Synthesis and Comparative Glycosidase Inhibitory Properties of Reducing Castanospermine Analogues

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The feasibility of the intramolecular nucleophilic addition of the nitrogen atom in cyclic (thio)carbamates with a pseudo-*C*-nucleoside structure to the masked carbonyl group in aldose precursors in the synthesis of reducing (i.e., 5-hydroxy)-6-oxaindolizidine frameworks is illustrated by the preparation of the 6-*epi*, 7-*epi*, 8-*epi* and 6,8a-di-*epi* diastereomers of the potent glycosidase inhibitor (+)-castanospermine. In all cases, the increased anomeric effect caused by the high sp^2 character of the pseudoamide-type nitrogen atom resulted in the pseudoanomeric hydroxy group being anchored in an axial orientation in aqueous solution, as in the aglycons in α-glycosides. These analogs of the natural alkaloid showed a higher selectivity in the inhibition of α-glucosidases. Structure/glycosidase inhibitory activity studies indicated that inversion of any hydroxy group resulted in a dramatic decrease in the inhibition potency, confirming the critical importance of a correct hydroxylation profile. In the case of (+)-8-*epi*-6-oxacastanospermine derivatives, with a hydroxylation profile with a structural complementarity to that of D-galactose, a moderate but very selective inhibition of α-galactosidase was observed, supporting the importance of a defined configuration at pseudoanomeric centres for anomeric specificity.

Introduction

Castanospermine (**1**) is one of a number of plant-derived polyhydroxyindolizidine alkaloids that exhibit glycosidase inhibition activity (Figure 1).[1–7] Thus, **1** is a potent, competitive and specific inhibitor of several glucosidases, including lysosomal glycoprotein processing enzymes, which gives it potential therapeutic value in the treatment of ailments as varied as cancer, viral infections and diabetes. The pronounced biological activity of **1** stems from its ability to mimic the transition state involved in enzymatic glycoside hydrolysis. However, contrary to the natural glucosides, neither **1** nor most of the analogues reported so far possess a defined configuration at the pseudoanomeric centre.[8–16] It is therefore not surprising that several α- and β-glucosidases can be simultaneously inhibited, which may be particularly problematic in clinical trials.

We have recently found that a subtle change in the structure of nitrogen-in-the-ring carbohydrate mimics (iminosugars, azasugars[17]), consisting of the replacement of the sp^3 imino nitrogen by a pseudoamide-type nitrogen atom with substantial sp^2 character, leads to a dramatic increase in the orbital contribution to the anomeric effect at amino acetal pseudoanomeric centres, resulting in a total preference for the axial orientation of the oxygen substituent and a notably enhanced stability,[18–20] even in the case of hemiaminal derivatives.[21–24] Thus, the reducing cyclic thiocarbamate and carbamate castanospermine analogues **2** and **3** (Figure 1) showed configurational integrity in water, with the C-5 hydroxy substituent anchored in the axial position, as in the natural aglycons in α-glucopyranosides. Noteworthy, these sp^2-azasugar-type glucomimetics exhibited a dramatic increase in the α-anomeric selectivity (up to 10000 times that of the parent compound **1**) when assayed against a panel of glycosidases, as well as a remarkable specificity within the α-glucosidase isoenzymes.[25,26] This marked specificity has been ascribed to the interplay of topographical and electronic characteristics, the main factors being: (i) a configurational pattern analogous to that of α-D-glucopyranosides; (ii) a locked conformation about the bond homologous to C-5–C-6 in the parent

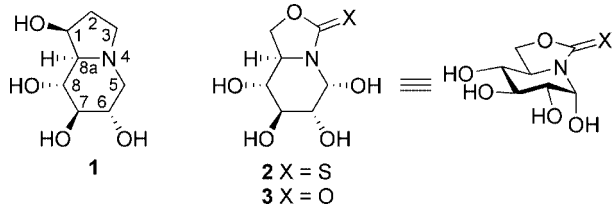

Figure 1. Structures of (+)-castanospermine and of the reducing thiocarbamic and carbamic analogues.

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sugar; and (iii) a partial positive charge at the region of the endocyclic heteroatom in the six-membered ring as a consequence of electron delocalization in the pseudoamide segment.[27] In order to further investigate the critical features of the specificity and potency of the inhibition, we have now prepared a series of reducing 3-oxo(thioxo)-2-oxaindolizidine diastereomers in which the four chiral centers at C-6, C-7, C-8 and C-8a in **2** and **3** have been systematically modified by inversion. This series has been assayed against several α- and β-glycosidases to map the geometrical requirements for biological activity in this family of compounds.

Results and Discussion

Synthesis and Structure of Reducing 2-Oxacastanospermine Diastereomers

The general synthetic strategy developed for the assembly of the bicyclic skeleton of 2-oxaindolizidines starts from hexofuranose precursors and is depicted in Figure 2. It involves the intramolecular nucleophilic addition of the nitrogen atom of five-membered cyclic (thio)carbamate derivatives with pseudo-*C*-nucleoside structure (II) to the masked carbonyl group of the aldose through the open chain *aldehydo* form (III). The key 5,6-(cyclic thiocarbamate) or (cyclic carbamate) intermediates are accessible from 5-amino-5-deoxyaldohexofuranose derivatives (I) by thiocarbonylation or carbonylation reactions, respectively. The stereochemical complementarity of the hydroxylation profiles of the piperidine ring of the natural (+)-castanospermine (**2**, **3**) and its 6-*epi* (**4**, **5**), 7-*epi* (**6**, **7**), 8-*epi* (**8**, **9**) and 6,8a-di-*epi* diastereomers (**10**, **11**) implies that the starting monosaccharide precursors have the D-*gluco*, D-*manno*, D-*allo*, D-*galacto* and L-*gulo* configurations, respectively (Figure 2).

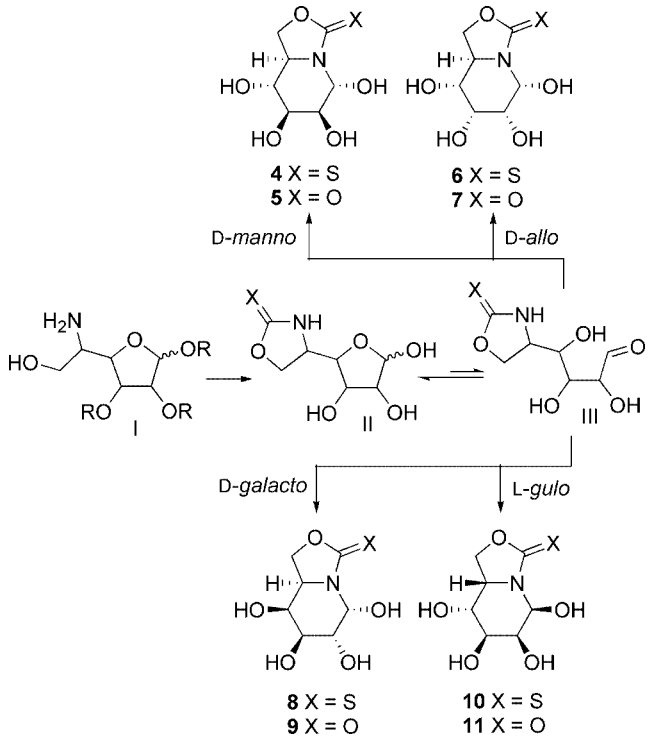
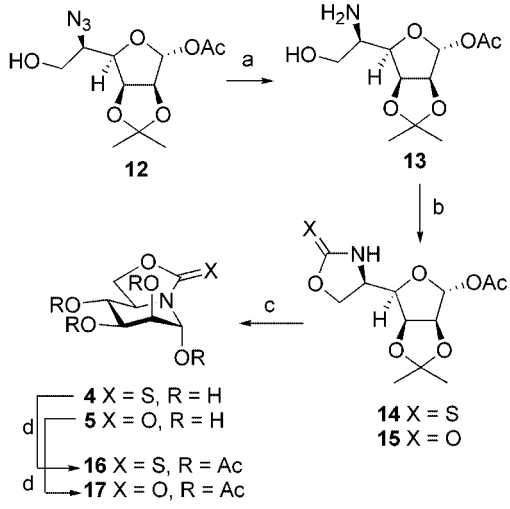


Figure 2. Synthetic strategy for the preparation of the reducing (+)-2-oxacastanospermine diastereomers from 5,6-cyclic (thio)carbamate hexofuranoses (II), obtained from 5-amino-5-deoxysugar precursors (I), via the open-chain *aldehydo* form (III).

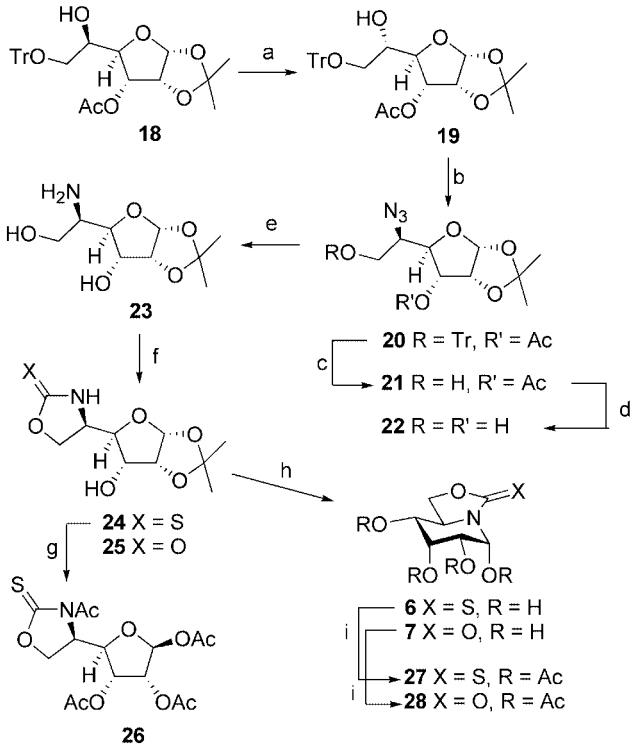
The 6-*epi*-castanospermine analogues **4** and **5** were synthesized from the previously reported 1-*O*-acetyl-5-azido-5-deoxy-2,3-*O*-isopropylidene-α-D-mannofuranose **12**[21] by reduction of the azido group. Thiocarbonylation of the resulting *vic* amino alcohol **13** with the carbon disulfide/dicyclohexylcarbodiimide system afforded the oxazolidine-2-thione derivative **14**. Similarly, carbonylation using triphosgene/diisopropylethylamine provided the corresponding cyclic carbamate **15**. Sequential removal of the anomeric acetyl and the cyclic acetal groups by treatment with methanolic sodium methoxide and aqueous trifluoroacetic acid provided, after neutralization with a basic ion-exchange resin, the target 2-oxaindolizidine derivatives **4** and **5**, whose structures were further confirmed by their transformation into the corresponding tetra-*O*-acetates **16** and **17** (Scheme 1).



Scheme 1. Reagents and conditions: a, H_2, Pd/C, MeOH, room temp., 2 h, quant.; b, for **14**: CS_2, DCC, CH_2Cl_2, –10 °C → room temp., 2.5 h, 78%; for **15**: triphosgene, DIPEA, CH_2Cl_2, 0 °C → room temp., 15 min, 65%; c, 1. NaOMe, MeOH; 2. 90% TFA/water, 0 °C, 15 min, 74–82%; d, Ac_2O/pyridine, 95–98%.

To access the 7-*epi*-2-oxacastanospermine derivatives **6** and **7**, a synthetic scheme analogous to that previously reported for the preparation of **2** and **3**,[24] involving the D-*allo*-configured amino alcohol **23** as pivotal intermediate, was considered. Compound **23** was obtained from the known selectively protected 1,2-*O*-isopropylidene-α-D-allofuranose derivative **18**[17] by double inversion at C-5, as depicted in Scheme 2. Trifluoromethanesulfonation at O-5 followed by S_N2 nucleophilic displacement using nitrite anion afforded, after work up, the corresponding L-talofuranose alcohol **19**. A second triflation/inversion process using the azide anion as the nucleophile provided the 5-azido-5-deoxy-D-allofuranose derivative **20**. Selective removal of the trityl group with boron trifluoride–diethyl ether complex

(→**21**), deacetylation (→**22**) and catalytic hydrogenation of the azido group led to **23**. The subsequent (thio)carbonylation reactions, using the above conditions, proceeded with total chemoselectivity to give the desired cyclic (thio)-carbamates **24** and **25**. Trifluoroacetic acid catalyzed hydrolysis of the isopropylidene group did not result in the expected furanose → piperidine rearrangement, however, even after prolonged treatment with Amberlite IRA-68 (OH^-) anion-exchange resin, probably because of the higher basicity of the endocyclic nitrogen in these compounds. Acetylation of the reaction mixture with acetic anhydride/pyridine afforded a mixture in which D-allofuranose derivatives predominated, as seen from the NMR spectra of the crude mixture, from which the β-peracetate **26** could be isolated. Deacetylation of the acetylated mixture with methanolic sodium methoxide proceeded with concomitant isomerization of the furanose thiocarbamates to give the desired 2-oxaindolizidine **6** as the only product.



