DOI: 10.1002/ejoc.200500601

Synthesis of Sugar Isocyanates and Their Application to the Formation of Ureido-Linked Disaccharides[‡]

Martín Ávalos,[a] Reyes Babiano,[a] Pedro Cintas,[a] Michael B. Hursthouse,[b]
José L. Jiménez,[a] Mark E. Light,[b] Juan C. Palacios,*[a] and Esther M. S. Pérez[a]

Dedicated to Professor Joaquín Plumet on the occasion of his 60th birthday

Keywords: Isocyanates / Ureas / Ureidosugars

The present work describes a facile and practical route to carbohydrate-based isocyanates, a reactive and appealing family of chiral heterocumulenes, wich can be easily converted into disaccharides and pseudodisaccharides interconnected by urea moieties. A full characterization of these substances by X-ray diffraction analysis and spectroscopic methods reveals further insights into their structures and preferred conformation.

Introduction

Although the preparation of urea and its derivatives dates back to the early history of organic synthesis, the enormous chemical and biological potential of this linkage has only been recognized and exploited within the last decades. Thus, urea itself is capable of forming inclusion complexes with long-chain alkanes and some functionalized molecules.[1,2] In such complexes, the urea molecules self-assemble through intermolecular hydrogen bonds giving rise to a helical lattice into which the guest compounds can be oriented and accommodated. Urea moieties also act as strong hydrogen-bond donors and acceptors,[3] and have been frequently used as functional groups for the formation of supramolecular architectures.[4] Substituted ureas and bisureas have also been shown to give gels with organic liquids and water,[5] and in some cases the gels are thermally reversible and require very low concentrations.[6]

Some thiourea-linked pseudodisaccharides, *O*-protected by acyl groups, have been prepared and structurally characterized.[7] However, the corresponding ureido disaccharides are seldom known. Some carbohydrate-based ureas exhibit relevant biological properties such as the antibiotics SF-1993,[8] CV-1,[9] and the family of glycocinnamoylspermidines.[10] A few glycosylureas have shown to be α-glycosidase inhibitors[11] and *N*-nitrosoureas, such as streptozotocin[12] and chlorozotocin,[13] possess antitumoral activity.[14] These substances induce crosslinking of DNA after in vivo decomposition. The generated isocyanate does not appear to be directly involved in the antitumor effect of nitrosoureas, but it does react with amines and proteins. More importantly, it inhibits DNA polymerase and other enzymes involved in the repair of DNA lesions. It also inhibits RNA synthesis and plays a role in the toxicity of nitrosoureas.[15]

Strategies for the construction of ureidosugars are relatively scarce and mainly involve the condensation of monosaccharides with ureas to give glycosylureas[16] and symmetrical ureidodisaccharides.[17] They also involve the reaction of glycosylamines[18,19] or amino sugars[20–24] with isocyanates or their synthetic equivalents such as carbamates,[25,26] addition of water to diglycosylcarbodiimides,[27,28] as well as side products in varied transformations of glycosyl isocyanates.[26,29]

A convenient synthetic protocol for the construction of structurally diverse glycoconjugates and pseudooligossacharides could be developed by reaction of protected sugar isocyanates with amino compounds. In this context, protected glycosyl isocyanates have been prepared by reaction of *O*-protected glycosylamines with phosgene,[30] or its safer synthetic surrogates,[31] e.g. triphosgene[23] or haloformates,[29] by reaction of glycosyl halides with silver cyanate,[32] through sugar phosphanimines,[33] or by oxidation of glycosyl isocyanides with pyridine *N*-oxide.[30,34,35] However, only one previous work addresses the preparation of a monosaccharide isocyanate at a non-anomeric position.[36]

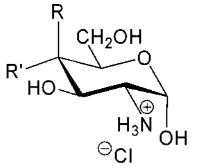
[‡] Part of this work has been presented at V Jornadas de Carbohidratos, Badajoz, Spain, **2000**, pp. 42; and 1er Congrés Maroco-Espagnol sur la Chimie Organique, Marrakech, Morocco, **2004**, A-124.

[a] Departamento de Química Orgánica, Facultad de Ciencias, Universidad de Extremadura,
Avenida de Elvas s/n, 06071 Badajoz, Spain
Fax: +34-924-271-149
E-mail: palacios@unex.es
[b] Departament of Chemistry, University of Southampton, Highfield,
Southampton S017 1BJ, UK

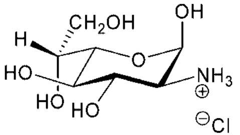
Herein, we describe a synthetic methodology for the preparation of a wide range of protected sugar isocyanates as well as symmetrical and unsymmetrical ureas linking non-anomeric carbon atoms.

Results and Discussion

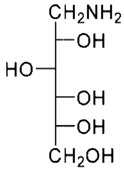
Synthesis of Raw Materials: A series of precursors have been required toward the synthesis of sugar isocyanates, such as those derived from amino sugars **1**–**3** and the aminoalditol **4**, some of them already described, while other substances have been prepared for the first time in this work. Although *O*-protected derivatives of 2-amino-2-deoxy-D-glucose (**1**) are well known, the corresponding analogs of 2-amino-2-deoxy-D-galactose (**2**) have seldom been reported, and therefore we have optimized the preparation of **7** and **10**.



1 R = H, R' = OH
2 R = OH, R' = H



3



4

The appropriate protection of an amino group at C-2 as an enamino derivative also controls the stereochemistry at the anomeric position. Thus, the synthesis of 1,3,4,6-tetra-*O*-acetyl-2-amino-2-deoxy-α-D-galactopyranose (**7**) is summarized in Scheme 1.

The condensation of **2** with diethyl ethoxymethylenemalonate affords exclusively the α-anomer of the enamine **5**, which is subsequently transformed into the per-*O*-acetylenamine **6** without affecting the configuration at the anomeric position. Its spectroscopic data are analogous to those of the enamine derived from **1**.[37] The large coupling constants between the NH and 2-H ($J_{NH,2} \approx$ 9–10 Hz) and between that NH and the CH= proton ($J_{NH,CH} \approx$ 14 Hz) clearly suggest an antiperiplanar disposition for such hydrogen atoms, which in turn indicates that the plane containing the enamino group and the mean plane of the pyranose ring form a dihedral angle of approximately 90° (Figure 1).

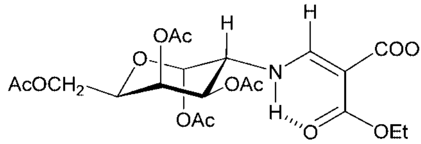


Figure 1. View of the dihedral angle between the main plain of the pyranose ring and the enamino group.

The remaining coupling constants of the sugar moiety are likewise consistent with a pyranose ring of α-D-*galacto* configuration exhibiting a $^4C_1$ conformation. It should also be pointed out that the large value of its optical rotation agrees with an α configuration at the anomeric position.

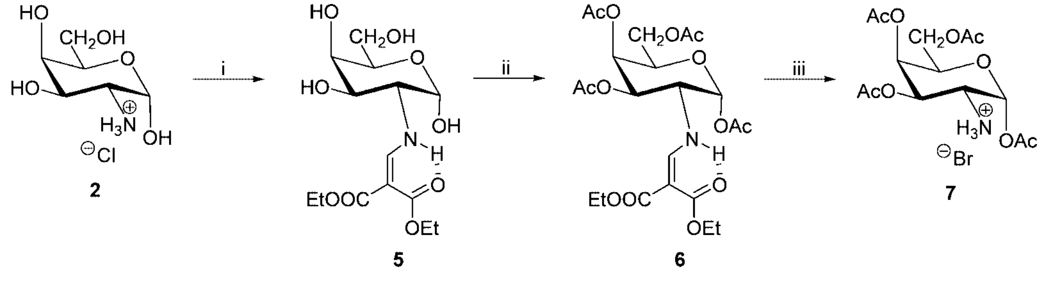
Finally, a facile and high-yielding *N*-deprotection could be accomplished with bromine and water in chloroform[7,38] giving rise to **7**.

The alternative preparation of the β-anomer **10** is depicted in Scheme 2. In this case the temporary protection of the amino group was effected with cinnamaldehyde. Conversion into the resulting imine **8** is accompanied by a selective formation of the β-anomer, which was further per-*O*-acetylated to give **9**, while preserving the stereochemistry at the anomeric position. After treatment with 5 M HCl in acetone, the amino group was deprotected. The β-configuration for **8**–**10** is inferred from the large values of $J_{1,2}$ coupling constants and the small values of their optical rotations.

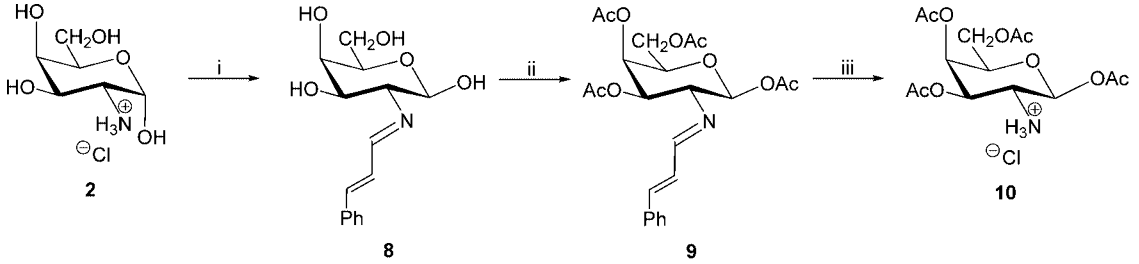
The known 1,3,4,6-tetra-*O*-acetyl-2-amino-2-deoxy-α-D-glucopyranose hydrobromide (**11**)[39] was prepared from **1** following the same route used for **7**.

A series of precursors derived from 2-amino-2-deoxy-D-glucopyranose, **12**,[40] **13**,[41] **14**,[42] as well as of 2-amino-2-deoxy-D-*glycero*-L-*gluco*-heptopyranose, **15**,[7] and **16**,[7] have also been prepared according to literature protocols.

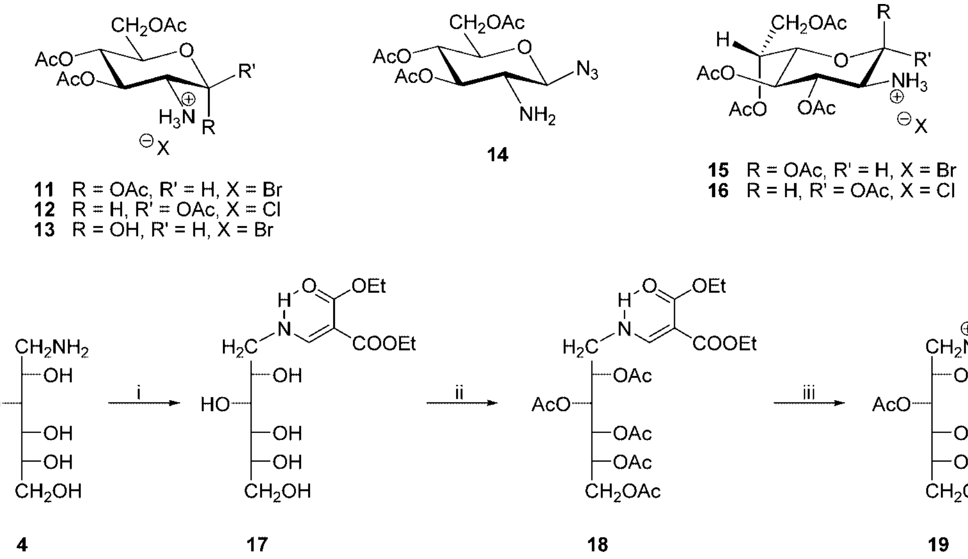
We have equally carried out the preparation of the hydrobromide derived from per-*O*-acetyl-D-glucamine (**19**). Its synthesis is no more than a peripheral modification employed for the synthesis of the hydrochloride,[43] and similar to the route described above for compounds **7** and **11** (Scheme 3). The main, yet relevant, variation is the cleavage of the enamine intermediate **18** with bromine instead of using a stream of chlorine.



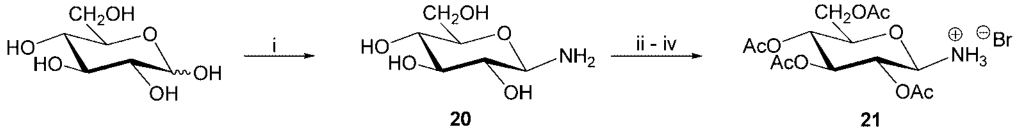
Scheme 1. Reagents: i: EtOCH=C(CO_2Et)$_2$, Et_3N; ii: Ac_2O, C_5H_5N; iii: Br_2, H_2O, Cl_3CH.



Scheme 2. Reagents: i: *trans*-PhCH=CHCHO, $NaHCO_3$; ii: Ac_2O, C_5H_5N; iii: 5 M HCl, CH_3COCH_3.



Scheme 3. Reagents: i: $EtOCH=C(CO_2Et)_2,Et_3N$; ii: Ac_2O, C_5H_5N; iii: Br_2, H_2O, Cl_3CH.

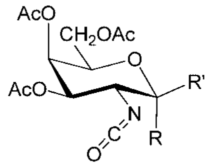


Scheme 4. Reagents: i: NH_3; ii: $EtOCH=C(CO_2Et)_2$, Et_3N; iii: Ac_2O, C_5H_5N; iv: Br_2, H_2O, Cl_3CH.

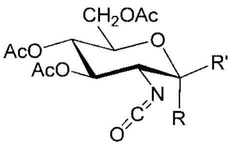
Finally, the enamine strategy has also been used for the synthesis of 2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosylamine hydrobromide (**21**),[38] starting from the β-D-glucopyranosylamine **20** (Scheme 4), which can be easily obtained by the reaction of D-glucose and ammonia.[44]

Syntheses of Sugar Isocyanates: Isocyanates have been frequently employed as building blocks in combinatorial chemistry to generate a library by reaction with amines or hydroxy groups. Accordingly, the isocyanates **22**–**31** have been synthesized by treatment of amino sugars **7**, **10**–**16**, **19**, and **21** with phosgene ($COCl_2$) or triphosgene ($Cl_3CO-COOCl_3$). The derivative **25** is the only non-anomeric isocyanate described so far; it was prepared by Jochims and Seeliger in 1965 using a stream of phosgene.[36] Given the inherent toxicity and hazards associated with the use of phosgene, a convenient, safer and easy-to-use reagent is a 1.93 M solution of phosgene in toluene, which has been employed by Norwick and co-workers for the preparation of amino acid ester isocyanates.[45] Thus, the first strategy (method A) involves the addition, under vigorous stirring, of a 1.93 M solution of phosgene in toluene to a mixture of the corresponding amino sugar hydrohalide and pyridine in CH_2Cl_2 at 0 °C. Pyridine can also be replaced by triethylamine without affecting product yields.

