Synthesis of Calystegine B_2, B_3, and B_4 Analogues: Mapping the Structure-Glycosidase Inhibitory Activity Relationships in the 1-Deoxy-6-oxacalystegine Series

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A practical synthesis of ring-modified calystegine analogues with a 6-oxa-*nor*-tropane structure has been developed. The methodology relies on the ability of the masked carbonyl group of hexose precursors to act as the electrophilic target for the nitrogen atom of pseudoamide (urea or thiourea) groups located at the C-5 position through the open-chain aldehyde form. The resulting piperidine species undergoes spontaneous intramolecular glycosylation reaction involving 6-OH provided that the resulting bicyclic aminoacetal fulfils the anomeric effect. The hydroxylation profile of the imino sugar glycomimetics thus obtained can be modified by judicious choice of the monosaccharide template. The validity of the strategy has been demonstrated by the preparation of *N*-thiocarbamoyl and *N*-carbamoyl derivatives of 1-deoxy-6-oxa-(+)-calystegine B_2, (–)-B_4, (+)-B_3, and (–)-B_2 from L-*ido*, L-*gulo*, L-*altro*, and D-*ido* precursors. The requested thioureas and ureas were obtained from 5-amino- or 5-azido-5-deoxyhexofuranose derivatives by a coupling reaction with isothiocyanates or a tandem Staudinger–aza-Wittig-type reaction with triphenylphosphane and an isothiocyanate followed by addition of water to the resulting carbodiimide, respectively. Attempts to prepare analogues with the unnatural 3-*epi*-(+)-calystegine B_2 hydroxylation profile from L-talofuranose (thio)ureas by this methodology led, however, to equilibrium mixtures of the furanose anomers, with only traces of the *nor*-tropane form. Evaluation of the inhibitory activity of the whole series of calystegine analogues against several glycosidases indicated that the main structural requirements for strong and specific inhibition of bovine liver β-glucosidase/β-galactosidase are the all-equatorial orientation of the triol system at the piperidine ring, the presence of a lipophilic substituent at the nitrogen atom and the location of the intramolecular aminoacetal oxygen atom at the 6-position of the *nor*-tropane core. On the basis of these data, a structural analogy of 6-oxa-(+)-calystegine B_2 derivatives with the natural calystegine C_1 has been established and a 1-azasugar inhibition mode is proposed.

Introduction

The calystegines are a recently discovered family of plant *nor*-tropane alkaloids bearing three (calystegine A), four (calystegine B) or five hydroxyl groups (calystegine C).[1–3] Similarly to other polyhydroxy alkaloids with a structural resemblance to sugars (imino sugars, "azasugars"),[4] many calystegines exhibit strong and specific glycoside hydrolase inhibitory activity, particularly for glucosidases and galactosidases, and are therefore interesting lead compounds for pharmaceutical research. However, in comparison to other sugar mimics with nitrogen in the ring, such as polyhydroxy pyrrolidine, piperidine, pyrrolizidine and indolizidine, which have been extensively investigated,[5–10] the calystegines have been significantly less explored, and the structural basis for glycosidase inhibition by this group of alkaloids has been only partially established.

Some of the most abundant calystegines in plants are calystegine B_2, B_3, B_4, and C_1 (Figure 1). The first of these is a potent inhibitor of β-glucosidases and α-galactosidases, while the epimeric calystegines B_3 and B_4 are moderate inhibitors of trehalases.[11] Calystegine C_1, which has a hydroxylation pattern around the piperidine ring identical to calystegine B_2 but bearing an additional hydroxyl substituent at the C-6 position on the pyrrolidine ring, is also a potent β-glucosidase inhibitor, although it is inactive against α-galactosidase.[11] A binding model has been proposed that invokes charge interactions with the carboxylic groups of the active site by analogy with the presumed glycosyl oxocarbenium cation intermediate of enzymatic glycoside hydrolysis.[12] This situation would be similar to that generally accepted for other azasugar glycomimetics such as 1-deoxynojirimycin. However, in the light of recent mechanistic studies on the β-glucosidase reaction,[13–15] the

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remarkable β-anomeric selectivity of calystegines B_2 and C_1 would rather suggest a correspondence with an anomeric carbocation species. Calystegines might then be regarded as rigid 1-azasugar-type glycomimetics, of which the potent β-glucosidase inhibitor isofagomine is a paradigmatic example (Figure 1).[16,17]

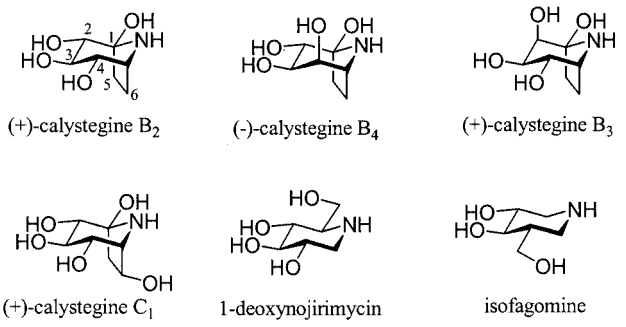


Figure 1. Structure of calystegines in comparison with that of 1-deoxynojirimycin and isofagomine

Several approaches to the synthesis of the natural calystegines have been reported in the last few years.[18−21] However, examples of unnatural calystegine analogues are much rarer,[22,23] and no systematic modifications of the topographical properties for structure-activity studies have been reported so far, probably due to the instability of the aminoacetal function characteristic of the calystegine bicyclic core. We have recently found that a subtle change in the structure of azasugars — replacing the sp^3-imino nitrogen by a pseudoamide-type nitrogen atom with substantial sp^2 character — leads to a dramatic increase of the orbital contribution to the anomeric effect at the aminoacetal pseudoanomeric center, resulting in a total preference for the axial orientation of the oxygen substituent and a notably enhanced stability.[24−28] This principle has been translated into a practical synthesis of calystegine B_2 analogues in which the hemiaminal bridgehead hydroxyl has been replaced by an endocyclic aminoacetal group, namely *N*-(thio)carbamoyl-1-deoxy-6-oxa-(+)-calystegine B_2 derivatives (**1**−**6**; Figure 2).[29,30] Some of the members of this new class of compounds (e.g., **1** and **2**) have been shown to be more potent and selective β-glucosidase inhibitors than the parent natural product, their inhibitory activity being strongly dependent on the nature of the exocyclic substituent. Here we report on the preparation of 6-oxacalystegine

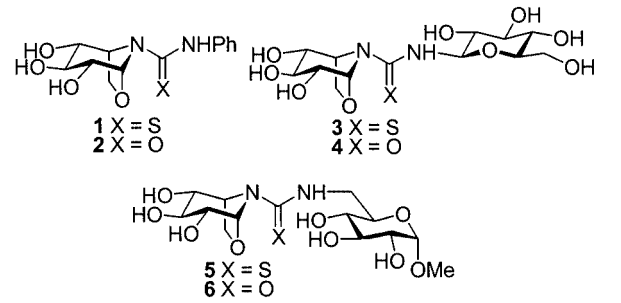


Figure 2. 6-oxa-(+)-calystegine B_2 derivatives

sp^2-azasugar-type glycomimetics[4] having all possible epimeric hydroxylation profiles at the piperidine ring, including calystegine B_2, B_3, B_4, and 3-*epi*-B_2 analogues. The latter are shown to exist only in a very minor proportion in aqueous solution. The inhibitory selectivity and potency relationships have been assayed in order to map the geometrical requirements for biological activity in this family of compounds.

Results and Discussion

The general synthetic strategy developed for the assembly of the bicyclic skeleton of 6-oxacalystegines starts from hexose precursors and is depicted in Figure 3. It consists of an intramolecular two-step tandem reaction involving sequential nucleophilic addition of a C-5 located pseudoamide-type (urea or thiourea) nitrogen atom to the masked aldehyde group of the monosaccharide template, to give a transient reducing piperidine derivative which undergoes spontaneous intramolecular glycosidation to form the primary hydroxyl group. The driving force for the whole transformation is probably the increase in stability due to the efficient delocalization interaction between the π-type lone-pair orbital of the sp^2-hybridized nitrogen atom in the ground state of *N*-(thio)carbonyl functionalities and the σ*-antibonding orbital of the contiguous C−O bond, which is axially anchored in the bridged 1,3-*O*,*N*-heterobicyclic system, fitting the anomeric effect.[29] Hydroxylation profiles of stereochemical complementarity with the natural (+)-calystegine B_2, (−)-calystegine B_4, and (+)-calystegine B_3 imply the L-*ido*, L-*gulo*, and L-*altro* configuration, respectively, of the starting monosaccharide precursors, while in the cases of derivatives having the 3-*epi*-(+)-calystegine B_2 and (−)-calystegine B_2 stereochemistry, hitherto not isolated from natural sources, the L-*talo* and D-*ido* configurational arrangements are required. In all cases, the key 5-deoxy-5-(thio)ureidohexofuranose intermediates were obtained through a reaction sequence that involved the inversion of the configuration at C-5 of the corresponding epimeric sugars at this position, that is D-glucose, D-mannose, D-galactose, D-allose, and L-glucose derivatives, respectively, which are much more readily accessible from commercially available monosaccharides.

Synthesis of 1-Deoxy-6-oxa-(−)-calystegine B_4 Derivatives

The preparation of the 5-deoxy-5-thioureido-L-gulofuranose derivatives **15**−**17** was accomplished in six steps from 1-*O*-acetyl-2,3:4,5-di-*O*-isopropylidene-α-D-mannofuranose[31] (**7**) through a reaction sequence that involved: (i) selective removal of the 5,6-*O*-acetonide group by treatment with 50% aqueous acetic acid (→ **8**), (ii) protection of the primary hydroxyl group as the corresponding triphenylmethyl ether (→ **9**), (iii) S_N2 displacement of the remaining hydroxy group by azide via a trifluoromethanesulfonate ester intermediate (→ **10**), (iv) hydrolysis of the *O*-6 trityl group with boron trifluoride diethyl etherate (→ **11**), (v) reduction of the azide group (→ **12**), and (vi) a chemose-

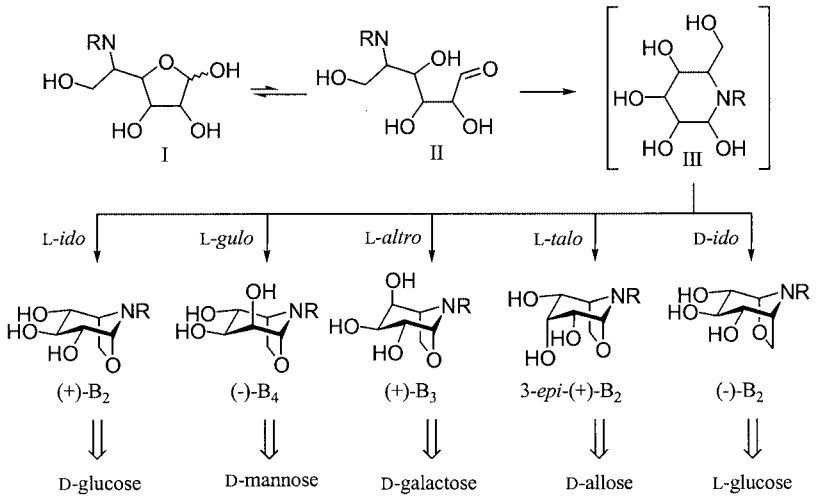
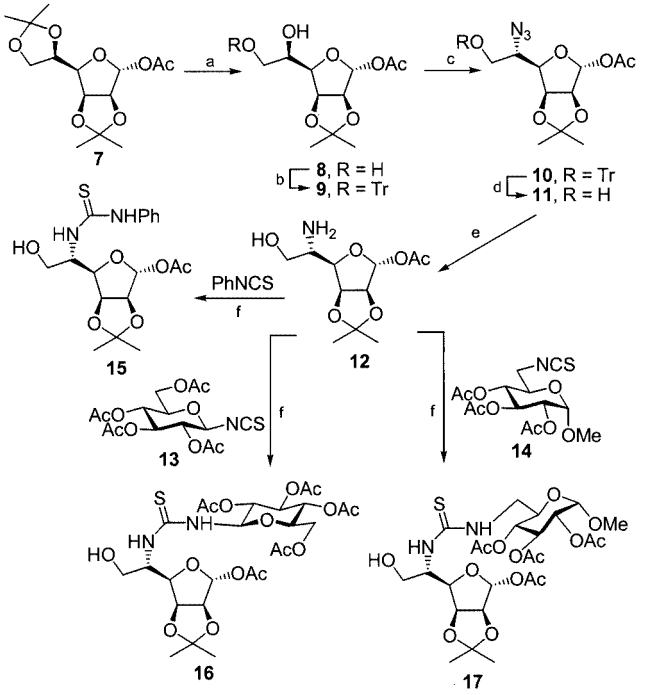


Figure 3. Synthetic strategy for the preparation of 6-oxacalystegines from 5-deoxy-5-(thio)ureidohexofuranoses (I) via the open-chain aldehyde form (II) and the piperidine intermediate (III)

lective coupling reaction of the generated amine with phenyl isothiocyanate, 2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl isothiocyanate[32] (**13**) or methyl 2,3,4-tri-O-acetyl-6-deoxy-6-isothiocyanato-α-D-glucopyranoside[33] (**14**), respectively (Scheme 1).[34]



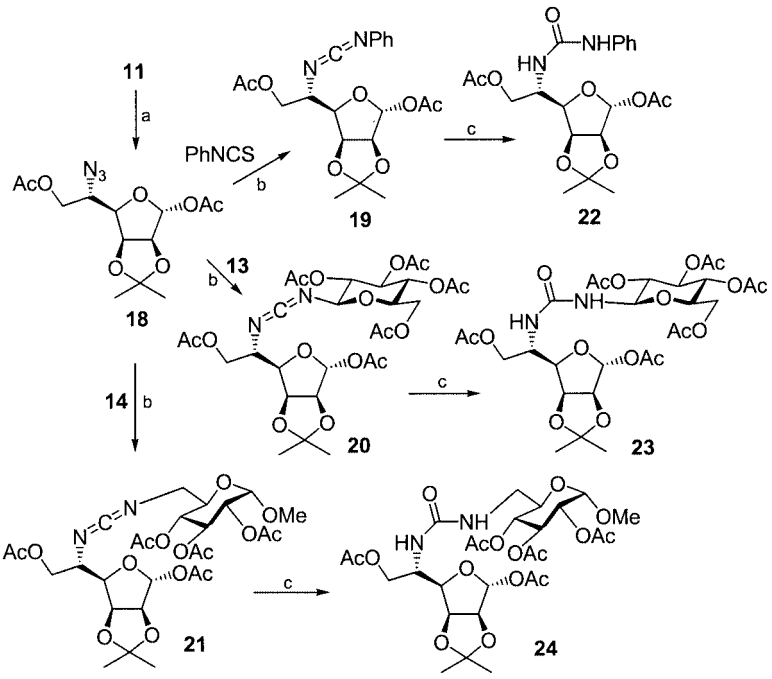
Scheme 1. Reagents and conditions: a, 50% AcOH/H_2O, 40 °C, 4 h, 90%; b, TrCl, pyridine, room temp., 36 h, 84%; c, 1. Tf_2O, CH_2Cl_2, pyridine, −25 °C, 1 h. 2. NaN_3, DMF, room temp., 18 h, 75%; d, $BF_3{\cdot}Et_2O$, CH_2Cl_2, 0 °C → room temp., 2 h, 80%; e, H_2, Pd/C, MeOH, room temp., 2 h, 88%; f, pyridine, room temp.,18 h, 75−85%

For the preparation of the urea analogues, a different synthetic strategy that avoids the use of hazardous isocyanate reagents was developed. Staudinger condensation of the per-*O*-protected azide **18** with triphenylphosphane and in situ aza-Wittig-type reaction with the corresponding isothiocyanate[35−37] afforded the carbodiimide adducts **19**−**21**. Further acid-catalyzed addition of water to the heterocumulene group[38] led to the corresponding 5-deoxy-5-ureido-L-gulofuranose derivatives **22**−**24** in 69−94% yield (Scheme 2).

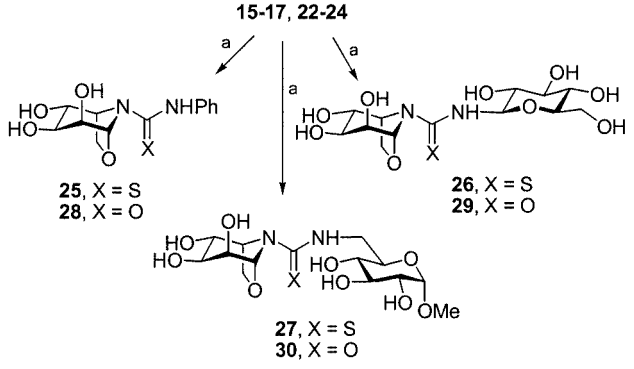
Full *O*-deprotection of the thioureas **15**−**17** and ureas **22**−**24** by deacetylation and treatment with 9:1 trifluoroacetic acid-water afforded the target 1-deoxy-6-oxa-(−)-calystegine B_4 derivatives **25**−**27** and **28**−**30**, respectively (Scheme 3). The ^1H NMR spectra, recorded in D_2O, exhibit coupling constant values around the piperidine ring characteristic of *trans*, *gauche*, *gauche*, dispositions between 2-H, 3-H, 4-H, and 5-H, confirming the axial orientation of 4-OH, while the long-range $^4J_{H,H}$ coupling constant between 2-H and the *exo*-oriented methylene proton 7b-H ($J_{4,7b}$ = 0.6 Hz), in a W arrangement, attests to the rigidity of the 6-oxa-*nor*-tropane core. The ^{13}C NMR spectra show the typical low-field resonance for the *N*-thiocarbonyl or *N*-carbonyl group. In the case of the pseudodisaccharide derivatives, the resonance of the corresponding linking carbon atom (C-1′ or C-6′) experiences a significant high-field shift relative to the parent monosaccharide, in agreement with the presence of the (thio)urea bridge.

Synthesis of 1-Deoxy-6-oxa-(+)-calystegine B_3 Derivatives

To implement the above synthetic strategy in order to access 6-oxa-(+)-calystegine B_3 analogues, the preparation of 5-amino and 5-azido-5-deoxy-L-altrofuranose derivatives was required. Their preparation started from the known 3-*O*-acetyl-1,2-*O*-isopropylidene-α-D-galactofuranose[39] (**31**) and paralleled the reaction pathway described above for the L-*gulo* derivatives. Sequential *O*-6 tritylation (→ **32**) and OH → N_3 exchange (→ **33**), with inversion of the configuration at C-5, followed by detritylation, afforded the pivotal azido alcohol **34**, which was subsequently deacetylated (→



Scheme 2. Reagents and conditions: a, Ac_2O/pyridine, 85%; b, TPP, toluene, room temp., 18 h, 41−86%; c, 1% TFA in 2:1 acetone/water, room temp., 8 h, 69−94%

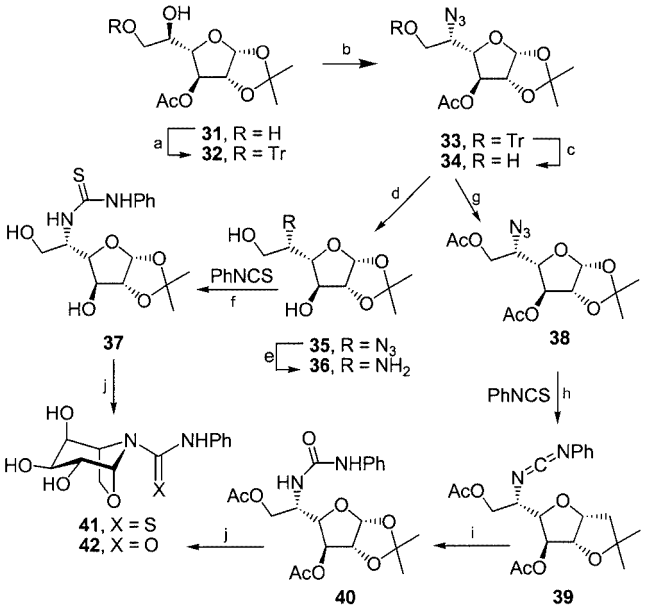


Scheme 3. Reagents and conditions: a, 1. NaOMe, MeOH. 2. 90% TFA-water, 0 °C, 15 min. 3. Amberlite® IRA 68 (OH^-), 65−85%

35) and reduced to the corresponding amino alcohol **36** or acetylated to the fully *O*-protected azide **38**. Since the natural compound calystegine B_3 is a rather poor glycosidase inhibitor, and in view of the glycosidase inhibition results obtained in the 6-oxacalystegine B_2 and B_4 series (see below), we limited further transformations in this case to the synthesis of the *N*-(*N*′-phenylthiocarbamoyl) and *N*-(*N*′-phenylcarbamoyl) derivatives **41** and **42**. Thus, reaction of **36** with phenyl isothiocyanate yielded the corresponding *N*,*N*′-disubstituted thiourea **37**, while Staudiger−aza-Wittig-type condensation of **38** with triphenylphosphane and the same isothiocyanate reagent, followed by acid-catalyzed addition of water to the carbodiimide intermediate **39**, provided urea **40**. Removal of the *O*-protecting groups as above led, initially, to α,β-anomeric mixtures of the corresponding L-altrofuranose derivatives, probably as the corresponding iso(thio)uronium salts, as seen from the ^{13}C NMR spectra of the corresponding reaction mixtures. A similar behavior has been previously observed in the L-idofuranose series.[29] After several coevaporations with water and, finally, neutralization of a water solution with Amberlite® IRA 68 (OH^-) ion-exchange resin, the furanose ring rearranged to give a transient piperidine species that underwent an intramolecular glycosylation in situ to afford the target (+)-calystegine B_3 analogues **41** and **42**, whose structure was confirmed by ^1H and ^{13}C NMR spectroscopy, MS and elemental analysis data (Scheme 4).