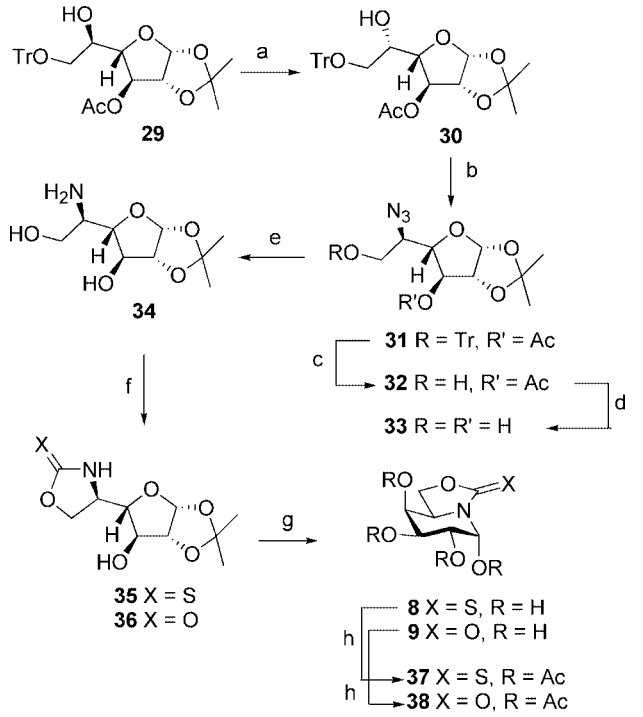
Scheme 2. Reagents and conditions: a, 1. Tf_2O, CH_2Cl_2, pyridine, –25 °C → room temp., 30 min; 2. $NaNO_2$, DMF, room temp., 18 h, 51%; b, 1. Tf_2O, CH_2Cl_2, pyridine, –25 °C → room temp., 30 min; 2. NaN_3, DMF, room temp., 18 h, 85%; c, BF_3–Et_2O, MeOH, 0 °C → room temp., 2 h, 80%; d, NaOMe, MeOH, 85%; e, H_2, Pd/C, MeOH, room temp., 1 h, quant.; f, for **24**: CS_2, DCC, CH_2Cl_2, –10 °C → room temp., 5 h, 89%; for **25**: triphosgene, DIPEA, CH_2Cl_2, 0 °C → room temp., 20 min, 89%; g, 1.90% TFA/water, 0 °C, 15 min; 2. Ac_2O/pyridine; h, 1. 90% TFA/water, 0 °C, 15 min; 2. Ac_2O/pyridine; 3. NaOMe, MeOH, 50–64%; i, Ac_2O/pyridine, 98%.

The above acetylation/deacetylation procedure proved to be very efficient in promoting the intramolecular nucleophilic addition of the nitrogen atom in pseudo-*C*-nucleoside (thio)carbamates to the aldehyde functionality in fully unprotected hexofuranose derivatives. Interestingly, the mixture of peracetates can easily be purified by silica gel column chromatography so that the subsequent deacetylation step provides the target bicyclic derivative in high purity, thus avoiding the need of a final purification by gel-permeation chromatography. In this way, the 3-oxo-2-oxaindolizidine glycomimetic **7** was obtained from carbamate **25**. Both **6** and **7** afforded the corresponding tetraacetates **27** and **28** upon conventional acetylation. No reversion into the furanose isomers was observed under these conditions (Scheme 2).

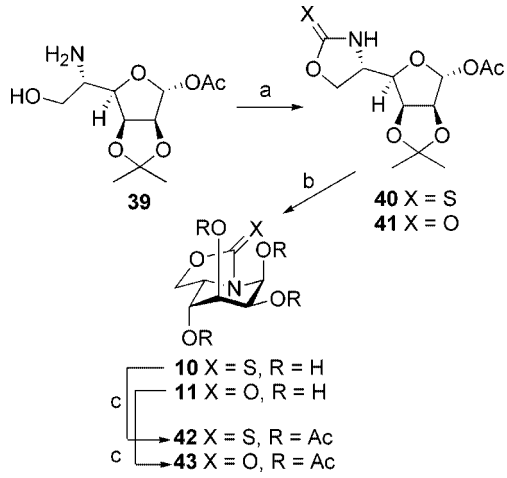
To access 8-*epi*-castanospermine analogues of the sp^2 azasugar type using the above strategy, D-*galacto*-configured precursors were required. The synthetic scheme parallels that already discussed above for the D-allose series but starts from the known 3-*O*-acetyl-1,2-*O*-isopropylidene-6-*O*-trityl-α-D-galactofuranose **29**.[17] Thus, double inversion at C-5 by triflation/nitrite addition (→**30**) followed by triflation/azide substitution (→**31**), detritylation (→**32**), deacetylation (→**33**) and reduction of the azide group provided the key D-*galacto* amino alcohol **34**. Thiocarbonylation with carbon disulfide/dicyclohexylcarbodiimide or carbonylation with triphosgene/diisopropylethylamine afforded the corresponding five-membered (thio)carbamate (**35** and **36**, respectively), which after deacetalation, acetylation and deacetylation as above led to the target reducing tetrahydroxyindolizidines **8** and **9**, respectively, with a substitution pattern at the six-membered ring analogous to that of α-D-galactopyranosides. Small samples of **8** and **9** were acetylated (→**37** and **38**, respectively) to confirm their structures (Scheme 3).

Inverting the configuration at position C-8a in any of the 2-oxaindolizidine derivatives **4**–**9** implies the need of a (thio)carbamate monosaccharide precursor of the non-natural L-series. Since the L-*gulo* vicinal amino alcohol **39**, the C-5 epimer of the D-mannofuranose derivative **13**, had been prepared previously by our group,[17] an investigation of its suitability as a precursor for 6,8-di-*epi*-castanospermine analogues seemed intriguing. After removal of the protecting groups in the corresponding cyclic (thio)carbamate (**40** and **41**) and subsequent acetylation/deacetylation, the furanose → pyranose rearrangement took place to give **10** and **11**, respectively, as the only detectable diastereomers. In accord with earlier reactions, further acetylation afforded exclusively the tetraacetoxyindolizidines **42** and **43**, respectively (Scheme 4).

All the new tetrahydroxy-2-oxaindolizidine analogues **4**–**11** existed in D_2O solution as single diastereomers. The high-field pseudoanomeric C-5 resonance (82.7–75.7 ppm) confirmed the amino acetal bicyclic structure, while the vicinal ^3J(H,H) values of the piperidine ring were in agreement with a configurational pattern that matched that of the related hexopyranoses. The configuration at the hemiaminal centre C-5 was inferred directly from the corresponding $J_{5,6}$ value, indicative of a 5*R* configuration in the cases of the 7- and 8-*epi*-castanospermine glycomimetics (**6**, **7** and **8**, **9**, respectively) and of a 5*S* configuration in the case of **10** and **11** ($J_{5,6}$ = 3.7–4.5 Hz for *cis* axial/equatorial relative dispositions). The 5*R* configuration of the 6-*epi* dia-



Scheme 3. Reagents and conditions: a, 1. Tf_2O, CH_2Cl_2, pyridine, –25 °C → room temp., 30 min; 2. $NaNO_2$, DMF, room temp., 24 h, 51%; b, 1. Tf_2O, CH_2Cl_2, pyridine, –25 °C → room temp., 30 min; 2. NaN_3, DMF, room temp., 24 h, 51%; c, BF_3–Et_2O, MeOH, 0 °C → room temp., 2 h, 75%; d, NaOMe, MeOH, 80%; e, H_2, Pd/C, MeOH, room temp., 1 h, 96%; f, for **35**: CS_2, DCC, CH_2Cl_2, –10 °C → room temp., 6 h, 86%; for **36**: triphosgene, DIPEA, CH_2Cl_2, 0 °C → room temp., 10 min, 90%; g, 1. 90% TFA/water, 0 °C, 15 min; 2. Ac_2O/pyridine; 3. NaOMe, MeOH, 65–89%; h, Ac_2O/pyridine, 82–85%.



Scheme 4. Reagents and conditions: a, for **40**: CS_2, DCC, CH_2Cl_2, –10 °C → room temp., 8 h, 70%; for **41**: triphosgene, DIPEA, CH_2Cl_2, 0 °C → room temp., 45 min, 43%; b, 1. 90% TFA/water, 0 °C, 15 min; 2. Ac_2O/pyridine; 3. NaOMe, MeOH, 50%; c, Ac_2O/pyridine, 87–90%.

stereomers **4** and **5** ($J_{5,6}$ = 2.9 and 2.8 Hz, respectively, for *trans* diequatorial relative dispositions of the corresponding protons) was confirmed by the absence of NOE contacts between H-5 and H-8a. In all cases, a single compound, with a pseudoanomeric configuration identical to that of its unprotected precursor, was detected after conventional acetylation, thus confirming the high configurational integrity imparted by the pseudoamide-type endocyclic nitrogen atom.

Mapping the Structure/Glycosidase Inhibitory Properties of Reducing 2-Oxacastanospermine Diastereomers

The inhibitory activities of the 2-oxacastanospermine diastereomers **4**–**11** were first screened against yeast α-glucosidase and almond β-glucosidase (Table 1). The (+)-castanospermine analogues **2** and **3** exhibited total anomeric selectivity with these two glycosidases, behaving as potent competitive inhibitors of the enzyme with α specificity (K_i = 40 and 2.2 μM, respectively).[24] Inverting the configuration at C-6 (**4**, **5** or **10**, **11**) or C-8 (**8**, **9**) was found to have a deleterious effect on the glucosidase inhibition ability, while the C-7 epimer **7** retained a certain amount of activity, although two orders of magnitude weaker than that of the D-*gluco* analogue **3** (K_i = 540 μM). These results are consistent with those obtained with the parent tetrahy-

Table 1. Comparison of inhibitory activities[a] (K_i, μM) for reducing (+)-2-oxacastanospermine derivatives (**2**, **3**),[b] and the corresponding 6-*epi* (**4**, **5**), 7-*epi* (**6**, **7**), 8-*epi* (**8**, **9**) and 6,8a-di-*epi* (**10**, **11**) diastereomers.[c,d]

Compound	α-Glucosidase (yeast)	α-Mannnosidase (Jack bean)	α-Galactosidase (coffee beans)	β-Galactosidase (bovine liver, cytosolic)
2	40	n.i.	n.i.	n.i.
3	2.2	n.i.	n.i.	n.i.
4	n.i.	n.i.	n.i.	n.i.
5	n.i.	n.i.	n.i.	n.i.
6	n.i.	n.i.	n.i.	n.i
7	540	n.i.	n.i.	n.i.
8	n.i.	n.i.	137	267
9	n.i.	n.i.	259	n.i.
10	n.i.	n.i.	n.i.	n.i.
11	n.i.	n.i.	n.i.	n.i.

[a] Inhibition, when detected, was always of the competitive type. [b] See ref.[24]. [c] The new compounds **4**–**11** showed no inhibition when assayed against β-glucosidase (almonds), trehalase (pig kidney), isomaltase (yeast), invertase (yeast), amyloglucosidase (*Aspergillus niger*) and α-L-fucosidase (pig kidney). [c] n.i. = no inhibition detected.

droxyindolizidine alkaloid series[28] and show the importance of the correct number and stereochemistry of the hydroxy groups for the specific inhibition of glycosidases.

Compounds **4** and **5** are related to α-D-mannopyranosides in the same way as **2** and **3** are related to α-D-glucopyranosides. Yet, neither **4** nor **5** inhibited Jack bean α-mannosidase, which may be due to an unfavourable disposition about the bond homologous to C-5–C-6 (i.e. C-8–C-8a) as compared with that in the bound substrates. The D-galactopyranoside analogues **8** and **9** behaved as moderate competitive inhibitors of green coffee α-galactosidase (K_i = 137 and 259 μM, respectively). Compound **9** exhibited total α-anomeric selectivity with bovine liver β-galactosidase, in agreement with the α-pseudoanomeric configuration at C-5, while the thioxo analogue **8** inhibited the β-enzyme with half the activity of the inhibition of the α form (K_i = 267 μM, respectively). No cross-configurational activity was observed in any case when a larger glycosidase panel, which included trehalase (pig kidney), isomaltase (yeast), invertase (yeast), amyloglucosidase (*Aspergillus niger*) and α-L-fucosidase (pig kidney), was considered.

Conclusions

The results described herein demonstrate the concept of stereoelectronic control of the stereochemistry at amino acetal centres which allows access to reducing glycomimetics of the sp^2 azasugar type that retain a defined pseudoanomeric configuration in aqueous solution. By exploiting the ability of the nitrogen atom of oxazolidine-2-(thi)one to act as a nucleophile in intramolecular addition to the masked aldehyde group in hexose precursors, a series of epimeric reducing castanospermine analogues has been prepared which has allowed structure/glycosidase inhibition specificity and potency relationships to be evaluated. The data obtained underline the critical influence of the hydroxylation profile on the inhibitory activity and support the importance of the configuration at pseudoanomeric centres in anomeric specificity.

Experimental Section

General Remarks: Optical rotations were measured at room temperature in 1-cm or 1-dm tubes. Unit for ε values: $mM^{-1}cm^{-1}$. IR spectra were recorded on a FTIR instrument. ^1H (and ^{13}C) NMR spectra were recorded at 500 (125.7) and 300 (75.5) MHz. 1D TOCSY as well as 2D COSY and HMQC experiments were carried out to assist in signal assignment. The FABMS spectra were recorded by using a primary beam consisting of Xe atoms with a maximum energy of 8 keV. The samples were dissolved in *m*-nitrobenzyl alcohol or thioglycerol as the matrices and the positive ions were separated and accelerated over a potential of 7 keV. NaI was added as a cationizing agent. TLC was performed with E. Merck precoated TLC plates, silica gel 30F-245, with visualization by UV light and by charring with 10% H_2SO_4 or 0.2% w/v cerium(IV) sulphate/5% ammonium molybdate in 2 M H_2SO_4. Column chromatography was carried out with silica gel 60 (E. Merck, 230–400 mesh). Fully deprotected compounds were purified by GPC (Sephadex G-10, 1:1 MeOH/H_2O). Acetylations were effected conventionally with 1:1 pyridine/Ac_2O (10 mL per 1 g of sample). Deacetylations were effected following the method of Zemplén by treatment with methanolic NaOMe (0.1 equiv. per mol of acetate) at room temperature for 1 h followed by neutralization with Amberlite IR-120 (H^+) ion-exchange resin or solid CO_2. Microanalyses were performed by the Instituto de Investigaciones Químicas (Sevilla, Spain).