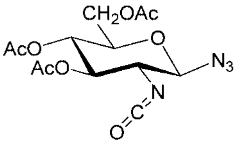
The second protocol (method B), analogous to that employed recently by Ichikawa et al. in the synthesis of Fischer's glucopyranosyl isocyanate (**31**),[23] involves the use of a solid synthetic equivalent of phosgene, triphosgene, under heterogeneous conditions similar to those of the Schotten–Baumann synthesis. This method is also reminiscent of the well-established preparation of sugar isothiocyanates using liquid thiophosgene.[7,36,46] Thus, to a solution of the corresponding amino sugar hydrohalide and a saturated solution of sodium hydrogen carbonate was added triphosgene, under vigorous stirring, at 0 °C in order to minimize the potential hydrolysis of the generated isocyanate. Table 1 collects our results, including the synthesis of **31** for comparative purposes.



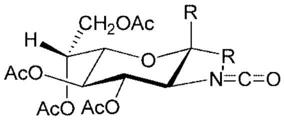
22 R = OAc, R' = H
23 R = H, R' = OAc



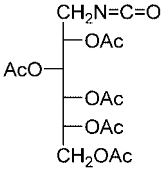
24 R = OAc, R' = H
25 R = H, R' = OAc
26 R = OH, R' = H



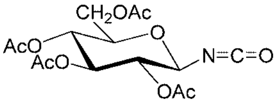
27



28 R = OAc, R' = H
29 R = H, R' = OAc



30



31

Table 1. Synthesis of sugar isocyanates.

Entry	Precursor	Product	Method[a]	Yield (%)
1	**7**	**22**	B	70
2	**10**	**23**	A, B	45, 65
3	**11**	**24**	A, B	65, 64
4	**12**	**25**	A, B	51, 96
5	**13**	**26**[b]	A	88
6	**14**	**27**	B	37
7	**15**	**28**	A, B	55, 52
8	**16**	**29**	A, B	63, 82
9	**17**	**30**	B	80
10	**18**	**31**	A, B	51, 86

[a] Method A (amino sugar/phosgene in toluene); Method B (amino sugar/triphosgene). [b] Isolated as **32**.

The structures and stereochemistries attributed to compounds **22**–**25**, **27**–**31** are consistent with their spectroscopic and analytical data, as well as with their optical rotations. All isocyanates exhibit a strong FT-IR absorption at about 2260 cm^{-1} and ^{13}C resonances at ca. 126 ppm, which are typical of the heterocumulene fragment. For compound **27**, the absorption at 2320 cm^{-1} is also characteristic of the azide group. Moreover, the structure of the acyclic isocyanate **30** could unambiguously be established by single-crystal diffraction analysis and its ORTEP diagram is collected in Figure 2.[47]

For compound **30**, an analysis of its proton–proton coupling constants reveals that this substance should be preferentially existing in solution as an equilibrium between $_2G^-$ and $_2G^-{}_5G^+$ conformations. An extended zig-zag conformation (*P*) or a $_2G^-{}_5G^-$ conformation would otherwise cause a strong 1,3-diaxial interaction between the acetate groups located at C-2 and C-4 or C-4 and C-6, respectively (Scheme 5).[48] Remarkably, a $_2G^-{}_5G^+$ conformation is the preferred geometry adopted by **30** in the crystal lattice (vide supra, Figure 2).

Compound **26** was generated as a transient species and intramolecularly trapped by its glucopyranoimidazolidin-2-one **32**, (Scheme 6) whose isolated yield should also reflect the extent at which the isocyanate was produced. The absence of the characteristic IR band at 2260 cm^{-1} and the N=C=O resonance at δ = 125 ppm, together with the presence of the NH absorption at 3300 cm^{-1}, δ_{NH} at δ = 6.31 ppm and δ_{NCOO} at δ = 156 ppm account for the suggested structure of imidazolidin-2-one.

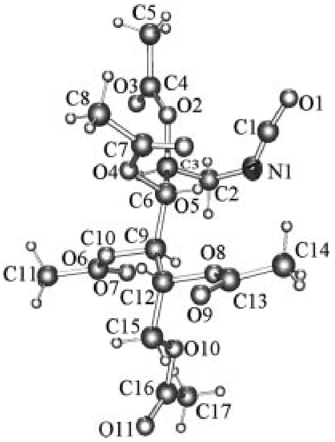
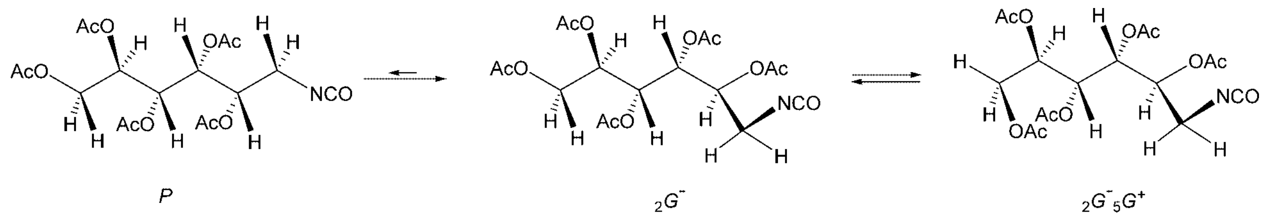
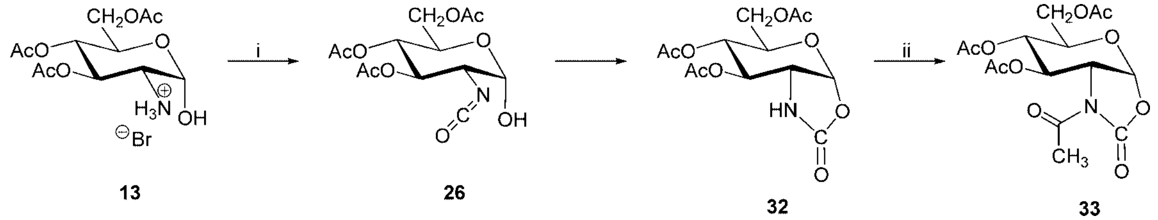


Figure 2. X-ray structure of **30** showing atomic numbering and thermal ellipsoids at the 50% probability level.

The bicyclic derivative **32** has been described previously resulting from diverse reactions of per-*O*-acetylcarbamates of **1**.[49–51] The above-mentioned synthesis is a new and straightforward procedure that gives **32** in high yield, an interesting aspect because such an oxazolidin-2-one could be employed as chiral auxiliary in asymmetric methodologies. Compound **32** could further be characterized by its *N*-acetyl derivative **33**.[13] A strong downfield peak for the *N*-acetyl group (δ_{AcN} = 2.53 ppm) and the shifted resonances of 2-H ($\Delta\delta_{2\text{-H}}$ = 0.64) and 3-H ($\Delta\delta_{3\text{-H}}$ = 0.46), presumably reflect the deshielding caused by the *N*-acetyl group and the heterocyclic C=O bond on the most stable conformation.



Scheme 5.



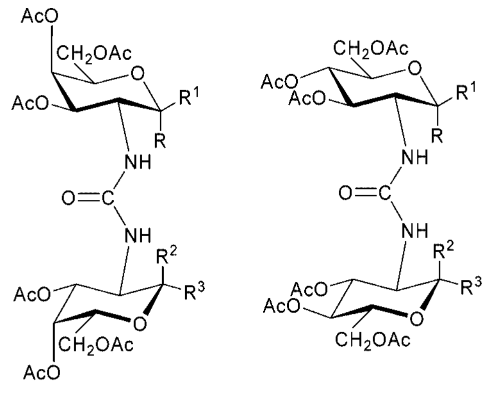
Scheme 6. Reagents: i, Cl_2CO, toluene; ii, Ac_2O, C_5H_5N.

This geometry reveals an antiperiplanar disposition between the carbonyl groups in order to reduce the dipole–dipole interaction. This arrangement has also been found in 3-acetyl-2-oxazolidones[52] and other five-membered *N*-acylated heterocycles,[53–55] and has a marked effect on the optical rotation causing a significant decrease (≈ 60°) going from **32** to **33**.[54,55]

The coupling constant $J_{1,2}$ exhibit an unusual large value (≈ 7 Hz) for an α-anomer derived from compound **1**, whereas $J_{2,3}$ (4.2 Hz) and $J_{3,4}$ (5.3 Hz) have unexpected small values. Overall, such data suggest a severe distortion of the $^4C_1$ conformation (characteristic of compounds derived from **1**) owing to the *cis* fusion with the oxazolidin-2-one ring. The sugar moiety of **32** and **33** should therefore adopt a preferential $^0S_2$ conformation in solution.[20,41,56] It should be mentioned that a *trans* fusion would provide larger coupling constants (≈ 9 Hz).[57]

Syntheses of Ureylenedisaccharides: The facile access to isocyanates **22**–**25** and **27**–**31** offers the possibility of preparing a wide variety of urea-tethered neoglyconjugates, glycopeptide mimetics, and pseudooligosaccharides with urea and carbamate bonds as the carbohydrate–peptide and carbohydrate–carbohydrate linkages. Probably, the most versatile method to synthesize both symmetrical and unsymmetrical carbohydrate-based ureas is the reaction of a sugar isocyanate with an appropriately protected amino sugar and, in fact this approach has been assessed throughout this study.

Formation of such ureidodisaccharides has been carried out by reacting equimolar amounts of the sugar isocyanate and the amino sugar hydrohalide in pyridine solution at room temperature. This heterocyclic base gives rise to the free amino sugar, which attacks then the electrophilic isocyanate group. There is a set of 55 possible synthetic combinations involving the starting isocyanates **22**–**31** with the amino derivatives **7**, **10**–**16**, **19**, and **21**. However, our study has been focused on 10 representative compounds (**34**–**43**). Thus, an ureido group interconnects the C-2 position of two identical fragments of 2-amino-2-deoxy-D-galactopyranose in compounds **34** and **35**, whereas the same spacer links the same position of two 2-amino-2-deoxy-D-glucopyranose units in **36** and **37**.

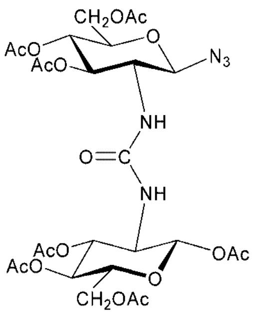


34 $R = R^2 = OAc$, $R^1 = R^3 = H$
35 $R = R^2 = H$, $R^1 = R^3 = OAc$
36 $R = R^2 = OAc$, $R^1 = R^3 = H$
37 $R = R^2 = H$, $R^1 = R^3 = OAc$
38 $R = R^3 = OAc$, $R^1 = R^2 = H$

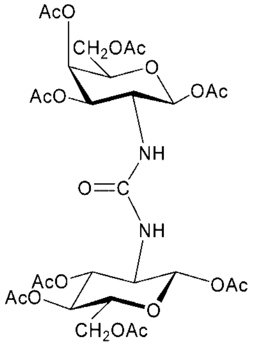
We should point out that compound **37** had already been prepared by Jochims and Seeliger by treatment of **12** with **25**.[36] The molecular symmetry (C_{2v}) present in **34**–**37** simplifies the structural elucidation as both ^1H and ^{13}C NMR spectra exhibit only one signal set for the two sugar moieties.

Likewise, the ureido disaccharides **38** and **39** contain two residues of 2-amino-2-deoxy-D-glucopyranose, albeit with different stereochemistry or functionality at the anomeric position. The α,α anomers **34** and **36** have larger optical rotations than their β,β counterparts **35** and **37**; as expected the α,β ureido derivative **38** exhibits an intermediate value.

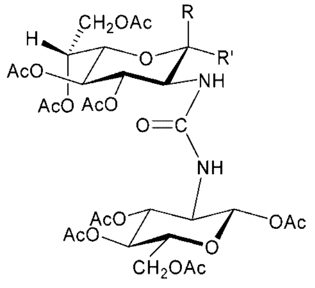
In compounds **40**–**42**, the urea spacer links two structurally different amino sugars. In all cases, one of the fragments comes from 2-amino-2-deoxy-β-D-glucopyranose, while the other involves either 2-amino-2-deoxy-β-D-galactopyranose (**40**) or 2-amino-2-deoxy-D-*glycero*-L-*gluco*-heptopyranose, having β (**41**) or α (**42**) anomeric configurations. Finally, the symmetrical urea **43** constitutes the first example of this kind of glycoconjugates interconnecting two acyclic amino sugars.



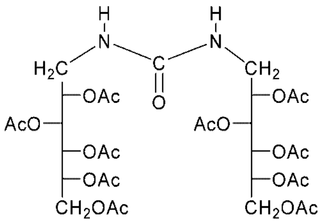
39



40



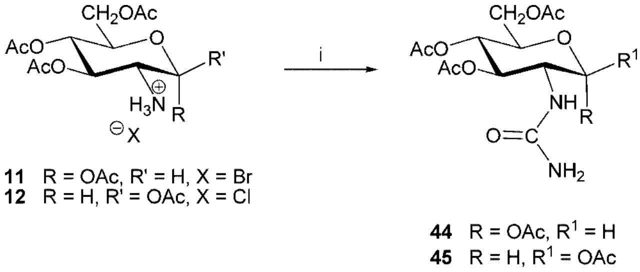
41 R = OAc, R^1 = H
42 R = H, R^1 = OAc



43

As expected, the proposed structures for compounds **34**–**43** can easily be inferred from their spectroscopic and analytical data, and other physical constants. In addition, the solid-state geometry for compound **40** could be determined by single-crystal X-ray diffractometry (Figure 3).[58]

The NH groups of the ureido group show FT-IR absorption bands at ca. 3300 and 1540 cm^{-1}, while the urea carbonyl groups appear at ca. 150 ppm in the ^{13}C NMR spectra. It is interesting to note that both proton and carbon resonances of compounds **36** and **37** are nearly coincidental with those of the ureidoanalogs **44**[59] and **45**,[60] which were prepared by reaction of **11** and **12** with silver cyanate in aqueous medium (Scheme 7).



11 R = OAc, R' = H, X = Br
12 R = H, R' = OAc, X = Cl

44 R = OAc, R^1 = H
45 R = H, R^1 = OAc

Scheme 7. Reagents: i, AgNCO, H_2O.