Synthesis of 1-Deoxy-6-oxa-3-*epi*-(+)-calystegine B_2 Derivatives

For the preparation of 6-oxa-(+)-calystegine B_2 analogues with the epimeric configuration at C-3, the general synthetic strategy proven successful for the C-2 and C-4 epimers was examined. Thus, 1,2:5,6-di-*O*-isopropylidene-α-D-allofuranose[40] (**43**) was transformed into the 5-amino- and 5-azido-5-deoxy-β-L-talofuranose derivatives **47** and **49**, respectively, via **44**−**46**, by standard protecting-group strategies and inversion of the configuration at C-5 (Scheme 5). Further coupling with phenyl isothiocyanate afforded the corresponding phenylthiourea **48** or carbodiimide adduct **50**, the latter being transformed into the phenylurea **51** by nucleophilic addition of water. However, in this particular case full *O*-deprotection of **48** or **51** and neutralization of the reaction mixtures with basic anion-exchange resin did not result in the expected furanose → piperidine rearrangement. Instead, an equilibrium between the L-talofuranose anomers **52** or **54**, with a very minor proportion (below 5%) of the bicyclic *nor*-tropane form, was observed in D_2O

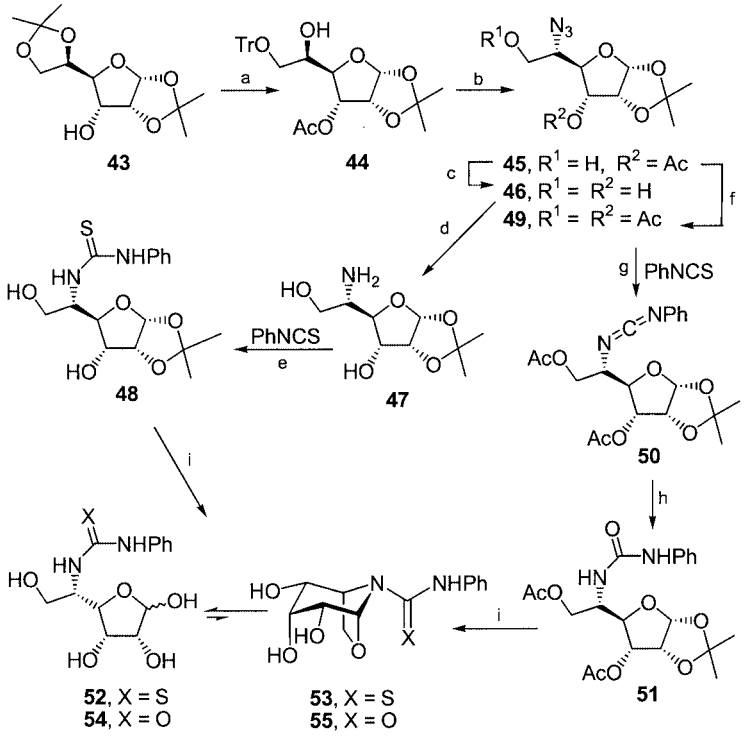


Scheme 4. a, TrCl, pyridine, room temp., 24 h, 74%; b, 1. Tf_2O, CH_2Cl_2, pyridine, −25 °C. 2. NaN_3, DMF, 12 h, 60% (global); c, $BF_3{\cdot}Et_2O$, CH_2Cl_2, 0 °C → room temp., 2 h, 75%; d, NaMeO, MeOH, 95%; e, H_2, Pd/C, MeOH, room temp., 2 h, quant; f, pyridine, room temp., 18 h, 75%; g, Ac_2O/pyridine, room temp., 83%; h, TPP, toluene, room temp., 18 h, 45%; i, 1% TFA in 2:1 acetone/water, room temp., 8 h, 88%; j, 1. NaOMe, MeOH (for **40**). 2. 90% TFA-water, 0 °C, 15 min. 3. Amberlite® IRA 68 (OH^-), 65−90%

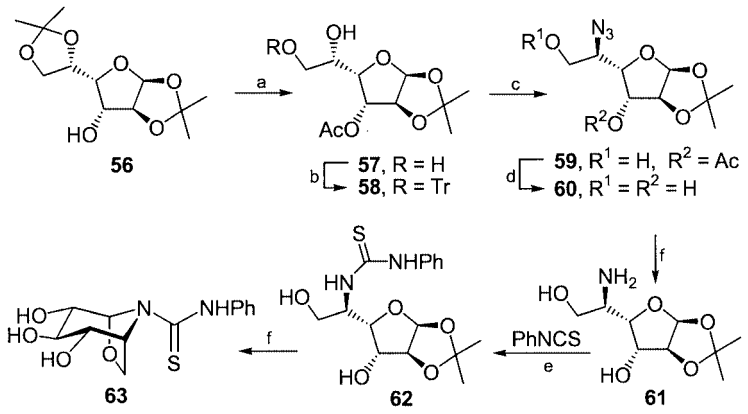
solutions (^1H NMR spectroscopy). Attempts to trap the bicyclic oxa-*nor*-tropanes **53** and **55** by provoking the intramolecular glycosylation reaction at different pHs failed. It is likely that the steric hindrance imposed by the 1,3-parallel disposition between the carbon and oxygen substituents at the piperidine ring in **53** and **55** overcomes, in this case, the stabilization due to the anomeric effect at the aminoacetal center.

Synthesis of 6-Oxa-(−)-calystegine B_2 Derivatives

In order to have a complete view of the contribution of all oxygen substituents at the *nor*-tropane ring to the binding affinity of oxacalystegine analogues for the active site of glycosidases, the preparation and assaying of a 7-oxa-(+)-calystegine B_2 derivative was also considered. Due to the pseudosymmetry of the molecule, moving the aminoacetal endocyclic oxygen atom from the 6-position to the 7-position in the *nor*-tropane skeleton leads to the enantiomeric 6-oxa-(−)-calystegine B_2 series. Consequently, a synthesis from D-idose precursors, matching the strategy previously developed for the 6-oxa-(+)-calystegine B_2 counterparts,[29] was elaborated. Thus, 1,2:4,5-di-*O*-isopropylidene-β-L-glucofuranose[41] **56** was transformed, after inversion of the configuration at C-5, via **57**−**60** following the reaction sequence already discussed in the previous examples, into 5-amino-5-deoxy-1,2-*O*-isopropylidene-α-D-idofuranose **61**.



Scheme 5. a, 1. Ac_2O-pyridine, room temp. 2. 40% AcOH/water, 40 °C, 24 h. 3. TrCl, pyridine, room temp., 24 h, 74%; b, 1. Tf_2O, CH_2Cl_2, pyridine, −25 °C, 30 min. 2. NaN_3, DMF, room temp. 3.5 h. 3. $BF_3{\cdot}Et_2O$, CH_2Cl_2, 0 °C → room temp., 2 h, 60%; c, NaMeO, MeOH, 92%; d, H_2, Pd/C, MeOH, room temp., 2 h, quant; e, pyridine, room temp., 18 h, 65%; f, Ac_2O/pyridine, room temp., 94%; g, TPP, toluene, 80 °C, 2.5 h, 71%; h, 1% TFA in acetone/water (2:1), room temp., 8 h, 92%; i, 1. NaOMe, MeOH (for **51**). 2. 90% TFA-water, 0 °C, 15 min. 3. Amberlite® IRA 68 (OH^-), 80−92%



Scheme 6. a, 40% AcOH/water, 40 °C, 4 h, 82%; b, TrCl, pyridine, room temp., 24 h, 74%; c, 1. Tf_2O, CH_2Cl_2, pyridine, −25 °C, 20 min. 2. NaN_3, DMF, room temp. 3.5 h. 3. $BF_3{\cdot}Et_2O$, CH_2Cl_2, 0 °C → room temp., 3.5 h, 66%; d, NaMeO, MeOH, quant.; e, H_2, Pd/C, MeOH, room temp., 2 h, quant; f, pyridine, room temp., 18 h, 71%; g, 1. TFA/water, 0 °C, 30 min. 2. Amberlite® IRA 68 (OH^-), 95%

The coupling reaction of **61** with phenyl isothiocyanate afforded the corresponding thiourea adduct **62** which, by trifluoroacetic acid-catalyzed hydrolysis of the acetal group and neutralization of the reaction mixture, led to the 6-oxa-*N*-(*N*′-phenylthiocarbamoyl)-(−)-calystegine B_2 derivative **63** having identical spectroscopic properties to the previously reported enantiomer **1** (Scheme 6).[29]

Mapping the Structure-Glycosidase Inhibitory Properties Relationships of 6-Oxacalystegine Analogues

The inhibitory activities of the 6-oxacalystegine (+)-B_2 (**1**−**6**), (−)-B_4 (**25**−**30**), (+)-B_3 (**41**, **42**), and (−)-B_2 (**63**) glycomimetics, as well as those of the L-talofuranose derivatives **52** and **54** containing small proportions of 3-*epi*-(+)-calystegine B_2 analogues **53** and **55**, for α-glucosidase (yeast), β-glucosidase (almonds) β-glucosidase/β-galactosidase (bovine liver, cytosolic) and α-galactosidase (green coffee beans), are summarized in Table 1. No inhibition was detected for any of the above compounds against trehalase (pig kidney), invertase (yeast), α-mannosidase (Jack beans), or amyloglucosidase (*Aspegillus niger*). The 6-oxa-(+)-calystegine-B_2 analogues **1** and **2**, bearing aromatic substituents at the nitrogen atom, are strong and selective competitive inhibitors of mammalian β-glucosidase/β-galactosidase, with inhibition constant (K_i) values in the low micromolar range. Actually, the *N*-(*N*′-phenylthiocarbamoyl) derivative **1** (K_i = 2.5 μM) inhibits this enzyme 18-fold more strongly than (+)-calystegine B_2 (K_i = 45 μM).[11] The enzyme specificity is also remarkable: while the natural compound also inhibits almond β-glucosidase (K_i = 1.5 μM) and α-galactosidase (K_i = 0.86 μM) simultaneously,[11] compounds **1** and **2** are very weak inhibitors of these two enzymes. The inhibition activity is strongly decreased for *N*-substituents at the 6-oxa-*nor*-tropane ring having a hydrophilic nature (**3**−**6**).

The high selectivity and potency observed for the 6-oxa-(+)-calystegine B_2 derivatives bearing aromatic substituents

Table 1. Comparison of inhibitory activities (K_i, μM) for 6-oxa-(+)-calystegine B_2 (**1**−**6**), (−)-B_4 (**25**−**30**), (+)-B_3 (**41**, **42**), and (−)-B_2 (**63**) derivatives, as well as for L-altrofuranose/3-*epi*-6-oxa-(+)-calystegine B_2 equilibrium mixtures (**52/53**, **54/55**)

Compound	α-glucosidase (yeast)	β-glucosidase (almonds)	β-glucosidase/β-galactosidase (bovine liver, cytosolic)	α-galactosidase (coffee beans)
1	n.i.[a]	970	2.5	137
2	n.i.	1500	30	172
3	n.i.	n.i.	148	n.i.
4	n.i.	n.i.	n.i.	160
5	n.i.	118	325	n.i
6	n.i.	n.i	1640	175
25	n.i.	895	n.i.	n.i.
26	n.i.	n.i.	n.i.	n.i.
27	n.i.	n.i.	n.i.	n.i.
28	n.i.	n.i.	n.i.	n.i.
29	n.i.	n.i.	n.i.	n.i.
30	n.i.	n.i.	n.i.	n.i.
41	138	n.i.	190	n.i.
42	n.i.	n.i.	870	n.i.
52/53	n.i.	n.i.	161	n.i.
54/55	n.i.	n.i.	750	n.i.
63	n.i.	207	424	149

[a] Inhibition, when detected, was always of the competitive type; n.i. = no inhibition detected.

in the inhibition of β-glucosidase/β-galactosidase from bovine liver, an enzyme known to possess a hydrophobic binding site and for which aromatic β-D-glucosides are good substrates,[42] supports the idea that the (thio)carbamoyl segment acts as an aglycon-mimicking group in a 1-azasugar inhibition mode. As already observed in the natural compounds, strong inhibition of β-glucosidase by 6-oxacalystegines is associated with the all-equatorial arrangement of the triol system at the piperidine ring. Changing the configuration at either C-4 (**25**−**30**) or C-2 (**41**, **42**) results in a dramatic increase in the inhibition constant values for β-glucosidase/β-galactosidase. It seemed at this point that this configurational arrangement, which resembles that of the natural D-glucopyranoside substrates, in combination with a lipophilic nitrogen substituent, was the main structural requirement for the biological activity of these glycomimetics. The high enzyme selectivity observed is probably a consequence of the neutral character of sp^2-azasugars as compared with classical imino sugars. Actually, the partial positive charge density at the nitrogen regions in pseudoamide functional groups[43] probably reflects more closely the situation at the anomeric region in the transition state, leading to enzymatic glycoside hydrolysis, than a protonated ammonium group.[44]

It must be noticed that, assuming the 1-azasugar model for the calystegines, the hydroxylation patterns of the (−)-B_4 and (+)-B_3 representatives, which would resemble D-mannose and D-galactose when considering a classical azasugar (1,5-imino sugar) mode of action, do not conform to the configurational pattern of any common monosaccharide (i.e. D-allose and L-idose, respectively). This is in agreement with the lack of activity against mannosidases and galactosidases of both the natural compounds and the 6-oxa analogues reported in this work. In contrast, the unnatural 3-*epi*-(+)-B_2 hydroxylation profile would match that of D-galactose. Since aromatic β-D-galactosides are also substrates of the cytosolic β-glucosidase/β-galactosidase, structures such as **53** and **55** would be expected to act as inhibitors of this enzyme. Although their apparent instability has prevented a confirmation of this point, the K_i value obtained for **53**, considering that the concentration of the active species is very low, is significant.

Notwithstanding this, the 6-oxa-(−)-calystegine B_2 derivative **63**, which fulfils the above requirements, is more than two orders of magnitude weaker as an inhibitor of β-glucosidase/β-galactosidase than its enantiomer **1** (K_i = 424 μM), indicating that the endocyclic oxygen atom is also playing an active role in enzyme binding for this particular enzyme. This result suggests that 6-oxa-(+)-calystegine B_2 glycomimetics are rather closer analogues of (+)-calystegine C_1 (K_i for β-glucosidase/β-galactosidase = 3.6 μM and no inhibition of α-galactosidase),[11] bearing an extra hydroxyl substituent at C-6 as compared to calystegine B_2. According to our data, the extra oxygen at this region probably acts as a hydrogen-bond acceptor in the active site of the mammalian cytosolic enzyme and also prevents efficient binding to α-galactosidase and almond β-glucosidase, leading to higher selectivities. Introducing stronger hydrogen-bond-acceptor groups at this position and optimizing the structure of the pseudoaglyconic substituent for optimal interaction with the enzyme may, thus, result in still more potent and selective inhibitors. Work in that direction is currently under way in our laboratories.

Conclusion

We have described here an efficient synthetic route to a new family of sp^2-azasugar glycomimetics endowed with the essential structural features of the calystegines. The reaction sequence involves: (i) a coupling reaction of an amino sugar with an isothiocyanate to give a thiourea adduct or tandem Staudinger−aza-Wittig-type coupling reaction of an azido sugar with triphenylphosphane and an isothiocyanate to give a carbodiimide, which is further transformed into the corresponding urea, (ii) rearrangement of the furanose intermediate through the open-chain aldehyde form to give a transient piperidine species, and (iii) intramolecular glycosylation reaction, with generation of an aminoacetal functional group, thus closing the bicyclic 6-oxa-*nor*-tropane skeleton. Several hydroxylation profiles are available by judicious choice of the monosaccharide precursor. The glycosidase inhibition studies show a remarkable influence of both the arrangement of the oxygen substituents on the bicyclic core and the nature of the *N*-substituent in the inhibitory properties towards mammalian cytosolic β-glucosidase/β-galactosidase. The ensemble of data suggests a parallelism between the behavior of 6-oxa-(+)-calystegine B_2 derivatives and the natural calystegine C_1, strongly supporting a 1-azasugar inhibition mode for the polyhydroxy-*nor*-tropane azasugar family.

Experimental Section

General Remarks: Optical rotations were measured at room temperature in 1-cm or 1-dm tubes. IR spectra were recorded on a FT-IR instrument. ^1H (^{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. In the FAB-MS spectra, the primary beam consisted 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 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) sulfate-5% ammonium molybdate in 2 M H_2SO_4. Column chromatography was carried out with Silica Gel 60 (E. Merk, 230−400 mesh). Fully deprotected compounds were purified by GPC (Sephadex G-10, MeOH/H_2O, 1:1). Acetylations were effected conventionally with pyridine/Ac_2O (1:1, 10 mL per 1 g of sample). Deacetylations were effected 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-Deoxy-6-oxa-*N*-(thiocarbamoyl and carbamoyl)-(+)-calystegine B_2 derivatives **1**−**6** were prepared from 5-deoxy-5-thioureido and ureido-L-idofuranose precursors as reported.[29] 1-*O*-Acetyl-2,3:5,6-di-*O*-isopropylidene-α-D-mannofuranose[31] (**7**), 3-*O*-acetyl-1,2-*O*-isopropylidene-α-D-galactofuranose[39] (**31**), 1,2:5,6-di-*O*-isopropylidene-α-D-allofuranose[40] (**43**), and 1,2:5,6-di-*O*-isopropylidene-β-L-glucofuranose[11] (**56**) were obtained from commercial D-mannose, D-galactose, D-glucose, and L-glucose, respectively. 2,3,4,6-Tetra-*O*-acetyl-β-D-glucopyranosyl isothiocyanate (**13**) was synthesized from the corresponding per-*O*-acetyl glucopyranosyl bromide by treatment with potassium thiocyanate and tetra-*n*-butylammonium hydrogensulfate in acetonitrile, following the procedure of Camarasa et al.[32] Methyl 2,3,4-tri-*O*-acetyl-6-deoxy-6-isothiocyanato-α-D-glucopyranoside (**14**) was obtained by isothiocyanation of the corresponding 6-amino-6-deoxy-sugar by thiophosgene, as reported previously.[33] The glycosidases α-glucosidase (from yeast), β-glucosidase (from almonds), β-glucosidase/β-galactosidase (from bovine liver, cytosolic), trehalase (from pig kidney), α-galactosidase (from green coffee beans), α-mannosidase (from jack beans), invertase (from yeast), and amyloglucosidase (from *Aspergillus Niger*), used in the inhibition studies, as well as α,α′-trehalose, sucrose and the corresponding *o*- and *p*-nitrophenyl glycoside substrates were purchased from Sigma Chemical Co.