Materials: 1-*O*-Acetyl-5-azido-5-deoxy-2,3-*O*-isopropylidene-α-D-mannofuranose (**12**) was obtained from 2,3:5,6-di-*O*-isopropylidene-L-gulonolactone as reported previously.[21] 3-*O*-Acetyl-1,2-*O*-isopropylidene-6-*O*-trityl-α-D-allofuranose (**18**) was prepared from 3-*O*-acetyl-1,2:5,6-di-*O*-isopropylidene-α-D-allofuranose.[17] 3-*O*-Acetyl-1,2-*O*-isopropylidene-6-*O*-trityl-α-D-galactofuranose (**29**) was prepared from 3-*O*-acetyl-1,2-*O*-isopropylidene-α-D-galactofuranose.[17] 1-*O*-Acetyl-5-amino-5-deoxy-2,3-*O*-isopropylidene-β-L-gulofuranose (**39**) was prepared from 1-*O*-acetyl-2,3:5,6-di-*O*-isopropylidene-α-D-mannofuranose following the previously reported procedure.[17] The glycosidases α-glucosidase (from yeast), β-glucosidase (from almonds), β-glucosidase (from bovine liver, cytosolic), trehalase (from pig kidney), α-galactosidase (from green coffee beans), α-mannosidase (from Jack beans), α-fucosidase (from bovine kidney) and amyloglucosidase (from *Aspergillus Niger*), used in the inhibition studies, as well as α,α′-trehalose and the corresponding *o*- and *p*-nitrophenyl glycoside substrates were purchased from Sigma Chemical Co.

1-*O*-Acetyl-5-amino-5-deoxy-2,3-*O*-isopropylidene-α-D-mannofuranose (13): A solution of 1-*O*-acetyl-5-azido-5-deoxy-2,3-*O*-isopropylidene-α-D-mannofuranose **12** (313 mg, 1.20 mmol) and 10% Pd/C (109 mg) in MeOH (10 mL) was hydrogenated under an atmospheric pressure of hydrogen using a balloon. The suspension was stirred for 2 h, filtered through Celite and concentrated to give **13** in quantitative yield, as seen by NMR, as a hygroscopic solid that was used in the next step without further purification. R_f = 0.35 (10:1:1 MeCN/H_2O/NH_4OH). $[a]_D^{22}$ = +55.3 (*c* = 1.0, MeOH). ^1H NMR (300 MHz, CD_3OD): δ = 1.51, 1.63 (2 s, 6 H, CMe_2), 2.23 (s, 3 H, MeCO), 3.10 (ddd, $J_{5,6a}$ = 3.3, $J_{5,6b}$ = 6.2, $J_{4,5}$ = 9.1 Hz, 1 H, H-5), 3.72 (dd, $J_{6a,6b}$ = 11.0 Hz, 1 H, H-6b), 3.92 (dd, 1 H, H-6a), 4.13 (dd, $J_{3,4}$ = 3.7 Hz, 1 H, H-4), 4.91 (d, $J_{2,3}$ = 5.9 Hz, 1 H, H-2), 5.19 (dd, 1 H, H-3), 6.04 (s, 1 H, H-1) ppm. ^{13}C NMR (75.5 MHz, CD_3OD): δ = 20.9 (*Me*CO), 24.7, 26.3 (C*Me*$_2$), 52.9 (C-5), 64.2 (C-6), 80.8 (C-3), 83.3 (C-4), 86.3 (C-2), 101.8 (C-1), 114.0 (*C*Me$_2$), 171.1 (CO) ppm. FABMS: *m*/*z* (%) = 262 (100) [M + H]$^+$. HRFABMS: *m*/*z* = 262.128786; calcd. for $C_{11}H_{20}NO_6$: 262.129063.

1-*O*-Acetyl-5-amino-5-deoxy-2,3-*O*-isopropylidene-α-D-mannofuranose 5,6-Cyclic Thiocarbamate (14): CS_2 (6.2 mmol) and DCC (0.62 mmol) were added to a stirred solution of **13** (161 mg, 0.62 mmol) in CH_2Cl_2 (2.6 mL) at –10 °C. The reaction mixture was allowed to reach room temperature and stirred for 2.5 h. The solvent was removed under reduced pressure and the residue was purified by column chromatography (1:3 → 1:1 EtOAc/petroleum ether) to give **14**. Yield: 145 mg (78%). R_f = 0.32 (1:1 EtOAc/petroleum ether). $[a]_D^{22}$ = +39.0 (*c* = 1.0, CH_2Cl_2). UV (CH_2Cl_2): λ = 248 nm (ε = 22.1). IR (KBr): $\tilde{\nu}_{max}$ = 3325, 2999, 1738, 1521, 1442, 1386, 1220, 1100 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$, 313 K): δ = 1.31, 1.46 (2s, 6 H, CMe_2), 2.07 (s, 3 H, MeCO), 4.21 (dd, $J_{3,4}$ = 3.8, $J_{4,5}$ = 7.4 Hz, 1 H, H-4), 4.29 (m, 1 H, H-5), 4.67 (dd, $J_{5,6b}$ = 5.4, $J_{6a,6b}$ = 9.3 Hz, 1 H, H-6b), 4.71 (d, $J_{2,3}$ = 5.9 Hz, 1 H, H-2), 4.74 (t, $J_{5,6a}$ = 9.3 Hz, 1 H, H-6a), 4.86 (dd, 1 H, H-3), 6.15 (s, 1 H, H-1), 8.00 (br. s, 1 H, NH) ppm. ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 20.8 (*Me*CO), 24.1, 25.5 (C*Me*$_2$), 55.4 (C-5), 73.2 (C-6), 77.3

(C-3), 81.7 (C-4), 84.6 (C-2), 100.1 (C-1), 113.6 (*C*Me$_2$), 169.1 (CO), 189.8 (CS) ppm. FABMS: *m*/*z* (%) = 326 (100) [M + Na]$^+$, 304 (80) [M + H]$^+$. $C_{12}H_{17}O_6NS$ (303.34): C 47.51, H 5.65, N 4.62; found C 47.45, H 5.67, N 4.64.

1-*O*-Acetyl-5-amino-5-deoxy-2,3-*O*-isopropylidene-α-D-mannofuranose 5,6-Cyclic Carbamate (15): Diisopropylethylamine (11.4 mmol) and triphosgene (1.71 mmol) were added to a stirred solution of **13** (299 mg, 1.14 mmol) in CH_2Cl_2 (5.9 mL) at 0 °C. The reaction mixture was allowed to reach room temperature and stirred for 15 min. The solvent was removed under reduced pressure and the residue was purified by column chromatography (2:1 EtOAc/petroleum ether) to give **15**. Yield: 210 mg (65%). R_f = 0.23 (3:1 EtOAc/petroleum ether). $[\alpha]_D^{22}$ = +28.0 (*c* = 1.0, CH_2Cl_2). IR (KBr): $\tilde{\nu}_{max}$ = 2990, 1752, 1657, 1426, 1259, 1093 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.27, 1.42 (2s, 6 H, CMe$_2$), 2.02 (s, 3 H, MeCO), 4.07 (ddd, $J_{5,6b}$ = 4.8, $J_{4,5}$ = 7.2, $J_{5,6a}$ = 8.1 Hz, 1 H, H-5), 4.12 (dd, $J_{3,4}$ = 3.7 Hz, 1 H, H-4), 4.38 (dd, $J_{6a,6b}$ = 9.2 Hz, 1 H, H-6b), 4.45 (dd, 1 H, H-6a), 4.67 (d, $J_{2,3}$ = 5.8 Hz, 1 H, H-2), 4.79 (dd, 1 H, H-3), 6.11 (s, 1 H, H-1), 6.11 (s, 1 H, NH) ppm. ^{13}C NMR (125.7 MHz, $CDCl_3$): δ = 21.0 (*Me*CO), 24.4, 25.7 (C*Me$_2$*), 51.6 (C-5), 67.8 (C-6), 78.9 (C-3), 82.8 (C-4), 84.8 (C-2), 100.4 (C-1), 113.5 (*C*Me$_2$), 159.5 (CO carbamate), 169.3 (CO ester) ppm. FABMS: *m*/*z* (%) = 310 (100) [M + Na]$^+$. $C_{12}H_{17}O_7N$ (287.28): C 50.17, H 5.96, N 4.87; found C 50.05, H 5.89, N 4.76.

(5*R*,6*S*,7*S*,8*R*,8a*R*)-5,6,7,8-Tetrahydroxy-3-thioxo-2-oxaindolizidine (4): Compound **14** (121 mg, 0.40 mmol) was subjected to conventional Zemplén *O*-deacetylation, followed by deacetalation with 90% TFA/water (5 mL). The reaction mixture was concentrated, and the residue was coevaporated several times with water to eliminate traces of acid and then purified by GPC (Sephadex G-10, 1:1 MeOH/H_2O) to give **4**. Yield: 72.5 mg (82%). R_f = 0.41 (45:5:3 EtOAc/EtOH/H_2O). $[\alpha]_D^{22}$ = +8.0 (*c* = 1.0, MeOH). UV (MeOH): λ = 248.0 nm (ε = 15.0). ^{1}H NMR (500 MHz, D_2O): δ = 3.81 (t, $J_{7,8}$ = $J_{8,8a}$ = 9.7 Hz, 1 H, H-8), 3.90 (dd, $J_{6,7}$ = 2.9 Hz, 1 H, H-7), 4.13 (t, $J_{5,6}$ = 2.9 Hz, 1 H, H-6), 4.17 (ddd, $J_{8a,1b}$ = 8.1, $J_{8a,1a}$ = 9.2 Hz, 1 H, H-8a), 4.55 (dd, $J_{1a,1b}$ = 9.2 Hz, 1 H, H-1b), 4.88 (t, 1 H, H-1a), 5.80 (d, 1 H, H-5) ppm. ^{13}C NMR (125.7 MHz, D_2O): δ = 59.9 (C-8a), 72.4 (C-1), 72.8 (C-7), 73.7 (C-8), 74.8 (C-6), 82.7 (C-5), 190.5 (CS) ppm. FABMS: *m*/*z* (%) = 244 (60) [M + Na]$^+$. $C_7H_{11}O_5NS$ (221.24): C 38.00, H 5.01, N 6.33; found C 37.98, H 5.10, N 6.38.

(5*R*,6*S*,7*S*,8*R*,8a*R*)-5,6,7,8-Tetrahydroxy-3-oxo-2-oxaindolizidine (5): Zemplén *O*-deacetylation of **15** (115 mg, 0.40 mmol), followed by deacetalation with 90% TFA/water (5 mL), elimination of the traces of acid by coevaporation with water and purification by GPC (Sephadex G-10, 1:1 MeOH/H_2O) afforded **5**. Yield: 60.7 mg (74%). R_f = 0.16 (45:5:3 EtOAc/EtOH/H_2O). $[\alpha]_D^{22}$ = +4.6 (*c* = 1.0, MeOH). ^{1}H NMR (500 MHz, D_2O): δ = 3.68 (t, $J_{7,8}$ = $J_{8,8a}$ = 9.5 Hz, 1 H, H-8), 3.75 (dd, $J_{6,7}$ = 2.8 Hz, 1 H, H-7), 3.87 (ddd, $J_{8a,1b}$ = 6.5, $J_{8a,1a}$ = 9.0 Hz, 1 H, H-8a), 4.00 (t, $J_{5,6}$ = 2.8 Hz, 1 H, H-6), 4.26 (dd, $J_{1a,1b}$ = 9.0 Hz, 1 H, H-1b), 4.56 (t, 1 H, H-1a), 5.20 (d, 1 H, H-5) ppm. ^{13}C NMR (125.7 MHz, D_2O): δ = 54.0 (C-8a), 67.6 (C-1), 70.1 (C-7), 70.3 (C-8), 71.0 (C-6), 77.2 (C-5), 158.6 (CO carbamate) ppm. FABMS: *m*/*z* (%) = 228 (10) [M + Na]$^+$. $C_7H_{11}O_6N$ (205.17): C 40.98, H 5.40, N 6.83; found C 41.06, H 5.42, N 6.87.