In addition, the NMR spectra of the sugar fragments present in the non-symmetrical urea **38** can be considered a superposition of those of **36** and **37**. A similar interpretation facilitates the structural assignment of the non-symmetrical derivatives **40**–**42**. Further two-dimensional NMR correlations, selective decoupling, and proton–deuterium exchange also corroborated our assessment. Coupling constants suggest that, in solution, the hexopyranose ring adopts a preferential $^4C_1$ conformation, whereas the $^1C_4$ arrangement is adopted by heptopyranoses. The anomeric configuration could easily be deduced from such coupling constants (a large value for β-anomers of hexoses and α-anomers of heptoses, characteristic of equatorial substituents, as well as small values for α-anomers in hexoses and β-anomers in heptoses, typical of axial groups); along with the ^{13}C resonances for the anomeric carbon atoms (a downfield shift is observed with equatorial groups at C-1). It is equally interesting the large value of the coupling constants $J_{CH,NH}$ (ca. 9 Hz), thus evidencing an antiperiplanar disposition between these protons. Again, the plane containing the urea fragment and the mean plane of the pyranose ring should form a dihedral angle of ca. 90°. Scheme 8 depicts the three possible conformers (*Z*,*Z*; *Z*,*E*, and *E*,*E*) that could exist in solution, assuming the above-mentioned antiperiplanar relationship.

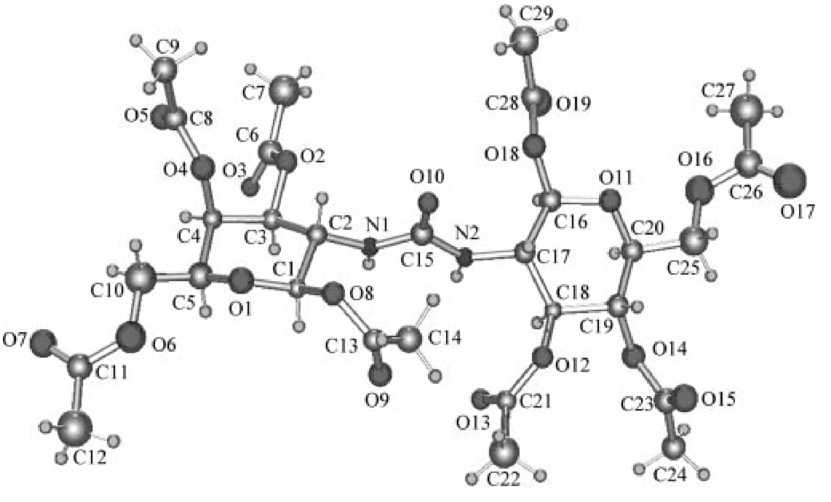
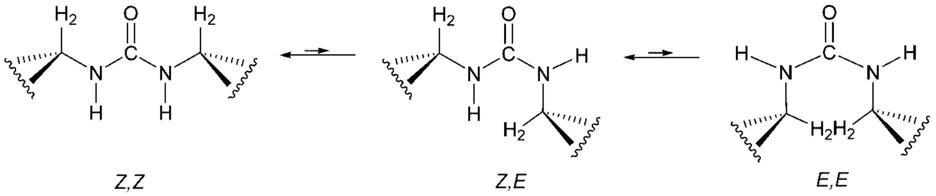
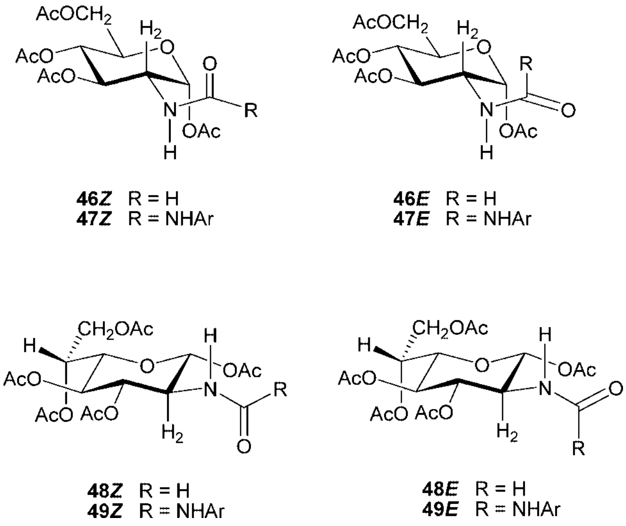


Figure 3. X-ray structure of **40** showing atomic numbering and thermal ellipsoids at the 50% probability level.



Scheme 8.

Because NMR spectra of compounds **34**–**37** evidence a symmetrical pattern, only *Z*,*Z* or *E*,*E* conformers may be observable. However, the latter should be particularly unstable due to 1,3-syndiaxial steric interactions. Furthermore, the chemical shift for the 2-H proton ($\delta_{2\text{-H}} \approx$ 4.0–4.4 ppm) is similar to that of *Z*-conformers in sugar formamides **46**[61] ($\delta^{Z}_{2\text{-H}}$ = 4.56 ppm, $\delta^{E}_{2\text{-H}}$ = 3.80 ppm) and **48**[62] ($\delta^{Z}_{2\text{-H}}$ = 4.34 ppm, $\delta^{E}_{2\text{-H}}$ = 3.57 ppm) as well as to that of ureido derivatives **47**[20] and **49**.[63] For the corresponding *E* conformers, the 2-H resonance should be shifted upfield ($\delta^{E}_{2\text{-H}} \approx$ 3.6 ppm) (Figure 4). Accordingly, the major, or exclusive, conformer in solution for the ureylenedisaccharides **34**–**43** should exhibit a *Z*,*Z* geometry, and the *Z*-conformer will also be the preferred arrangement of models compounds **44** and **45**.


46*Z* R = H
47*Z* R = NHAr

46*E* R = H
47*E* R = NHAr

48*Z* R = H
49*Z* R = NHAr

48*E* R = H
49*E* R = NHAr

Figure 4. *Z*-conformers for compounds **46**–**49**.

Further evidences about the preferential conformation of these glycoconjugates arise from the solid-state structure of **40** (vide supra), in which the molecular disposition adopted in the crystal unit is virtually coincidental with a *Z*-*trans*,*Z*-*trans* conformation. The urea linkage shows a *Z*,*Z* arrangement and one of the sugar fragments (D-*gluco*) exhibits a *trans* relationship between the vicinal 2-H and NH protons. For the other sugar moiety (D-*galacto*), an approximate *trans* geometry can also be found (Figure 3). Finally, it is worth pointing out the macromolecular association of the ureidosugars in the crystalline state (Table 2). Hydrogen bonds connect the NH groups with two different oxygen atoms of a vicinal molecule, the urea carbonyl and the anomeric acetate.

Table 2. Hydrogen bonds [Å and degrees] in the crystalline state of the ureidodisaccharide **40**.[a]

D–H··A	δ(D–H)	δ(H···A)	δ(D···A)	<(D–H–A)
N1–H1···O10[b]	0.88	2.40	3.076(6)	134.3
N2–H2···O18[b]	0.88	2.38	3.201(6)	154.9

[a] For atom numbering, see Figure 3. [b] Symmetry transformations used to generate equivalent atoms: (i) *x* + 1, *y*, *z*.

The crystal data and refinement parameters of **30** and **40** are summarized in Table 3.

Conclusion

A series of sugar isocyanates have been prepared, by means of useful and safe methods, starting from diversely substituted amino sugars, which can also be obtained in a few steps from commercially available sources. These isocyanates could be advantageously employed for the construction of libraries of new glycoconjugates, namely ureidodisaccharides, exemplified here by a series of substances combining different sugar skeleta and configurations. The synthetic protocol is simple and products can easily be isolated and purified. Both spectroscopic and crystallographic analyses reveal a well-defined conformational trend, including the association of such substances at a supramolecular level in the solid state, which could be relevant in crystal engineering. These results should therefore be of benefit to readers interested in the development and application of glycomimetics.

Experimental Section

General Methods: All solvents were purchased from commercial sources and used as received unless otherwise stated. Melting points were determined with Gallenkamp and Electrothermal apparatus and are uncorrected. Analytical TLC were performed on precoated Merck 60 GF_{254} silica gel plates with a fluorescent indicator, and detection by means of UV light at 254 and 360 nm and iodine vapours. Optical rotations were measured at 20 ± 2 °C with a Perkin–Elmer 241 polarimeter. IR spectra were recorded in the range 4000–600 cm^{-1} with FT-IR THERMO spectrophotometer. Solid samples were recorded on KBr (Merck) pellets. ^{1}H- and ^{13}C NMR spectra were recorded on a Bruker 400 AC/PC instrument at 400 and 100 MHz, respectively, or with a Bruker AC 200-E instrument at 200 and 50.3 MHz, respectively, in different solvent systems. Assignments were confirmed by homo- and hetero-nuclear double-resonance, DEPT (distortionless enhancement by polarization transfer), and variable-temperature experiments. TMS was used as the internal standard (δ = 0.00 ppm) and all *J* values are

Table 3. Crystal data and structure refinement parameters of **30** and **40**.

Compound	**30**	**40**
Empirical formula	$C_{17}H_{23}NO_{11}$	$C_{29}H_{40}N_2O_{19}$
Formula weight	417.36	720.63
Temperature [K]	120(2)	120(2)
Wavelength [Å]	0.71069	0.71073
Crystal system	monoclinic	triclinic
Space group	$P2_1$	$P1$
Unit cell dimensions		
a [Å]	9.310(5)	5.2656(6)
b [Å]	7.112(5)	9.8828(15)
c [Å]	16.117(5)	16.498(2)
A [°]		81.199(11)
B [°]	β = 100.563(5)	84.504(10)
Γ [°]		87.274(11)
V [Å^3]	1049.1(10)	844.0(2)
Z	2	1
$D_{calcd.}$ [Mg/m^3]	1.321	1.418
M [mm^{-1}]	0.112	0.120
F(000)	440	380
Crystal size [mm]	0.2 × 0.2 × 0.1	0.6 × 0.2 × 0.1
Diffractometer	Nonius-KappaCCD	Nonius-KappaCCD
θ Range for data collections (°)	3.14–25.03	3.01–25.03°
Limiting indices	$-10 \le h \le 11$ $-8 \le k \le 8$ $-18 \le l \le 19$	$-6 \le h \le 6$ $-11 \le k \le 11$ $-19 \le l \le 19$
Reflections collected	13364	14059
Refinement method	Full-matrix least-squares on F^2	Full-matrix least-squares on F^2
Parameters / restrains	3673 / 1 / 268	5677 / 3 / 460
Goodness-of-fit on F^2	1.029	1.109
Final R indices [$I > 2\sigma(I)$]	R_1 = 0.0455 wR_2 = 0.1042	R_1 = 0.0812 wR_2 = 0.2107
R indices (all data)	R_1 = 0.0616 wR_2 = 0.1107	R_1 = 0.1124 wR_2 = 0.2393
Largest diff. peak/ hole [e·Å^{-3}]	0.211 and –0.160	0.392 and –0.504

given in Hz. Microanalyses were determined with a Leco 932 analyser at the University of Extremadura (Spain). High-resolution mass spectra (chemical ionization) were recorded with a Micromass Autospec spectrometer by the 'Servicio de Espectrometría de Masas'of the university of Santiago de Compostela (Spain).

2-Deoxy-2-[1-(2,2-diethoxycarbonylvinyl)amino]-α-D-galactopyranose (5): To a stirred solution of **2** (3.0 g, 13.9 mmol) and sodium hydrogen carbonate (0.75 g, 6.9 mmol) in water (11 mL) was added diethyl ethoxymethylenemalonate (5.7 mL, 27.8 mmol). A white solid appeared in a few minutes, which was collected by filtration and washed with water, cold ethanol and diethyl ether to yield **5** (3.7 g, 77%); recrystallized from ethanol; m.p. 165–166 °C. $[\alpha]_D^{20}$ = +117.2. $[\alpha]_{578}^{20}$ = +123.0. $[\alpha]_{546}^{20}$ = +141.0. $[\alpha]_{436}^{20}$ = +258.8 (c = 0.5, pyridine). IR (KBr): $\tilde{\nu}$ = 3500–2300 (OH, NH), 1678 (C=O), 1633 (C=O, H bonded), 1589 (C=C), 1239 (C–O–C), 1081, 1011 (C–O) cm^{-1}. ^{1}H NMR (400 MHz, [D$_6$]DMSO): δ = 9.07 (dd, J_{NH-CH} = 14.5 Hz, $J_{NH,2}$ = 8.9 Hz, 1 H, NH), 7.99 (d, J_{NH-CH} = 14.4 Hz, 1 H, CH=C), 6.90 (d, $J_{OH,1}$ = 4.3 Hz, 1 H, 1-OH), 5.11 (t, $J_{1,2}$ = 3.8 Hz, 1 H, 1-H), 5.07 (d, $J_{OH,3}$ = 6.8 Hz, 1 H, 3-OH), 4.71 (d, $J_{OH,4}$ = 4.5 Hz, 1 H, 4-OH), 4.64 (t, $J_{OH,6}$ = 5.7 Hz, 1 H, 6-OH), 4.08 (c, $J_{CH2-CH3}$ = 6.1 Hz, 2 H, CH$_2$), 4.04 (c, $J_{CH2-CH3}$ = 5.1 Hz, 2 H, CH$_2$), 3.81 (t, $J_{5,6} \approx J_{5,6'}$ 6.4 Hz, 1 H, 5-H), 3.75 (t, 1 H, 4-H), 3.58 (m, 3 H, 3-H, 6-H, 2-H), 3.43 (dd, $J_{5,6'}$ = 5.2 Hz, $J_{6,6'}$ = 10.6 Hz, 1 H, 6′-H), 1.18 (c, $J_{CH2-CH3}$ = 6.6 Hz, 6 H, 2 CH$_3$) ppm. ^{13}C NMR (100 MHz, [D$_6$]DMSO): δ = 168.44 (C=O), 165.41 (C=O), 160.33 (*CH*=C), 90.98 (C-1), 88.27 (CH=*C*), 71.04 (C-5), 68.47 (C-4), 68.20 (C-3), 60.68 (C-6), 60.33 (C-2), 59.07 (CH$_2$), 58.89 (CH$_2$), 14.66 (CH$_3$), 14.57 (CH$_3$) ppm. $C_{14}H_{25}NO_{10}$ (367.35): calcd. C 45.77, H 6.86, N 3.81; found C 45.76, H 6.81, N 3.47.