1-*O*-Acetyl-2,3-*O*-isopropylidene-α-D-mannofuranose (8): 1-*O*-Acetyl-2,3:5,6-di-*O*-isopropylidene-α-D-mannofuranose (**7**) (2.0 g, 6.62 mmol) was suspended in 50% aqueous AcOH (6 mL) and heated at 40 °C for 4 h. The resulting solution was concentrated and coevaporated several times with water and toluene to eliminate traces of the acid. The residue was purified by column chromatography using EtOAc/petroleum ether (2:1) → EtOAc as an eluent. Yield: 1.55 g (90%). R_f = 0.38 (EtOAc/petroleum ether, 3:1). $[\alpha]_D^{22}$ = +55.0 (c = 1.0, CH_2Cl_2). IR (KBr): $\tilde{\nu}_{max}$ = 3459, 2988, 1746, 1408, 1379, 1235, 1213, 1094 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 1.34 (s, 3 H, Me), 1.47 (s, 3 H, Me), 2.05 (s, 3 H, MeCO), 2.87 (br. s, 1 H, OH), 2.88 (br. s, 1 H, OH), 3.71 (dd, $J_{5,6b}$ = 4.9, $J_{6a,6b}$ = 11.3 Hz, 1 H, 6b-H), 3.85 (d, $J_{6a,6b}$ = 11.3 Hz, 1 H, 6a-H), 4.00 (dd, $J_{4,5}$ = 8.2, $J_{5,6b}$ = 4.9 Hz, 1 H, 5-H), 4.09 (dd, $J_{3,4}$ = 3.8, $J_{4,5}$ = 8.2 Hz, 1 H, 4-H), 4.69 (d, $J_{2,3}$ = 5.9 Hz, 1 H, 2-H), 4.91 (dd, $J_{2,3}$ = 5.9, $J_{3,4}$ = 3.8 Hz, 1 H, 3-H), 6.15 (s, 1 H, 1-H). ^{13}C NMR (125.7 MHz, $CDCl_3$): δ = 20.9 (*Me*CO), 24.7, 25.9 (C*Me*$_2$), 64.0 (C-6), 70.0 (C-5), 79.8 (C-4), 81.3 (C-3), 84.8 (C-2), 100.6 (C-1), 113.3 (*C*Me$_2$), 169.2 (CO) ppm. FAB-MS: m/z = 285 (100) [M + Na]$^+$, 263 (40) [M + H]$^+$. $C_{11}H_{18}O_7$ (262.26): calcd. C 50.38, H 6.92; found C 50.15, H 6.62.

1-*O*-Acetyl-2,3-*O*-isopropylidene-6-*O*-trityl-α-D-mannofuranose (9): Trityl chloride (1.9 g, 6.8 mmol, 1.5 equiv.) was added to a solution of **8** (1.25 g, 4.59 mmol) in pyridine (8 mL) and the solution was stirred at room temperature for 36 h. The reaction mixture was poured into ice-water (80 mL) and the resulting solid was dissolved in toluene (40 mL) and washed with iced aqueous 10% AcOH (10 mL), saturated aqueous $NaHCO_3$ (10 mL), dried ($MgSO_4$), and the solvents evaporated under reduced pressure. The residue was purified by column chromatography eluting with EtOAc/petroleum ether (1:3). Yield: 1.94 g (84%). R_f = 0.58 (EtOAc/petroleum ether, 1:1). $[\alpha]_D^{22}$ = +25.8 (c = 1.0, CH_2Cl_2). IR (KBr): $\tilde{\nu}_{max}$ = 3445, 2988, 1748, 1402, 1379, 1262, 1211, 1094 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 1.36 (s, 3 H, Me), 1.49 (s, 3 H, Me), 2.04 (s, 3 H, MeCO), 2.82 (d, $J_{5,OH}$ = 6.2 Hz, 1 H, OH), 3.44−3.36 (m, 2 H, 6a-H, 6b-H), 4.11 (m, 1 H, 5-H), 4.20 (dd, $J_{3,4}$ = 3.4, $J_{4,5}$ = 7.8 Hz, 1 H, 4-H), 4.71 (d, $J_{2,3}$ = 5.9 Hz, 1 H, 2-H), 4.94 (dd, $J_{2,3}$ = 5.9, $J_{3,4}$ = 3.4 Hz, 1 H, 3-H), 6.18 (s, 1 H, 1-H), 7.18−7.48 (m, 15 H, 3 Ph) ppm. ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 20.9 (*Me*CO), 24.7, 25.9 (C*Me*$_2$), 64.7 (C-6), 68.7 (C-5), 79.9 (C-3), 81.0 (C-4), 84.8 (C-2), 86.6 (*C*Ph$_3$), 100.5 (C-1), 113.1 (*C*Me$_2$), 127.0−143.7 (Ph), 169.2 (CO) ppm. FAB-MS: m/z = 527 (80) [M + Na]$^+$. $C_{30}H_{32}O_7$ (504.57): calcd. C 71.41, H 6.39; found C 71.27, H 6.20.

1-*O*-Acetyl-5-azido-5-deoxy-2,3-*O*-isopropylidene-6-*O*-trityl-β-L-gulofuranose (10): Pyridine (0.72 mL) and trifluoromethanesulfonic anhydride (1.05 mL, 6.36 mmol) were added to a solution of **9** (2.3 g, 4.59 mmol) in CH_2Cl_2 (20 mL) at −25 °C under N_2. The reaction mixture was allowed to reach room temperature and, after stirring for 1 h, the mixture was diluted with CH_2Cl_2 (15 mL), washed with saturated aqueous $NaHCO_3$ (15 mL), dried ($MgSO_4$), and concentrated. The resulting crude triflate ester was dissolved in DMF (18 mL), NaN_3 (3.04 g, 32.13 mmol, 7 equiv.) 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 and washed with water. The organic extract was dried ($MgSO_4$) and the solvents evaporated to give a solid which was purified by column chromatography using EtOAc/petroleum ether (1:5). Yield: 1.8 g (75%). R_f = 0.54 (EtOAc/petroleum ether, 1:2). $[\alpha]_D^{22}$ = +27.4 (c = 1.0, CH_2Cl_2). IR (KBr): $\tilde{\nu}_{max}$ = 2990, 2101, 1746, 1379, 1235, 1213, 1105 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 1.15 (s, 3 H, Me), 1.39 (s, 3 H, Me), 2.08 (s, 3 H, MeCO), 3.24 (dd, $J_{5,6b}$ = 4.9, $J_{6a,6b}$ = 9.9 Hz, 1 H, 6b-H), 3.55 (dd, $J_{5,6a}$ = 3.1, $J_{6a,6b}$ = 9.9 Hz, 1 H, 6a-H), 3.84 (ddd, $J_{4,5}$ = 8.9, $J_{5,6a}$ = 3.1, $J_{5,6b}$ = 4.9 Hz, 1 H, 5-H), 4.24 (dd, $J_{3,4}$ = 3.4, $J_{4,5}$ = 8.9 Hz, 1 H, 4-H), 4.32 (dd, $J_{2,3}$ = 5.8, $J_{3,4}$ = 3.4 Hz, 1 H, 3-H), 4.59 (d, $J_{2,3}$ = 5.8 Hz, 1 H, 2-H), 6.15 (s, 1 H, 1-H), 7.48−7.24 (m, 15 H, 3 Ph) ppm. ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 20.9 (*Me*CO), 24.5, 25.8 (C*Me*$_2$), 61.2 (C-5), 62.8 (C-6), 78.8 (C-3), 81.4 (C-4), 85.1 (C-2), 86.9 (*C*Ph$_3$), 100.5 (C-1), 112.9 (*C*Me$_2$), 127.0−143.3 (Ph), 169.2 (CO) ppm. FAB-MS: m/z = 552 (100) [M + Na]$^+$. $C_{30}H_{31}N_3O_6$ (529.58): calcd. C 68.04, H 5.90, N 7.94; found C 67.88, H 5.71, N 7.84.

1-*O*-Acetyl-5-azido-5-deoxy-2,3-*O*-isopropylidene-β-L-gulofuranose (11): $BF_3{\cdot}Et_2O$ (391 μL) and MeOH (1 mL) were added to a solution of the tritylated azido derivative **10** (1.5 g, 2.8 mmol) in CH_2Cl_2 (19 mL), at 0 °C under Ar. The reaction mixture was allowed to reach room temperature and stirred for 2 h, then washed with saturated aqueous $NaHCO_3$ (2 × 10 mL), dried ($MgSO_4$), and concentrated. The resulting residue was purified by column chromatography (EtOAc/petroleum ether, 1:4 → 1:1). Yield: 644 mg (80%). R_f = 0.24 (EtOAc/petroleum ether, 1:2). $[\alpha]_D^{22}$ = +44.0 (c = 1.0, CH_2Cl_2). IR (KBr): $\tilde{\nu}_{max}$ = 3503, 2990, 2104, 1748, 1379, 1231, 1100 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 1.32 (s, 3 H, Me), 1.49 (s, 3 H, Me), 2.08 (s, 3 H, MeCO), 3.75 (dd, $J_{5,6b}$ = 5.8, $J_{6a,6b}$ = 12.4 Hz, 1 H, 6b-H), 3.87 (dd, $J_{5,6a}$ = 3.1, $J_{6a,6b}$ = 12.4 Hz, 1 H, 6a-H), 3.88 (m, 1 H, 5-H), 4.22 (dd, $J_{3,4}$ = 3.5, $J_{4,5}$ = 8.5 Hz, 1 H, 4-H), 4.71 (d, $J_{2,3}$ = 5.8 Hz, 1 H, 2-H), 4.79 (dd, $J_{2,3}$ = 5.8, $J_{3,4}$ = 3.5 Hz, 1 H, 3-H), 6.20 (s, 1 H, 1-H) ppm. ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 20.9 (*Me*CO), 24.7, 25.9 (C*Me*$_2$), 61.9 (C-5), 63.1 (C-6), 78.9 (C-3), 82.0 (C-4), 85.2 (C-2), 100.2 (C-1), 113.3 (*C*Me$_2$), 169.4 (CO) ppm. FAB-MS: m/z = 272 (30) [M − Me]$^+$. $C_{11}H_{17}N_3O_6$ (287.27): calcd. C 45.99, H 5.96, N 14.63; found C 45.95, H, 5.95, N 14.53.

1-*O*-Acetyl-5-amino-5-deoxy-2,3-*O*-isopropylidene-β-L-gulofuranose (12): A solution of **11** (474 mg, 1.65 mmol) in MeOH (30 mL) was hydrogenated at atmospheric pressure for 2 h using 10% Pd/C (163.3 mg) as catalyst. The suspension was filtered through Celite and concentrated to give **13** as a hygroscopic solid which was used in the next step without further purification.

L-Gulofuranose-derived Thioureas 15−17. General Procedure: The corresponding isothiocyanate (phenyl isothiocyanate, **13** or **14**;

0.5 mmol) was added to a solution of amine **12** (0.5 mmol) in pyridine (5 mL). The resulting mixture was stirred at room temperature for 18 h, then coevaporated several times with toluene under vacuum. The resulting residue was purified by column chromatography using EtOAc/petroleum ether (1:1 → 3:1) to afford the thioureido derivatives **15**−**17**.

1-*O*-Acetyl-5-deoxy-2,3-*O*-isopropylidene-5-(*N*′-phenylthioureido)-β-L-gulofuranose (15): Yield: 158 mg, (80%). R_f = 0.60 (EtOAc/petroleum ether, 4:1). $[\alpha]_D^{22}$ = +78.0 (*c* = 1.0, CH_2Cl_2). UV (CH_2Cl_2) 267 nm (ε_mM 26.3). IR (KBr): $\tilde{\nu}_{max}$ = 3339, 2961, 1740, 1651, 1537, 1260, 1094, 1013 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 1.29 (s, 3 H, Me), 1.41 (s, 3 H, Me), 2.06 (s, 3 H, MeCO), 3.87 (dd, $J_{5,6b}$ = 4.8, $J_{6a,6b}$ = 11.5 Hz, 1 H, 6b-H), 3.93 (dd, $J_{5,6a}$ = 3.8, $J_{6a,6b}$ = 11.5 Hz, 1 H, 6a-H), 4.45 (dd, $J_{3,4}$ = 3.5, $J_{4,5}$ = 6.8 Hz, 1 H, 4-H), 4.69 (d, $J_{2,3}$ = 5.8 Hz, 1 H, 2-H), 4.77 (dd, $J_{2,3}$ = 5.8, $J_{3,4}$ = 3.5 Hz, 1 H, 3-H), 4.87 (ddd, $J_{4,5}$ = 6.8, $J_{5,6a}$ = 3.8, $J_{5,6b}$ = 4.8 Hz, 1 H, 5-H), 6.13 (s, 1 H, 1-H), 6.80 (br. s, 1 H, NH), 7.40−7.20 (m, 5 H, Ph), 8.50 (br. s, 1 H, N′H) ppm. ^{13}C NMR (125.7 MHz, $CDCl_3$): δ = 21.0 (*Me*CO), 24.5, 25.8 (C*Me*$_2$), 55.4 (C-5), 61.4 (C-6), 79.1 (C-3, C-4), 85.1 (C-2), 100.0 (C-1), 113.5 (*C*Me$_2$), 124.3−130.0 (Ph), 169.3 (CO), 180.5 (CS) ppm. FAB-MS: *m*/*z* = 419 (100) $[M + Na]^+$, 397 (40) $[M + H]^+$. $C_{18}H_{24}N_2O_6S$ (396.46): calcd. C 54.53, H 6.10, N 7.07; found C 54.65, H 6.02, N 6.92.

1-*O*-Acetyl-5-deoxy-2,3-*O*-isopropylidene-5-[*N*′-(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl)thioureido]-β-L-gulofuranose (16): Yield: 275 mg (85%). R_f = 0.47 (EtOAc/petroleum ether, 4:1). $[\alpha]_D^{22}$ = +16 (*c* = 1.0, CH_2Cl_2). UV (CH_2Cl_2) 257 nm (ε_mM 19.1). IR (KBr): $\tilde{\nu}_{max}$ = 3308, 2961, 1750, 1651, 1514, 1260, 1094, 1034 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$, 313 K): δ = 1.33 (s, 3 H, Me), 1.51 (s, 3 H, Me), 2.00 (s, 3 H, MeCO), 2.01 (s, 3 H, MeCO), 2.03 (s, 3 H, MeCO), 2.05 (s, 3 H, MeCO), 2.06 (s, 3 H, MeCO), 3.81 (dd, $J_{5,6b}$ = 4.5, $J_{6a,6b}$ = 11.6 Hz, 1 H, 6b-H), 3.84 (ddd, $J_{5',6b'}$ = 2.5, $J_{5',6a'}$ = 4.4, $J_{4',5'}$ = 9.5 Hz, 1 H, 5′-H), 3.88 (dd, $J_{5,6a}$ = 3.7, $J_{6a,6b}$ = 11.6 Hz, 1 H, 6a-H), 4.16 (dd, $J_{6a',6b'}$ = 12.5, $J_{5',6b'}$ = 2.5 Hz, 1 H, 6b′-H), 4.33 (dd, $J_{5',6a'}$ = 4.4, $J_{6a',6b'}$ = 12.5 Hz, 1 H, 6a′-H), 4.39 (m, 1 H, 4-H), 4.68 (m, 1 H, 5-H), 4.69 (d, $J_{2,3}$ = 5.8 Hz, 1 H, 2-H), 4.80 (dd, $J_{2,3}$ = 5.8, $J_{3,4}$ = 3.5 Hz, 1 H, 3-H), 5.01 (t, $J_{1',2'}$ = $J_{2',3'}$ = 9.5 Hz, 1 H, 2′-H), 5.11 (t, $J_{3',4'}$ = $J_{4',5'}$ = 9.5 Hz, 1 H, 4′-H), 5.33 (t, $J_{2',3'}$ = $J_{3',4'}$ = 9.5 Hz, 1 H, 3′-H), 5.63 (t, $J_{1',N'H}$ = $J_{1',2'}$ = 9.5 Hz, 1 H, 1′-H), 6.16 (s, 1 H, 1-H), 6.80 (br. s, 1 H, N′H), 7.20−7.40 (m, 5 H, Ph), 8.30 (br. s, 1 H, NH) ppm. ^{13}C NMR (75.5 MHz, $CDCl_3$, 313 K): δ = 21.7−22.0 (5 *Me*CO), 24.6, 25.9 (C*Me*$_2$), 55.1 (C-5), 61.5 (C-6, C-6′), 68.4 (C-4′), 70.8 (C-2′), 73.6 (C-5′), 73.8 (C-3′), 79.2 (C-3, C-4), 83.1 (C-1′), 85.3 (C-2), 100.2 (C-1), 113.6 (*C*Me$_2$), 169.2, 169.4, 169.7, 170.5, 171.1 (CO), 183.9 (CS) ppm. FAB-MS: *m*/*z* = 673 (80) $[M + Na]^+$, 651 (20) $[M + H]^+$. $C_{26}H_{38}N_2O_{15}S$ (650.65): calcd. C 47.99, H 5.89, N 4.31; found C 48.11, H 5.69, N 4.29.

1-*O*-Acetyl-5-deoxy-2,3-*O*-isopropylidene-5-[*N*′-(methyl 2,3,4-tri-*O*-acetyl-α-D-glucopyranosid-6-yl)thioureido]-β-L-gulofuranose (17): Yield: 233 mg (75%). R_f = 0.38 (EtOAc/petroleum ether, 3:1). $[\alpha]_D^{22}$ = +133 (*c* = 1.0, CH_2Cl_2). UV (CH_2Cl_2) 250 nm (ε_mM 12.5). IR (KBr): $\tilde{\nu}_{max}$ = 3366, 2984, 1750, 1678, 1516, 1254, 1092, 1040 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$, 323 K): δ = 1.30 (s, 3 H, Me), 1.40 (s, 3 H, Me), 1.95 (s, 3 H, MeCO), 1.97 (s, 3 H, MeCO), 2.00 (s, 3 H, MeCO), 2.02 (s, 3 H, MeCO), 3.73 (m, 1 H, 5′-H), 3.75 (m, 1 H, 6b′-H), 3.84 (dd, $J_{5,6b}$ = 3.5, $J_{6a,6b}$ = 11.5 Hz, 1 H, 6b-H), 3.89 (dd, $J_{5,6a}$ = 4.0, $J_{6a,6b}$ = 11.5 Hz, 1 H, 6a-H), 3.93 (m, 1 H, 6a′-H), 4.36 (dd, $J_{3,4}$ = 3.5, $J_{4,5}$ = 7.5 Hz, 1 H, 4-H), 4.50 (m, 1 H, 5-H), 4.66 (d, $J_{2,3}$ = 5.5 Hz, 1 H, 2-H), 4.78 (dd, $J_{2,3}$ = 5.5, $J_{3,4}$ = 3.5 Hz, 1 H, 3-H), 4.81 (dd, $J_{2',3'}$ = 9.6, $J_{1',2'}$ = 3.7 Hz, 1 H, 2′-H), 4.88 (t, $J_{3',4'}$ = $J_{4',5'}$ = 9.6 Hz, 1 H, 4′-H), 4.90 (d, $J_{1',2'}$ = 3.7 Hz, 1 H, 1′-H), 5.42 (t, $J_{2',3'}$ = $J_{3',4'}$ = 9.6 Hz, 1 H, 3′-H), 6.12 (s, 1 H, 1-H), 6.57 (bd, $J_{N'H,6a'}$ 5.0 Hz, 1 H, N′H), 6.80 (br. s, 1 H, NH) ppm. ^{13}C NMR (125.7 MHz, $CDCl_3$, 313 K): δ = 20.4−20.8 (*Me*CO), 24.7, 26.0 (C*Me*$_2$), 44.9 (C-6′), 55.4 (OMe), 55.5 (C-5), 61.7 (C-6), 68.3 (C-5′), 69.6 (C-4′), 70.1 (C-3′), 71.1 (C-2′), 79.2 (C-3), 80.9 (C-4), 85.3 (C-2), 96.9 (C-1′), 100.3 (C-1), 113.4 (*C*Me$_2$), 169.1−170.1 (CO), 183.9 (CS) ppm. FAB-MS: *m*/*z* = 645 (100) $[M + Na]^+$, 623 (45) $[M + H]^+$. $C_{25}H_{38}O_{14}N_2S$ (622.64): calcd. C 48.22, H 6.15, N 4.50; found C 47.87, H 5.93, N 4.30.