(5*R*,6*S*,7*S*,8*R*,8a*R*)-5,6,7,8-Tetraacetoxy-3-thioxo-2-oxaindolizidine (16): Conventional acetylation of **4** (30 mg, 0.13 mmol) afforded **16**. Yield: 53 mg (98%). R_f = 0.51 (3:1 EtOAc/petroleum ether). $[\alpha]_D^{22}$ = +5.0 (*c* = 1.0, CH_2Cl_2). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 2.00–2.20 (4 s, 12 H, 4 MeCO), 4.16 (ddd, $J_{8a,1b}$ = 6.8, $J_{8a,1a}$ = 9.5, $J_{8,8a}$ = 10.0 Hz, 1 H, H-8a), 4.55 (dd, $J_{1a,1b}$ = 9.5 Hz, 1 H, H-1b), 4.65 (t, 1 H, H-1a), 5.25 (t, $J_{7,8}$ = 10.0 Hz, 1 H, H-8), 5.35 (dd, 1 H, H-7), 5.40 (t, $J_{5,6}$ = $J_{6,7}$ = 2.8 Hz, 1 H, H-6), 6.89 (d, 1 H, H-5) ppm. ^{13}C NMR (125.7 MHz, $CDCl_3$): δ = 20.6 (*Me*CO), 56.7 (C-8a), 67.8 (C-6), 68.2 (C-7), 69.0 (C-8), 71.0 (C-1), 77.0 (C-5), 167.6, 169.4, 169.7, 170.0, (CO), 187.6 (CS) ppm. FABMS: *m*/*z* (%) = 412 (60) [M + Na]$^+$. $C_{15}H_{19}O_9NS$ (389.39): C 46.27, H 4.92, N 3.60, S 8.23; found C 46.25, H 4.99, N 3.57, S 8.42.

(5*R*,6*S*,7*R*,8*R*,8a*R*)-5,6,7,8-Tetraacetoxy-3-oxo-2-oxaindolizidine (17): Conventional acetylation of **5** (30 mg, 0.15 mmol) afforded **17**. Yield: 52 mg (95%). R_f = 0.24 (1:1 EtOAc/petroleum ether). $[\alpha]_D^{22}$ = +7.1 (*c* = 1.0, CH_2Cl_2). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.07–2.09 (4 s, 12 H, 4 MeCO), 3.96 (ddd, $J_{8a,1b}$ = 5.7, $J_{8a,1a}$ = 8.3, $J_{8,8a}$ = 9.2 Hz, 1 H, H-8a), 4.32 (dd, $J_{1a,1b}$ = 9.2 Hz, 1 H, H-1b), 4.42 (dd, 1 H, H-1a), 5.21 (t, $J_{7,8}$ = 9.2 Hz, 1 H, H-8), 5.30 (dd, $J_{6,7}$ = 2.4 Hz, 1 H, H-7), 5.34 (t, $J_{5,6}$ = 2.4 Hz, 1 H, H-6), 6.34 (d, 1 H, H-5) ppm. ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 20.5 (*Me*CO), 53.1 (C-8a), 66.1 (C-1), 67.7 (C-7), 68.3 (C-8), 68.9 (C-6), 74.4 (C-5), 154.8 (CO carbamate), 167.7, 169.1, 169.6, 169.9 (CO ester) ppm. FABMS: *m*/*z* (%) = 396 (100) [M + Na]$^+$. $C_{15}H_{19}O_{10}N$ (373.32): C 48.26, H 5.13, N 3.75; found C 48.16, H 5.17, N 3.70.

3-*O*-Acetyl-1,2-*O*-isopropylidene-6-*O*-trityl-β-L-talofuranose (19): Pyridine (0.92 mL) and trifluoromethanesulfonic anhydride (1.22 mL, 7.38 mmol) were added under nitrogen to a solution of 3-*O*-acetyl-1,2-*O*-isopropylidene-6-*O*-trityl-α-D-allofuranose (**18**) (2.74 g, 5.43 mmol) in CH_2Cl_2 (15 mL) at –25 °C. The reaction mixture was allowed to reach room temperature and after stirring for 30 min, the mixture was diluted with CH_2Cl_2 (15 mL), washed with iced saturated aqueous $NaHCO_3$ (15 mL), dried ($MgSO_4$) and concentrated. The resulting triflate ester was dissolved in DMF (14 mL), $NaNO_2$ (1.75 g, 25.4 mmol) was added and the reaction mixture was stirred at room temperature for 18 h. The solvent was removed under reduced pressure and the resulting residue was dissolved in CH_2Cl_2 (15 mL) and washed with water (2 × 10 mL). The organic extract was dried ($MgSO_4$) and concentrated. The resulting residue was purified by column chromatography using 1:6 → 1:4 EtOAc/petroleum ether as eluent to give **19**. Yield: 1.40 g (51%). R_f = 0.30 (1:2 EtOAc/petroleum ether). $[\alpha]_D^{22}$ = +37.6 (*c* = 1.0, CH_2Cl_2). IR (KBr): $\tilde{\nu}_{max}$ = 3436, 3047, 2991, 1736, 1363, 1236, 1061 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.34, 1.54 (2 s, 6 H, CMe$_2$), 2.10 (s, 3 H, MeCO), 2.27 (d, $J_{OH,5}$ = 7.0 Hz, 1 H, OH), 3.25 (dd, $J_{5,6b}$ = 5.6, $J_{6a,6b}$ = 9.5 Hz, 1 H, H-6b), 3.34 (dd, $J_{5,6a}$ = 7.3 Hz, 1 H, H-6a), 3.75 (m, 1 H, H-5), 4.23 (dd, $J_{4,5}$ = 2.0, $J_{3,4}$ = 8.9 Hz, 1 H, H-4), 4.81 (dd, $J_{1,2}$ = 3.7, $J_{2,3}$ = 4.7 Hz, 1 H, H-2), 4.88 (dd, 1 H, H-3), 5.80 (d, 1 H, H-1), 7.23–7.54 (m, 15 H, Ph) ppm. ^{13}C NMR (125.7 MHz, $CDCl_3$): δ = 20.7 (*Me*CO), 26.4, 26.6 (C*Me$_2$*), 60.4 (C-6), 64.9 (C-5), 71.9 (C-3), 77.3 (C-4), 77.4 (C-2), 86.8 (*C*Ph$_3$), 104.3 (C-1), 113.1 (*C*Me$_2$), 127.0–143.7 (Ph), 170.3 (CO) ppm. FABMS: *m*/*z* (%) = 527 (100) [M + Na]$^+$. $C_{30}H_{32}O_7$ (504.59): C 71.41, H 6.39; found C 71.36, H 6.24.

3-*O*-Acetyl-5-azido-5-deoxy-1,2-*O*-isopropylidene-6-*O*-trityl-α-D-allofuranose (20): Pyridine (0.47 mL) and trifluoromethanesulfonic anhydride (0.62 mL, 3.75 mmol) were added under nitrogen to a solution of **19** (1.40 g, 2.77 mmol) in CH_2Cl_2 (7.5 mL) at –25 °C. The reaction mixture was allowed to reach room temperature and, after stirring for 30 min, the mixture was diluted with CH_2Cl_2 (15 mL), washed with iced saturated aqueous $NaHCO_3$ (15 mL), dried ($MgSO_4$) and concentrated. The resulting triflate ester was dissolved in DMF (11 mL), NaN_3 (1.26 g, 19.38 mmol) was added and the reaction mixture was stirred at room temperature for 18 h. The solvent was removed under reduced pressure and the resulting residue was dissolved in CH_2Cl_2 (10 mL) and washed with water (2 × 5 mL). The organic extract was dried ($MgSO_4$) and concen-

trated. The resulting residue was purified by column chromatography to give **20**. Yield: 1.24 g (85%). $[\alpha]_D^{22}$ = +49.2 (*c* = 1.0, CH_2Cl_2). IR (KBr): $\tilde{\nu}_{max}$ = 3150, 2101, 1744, 1633, 1386, 1236, 1093 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 1.32, 1.52 (2 s, 6 H, CMe_2), 1.92 (s, 3 H, MeCO), 3.18 (dd, $J_{5,6b}$ = 8.5, $J_{6a,6b}$ = 9.9 Hz, 1 H, H-6b), 3.28 (dd, $J_{5,6a}$ = 4.1 Hz, 1 H, H-6a), 3.89 (dt, $J_{4,5}$ = 4.1 Hz, 1 H, H-5), 4.21 (dd, $J_{3,4}$ = 8.5 Hz, 1 H, H-4), 4.74 (dd, $J_{2,3}$ = 4.1 Hz, 1 H, H-3), 4.78 (dd, $J_{1,2}$ = 3.6 Hz, 1 H, H-2), 5.78 (d, 1 H, H-1), 7.25–7.47 (m, 15 H, Ph) ppm. ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 20.4 (*Me*CO), 26.5 (C*Me*$_2$), 62.4 (C-6), 63.1 (C-5), 72.3 (C-3), 76.4 (C-4), 77.3 (C-2), 87.2 (*C*Ph$_3$), 103.9 (C-1), 113.0 (*C*Me$_2$), 127.1–143.3 (Ph), 169.6 (CO) ppm. FABMS: *m*/*z* (%) = 552 (100) $[M + Na]^+$. $C_{30}H_{31}N_3O_6$ (529.60): C 68.04, H 5.90, N 7.94; found C 68.14, H 5.81, N 7.84.

3-*O*-Acetyl-5-azido-5-deoxy-1,2-*O*-isopropylidene-α-D-allofuranose (21): $BF_3{\cdot}Et_2O$ complex (0.84 mL) and MeOH (5 mL) were added to a solution of the tritylated azido derivative **20** (1.85 g, 3.5 mmol) in CH_2Cl_2 (25 mL) at 0 °C under argon. The reaction mixture was allowed to reach room temperature and stirred for 2 h, diluted with CH_2Cl_2 (15 mL), then washed with saturated aqueous $NaHCO_3$ (2×15 mL), dried ($MgSO_4$) and concentrated. The resulting residue was purified by column chromatography (1:2 → 1:1 EtOAc/petroleum ether) to give **21** (804 mg, 80%) as an amorphous solid. R_f = 0.27 (1:2 EtOAc/petroleum ether). $[\alpha]_D^{22}$ = +165.8 (*c* = 1.0, CH_2Cl_2). IR (KBr): $\tilde{\nu}_{max}$ = 3443, 2990, 2114, 1740, 1374, 1231, 1064 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 1.32, 1.53 (2 s, 6 H, CMe_2), 2.12 (s, 3 H, MeCO), 3.60 (dd, $J_{5,6b}$ = 7.0, $J_{6a,6b}$ = 11.5 Hz, 1 H, H-6b), 3.75 (dd, $J_{5,6a}$ = 4.5 Hz, 1 H, H-6a), 3.79 (dt, $J_{4,5}$ = 4.5 Hz, 1 H, H-5), 4.25 (dd, 1 H, H-4), 4.84 (m, 2 H, H-2, H-3), 5.82 (d, $J_{1,2}$ = 3.7 Hz, 1 H, H-1) ppm. ^{13}C NMR (125.7 MHz, $CDCl_3$): δ = 20.8 (*Me*CO), 26.8 (C*Me*$_2$), 62.1 (C-6), 64.3 (C-5), 72.9 (C-3), 77.4 (C-4), 77.7 (C-2), 104.3 (C-1), 113.6 (*C*Me$_2$), 170.3 (CO) ppm. FABMS: *m*/*z* (%) = 310 (100) $[M + Na]^+$. $C_{11}H_{17}N_3O_6$ (287.28): C 45.99, H 5.96, N 14.63; found C 45.97, H 5.90, N 14.58.

5-Azido-5-deoxy-1,2-*O*-isopropylidene-α-D-allofuranose (22): Conventional deacetylation of **21** (2.8 mmol) and purification by column chromatography (1:1 EtOAc/petroleum ether) afforded **22**. Yield: 584 mg (85%). R_f = 0.24 (1:1 EtOAc/petroleum ether). $[\alpha]_D^{22}$ = +48.0 (*c* = 1.0, CH_2Cl_2). IR (KBr): $\tilde{\nu}_{max}$ = 3420, 2125, 1641, 1386, 1093 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 1.36, 1.57 (2 s, 6 H, CMe_2), 2.81 (t, $J_{OH,6a}$ = 5.0 Hz, 1 H, OH), 3.25 (d, $J_{OH,3}$ = 8.2 Hz, 1 H, OH), 3.77 (dd, $J_{5,6b}$ = 4.4, $J_{6a,6b}$ = 12.2 Hz, 1 H, H-6b), 3.85 (ddd, $J_{5,6a}$ = 6.2 Hz, 1 H, H-6a), 3.96 (ddd, $J_{4,5}$ = 3.1 Hz, 1 H, H-5), 4.00 (dd, $J_{3,4}$ = 8.2 Hz, 1 H, H-4), 4.18 (td, $J_{2,3}$ = 5.0 Hz, 1 H, H-3), 4.65 (dd, $J_{1,2}$ = 3.7 Hz, 1 H, H-2), 5.84 (d, 1 H, H-1) ppm. ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 26.3, 26.4 (C*Me*$_2$), 61.6 (C-6), 62.8 (C-5), 70.4 (C-3), 78.8 (C-2), 81.1 (C-4), 103.6 (C-1), 113.0 (*C*Me$_2$) ppm. FABMS: *m*/*z* (%) = 268 (100) $[M + Na]^+$. $C_9H_{15}N_3O_5$ (245.24): C 44.08, H 6.16, N 17.13; found C 43.90, H 6.19, N 16.88.

