2Ph); HRMS (Cl, NH_3) MH^+, found 706.1938. $C_{36}H_{38}N_2O_9S_2$ requires 706.1940.

3.3.38. (6*R*,7*S*)-7,9-Dibenzyloxy-6,7-dihydro-5*H*-imidazo[1,5-*a*]azepin-6-ol (45). To a stirred solution of compound **43a** (69 mg, 0.10 mmol) in anhydrous DMF (1.5 mL) was added under argon atmosphere $NaNH_2$ (10 mg, 0.26 mmol) and the mixture was stirred at room temperature overnight. The mixture was quenched with MeOH, neutralised with AcOH and evaporated to dryness. The residue was diluted with 5% aq. K_2CO_3 solution and extracted with $CHCl_3$. The organic layer was dried ($MgSO_4$), filtered and evaporated. The residue was purified by flash chromatography ($CHCl_3$/MeOH 9:1) to give the title *compound* **45** (30 mg, 0.08 mmol, 85%) as a colourless amorphous solid). $[\alpha]_D^{20}=+57$ (*c*=1.5; $CHCl_3$); ν_{max} (film): 3112, 2992, 2928, 1708, 1656, 1492, 1452, 1356, 1256, 1216, 1152, 1144, 1136, 1128, 1096, 1028, 760, 696 cm^{-1}; δ_H (250 MHz, $CDCl_3$+C_6D_6) 7.46 (1H, s, C(3)*H*), 7.30–7.00 (10H, m, 2Ph), 7.00 (1H, s, C(1)*H*), 4.70 (1H, d, *J*=6.0 Hz, C(8)*H*), 4.61 and 4.58 (2H, AB, *J*=12 Hz, OCH_2Ph), 4.36 and 4.21 (2H, AB, *J*=11.5 Hz, OCH_2Ph), 3.88 (1H, dd, *J*=6.0, 3.1 Hz, C(7)*H*), 3.83 (1H, dd, *J*=13.2, 9.0 Hz, C(5)H_aH_b), 3.74 (1H, ddd, *J*=9.0, 3.1, 2.6 Hz, C(6)*H*), 3.51 (1H, dd, *J*=13.2, 2.6 Hz, C(5)H_aH_b); δ_C (250 MHz, $CDCl_3$+C_6D_6) 147.8 (*C*-9), 140.0 (*C*-1), 138.0 (*C*-9a), 139.4, 137.7 (*C* s-arom.), 131.0 (*C*-3), 129.0–127.5 (m, *C*H arom.), 95.8 (*C*-8), 76.4 (*C*-7), 71.2 (O*C*H_2Ph), 70.3 (O*C*H_2Ph), 69.9 (*C*-6), 47.9 (*C*-5); HRMS (Cl, NH_3) MH^+, found 363.1706. $C_{22}H_{23}N_2O_3$ requires 363.1708.

3.3.39. (5*R*,6*S*)-6,8-Dibenzyloxy-5,6-dihydro-5-hydroxymethyl-imidazo[1,5-*a*]pyridine (46). The same procedure as for the preparation of **45** was used staring from **44** (49 mg, 0.09 mmol) to give after workup and flash chromatography (acetone/CH_2Cl_2) 6:1) the title *compound* **46** (28 mg, 0.08 mmol, 84%) as a colourless amorphous solid. $[\alpha]_D^{20}=+172$ (c=0.9; $CHCl_3$); ν_{max} (film): 3128, 3032, 2856, 1648, 1560, 1492, 1456, 1392, 1364, 1292, 1256, 1212, 1088, 1068, 1052, 748, 696, 656 cm^{-1}; δ_H (250 MHz, $CDCl_3$) 7.50 (1H, s, C(3)*H*), 7.40–7.20 (10H, m, 2Ph), 6.94 (1H, s, C(1)*H*), 4.95 (2H, s, OCH_2Ph), 4.88 (1H, d, J=6.3 Hz, C(7)*H*), 4.47 and 4.42 (2H, AB, J=12.3 Hz, OCH_2Ph), 4.41 (1H, ddd, J=8.8, 5.0, 1.3 Hz, C(5)*H*), 4.24 (1H, dd, J=6.3, 1.3 Hz, C(6)*H*), 3.60 (1H, dd, J=11.3, 1.0 Hz, C(9)H_aH_b), 3.47 (1H, dd, J=11.3, 8.8 Hz, C(9)H_aH_b); δ_C (60 MHz, $CDCl_3$) 140.0 (*C*-8), 139.2 (*C*-8a), 138.3 (*C*-3), 129.0–127.5 (m, *C*H arom.), 124.8 (*C*-1), 89.8 (*C*-7), 71.2 (*C*-6), 69.3 (O*C*H_2Ph), 69.2 (O*C*H_2Ph), 62.8 (*C*-9), 60.5 (*C*-5); HRMS (Cl, NH_3) MH^+, found 363.1707. $C_{22}H_{23}N_2O_3$ requires 363.1708.