1,6-Di-*O*-acetyl-5-azido-5-deoxy-2,3-*O*-isopropylidene-β-L-gulofuranose (18): Conventional acetylation of **11** (100 mg, 0.35 mmol) and purification of the crude reaction mixture by column chromatography (EtOAc/petroleum ether, 1:3 → 1:2) gave **18**. Yield: 98 mg (85%). R_f = 0.47 (EtOAc/petroleum ether, 1:2). $[\alpha]_D^{22}$ = +55.9 (*c* = 0.85, CH_2Cl_2). IR (KBr): $\tilde{\nu}_{max}$ = 2989, 2104, 1748, 1377, 1231, 1094 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 1.29 (s, 3 H, Me), 1.47 (s, 3 H, Me), 2.06 (s, 3 H, Me), 2.11 (s, 3 H, MeCO), 3.96 (ddd, $J_{5,6a}$ = 3.7, $J_{5,6b}$ = 5.7, $J_{4,5}$ = 9.8 Hz, 1 H, 5-H), 4.09 (dd, $J_{3,4}$ = 3.1, $J_{4,5}$ = 9.8 Hz, 1 H, 4-H), 4.24 (dd, $J_{6a,6b}$ = 12.0, $J_{5,6b}$ = 5.7 Hz, 1 H, 6b-H), 4.30 (dd, $J_{5,6a}$ = 3.7, $J_{6a,6b}$ = 12.0 Hz, 1 H, 6a-H), 4.70 (d, $J_{2,3}$ = 5.8 Hz, 1 H, 2-H), 4.73 (dd, $J_{2,3}$ = 5.8, $J_{3,4}$ = 3.1 Hz, 1 H, 3-H), 6.17 (s, 1 H, 1-H) ppm. ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 20.6, 20.8 (*Me*CO), 24.6, 25.8 (C*Me*$_2$), 59.8 (C-5), 63.1 (C-6), 78.8 (C-3), 81.5 (C-4), 85.2 (C-2), 100.1 (C-1), 113.4 (*C*Me$_2$), 169.0, 170.4 (CO) ppm. FAB-MS: *m*/*z* = 352 (70) $[M + Na]^+$. $C_{13}H_{19}N_3O_7$ (329.31): calcd. C 47.41, H 5.82, N 12.76; found C 47.44, H 5.95, N 12.76.

L-Gulofuranose-Derived Carbodiimides 19−21. General Procedure: A solution of furanose **18** (0.2 g, 0.6 mmol) in toluene (4 mL) was stirred at room temperature under N_2 for 30 min. Then, the corresponding isothiocyanate (0.73 mmol, 1.2 equiv.) and a solution of TPP (0.67 mmol, 1.1 equiv.) in toluene (2 mL) were added successively. The resulting solution was stirred overnight, concentrated under vacuum and the resulting residue was purified by column chromatography using the eluent indicated in each case.

1,6-Di-*O*-acetyl-5-deoxy-2,3-*O*-isopropylidene-5-(*N*′-phenylcarbodiimido)-β-L-gulofuranose (19): Eluent: EtOAc/petroleum ether (1:5 → 1:1). Yield: 136 mg (56%). R_f = 0.25 (EtOAc/petroleum ether, 1:5). $[\alpha]_D^{22}$ = +74.5 (*c* = 1.0, CH_2Cl_2). IR (KBr): $\tilde{\nu}_{max}$ = 2988, 2133, 1744, 1539, 1505, 1379, 1225, 1094 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 1.30 (s, 3 H, Me), 1.50 (s, 3 H, Me), 1.99 (s, 3 H, MeCO), 2.06 (s, 3 H, MeCO), 4.12 (ddd, $J_{5,6b}$ = 3.6, $J_{5,6a}$ = 4.8, $J_{4,5}$ = 8.9 Hz, 1 H, 5-H), 4.18 (dd, $J_{3,4}$ = 3.3, $J_{4,5}$ = 8.9 Hz, 1 H, 4-H), 4.32 (dd, $J_{5,6b}$ = 3.6, $J_{6a,6b}$ = 11.7 Hz, 1 H, 6b-H), 4.35 (dd, $J_{5,6a}$ = 4.8, $J_{6a,6b}$ = 11.7 Hz, 1 H, 6a-H), 4.73 (d, $J_{2,3}$ = 5.8 Hz, 1 H, 2-H), 4.78 (dd, $J_{2,3}$ = 5.8, $J_{3,4}$ = 3.3 Hz, 1 H, 3-H), 6.22 (s, 1 H, 1-H), 7.10−7.30 (m, 5 H, Ph) ppm. ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 20.6, 20.8, (*Me*CO), 24.6, 25.9 (C*Me*$_2$), 56.4 (C-5), 63.8 (C-6), 78.6 (C-3), 82.0 (C-4), 85.4 (C-2), 99.9 (C-1), 113.4 (*C*Me$_2$), 123.9−138.1 (Ph), 139.2 (NCN), 168.9, 170.5 (CO) ppm. FAB-MS: *m*/*z* = 427 (60) $[M + Na]^+$. $C_{20}H_{24}N_2O_7$ (404.41): calcd. C 59.40, H 5.94, N 6.93; found C 59.16, H 6.03, N 6.92.

1,6-Di-*O*-acetyl-5-deoxy-2,3-*O*-isopropylidene-5-[*N*′-(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl)carbodiimido]-β-L-gulofuranose (20): Eluent: EtOAc/petroleum ether (1:3 → 2:1). Yield: 340 mg (86%). R_f = 0.29 (EtOAc/petroleum ether, 1:1). $[\alpha]_D^{22}$ = +60.1 (*c* = 0.8 CH_2Cl_2). IR (KBr): $\tilde{\nu}_{max}$ = 2988, 2141, 1750, 1626, 1377, 1227, 1094 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 1.28 (s, 3 H, Me), 1.45 (s, 3 H, Me), 1.98 (s, 3 H, MeCO), 1.99 (s, 3 H, MeCO), 2.01 (s, 3 H, MeCO), 2.02 (s, 3 H, MeCO), 2.08 (s, 3 H, MeCO), 2.12 (s,

3 H, MeCO), 3.83 (ddd, $J_{5',6b'}$ = 2.5, $J_{5',6a'}$ = 4.7, $J_{4',5'}$ = 9.4 Hz, 1 H, 5′-H), 3.99 (dd, $J_{3,4}$ = 3.3, $J_{4,5}$ = 9.3 Hz, 1 H, 4-H), 4.10 (ddd, $J_{4,5}$ = 9.3, $J_{5,6b}$ = 2.6, $J_{5,6a}$ = 5.2 Hz, 1 H, 5-H), 4.11 (dd, $J_{5',6b'}$ = 2.5, $J_{6a',6b'}$ = 12.4 Hz, 1 H, 6b′-H), 4.12 (dd, $J_{5,6b}$ = 2.6, $J_{6a,6b}$ = 11.8 Hz, 1 H, 6b-H), 4.17 (dd, $J_{5,6a}$ = 5.2, $J_{6a,6b}$ = 11.8 Hz, 1 H, 6a-H), 4.22 (dd, $J_{5',6a'}$ = 4.7, $J_{6a',6b'}$ = 12.4 Hz, 1 H, 6a′-H), 4.71 (dd, $J_{2,3}$ = 5.8, $J_{3,4}$ = 3.3 Hz, 1 H, 3-H), 4.74 (d, $J_{2,3}$ = 5.8 Hz, 1 H, 2-H), 4.96 (dd, $J_{1',2'}$ = 8.7, $J_{2',3'}$ = 9.4 Hz, 1 H, 2′-H), 4.97 (d, $J_{1',2'}$ = 8.7 Hz, 1 H, 1′-H), 5.08 (t, $J_{3',4'}$ = $J_{4',5'}$ = 9.4 Hz, 1 H, 4′-H), 5.25 (t, $J_{2',3'}$ = $J_{3',4'}$ = 9.4 Hz, 1 H, 3′-H), 6.13 (s, 1 H, 1′-H) ppm. ^{13}C NMR (125.7 MHz, $CDCl_3$): δ = 20.6−20.9 (*Me*CO), 24.7, 26.0 (C*Me*$_2$), 55.9 (C-5), 61.9 (C-6′), 63.6 (C-6), 68.1 (C-3′), 72.9 (C-2′), 73.1 (C-4′), 73.4 (C-5′), 78.4 (C-3), 81.5 (C-4), 84.1 (C-1′), 86.3 (C-2), 99.7 (C-1), 113.6 (*C*Me$_2$), 139.6 (NCN), 169.2−170.5 (CO) ppm. FAB-MS: *m*/*z* = 681 (30) [M + Na]$^+$. $C_{28}H_{38}N_2O_{16}$ (658.61): calcd. C 51.06, H 5.82, N 4.25; found C 51.08, H 5.84, N 4.25.

1,6-Di-*O*-acetyl-5-deoxy-2,3-*O*-isopropylidene-5-[*N*′-(methyl 2,3,4-tri-*O*-acetyl-6-deoxy-β-D-glucopyranosid-6-yl)carbodiimido]-β-L-gulofuranose (21): Eluent: EtOAc/petroleum ether (1:1). Yield: 155 mg (41%). R_f = 0.37 (EtOAc/petroleum ether, 1:1). $[\alpha]_D^{22}$ = +109.5 (*c* = 1.0, CH_2Cl_2). IR (KBr): $\tilde{\nu}_{max}$ = 2959, 2137, 1750, 1626, 1373, 1225, 1094 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.26 (s, 3 H, Me), 1.44 (s, 3 H, Me), 1.96 (s, 3 H, MeCO), 1.98 (s, 3 H, MeCO), 2.00 (s, 3 H, MeCO), 2.06 (s, 3 H, MeCO), 2.10 (s, 3 H, MeCO), 3.38 (s, 3 H, OMe), 3.36 (dd, $J_{5',6b'}$ = 5.8, $J_{6a',6b'}$ = 13.7 Hz, 1 H, 6b′-H), 3.40 (dd, $J_{5',6a'}$ = 3.3, $J_{6a',6b'}$ = 13.7 Hz, 1 H, 6a′-H), 3.81 (ddd, $J_{4',5'}$ = 9.5, $J_{5',6a'}$ = 3.3, $J_{5',6b'}$ = 5.8 Hz, 1 H, 5′-H), 3.99 (ddd, $J_{5,6b}$ = 3.3, $J_{5,6a}$ = 5.2, $J_{4,5}$ = 5.8 Hz, 1 H, 5-H), 4.17 (dd, $J_{5,6b}$ = 3.3, $J_{6a,6b}$ = 11.5 Hz, 1 H, 6b-H), 4.21 (dd, $J_{5,6a}$ = 5.2, $J_{6a,6b}$ = 11.5 Hz, 1 H, 6a-H), 4.68 (dd, $J_{3,4}$ = 3.1, $J_{4,5}$ = 5.8 Hz, 1 H, 4-H), 4.69 (d, $J_{2,3}$ = 5.9 Hz, 1 H, 2-H), 4.70 (dd, $J_{2,3}$ = 5.9, $J_{3,4}$ = 3.1 Hz, 1 H, 3-H), 4.83 (dd, $J_{1',2'}$ = 3.6, $J_{2',3'}$ = 10.1 Hz, 1 H, 2′-H), 4.90 (d, $J_{1',2'}$ = 3.6 Hz, 1 H, 1′-H), 4.99 (t, $J_{3',4'}$ = $J_{4',5'}$ = 9.5 Hz, 1 H, 4′-H), 5.42 (dd, $J_{2',3'}$ = 10.1, $J_{3',4'}$ = 9.5 Hz, 1 H, 3′-H), 6.11 (s, 1 H, 1-H) ppm. ^{13}C NMR (125.7 MHz, $CDCl_3$): δ = 20.6−20.8 (5 *Me*CO), 24.8, 26.0 (C*Me*$_2$), 46.7 (C-6′), 55.5 (OMe), 55.8 (C-5), 64.2 (C-6), 68.1 (C-5′), 69.8 (C-4′), 70.2 (C-3′), 70.9 (C-2′), 78.7 (C-3), 82.1 (C-4), 85.5 (C-2), 96.7 (C-1′), 100.1 (C-1), 113.4 (*C*Me$_2$), 140.6 (NCN), 170.7−169.3 (CO) ppm. FAB-MS: *m*/*z* = 631 (80) [M + H]$^+$. $C_{27}H_{38}N_2O_{15}$ (630.60): calcd. C 51.42, H 6.07, N 4.44; found C 51.30, H 5.72, N 4.33.

L-Gulofuranose-Derived Ureas 22−24. General Procedure: TFA (0.1 mL) was added to a solution of the corresponding carbodiimido derivative **19**−**21** (0.6 mmol) in acetone/water (2:1, 13.5 mL). The reaction mixture was stirred at room temperature for 8 h, then the solvents were evaporated under vacuum and the resulting residue was purified by column chromatography using the eluent indicated in each case.

1,6-Di-*O*-acetyl-5-deoxy-2,3-*O*-isopropylidene-5-(*N*′-phenylureido)-β-L-gulofuranose (22): Eluent: EtOAc/petroleum ether (1:1 → 2:1). Yield: 204 mg (81%). R_f = 0.56 (EtOAc/petroleum ether, 3:1). $[\alpha]_D^{22}$ = +21.5 (*c* = 1.0, CH_2Cl_2). IR (KBr): $\tilde{\nu}_{max}$ = 3391, 3364, 1742, 1601, 1559, 1524, 1379, 1227, 1094 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.30 (s, 3 H, Me), 1.40 (s, 3 H, Me), 2.05 (s, 3 H, MeCO), 2.06 (s, 3 H, MeCO), 4.21 (dd, $J_{5,6b}$ = 6.2, $J_{6a,6b}$ = 13.5 Hz, 1 H, 6b-H), 4.23 (dd, $J_{3,4}$ = 3.6, $J_{4,5}$ = 6.2 Hz, 1 H, 4-H), 4.47 (td, $J_{5,6a}$ = 5.2, $J_{4,5}$ = $J_{5,6b}$ = 6.2 Hz, 1 H, 5-H), 4.48 (dd, $J_{5,6a}$ = 5.2, $J_{6a,6b}$ = 13.5 Hz, 1 H, 6a-H), 4.68 (d, $J_{2,3}$ = 5.9 Hz, 1 H, 2-H), 4.79 (dd, $J_{2,3}$ = 5.9, $J_{3,4}$ = 3.6 Hz, 1 H, 3-H), 5.37 (br. s, 1 H, NH), 6.16 (s, 1 H, 1-H), 6.98 (br. s, 1 H, N′H), 7.26−7.33 (m, 5 H, Ph) ppm. ^{13}C NMR (125.7 MHz, $CDCl_3$): δ = 20.8, 20.9 (MeCO), 24.3, 25.7 (C*Me*$_2$), 48.9 (C-5), 64.3 (C-6), 79.4 (C-3), 80.5 (C-4), 84.8 (C-2), 100.0 (C-1), 113.3 (*C*Me$_2$), 120.1−138.6 (Ph), 155.1 (CO urea), 169.4, 171.1 (CO ester) ppm. FAB-MS: *m*/*z* = 445 (100) [M + Na]$^+$. $C_{20}H_{26}N_2O_8$ (422.43): calcd. C 56.87, H 6.16, N 6.63; found C 56.56, H 6.24, N 6.62.

1,6-Di-*O*-acetyl-5-deoxy-2,3-*O*-isopropylidene-5-[*N*′-(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl)ureido]-β-L-gulofuranose (23): Eluent: EtOAc/petroleum ether (1:1) → EtOAc. Yield: 382 mg (94%). R_f = 0.45 (EtOAc/petroleum ether, 3:1). $[\alpha]_D^{22}$ = +24.4 (*c* = 1.0 CH_2Cl_2). IR (KBr): $\tilde{\nu}_{max}$ = 3397, 2959, 1748, 1547, 1377, 1229, 1094 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$, 313 K): δ = 1.28 (s, 3 H, Me), 1.45 (s, 3 H, Me), 1.99 (s, 3 H, MeCO), 2.00 (s, 3 H, MeCO), 2.02 (s, 3 H, MeCO), 2.03 (s, 3 H, MeCO), 2.05 (s, 3 H, MeCO), 2.06 (s, 3 H, MeCO), 3.79 (ddd, $J_{5',6b'}$ = 2.0, $J_{5',6a'}$ = 4.2, $J_{4',5'}$ = 9.5 Hz, 1 H, 5′-H), 4.06 (dd, $J_{6a',6b'}$ = 12.5, $J_{5',6b'}$ = 2.0 Hz, 1 H, 6b′-H), 4.10 (m, 1 H, 4-H), 4.12 (dd, $J_{5,6b}$ = 2.6, $J_{6a,6b}$ = 12.5 Hz, 1 H, 6b-H), 4.31 (dd, $J_{5',6a'}$ = 4.2, $J_{6a',6b'}$ = 12.5 Hz, 1 H, 6a′-H), 4.43 (dd, $J_{5,6a}$ = 4.2, $J_{6a,6b}$ = 12.5 Hz, 1 H, 6a-H), 4.44 (m, 1 H, 5-H), 4.66 (d, $J_{2,3}$ = 5.9 Hz, 1 H, 2-H), 4.74 (dd, $J_{2,3}$ = 5.9, $J_{3,4}$ = 3.7 Hz, 1 H, 3-H), 4.89 (t, $J_{1',2'}$ = $J_{2',3'}$ = 9.5 Hz, 1 H, 2′-H), 5.05 (t, $J_{3',4'}$ = $J_{4',5'}$ = 9.5 Hz, 1 H, 4′-H), 5.11 (d, $J_{NH,5}$ = 8.0 Hz, 1 H, NH), 5.14 (t, $J_{N'H,1'}$ = $J_{1',2'}$ = 9.5 Hz, 1 H, 1′-H), 5.27 (t, $J_{2',3'}$ = $J_{3',4'}$ = 9.5 Hz, 1 H, 3′-H), 5.41 (d, $J_{N'H,1'}$ = 9.5 Hz, 1 H, N′H), 6.11 (s, 1 H, 1-H) ppm. ^{13}C NMR (125.7 MHz, $CDCl_3$): δ = 20.4−20.9 (*Me*CO), 24.5, 25.8 (C*Me*$_2$), 48.8 (C-5), 61.6 (C-6′), 64.2 (C-6), 68.2 (C-4′), 70.4 (C-2′), 72.9 (C-3′), 73.0 (C-5′), 79.2 (C-3), 80.2 (C-1′), 80.5 (C-4), 84.9 (C-2), 100.0 (C-1), 113.4 (*C*Me$_2$), 155.6 (CO urea), 169.1−171.1 (CO ester) ppm. FAB-MS: *m*/*z* = 699 (100) [M + Na]$^+$. $C_{28}H_{40}N_2O_{17}$ (676.62): calcd. C 49.70, H 5.96, N 4.14; found C 49.45, H 5.82, N 4.00.

1,6-Di-*O*-acetyl-5-deoxy-2,3-*O*-isopropylidene-5-[*N*′-(methyl 2,3,4-tri-*O*-acetyl-6-deoxy-β-D-glucopyranosid-6-yl)ureido]-β-L-gulofuranose (24): Eluent: EtOAc/petroleum ether (3:1) → EtOAc. Yield: 269 mg (69%). R_f = 0.49 (EtOAc). $[\alpha]_D^{22}$ = +106.9 (*c* = 1.0, CH_2Cl_2). IR (KBr): $\tilde{\nu}_{max}$ = 3412, 2986, 1748, 1649, 1551, 1375, 1227, 1092 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.23 (s, 3 H, Me), 1.45 (s, 3 H, Me), 1.95 (s, 3 H, MeCO), 1.99 (s, 3 H, MeCO), 2.01 (s, 3 H, MeCO), 2.04 (s, 3 H, MeCO), 2.09 (s, 3 H, MeCO), 3.26 (dd, $J_{5',6b'}$ = 5.9, $J_{6a',6b'}$ = 14.5 Hz, 1 H, 6b′-H), 3.45 (s, 3 H, OMe), 3.46 (dd, $J_{5',6a'}$ = 2.4, $J_{6a',6b'}$ = 14.5 Hz, 1 H, 6a′-H), 3.83 (ddd, $J_{4',5'}$ = 10.1, $J_{5',6a'}$ = 2.4, $J_{5',6b'}$ = 5.9 Hz, 1 H, 5′-H), 4.13 (dd, $J_{3,4}$ = 3.6, $J_{4,5}$ = 6.9 Hz, 1 H, 4-H), 4.16 (dd, $J_{5,6b}$ = 4.2, $J_{6a,6b}$ = 11.5 Hz, 1 H, 6b-H), 4.32 (ddd, $J_{4,5}$ = 6.9, $J_{5,6a}$ = 4.8, $J_{5,6b}$ = 4.2 Hz, 1 H, 5-H), 4.43 (dd, $J_{5,6a}$ = 4.8, $J_{6a,6b}$ = 11.5 Hz, 1 H, 6a-H), 4.64 (d, $J_{2,3}$ = 5.9 Hz, 1 H, 2-H), 4.73 (dd, $J_{2,3}$ = 5.9, $J_{3,4}$ = 3.6 Hz, 1 H, 3-H), 4.81 (dd, $J_{1',2'}$ = 3.7, $J_{2',3'}$ = 10.2 Hz, 1 H, 2′-H), 4.87 (dd, $J_{3',4'}$ = 9.5, $J_{4',5'}$ = 10.1 Hz, 1 H, 4′-H), 4.88 (d, $J_{1',2'}$ = 3.7 Hz, 1 H, 1′-H), 4.95 (m, 2 H, NH, N′H), 5.43 (dd, $J_{2',3'}$ = 10.2, $J_{3',4'}$ = 9.5 Hz, 1 H, 3′-H), 6.12 (s, 1 H, 1-H) ppm. ^{13}C NMR (125.7 MHz, $CDCl_3$): δ = 20.7−21.0 (*Me*CO), 24.6, 26.0 (C*Me*$_2$), 40.3 (C-6′), 49.3 (C-5), 55.4 (OMe), 64.5 (C-6), 68.3 (C-5′), 69.5 (C-4′), 70.0 (C-3′), 71.0 (C-2′), 79.4 (C-3), 80.9 (C-4), 84.9 (C-2), 96.5 (C-1′), 100.2 (C-1), 113.4 (*C*Me$_2$), 157.4 (CO urea), 169.4−171.2 (CO ester) ppm. FAB-MS: *m*/*z* = 671 (100) [M + Na]$^+$. $C_{27}H_{40}N_2O_{16}$ (648.61): calcd. C 49.99, H 6.22, N 4.32; found C 50.29, H 6.26, N 4.27.