5-Amino-5-deoxy-1,2-*O*-isopropylidene-α-D-allofuranose (23): A solution of azido sugar **22** (235 mg, 0.96 mmol) and 10% Pd/C (95 mg) in MeOH (8.8 mL) was hydrogenated under an atmospheric pressure of hydrogen using a balloon. The mixture was stirred for 1 h, filtered through Celite and concentrated to give **23** (210 mg, 99%) as a hygroscopic solid that was used in the next step without further purification. $[\alpha]_D^{22}$ = +44.8 (*c* = 1.0, MeOH). IR (KBr): $\tilde{\nu}_{max}$ = 3396, 1641, 1450, 1386, 1093 cm^{-1}. ^1H NMR (300 MHz, CD_3OD): δ = 1.33, 1.53 (2 s, 6 H, CMe_2), 3.58 (dd, $J_{5,6b}$ = 5.5, $J_{6a,6b}$ = 11.2 Hz, 1 H, H-6b), 3.70 (dd, $J_{5,6a}$ = 4.0 Hz, 1 H, H-6a), 3.00 (td, $J_{4,5}$ = 5.5 Hz, 1 H, H-5), 3.83 (dd, $J_{3,4}$ = 9.1 Hz, 1 H, H-4), 3.95 (dd, $J_{2,3}$ = 3.7 Hz, 1 H, H-3), 4.56 (t, $J_{1,2}$ = 3.7 Hz, 1 H, H-2), 5.72 (d, 1 H, H-1) ppm. ^{13}C NMR (75.5 MHz, CD_3OD): δ = 26.6, 26.8 (C*Me*$_2$), 55.1 (C-5), 63.9 (C-6), 73.6 (C-3), 80.7 (C-4), 81.0 (C-2), 105.1 (C-1), 113.7 (*C*Me$_2$) ppm. FABMS: *m*/*z* (%) = 242 (100) $[M + Na]^+$, 220 (60) $[M + H]^+$. HRFABMS: *m*/*z* = 220.118101; calcd. for $C_9H_{18}NO_5$: 220.118498.

5-Amino-5-deoxy-1,2-*O*-isopropylidene-α-D-allofuranose 5,6-Cyclic Thiocarbamate (24): Thiocarbonylation of **23** (193 mg, 0.88 mmol) by treatment with CS_2/DCC for 5 h as above described for the preparation of **14**, followed by purification by column chromatography (2:1 → 3:1 EtOAc/petroleum ether) yielded **24**. Yield: 204 mg (89%). R_f = 0.36 (3:1 EtOAc/petroleum ether). $[\alpha]_D^{22}$ = +5.6 (*c* = 0.5, MeOH). UV (MeOH): λ = 243 nm (ε = 15.9). IR (KBr): $\tilde{\nu}_{max}$ = 3364, 2983, 1641, 1514, 1386, 1093 cm^{-1}. ^1H NMR (300 MHz, CD_3OD): δ = 1.33, 1.52 (2 s, 6 H, CMe_2), 3.80 (dd, $J_{2,3}$ = 4.6, $J_{3,4}$ = 9.2 Hz, 1 H, H-3), 3.94 (dd, $J_{4,5}$ = 3.1 Hz, 1 H, H-4), 4.33 (ddd, $J_{5,6a}$ = 6.3, $J_{5,6b}$ = 9.1 Hz, 1 H, H-5), 4.56 (dd, $J_{1,2}$ = 3.6 Hz, 1 H, H-2), 4.63 (t, $J_{6a,6b}$ = 9.1 Hz, 1 H, H-6b), 4.68 (dd, 1 H, H-6a), 5.74 (d, 1 H, H-1) ppm. ^{13}C NMR (125.7 MHz, CD_3OD): δ = 26.6, 26.9 (C*Me*$_2$), 58.2 (C-5), 71.5 (C-6), 72.9 (C-3), 79.9 (C-4), 81.1 (C-2), 105.3 (C-1), 114.1 (*C*Me$_2$), 191.7 (CS) ppm. FABMS: *m*/*z* (%) = 284 (70) $[M + Na]^+$, 262 (100) $[M + H]^+$. $C_{10}H_{15}NO_5S$ (261.30): C 45.96, H 5.79, N 5.36; found C 46.06, H 5.72, N 5.43.

5-Amino-5-deoxy-1,2-*O*-isopropylidene-α-D-allofuranose 5,6-Cyclic Carbamate (25): Carbonylation of **23** (210 mg, 0.96 mmol) by treatment with triphosgene/diisopropyl(ethyl)amine for 20 min, as described for the preparation of **15**, and purification by column chromatography (EtOAc → 45:5:3 EtOAc/EtOH/H_2O) afforded **25**. Yield: 210 mg (89%). R_f = 0.55 (45:5:3 EtOAc/EtOH/H_2O). $[\alpha]_D^{22}$ = +22.5 (*c* = 0.52, MeOH). IR (KBr): $\tilde{\nu}_{max}$ = 3396, 2985, 1744, 1633, 1402, 1093 cm^{-1}. ^1H NMR (500 MHz, CD_3OD): δ = 1.33, 1.52 (2 s, 6 H, CMe_2), 3.85 (dd, $J_{2,3}$ = 3.6, $J_{3,4}$ = 9.1 Hz, 1 H, H-3), 3.90 (dd, $J_{4,5}$ = 3.4 Hz, 1 H, H-4), 4.13 (ddd, $J_{5,6a}$ = 6.2, $J_{5,6b}$ = 9.6 Hz, 1 H, H-5), 4.43 (m, 2 H, H-6a, H-6b), 4.57 (t, $J_{1,2}$ = 3.6 Hz, 1 H, H-2), 5.73 (d, 1 H, H-1) ppm. ^{13}C NMR (125.7 MHz, CD_3OD): δ = 26.7, 26.9 (C*Me*$_2$), 54.3 (C-5), 66.7 (C-6), 73.0 (C-3), 80.5 (C-4), 81.1 (C-2), 105.3 (C-1), 114.0 (*C*Me$_2$), 162.4 (CO carbamate) ppm. FABMS: *m*/*z* (%) = 268 (100) $[M + Na]^+$. $C_{10}H_{15}O_6N$ (245.24): C 48.98, H 6.16, N 5.71; found C 49.00, H 6.17, N 5.64.

***N*-Acetyl-1,2,3-tri-*O*-acetyl-5-amino-5-deoxy-α-D-allofuranose 5,6-Cyclic Thiocarbamate (26):** Compound **24** (104 mg, 0.40 mmol) was deacetalated by treatment with 90% TFA/water (5 mL). The reaction mixture was concentrated and the residue was coevaporated several times with water to eliminate traces of acid. The resulting residue was subjected to conventional acetylation with Ac_2O/pyridine (1:1, 5.0 mL) and the peracetylated mixture was purified by column chromatography using 1:1 EtOAc/petroleum ether as eluent. A mixture of furanose and indolizidine isomers was obtained according to NMR spectroscopy. A second column chromatography using 4:1 Et_2O/petroleum ether as eluent allowed a pure sample of **26** to be isolated. Yield: 21 mg (14%). R_f = 0.26 (4:1 Et_2O/petroleum ether). $[\alpha]_D^{22}$ = +53.7 (*c* = 1.0, CH_2Cl_2). UV (CH_2Cl_2): λ = 266 nm (ε = 12.5). IR (KBr): $\tilde{\nu}_{max}$ = 3301, 2920, 1752, 1698, 1426, 1371, 1220, 1088 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 2.07, 2.12, 2.13, (3 s, 9 H, MeCO ester), 2.82 (s, 3 H, MeCO amide), 4.49 (dd, $J_{5,6b}$ = 8.4, $J_{6a,6b}$ = 9.0 Hz, 1 H, H-6b), 4.54 (dd, $J_{4,5}$ = 3.9, $J_{3,4}$ = 8.9 Hz, 1 H, H-4), 4.65 (dd, $J_{5,6a}$ = 2.7 Hz, 1 H, H-6a), 4.95 (ddd, 1 H, H-5), 5.24 (dd, $J_{2,3}$ = 4.5 Hz, 1 H, H-3), 5.34 (d, 1 H, H-2), 6.16 (s, 1 H, H-1) ppm. ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 20.3–20.8 (*Me*CO ester), 26.0 (*Me*CO amide), 59.0 (C-5), 67.3 (C-6), 70.3 (C-3), 73.9 (C-2), 78.4 (C-4), 97.4 (C-1), 168.1–171.2 (CO), 185.5 (CS) ppm. FABMS: *m*/*z* (%) = 412 (80) $[M + Na]^+$. $C_{15}H_{19}NO_9S$ (389.39): C 46.27, H 4.92, N 3.60; found C 46.12, H 4.71, N 3.51

(5*R*,6*R*,7*R*,8*R*,8a*R*)-5,6,7,8-Tetrahydroxy-3-thioxo-2-oxaindolizidine (6): Compound **24** (104 mg, 0.40 mmol) was deacetalated by treatment with 90% TFA/water (5 mL). The reaction mixture was concentrated, and the residue coevaporated several times with water to eliminate traces of acid. The resulting residue was subjected to conventional acetylation with Ac_2O/pyridine (1:1, 5.0 mL) and the peracetylated mixture was purified by column chromatography using 1:1 EtOAc/petroleum ether as eluent. The resulting crude peracetylated mixture of furanose and indolizidine isomers, according to NMR, was deacetylated with methanolic NaOMe to give **6** as the only reaction product. Yield: 44 mg (50%). R_f = 0.41 (45:5:3 EtOAc/EtOH/H_2O). $[\alpha]_D^{22}$ = –27.5 (*c* = 1.0, H_2O). UV (H_2O): λ = 243 nm (ε = 16.0). ^{1}H NMR (500 MHz, D_2O): δ = 3.63 (dd, $J_{7,8}$ = 2.7, $J_{8,8a}$ = 9.1 Hz, 1 H, H-8), 3.67 (dd, $J_{6,7}$ = 2.7, $J_{5,6}$ = 4.4 Hz, 1 H, H-6), 4.03 (t, 1 H, H-7), 4.24 (td, $J_{8a,1b}$ = 7.8, $J_{8a,6a}$ = 9.1 Hz, 1 H, H-8a), 4.41 (dd, $J_{1a,1b}$ = 9.1 Hz, 1 H, H-1b), 4.66 (t, 1 H, H-1a), 5.64 (d, 1 H, H-5) ppm. ^{13}C NMR (125.7 MHz, D_2O): δ = 52.6 (C-8a), 66.7 (C-6), 70.2 (C-8), 72.1 (C-7, C-1), 78.1 (C-5), 187.4 (CS) ppm. FABMS: *m*/*z* (%) = 244 (60) $[M + Na]^+$. $C_7H_{11}NO_5S$ (221.24): C 38.00, H 5.01, N 6.33; found C 37.92, H 4.93, N 6.31.

(5*R*,6*R*,7*R*,8*R*,8a*R*)-5,6,7,8-Tetrahydroxy-3-oxo-2-oxaindolizidine (7): Compound **25** (99 mg, 0.40 mmol) was deacetalated by treatment with 90% TFA/water (5 mL). The reaction mixture was concentrated, and the residue coevaporated several times with water to eliminate traces of acid. The resulting residue was subjected to conventional acetylation with Ac_2O/pyridine (1:1, 7.3 mL) and the peracetylated mixture was purified by column chromatography using 5:2 EtOAc/petroleum ether as eluent. The resulting crude peracetylated mixture of furanose and indolizidine isomers, according to NMR, was deacetylated with methanolic NaOMe to give **7** as the only reaction product. Yield: 44.7 mg (64%). R_f = 0.61 (6:3:1 MeCN/H_2O/NH_4OH). $[\alpha]_D^{22}$ = +33.0 (*c* = 1.0, H_2O). ^{1}H NMR (500 MHz, D_2O): δ = 3.67 (t, $J_{7,8}$ = 2.8 Hz, $J_{8,8a}$ = 10.0 Hz, 1 H, H-8), 3.69 (dd, $J_{6,7}$ = 2.8, $J_{5,6}$ = 4.4 Hz, 1 H, H-6), 4.07 (t, 1 H, H-7), 4.11 (m, 1 H, H-8a), 4.25 (dd, $J_{8a,1b}$ = 7.2, $J_{1a,1b}$ = 8.7 Hz, 1 H, H-1b), 4.61 (t, $J_{8a,1a}$ = 8.7 Hz, 1 H, H-1a), 5.22 (d, 1 H, H-5) ppm. ^{13}C NMR (125.7 MHz, D_2O): δ = 50.1 (C-8a), 68.5 (C-8), 68.8 (C-1), 71.8 (C-6), 73.5 (C-7), 75.7 (C-5), 159.1 (CO) ppm. FABMS: *m*/*z* (%) = 228 (100) $[M + Na]^+$. HRFABMS: *m*/*z* = 206.066916; calcd. for $C_7H_{12}O_6N$: 206.066462. $C_7H_{11}O_6N$ (205.17): C 40.98, H 5.40, N 6.83; found C 40.90, H 5.47, N 6.78.

(5*R*,6*R*,7*R*,8*R*,8a*R*)-5,6,7,8-Tetraacetoxy-3-thioxo-2-oxaindolizidine (27): Conventional acetylation of **6** (20.4 mg, 0.09 mmol) afforded **27**. Yield: 34 mg (98%). R_f = 0.55 (2:1 EtOAc/petroleum ether). $[\alpha]_D^{22}$ = +31.0 (*c* = 1.0, CH_2Cl_2). UV (CH_2Cl_2): λ = 249.6 nm (ε = 12.2). IR (KBr): $\tilde{\nu}_{max}$ = 2983, 1752, 1434, 1371, 1220, 1053 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.00–2.23 (4 s, 12 H, 4 MeCO), 4.49 (t, $J_{8a,1b}$ = $J_{1a,1b}$ = 8.5 Hz, 1 H, H-1b), 4.46 (td, $J_{1a,8a}$ = 8.5, $J_{8,8a}$ = 10.0 Hz, 1 H, H-8a), 4.71 (t, 1 H, H-1a), 4.95 (dd, $J_{3,4}$ = 2.9 Hz, 1 H, H-8), 5.18 (dd, $J_{6,7}$ = 2.9, $J_{5,6}$ = 4.5 Hz, 1 H, H-6), 5.65 (t, 1 H, H-7), 7.11 (d, 1 H, H-5) ppm. ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 20.2–20.4 (*Me*CO), 52.2 (C-8a), 65.7 (C-6), 67.0 (C-7), 69.3 (C-8), 70.9 (C-1), 74.0 (C-5), 168.3–169.5 (CO), 187.1 (CS) ppm. FABMS: *m*/*z* (%) = 412 (100) $[M + Na]^+$. $C_{15}H_{19}NO_9S$ (389.39): C 46.27, H 4.92, N 3.60; found C 46.39, H 4.78, N 3.54.