1,3,4,6-Tetra-*O*-acetyl-2-deoxy-2-[1-(2,2-diethoxycarbonylvinyl)-amino]-α-D-galactopyranose (6): To a solution of **5** (1.73 g, 4.95 mmol) in pyridine (17.3 mL) was added acetic anhydride (8.6 mL) and the mixture was kept at 0 °C overnight. Then, it was poured into ice-water. The oily product was extracted with chloroform and the organic layer was washed with 1 M HCl, saturated solution of NaHCO$_3$ and water. Finally, the organic layer was dried (MgSO$_4$) and concentrated to dryness to give an amorphous powder (2.5 g, 99%) which was crystallized from ethanol/water; m.p. 103–104 °C. $[\alpha]_D^{21}$ = +94.8. $[\alpha]_{578}^{21}$ = +98.6. $[\alpha]_{546}^{21}$ = +108.2. $[\alpha]_{436}^{21}$ = +172.6. $[\alpha]_{365}^{21}$ = +257.2 (c = 0.5, CHCl$_3$). IR (KBr): $\tilde{\nu}$ = 3275 (NH), 1757, 1751 (C=O, acetates), 1709 (C=O, H bonded), 1660 (C=O), 1604 (C=C), 1252, 1209 (C–O–C), 1106, 1072, 1013 (C–O) cm^{-1}. ^{1}H NMR (400 MHz, CDCl$_3$): δ = 9.08 (dd, J_{NH-CH} = 13.3 Hz, $J_{NH,2}$ = 10.0 Hz, 1 H, NH), 7.94 (d, $J_{NH,CH}$ = 13.4 Hz, 1 H, NH–C*H*=C), 6.28 (d, $J_{1,2}$ = 3.8 Hz, 1 H, 1-H), 5.48 (d, $J_{3,4}$ = 2.5 Hz, $J_{4,5}$ = 0.0 Hz, 1 H, 4-H), 5.22 (dd, $J_{3,4}$ = 3.2 Hz, $J_{2,3}$ = 11.0 Hz, 1 H, 3-H), 4.29 (c, $J_{5,6} \approx J_{5,6'}$ 10.0 Hz, 1 H, 5-H), 4.20 (c, 2 H, CH$_2$), 4.10 (m, 2 H, 6-H, 6′-H), 3.87 (dt, $J_{1,2}$ = 3.7 Hz, $J_{NH,2}$ = 10.5 Hz, 1 H, 2-H), 2.24, 2.19, 2.04, 2.00 (s, 4 × 3 H, OAc), 1.30 (c, 6 H, 2 CH$_3$) ppm. ^{13}C NMR (100 MHz, CDCl$_3$): δ = 170.17, 169.74, 168.66, 168.58, 165.69 (C=O),158.93 (*CH*=C), 92.37 (CH=*C*), 90.92 (C-1), 68.54 (C-5), 68.33 (C-4), 66.29 (C-3), 60.91 (C-6), 59.97 (CH$_2$), 59.81 (CH$_2$), 56.36 (C-2), 20.63 (OAc), 20.48 (2 OAc), 20.39 (OAc), 14.26 (CH$_3$), 14.09 (CH$_3$) ppm. $C_{22}H_{31}NO_{13}$ (517.48): calcd: C 51.06, H 6.04, N 2.71; found C 51.02, H 5.68, N 2.97.

1,3,4,6-Tetra-*O*-acetyl-2-amino-2-deoxy-α-D-galactopyranose Hydrobromide (7): To a solution of **6** (1.47 g, 3.1 mmol) in chloroform (11 mL) was added gradually a solution of bromine (0.14 mL) in chloroform (8.4 mL) and water (0.05 mL). The mixture was kept at room temperature; and the product crystallized within 30 minutes. Then, the flask was kept at 0 °C for 4 hours, diethyl ether was added (4.8 mL), and the product was collected by filtration (0.9 g, 70%). M.p. 185–186 °C. $[\alpha]_{\mathrm{D}}^{20}$ = +96.2. $[\alpha]_{578}^{20}$ = +100.8. $[\alpha]_{546}^{20}$ = +114.2. $[\alpha]_{436}^{20}$ = +186.4 (*c* = 0.5, pyridine). IR (KBr): $\tilde{\nu}$ = 3000–2544, 1999 (NH_3^+), 1766, 1746 (C=O), 1509 (NH_3^+), 1255, 1242 (C–O–C), 1122, 1049, 1002 (C–O) cm^{-1}. ^{1}H NMR (400 MHz, [D$_6$]DMSO): δ = 8.43 (br. s, 3 H, NH), 6.23 (d, $J_{1,2}$ = 3.5 Hz, 1 H, 1-H), 5.37 (d, $J_{3,4}$ = 2.6 Hz, $J_{4,5}$ = 0.0 Hz, 1 H, 4-H), 5.20 (dd, $J_{3,4}$ = 3.2 Hz, $J_{2,3}$ = 11.4 Hz, 1 H, 3-H), 4.38 (t, $J_{5,6} \approx J_{6,6'}$ 6.29 Hz, 1 H, 6-H), 4.02 (m, 2 H, 5-H, 6′-H), 3.82 (m, 1 H, 2-H), 2.16, 2.12, 2.01, 1.97 (s, 4×3 H, OAc) ppm. ^{13}C NMR (100 MHz, [D$_6$]DMSO): δ = 170.09, 170.04, 169.63, 168.97 (C=O, acetates), 88.98 (C-1), 68.21 (C-3), 67.15 (C-5), 66.25 (C-4), 61.13 (C-6), 47.14 (C-2), 20.99, 20.81, 20.70, 20.59 (OAc) ppm. $C_{14}H_{22}BrNO_9$ (428.23): calcd. C 39.27, H 5.18, N 3.27; found C 39.10, H 5.29, N 3.58.

2-[(*E*)-Cinnamylidene]amino-2-deoxy-β-D-galactopyranose (8): To a stirred solution of **2** (1.0 g, 4.7 mmol) and sodium hydrogen carbonate (0.5 g, 6.0 mmol) in water (6 mL) was added gradually a solution of *trans*-cinnamaldehyde (0.63 mL, 5.0 mmol) in methanol (5 mL). The title compound crystallized in a few minutes, which was washed with water, cold ethanol and diethyl ether (0.8 g, 62%) followed by recrystallization from methanol; m.p. 171–172 °C. $[\alpha]_{\mathrm{D}}^{19}$ = +55.0. $[\alpha]_{578}^{19}$ = +58.0. $[\alpha]_{546}^{19}$ = +70.0. $[\alpha]_{436}^{19}$ = +122.2 (*c* = 0.5, pyridine). IR (KBr): $\tilde{\nu}$ = 3500–2800 (OH), 1636 (CH=CH–C=N), 1449 (arom.), 1163, 1067 (C–O), 750, 690 (arom.) cm^{-1}. ^{1}H NMR (400 MHz, [D$_6$]DMSO): δ = 7.95 (d, $J_{=CH\text{–}CH}$ = 8.8 Hz, 1 H, N=C*H*–CH), 7.59 (d, *J* = 8.3 Hz, 2 H, Ar), 7.36 (m, 3 H, Ar), 7.09 (d, $J_{CH=CH}$ = 16.1 Hz, 1 H, CH=C*H*–Ar), 6.89 (dd, $J_{CH=CH}$ = 16.1 Hz, $J_{CH\text{–}Ar}$ = 8.8 Hz, 1 H, C*H*=CH–Ar), 6.49 (d, $J_{1,OH}$ = 6.9 Hz, 1 H, 1-OH), 4.63 (t, $J_{6,OH}$ = 5.6 Hz, 1 H, 6-OH), 4.58 (m, $J_{1,2}$ = 7.5 Hz, $J_{3,OH}$ = 5.7 Hz, 2 H, 1-H, 3-OH), 4.45 (d, $J_{4,OH}$ = 4.5 Hz, 1 H, 4-OH), 3.66 (t, $J_{3,4}$ = 3.8 Hz, $J_{4,5}$ = 0.0 Hz, 1 H, 4-H), 3.58 (m, 2 H, 3-H, 6-H), 3.52 (dd, $J_{6,6'}$ = 10.7 Hz, $J_{5,6'}$ = 6.3 Hz, 1 H, 6′-H), 3.43 (t, $J_{4,5}$ = 0.0 Hz, $J_{5,6}$ = $J_{5,6'}$ = 6.1 Hz, 1 H, 5-H), 3.02 (dd, $J_{1,2}$ = 7.7 Hz, $J_{2,3}$ = 9.6 Hz, 1 H, 2-H) ppm. ^{13}C NMR (100 MHz, [D$_6$]DMSO): δ = 163.93 (N=C), 141.03 (2 C, CH=CH), 136.00, 129.25, 129.12, 128.64, 127.39 (C, arom.), 96.32 (C-1), 75.44 (C-5), 74.87 (C-2), 71.87 (C-3), 67.40 (C-4), 60.98 (C-6) ppm. $C_{15}H_{19}NO_5$ (293.32): calcd. C 61.42, H 6.53, N 4.78; found C 61.09, H 6.54, N 4.87.

1,3,4,6-Tetra-*O*-acetyl-2-[(*E*)-cinnamylidene]amino-2-deoxy-β-D-galactopyranose (9): To a stirred and cooled suspension (0 °C) of **8** (0.25 g, 0.9 mmol) in pyridine (1.2 mL) was added acetic anhydride (1.1 mL). The mixture was kept at 0 °C for 12 hours. Then, it was poured into ice-water and, on stirring and scrapping, the title compound was obtained as a solid that was filtered and washed with plenty cold water (0.29 g, 71%). M.p. 205–206 °C. $[\alpha]_{\mathrm{D}}^{21}$ = +41.4. $[\alpha]_{578}^{21}$ = +101.0. $[\alpha]_{546}^{21}$ = +289.4 (*c* = 0.5, CHCl$_3$). IR (KBr): $\tilde{\nu}$ = 1748 (C=O, acetates), 1643 (CH=CH–C=N), 1449 (arom.), 1244 (C–O–C), 1065 (C–O), 763, 698 (arom.) cm^{-1}. ^{1}H NMR (400 MHz, CDCl$_3$): δ = 8.06 (d, $J_{=CH\text{–}CH}$ = 8.8 Hz, 1 H, N=C*H*–CH), 7.49 (d, *J* = 6.6 Hz, 2 H, Ar), 7.37 (m, 3 H, Ar), 7.04 (d, $J_{CH=CH}$ = 16.0 Hz, 1 H, CH=C*H*–Ar), 6.86 (dd, $J_{CH=CH}$ = 16.0 Hz, $J_{CH\text{–}CH}$ = 8.8 Hz, 1 H, C*H*=CH–Ar), 5.88 (d, $J_{1,2}$ = 8.2 Hz, 1 H, 1-H), 5.46 (d, $J_{3,4}$ = 3.1 Hz, $J_{4,5}$ = 0.0 Hz, 1 H, 4-H), 5.20 (dd, $J_{3,4}$ = 3.2 Hz, $J_{2,3}$ = 10.4 Hz, 1 H, 3-H), 4.19 (m, 3 H, 5-H, 6-H, 6′-H), 3.55 (dd, $J_{1,2}$ = 8.4 Hz, $J_{2,3}$ = 10.3 Hz, 1 H, 2-H), 2.18 (s, 3 H, OAc), 2.08 (s, 3 H, OAc), 2.06 (s, 3 H, OAc), 1.95 (s, 3 H, OAc) ppm. ^{13}C NMR (100 MHz, CDCl$_3$): δ = 170.42 (C=O), 170.06 (C=O), 169.57 (C=O), 168.63 (C=O), 167.05 (N=C), 143.67 (2×C, CH=CH), 135.09, 129.70, 128.90 (arom.), 127.41 (2 C, arom.), 127.32 (arom.), 93.32 (C-1), 71.69 (C-2), 71.48 (C-5), 68.81 (C-3), 65.79 (C-4), 61.22 (C-6), 20.77 (CH$_3$), 20.67 (2×CH$_3$), 20.51 (CH$_3$) ppm. $C_{23}H_{27}NO_9$ (461.46): calcd. C 59.86, H 5.90, N 3.04; found C 59.48, H 5.85, N 2.83.

1,3,4,6-Tetra-*O*-acetyl-2-amino-2-deoxy-β-D-galactopyranose Hydrochloride (10): A solution of **9** (1.84 g, 4.0 mmol) in acetone (8.6 mL) was heated at reflux. Then, 5 N HCl (0.92 mL) was added while the temperature was maintained at 40–50 °C. The title compound suddenly crystallized. Then, it was kept at room temperature for half an hour and subsequently cooled to 0 °C, diethyl ether (6.2 mL) was added and the product was collected by filtration to yield pure **10** (1.1 g, 73%). M.p. 204–206 °C. $[\alpha]_{\mathrm{D}}^{22}$ = +4.2. $[\alpha]_{578}^{22}$ = +3.4. $[\alpha]_{546}^{22}$ = +5.2. $[\alpha]_{436}^{22}$ = +22.8 (*c* = 0.5, pyridine). IR (KBr): $\tilde{\nu}$ = 3100–2545 (NH_3^+), 2008 (NH_3^+), 1778, 1751, 1747 (C=O), 1599, 1510 (NH_3^+), 1250, 1222, 1209 (C–O–C), 1113, 1074, 1065 (C–O) cm^{-1}. ^{1}H NMR (400 MHz, [D$_6$]DMSO): δ = 8.77 (br. s, 3 H, NH), 5.89 (d, $J_{1,2}$ = 8.7 Hz, 1 H, 1-H), 5.29 (m, 2 H, 3-H, 4-H), 4.29 (t, $J_{5,6} \approx J_{6,6'}$ 6.2 Hz, 1 H, 6-H), 3.37 (m, 3 H, 2-H, 5-H, 6′-H), 2.16 (s, 3 H, OAc), 2.12 (s, 3 H, OAc), 2.05 (s, 3 H, OAc), 1.99 (s, 3 H, OAc) ppm. ^{13}C NMR (100 MHz, [D$_6$]DMSO): δ = 170.08 (C=O), 169.51 (C=O), 168.83 (C=O), 92.46 (C-1), 71.23 (C-3), 68.99 (C-5), 65.95 (C-4), 61.35 (C-6), 49.54 (C-2), 21.03 (CH$_3$), 20.87 (CH$_3$), 20.67 (CH$_3$), 20.51 (CH$_3$) ppm. $C_{14}H_{22}ClNO_9$ (383.78): calcd. C 43.81, H 5.78, N 3.65; found C 44.09, H 6.23, N 3.96.