***N*-Thiocarbamoyl- and *N*-Carbamoyl-6-oxa-(−)-calystegine B_4 Derivatives 25−27 and 28−30. General Procedure:** Thioureas **15**−**17** and ureas **22**−**24** (0.5 mmol) were conventionally deacetylated by treatment with methanolic NaOMe (1 M, 0.1 equiv. per mol of acetate). The resulting product was dissolved in a mixture of TFA/H_2O (9:1, 3 mL) and stirred at 0 °C for 15 min until disappearance of

the starting material (TLC). The solvent was removed under vacuum, the residue was coevaporated several times with water and finally the aqueous solution was neutralized by treatment with Amberlite IRA 68 (OH^-) ion-exchange resin and freeze dried. The resulting residue was purified by column chromatography with the eluent indicated in each case. The corresponding 6-oxa-(−)-calystegine B_4 derivatives **25**−**27** and **28**−**30** were isolated as white foams after freeze-drying of water solutions.

(1*S*,2*R*,3*S*,4*S*,5*R*)-2,3,4-Trihydroxy-6-oxa-*N*-(*N*′-phenylthiocarbamoyl)-*nor*-tropane (25): Eluent: CH_2Cl_2/MeOH (20:1 → 9:1). Yield: 104 mg (70%). R_f = 0.51 (CH_2Cl_2/MeOH, 4:1). $[\alpha]_D^{22}$ = +38.4 (*c* = 1.0, H_2O). UV (MeOH): 250 nm (ε_mM 20.9). ^{1}H NMR (500 MHz, D_2O, 313 K): δ = 3.95 (dd, $J_{1,7b}$ = 4.5, $J_{7a,7b}$ = 8.5 Hz, 1 H, 7b-H), 3.99 (dd, $J_{3,4}$ = 4.8, $J_{2,3}$ = 9.2 Hz, 1 H, 3-H), 4.14 (dd, $J_{1,2}$ = 4.5 Hz, 1 H, 2-H), 4.26 (d, $J_{7a,7b}$ = 8.5 Hz, 1 H, 7a-H), 4.30 (dd, $J_{3,4}$ = 4.8, $J_{4,5}$ = 3.7 Hz, 1 H, 4-H), 5.26 (t, $J_{1,2}$ = $J_{1,7b}$ = 4.5 Hz, 1 H, 1-H), 6.35 (d, $J_{4,5}$ = 3.7 Hz, 1 H, 5-H), 7.50−7.60 (m, 5 H, Ph) ppm. ^{13}C NMR (125.7 MHz, D_2O, 313 K): δ = 61.7 (C-1), 66.6 (C-7), 72.2 (C-2), 72.3 (C-3), 72.8 (C-4), 89.1 (C-5), 129.6−141.5 (Ph), 182.7 (CS) ppm. FAB-MS: *m*/*z* = 297 (100) [M + H]$^+$. $C_{13}H_{16}N_2O_4S$ (296.34): calcd. C 52.69, H 5.44, N 9.45; found C 52.65, H 5.45, N 9.44.

(1*S*,2*R*,3*S*,4*S*,5*R*)-*N*-[*N*′-(β-D-Glucopyranosyl)thiocarbamoyl]-2,3,4-trihydroxy-6-oxa-*nor*-tropane (26): Eluent: MeCN/H_2O (7:1). Yield: 124 mg (65%). R_f = 0.52 (MeCN/H_2O/NH_4OH, 6:3:1). $[\alpha]_D^{22}$ = −23.7 (*c* = 0.97, MeOH). UV (MeOH): 241 nm (ε_mM 19.1). ^{1}H NMR (500 MHz, D_2O, 313 K): δ = 3.44 (dd, $J_{1',2'}$ = 6.5, $J_{2',3'}$ = 9.1 Hz, 1 H, 2′-H), 3.53 (m, 1 H, 5′-H), 3.55 (t, $J_{4',5'}$ = $J_{3',4'}$ = 9.1 Hz, 1 H, 4′-H), 3.57 (t, $J_{2',3'}$ = $J_{3',4'}$ = 9.1 Hz, 1 H, 3′-H), 3.74 (dd, $J_{5',6b'}$ = 5.2, $J_{6a',6b'}$ = 12.5 Hz, 1 H, 6b′-H), 3.77 (dd, $J_{1,7b}$ = 4.3, $J_{7a,7b}$ = 8.5 Hz, 1 H, 7b-H), 3.81 (dd, $J_{3,4}$ = 4.8, $J_{2,3}$ = 9.2 Hz, 1 H, 3-H), 3.87 (dd, $J_{5',6b'}$ = 2.1, $J_{6a',6b'}$ = 12.5 Hz, 1 H, 6a′-H), 3.93 (dd, $J_{1,2}$ = 4.3, $J_{2,3}$ = 9.2 Hz, 1 H, 2-H), 4.08 (d, $J_{7a,7b}$ = 8.5 Hz, 1 H, 7a-H), 4.11 (dd, $J_{3,4}$ = 4.8, $J_{4,5}$ = 3.6 Hz, 1 H, 4-H), 5.10 (t, $J_{1,2}$ = $J_{1,7b}$ = 4.3 Hz, 1 H, 1-H), 5.66 (d, $J_{1',2'}$ = 6.5 Hz, 1 H, 1′-H), 6.24 (d, $J_{4,5}$ = 3.6 Hz, 1 H, 5-H) ppm. ^{13}C NMR (75.5 MHz, D_2O, 313 K): δ = 58.9 (C-1), 60.6 (C-6′), 64.1 (C-7), 69.3 (C-4′), 69.4 (C-4), 70.1 (C-2), 70.6 (C-3), 71.9 (C-2′), 76.6 (C-3′), 77.6 (C-5′), 84.9 (C-1′), 86.3 (C-5), 184 (CS) ppm. FAB-MS: *m*/*z* = 405 (30) [M + Na]$^+$. $C_{13}H_{22}N_2O_9S$ (280.28): calcd. C 40.83, H 5.80, N 7.33; found C 40.68, H 5.86, N 7.24.

(1*S*,2*R*,3*S*,4*S*,5*R*)-2,3,4-Trihydroxy-*N*-[*N*′-(methyl α-D-glucopyranosid-6-yl)thiocarbamoyl]-6-oxa-*nor*-tropane (27): Eluent: EtOAc/EtOH (20:1 → 3:1). Yield: 141 mg (71%). R_f = 0.54 (EtOAc/EtOH, 1:1). $[\alpha]_D^{22}$ = +83.7 (*c* = 1.0, H_2O). UV (MeOH): 249 nm (ε_mM 12.9). ^{1}H NMR (500 MHz, D_2O, 313 K): δ = 3.30 (t, $J_{4',5'}$ = $J_{3',4'}$ = 9.5 Hz, 1 H, 4′-H), 3.37 (s, 3 H, OMe), 3.41 (dd, $J_{1',2'}$ = 4.0, $J_{2',3'}$ = 9.5 Hz, 1 H, 2′-H), 3.65 (t, $J_{2',3'}$ = $J_{3',4'}$ = 9.5 Hz, 1 H, 3′-H), 3.69 (ddd, $J_{2,7b}$ = 1.0, $J_{1,7b}$ = 4.5, $J_{7a,7b}$ = 8.5 Hz, 1 H, 7b-H), 3.79 (dd, $J_{3,4}$ = 5.0, $J_{2,3}$ = 9.0 Hz, 1 H, 3-H), 3.80 (dd, $J_{5',6b'}$ = 8.0, $J_{6a',6b'}$ = 13.0 Hz, 1 H, 6b′-H), 3.83 (ddd, $J_{4',5'}$ = 9.5, $J_{5',6a'}$ = 2.5, $J_{5',6b'}$ = 8.0 Hz, 1 H, 5′-H), 3.88 (ddd, $J_{1,2}$ = 4.3, $J_{2,3}$ = 9.0, $J_{2,7b}$ = 1.0 Hz, 1 H, 2-H), 4.06 (d, $J_{7a,7b}$ = 8.5 Hz, 1 H, 7a-H), 4.12 (dd, $J_{4,5}$ = 3.5, $J_{3,4}$ = 5.0 Hz, 1 H, 4-H), 4.13 (dd, $J_{5',6a'}$ = 2.5, $J_{6a',6b'}$ = 13.0 Hz, 1 H, 6a′-H), 4.78 (d, $J_{1',2'}$ = 4.0 Hz, 1 H, 1′-H), 5.06 (t, $J_{1,2}$ = $J_{1,7b}$ = 4.3 Hz, 1 H, 1-H), 6.09 (d, $J_{4,5}$ = 3.5 Hz, 1 H, 5-H) ppm. ^{13}C NMR (125.7 MHz, D_2O, 313 K): δ = 46.4 (C-6′), 55.1 (OMe), 58.9 (C-1), 63.8 (C-7), 69.8 (C-2), 69.9 (C-5′), 70.3 (C-3), 70.5 (C-4), 71.5 (C-2′), 71.8 (C-4′), 73.1 (C-3′), 86.4 (C-5), 99.3 (C-1′), 180.1 (CS) ppm. FAB-MS: *m*/*z* = 419 (80) [M + Na]$^+$, 397 (75) [M + H]$^+$. $C_{14}H_{24}N_2O_9S$ (396.41): calcd. C 42.42, H 6.10, N 7.07; found C 42.23, H 6.06, N 7.06.

(1*S*,2*R*,3*S*,4*S*,5*R*)-2,3,4-Trihydroxy-6-oxa-*N*-(*N*′-phenylcarbamoyl)-*nor*-tropane (28): Eluent: CH_2Cl_2/MeOH (7:1 → 3:1). Yield: 122 mg (87%). R_f = 0.44 (EtOAc/EtOH/H_2O, 45:5:3). $[\alpha]_D^{22}$ = +13.5 (*c* = 1.0, MeOH). ^{1}H NMR (500 MHz, D_2O): δ = 3.53 (ddd, $J_{2,7b}$ = 0.6, $J_{1,7b}$ = 4.3, $J_{7a,7b}$ = 8.4 Hz, 1 H, 7b-H), 3.62 (dd, $J_{3,4}$ = 4.8, $J_{2,3}$ = 9.3 Hz, 1 H, 3-H), 3.81 (dd, $J_{1,2}$ = 4.3, $J_{2,3}$ = 9.3 Hz, 1 H, 2-H), 3.91 (dd, $J_{3,4}$ = 4.8, $J_{4,5}$ = 3.7 Hz, 1 H, 4-H), 4.49 (t, $J_{1,2}$ = $J_{1,7b}$ = 4.3 Hz, 1 H, 1-H), 5.70 (d, $J_{4,5}$ = 3.7 Hz, 1 H, 5-H), 7.20−7.40 (m, 5 H, Ph) ppm. ^{13}C NMR (125.7 MHz, D_2O): δ = 56.6 (C-1), 63.6 (C-7), 69.6 (C-4), 70.1 (C-3), 70.2 (C-2), 85.1 (C-5), 122.7−137.2 (Ph), 156.8 (CO urea) ppm. FAB-MS: *m*/*z* = 281 (70) [M + H]$^+$. $C_{13}H_{16}N_2O_5$ (280.28): calcd. C 55.71, H 5.75, N 9.99; found C 55.60, H 5.60, N 9.84.

(1*S*,2*R*,3*S*,4*S*,5*R*)-*N*-[*N*′-(β-D-Glucopyranosyl)carbamoyl]-2,3,4-trihydroxy-6-oxa-*nor*-tropane (29): Yield: 137 mg (75%). Eluent: MeCN/H_2O (7:1 → 4:1). R_f = 0.38 (MeCN/H_2O/NH_4OH, 6:3:1). $[\alpha]_D^{22}$ = −11.0 (*c* = 1.0, H_2O). ^{1}H NMR (500 MHz, D_2O): δ = 3.38 (dd, $J_{3',4'}$ = 9.1, $J_{4',5'}$ = 9.5 Hz, 1 H, 4′-H), 3.42 (t, $J_{1',2'}$ = $J_{2',3'}$ = 9.1 Hz, 1 H, 2′-H), 3.45 (ddd, $J_{5',6a'}$ = 2.2, $J_{5',6b'}$ = 5.4 Hz, 1 H, 5′-H), 3.50 (t, $J_{2',3'}$ = $J_{3',4'}$ = 9.1 Hz, 1 H, 3′-H), 3.58 (dd, $J_{1,7b}$ = 4.3, $J_{7a,7b}$ = 8.5 Hz, 1 H, 7b-H), 3.67 (dd, $J_{3,4}$ = 4.8, $J_{2,3}$ = 9.2 Hz, 1 H, 3-H), 3.68 (dd, $J_{5',6b'}$ = 5.4, $J_{6a',6b'}$ = 12.4 Hz, 1 H, 6b′-H), 3.83 (dd, $J_{5',6a'}$ = 2.2, $J_{6a',6b'}$ = 12.4 Hz, 1 H, 6a′-H), 3.84 (dd, $J_{1,2}$ = 4.3, $J_{2,3}$ = 9.2 Hz, 1 H, 2-H), 3.96 (d, $J_{7a,7b}$ = 8.5 Hz, 1 H, 7a-H), 3.97 (dd, $J_{3,4}$ = 4.8, $J_{4,5}$ = 3.7 Hz, 1 H, 4-H), 4.51 (t, 1 H, 1-H), 4.87 (d, $J_{1,2}$ = $J_{1,7b}$ = 4.3 Hz, 1 H, 1′-H), 5.75 (d, $J_{4,5}$ = 3.7 Hz, 1 H, 5-H) ppm. ^{13}C NMR (125.7 MHz, D_2O): δ = 57.5 (C-1), 61.7 (C-6′), 64.9 (C-7), 70.4 (C-4′), 70.7 (C-4), 71.2 (C-3, C-2), 72.7 (C-2′), 77.6 (C-3′), 78.5 (C-5′), 82.5 (C-1′), 86.4 (C-5), 158.9 (CO urea) ppm. FAB-MS: *m*/*z* = 389 (100) [M + Na]$^+$. $C_{13}H_{22}N_2O_{10}$ (366.32): calcd. C 42.68, H 6.05, N 7.65; found C 42.92, H 6.22, N 7.67.

(1*S*,2*R*,3*S*,4*S*,5*R*)-2,3,4-Trihydroxy-*N*-[*N*′-(methyl 6-deoxy-α-D-glucopyranosid-6-yl)carbamoyl]-6-oxa-*nor*-tropane (30): Eluent: MeCN/H_2O (7:1 → 4:1). Yield: 162 mg (85%). R_f = 0.51 (MeCN/H_2O/NH_4OH, 6:3:1). $[\alpha]_D^{22}$ = +62 (*c* = 1.0, H_2O). ^{1}H NMR (500 MHz, D_2O): δ = 3.30 (t, $J_{3',4'}$ = $J_{4',5'}$ = 9.5 Hz, 1 H, 4′-H), 3.40 (s, 3 H, OMe), 3.42 (dd, $J_{5',6b'}$ = 7.8, $J_{6a',6b'}$ = 14.5 Hz, 1 H, 6b′-H), 3.55 (dd, $J_{1,7b}$ = 4.2, $J_{7a,7b}$ = 8.5 Hz, 1 H, 7b-H), 3.57 (dd, $J_{1',2'}$ = 3.8, $J_{2',3'}$ = 9.9 Hz, 1 H, 2′-H), 3.63 (ddd, $J_{4',5'}$ = 9.5, $J_{5',6a'}$ = 2.7, $J_{5',6b'}$ = 7.8 Hz, 1 H, 5′-H), 3.64 (dd, $J_{5',6a'}$ = 2.7, $J_{6a',6b'}$ = 14.5 Hz, 1 H, 6a′-H), 3.65 (dd, $J_{2',3'}$ = 9.9, $J_{3',4'}$ = 9.5 Hz, 1 H, 3′-H), 3.71 (dd, $J_{3,4}$ = 4.9, $J_{2,3}$ = 9.2 Hz, 1 H, 3-H), 3.87 (dd, $J_{1,2}$ = 4.2, $J_{2,3}$ = 9.2 Hz, 1 H, 2-H), 4.00 (d, $J_{7a,7b}$ = 8.5 Hz, 1 H, 7a-H), 4.02 (dd, $J_{3,4}$ = 4.9, $J_{4,5}$ = 3.7 Hz, 1 H, 4-H), 4.52 (t, $J_{1,2}$ = $J_{1,7b}$ = 4.2 Hz, 1 H, 1-H), 4.79 (d, $J_{1',2'}$ = 3.8 Hz, 1 H, 1′-H), 5.73 (d, $J_{4,5}$ = 3.7 Hz, 1 H, 5-H) ppm. ^{13}C NMR (125.7 MHz, D_2O): δ = 41.5 (C-6′), 55.3 (OMe), 56.9 (C-1), 63.8 (C-7), 69.9 (C-5′), 70.6 (C-2), 70.7 (C-3), 70.8 (C-4), 71.8 (C-2′, C-4′), 73.4 (C-3′), 86.5 (C-5), 99.6 (C-1′), 159.3 (CO urea) ppm. FAB-MS: *m*/*z* = 403 (100) [M + Na]$^+$. $C_{14}H_{24}N_2O_{10}$ (380.35): calcd. C 44.21, H 6.36, N 7.36; found C 44.26, H 6.37, N 7.36.

3-*O*-Acetyl-1,2-*O*-isopropylidene-6-*O*-trityl-α-D-galactofuranose (32): Trityl chloride (1.9 g, 6.8 mmol, 1.5 equiv.) was added to a solution of 3-*O*-acetyl-1,2-*O*-isopropylidene-α-D-galactofuranose (**31**) (1.25 g, 4.59 mmol) in pyridine (8 mL),. The reaction mixture was stirred at room temperature for 24 h, then poured into ice-water (80 mL) and decanted. A solution of the solid in toluene (20 mL) was washed with iced aqueous 10% acetic acid (10 mL), aqueous saturated $NaHCO_3$ (10 mL), the organic phase was dried ($MgSO_4$), and concentrated. The resulting residue was purified by column chromatography using EtOAc/petroleum ether (1:3). Yield:

1.7 g (74%). R_f = 0.67 (EtOAc/petroleum ether, 1:1). $[\alpha]_D^{22}$ = −3.0 (c = 1.0, CH_2Cl_2). IR (KBr): $\tilde{\nu}_{max}$ = 3503, 3059, 2988, 1746, 1377, 1229, 1092 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 1.32 (s, 3 H, Me), 1.61 (s, 3 H, Me), 2.05 (s, 3 H, MeCO), 3.23 (dd, $J_{5,6b}$ = 5.6, $J_{6a,6b}$ = 9.8 Hz, 1 H, 6b-H), 3.28 (dd, $J_{5,6a}$ = 5.4, $J_{6a,6b}$ = 9.8 Hz, 1 H, 6a-H), 3.98 (ddd, $J_{4,5}$ = 6.7, $J_{5,6a}$ = 5.4, $J_{5,6b}$ = 5.6 Hz, 1 H, 5-H), 4.23 (dd, $J_{3,4}$ = 2.4, $J_{4,5}$ = 6.7 Hz, 1 H, 4-H), 4.59 (d, $J_{1,2}$ = 4.1 Hz, 1 H, 2-H), 5.12 (d, $J_{3,4}$ = 2.4 Hz, 1 H, 3-H), 5.91 (d, $J_{1,2}$ = 4.1 Hz, 1 H, 1-H), 7.23−7.46 (m, 15 H, 3 Ph) ppm. ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 20.6 (*Me*CO), 25.9, 26.5 (C*Me*$_2$), 64.8 (C-6), 69.6 (C-5), 77.9 (C-3), 84.9 (C-2), 86.1 (C-4), 87.2 (*C*Ph_3), 105.3 (C-1), 112.8 (*C*Me_2), 126.9−143.7 (Ph), 170.0 (CO) ppm. FAB-MS: m/z = 527 (100) $[M + Na]^+$. $C_{30}H_{32}O_7$ (504.57): calcd. C 71.41, H 6.39; found C 71.60, H 6.41.