(5*R*,6*R*,7*R*,8*R*,8a*R*)-5,6,7,8-Tetracetoxy-3-oxo-2-oxaindolizidine (28): Conventional acetylation of **7** (60 mg, 0.29 mmol) afforded **28**. Yield: 106 mg (98%). R_f = 0.50 (2:1 EtOAc/petroleum ether). $[\alpha]_D^{22}$ = +38.6 (*c* = 1.0, CH_2Cl_2). IR (NaCl): $\tilde{\nu}_{max}$ = 2991, 2928, 1776, 1752, 1418, 1371, 1228, 1053 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.00–2.17 (4 s, 12 H, 4 MeCO), 4.16 (dd, $J_{8a,1b}$ = 8.0, $J_{1a,1b}$ = 8.6 Hz, 1 H, H-1b), 4.30 (dt, $J_{8a,1a}$ = 8.0, $J_{8,8a}$ = 10.0 Hz, 1 H, H-8a), 4.49 (dd, 1 H, H-1a), 4.93 (dd, $J_{7,8}$ = 3.0 Hz, 1 H, H-8), 5.13 (dd, $J_{6,7}$ = 3.0, $J_{5,6}$ = 4.6 Hz, 1 H, H-6), 5.63 (t, 1 H, H-7), 6.65 (d, 1 H, H-5) ppm. ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 20.2–20.5 (*Me*CO), 48.5 (C-8a), 66.1 (C-6), 66.2 (C-1), 67.4 (C-7), 69.8 (C-8), 71.4 (C-5), 154.5 (CO carbamate), 168.6–169.7 (CO ester) ppm. FABMS: *m*/*z* (%) = 396 (100) $[M + Na]^+$. $C_{15}H_{19}O_{10}N$ (373.32): C 48.26, H 5.13, N 3.75; found C 48.44, H 5.47, N 3.52.

3-*O*-Acetyl-1,2-*O*-isopropylidene-6-*O*-trityl-β-L-altrofuranose (30): Pyridine (0.67 mL) and trifluoromethanesulfonic anhydride (0.88 mL, 5.3 mmol) were added under nitrogen to a solution of 3-*O*-acetyl-1,2-*O*-isopropylidene-6-*O*-trityl-α-D-galactofuranose **29** (1.99 g, 3.95 mmol) in CH_2Cl_2 (10.6 mL) at –25 °C. The reaction mixture was allowed to reach room temperature and after stirring for 30 min, the mixture was diluted with CH_2Cl_2 (15 mL), washed with iced saturated aqueous $NaHCO_3$ (15 mL), dried ($MgSO_4$) and concentrated. The resulting triflate ester was dissolved in DMF (10 mL), $NaNO_2$ (1.27 g, 18.4 mmol) was added and the reaction mixture was stirred at room temperature for 24 h. The solvent was removed under reduced pressure and the resulting residue was dissolved in CH_2Cl_2 (20 mL) and washed with water (2 × 10 mL). The organic extract was dried ($MgSO_4$) and concentrated. The resulting residue was purified by column chromatography using 1:6 EtOAc/petroleum ether as eluent to give **30**. Yield: 1.0 g (51%). R_f = 0.49 (1:2 EtOAc/petroleum ether). $[\alpha]_D^{22}$ = –16.1 (*c* = 1.0, CH_2Cl_2). IR (KBr): $\tilde{\nu}_{max}$ = 3476, 1744, 1386, 1220, 1093 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.29, 1.48 (2 s, 6 H, CMe_2), 2.07 (s, 3 H, MeCO), 2.58 (d, $J_{OH,5}$ = 5.4 Hz, 1 H, OH), 3.32 (dd, $J_{5,6b}$ = 5.4, $J_{6a,6b}$ = 9.6 Hz, 1 H, H-6b), 3.38 (dd, $J_{5,6a}$ = 3.6 Hz, 1 H, H-6a), 4.01 (m, 1 H, H-5), 4.18 (dd, $J_{3,4}$ = 1.2, $J_{4,5}$ = 9.6 Hz, 1 H, H-4), 4.56 (d, $J_{1,2}$ = 4.1 Hz, 1 H, H-2), 5.39 (d, 1 H, H-3), 5.89 (d, 1 H, H-1), 7.21–7.37 (m, 15 H, Ph) ppm. ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 20.8 (*Me*CO), 25.6, 26.5 (C*Me*$_2$), 63.1 (C-6), 70.1 (C-5), 77.6 (C-3), 86.8 (*C*Ph$_3$), 84.6 (C-2), 85.6 (C-4), 105.7 (C-1), 112.4 (*C*Me$_2$), 127.0–143.7 (Ph), 169.8 (CO) ppm. FABMS: *m*/*z* (%) = 527 (100) $[M + Na]^+$. $C_{30}H_{32}O_7$ (504.59): C 71.41, H 6.39; found C 71.29, H 6.36.

3-*O*-Acetyl-5-azido-5-deoxy-1,2-*O*-isopropylidene-6-*O*-trityl-α-D-galactofuranose (31): Pyridine (0.31 mL) and trifluoromethanesulfonic anhydride (0.38 mL, 2.3 mmol) were added under nitrogen to a solution of **30** (878 mg, 1.74 mmol) in CH_2Cl_2 (4.8 mL) at –25 °C. The reaction mixture was allowed to reach room temperature and, after stirring for 30 min, the mixture was diluted with CH_2Cl_2 (15 mL), washed with iced saturated aqueous $NaHCO_3$ (15 mL), dried ($MgSO_4$) and concentrated. The resulting triflate ester was dissolved in DMF (7 mL), NaN_3 (1.15 g, 17.7 mmol) was added and the reaction mixture was stirred at room temperature for 24 h. The solvent was removed under reduced pressure and the resulting residue was dissolved in CH_2Cl_2 (15 mL) and washed with water (2 × 10 mL). The organic extract was dried ($MgSO_4$) and concentrated. The resulting residue was purified by column chromatography using 1:8 → 1:6 EtOAc/petroleum ether as eluent to give **31**. Yield: 475 mg (51%). R_f = 0.18 (1:6 EtOAc/petroleum ether). $[\alpha]_D^{22}$ = –22.7 (*c* = 1.0, CH_2Cl_2). IR (KBr): $\tilde{\nu}_{max}$ = 3420, 2101, 1744, 1633, 1379, 1220, 1093 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.32, 1.57 (2 s, 6 H, CMe_2), 2.02 (s, 3 H, MeCO), 3.30 (dd, $J_{5,6b}$ = 6.5, $J_{6a,6b}$ = 10.3 Hz, 1 H, H-6b), 3.38 (dd, $J_{5,6a}$ = 3.8 Hz, 1 H, H-6a), 3.80 (ddd, $J_{4,5}$ = 7.8 Hz, 1 H, H-5), 4.08 (dd, $J_{3,4}$ = 3.0 Hz, 1 H, H-4), 4.54 (d, $J_{1,2}$ = 4.0 Hz, 1 H, H-2), 4.97 (d, 1 H, H-3), 5.87 (d, 1 H, H-1), 7.25–7.46 (m, 15 H, Ph) ppm. ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 20.6 (*Me*CO), 26.8, 26.0 (C*Me*$_2$), 62.3 (C-5), 63.7 (C-6), 77.1 (C-3), 83.9 (C-4), 84.6 (C-2), 87.2 (*C*Ph$_3$), 105.2 (C-1), 113.3 (*C*Me$_2$), 127.0–143.6 (Ph), 169.5 (CO) ppm. FABMS: *m*/*z* (%) =

552 (10) $[M + Na]^+$. $C_{30}H_{31}N_3O_6$ (529.60): C 68.04, H 5.90, N 7.94; found C 68.31, H 5.81, N 7.80.

3-*O*-Acetyl-5-azido-5-deoxy-1,2-*O*-isopropylidene-α-D-galactofuranose (32): BF_3–Et_2O complex (318 mL) and MeOH (1.6 mL) were added to a solution of the tritylated azido derivative **31** (572 mg, 1.08 mmol) in CH_2Cl_2 (8.5 mL) at 0 °C under argon. The reaction mixture was allowed to reach room temperature and stirred for 2 h, diluted with CH_2Cl_2 (10 mL), then washed with saturated aqueous $NaHCO_3$ (2×10 mL), dried ($MgSO_4$) and concentrated. The resulting residue was purified by column chromatography (1:3 → 1:1 EtOAc/petroleum ether) to give **32**. Yield: 233 mg (75%). R_f 0.22 (1:2 EtOAc/petroleum ether). $[\alpha]_D^{22}$ = –57.1 (*c* = 0.98, CH_2Cl_2). IR (KBr): $\tilde{\nu}_{max}$ = 3435, 2991, 2101, 1746, 1375, 1233, 1053 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 1.32, 1.59 (2 s, 6 H, CMe_2), 2.11 (s, 3 H, MeCO), 3.75 (dd, $J_{5,6b}$ = 5.6, $J_{6a,6b}$ = 12.1 Hz, 1 H, H-6b), 3.79 (td, $J_{4,5}$ = $J_{5,6a}$ = 9.3 Hz, 1 H, H-5), 3.84 (dd, 1 H, H-6a), 4.15 (dd, $J_{3,4}$ = 1.4 Hz, 1 H, H-4), 4.69 (d, $J_{1,2}$ = 4.0 Hz, 1 H, H-2), 5.12 (d, 1 H, H-3), 6.00 (d, 1 H, H-1) ppm. ^{13}C NMR (125.7 MHz, $CDCl_3$): δ = 20.9 (*Me*CO), 25.9, 26.8 (C*Me*$_2$), 62.7 (C-6), 63.6 (C-5), 77.8 (C-3), 84.4 (C-4), 86.4 (C-2), 106.0 (C-1), 113.2 (*C*Me_2), 170.9 (CO) ppm. FABMS: *m*/*z* (%) = 310 (100) $[M + Na]^+$. $C_{11}H_{17}N_3O_6$ (287.28): C 45.99, H 5.96, N 14.63; found C 45.61, H 5.78, N 14.47.

5-Azido-5-deoxy-1,2-*O*-isopropylidene-α-D-galactofuranose (33): Conventional deacetylation of **32** (0.8 mmol) and purification by column chromatography (1:1 → 2:1 EtOAc/petroleum ether) afforded **33**. Yield: 171 mg (80%). R_f = 0.41 (2:1 EtOAc/petroleum ether). $[\alpha]_D^{22}$ = –113.8 (*c* = 1.0, CH_2Cl_2). IR (KBr): $\tilde{\nu}_{max}$ = 3412, 2991, 2109, 1641, 1386, 1093 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 1.34, 1.55 (2 s, 6 H, CMe_2), 2.65 (br. s, 1 H, OH), 3.33 (br. s, 1 H, OH), 3.75 (dd, $J_{5,6b}$ = 4.3, $J_{6a,6b}$ = 10.9 Hz, 1 H, H-6b), 3.81 (m, 1 H, H-6a), 3.94 (m, 1 H, H-5), 4.04 (dd, $J_{3,4}$ = 3.3, $J_{4,5}$ = 5.6 Hz, 1 H, H-4), 4.27 (br. d, 1 H, H-3), 4.59 (dd, $J_{2,3}$ = 0.9, $J_{1,2}$ = 4.0 Hz, 1 H, H-2), 5.92 (d, 1 H, H-1) ppm. ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 26.0, 26.8 (C*Me*$_2$), 62.2 (C-6), 63.2 (C-5), 75.9 (C-3), 86.5 (C-2), 86.8 (C-2), 105.1 (C-1), 113.2 (*C*Me_2) ppm. FABMS: *m*/*z* (%) = 268 (100) $[M + Na]^+$. HRFABMS: *m*/*z* = 246.109779; calcd. for $C_9H_{16}N_3O_5$: 246.108996.

5-Amino-5-deoxy-1,2-*O*-isopropylidene-α-D-galactofuranose (34): A solution of azido sugar **33** (69.8 mg, 0.29 mmol) and 10% Pd/C (28.2 mg) in MeOH (2.6 mL) was hydrogenated under an atmospheric pressure of hydrogen using a balloon. The mixture was stirred for 1 h, filtered through Celite and concentrated to give **34** as a hygroscopic solid that was used in the next step without further purification. Yield: 59 mg (96%). $[\alpha]_D^{22}$ = –25.3 (*c* = 1.0, MeOH). IR (KBr): $\tilde{\nu}_{max}$ = 3357, 2991, 1379, 1212, 1013 cm^{-1}. ^1H NMR (500 MHz, CD_3OD): δ = 1.29, 1.47 (2 s, 6 H, CMe_2), 3.08 (m, 1 H, H-5), 3.49 (dd, $J_{5,6b}$ = 6.0, $J_{6a,6b}$ = 11.1 Hz, 1 H, H-6b), 3.63 (dd, $J_{5,6a}$ = 4.4 Hz, 1 H, H-6a), 3.77 (dd, $J_{3,4}$ = 1.7, $J_{4,5}$ = 9.2 Hz, 1 H, H-4), 4.17 (d, 1 H, H-3), 4.52 (d, $J_{1,2}$ = 4.0 Hz, 1 H, H-2), 5.82 (d, 1 H, H-1) ppm. ^{13}C NMR (125.7 MHz, CD_3OD): δ = 26.1, 27.1 (C*Me*$_2$), 58.4 (C-5), 64.2 (C-6), 77.2 (C-3), 88.6 (C-2), 89.8 (C-4), 106.8 (C-1), 113.4 (*C*Me_2) ppm. FABMS: *m*/*z* (%) = 242 (100) $[M + Na]^+$, 220 (40) $[M + H]^+$. HRFABMS: *m*/*z* = 220.118354; calcd. for $C_9H_{18}NO_5$: 220.118498.