1,3,4,6-Tetra-*O*-acetyl-2-amino-2-deoxy-α-D-glucopyranose Hydrobromide (11): From 1,3,4,6-tetra-*O*-acetyl-2-deoxy-2-[1-(2,2-diethoxycarbonylvinyl)amino]-α-D-glucopyranose[37] (13.9 g, 26.8 mmol) following the same route as for compound **7** the title compound **11** was obtained. (7.42 g, 65%), (ref.[39] $[\alpha]_{\mathrm{D}}$ = +118.2). M.p. 190–192 °C. $[\alpha]_{\mathrm{D}}^{23}$ = +117.2. $[\alpha]_{578}^{23}$ = +121.2. $[\alpha]_{546}^{23}$ = +136.8. $[\alpha]_{436}^{23}$ = +228.0 (*c* = 0.5, H$_2$O). IR (KBr): $\tilde{\nu}$ = 3100–2535, 1765 (C=O), 1510 (NH_3^+), 1223 (C–O–C), 1030 (C–O) cm^{-1}. ^{1}H NMR (400 MHz, [D$_6$]DMSO): δ = 8.57 (br. s, 3 H, NH), 6.19 (d, $J_{1,2}$ = 3.2 Hz, 1 H, 1-H), 5.25 (d, $J_{3,4}$ = $J_{4,5}$ = 10.0 Hz, 1 H, 4-H), 5.00 (dd, $J_{2,3}$ = $J_{3,4}$ = 9.7 Hz, 1 H, 3-H), 4.18 (m, 2 H, 5-H, 6-H), 3.98 (d, 1 H, $J_{6,6'}$ = 11.6 Hz, 6′-H), 3.91 (dd, 1 H, $J_{1,2}$ = 3.1 Hz, $J_{2,3}$ = 10.6 Hz, 2-H), 2.24, 2.19, 2.04, 1.98 (s, 4×3 H, OAc) ppm. ^{13}C NMR (100 MHz, [D$_6$]DMSO): δ = 170.18, 169.43, 168.94 (C=O, acetates), 88.36 (C-1), 69.20 (C-3), 69.04 (C-5), 67.49 (C-6), 61.20 (C-4), 50.37 (C-2), 21.09, 20.73, 20.54 (OAc) ppm.

1-Deoxy-1-[(2,2-diethoxycarbonyvinyl)]amino-D-glucitol (17): To a solution of **4** (8.4 g, 46.42 mmol) in methanol (250 mL) was added diethyl ethoxymethylenemalonate (15.5 mL, 62.5 mmol). The mixture was stirred at room temperature for 24 hours, resulting in the formation of a solid that was filtered (13.7 g 84%). M.p. 204–206 °C. IR (KBr): $\tilde{\nu}$ = 3500–3200 (OH), 1651, 1605 (C=C), 1271 (C–O–C), 1150, 1013 cm^{-1} (C–O). ^{1}H NMR (400 MHz, CDCl$_3$): δ = 9.19 (dt, $J_{NH,CH2}$ = 6.6 Hz, $J_{NH,CH=}$ = 13.2 Hz, 1 H, NH), 7.98 (d, $J_{NH,CH=}$ = 14.8 Hz, 1 H, CH=), 4.99 (d, 1 H, $J_{2,OH}$ = 5.6 Hz, 2-OH), 4.50 (d, 1 H, $J_{4,OH}$ = 5.2 Hz, 4-OH), 4.43 (m, 2 H, 3-OH, 5-OH), 4.35 (t, 1 H, $J_{6,OH} \approx J_{6',OH}$ 5.6 Hz, 6-OH), 4.09 (2 H, c, $J_{CH3,\mathit{CH2}}$ = 7.2 Hz, *CH$_2$*CH$_3$), 4.05 (2 H, c, $J_{CH3,\mathit{CH2}}$ = 7.1 Hz, *CH$_2$*CH$_3$), 3.64–3.28 (m, 8 H, 1-H, 1′-H, 2-H, 3-H, 4-H, 5-H, 6-H, 6′-H), 1.20 (t, $J_{\mathit{CH3},CH2}$ = 7.1 Hz, 3 H, CH$_3$), 1.18 (t, $J_{\mathit{CH3},CH2}$ = 7.1 Hz, 1 H, CH$_3$) ppm. ^{13}C NMR (100 MHz, CDCl$_3$): δ = 168.07, 165.45 (C=O), 160.40 (C=*CH*), 87.96 (*C*=CH), 72.02 (C-2), 71.46 (C-4), 71.27 (C-5), 70.16 (C-3), 63.50 (C-6), 58.88, 58.79 (2 C, CH$_2$), 52.10 (C-1), 14.52, 14.46 (2 C, CH$_3$) ppm.

2,3,4,5,6-Penta-*O*-acetyl-1-deoxy-1-[(2,2-diethoxycarbonylvinyl)]amino-D-glucitol (18): To a cooled solution of **17** (12.7 g, 36.3 mmol) in pyridine (105 mL) was added gradually acetic anhydride (158 mL). The mixture was kept at 0 °C for 2 hours. Then it was poured into ice-water and was extracted with chloroform (3 × 125 mL). The organic layer was washed with a solution of 1 N HCl (2 × 250 mL), a saturated solution of $NaHCO_3$ (2 × 250 mL), water (2 × 250 mL), and dried (anhydrous $MgSO_4$). The solution was evaporated to dryness and the title compound was obtained as an oily residue (20.3 g, 100%). IR (KBr): $\tilde{\nu}$ = 1748, (C=O, acetates), 1658 (C=O), 1610 (CH=CH), 1431 (arom.), 1219 (C–O–C), 1048 (C–O), 803, 756 (arom.) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 9.19 (dt, $J_{NH,CH2}$ = 6.9 Hz, $J_{NH,CH=}$ = 13.9 Hz, 1 H, NH), 7.92 (d, $J_{NH,CH=}$ = 13.9 Hz, 1 H, CH=), 5.40 (m, 2 H, 3-H, 4-H), 5.17 (dd, $J_{2,3}$ = 5.1 Hz, 1 H, 2-H), 5.05 (dd, 1 H, 5-H), 4.26–4.13 (m, 4 H, 6-H, 6′-H, 2 CH_2CH_3), 3.62 (dt, 1 H, 1-H), 3.49 (dt, $J_{1,1'}$ = 14.1 Hz, $J_{1,2}$ = 7.4 Hz, 1 H, 1′-H), 2.14, 2.13, 2.11, 2.10, 2.05, 2.04 (s, 4 × 3 H, OAc), 1.32 (t, $J_{CH3,CH2}$ = 7.4 Hz, 3 H, CH_3), 1.27 (t, $J_{CH3,CH2}$ = 7.4 Hz, 3 H, CH_3) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 169.98, 169.68, 169.48, 169.43, 169.32, 168.40, 165.32 (C=O), 159.74 (C=*CH*), 90.90 (*C*=CH), 70.05 (C-2), 68.45 (C-3), 68.31 (C-4), 68.17 (C-5), 60.89 (C-6), 59.46, 59.24 (2 C, CH_2), 48.81 (C-1), 20.16, 20.00 (CH_3), 14.01, 13.90 (2 C, CH_3CH_2) ppm.

2,3,4,5,6-Penta-*O*-acetyl-1-amino-1-deoxy-D-glucitol Hydrobromide (19): To a solution of **18** (21.9 g, 36.3 mmol) in chloroform (300 mL) was added gradually a solution of bromine (1.57 mL) in chloroform (98 mL) and water (0.6 mL) until the solution showed a persistent orange color. The mixture was kept at 0 °C for 4 hours. Then, the product was filtered off and washed with diethyl ether to give **19** (12.2 g, 73%). M.p. 205–207 °C. $[\alpha]^{20}_{D}$ = –2.6. $[\alpha]^{20}_{578}$ = –1.8. $[\alpha]^{20}_{546}$ = –1.6. $[\alpha]^{20}_{436}$ = –1.0. $[\alpha]^{20}_{365}$ = –1.4 (*c* = 0.5, H_2O). IR (KBr): $\tilde{\nu}$ = 3200–2900 (NH_3^+), 1755 (C=O), 1501 (NH_3^+), 1215 (C–O–C), 1073, 1048, 1027 cm^{-1} (C–O). ^1H NMR (400 MHz, $CDCl_3$): δ = 8.07 (br. s, 3 H, NH_3^+), 5.29 (m, 2 H, 3-H, 4-H), 5.18 (m, 1 H, 2-H), 4.99 (dt, $J_{5,6}$ = 2.9 Hz, $J_{5,6'}$ = 6.2 Hz, 1 H, 5-H), 4.22 (dd, $J_{5,6'}$ = 2.9 Hz, $J_{6,6'}$ = 12.4 Hz, 1 H, 6-H), 4.07 (dd, $J_{5,6'}$ = 6.4 Hz, $J_{6,6'}$ = 12.4 Hz, 1 H, 6′-H), 3.41 (br. s, 1 H, 1-H), 3.02 (br. s, 1 H, 1′-H), 2.10, 2.05, 2.03, 1.99, 1.98 (s, 4 × 3 H, OAc) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 170.23, 170.18, 169.88, 169.74, 169.68 (C=O), 68.95 (C-2), 68.62 (C-3), 68.35 (C-4), 68.30 (C-5), 61.51 (C-6), 39.08 (C-1), 21.25, 20.89, 20.78, 20.67, 20.62 (CH_3, acetates) ppm. $C_{16}H_{26}BrNO_{10}$ (472.28): calcd. C 40.69, H 5.55, N 2.87; found C 40.33, H 5.33, N 2.51.

General Procedures for the Synthesis of Protected Sugar Isocyanates. Method A: To a cooled solution of pyridine (0.32 mL) in anhydrous dichloromethane (10 mL) was added the corresponding *O*-protected amino sugar (1.0 mmol) and the mixture was stirred vigorously at 0 °C for 30 min. Then, it was added dropwise a solution of phosgene in toluene (1.93 M, 1.1 mL, 2.0 mmol). The mixture was stirred at 0 °C for 2 additional hours. The reaction mixture was washed with 0.5 N HCl (2 × 5 mL), a saturated solution of NaCl (5 mL), dried with anhydrous $MgSO_4$, and concentrated to dryness. The oily residue was crystallized from diethyl ether/petroleum ether. **Method B:** To a heterogeneus mixture of the corresponding *O*-protected amino sugar (4.6 mmol) in dichloromethane (50 mL) and saturated solution of $NaHCO_3$ (30 mL) was added triphosgene (1.35 g, 4.6 mmol) The mixture was stirred vigorously at 0 °C for 30 min. The organic layer was separated, washed with a saturated solution of NaCl, dried (Na_2SO_4), and concentrated to dryness. The white powder obtained was further crystallized from diethyl ether/petroleum ether.

1,3,4,6-Tetra-*O*-acetyl-2-deoxy-2-isocyanato-α-D-galactopyranose (22): From **7** and following the method B the isocyanate **22** was obtained (70%). M.p. 106–107 °C. $[\alpha]^{20}_{D}$ = +115. $[\alpha]^{20}_{578}$ = +116.2. $[\alpha]^{20}_{540}$ = +128.0. $[\alpha]^{20}_{436}$ = +195.4 (*c* = 0.5, $CHCl_3$). IR (KBr): $\tilde{\nu}$ = 2275 (N=C=O), 1745 (C=O), 1250, 1209 (C–O–C, ester), 1042, 1015 (C–O) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 6.29 (d, $J_{1,2}$ = 3.5 Hz, 1 H, 1-H), 5.46 (d, $J_{3,4}$ = 1.9 Hz, $J_{4,5}$ = 0.0 Hz, 1 H, 4-H), 5.24 (dd, $J_{3,4}$ = 3.1 Hz, $J_{2,3}$ = 11.0 Hz, 1 H, 3-H), 4.30 (t, $J_{5,6} \approx J_{5,6'}$ 6.7 Hz, $J_{4,5}$ = 0.0 Hz, 1 H, 5-H), 4.09 (m, 3 H, 2-H, 6-H, 6′-H), 2.20, 2.16, 2.08, 2.04 (s, 4 × 3 H, OAc) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 170.32, 169.97, 169.89, 168.78 (C=O, acetate), 125.92 (NCO), 90.41 (C-1), 69.65 (C-4), 68.70 (C-3), 66.53 (C-5), 60.99 (C-6), 51.90 (C-2), 20.83 (OAc), 20.61 (2 OAc), 20.53 (2 OAc) ppm. $C_{15}H_{19}NO_{10}$ (373.31): calcd. C 48.26, H 5.13, N 3.75; found C 48.11, H 5.19, N 3.93.

1,3,4,6-Tetra-*O*-acetyl-2-deoxy-2-isocyanato-β-D-galactopyranose (23): From **10** and following the methods A (45%) and B (65%) the title compound **23** was obtained. Recrystallized from diethyl ether/petroleum ether. M.p. 149–150 °C. $[\alpha]^{19}_{D}$ = +27.2. $[\alpha]^{19}_{578}$ = +29.0. $[\alpha]^{19}_{546}$ = +32.6. $[\alpha]^{19}_{436}$ = +57.2 (*c* = 0.5, $CDCl_3$). IR (KBr): $\tilde{\nu}$ = 2260 (N=C=O), 1756, 1741 (C=O), 1245, 1216 (C–O–C), 1048 (C–O) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 5.59 (d, $J_{1,2}$ = 8.7 Hz, 1 H, 1-H), 5.40 (d, $J_{3,4}$ = 3.1 Hz, $J_{4,5}$ = 0.0 Hz, 1 H, 4-H), 4.95 (dd, $J_{3,4}$ = 3.4 Hz, $J_{2,3}$ = 10.7 Hz, 1 H, 3-H), 4.15 (dd, $J_{5,6}$ = 7.2 Hz, $J_{6,6'}$ = 11.0 Hz, 6-H), 4.12 (d, $J_{5,6'}$ = 6.7 Hz, 1 H, 6′-H), 4.05 (m, $J_{5,6'}$ = 6.6 Hz, $J_{4,5}$ = 0.0 Hz, 1 H, 5-H), 3.77 (t, $J_{1,2} \approx J_{2,3}$ 9.4 Hz, 1 H, 2-H), 2.20, 2.16, 2.08, 2.04 (s, 3 H, OAc) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 170.30, 169.88, 169.69, 168.65 (C=O, acetates), 126.99 (NCO), 92.76 (C-1), 71.85 (C-3, C-5), 65.96 (C-4), 60.86 (C-6), 53.77 (C-2), 20.73, 20.61, 20.52, 20.43 (OAc) ppm. $C_{15}H_{19}NO_{10}$ (373.31): calcd. C 48.26, H 5.13, N 3.75; found C 48.48, H 4.93, N 3.86.