3-*O*-Acetyl-5-azido-5-deoxy-1,2-*O*-isopropylidene-6-*O*-trityl-β-L-altrofuranose (33): Pyridine (0.4 mL) and trifluoromethanesulfonic anhydride (0.48 mL, 2.9 mmol) were added to a solution of **32** (1.0 g, 2.0 mmol) in CH_2Cl_2 (9 mL) at −25 °C under N_2. The reaction mixture was allowed to reach room temperature and stirred for 20 min, then diluted with CH_2Cl_2 (10 mL), washed with saturated aqueous $NaHCO_3$ (8 mL), dried ($MgSO_4$), and concentrated. The resulting crude triflate ester was dissolved in DMF (8 mL), NaN_3 (1.40 g, 14 mmol, 7 equiv.) was added and the reaction mixture was stirred at room temperature for 12 h. The solvent was eliminated under reduced pressure and the resulting residue was purified by column chromatography using EtOAc/petroleum ether (1:4). Yield: 0.63 g (60%). R_f = 0.65 (EtOAc/petroleum ether, 1:2). $[\alpha]_D^{22}$ = −17.0 (c = 1.0, CH_2Cl_2). IR (KBr): $\tilde{\nu}_{max}$ = 2959, 2099, 1746, 1348, 1227, 1094 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 1.31 (s, 3 H, Me), 1.51 (s, 3 H, Me), 2.07 (s, 3 H, MeCO), 3.30 (dd, $J_{5,6b}$ = 7.3, $J_{6a,6b}$ = 9.8 Hz, 1 H, 6b-H), 3.56 (dd, $J_{5,6a}$ = 2.8, $J_{6a,6b}$ = 9.8 Hz, 1 H, 6a-H), 3.89 (ddd, $J_{4,5}$ = 9.9, $J_{5,6a}$ = 2.8, $J_{5,6b}$ = 7.3 Hz, 1 H, 5-H), 3.98 (dd, $J_{3,4}$ = 1.4, $J_{4,5}$ = 9.9 Hz, 1 H, 4-H), 4.53 (d, $J_{1,2}$ = 3.8 Hz, 1 H, 2-H), 5.64 (d, $J_{3,4}$ = 1.4 Hz, 1 H, 3-H), 5.85 (d, $J_{1,2}$ = 3.8 Hz, 1 H, 1-H), 7.24−7.49 (m, 15 H, 3 Ph) ppm. ^{13}C NMR (125.7 MHz, $CDCl_3$): δ = 20.7 (*Me*CO), 25.7, 26.6 (C*Me*$_2$), 62.3 (C-5), 63.5 (C-6), 77.6 (C-3), 83.4 (C-2), 84.4 (C-4), 87.2 (*C*Ph_3), 105.9 (C-1), 112.8 (*C*Me_2), 127.0−143.6 (Ph), 169.5 (CO) ppm. FAB-MS: m/z = 552 (100) $[M + Na]^+$. $C_{30}H_{31}N_3O_6$ (529.58): calcd. C 68.04, H 5.90, N 7.94; found C 67.96, H 5.73, N 7.91.

3-*O*-Acetyl-5-azido-5-deoxy-1,2-*O*-isopropylidene-β-L-altrofuranose (34): $BF_3{\cdot}Et_2O$ (391 mL) and MeOH (1 mL) were added to a solution of **33** (1.5 g, 2.8 mmol) in CH_2Cl_2 (18 mL) at 0 °C under Ar. The reaction mixture was allowed to reach room temperature and stirred for 2 h, then washed with saturated aqueous $NaHCO_3$ (2 × 10 mL), dried ($MgSO_4$), and concentrated. The resulting residue was purified by column chromatography (EtOAc/petroleum ether, 1:4 → 1:1). Yield: 604 mg (75%). R_f = 0.30 (EtOAc/petroleum ether, 1:2). $[\alpha]_D^{22}$ = −5.0 (c = 1.0, CH_2Cl_2). IR (KBr): $\tilde{\nu}_{max}$ = 3480, 2939, 2103, 1744, 1379, 1260, 1094 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 1.31 (s, 3 H, Me), 1.55 (s, 3 H, Me), 2.10 (s, 3 H, MeCO), 3.76 (ddd, $J_{5,6a}$ = 4.1, $J_{5,6b}$ = 5.2, $J_{4,5}$ = 9.7 Hz, 1 H, 5-H), 3.84 (dd, $J_{5,6b}$ = 5.2, $J_{6a,6b}$ = 11.5 Hz, 1 H, 6b-H), 3.99 (dd, $J_{5,6a}$ = 4.1, $J_{6a,6b}$ = 11.5 Hz, 1 H, 6a-H), 4.04 (dd, $J_{3,4}$ = 1.4, $J_{4,5}$ = 9.7 Hz, 1 H, 4-H), 4.59 (d, $J_{1,2}$ = 3.8 Hz, 1 H, 2-H), 5.30 (d, $J_{3,4}$ = 1.4 Hz, 1 H, 3-H), 5.92 (d, $J_{1,2}$ = 3.8 Hz, 1 H, 1-H) ppm. ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 20.7 (*Me*CO), 25.4, 26.4 (C*Me*$_2$), 62.7 (C-5), 62.9 (C-6), 77.4 (C-3), 84.1 (C-2), 84.4 (C-4), 87.2 (*C*Ph_3), 105.9 (C-1), 112.9 (*C*Me_2), 169.8 (CO) ppm. FAB-MS: m/z = 310 (40) $[M + Na]^+$. $C_{11}H_{17}N_3O_6$ (287.27): calcd. C 45.99, H 5.96, N 14.63; found C 45.90, H 6.02, N 14.63.

5-Azido-5-deoxy-1,2-*O*-isopropylidene-β-L-altrofuranose (35): Conventional deacetylation of **34** (0.3 g, 1.07 mmol) gave **33**. Yield: 250 mg (95%). R_f = 0.43 (EtOAc/petroleum ether, 2:1). $[\alpha]_D^{22}$ = −11.0 (c = 1.0, MeOH). IR (KBr): $\tilde{\nu}_{max}$ = 3445, 2988, 2101, 1382, 1092 cm^{-1}. ^1H NMR (300 MHz, CD_3OD): δ = 1.29 (s, 3 H, Me), 1.49 (s, 3 H, Me), 3.63 (dd, $J_{5,6b}$ = 6.9, $J_{6a,6b}$ = 11.1 Hz, 1 H, 6b-H), 3.67 (ddd, $J_{4,5}$ = 9.4, $J_{5,6a}$ = 2.1, $J_{5,6b}$ = 6.9 Hz, 1 H, 5-H), 3.79 (dd, $J_{3,4}$ = 1.4, $J_{4,5}$ = 9.4 Hz, 1 H, 4-H), 3.95 (dd, $J_{5,6a}$ = 2.1, $J_{6a,6b}$ = 11.1 Hz, 1 H, 6a-H), 4.28 (d, $J_{3,4}$ = 1.4 Hz, 1 H, 3-H), 4.52 (d, $J_{1,2}$ = 3.8 Hz, 1 H, 2-H), 5.88 (d, $J_{1,2}$ = 3.8 Hz, 1 H, 1-H) ppm. ^{13}C NMR (75.5 MHz, CD_3OD): δ = 25.9, 27.0 (C*Me*$_2$), 63.2 (C-5), 65.6 (C-6), 76.9 (C-3), 87.5 (C-2), 88.0 (C-4), 107.9 (C-1), 113.5 (*C*Me_2) ppm. FAB-MS: m/z = 268 (50) $[M + Na]^+$. $C_9H_{15}N_3O_5$ (245.23): calcd. C 44.08, H 6.16, N 17.13; found C 44.07, H 6.03, N 17.12.

5-Amino-5-deoxy-1,2-*O*-isopropylidene-β-L-altrofuranose (36): A solution of **35** (1.07 mmol) in MeOH (10 mL) was hydrogenated at atmospheric pressure for 2 h using 10% Pd/C (107 mg) as catalyst. The suspension was filtered through Celite and concentrated to give **34** as a hygroscopic solid which was used in the next step without further purification.

5-Deoxy-1,2-*O*-isopropylidene-5-(*N*′-phenylthioureido)-β-L-altrofuranose (37): Phenyl isothiocyanate was added to a solution of the crude amine **36** (1.08 mmol) in pyridine (1 mL). The reaction mixture was stirred at room temperature for 12 h, then coevaporated several times with toluene under vacuum. The resulting residue was purified by column chromatography using CH_2Cl_2/MeOH, 30:1. Yield: 287 mg (75%). R_f = 0.58 (CH_2Cl_2/MeOH, 20:1). $[\alpha]_D^{22}$ = +27.0 (c = 1.0, CH_2Cl_2). UV (CH_2Cl_2): 269 nm (ε_{mM} 12.7). IR (KBr): $\tilde{\nu}_{max}$ = 3362, 3065, 2990, 1537, 1379, 1092 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$, 313 K): δ = 1.31 (s, 3 H, Me), 1.52 (s, 3 H, Me), 3.80 (bd, $J_{6a,6b}$ = 11.4 Hz, 1 H, 6b-H), 3.99 (dd, $J_{5,6a}$ = 2.6, $J_{6a,6b}$ = 11.4 Hz, 1 H, 6a-H), 4.01 (dd, $J_{3,4}$ = 3.5, $J_{4,5}$ = 7.5 Hz, 1 H, 4-H), 4.52 (d, $J_{3,4}$ = 3.5 Hz, 1 H, 3-H), 4.58 (d, $J_{1,2}$ = 3.8 Hz, 1 H, 2-H), 4.78 (m, 1 H, 5-H), 5.85 (d, $J_{1,2}$ = 3.8 Hz, 1 H, 1-H), 6.95 (br. s, 1 H, NH), 7.20−7.40 (m, 5 H, Ph), 8.40 (br. s, 1 H, N′H) ppm. ^{13}C NMR (75.5 MHz, $CDCl_3$, 313 K): δ = 26.2, 26.9, (C*Me*$_2$), 56.9 (C-5), 61.4 (C-6), 76.2 (C-3), 86.2 (C-4), 87.3 (C-2), 105.1 (C-1), 113.4 (*C*Me_2), 124.4, 126.6, 129.6 (Ph), 180.6 (CS) ppm. FAB-MS: m/z = 377 (100) $[M + Na]^+$. $C_{16}H_{22}N_2O_5S$ (354.42): calcd. C 54.22, H 6.25, N 7.90; found C 54.05, H 6.38, N 7.81.

3,6-Di-*O*-acetyl-5-azido-5-deoxy-1,2-*O*-isopropylidene-β-L-altrofuranose (38): Conventional acetylation of **34** (245 mg, 0.86 mmol) and purification by column chromatography using EtOAc/petroleum ether (1:2) as an eluent gave **36**. Yield: 235 mg (83%). R_f = 0.50 (EtOAc/petroleum ether, 1:2). $[\alpha]_D^{22}$ = −7.0 (c = 0.99, CH_2Cl_2). IR (KBr): $\tilde{\nu}_{max}$ = 2990, 2104, 1748, 1375, 1227, 1032 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 1.29 (s, 3 H, Me), 1.51 (s, 3 H, Me), 2.07 (s, 3 H, MeCO), 2.08 (s, 3 H, MeCO), 3.89 (ddd, $J_{5,6a}$ = 2.8, $J_{5,6b}$ = 6.9, $J_{4,5}$ = 10.1 Hz, 1 H, 5-H), 3.96 (dd, $J_{3,4}$ = 1.4, $J_{4,5}$ = 10.1 Hz, 1 H, 4-H), 4.20 (dd, $J_{5,6b}$ = 6.9, $J_{6a,6b}$ = 11.7 Hz, 1 H, 6b-H), 4.53 (dd, $J_{5,6a}$ = 2.8, $J_{6a,6b}$ = 11.7 Hz, 1 H, 6a-H), 4.55 (d, $J_{1,2}$ = 3.8 Hz, 1 H, 2-H), 5.29 (d, $J_{3,4}$ = 1.4 Hz, 1 H, 3-H), 5.90 (d, $J_{1,2}$ = 3.8 Hz, 1 H, 1-H) ppm. ^{13}C NMR (125.7 MHz, $CDCl_3$): δ = 20.6, 20.7 (*Me*CO), 25.5, 26.5 (C*Me*$_2$), 60.4 (C-5), 63.9 (C-6), 77.4 (C-3), 83.5 (C-2), 84.1 (C-4), 106.2 (C-1), 112.8 (*C*Me_2), 169.5, 170.3 (CO) ppm. FAB-MS: m/z = 314 (100) $[M - Me]^+$. $C_{13}H_{19}N_3O_7$ (329.31): calcd. C 47.41, H 5.81, N 12.76; found C 47.31, H 5.63, N 12.61.

3,6-Di-*O*-acetyl-5-deoxy-1,2-*O*-isopropylidene-5-(*N*′-phenylcarbodiimido)-β-L-altrofuranose (39): Compound **39** was obtained

from azide **38** (235 mg, 0.71 mmol) by an aza-Wittig-type reaction with phenyl isothiocyanate (115 mg, 0.85 mmol, 1.2 equiv.), and TPP (205 mg, 0.78 mmol, 1.1 equiv.) in toluene (2 mL), following the procedure described above for the preparation of L-gulofuranose-derived carbodiimides. Purification was effected by column chromatography using EtOAc/petroleum ether (1:5 → 1:3) as an eluent. Yield: 129 mg (45%). R_f = 0.36 (EtOAc/petroleum ether, 1:3). $[\alpha]_D^{22}$ = −12.3 (*c* = 1.0, CH_2Cl_2). IR (KBr): $\tilde{\nu}_{max}$ = 3061, 2988, 2137, 1748, 1593, 1501, 1375, 1225, 1101 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 1.29 (s, 3 H, Me), 1.53 (s, 3 H, Me), 1.91 (s, 3 H, MeCO), 2.08 (s, 3 H, MeCO), 4.07 (ddd, $J_{5,6a}$ = 2.6, $J_{5,6b}$ = 5.4, $J_{4,5}$ = 10.0 Hz, 1 H, 5-H), 4.09 (d, $J_{4,5}$ = 10.0 Hz, 1 H, 4-H), 4.22 (dd, $J_{5,6b}$ = 5.4, $J_{6a,6b}$ = 11.7 Hz, 1 H, 6b-H), 4.54 (dd, $J_{5,6a}$ = 2.6, $J_{6a,6b}$ = 11.7 Hz, 1 H, 6a-H), 4.56 (d, $J_{1,2}$ = 3.8 Hz, 1 H, 2-H), 5.39 (s, 1 H, 3-H), 5.92 (d, $J_{1,2}$ = 3.8 Hz, 1 H, 1-H), 7.08−7.29 (m, 5 H, Ph) ppm. ^{13}C NMR (125.7 MHz, $CDCl_3$): δ = 20.4, 20.7 (2 *Me*CO), 25.5, 26.5 (C*Me*$_2$), 57.3 (C-5), 64.3 (C-6), 77.6 (C-3), 84.1 (C-2), 84.7 (C-4), 106.2 (C-1), 112.7 (*C*Me$_2$), 123.7, 125.1, 129.3, 136.9 (Ph), 138.9 (NCN), 169.4, 170.3 (CO) ppm. FAB-MS: *m*/*z* = 427 (100) $[M + Na]^+$. $C_{20}H_{24}N_2O_7$ (404.41): calcd. C 59.40, H 5.98, N 6.93; found C 59.77, H 6.16, N 6.69.

3,6-Di-*O*-acetyl-5-deoxy-1,2-*O*-isopropylidene-5-(*N*′-phenylureido)-β-L-altrofuranose (40): Compound **40** was obtained from carbodiimide **39** (243 mg, 0.6 mmol) by TFA-catalyzed addition of water, following the procedure described above for the preparation of L-gulofuranose-derived ureas. Purification was effected by column chromatography using EtOAc/petroleum ether (2:1) as an eluent. Yield: 223 mg (88%). R_f = 0.55 (EtOAc/petroleum ether, 3:1). $[\alpha]_D^{22}$ = +42.0 (*c* = 1.0, CH_2Cl_2). IR (KBr): $\tilde{\nu}_{max}$ = 3360, 3057, 2988, 1746, 1557, 1377, 1233, 1099 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 1.30 (s, 3 H, Me), 1.87 (s, 3 H, Me), 2.04 (s, 3 H, MeCO), 2.08 (s, 3 H, MeCO), 4.03 (d, $J_{4,5}$ = 10.6 Hz, 1 H, 4-H), 4.31 (dd, $J_{5,6b}$ = 3.2, $J_{6a,6b}$ = 11.3 Hz, 1 H, 6b-H), 4.39 (dd, $J_{5,6a}$ = 4.0, $J_{6a,6b}$ = 11.3 Hz, 1 H, 6a-H), 4.53 (m, 1 H, 5-H), 4.66 (d, $J_{1,2}$ = 3.9 Hz, 1 H, 2-H), 5.20 (br. s, 1 H, NH), 5.24 (s, 1 H, 3-H), 5.96 (d, $J_{1,2}$ = 3.9 Hz, 1 H, 1-H), 6.79 (br. s, 1 H, N′H), 7.03−7.36 (m, 5 H, Ph) ppm. ^{13}C NMR (125.7 MHz, $CDCl_3$): δ = 20.7, 20.8, (*Me*CO), 25.5, 26.4 (C*Me*$_2$), 50.1 (C-5), 63.6 (C-6), 78.4 (C-3), 83.9 (C-2), 84.9 (C-4), 106.2 (C-1), 112.8 (*C*Me$_2$), 120.8−138.2 (Ph), 154.9 (CO urea), 170.3, 170.7 (CO) ppm. FAB-MS: *m*/*z* = 445 (100) $[M + Na]^+$. $C_{20}H_{26}N_2O_8$ (422.43): calcd. C 56.69, H 6.20, N 6.63; found C 56.65, H 6.23, N 6.56.

***N*-Thiocarbamoyl and *N*-Carbamoyl-6-oxa-(+)-calystegine B_3 Derivatives 41 and 42. General Procedure:** Compounds **41** and **42** were obtained from thiourea **37** and urea **40** (0.5 mmol), respectively, by sequential deacetylation (for **40**) and TFA-catalyzed hydrolysis of the isopropylidene group, following the procedure described above for the preparation of 6-oxa-(−)-calystegine B_4 derivatives.

(1*S*,2*S*,3*S*,4*R*,5*R*)-2,3,4-Trihydroxy-6-oxa-*N*-(*N*′-phenylthiocarbamoyl)-*nor*-tropane (41): Purification by column chromatography using EtOAc/EtOH (50:1) as an eluent. Yield: 95 mg (64%). R_f = 0.38 (EtOAc/EtOH/H_2O, 45:5:3). $[\alpha]_D^{22}$ = +71.0 (*c* = 1.0, H_2O). UV (MeOH): 248 nm (ε_mM 18.0). ^1H NMR (500 MHz, D_2O): δ = 3.74 (dd, $J_{2,3}$ = 3.5, $J_{3,4}$ = 8.7 Hz, 1 H, 3-H), 3.76 (dd, $J_{3,4}$ = 8.7, $J_{4,5}$ = 1.5 Hz, 1 H, 4-H), 3.85 (d, $J_{1,7a}$ = $J_{1,7b}$ = 2.9 Hz, 2 H, 7a-H, 7b-H), 4.08 (t, $J_{1,2}$ = $J_{2,3}$ = 3.5 Hz, 1 H, 2-H), 5.07 (dt, $J_{1,2}$ = 3.5, $J_{1,7a}$ = $J_{1,7b}$ = 2.9 Hz, 1 H, 1-H), 6.01 (d, $J_{4,5}$ = 1.5 Hz, 1 H, 5-H), 7.16−7.26 (m, 5 H, Ph) ppm. ^{13}C NMR (125.7 MHz, D_2O): δ = 60.8 (C-1), 70.3 (C-7), 71.7 (C-2), 71.8 (C-3), 74.6 (C-4), 90.3 (C-5), 128.3−140.1 (Ph), 180.8 (CS) ppm. FAB-MS: *m*/*z* = 297 (100) $[M + H]^+$. $C_{13}H_{16}N_2O_4S$ (296.34): calcd. C 52.69, H 5.44, N 9.45; found C 52.51, H 5.38, N 9.33.