5-Amino-5-deoxy-1,2-*O*-isopropylidene-α-D-galactofuranose 5,6-Cyclic Thiocarbamate (35): Thiocarbonylation of **34** (57 mg, 0.26 mmol) by treatment with CS_2/DCC for 6 h, as above described for the preparation of **14**, followed by purification by column chromatography (2:1 EtOAc/petroleum ether) gave **35**. Yield: 58 mg (86%). R_f = 0.40 (3:1 EtOAc/petroleum ether). $[\alpha]_D^{22}$ = –142.6 (*c* = 0.54, MeOH). UV (MeOH): λ = 244 nm (ε = 15.5). IR (KBr): $\tilde{\nu}_{max}$ = 3237, 2928, 1514, 1386, 1283, 1090 cm^{-1}. ^1H NMR (500 MHz, CD_3OD): δ = 1.30, 1.50 (2 s, 6 H, CMe_2), 3.84 (dd, $J_{3,4}$ = 2.7, $J_{4,5}$ = 8.5 Hz, 1 H, H-4), 4.02 (d, 1 H, H-3), 4.31 (ddd, $J_{6b,5}$ = 5.8, $J_{6a,5}$ = 9.2, H-5), 4.44 (dd, $J_{6a,6b}$ = Hz, 1 H, H-6b), 4.51 (d, $J_{1,2}$ = 3.7 Hz, 1 H, H-2), 4.71 (t, 1 H, H-6a), 5.82 (s, 1 H, H-1) ppm. ^{13}C NMR (125.7 MHz, CD_3OD): δ = 26.3, 27.5 (C*Me*$_2$), 59.4 (C-5), 72.8 (C-6), 76.2 (C-3), 88.5 (C-2), 89.4 (C-4), 107.0 (C-1), 114.2 (*C*Me_2), 191.3 (CS) ppm. FABMS: *m*/*z* (%) = 284 (100) $[M + Na]^+$, 262 (20) $[M + H]^+$. $C_{10}H_{15}NO_5S$ (261.30): C 45.96, H 5.79, N 5.36; found C 45.84, H 5.75, N 5.25.

5-Amino-5-deoxy-1,2-*O*-isopropylidene-α-D-galactofuranose 5,6-Cyclic Carbamate (36): Carbonylation of **34** (90 mg, 0.41 mmol) by treatment with triphosgene/diisopropylethylamine for 10 min, as described for the preparation of **15**, and purification by column chromatography (EtOAc and 40:1 EtOAc/EtOH) yielded **36**. Yield: 90 mg (90%). R_f = 0.53 (20:1 EtOAc/EtOH). $[\alpha]_D^{22}$ = –50.6 (*c* = 1.0, MeOH). IR (KBr): $\tilde{\nu}_{max}$ = 3420, 2935, 1752, 1641, 1379, 1212, 1108, 1061 cm^{-1}. ^1H NMR (300 MHz, CD_3OD): δ = 1.30, 1.49 (2 s, 6 H, CMe_2), 3.81 (dd, $J_{3,4}$ = 2.8, $J_{4,5}$ = 8.5 Hz, 1 H, H-4), 3.99 (d, 1 H, H-3), 4.13 (td, $J_{5,6b}$ = 5.2, $J_{5,6a}$ = 8.5 Hz, 1 H, H-5), 4.19 (dd, $J_{6a,6b}$ = 8.5 Hz, 1 H, H-6b), 4.49 (t, 1 H, H-6a), 4.51 (d, $J_{1,2}$ = 3.8 Hz, 1 H, H-2), 5.87 (d, 1 H, H-1) ppm. ^{13}C NMR (75.5 MHz, CD_3OD): δ = 26.3, 27.4 (C*Me*$_2$), 55.4 (C-6), 67.8 (C-6), 76.1 (C-3), 88.6 (C-2), 90.3 (C-4), 106.9 (C-1), 114.1 (*C*Me_2), 162.0 (CO) ppm. CIMS: *m*/*z* (%) = 246 (25) $[M + H]^+$. $C_{10}H_{15}NO_6$ (245.24): C 48.98, H 6.16, N 5.71; found C, 48.92, H 6.08, N 5.68.

(5*R*,6*R*,7*S*,8*S*,8a*R*)-5,6,7,8-Tetrahydroxy-3-thioxo-2-oxaindolizidine (8): Compound **35** (102.5 mg, 0.40 mmol) was deacetalated by treatment with 90% TFA/water (5 mL). The reaction mixture was concentrated and the residue coevaporated several times with water to eliminate traces of acid. The resulting residue was subjected to conventional acetylation with Ac_2O/pyridine (1:1, 1.6 mL) and the peracetylated mixture was purified by column chromatography using 1:1 EtOAc/petroleum ether as eluent. The resulting crude peracetylated mixture of furanose and indolizidine isomers, according to NMR, was deacetylated with methanolic NaOMe to give **8** as the only reaction product. Yield: 60.9 mg (65%) R_f = 0.31 (45:5:3 EtOAc/EtOH/H_2O). $[\alpha]_D^{22}$ = –10.5 (*c* = 1.0, H_2O). UV (H_2O): λ = 244.0 nm (ε = 14.1). ^1H NMR (300 MHz, D_2O): δ = 3.80 (dd, $J_{5,6}$ = 3.7, $J_{6,7}$ = 10.2 Hz, 1 H, H-6), 3.90 (dd, $J_{7,8}$ = 2.7 Hz, 1 H, H-7), 4.01 (br. t, $J_{8,8a}$ = 2.0 Hz, 1 H, H-8), 4.44 (ddd, $J_{8a,1b}$ = 6.5, $J_{8a,1a}$ = 9.4 Hz, 1 H, H-8a), 4.55 (dd, $J_{1a,1b}$ = 9.4 Hz, 1 H, H-1b), 4.68 (t, 1 H, H-1a), 5.84 (d, 1 H, H-5) ppm. ^{13}C NMR (125.7 MHz, D_2O): δ = 57.7 (C-8a), 68.2 (C-6), 69.9 (C-8), 70.1 (C-1), 70.2 (C-7), 79.2 (C-5), 187.8 (CS) ppm. CIMS: *m*/*z* (%) = 221 (15) $[M]^+$, 222 (60) $[M + H]^+$. HRCIMS: *m*/*z* = 221.036008; calcd. for $C_7H_{11}NO_5S$: 221.035794. $C_7H_{11}NO_5S$ (221.24): C 38.00, H 5.01, N 6.33; found C 38.01, H 4.94, N 6.27.

(5*R*,6*R*,7*S*,8*S*,8a*R*)-5,6,7,8-Tetrahydroxy-3-oxo-2-oxaindolizidine (9): Compound **36** (98.9 mg, 0.40 mmol) was deacetalated by treatment with 90% TFA/water (5 mL). The reaction mixture was concentrated and the residue coevaporated several times with water to eliminate traces of acid. The resulting residue was subjected to conventional acetylation with Ac_2O/pyridine (1:1, 2.6 mL) and the peracetylated mixture was purified by column chromatography using 2:1 EtOAc/petroleum ether as eluent. The resulting crude peracetylated mixture of furanose and indolizidine isomers, according to NMR, was deacetylated with methanolic NaOMe to give **9** as the only reaction product. Yield: 73 mg (89%). R_f = 0.56 (6:3:1 MeCN/H_2O/NH_4OH). $[\alpha]_D^{22}$ = +40.0 (*c* = 1.0, H_2O). ^1H NMR (300 MHz, D_2O): δ = 3.75 (dd, $J_{5,6}$ = 4.1 Hz, 1 H, H-6), 3.84 (dd, $J_{7,8}$ = 2.7, $J_{6,7}$ = 10.3 Hz, 1 H, H-7), 3.96 (dd, $J_{8,8a}$ = 1.8 Hz, 1 H,

H-8), 4.22 (ddd, $J_{8a,1b}$ = 6.3, $J_{8a,1a}$ = 9.0 Hz, 1 H, H-5), 4.34 (dd, $J_{1a,1b}$ = 9.0 Hz, 1 H, H-1b), 4.47 (t, 1 H, H-1a) ppm. ^{13}C NMR (125.7 MHz, D_2O): δ = 54.9 (C-8a), 66.7 (C-1), 69.8 (C-6), 71.1 (C-8), 71.5 (C-7), 76.9 (C-5), 160.5 (CS) ppm. CIMS: *m*/*z* (%) = 206 (5) $[M + H]^+$. $C_7H_{11}NO_6$ (205.27): C 40.98, H 5.40, N 6.83; found C 40.90, H 5.47, N 6.78.

(5*R*,6*R*,7*S*,8*S*,8a*R*)-5,6,7,8-Tetraacetoxy-3-thioxo-2-oxaindolizidine (37): Conventional acetylation of **8** (46 mg, 0.21 mmol) gave **37**. Yield: 67 mg (82%). R_f = 0.54 (2:1 EtOAc/petroleum ether). $[\alpha]_D^{22}$ = +74.5 (*c* = 1.0, CH_2Cl_2). UV (CH_2Cl_2): λ = 249.6 nm (ε = 17.3). IR (NaCl): $\tilde{\nu}_{max}$ = 2999, 2920, 1752, 1752, 1553, 1371, 1212, 1077 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.02–2.20 (4 s, 12 H, 4 MeCO), 4.21 (t, $J_{1a,1b}$ = $J_{8a,1b}$ = 8.5 Hz, 1 H, H-1b), 4.50 (td, $J_{8,8a}$ = 1.8, $J_{8a,1a}$ = 8.5 Hz, 1 H, H-8a), 4.61 (t, 1 H, H-1a), 5.31 (dd, $J_{7,8}$ = 2.6, $J_{6,7}$ = 10.7 Hz, 1 H, H-7), 5.39 (dd, $J_{5,6}$ = 3.8 Hz, 1 H, H-6), 5.53 (dd, 1 H, H-8), 7.23 (d, 1 H, H-5) ppm. ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 20.2–20.5 (*Me*CO), 55.1 (C-8a), 65.2 (C-6), 66.7 (C-8), 67.3 (C-1), 67.7 (C-7), 75.4 (C-5), 168.2–170.0 (CO), 186.6 (CS) ppm. FABMS: *m*/*z* (%) = 412 (100) $[M + Na]^+$. $C_{15}H_{19}NO_9S$ (389.39): C 46.27, H 4.92, N 3.60; found C 46.55, H 4.67, N 3.59.

(5*R*,6*R*,7*S*,8*S*,8a*R*)-5,6,7,8-Tetraacetoxy-3-oxo-2-oxaindolizidine (38): Conventional acetylation of **9** (25 mg, 0.12 mmol) gave **38**. Yield: 38 mg (85%). R_f = 0.42 (2:1 EtOAc/petroleum ether). $[\alpha]_D^{22}$ = +59.6 (*c* = 1.0, CH_2Cl_2). IR (NaCl): $\tilde{\nu}_{max}$ = 2999, 2928, 1752, 1537, 1371, 1212, 1077 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.00–2.20 (4 s, 12 H, 4 MeCO), 4.02 (dd, $J_{8a,1b}$ = 5.9, $J_{1a,1b}$ = 8.5 Hz, 1 H, H-1b), 4.32 (ddd, $J_{8,8a}$ = 1.7, $J_{8a,1a}$ = 8.5 Hz, 1 H, H-8a), 4.41 (t, 1 H, H-1a), 5.29 (dd, $J_{7,8}$ = 2.3, $J_{6,7}$ = 10.9 Hz, 1 H, H-7), 5.34 (dd, $J_{5,6}$ = 3.5 Hz, 1 H, H-6), 5.49 (dd, 1 H, H-8), 6.78 (d, 1 H, H-5) ppm. ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 20.0–20.4 (*Me*CO), 51.3 (C-8a), 65.5 (C-6), 67.2 (C-8), 67.8 (C-7), 62.7 (C-1), 72.8 (C-5), 154.1 (CO carbamate), 168.4, 169.2, 169.9, 170.1 (CO ester) ppm. FABMS: *m*/*z* (%) = 396 (100) $[M + Na]^+$. $C_{15}H_{19}NO_{10}$ (373.32): C 48.26, H 5.13, N 3.75; found C 48.15, H 4.95, N 3.74.