1,3,4,6-Tetra-*O*-acetyl-2-deoxy-2-isocyanato-α-D-glucopyranose (24): From **11** and following the methods A (65%) and B (64%) the title isocyanate **24** was obtained. M.p. 113–114 °C. $[\alpha]^{20}_{D}$ = +143.6. $[\alpha]^{20}_{578}$ = +145.0. $[\alpha]^{20}_{546}$ = +164.0. $[\alpha]^{20}_{436}$ = +254.8 (*c* = 0.5, $CHCl_3$). IR (KBr): $\tilde{\nu}$ = 2259 (N=C=O, isocyanate), 1753 (C=O), 1221 (C–O–C), 1154 cm^{-1} (C–O). ^1H NMR (400 MHz, $CDCl_3$): δ = 6.23 (d, $J_{1,2}$ = 3.6 Hz, 1 H, 1-H), 5.37 (t, $J_{2,3} \approx J_{3,4}$ 9.9 Hz, 1 H, 3-H), 5.05 (t, $J_{3,4} \approx J_{4,5}$ 9.7 Hz, 1 H, 4-H), 4.27 (dd, $J_{5,6}$ = 3.7 Hz, $J_{6,6'}$ = 12.3 Hz, 1 H, 6-H), 4.08 (dddd, $J_{5,6}$ = 3.8 Hz, $J_{5,6'}$ = 2.3 Hz, $J_{4,5}$ = 10.2, 1 H, 5-H), 4.02 (dd, $J_{5,6'}$ = 2.3 Hz, $J_{6,6'}$ = 12.3 Hz, 1 H, 6′-H), 3.78 (dd, $J_{1,2}$ = 3.6 Hz, $J_{2,3}$ = 10.5 Hz, 1 H, 2-H), 2.20, 2.09, 2.05, 2.02 (s, 3 H, OAc) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 170.4, 170.1, 169.4, 168.5 (C=O, acetates), 125.8 (NCO), 89.8 (C-1), 71.8 (C-3), 69.8 (C-5), 67.4 (C-4), 61.3 (C-6), 55.5 (C-2), 20.7, 20.6, 20.5 (4 OAc) ppm. $C_{15}H_{19}NO_{10}$ (373.31): calcd. C 48.26, H 5.13, N 3.75; found C 48.10, H 5.20, N 3.79.

1,3,4,6-Tetra-*O*-acetyl-2-deoxy-2-isocyanato-β-D-glucopyranose (25): From **12** and following the methods A (51%) and B (96%) compound **25** was obtained. M.p. 75–76 °C. $[\alpha]^{21}_{D}$ = +35.2. $[\alpha]^{21}_{578}$ = +37.0. $[\alpha]^{21}_{546}$ = +41.4. $[\alpha]^{21}_{436}$ = +74.6. $[\alpha]^{21}_{365}$ = +121.2 (*c* 0.5, $CDCl_3$). [ref.[42] m.p. 71–72 °C. $[\alpha]_D$ = 35.9. $[\alpha]_{578}$ = 37.5 (*c* = 1.0, $HCONMe_2$)]. IR (KBr): $\tilde{\nu}$ = 2263 (N=C=O), 1742 (C=O), 1236 (C–O–C), 1047 (C–O) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 5.59 (d, $J_{1,2}$ = 8.6 Hz, 1 H, 1-H), 5.15 (t, $J_{2,3} \approx J_{3,4}$ 9.8 Hz, 1 H, 3-H), 5.00 (t, $J_{3,4} \approx J_{4,5}$ 9.5 Hz, 1 H, 4-H), 4.28 (dd, $J_{5,6}$ = 4.2 Hz, $J_{6,6'}$ = 12.5 Hz, 1 H, 6-H), 4.06 (dd, $J_{6,6'}$ = 12.5 Hz, 1 H, 6′-H), 3.84 (dddd, $J_{5,6'}$ = 2.1 Hz, $J_{5,6}$ = 4.1 Hz, $J_{4,5}$ = 10.0 Hz, 1 H, 5-H), 3.77 (t, $J_{1,2} \approx J_{2,3}$ 9.4 Hz, 1 H, 2-H), 2.17, 2.08, 2.06, 2.01 (s, 3 H, OAc) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 170.4, 169.7, 169.5, 168.6 (C=O, acetates), 126.6 (NCO), 92.4 (C-1), 73.2 (C-3), 72.8 (C-5), 67.5 (C-4), 61.3 (C-6), 56.8 (C-2), 20.6 (OAc), 20.6 (OAc), 20.4 (2 OCH_3) ppm. $C_{15}H_{19}NO_{10}$ (373.31): calcd. C 48.26, H 5.13, N 3.75; found C 48.42, H 5.10, N 3.99.

3,4,6-Tri-*O*-acetyl-2-deoxy-2-isocyanato-β-D-glucopyranosyl Azide (27): To a solution of **14** (1.0 g, 3.0 mmol) in dichloromethane

(33 mL) was added triphosgene (0.89 g, 3.0 mmol) and the mixture was stirred vigorously at 0 °C for 30 min. Then, it was concentrated to dryness, and the white residue was recrystallized from diethyl ether/petroleum ether to give **27** (0.39 g, 37%). M.p. 109–110 °C. $[\alpha]_D^{20} = +3.6$. $[\alpha]_{578}^{20} = +4.2$. $[\alpha]_{546}^{20} = +5.2$. $[\alpha]_{436}^{20} = +11.8$ ($c = 0.5$, $CDCl_3$). IR (KBr): $\tilde{\nu}$ = 2240 (N=C=O), 2119 (N=N=N), 1750 (C=O), 1240, 1222 (C–O–C), 1113, 1067, 1039 cm^{-1} (C–O). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.10 (t, $J_{2,3} \approx J_{3,4}$ 9.8 Hz, 1 H, 3-H), 5.00 (t, $J_{4,5} \approx J_{3,4}$ 9.7, 1 H, 4-H), 4.70 (d, $J_{1,2}$ = 8.9 Hz, 1 H, 1-H), 4.30 (dd, $J_{5,6}$ = 4.8 Hz, $J_{6,6'}$ = 12.5 Hz, 1 H, 6-H), 4.15 (dd, $J_{5,6'}$ = 2.2 Hz, $J_{6,6'}$ = 12.5 Hz, 1 H, 6′-H), 3.81 (dddd, $J_{5,6'}$ = 2.3 Hz, $J_{5,6}$ = 4.7 Hz, $J_{4,5}$ = 10.0, 1 H, 5-H), 3.57 (dd, $J_{1,2}$ = 9.1 Hz, $J_{2,3}$ = 9.9 Hz, 1 H, 2-H), 2.10 (s, 6 H, OAc), 2.04 (s, 3 H, OAc) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 170.5, 169.8, 169.4 (C=O, acetates), 126.6 (NCO), 89.2 (C-1), 74.1 (C-5), 73.3 (C-3), 67.6 (C-4), 61.5 (C-6), 57.7 (C-2), 20.6 (OAc), 20.5 (2 OAc) ppm. $C_{13}H_{16}N_4O_8$ (356.29): calcd. C 43.82, H 4.53, N 15.73; found C 44.12, H 4.80, N 15.70.

1,3,4,6,7-Penta-*O*-acetyl-2-deoxy-2-isocyanato-β-D-*glycero*-L-*gluco*-heptopyranose (28): From **15** and following the methods A (55%) and B (52%) the title compound **28** was obtained. M.p. 112–113 °C. $[\alpha]_D^{22} = +115.4$. $[\alpha]_{578}^{22} = +116.0$. $[\alpha]_{546}^{22} = +133.0$. $[\alpha]_{436}^{22} = +211.8$ ($c = 0.5$, $CHCl_3$). IR (KBr): $\tilde{\nu}$ = 2265 (N=C=O), 1755 (C=O), 1223 (C–O–C), 1142, 1032 (C–O) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.25 (d, $J_{1,2}$ = 3.6 Hz, 1 H, 1-H), 5.37 (t, $J_{2,3} \approx J_{3,4}$ 9.9 Hz, 1 H, 3-H), 5.24 (t, $J_{6,7} \approx J_{6,7'}$ 6.1 Hz, 1 H, 6-H), 5.01 (t, $J_{4,5} \approx J_{3,4}$ 9.9 Hz, 1 H, 4-H), 4.22 (dd, $J_{6,7}$ = 5.2 Hz, $J_{7,7'}$ = 11.6 Hz, 1 H, 7-H), 4.14 (m, $J_{6,7'}$ = 7.5 Hz, $J_{7,7'}$ = 11.4 Hz, 2 H, 7′-H, 5-H), 3.81 (dd, $J_{1,2}$ = 3.7 Hz, $J_{2,3}$ = 10.4 Hz, 1 H, 2-H), 2.27 (s, 3 H, OCH_3), 2.11 (s, 6 H, OCH_3), 2.03 (s, 3 H, OCH_3), 2.03 (s, 3 H, OCH_3) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 170.3 (CH_3-*C*O), 170.1 (2 CH_3–*C*O), 169.5 (CH_3–*C*O), 168.3 (CH_3–*C*O), 126.9 (NCO), 89.8 (C-1), 72.0 (C-3), 70.0 (C-5), 66.7 (C-4), 66.5 (C-6), 61.9 (C-7), 55.5 (C-2), 20.7 (*C*H_3–CO), 20.6 (3 *C*H_3–CO), 20.4 (2 *C*H_3–CO) ppm. $C_{18}H_{23}NO_{12}$ (445.37): calcd. C 48.54, H 5.21, N 3.14; found C 48.31, H 5.30, N 3.20.

1,3,4,6,7-Penta-*O*-acetyl-2-deoxy-2-isocyanato-α-D-*glycero*-L-*gluco*-heptopyranose (29): From **16** and following the methods A (63%) and B (82%) the title compound **29** was obtained. M.p. 140–141 °C. $[\alpha]_D^{19} = 0.0$. $[\alpha]_{578}^{19} = -3.6$. $[\alpha]_{546}^{19} = -8.8$. $[\alpha]_{436}^{19} = -36.6$ ($c = 0.5$, $CHCl_3$). IR (KBr): $\tilde{\nu}$ = 2261 (N=C=O), 1755 (C=O), 1242 (C–O–C), 1109, 1072, 961 (C–O) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.54 (d, 1 H, $J_{1,2}$ = 8.4 Hz, 1-H), 5.28 (dt, 1 H, $J_{6,7} \approx J_{6,7'}$ 5.4 Hz, $J_{5,6}$ = 2.3 Hz, 6-H), 5.16 (t, $J_{3,4} \approx J_{2,3}$ 9.9 Hz, 1 H, 3-H), 5.01 (t, $J_{4,5} \approx J_{3,4}$ 9.7, 1 H, 4-H), 4.27 (dd, $J_{6,7}$ = 5.3 Hz, $J_{7,7'}$ = 11.6 Hz, 1 H, 7-H), 4.11(dd, $J_{6,7'}$ = 7.7 Hz, $J_{7,7'}$ = 11.2 Hz, 1 H, 7′-H), 3.90 (d, $J_{4,5}$ = 10.1 Hz, $J_{5,6}$ = 2.2 Hz, 1 H, 5-H), 3.80 (t, $J_{1,2} \approx J_{2,3}$ 9.4 Hz, 1 H, 2-H), 2.19 (s, 3 H, OAc), 2.09 (s, 6 H, OAc), 2.05, 2.01 (s, 3 H, OAc) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 170.4, 170.0, 169.75, 168.4 (5 C=O, acetates), 126.6 (NCO), 92.8 (C-1), 73.4 (C-3), 73.0 (C-5), 66.7 (C-4), 66.3 (C-6), 61.8 (C-7), 56.7 (C-2), 20.6 (3 OAc), 20.4 (2 OAc) ppm. $C_{18}H_{23}NO_{12}$ (445.37): calcd. C 48.54, H 5.21, N 3.14; found C 48.54, H 5.21, N 3.34.

2,3,4,5,6-Tetra-*O*-acetyl-1-deoxy-1-isocyanato-D-glucitol (30): To a solution of triphosgene (0.17 g, 0.56 mmol) in dichloromethane (6 mL) was added a saturated solution of $NaHCO_3$ (4 mL) and then **19** (0.30 g, 0.56 mmol). The mixture was stirred vigorously at 0 °C for 30 min. The organic layer was separated, washed with a saturated solution of NaCl, and dried (anhydrous Na_2SO_4). It was concentrated to dryness and a white powder was obtained (0.21 g, 80%). Recrystallized from diethyl ether/petroleum ether it had m.p. 95–97 °C. $[\alpha]_D^{19} = +20.8$. $[\alpha]_{578}^{19} = +22.8$. $[\alpha]_{546}^{19} = +24.8$. $[\alpha]_{436}^{19} = +43.6$. $[\alpha]_{365}^{19} = +69.8$ ($c = 0.5$, $CHCl_3$). IR (KBr): $\tilde{\nu}$ = 2267, 2241 (N=C=O), 1745 (C=O), 1223 (C–O–C, ester), 1078, 1045 (C–O) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.47 (dd, $J_{3,4}$ = 3.5 Hz, $J_{4,5}$ = 7.0 Hz, 1 H, 4-H), 5.36 (dd, $J_{2,3}$ = 7.6 Hz, $J_{3,4}$ = 3.5 Hz, 1 H, 3-H), 5.04 (m, 2 H, 2-H, 5-H), 4.25 (dd, $J_{5,6}$ = 3.2 Hz, $J_{6,6'}$ = 12.5 Hz, 1 H, 6-H), 4.14 (dd, $J_{5,6'}$ = 4.8 Hz, $J_{6,6'}$ = 12.5 Hz, 1 H, 6′-H), 3.59 (dc, $J_{1,1'}$ = 4.7 Hz, $J_{1,2}$ = 4.4 Hz, 2 H, 1-H), 2.14, 2.12, 2.09, 2.08 (s, 4 × 3 H, OAc) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 170.45, 169.90, 169.84, 169.66 (C=O acetates), 124.11 (NCO), 69.91 (C-4), 68.32 (C-3), 68.26 (C-2, C-5), 61.27 (C-6), 42.87 (C-1), 20.67 (OAc), 20.61 (2 OAc), 20.37 (OAc) ppm. $C_{17}H_{23}NO_{11}$ (417.36): calcd. C 48.92, H 5.55, N 3.36; found C 48.95, H 5.73, N 3.00.

2,3,4,6-Tetra-*O*-acetyl-β-D-glucopyranosyl Isocyanate (31): From **21** and following the methods A (51%) and B (86%) the title compound **31** was obtained. M.p. 117–119 °C (ref.[23] m.p. 118–120 °C).