(1*S*,2*S*,3*S*,4*R*,5*R*)-2,3,4-Trihydroxy-6-oxa-*N*-(*N*′-phenylcarbamoyl)-*nor*-tropane (42): Purification by column chromatography using EtOAc/EtOH (50:1 → 10:1) as an eluent. Yield: 133 mg (95%). R_f = 0.26 (EtOAc/EtOH/H_2O, 45:5:3). $[\alpha]_D^{22}$ = +82.9 (*c* = 0.82, H_2O). ^1H NMR (500 MHz, D_2O): δ = 3.75 (m, 2 H, 3-H, 4-H), 3.84 (bd, $J_{7a,7b}$ = 8.6 Hz, 1 H, 7a-H), 3.88 (dd, $J_{1,7b}$ = 4.5, $J_{7a,7b}$ = 8.6 Hz, 1 H, 7b-H), 4.10 (m, 1 H, 2-H), 4.80 (t, $J_{1,2}$ = $J_{1,7b}$ = 4.5 Hz, 1 H, 1-H), 5.71 (d, $J_{4,5}$ = 1.0 Hz, 1 H, 5-H), 7.21−7.40 (m, 5 H, Ph) ppm. ^{13}C NMR (125.7 MHz, D_2O): δ = 59.3 (C-1), 67.6 (C-7), 70.6 (C-2), 71.6 (C-3), 74.2 (C-4), 88.3 (C-5), 123.9−138.5 (Ph), 158.2 (CO) ppm. FAB-MS: *m*/*z* = 281 (70) $[M + H]^+$. $C_{13}H_{16}N_2O_5$ (280.28): calcd. C 55.71, H 5.75, N 9.99; found C 55.69, H 6.03, N 10.02.

3-*O*-Acetyl-1,2-*O*-isopropylidene-6-*O*-trityl-α-D-allofuranose (44): 1,2:5,6-Di-*O*-isopropylidene-α-D-allofuranose (**43**) (1.6 g, 6.2 mmol) was acetylated and the crude acetate was treated with 40% aqueous acetic acid (16 mL) at 40 °C for 24 h. The solvents were eliminated under reduced pressure, and coevaporated several times with water to give the corresponding 5,6-diol as a homogeneous product (TLC), which was dissolved in pyridine (10 mL). Trityl chloride (2.0 g, 7.2 mmol, 1.2 equiv.) was added and the reaction mixture was stirred at room temperature for 24 h, then poured into ice-water (60 mL) and decanted. The resulting solid was dissolved in toluene (30 mL), washed with iced aqueous 10% acetic acid (12 mL), aqueous saturated $NaHCO_3$ (12 mL), dried ($MgSO_4$), and concentrated. The residue was purified by column chromatography using EtOAc/petroleum ether (1:3). Yield: 2.3 g (74%). R_f = 0.68 (EtOAc/petroleum ether, 1:3). $[\alpha]_D^{22}$ = +60.0 (*c* = 1.0, CH_2Cl_2). IR (KBr): $\tilde{\nu}_{max}$ = 3489, 3059, 2988, 1744, 1375, 1240, 1074 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 1.32 (s, 3 H, Me), 1.54 (s, 3 H, Me), 1.99 (s, 3 H, MeCO), 3.16 (dd, $J_{5,6b}$ = 7.6, $J_{6a,6b}$ = 9.7 Hz, 6b-H), 3.23 (dd, $J_{5,6a}$ = 4.1, $J_{6a,6b}$ = 9.7 Hz, 1 H, 6a-H), 4.13 (ddd, $J_{4,5}$ = 3.8, $J_{5,6a}$ = 4.1, $J_{5,6b}$ = 7.6 Hz, 1 H, 5-H), 4.18 (dd, $J_{3,4}$ = 8.6, $J_{4,5}$ = 3.8 Hz, 1 H, 4-H), 4.79 (dd, $J_{1,2}$ = 3.8, $J_{2,3}$ = 5.0 Hz, 1 H, 2-H), 4.85 (dd, $J_{2,3}$ = 5.0, $J_{3,4}$ = 8.6 Hz, 1 H, 3-H), 5.78 (d, $J_{1,2}$ = 3.8 Hz, 1 H, 1-H), 7.23−7.43 (m, 15 H, 3 Ph) ppm. ^{13}C NMR (125.7 MHz, $CDCl_3$): δ = 20.6 (*Me*CO), 26.6, 26.7 (C*Me*$_2$), 64.2 (C-6), 70.3 (C-5), 71.8 (C-3), 77.7 (C-4), 77.8 (C-2), 87.0 (*C*Ph$_3$), 104.1 (C-1), 113.0 (*C*Me$_2$), 127.2−143.7 (Ph), 170.0 (CO) ppm. FAB-MS: *m*/*z* = 527 (90) $[M + Na]^+$. $C_{30}H_{32}O_7$ (504.57): calcd. C 71.41, H 6.39; found C 71.80, H, 6.42.

3-*O*-Acetyl-5-azido-5-deoxy-1,2-*O*-isopropylidene-β-L-talofuranose (45): Pyridine (0.4 mL) and trifluoromethanesulfonic anhydride (0.83 mL, 5.0 mmol) were added to a solution of **44** (1.8 g, 3.6 mmol) in CH_2Cl_2 (10 mL) at −25 °C under N_2. The reaction mixture was allowed to reach room temperature and stirred for 30 min, then diluted with CH_2Cl_2 (10 mL), washed with saturated aqueous $NaHCO_3$ (8 mL), dried ($MgSO_4$), and concentrated. The resulting crude triflate ester was dissolved in DMF (15 mL), NaN_3 (2.4 g, 36.9 mmol, 7 equiv.) was added and the reaction mixture was stirred at room temperature for 3.5 h. The solvent was eliminated under reduced pressure and the resulting residue was dissolved in CH_2Cl_2 (20 mL), the organic solution was washed with water (2 × 10 mL), dried, and concentrated. $BF_3{\cdot}Et_2O$ (1.1 mL) and MeOH (5.4 mL) were added to a solution of the crude tritylated azido derivative thus obtained in CH_2Cl_2 (29 mL) at 0 °C under Ar. The reaction mixture was allowed to reach room temperature and stirred for 2 h, then washed with saturated aqueous $NaHCO_3$ (2 × 10 mL), dried ($MgSO_4$), and concentrated. The resulting residue was purified by column chromatography using EtOAc/petroleum ether (1:3 → 1:2). Yield: 620 mg (60%). R_f = 0.18 (EtOAc/petroleum ether, 1:2). $[\alpha]_D^{22}$ = +137.1 (*c* = 0.97, CH_2Cl_2). IR (KBr):

$\tilde{\nu}_{max}$ = 3489, 2988, 2114, 1746, 1377, 1242, 1074 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 1.32 (s, 3 H, Me), 1.54 (s, 3 H, Me), 2.13 (s, 3 H, MeCO), 3.51 (ddd, $J_{4,5}$ = 3.1, $J_{5,6a}$ = 5.2, $J_{5,6b}$ = 6.8 Hz, 1 H, 5-H), 3.91 (m, 2 H, 6a-H, 6b-H), 4.25 (dd, $J_{3,4}$ = 8.6, $J_{4,5}$ = 3.1 Hz, 1 H, 4-H), 4.84 (dd, $J_{1,2}$ = 3.6, $J_{2,3}$ = 4.9 Hz, 1 H, 2-H), 4.87 (dd, $J_{2,3}$ = 4.9, $J_{3,4}$ = 8.6 Hz, 1 H, 3-H), 5.83 (d, $J_{1,2}$ = 3.6 Hz, 1 H, 1-H) ppm. ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 20.5 (*Me*CO), 26.4, 26.5 (C*Me*$_2$), 61.5 (C-5), 62.8 (C-6), 72.7 (C-3), 76.9 (C-4), 77.4 (C-2), 104.2 (C-1), 113.3 (*C*Me$_2$), 170.3 (CO) ppm. FAB-MS: *m*/*z* = 310 (85) $[M + Na]^+$. $C_{11}H_{17}N_3O_6$ (287.27): calcd. C 45.99, H 5.96, N 14.63; found C 45.95, H 5.91, N 14.34.

5-Azido-5-deoxy-1,2-*O*-isopropylidene-β-L-talofuranose (46): Conventional deacetylation of **45** (209 mg, 0.73 mmol) afforded **45**. Yield: 165 mg (92%). R_f = 0.35 (EtOAc/petroleum ether, 1:2). $[\alpha]_D^{22}$ = +43.3 (*c* = 0.9, MeOH). IR (KBr): $\tilde{\nu}_{max}$ = 3468, 2988, 2104, 1377, 1107 cm^{-1}. ^1H NMR (300 MHz, CD_3OD): δ = 1.33 (s, 3 H, Me), 1.51 (s, 3 H, Me), 3.46 (ddd, $J_{4,5}$ = 3.6, $J_{5,6a}$ = 5.4, $J_{5,6b}$ = 7.7 Hz, 1 H, 5-H), 3.76 (dd, $J_{5,6b}$ = 7.7, $J_{6a,6b}$ = 11.6 Hz, 1 H, 6b-H), 3.81 (dd, $J_{5,6a}$ = 5.4, $J_{6a,6b}$ = 11.6 Hz, 1 H, 6a-H), 3.89 (dd, $J_{3,4}$ = 9.0, $J_{4,5}$ = 3.6 Hz, 1 H, 4-H), 4.00 (dd, $J_{2,3}$ = 4.5, $J_{3,4}$ = 9.0 Hz, 1 H, 3-H), 4.56 (dd, $J_{1,2}$ = 3.6, $J_{2,3}$ = 4.5 Hz, 1 H, 2-H), 5.72 (d, $J_{1,2}$ = 3.6 Hz, 1 H, 1-H) ppm. ^{13}C NMR (75.5 MHz, CD_3OD): δ = 26.6, 26.9 (C*Me*$_2$), 63.1 (C-5), 64.4 (C-6), 73.5 (C-3), 80.2 (C-4), 80.7 (C-2), 105.3 (C-1), 114.0 (*C*Me$_2$) ppm. FAB-MS: *m*/*z* = 268 (100) $[M + Na]^+$. $C_9H_{15}N_3O_5$ (245.23): calcd. C 44.08, H 6.16, N. 17.13; found C 43.96, H. 6.05, N 17.07.

5-Amino-5-deoxy-1,2-*O*-isopropylidene-β-L-talofuranose (47): A solution of **46** (277 mg, 1.13 mmol) in MeOH (11 mL) was hydrogenated at atmospheric pressure for 2 h using 10% Pd/C (112 mg) as catalyst. The suspension was filtered through Celite and concentrated to give **46** as a hygroscopic solid which was used in the next step without further purification.

5-Deoxy-1,2-*O*-isopropylidene-5-(*N*′-phenylthioureido)-β-L-talofuranose (48): Compound **48** was obtained by the coupling reaction of amine **47** (138 mg, 0.63 mmol) with phenyl isothiocyanate, following the procedure described above for the preparation of L-gulofuranose-derived thioureas. Purification was effected by column chromatography using EtOAc/petroleum ether (2:1) as an eluent. Yield: 145 mg (65%). R_f = 0.33 (EtOAc/petroleum ether, 3:1). $[\alpha]_D^{22}$ = +13.0 (*c* = 1.0, CH_2Cl_2). UV (CH_2Cl_2): 267 nm (ε_m 15.7). IR (KBr): $\tilde{\nu}_{max}$ = 3350, 2934, 1603, 1589, 1387, 1072 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$, 313 K): δ = 1.32 (s, 3 H, Me), 1.55 (s, 3 H, Me), 3.79 (dd, $J_{5,6b}$ = 4.8, $J_{6a,6b}$ = 11.6 Hz, 1 H, 6b-H), 3.89 (dd, $J_{2,3}$ = 4.5, $J_{3,4}$ = 9.0 Hz, 1 H, 3-H), 3.94 (dd, $J_{5,6a}$ = 3.5, $J_{6a,6b}$ = 11.6 Hz, 1 H, 6a-H), 4.10 (dd, $J_{3,4}$ = 9.0, $J_{4,5}$ = 1.9 Hz, 1 H, 4-H), 4.57 (dd, $J_{1,2}$ = 3.6, $J_{2,3}$ = 4.5 Hz, 1 H, 2-H), 4.88 (dddd, $J_{4,5}$ = 1.9, $J_{5,6a}$ = 3.5, $J_{5,6b}$ = 4.8, $J_{5,NH}$ = 8.6 Hz, 1 H, 5-H), 6.14 (d, $J_{1,2}$ = 3.6 Hz, 1 H, 1-H), 6.84 (d, $J_{5,NH}$ = 8.6 Hz, 1 H, NH), 7.22−7.44 (s, 5 H, Ph), 8.30 (br. s, 1 H, N′H) ppm. ^{13}C NMR (75.5 MHz, $CDCl_3$, 313 K): δ = 26.0, 26.4 (C*Me*$_2$), 54.4 (C-5), 64.1 (C-6), 71.4 (C-3), 78.3 (C-2), 81.2 (C-4), 103.8 (C-1), 113.2 (*C*Me$_2$), 181.0 (CS) ppm. FAB-MS: *m*/*z* = 377 (100) $[M + Na]^+$. $C_{16}H_{22}N_2O_5S$ (354.42): calcd. C 54.22, H 6.25, N 7.90; found C 54.28, H 6.24, N 7.83.

3,6-Di-*O*-acetyl-5-azido-5-deoxy-1,2-*O*-isopropylidene-β-L-talofuranose (49): Conventional acetylation of **45** (219 mg, 0.76 mmol) and purification by column chromatography using EtOAc/petroleum ether (1:3) as an eluent gave **49**. Yield: 236 mg (94%). R_f = 0.28 (EtOAc/petroleum ether, 1:3). $[\alpha]_D^{22}$ = +102.2 (*c* = 0.91, CH_2Cl_2). IR (KBr): $\tilde{\nu}_{max}$ = 2990, 2120, 1746, 1375, 1235, 1024 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 1.33 (s, 3 H, Me), 1.53 (s, 3 H, Me), 2.11 (s, 3 H, MeCO), 2.13 (s, 3 H, MeCO), 3.66 (ddd, $J_{4,5}$ = 2.9, $J_{5,6a}$ = 4.6, $J_{5,6b}$ = 8.4 Hz, 1 H, 5-H), 4.19 (dd, $J_{3,4}$ = 8.7, $J_{4,5}$ = 2.9 Hz, 1 H, 4-H), 4.33 (dd, $J_{5,6b}$ = 8.4, $J_{6a,6b}$ = 11.7 Hz, 1 H, 6b-H), 4.38 (dd, $J_{5,6a}$ = 4.6, $J_{6a,6b}$ = 11.7 Hz, 1 H, 6a-H), 4.82 (dd, $J_{1,2}$ = 3.6, $J_{2,3}$ = 4.8 Hz, 1 H, 2-H), 4.87 (dd, $J_{2,3}$ = 4.8, $J_{3,4}$ = 8.7 Hz, 1 H, 3-H), 5.82 (d, $J_{1,2}$ = 3.6 Hz, 1 H, 1-H) ppm. ^{13}C NMR (125.7 MHz, $CDCl_3$): δ = 20.6 (*Me*CO), 26.5, 26.6 (C*Me*$_2$), 59.2 (C-5), 64.0 (C-6), 72.7 (C-3), 77.0 (C-4), 77.2 (C-2), 104.3 (C-1), 113.4 (*C*Me$_2$), 170.0, 170.4 (CO) ppm. FAB-MS: *m*/*z* = 100 (40) $[M + H]^+$. $C_{13}H_{19}N_3O_7$ (329.31): calcd. C 47.41, H 5.81, N 12.76; found C 47.26, H 5.75, N 12.60.

3,6-Di-*O*-acetyl-5-deoxy-1,2-*O*-isopropylidene-5-(*N*′-phenylcarbodiimido)-β-L-talofuranose (50): Compound **50** was obtained from azide **49** (198 mg, 0.60 mmol) by an aza-Wittig-type reaction with phenyl isothiocyanate (97 mg, 0.72 mmol, 1.2 equiv.) and TPP (173 mg, 0.66 mmol, 1.1 equiv.) in toluene (1.5 mL), following the procedure described above for the preparation of L-gulofuranose-derived carbodiimides. Purification was effected by column chromatography using EtOAc/petroleum ether (1:4) as an eluent. Yield: 175 mg (71%). R_f = 0.14 (EtOAc/petroleum ether, 1:3). $[\alpha]_D^{22}$ = +110.0 (*c* = 1.1, CH_2Cl_2). IR (KBr): $\tilde{\nu}_{max}$ = 3063, 2990, 2131, 1748, 1589, 1381, 1231, 1101 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 1.34 (s, 3 H, Me), 1.55 (s, 3 H, Me), 1.98 (s, 3 H, MeCO), 2.15 (s, 3 H, MeCO), 3.93 (ddd, $J_{4,5}$ = 2.2, $J_{5,6a}$ = 5.0, $J_{5,6b}$ = 8.1 Hz, 1 H, 5-H), 4.23 (dd, $J_{3,4}$ = 8.7, $J_{4,5}$ = 2.2 Hz, 1 H, 4-H), 4.33 (dd, $J_{5,6b}$ = 8.1, $J_{6a,6b}$ = 11.4 Hz, 1 H, 6b-H), 4.39 (dd, $J_{5,6a}$ = 5.0, $J_{6a,6b}$ = 11.4 Hz, 1 H, 6a-H), 4.84 (dd, $J_{1,2}$ = 3.6, $J_{2,3}$ = 4.7 Hz, 1 H, 2-H), 4.93 (dd, $J_{2,3}$ = 4.7, $J_{3,4}$ = 8.7 Hz, 1 H, 3-H), 5.82 (d, $J_{1,2}$ = 3.6 Hz, 1 H, 1-H), 7.10−7.32 (m, 5 H, Ph) ppm. ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 20.5 (*Me*CO), 26.5, 26.6 (C*Me*$_2$), 56.2 (C-5), 64.9 (C-6), 72.7 (C-3), 76.7 (C-4), 77.1 (C-2), 104.2 (C-1), 113.3 (*C*Me$_2$), 123.7−134.7 (Ph), 139.0 (NCN), 169.9, 170.4 (CO) ppm. FAB-MS: *m*/*z* = 427 (40) $[M + Na]^+$, 405 (100) $[M + H]^+$. $C_{20}H_{24}N_2O_7$ (404.41): calcd. C 59.39, H 5.98, N, 6.93; found C 59.56, H 5.75, N 6.89.

3,6-Di-*O*-acetyl-5-deoxy-1,2-*O*-isopropylidene-5-(*N*′-phenylureido)-β-L-talofuranose (51): Compound **51** was obtained from carbodiimide **50** (150 mg, 0.37 mmol) by TFA-catalyzed addition of water, following the procedure described above for the preparation of L-gulofuranose-derived ureas. Purification was effected by column chromatography using EtOAc/petroleum ether (2:1) as an eluent. Yield: 144 mg (92%). R_f = 0.69 (EtOAc/petroleum ether, 3:1). $[\alpha]_D^{22}$ = +84.3 (*c* = 1.02, CH_2Cl_2). IR (KBr): $\tilde{\nu}_{max}$ = 3351, 3055, 2988, 1746, 1533, 1375, 1238, 1074 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 1.31 (s, 3 H, Me), 1.53 (s, 3 H, Me), 2.05 (s, 3 H, MeCO), 2.12 (s, 3 H, MeCO), 4.12 (dd, $J_{5,6b}$ = 5.7, $J_{6a,6b}$ = 10.8 Hz, 1 H, 6b-H), 4.27 (dd, $J_{4,5}$ = 1.3, $J_{3,4}$ = 9.2 Hz, 1 H, 4-H), 4.30 (dd, $J_{5,6a}$ = 6.7, $J_{6a,6b}$ = 10.8 Hz, 1 H, 6a-H), 4.33 (m, 1 H, 5-H), 4.63 (dd, $J_{2,3}$ = 4.6, $J_{3,4}$ = 9.2 Hz, 1 H, 3-H), 4.80 (dd, $J_{1,2}$ = 3.7, $J_{2,3}$ = 4.6 Hz, 1 H, 2-H), 5.21 (d, $J_{5,NH}$ = 9.1 Hz, 1 H, NH), 5.71 (d, $J_{1,2}$ = 3.7 Hz, 1 H, 1-H), 6.91 (br. s, 1 H, N′H), 7.05−7.29 (m, 5 H, Ph) ppm. ^{13}C NMR (125.7 MHz, $CDCl_3$): δ = 20.6, 20.8 (*Me*CO), 26.5, 26.6 (C*Me*$_2$), 48.1 (C-5), 64.3 (C-6), 72.4 (C-3), 76.4 (C-4), 77.1 (C-2), 104.2 (C-1), 113.4 (*C*Me$_2$), 120.7−138.3 (Ph), 155.2 (CO urea), 171.1, 170.3 (CO) ppm. FAB-MS: *m*/*z* = 445 (100) $[M + Na]^+$. $C_{20}H_{26}N_2O_8$ (422.43): calcd. C 56.69, H 6.20, N 6.63; found C 56.49, H 6.23, N 6.46.