3.3.40. (6*S*,7*R*,9*R*)-6,7,8,9-Tetrahydro-5*H*-imidazo[1,5-*a*]azepin-6,7,9-triol (47). To a solution of compound **45** (66 mg, 0.18 mmol) in 95% ethanol (6 mL) was added 10% Pd/C catalyst (135 mg) and the mixture was stirred overnight under H_2 atmosphere at room temperature. The stirring was continued for next 4 days under H_2 after addition of the two new portions of the catalyst (2×100 mg) until complete disappearance of the substrate (TLC). The mixture was filtered through celite, evaporated and purified by chromatography (EtOH/aq. NH_3 11:1) to give the title *compound* **47** (8 mg, 0.043 mmol, 24%) as a white foam. $[\alpha]_D^{20}=-17$ (c=0.4; MeOH); δ_H (250 MHz, D_2O) 7.73 (1H, s, C(3)*H*), 6.95 (1H, s, C(1)*H*), 4.89 (1H, dd, J=10.5, 3.0 Hz, C(9)*H*), 4.37 (1H, dd, J=15.0, 6.5 Hz, C(5)H_aH_b), 4.15 (1H, dd, J=6.5, 1.8 Hz, C(6)*H*), 4.06 (1H, ddd, J=10.8, 4.0, 1.8 Hz, C(7)*H*), 3.99 (1H, d, J=15.0 Hz, C(5)H_aH_b), 2.14 (1H, ddd, J=12.5, 10.8, 3.0 Hz, C(8)H_aH_b), 2.03 (1H, ddd, J=12.5, 10.5, 4.0 Hz, C(8)H_aH_b); δ_C (60 MHz, D_2O) 134.1 (*C*-9a), 126.8 (*C*-3), 120.6 (*C*-1), 69.4 (*C*-6), 66.9 (*C*-7), 61.6 (*C*-9), 45.3 (*C*-5), 35.8 (*C*-8); HRMS (Cl, NH_3) MH^+, found 185.09289. $C_8H_{13}N_2O_3$ requires 185.092617.

3.3.41. (5*S*,6*S*,8*R*)-5,6,7,8,-Tetrahydro-5-hydroxymethyl-imidazo[1,5-*a*]pyridin-6,8-diol (48). To a solution of compound **46** (39 mg, 0.11 mmol) in 95% ethanol (4 mL) was added 10% Pd/C catalyst (80 mg) and the mixture was stirred at room temperature overnight in H_2 atmosphere. A new portion of catalyst (80 mg) was added and mixture was stirred for the next 2 days. After workup as for **47** and chromatography ($CHCl_3$/MeOH 2:1) the title *compound* **48** (7 mg, 0.038 mmol, 35%) was given as a white foam. $[\alpha]_D^{20}=-32$ (c=0.35; MeOH); δ_H (250 MHz, D_2O) 7.73 (1H, s, C(3)*H*), 6.95 (1H, s, C(1)*H*), 4.89 (1H, dd, J=7.5, 5.8 Hz, C(8)*H*), 4.12 (1H, ddd, J=8.8, 6.5, 3.0 Hz, C(6)*H*), 4.03 (1H, ddd, J=6.5, 4.3, 3.5 Hz, C(5)*H*), 3.90 (1H, dd, J=12.3, 3.5 Hz, C(9)H_aH_b), 3.78 (1H, dd, J=12.3, 4.3 Hz, C(9)H_aH_b), 2.32 (1H, ddd, J=13.0, 5.8, 3.0 Hz, C(7)H_aH_b), 1.86 (1H, ddd, J=13.0, 8.8, 7.5 Hz, C(7)H_aH_b); δ_C (250 MHz, D_2O) 143.0 (*C*-8a), 131.2 (*C*-3), 64.0 (*C*-6), 124.0 (*C*-1), 61.0 (*C*-5), 60.3 (*C*-8), 60.2 (*C*-9), 35.9 (*C*-7); HRMS (Cl, NH_3) MH^+, found 185.09231. $C_8H_{13}N_2O_3$ requires 185.092617.