Tetrahydro-(3,4,6-tri-*O*-acetyl-1,2-dideoxy-α-D-glucopyranoso)[2,1-*d*]-1,3-oxazol-2-one (32): To a mixture of **13** (3.4 g, 9.0 mmol) in chloroform (40 mL) was added a solution of sodium carbonate (3.24 g, 30.6 mmol) in water (20 mL) and, finally, a 1.93 M solution of phosgene in toluene (7.0 mL). The mixture was stirred vigorously for 12 h. Then, it was filtered and the organic layer was separated, washed with water, dried (anhydrous $CaCl_2$) and the solvents evaporated. The resulting residue was crystallized from diethyl ether-petroleum ether to give the title product (2.53 g, 88%). M.p. 175–177 °C. $[\alpha]_D^{20} = +23.4$. $[\alpha]_{578}^{20} = +25.4$. $[\alpha]_{546}^{20} = +28.8$. $[\alpha]_{436}^{20} = +47.4$. $[\alpha]_{365}^{20} = +71.6$ ($c = 0.5$, $CHCl_3$). [ref.[13,50,51] m.p. 171.0–172.5 or 170 or 174–175 °C, $[\alpha]_D = +23 \pm 5$ ($c = 2.0$, $CHCl_3$) or 33.0 ($c = 2$, $CHCl_3$) or 29 ($c = 1$, $CHCl_3$)]. IR (KBr): $\tilde{\nu}$ = 3249 (NH), 1744 (C=O, ester), 1261, 1224, 1190 (C–O–C, ester), 1079, 1046, 1015 (C–O) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.31 (s, 1 H, NH), 5.98 (d, $J_{1,2}$ = 7.0 Hz, 1 H, 1-H), 5.04 (dd, $J_{3,4}$ = 5.4 Hz, $J_{4,5}$ = 9.1 Hz, 1 H, 4-H), 4.97 (dd, $J_{2,3}$ = 4.1 Hz, $J_{3,4}$ = 5.3 Hz, 1 H, 3-H), 4.32 (dd, $J_{5,6}$ = 5.3 Hz, $J_{6,6'}$ = 12.3 Hz, 1 H, 6-H), 4.21 (dd, $J_{5,6'}$ = 2.6 Hz $J_{6,6'}$ = 12.5 Hz, 1 H, 6′-H), 4.12 (ddd, $J_{5,6'}$ = 2.7 Hz, $J_{5,6}$ = 5.2 Hz, $J_{4,5}$ = 8.4 Hz, 1 H, 5-H), 3.93 (dd, $J_{1,2}$ = 6.9 Hz, $J_{2,3}$ = 3.9 Hz, 1 H, 2-H), 2.13, 2.10, 2.09 (s, 3 H, OAc each one) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 170.57, 170.42, 169.45 (C=O, acetates), 156.32 (C=O), 96.39 (C-1), 73.53 (C-3), 68.39 (C-5), 66.24 (C-4), 62.20 (C-6), 54.28 (C-2), 20.69 (OAc) ppm.

3-Acetyltetrahydro-(3,4,6-tri-*O*-acetyl-1,2-dideoxy-α-D-glucopyranoso)[2,1-*d*]-1,3-oxazol-2-one (33): To a solution of **32** (0.35 g, 1.1 mmol) in pyridine (4 mL) was added acetic anhydride (4 mL) and the mixture was kept at room temperature overnight. Then it was poured into ice-water and extracted with chloroform (3 × 25 mL). The combined extracts were washed with 1 M HCl, saturated solution of aqueous $NaHCO_3$ and water; dried ($MgSO_4$), and the solvents evaporated. A colourless oil that further solidified could be obtained (0.43 g, 100%). M.p. 108–109 °C. $[\alpha]_D^{20} = -31.4$. $[\alpha]_{578}^{20} = -32.8$. $[\alpha]_{546}^{20} = -37.6$. $[\alpha]_{436}^{20} = -75.2$. $[\alpha]_{365}^{20} = -134.8$ ($c = 0.5$, $CHCl_3$). HRMS-CI ($C_{15}H_{19}NO_{10}$ $[M + H]^+$): calcd. for 374.10872; found: 374.10958.

General Procedures for the Synthesis of Protected Ureas: To a solution of the corresponding isocyanate (1.0 mmol) in pyridine (6 mL) was added the *O*-protected amino sugar (1.0 mmol) and the mixture was kept at room temperature for 24 h. Then, it was poured into ice-water and the resulting white solid was collected by filtration, washed with cold water and recrystallized from ethanol/water.

***N*,*N*′-Bis(1,3,4,6-tetra-*O*-acetyl-2-deoxy-α-D-galactopyranos-2-yl)urea (34):** From **7** and **22**, the title compound was obtained (64%). M.p. 146–148 °C. $[\alpha]_D^{20} = +107.0$. $[\alpha]_{578}^{20} = +112.0$. $[\alpha]_{546}^{20} = +126.4$.

$[\alpha]^{20}_{436}$ = +212.0. $[\alpha]^{20}_{365}$ = +212.0 (*c* = 0.5, CHCl$_3$). IR (KBr): $\tilde{\nu}$ = 3417, 3375 (NH), 1750 (C=O), 1697 (C=O, urea),1552 (NH), 1256, 1225 (C–O–C, ester), 1165, 1137, 1067 (C–O) cm^{-1}. ^{1}H NMR (400 MHz, CDCl$_3$): δ = 6.16 (d, $J_{1,2}$ = 3.6 Hz, 2 H, 1-H), 5.40 (d, $J_{3,4}$ = 2.3 Hz, $J_{4,5}$ = 0.0 Hz, 2 H, 4-H), 5.14 (dd, $J_{3,4}$ = 3.2 Hz, $J_{2,3}$ = 11.4 Hz, 2 H, 3-H), 4.85 (d, $J_{NH,2}$ = 9.6 Hz, 2 H, NH), 4.52 (ddd, $J_{1,2}$ = 3.7 Hz, $J_{NH,2} \approx J_{2,3}$ 9.7 Hz, 2 H, 2-H), 4.23 (t, $J_{5,6'} \approx J_{5,6}$ 6.8 Hz, $J_{4,5}$ = 0.0 Hz, 2 H, 5-H), 4.14 (m, $J_{5,6}$ = 6.8 Hz, $J_{6,6'}$ = 11.3 Hz, 4 H, 6-H, 6′-H), 2.18 (s, 3 H, OAc), 2.15 (s, 3 H, OAc), 2.04 (s, 3 H, OAc), 2.03 (s, 2 × 3 H, OAc) ppm. ^{13}C NMR (100 MHz, CDCl$_3$): δ = 171.54, 170.45, 170.21, 168.84 (2 C, C=O, acetates), 156.01 (C=O, urea), 91.78 (2 C, C-1), 68.60 (1 C, C-4), 67.94 (2 C, C-3), 66.81 (2 C, C-5), 61.32 (2 C, C-6), 47.79 (2 C, C-2), 20.77 (2 C, OAc), 20.71 (2 C, OAc), 20.59 (4C, OAc) ppm. $C_{29}H_{40}N_2O_{19}$ (720.63): calcd. C 48.33, H 5.59, N 3.89; found C 47.79, H 5.63, N 4.06. HRMS-FAB ($C_{29}H_{40}N_2O_{19}Na$ [M + Na]$^+$): calcd. for 743.2120; found 743.2130.

***N*,*N*′-Bis(1,3,4,6-tetra-*O*-acetyl-2-deoxy-β-D-galactopyranos-2-yl)urea (35):** From **10** and **23**, compound **35** was obtained (62%). M.p. 208–209 °C. $[\alpha]^{22}_{\mathrm{D}}$ = +10.2. $[\alpha]^{22}_{578}$ = +12.0. $[\alpha]^{22}_{546}$ = +13.0. $[\alpha]^{22}_{436}$ = +24.2. $[\alpha]^{22}_{365}$ = +40.0 (*c* = 0.5, CHCl$_3$). IR (KBr): $\tilde{\nu}$ = 3414 (NH), 1752 (C=O), 1698 (C=O, urea), 1547 (NH), 1241 (C–O–C, ester), 1146, 1089, 1075, 1046 (C–O) cm^{-1}. ^{1}H NMR (400 MHz, CDCl$_3$): δ = 5.76 (d, $J_{1,2}$ = 8.7 Hz, 2 H, 1-H), 5.36 (d, $J_{3,4}$ = 3.3 Hz, $J_{4,5}$ = 0.0 Hz, 2 H, 4-H), 5.16 (dd, $J_{3,4}$ = 2.6 Hz, $J_{2,3}$ = 10.9 Hz, 2 H, 3-H), 4.89 (d, $J_{NH,2}$ = 9.1 Hz, 2 H, NH), 4.12 (m, 8 H, 2-H, 5-H, 6-H, 6′-H), 2.18, 2.13, 2.05, 2.03 (s, 2 × 3 H, OAc) ppm. ^{13}C NMR (100 MHz, CDCl$_3$): δ = 170.78, 170.42, 170.24, 169.60 (2 C × 2, C=O, acetates), 156.35 (C=O, urea), 93.24 (2 C, C-1), 71.69 (1 C, C-3), 70.54 (2 C, C-5), 66.56 (2 C, C-4), 61.36 (2 C, C-6), 51.19 (2 C, C-2), 20.86 (2 C, OAc), 20.67 (2 C, OAc) ppm. $C_{29}H_{40}N_2O_{19}$ (720.63): calcd. C 48.33, H 5.59, N 3.89; found C 48.42, H 5.66, N 3.98.

***N*,*N*′-Bis(1,3,4,6-tetra-*O*-acetyl-2-deoxy-α-D-glucopyranos-2-yl)urea (36):** From **11** and **24**, compound **36** was obtained (60%). M.p. 199–201 °C. $[\alpha]^{21}_{\mathrm{D}}$ = +115.8. $[\alpha]^{21}_{578}$ = +121.6. $[\alpha]^{21}_{546}$ = +138.4. $[\alpha]^{21}_{436}$ = +233.0. $[\alpha]^{21}_{365}$ = +353.2 (*c* = 0.5, CHCl$_3$). IR (KBr): $\tilde{\nu}$ = 3408 (NH), 1749 (C=O), 1668 (C=O, urea), 1559 (NH), 1227 (C–O–C, ester), 1125, 1040 (C–O) cm^{-1}. ^{1}H NMR (400 MHz, CDCl$_3$): δ = 6.11 (d, $J_{1,2}$ = 3.7 Hz, 2 H, 1-H), 5.19 (t, $J_{3,4} \approx J_{2,3}$ 9.7 Hz, 2 H, 3-H), 5.13 (t, $J_{3,4} \approx J_{4,5}$ 10.0 Hz, 2 H, 4-H), 4.69 (d, $J_{2,NH}$ = 9.3 Hz, 2 H, NH), 4.30 (dt, $J_{NH,2} \approx J_{2,3}$ 9.9 Hz, $J_{1,2}$ = 3.6 Hz, 2 H, 2-H), 4.24 (dd, $J_{6,6'}$ = 12.5 Hz, $J_{5,6}$ = 4.1 Hz, 2 H, 6-H), 4.06 (dd, $J_{6,6'}$ = 12.5 Hz, $J_{5,6'}$ = 2.2 Hz, 2 H, 6′-H), 3.97 (ddd, $J_{5,6'}$ = 2.4 Hz, $J_{5,6}$ = 3.7 Hz, $J_{4,5}$ = 9.8 Hz, 2 H, 5-H), 2.18, 2.09 (s, 3 H, OAc), 2.04 (s, 2 × 3 H, OAc) ppm. ^{13}C NMR (100 MHz, CDCl$_3$): δ = 170.82, 170.73, 169.00, 168.63 (2 C=O, acetates), 155.70 (C=O, urea), 90.83 (C-1), 70.72 (C-3), 69.60 (C-5), 67.45 (C-4), 61.55 (C-6), 51.70 (C-2), 20.60 (5 OAc), 20.41 (3 OAc) ppm. $C_{29}H_{40}N_2O_{19}$ (720.63): calcd. C 48.33, H 5.59, N 3.89; found C 48.32, H 5.65, N 3.79.

***N*,*N*′-Bis(1,3,4,6-tetra-*O*-acetyl-2-deoxy-β-D-glucopyranos-2-yl)urea (37):** From **12** and **25**, compound **37** was obtained (81%). M.p. 231–232 °C. $[\alpha]^{21}_{\mathrm{D}}$ = +16.8. $[\alpha]^{21}_{578}$ = +19.0. $[\alpha]^{21}_{546}$ = +20.8. $[\alpha]^{21}_{436}$ = +39.8. $[\alpha]^{21}_{365}$ = +66.8 (*c* = 0.5, CHCl$_3$). [ref.[42] m.p. 230–232 °C, $[\alpha]_{\mathrm{D}}$ = +44.7, $[\alpha]_{578}$ = +45.4 (*c* = 0.95, HCONMe$_2$)]. IR (KBr): $\tilde{\nu}$ = 3343 (NH), 1757 (C=O, ester), 1653 (C=O, urea), 1550 (NH), 1252 (C–O–C, ester), 1084 cm^{-1}(C–O). ^{1}H NMR (400 MHz, CDCl$_3$): δ = 5.75 (d, $J_{1,2}$ = 8.7 Hz, 2 H, 1-H), 5.47 (d, $J_{NH,2}$ = 9.4 Hz, 2 H, NH), 5.21 (t, $J_{2,3} \approx J_{3,4}$ 9.9 Hz, 2 H, 3-H), 5.12 (t, $J_{3,4} \approx J_{4,5}$ 9.6 Hz, 2 H, 4-H), 4.27 (dd, $J_{6,6'}$ = 12.4 Hz, $J_{5,6}$ = 5.2 Hz, 2 H, 6-H), 4.16 (m, $J_{1,2} \approx J_{NH,2} \approx J_{2,3}$ 9.4 Hz, 2 H, 2-H), 4.12 (dd, 2 H, 6′-H), 3.86 (ddd, $J_{5,6'}$ = 2.0 Hz, $J_{5,6}$ = 5.0 Hz, $J_{4,5}$ = 9.7 Hz, 2 H, 5-H), 2.10 (s, 3 H, OAc), 2.09 (s, 3 H, OAc), 2.07 (s, 2 × 3 H, OAc) ppm. ^{13}C NMR (100 MHz, CDCl$_3$): δ = 171.22, 170.66, 169.66, 169.45 (8 C=O, acetates), 156.47 (C=O, urea), 93.35 (C-1), 72.60 (C-3), 72.54 (C-5), 68.14 (C-4), 61.88 (C-6), 54.01 (C-2), 20.73 (3 OAc), 20.65 (2 OAc), 20.52 (3 OAc) ppm. $C_{29}H_{40}N_2O_{19}$ (720.63): calcd. C 48.33, H 5.59, N 3.89; found C 48.11, H 5.73, N 4.08.