5-Deoxy-5-(*N*′-phenylthioureido)-L-talofuranose (52) and (1*S*,2*R*,3*R*,4*R*,5*R*)-2,3,4-Trihydroxy-6-oxa-*N*-(*N*′-phenylthiocarbamoyl)-*nor*-tropane (53): TFA-catalyzed hydrolysis of the isopropylidene group of the protected thiourea **50** (150 mg, 0.42 mmol) and neutralization, following the procedure indicated above for the prep-

aration of calystegine B_4 derivatives afforded a mixture of **52** and **53** (5-H resonance at δ = 5.98 ppm) in a ratio of 95:5 (^{1}H NMR in D_2O). Purification was effected by column chromatography using EtOAc → EtOAc/EtOH/H_2O (45:5:3) as an eluent. Yield: 122 mg (92%). R_f = 0.50 (EtOAc/EtOH/H_2O, 45:5:3). UV (MeOH) 250 nm (ε_{mM} 13.0). The following data correspond to the furanose species **52**: Anomer ratio β/α = 2:1 (1-H integration). ^{1}H NMR (500 MHz, D_2O, 313 K): δ = 4.07 (m, 2 H, 6aα-H, 6bα-H), 4.40 (t, $J_{1,2}$ = $J_{2,3}$ = 5.7 Hz, 1 H, 2α-H), 4.08 (dd, $J_{5,6a}$ = 6.5, $J_{6a,6b}$ = 11.5 Hz, 1 H, 6aβ-H), 4.09 (m, 1 H, 6bβ-H), 4.20 (d, $J_{2,3}$ = 4.5 Hz, 1 H, 2β-H), 4.31 (m, 1 H, 3α-H), 4.45 (dd, $J_{4,5}$ = 2.5, $J_{3,4}$ = 7.5 Hz, 1 H, 4β-H), 4.51 (dd, $J_{2,3}$ = 4.5, $J_{3,4}$ = 7.5 Hz, 1 H, 3β-H), 4.52 (m, 1 H, 4α-H), 5.06 (m, 2 H, 5α-H, 5β-H), 5.43 (s, 1 H, 1β-H), 5.54 (br. s, 1 H, 1α-H), 7.21−7.43 (m, 5 H, Ph) ppm. ^{13}C NMR (125.7 MHz, D_2O, 313 K): δ = 56.1 (C-5β), 56.6 (C-5α), 61.5 (C-6α), 61.7 (C-6β), 70.5 (C-3β), 70.8 (C-3α), 74.9 (C-2α, C-2β), 80.3 (C-4β), 81.1 (C-4α), 96.8 (C-1α), 100.8 (C-1β), 126.2−136.1 (Ph), 180.4 (CS) ppm. FAB-MS: *m*/*z* = 315 (100) [M + H]$^+$. $C_{13}H_{18}N_2O_5S$ (296.34): calcd. C 49.67, H 5.68, N 8.91; found C 46.61, H 5.60, N 8.82.

5-Deoxy-5-(*N*′-phenylureido)-L-talofuranose (54) and (1*S*,2*R*,3*R*,4*R*,5*R*)-2,3,4-Trihydroxy-6-oxa-*N*-(*N*′-phenylcarbamoyl)*nor*-tropane (55): Sequential deacetylation and TFA-catalyzed hydrolysis of the isopropylidene group of the protected urea **51** (130 mg, 0.31 mmol) and further neutralization, following the procedure indicated above for the preparation of calystegine B_4 derivatives, afforded a mixture of **54** and **55** (5-H resonance at δ = 5.59 ppm) in 95:2 relative proportions (^{1}H NMR in D_2O). Purification was effected by column chromatography using EtOAc → EtOAc/EtOH/H_2O (45:5:3) as an eluent. Yield: 74 mg (80%). R_f = 0.34 (EtOAc/EtOH/H_2O, 45:5:3). The following data correspond to the furanose species **54**: Anomer ratio β/α = 1.9:1 (1-H integration). ^{1}H NMR (500 MHz, D_2O, 313 K): δ = 3.68 (dd, $J_{5,6b}$ = 7.0, $J_{6a,6b}$ = 11.0 Hz, 1 H, 6bα-H), 3.70 (dd, $J_{5,6b}$ = 7.0, $J_{6a,6b}$ = 11.0 Hz, 1 H, 6bβ-H), 3.73 (dd, $J_{5,6a}$ = 6.5, $J_{6a,6b}$ = 11.0 Hz, 1 H, 6aα-H), 3.75 (dd, $J_{5,6a}$ = 6.0, $J_{6a,6b}$ = 11.0 Hz, 1 H, 6aβ-H), 4.00 (dd, $J_{1,2}$ = 1.0, $J_{2,3}$ = 5.0 Hz, 1 H, 2β-H), 4.10 (m, 3 H, 2α-H, 3α-H, 5β-H), 4.15 (dd, $J_{4,5}$ = 2.5, $J_{3,4}$ = 7.5 Hz, 1 H, 4β-H), 4.24 (m, 2 H, 4α-H, 5α-H), 4.26 (dd, $J_{2,3}$ = 5.0, $J_{3,4}$ = 7.5 Hz, 1 H, 3β-H), 5.27 (d, $J_{1,2}$ = 1.0 Hz, 1 H, 1β-H), 5.43 (br. s, 1 H, 1α-H), 7.18−7.36 (m, 5 H, Ph) ppm. ^{13}C NMR (125.7 MHz, D_2O, 313 K): δ = 51.8 (C-5β), 52.1 (C-5α), 62.2 (C-6α), 62.4 (C-6β), 70.9 (C-3α, C-3β), 71.1 (C-2α), 75.2 (C-2β), 80.9 (C-4β), 81.7 (C-4α), 96.9 (C-1α), 101.1 (C-1β), 126.2−136.1 (Ph), 121.4−138.1 (Ph), 158.2 (CO urea), 180.4 (CS) ppm. FAB-MS: *m*/*z* = 321 (100) [M + Na]$^+$. $C_{13}H_{18}N_2O_6$ (298.30): calcd. C 52.34, H 6.08, N 9.39; found C 52.13, H 5.74, N 9.20.

3-*O*-Acetyl-1,2-*O*-isopropylidene-α-L-glucofuranose (57): 1,2:5,6-Di-*O*-isopropylidene-α-L-glucofuranose (**56**) (468.50 mg, 1.8 mmol) was sequentially acetylated and treated with 40% aqueous AcOH (5 mL) at 40 °C for 4 h. The solvents were eliminated under reduced pressure, coevaporated several times with water and the resulting residue was purified by column chromatography using EtOAc/petroleum ether (1:1 → 4:1) as an eluent. Yield: 419 mg (82%). R_f = 0.14 (EtOAc/petroleum ether, 1:1). $[\alpha]_D^{22}$ = −23.3 (*c* = 0.6, CH_2Cl_2). IR (KBr): $\tilde{\nu}_{max}$ = 3457, 2969, 1744, 1381, 1258, 1092 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.30 (s, 3 H, Me), 1.50 (s, 3 H, Me), 2.13 (s, 3 H, MeCO), 3.68 (ddd, $J_{5,6a}$ = 2.7, $J_{5,6b}$ = 5.7, $J_{4,5}$ = 8.8 Hz, 1 H, 5-H), 3.71 (dd, $J_{5,6b}$ = 5.7, $J_{6a,6b}$ = 10.9 Hz, 1 H, 6b-H), 3.83 (dd, $J_{5,6a}$ = 2.7, $J_{6a,6b}$ = 10.9 Hz, 1 H, 6a-H), 4.16 (dd, $J_{3,4}$ = 2.6, $J_{4,5}$ = 8.8 Hz, 1 H, 4-H), 4.55 (d, $J_{1,2}$ = 3.7 Hz, 1 H, 2-H), 5.26 (d, $J_{3,4}$ = 2.6 Hz, 1 H, 3-H), 5.89 (d, $J_{1,2}$ = 3.7 Hz, 1 H, 1-H) ppm. ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 20.6 (*Me*CO), 26.0, 26.4 (C*Me*$_2$), 63.9 (C-6), 68.0 (C-5), 76.4 (C-3), 79.2 (C-4), 82.9 (C-2), 104.7 (C-1), 112.2 (*C*Me$_2$), 171.0 (CO) ppm. FAB-MS: *m*/*z* = 285 (25) [M + Na]$^+$, 263 (25) [M + H]$^+$. $C_{11}H_{18}O_7$ (262.26): calcd. C 50.38, H 6.92; found C 50.22, H 6.81.

3-*O*-Acetyl-1,2-*O*-isopropylidene-6-*O*-trityl-α-L-glucofuranose (58): Trityl chloride (543 mg, 1.94 mmol, 1.3 equiv.) was added to a solution of **57** (368 mg, 1.4 mmol) in pyridine (3 mL). The reaction mixture was stirred at room temperature for 24 h, then poured into ice-water (10 mL), and decanted. A solution of the resulting solid in toluene (10 mL) was washed with iced aqueous 10% AcOH (6 mL), aqueous saturated $NaHCO_3$ (6 mL), dried ($MgSO_4$), and concentrated. The residue was purified by column chromatography using EtOAc/petroleum ether (1:3). Yield: 523 mg (74%). R_f = 0.43 (EtOAc/petroleum ether, 1:1). $[\alpha]_D^{22}$ = +19.8 (*c* = 1.01, CH_2Cl_2). IR (KBr): $\tilde{\nu}_{max}$ = 3063, 2974, 1746, 1487, 1377, 1231, 1092 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.31 (s, 3 H, Me), 1.51 (s, 3 H, Me), 2.09 (s, 3 H, MeCO), 3.39 (m, 2 H, 6a-H, 6b-H), 3.83 (m, 1 H, 5-H), 4.38 (dd, $J_{3,4}$ = 1.0, $J_{4,5}$ = 9.1 Hz, 1 H, 4-H), 4.51 (d, $J_{1,2}$ = 3.3 Hz, 1 H, 2-H), 5.34 (d, $J_{3,4}$ = 1.0 Hz, 1 H, 3-H), 5.86 (d, $J_{1,2}$ = 3.3 Hz, 1 H, 1-H), 7.46−7.22 (m, 15 H, 3 Ph) ppm. ^{13}C NMR (125.7.5 MHz, $CDCl_3$): δ = 20.6 (*Me*CO), 26.0, 26.6 (C*Me*$_2$), 64.8 (C-6), 67.7 (C-5), 76.2 (C-3), 78.6 (C-4), 83.1 (C-2), 86.7 (*C*Ph$_3$), 104.9 (C-1), 112.1 (*C*Me$_2$), 127.0−143.7 (Ph), 169.9 (CO) ppm. FAB-MS: *m*/*z* = 527 (40) [M + Na]$^+$. $C_{30}H_{32}O_7$ (504.57): calcd. C 71.41, H 6.39; found C 71.53, H 6.44.

3-*O*-Acetyl-5-azido-5-deoxy-1,2-*O*-isopropylidene-β-D-idofuranose (59): Pyridine (0.18 mL) and trifluoromethanesulfonic anhydride (0.23 mL, 1.39 mmol) were added to a solution of **58** (514 mg, 1.02 mmol) in CH_2Cl_2 (4 mL), at −25 °C under N_2. The reaction mixture was allowed to reach room temperature and stirred for 20 min, then diluted with CH_2Cl_2 (10 mL), washed with saturated aqueous $NaHCO_3$ (8 mL), dried ($MgSO_4$), and concentrated. The resulting crude triflate ester was dissolved in DMF (4 mL), NaN_3 (464 mg, 7.13 mmol, 7 equiv.) was added and the reaction mixture was stirred at room temperature for 3.5 h. The solvent was eliminated under reduced pressure and the resulting residue was dissolved in CH_2Cl_2 (20 mL), the organic solution was washed with water (2 × 10 mL), dried, and concentrated. The crude tritylated azido derivative thus obtained was dissolved in CH_2Cl_2 (8 mL) and $BF_3{\cdot}Et_2O$ (300 mL) and MeOH (1.5 mL) were added at 0 °C under Ar. The reaction mixture was allowed to reach room temperature, stirred for 3.5 h, washed with saturated aqueous $NaHCO_3$ (2 × 4 mL), dried ($MgSO_4$), and concentrated. The residue was purified by column chromatography using EtOAc/petroleum ether (1:3). Yield: 193 mg (66%). R_f = 0.12 (EtOAc/petroleum ether, 1:2). $[\alpha]_D^{22}$ = +33.6 (*c* = 1.0, CH_2Cl_2). IR (KBr): $\tilde{\nu}_{max}$ = 2988, 2106, 1748, 1379, 1223, 1092 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.31 (s, 3 H, Me), 1.52 (s, 3 H, Me), 2.12 (s, 3 H, MeCO), 3.56 (dd, $J_{5,6b}$ = 5.9, $J_{6a,6b}$ = 11.3 Hz, 1 H, 6b-H), 3.70 (m, 1 H, 5-H), 3.74 (dd, $J_{5,6a}$ = 3.9, $J_{6a,6b}$ = 11.3 Hz, 1 H, 6a-H), 4.35 (dd, $J_{3,4}$ = 3.0, $J_{4,5}$ = 7.8 Hz, 1 H, 4-H), 4.51 (d, $J_{1,2}$ = 3.8 Hz, 1 H, 2-H), 5.20 (d, $J_{3,4}$ = 3.0 Hz, 1 H, 3-H), 5.95 (d, $J_{1,2}$ = 3.8 Hz, 1 H, 1-H) ppm. ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 20.6 (*Me*CO), 26.0, 26.5 (C*Me*$_2$), 62.1 (C-6), 62.2 (C-5), 76.0 (C-3), 78.7 (C-4), 83.4 (C-2), 104.3 (C-1), 112.3 (*C*Me$_2$), 169.6 (CO) ppm. FAB-MS: *m*/*z* = 310 (15) [M + Na]$^+$, 288 (20) [M + H]$^+$. $C_{11}H_{17}O_6N_3$ (287.27): calcd. C 45.99, H 5.96, N 14.63; found C 45.99, H 5.87, N 14.64.

5-Azido-5-deoxy-1,2-*O*-isopropylidene-β-D-idofuranose (60): Compound **60** was obtained by conventional deacetylation of **59** (170 mg, 0.59 mmol) and showed spectroscopic properties identical to those of the known α-L-ido enantiomer. It was used in the next step without further purification.

5-Amino-5-deoxy-1,2-*O*-isopropylidene-β-D-idofuranose (61): A solution of azide **60** (0.59 mmol) in MeOH (5.6 mL) was hydrogenated at atmospheric pressure for 2 h using 10% Pd/C (59 mg) as catalyst. The suspension was filtered through Celite, and concentrated to give **61** as a hygroscopic solid that was used in next step without further purification.

5-Deoxy-1,2-*O*-isopropylidene-5-(*N*′-phenylthioureido)-β-D-idofuranose (62): Phenyl isothiocyanate (80 mg, 0.59 mmol) was added to a solution of amine **61** (170 mg, 0.59 mmol) in pyridine (5 mL). The reaction mixture was stirred at room temperature for 18 h and coevaporated several times with toluene. The resulting residue was purified by column chromatography using EtOAc/petroleum ether (2:1) as an eluent. Yield: 149 mg (71%). R_f = 0.41 (EtOAc/petroleum ether, 3:1). $[\alpha]_D^{22}$ = −15.5 (*c* = 1.0, MeOH). UV (MeOH): 249 nm (ε_{mM} 13.1). IR (KBr): $\tilde{\nu}_{max}$ = 3368, 3065, 2988, 1534, 1381, 1092 cm^{-1}. ^{1}H NMR (300 MHz, CD_3OD, 313 K): δ = 1.29 (s, 3 H, Me), 1.44 (s, 3 H, Me), 3.73 (dd, $J_{5,6b}$ = 5.3, $J_{6a,6b}$ = 11.1 Hz, 1 H, 6b-H), 3.79 (dd, $J_{5,6a}$ = 3.9, $J_{6a,6b}$ = 11.1 Hz, 1 H, 6a-H), 4.15 (d, $J_{3,4}$ = 2.7 Hz, 1 H, 3-H), 4.37 (dd, $J_{3,4}$ = 2.7, $J_{4,5}$ = 7.0 Hz, 1 H, 4-H), 4.50 (d, $J_{1,2}$ = 3.7 Hz, 1 H, 2-H), 4.78 (m, 1 H, 5-H), 5.87 (d, $J_{1,2}$ = 3.7 Hz, 1 H, 1-H), 7.17−7.39 (m, 5 H, Ph) ppm. ^{13}C NMR (75.5 MHz, CD_3OD, 313 K): δ = 26.4, 27.1 (C*Me*$_2$), 56.6 (C-5), 62.4 (C-6), 75.9 (C-3), 80.6 (C-4), 87.0 (C-2), 104.9 (C-1), 112.8 (*C*Me$_2$), 125.4−139.6 (Ph), 181.6 (CS) ppm. FAB-MS: *m*/*z* = 377 (50) $[M + Na]^+$, 355 (100) $[M + H]^+$. $C_{16}H_{22}N_2O_5S$ (354.42): calcd. C 54.22, H 6.25, N 7.90; found C 54.13, H 6.46, N 7.84.

6-Oxa-(−)-calystegine B$_2$ Derivative. (1*R*,2*S*,3*R*,4*S*,5*S*)-2,3,4-Trihydroxy-*N*-(*N*′-phenylthiocarbamoyl)-6-oxa-*nor*-tropane (63): A solution of **62** (130 mg, 0.37 mmol) in 90% TFA/H_2O (2 mL) was stirred at room temperature for 15 min. The solvent was eliminated under reduced pressure and the residue was coevaporated several times with water. An aqueous solution was further neutralized with Amberlite® IRA 68 (OH^-) ion-exchange resin, filtered, and freeze-dried. The residue was purified by column chromatography using EtOAc → EtOAc/EtOH (20:1) → EtOAc/EtOH/H_2O (45:5:3). Yield: 103 mg (95%). R_f = 0.47 (EtOAc/EtOH/H_2O, 45:5:3). $[\alpha]_D^{22}$ = −55.6 (*c* = 1.0, H_2O). UV (MeOH): 241 nm (ε_{mM} 13.9). ^{1}H NMR (300 MHz, D_2O, 313 K): δ = 3.64 (t, $J_{3,4}$ = $J_{2,3}$ = 8.1 Hz, 1 H, 3-H), 3.70 (dd, $J_{4,5}$ = 1.5, $J_{3,4}$ = 8.1 Hz, 1 H, 4-H), 3.84 (dd, $J_{1,2}$ = 4.3, $J_{2,3}$ = 8.1 Hz, 1 H, 2-H), 3.91 (dd, $J_{1,7b}$ = 4.3, $J_{7a,7b}$ = 8.5 Hz, 1 H, 7b-H), 4.17 (d, $J_{7a,7b}$ = 8.5 Hz, 1 H, 7a-H), 4.93 (t, $J_{1,2}$ = $J_{1,7b}$ = 4.3 Hz, 1 H, 1-H), 5.99 (d, $J_{4,5}$ = 1.5 Hz, 1 H, 5-H), 7.24−7.44 (m, 5 H, Ph) ppm. ^{13}C NMR (75.5 MHz, D_2O, 313 K): δ = 58.9 (C-1), 66.4 (C-7), 70.6 (C-2), 73.8 (C-4), 75.0 (C-3), 88.7 (C-5), 127.3−138.6 (Ph), 178.3 (CS) ppm. FAB-MS: *m*/*z* = 319 (100) $[M + Na]^+$, 297 (60) $[M + H]^+$. $C_{13}H_{16}N_2O_4S$ (296.34): calcd. C 52.69, H 5.44, N 9.45; found C 52.32, H 5.42, N 9.37.

General Procedure for Inhibition Assay: Inhibitory potencies were determined by spectrophotometrically measuring the residual hydrolytic activities of the glycosidases against the respective *o*- (for β-glucosidase/β-galactosidase from bovine liver) or *p*-nitrophenyl α- or β-D-glycopyranoside, sucrose (for invertase) or α,α′-trehalose (for trehalase) in the presence of the corresponding calystegine derivative. Each assay was performed in phosphate buffer or phosphate-citrate buffer (for α-mannosidase and amyloglucosidase) at the optimal pH for each enzyme. The reactions were initiated by addition of enzyme to a solution of the substrate in the absence or presence of various concentrations of inhibitor. After the mixture was incubated for 10−30 min at 37 °C or 55 °C (for amyloglucosidase) the reaction was quenched by addition of 1 M Na_2CO_3 or a solution of GLC-Trinder (Sigma, for trehalase and invertase). The absorbance of the resulting mixture was determined at 405 nm or at 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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