3.3.42. (2*R*,5*R*,6*R*,11*S*)-5,11-Dibenzyloxy-4-oxa-1,9-diazatricyclo[5,3,0,$1^{2,6}$]-7(8),9-undecadiene (49). The same procedure as for the preparation of **45** was used starting from **43b** (35 mg, 0.05 mmol) to give after workup and flash chromatography ($CHCl_3$/MeOH 9:1) the title *compound* **49** (10 mg, 0.03 mmol, 56%) as a white foam. $[\alpha]_D^{20}=-82$ (c=1.75; $CHCl_3$); ν_{max} (film): 2928, 2856, 1496, 1460, 1360, 1248, 1216, 1124, 1044, 960, 912, 788, 756, 696, 656 cm^{-1}; δ_H (250 MHz, $CDCl_3$) 7.51 (1H, s, C(3)*H*), 7.42–7.19 (10H, m, 2Ph), 6.86 (1H, s, C(1)*H*), 4.89 (1H, s, C(6)*H*), 4.88 (1H, d, J=2.5 Hz, C(8)*H*), 4.73 and 4.51 (2H, AB, J=12 Hz, OCH_2Ph), 4.62 and 4.54 (2H, AB, J=11.5 Hz, OCH_2Ph), 4.40 (1H, d, J=3.3 Hz, C(5)*H*), 3.85 (1H, dd, J=11.3, 3.3 Hz, C(9)H_aH_b), 3.60 (1H, d, J=11.3 Hz, C(9)H_aH_b), 3.48 (1H, bd, J=2.5 Hz, C(7)*H*); δ_C (60 MHz, $CDCl_3$) 138.9, 138.8 (*C* s-arom.), 135.2 (*C*-7a), 131.1 (*C*-3), 129.0–128.0 (m, *C*H arom.), 121.2 (*C*-1), 98.6 (*C*-8), 85.2 (*C*-6), 70.7 (O*C*H_2Ph), 69.5 (O*C*H_2Ph), 63.5 (*C*-9), 59.2 (*C*-5), 43.5 (*C*-7); HRMS (Cl, NH_3) MH^+, found 363.1708. $C_{22}H_{23}N_2O_3$ requires 363.1709.

3.3.43. (5*R*,6*S*,7*S*)-6,7-Dihydro-5,7-dihydroxymethyl-5*H*-pyrrolo[1,2-*c*]imidazole-6-ol (50). To a solution of compound **49** (39 mg, 0.11 mmol) in 95% ethanol (4 mL) was added 10% Pd/C catalyst (80 mg) and the mixture was stirred at room temperature overnight in H_2 atmosphere. A new portion of catalyst (90 mg) was added and mixture was stirred for the next 2 days. After workup as for **47** and chromatography (EtOH/NH_3aq. 9:1) the title *compound* **50** (16 mg, 0.09 mmol, 81%) was given as a white foam. $[\alpha]_D^{20}=-16$ (c=0.3; MeOH); δ_H (250 MHz, D_2O) 8.61 (1H, s, C(3)*H*), 7.24 (1H, s, C(1)*H*), 4.61 (1H, t, J=6.6 Hz, C(6)*H*), 4.50 (1H, dt, J=6.6, 3.7 Hz, C(7)*H*), 4.22 (1H, dd, J=5.8, 3.7 Hz, C(8)H_aH_b), 4.00 (1H, dd, J=11.3, 5.1 Hz, C(9)H_aH_b), 3.90 (1H, dd, J=6.6, 5.8 Hz, C(8)H_aH_b), 3.85 (1H, dd, J=11.3, 6.2 Hz, C(9)H_aH_b), 3.43 (1H, ddd, J=6.6, 6.2, 5.1 Hz, C(5)*H*), δ_C (60 MHz, D_2O) 134.6 (*C*-7a), 127.0 (*C*-3), 111.6 (*C*-1), 75.0 (*C*-6), 65.5 (*C*-7), 58.3 (*C*-9), 58.2 (*C*-8), 45.0 (*C*-5); HRMS (Cl, NH_3) MH^+, found 185.09256. $C_8H_{13}N_2O_3$ requires 185.092617.

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