1-*O*-Acetyl-5-amino-5-deoxy-2,3-*O*-isopropylidene-β-L-gulofuranose 5,6-Cyclic Thiocarbamate (40): Thiocarbonylation of 1-*O*-acetyl-5-amino-5-deoxy-2,3-*O*-isopropylidene-β-L-gulofuranose **39** (201 mg, 0.87 mmol) by treatment with CS_2/DCC for 8 h, as above described for the preparation of **14**, followed by purification by column chromatography (1:2 → 2:1 EtOAc/petroleum ether) gave **40**. Yield: 185 mg (70%). R_f = 0.33 (1:1 EtOAc/petroleum ether). $[\alpha]_D^{22}$ = +73 (*c* = 1.0, CH_2Cl_2). UV (CH_2Cl_2): λ = 249 nm (ε = 22.4). IR (KBr): $\tilde{\nu}_{max}$ = 3330, 2988, 1742, 1505, 1466, 1379, 1265, 1094 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.26, 1.45 (2 s, 6 H, CMe_2), 2.04 (s, 3 H, MeCO), 4.13 (dd, $J_{3,4}$ = 4.0, $J_{4,5}$ = 7.3 Hz, 1 H, H-4), 4.32 (ddd, $J_{5,6b}$ = 6.5, $J_{5,6a}$ = 9.5 Hz, 1 H, H-5), 4.45 (dd, $J_{6a,6b}$ = 9.5 Hz, 1 H, H-6b), 4.71 (d, $J_{2,3}$ = 5.9 Hz, 1 H, H-2), 4.76 (t, 1 H, H-6a), 4.82 (dd, 1 H, H-3), 6.13 (s, 1 H, H-1), 7.51 (br. s, 1 H, NH) ppm. ^{13}C NMR (125.7 MHz, $CDCl_3$): δ = 20.9 (*Me*CO), 24.3, 25.7 (CMe_2), 56.2 (C-5), 71.8 (C-6), 78.8 (C-3), 82.4 (C-4), 84.9 (C-2), 100.0 (C-1), 113.8 (CMe_2), 169.2 (CO), 189.6 (CS) ppm. FABMS: *m*/*z* (%) = 326 (100) $[M + Na]^+$. $C_{12}H_{17}O_6NS$ (303.34): C 47.51, H 5.65, N 4.62; found C 47.60, H 5.53, N 4.67.

1-*O*-Acetyl-5-amino-5-deoxy-2,3-*O*-isopropylidene-β-L-gulofuranose 5,6-Cyclic Carbamate (41): Carbonylation of **39** (211 mg, 0.81 mmol) by treatment with triphosgene/diisopropyl ethylamine for 45 min, as described for the preparation of **15**, and purification by column chromatography (1:1 EtOAc/petroleum ether → EtOAc) yielded **41**. Yield: 100 mg (43%). R_f = 0.24 (3:1 EtOAc/petroleum ether). $[\alpha]_D^{22}$ = +78 (*c* = 1.0, CH_2Cl_2). IR (KBr): $\tilde{\nu}_{max}$ = 3405, 2955, 1753, 1537, 1414, 1238, 1094 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.25, 1.42 (2 s, 6 H, CMe_2), 2.01 (s, 3 H, MeCO), 4.05 (dd, $J_{3,4}$ = 3.8, $J_{4,5}$ = 7.1 Hz, 1 H, H-4), 4.13 (m, 1 H, H-5), 4.15 (dd, $J_{5,6b}$ = 5.7, $J_{6a,6b}$ = 6.9 Hz, 1 H, H-6b), 4.49 (m, 1 H, H-6a), 4.68 (d, $J_{2,3}$ = 5.9 Hz, 1 H, H-2), 4.78 (dd, 1 H, H-3), 5.75 (br. s, 1 H, NH), 6.11 (s, 1 H, H-1) ppm. ^{13}C NMR (125.7 MHz, $CDCl_3$): δ = 20.8 (*Me*CO), 24.3, 25.7 (CMe_2), 52.2 (C-5), 66.3 (C-6), 78.8 (C-3), 83.3 (C-4), 85.0 (C-2), 100.2 (C-1), 113.6 (CMe_2), 158.9 (CO carbamate), 169.1 (CO ester) ppm. FABMS: *m*/*z* (%) = 283 (30) $[M + H]^+$. $C_{12}H_{17}O_7N$ (287.28): C 50.17, H 5.96, N 4.87; found C 50.07, H 5.85, N 4.75.

(5*R*,6*S*,7*S*,8*R*,8a*S*)-5,6,7,8-Tetrahydroxy-3-thioxo-2-oxaindolizidine (10): Compound **40** (90 mg, 0.31 mmol) was deacetalated by treatment with 90% TFA/water (5 mL). The reaction mixture was concentrated and the residue coevaporated several times with water to eliminate traces of acid. The resulting residue was subjected to conventional acetylation with Ac_2O/pyridine (1:1, 1.6 mL) and the peracetylated mixture was purified by column chromatography using 100:1 CH_2Cl_2/MeOH as eluent. The resulting crude peracetylated mixture of furanose and indolizidine isomers, according to NMR, was deacetylated with methanolic NaOMe to give **10** as the only reaction product. Yield: 34 mg (50%). R_f = 0.45 (45:5:3 EtOAc/EtOH/H_2O). $[\alpha]_D^{22}$ = +77 (*c* = 1.0, H_2O). UV (CH_2Cl_2): λ = 247nm (ε = 10.8). ^{1}H NMR (500 MHz, D_2O): δ = 3.97 (dd, $J_{6,7}$ = 3.4, $J_{5,6}$ = 4.4 Hz, 1 H, H-6), 4.06 (dd, $J_{4,5}$ = 1.9, $J_{7,8}$ = 3.4 Hz, 1 H, H-8), 4.13 (t, 1 H, H-7), 4.63 (dd, $J_{8a,1b}$ = 6.7, $J_{1a,1b}$ = 9.0 Hz, 1 H, H-1b), 4.70 (ddd, $J_{8a,1a}$ = 9.0 Hz, 1 H, H-8a), 4.79 (t, 1 H, H-1a), 5.86 (d, 1 H, H-5) ppm. ^{13}C NMR (125.7 MHz, D_2O): δ = 55.4 (C-8a), 66.6 (C-6), 70.9 (C-8), 71.4 (C-1), 73.7 (C-7), 81.2 (C-5), 189.5 (CS) ppm. FABMS: *m*/*z* (%) = 222 (60) $[M + H]^+$. $C_7H_{11}O_5NS$ (221.24): C 38.00, H 5.01, N 6.33; found C 37.68, H 4.69, N 6.33.

(5*R*,6*S*,7*S*,8*R*,8a*S*)-5,6,7,8-Tetrahydroxy-3-oxo-2-oxaindolizidine (11): Compound **41** (90 mg, 0.31 mmol) was deacetalated by treatment with 90% TFA/water (5 mL). The reaction mixture was concentrated and the residue coevaporated several times with water to eliminate traces of acid. The resulting residue was subjected to conventional acetylation with Ac_2O/pyridine (1:1, 2.6 mL) and the peracetylated mixture was purified by column chromatography using 100:1 CH_2Cl_2/MeOH as eluent. The resulting crude peracetylated mixture of furanose and indolizidine isomers, according to NMR, was deacetylated with methanolic NaOMe to give **11** as the only reaction product. Yield: 32 mg (50%). R_f = 0.28 (45:5:3 EtOAc/EtOH/H_2O). $[\alpha]_D^{22}$ = +52 (*c* = 1.0, MeOH). ^{1}H NMR (300 MHz, D_2O): δ = 3.92 (dd, $J_{6,7}$ = 3.2, $J_{5,6}$ = 4.5 Hz, 1 H, H-6), 4.00 (dd, $J_{8,8a}$ = 1.8, $J_{7,8}$ = 4.2 Hz, 1 H, H-8), 4.09 (t, 1 H, H-7), 4.40 (dd, $J_{8a,1b}$ = 8.6, $J_{1a,1b}$ = 8.6 Hz, 1 H, H-1b), 4.48 (ddd, $J_{8a,1a}$ = 7.5 Hz, 1 H, H-8a), 4.57 (t, 1 H, H-6a), 5.34 (d, 1 H, H-1) ppm. ^{13}C NMR (75.5 MHz, D_2O): δ = 48.8 (C-8a), 64.4 (C-1), 64.5 (C-6), 68.2 (C-8), 71.4 (C-7), 75.2 (C-5), 158.6 (CO) ppm. CIMS: *m*/*z* (%) = 206 (30) $[M + H]^+$. $C_7H_{11}O_6N$ (205.17): C 40.98, H 5.40, N 6.83; found C 41.03, H 5.40, N 6.65.

(5*R*,6*S*,7*S*,8*R*,8a*S*)-5,6,7,8-Tetraacetoxy-3-thioxo-2-oxaindolizidine (42): Conventional acetylation of **10** (35 mg, 0.16 mmol) gave **42**. Yield: 54 mg (87%). R_f = 0.53 (70:1 CH_2Cl_2/MeOH). $[\alpha]_D^{22}$ = –50.4 (*c* = 1.0, CH_2Cl_2). IR (KBr): $\tilde{\nu}_{max}$ = 2988, 1750, 1371, 1227, 1094 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 2.00–2.17 (4 s, 12 H, 4 MeCO), 4.23 (m, 1 H, H-1b), 4.64 (m, 2 H, H-8a, H-1a), 5.14 (dd, $J_{8,8a}$ = 2.0, $J_{7,8}$ = 4.0 Hz, 1 H, H-8), 5.29 (t, $J_{6,7}$ = 4.0 Hz, 1 H, H-7), 5.36 (t, $J_{5,6}$ = 4.0 Hz, 1 H, H-6), 7.14 (d, 1 H, H-5) ppm. ^{13}C NMR (125.7 MHz, $CDCl_3$): δ = 20.4–20.7 (*Me*CO), 52.8 (C-8a), 64.4 (C-1), 66.0 (C-6), 66.8 (C-7), 67.6 (C-8), 74.8 (C-5), 168.3–169.6 (CO ester), 187.2 (CS) ppm. FABMS: *m*/*z* (%) = 412 (100)

$[M + Na]^+$. $C_{15}H_{19}O_9NS$ (389.39): C 46.27, H 4.92, N 3.60; found C 46.27, H 4.80, N 3.53.

(5*R*,6*S*,7*S*,8*R*,8a*S*)-5,6,7,8-Tetraacetoxy-3-oxo-2-oxaindolizidine (43): Conventional acetylation of **11** (30 mg, 0.14 mmol) gave **43**. Yield: 47 mg (90%). R_f = 0.47 (20:1 CH_2Cl_2/MeOH). $[\alpha]_D^{22}$ = –48.4 (c = 1.0, CH_2Cl_2). IR (KBr): $\tilde{\nu}_{max}$ = 2963, 1750, 1559, 1374, 1258, 1094 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 1.99–2.17 (4 s, 12 H, 4 MeCO), 4.03 (dd, $J_{8a,1b}$ = 6.0, $J_{1a,1b}$ = 8.5 Hz, 1 H, H-1b), 4.41 (t, $J_{8a,1a}$ = 8.5 Hz, 1 H, H-1a), 4.46 (ddd, $J_{8,8a}$ = 2.0 Hz, 1 H, H-8a), 5.11 (dd, $J_{7,8}$ = 4.5 Hz, 1 H, H-8), 5.25 (dd, $J_{6,7}$ = 3.5, $J_{5,6}$ = 4.5 Hz, 1 H, H-6), 5.35 (dd, 1 H, H-7), 6.68 (d, 1 H, H-5) ppm. ^{13}C NMR (125.7 MHz, $CDCl_3$): δ = 20.4–20.7 (*Me*CO), 48.8 (C-8a), 63.1 (C-1), 64.7 (C-6), 66.3 (C-7), 67.2 (C-8), 72.2 (C-5), 154.8 (CO carbamate), 168.6–169.7 (CO ester) ppm. FABMS: m/z (%) = 396 (100) $[M + Na]^+$. $C_{15}H_{19}O_{10}N$ (373.32): C 48.26, H 5.13, N 3.75; found C 48.25, H 5.17, N 3.76.

General Procedure for the Inhibition Assay: Inhibitory potencies were determined by spectrophotometrically measuring the residual hydrolytic activities of the glycosidases against the respective *o*- (for β-glucosidase from bovine liver) or *p*-nitrophenyl α- or β-D-glycopyranoside, or α,α′-trehalose (for trehalase) in the presence of the corresponding iminoindolizidine derivative. Each assay was performed in phosphate or phosphate/citrate buffer (for α-mannosidase and amyloglucosidase) at the optimal pH for each enzyme. The K_m values for the different glycosidases used in the tests and the corresponding working pHs are listed as follows: α-glucosidase (yeast), K_m = 0.35 mM (pH 6.8); β-glucosidase (almonds), K_m = 3.5 mM (pH 5.5 and 7.0); β-glucosidase (bovine liver), K_m = 1.8 mM (pH 6.8); trehalase (pig kidney), K_m = 5.0 mM (pH 6.0); α-galactosidase (coffee beans), K_m = 2.02 mM (pH 6.8); α-mannosidase (Jack beans), K_m = 2.0 mM (pH 5.5); α-fucosidase (bovine kidney), K_m = 0.2 mM (pH 5.5); amyloglucosidase (*Aspergillus niger*), K_m = 3.0 mM (pH 4.5). The reactions were initiated by addition of the enzyme to a solution of the substrate in the absence or presence of various concentrations of inhibitor. After incubating the mixture for 10–30 min at 37 or 55 °C (for amyloglucosidase) the reaction was quenched by the addition of 1 M Na_2CO_3 or a solution of GLC-Trinder (Sigma, for trehalase). The absorbance of the resulting mixture was determined at 405 or 505 nm (for trehalase). The K_i value and enzyme inhibition mode were determined from the slope of Lineweaver–Burk plots and double reciprocal analysis using a Sigma Plot program (version 4.14, Jandel Scientific).

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