***N*-(1,3,4,6-Tetra-*O*-acetyl-2-deoxy-α-D-glucopyranos-2-yl)-*N*′-(1,3,4,6-tetra-*O*-acetyl-2-deoxy-β-D-glucopyranos-2-yl)urea (38):** From **12** and **24** urea **38** was obtained (86%). M.p. 213-214 °C. $[\alpha]^{21}_{\mathrm{D}}$ = +60.4. $[\alpha]^{21}_{578}$ = +62.6. $[\alpha]^{21}_{546}$ = +71.2. $[\alpha]^{21}_{436}$ = +120.2. $[\alpha]^{21}_{365}$ = +183.8 (*c* = 0.5, CHCl$_3$). IR (KBr): $\tilde{\nu}$ = 3410 (NH), 1750 (C=O), 1674 (C=O, urea), 1561 (NH), 1235 (C–O–C, ester), 1042 (C–O) cm^{-1}. ^{1}H NMR (400 MHz, CDCl$_3$): (α-glucose and β-glucose residues have been labelled A and B, respectively): δ = 6.18 (d, $J_{1,2}$ = 3.6 Hz, 1 H, 1-H$_A$), 5.70 (d, $J_{1,2}$ = 8.6 Hz, 1 H, 1-H$_B$), 5.29 (d, $J_{NH,2}$ = 9.0 Hz, 1 H, NH$_B$), 5.19 (d, $J_{NH,2}$ = 2.4 Hz, 1 H, NH$_A$), 5.19 (t, $J_{2,3} \approx J_{3,4}$ 10.0 Hz, 2 H, 3-H$_A$ and 3-H$_B$), 5.09 (t, $J_{3,4} \approx J_{4,5}$ 9.4 Hz, 2 H, 4-H$_A$ and 4-H$_B$), 4.33 (dt, $J_{1,2}$ = 3.5 Hz, $J_{2,3}$ = 7.7 Hz, 1 H, 2-H$_A$), 4.26 (dd, $J_{6,6'}$ = 12.6 Hz, $J_{5,6}$ = 5.0 Hz, 2 H, 6-H$_A$ and 6-H$_B$), 4.13 (dd, $J_{6,6'}$ = 12.3 Hz, $J_{5,6'}$ = 1.8 Hz, 1 H, 6′-H$_A$), 4.11 (t, 1 H, 2-H$_B$), 4.07 (dd, $J_{6,6'}$ = 12.4 Hz, $J_{5,6'}$ = 2.2 Hz, 1 H, 6′-H$_B$), 4.02 (dd, $J_{5,6'}$ = 2.0 Hz, $J_{5,6}$ = 5.9 Hz, 1 H, 5-H$_B$), 3.87 (ddd, $J_{5,6'}$ = 2.2 Hz, $J_{5,6}$ = 4.9 Hz, $J_{4,5}$ = 9.3 Hz, 1 H, 5-H$_A$), 2.14 (s, 3 H, OCH$_3$), 2.09 (s, 2 × 3 H, OAc), 2.05 (s, 4 × 3 H, OAc), 2.04 (s, 3 H, OAc) ppm. ^{13}C NMR (100 MHz, CDCl$_3$): δ = 171.20 (2 × C=O), 170.60 (2 × C=O), 169.33 (2 × C=O), 169.15 (C=O, acetates), 159.17 (C=O, urea), 92.99 (C-1$_B$), 90.77 (C-1$_A$), 72.45 (C-3$_B$, C-5$_B$), 70.27 (C-3$_A$), 69.68 (C-5$_A$), 68.05 (C-4$_B$), 67.63 (C-4$_A$), 61.74 (C-6$_B$), 61.69 (C-6$_A$), 53.83 (C-2$_B$), 51.76 (C-2$_A$), 20.52 (3 OAc), 20.38 (5 OAc) ppm. $C_{29}H_{40}N_2O_{19}$ (720.63): calcd. C 48.33, H 5.59, N 3.89; found C 48.77, H 5.51, N 4.14. HRMS-FAB ($C_{29}H_{40}N_2O_{19}Na$ [M + Na]$^+$): calcd. for 743.2120; found 743.2134.

***N*-(1,3,4,6-Tetra-*O*-acetyl-2-deoxy-2-α-D-glucopyranos-2-yl)-*N*′-(3,4,6-tri-*O*-acetyl-1-azido-1,2-dideoxy-β-D-glucopyranos-2-yl)urea (39):** To a solution of **25** (0.20 g, 0.53 mmol) in freshly distilled chloroform (6.0 mL) **14** (0.20 g, 0.53 mmol) was added. The mixture was kept at room temperature for 24 h. Then, it was concentrated to dryness to give the title compound (0.33 g, 88%) that was recrystallized from ethanol/water. M.p. 172–174 °C. IR (KBr): $\tilde{\nu}$ = 3435, 3364 (NH), 2117 (N=N=N), 1747 (C=O), 1671 (C=O), 1556 (NH), 1232 (C–O–C), 1124, 1037 (C–O) cm^{-1}. ^{1}H NMR (400 MHz, CDCl$_3$) (the glucosyl azide and glucose residues have been labelled A and B, respectively): δ = 6.18 (d, $J_{1,2}$ = 3.6 Hz, 1 H, 1-H$_B$), 5.70 (d, 1 H, $J_{1,2}$ = 8.6 Hz, 1-H$_A$), 5.21 (t, 2 H, 3-H$_A$ and 3-H$_B$), 5.08 (t, 2 H, 4-H$_A$ and 4-H$_B$), 4.92 (d, $J_{NH,2}$ = 9.1 Hz, 1 H, NH$_B$), 4.81 (d, $J_{NH,2}$ = 8.9 Hz, 1 H, NH$_A$), 4.62 (t, $J_{1,2}$ = 9.2 Hz, 1 H, 1-H$_A$), 4.34 (dt, $J_{2,3} \approx J_{NH,2}$ 9.6 Hz, $J_{1,2}$ = 3.8 Hz, 1 H, 2-H$_B$), 4.25 (m, $J_{5,6}$ = 5.6 Hz, $J_{6,6'}$ = 12.4 Hz, 2 H, 6-H$_A$ and 6-H$_B$), 4.16 (dd, $J_{6,6'}$ = 12.4 Hz, $J_{5,6'}$ = 1.9 Hz, 1 H, 6′-H$_A$), 4.07 (dd, $J_{6,6'}$ = 12.5 Hz, $J_{5,6'}$ = 2.0 Hz, 1 H, 6′-H$_B$), 4.01 (m, $J_{5,6}$ = 5.7 Hz, $J_{4,5}$ = 9.1 Hz, 1 H, 5-H$_B$), 3.77 (m, 2 H, 5-H$_A$, 2-H$_A$), 2.14, 2.11 (s, 3 H, OAc), 2.09 (s, 2 × 3 H, OAc), 2.08, 2.05, 2.03 (s, 3 H, OAc) ppm. ^{13}C NMR (100 MHz, CDCl$_3$): δ = 171.91 (C=O), 171.27 (2 × C=O), 170.75, 169.27, 169.12, 168.72 (C=O), 156.01 (C=O, urea), 91.06 (C-1$_A$), 89.20 (C-1$_B$), 73.84 (C-3$_A$), 72.57 (C-5$_A$), 70.76 (C-3$_B$), 69.80 (C-5$_B$), 68.06 (C-4$_A$), 67.56 (C-4$_B$), 61.86 (C-6$_A$), 61.62 (C-6$_B$), 55.03 (C-2$_A$), 51.98 (C-2$_B$), 20.70 (5 OAc), 20.55 (3 OAc) ppm. $C_{27}H_{37}N_5O_{17}$ (703.61): calcd. C 46.09, H 5.30, N 9.95; found C 46.07, H 5.26, N 9.66.

***N*-(1,3,4,6-tetra-*O*-acetyl-2-deoxy-β-D-galactopyranos-2-yl)-*N*′-(1,3,4,6-tetra-*O*-acetyl-2-deoxy-β-D-glucopyranos-2-yl)urea (40):** To a solution of **23** (0.20 g, 0.53 mmol) in freshly distilled chloroform

(6.0 mL) was added the 1,3,4,6-tetra-*O*-acetyl-2-amino-2-deoxy-β-D-glucopyranose (0.18 g, 0.53 mmol), easily generated by washing a solution of the hydrochloride in chloroform with a saturated solution of $NaHCO_3$, then dried, and the solvents evaporated to dryness. The mixture was kept at room temperature for 24 hours. Then, it was concentrated to dryness to give a solid (0.27 g, 72%) which was recrystallized from ethanol-water. M.p. 214–215 °C. $[\alpha]_{D}^{19} = +15.0$. $[\alpha]_{578}^{19} = +15.4$. $[\alpha]_{546}^{19} = +18.2$. $[\alpha]_{436}^{19} = +32.2$. $[\alpha]_{365}^{19} = +53.8$ ($c = 0.5$, $CHCl_3$). IR (KBr): $\tilde{\nu} = 3408$, 3326 (NH), 1750 (C=O), 1679 (C=O), 1553 (NH), 1226 (C–O–C), 1084, 1040 (C–O) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): (the glucose and galactose residues have been labelled A and B, respectively): $\delta = 5.76$ (d, $J_{1,2} = 8.7$ Hz, 2 H, 1-H_A and 1-H_B), 5.36 (d, $J_{3,4} = 3.3$ Hz, $J_{4,5} = 0.0$ Hz, 1 H, 4-H_B), 5.18 (m, 4 H, 3-H_A and 3-H_B, NH_A and NH_B), 5.10 (t, $J_{3,4} = 9.7$ Hz, 1 H, 4-H_A), 4.28 (dd, $J_{5,6} = 4.8$ Hz, $J_{6,6'} = 12.5$ Hz, 1 H, 6-H_A), 4.04 (m, $J_{1,2} \approx J_{2,3} \approx J_{NH,2}$ 9.4 Hz, 1 H, 2-H_A), 3.88 (ddd, $J_{5,6'} = 2.2$ Hz, $J_{5,6} = 4.7$ Hz, $J_{4,5} = 9.8$ Hz, 1 H, 5-H_A), 4.17 (m, 5 H, 6-H_B, 6′-H_A and 6′-H_B, 5-H_B, 2-H_B), 2.16 (s, 3 H, OAc), 2.14 (s, 3 H, OAc), 2.11 (s, 3 H, OAc), 2.09 (s, 3 H, OAc), 2.08 (s, 3 H, OAc), 2.03 (s, 3 H, OAc), 2.04 (s, 2×3 H, OAc) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 171.27$ (C=O), 170.72 (C=O), 170.63 (2×C=O), 170.33 (2 ×C=O), 169.51 (C=O), 169.44 (C=O), 156.34 (C=O, urea), 93.47 (C-1_A), 93.05 (C-1_B), 72.66 (C-3_A), 72.52 (C-5_A), 71.56 (C-3_B), 70.38 (C-5_B), 68.13 (C-4_A), 66.51 (C-4_B), 61.75 (C-6_A), 61.40 (C-6_B), 54.16 (C-2_A), 50.92 (C-2_B), 20.83 (2 OAc), 20.73 (3 OAc), 20.56 (3 OAc) ppm. $C_{29}H_{40}N_2O_{19}$ (720.63): calcd. C 48.33, H 5.59, N 3.89; found C 48.40, H 5.67, N 3.62.

***N*-(1,3,4,6,7-Penta-*O*-acetyl-2-deoxy-β-D-*glycero*-L-*gluco*-heptopyranos-2-yl)–*N*′-(1,3,4,6-tetra-*O*-acetyl-2-deoxy-β-D-glucopyranos-2-yl)urea (41):** From **15** and **25**, compound **41** was obtained. (76%). M.p. 147–149 °C. $[\alpha]_{D}^{21} = -30.0$. $[\alpha]_{578}^{21} = -31.6$. $[\alpha]_{546}^{21} = -35.6$. $\alpha]_{436}^{21} = -58.4$. $[\alpha]_{365}^{21} = -82.0$ ($c = 0.5$, $CHCl_3$). IR (KBr): $\tilde{\nu} = 3383$ (NH), 1751 (C=O), 1690 (C=O), 1543 (NH), 1217 (C–O–C), 1045 (C–O) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): (the glucose and heptose residues have been labelled A and B, respectively): $\delta = 6.17$ (d, $J_{1,2} = 3.7$ Hz, 1 H, 1-H_B), 5.62 (d, $J_{1,2} = 8.7$ Hz, 1 H, 1-H_A), 5.18 (dt, $J_{5,6} = 2.0$ Hz, $J_{6,7} \approx J_{6,7'}$ 4.7 Hz, 1 H, 6-H_B), 5.13 (m, 2 H, 3-H_A and 3-H_B, 4-H_A), 5.05 (t, $J_{3,4} \approx J_{4,5}$ 9.9 Hz, 1 H, 4-H_B), 4.80 (d, 1 H, $J_{2,NH} = 9.0$ Hz, NH), 4.67 (d, 1 H, $J_{2,NH} = 9.3$ Hz, NH), 4.24 (m, 3 H, 6-H_A, 7-H_B, 2-H_A), 4.13 (m, $J_{7,7'} = 11.6$ Hz, $J_{7,6} = 4.5$ Hz, $J_{6,6'} = 12.8$ Hz, $J_{5,6} = 2.5$ Hz, 2 H, 6′-H_A, 7′-H_B), 4.05 (m, $J_{5,6} = 2.4$ Hz, $J_{4,5} = 9.5$ Hz, 5-H_B, 2-H_B), 3.78 (ddd, $J_{4,5} = 9.8$ Hz, $J_{5,6} = 2.3$ Hz, $J_{5,6'} = 4.6$ Hz 1 H, 5-H_A), 2.14, 2.11, 2.09, 2.07, 2.04, 2.02, 2.01 (s, 9 x 3 H, OAc) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 171.60$, 171.28, 170.68, 170.59, 170.36, 169.79, 169.21, 169.06, 168.24 (C=O, acetates), 155.84 (C=O, urea), 92.86 (C-1_A), 90.80 (C-1_B), 72.92 (C-3_A), 72.67 (C-5_A), 70.80 (C-3_B), 69.99 (C-5_B), 67.77 (C-4_A), 66.62 (C-4_B, C-6_B), 62.23 (C-7_B), 61.69 (C-6_A), 54.01 (C-2_A), 52.11 (C-2_B), 20.61 (9 OAc) ppm. HRMS-ESI ($C_{32}H_{44}N_2O_{21}Na$ $[M + Na]^+$): calcd. for 815.2329; found 815.2348.

***N*-(1,3,4,6,7-Penta-*O*-acetyl-2-deoxy-α-D-*glycero*-L-*gluco*-heptopyranos-2-yl)-*N*′-(1,3,4,6-tetra-*O*-acetyl-2-deoxy-β-D-glucopyranos-2-yl)urea (42):** From **16** and **25**, compound **42** was obtained (68%). M.p. 229–230 °C. $[\alpha]_{D}^{21} = +14.6$. $[\alpha]_{578}^{21} = +15.4$. $[\alpha]_{546}^{21} = +18.2$. $[\alpha]_{436}^{21} = +31.0$. $[\alpha]_{365}^{21} = +50.6$ ($c = 0.5$, $CHCl_3$). IR (KBr): $\tilde{\nu} = 3408$, 3336 (NH), 1748 (C=O), 1665 (C=O, urea), 1545 (NH), 1234 (C–O–C, ester), 1071, 1038 cm^{-1}(C–O). ^1H NMR (400 MHz, $CDCl_3$): (the glucose and heptose residues have been labelled A and B, respectively): $\delta = 5.75$ (d, $J_{1,2} = 8.8$ Hz, 1 H, 1-H_A), 5.72 (d, $J_{1,2} = 9.0$ Hz, 1 H, 1-H_B), 5.24 (dt, $J_{6,7} \approx J_{6,7'}$ 5.1 Hz, $J_{5,6} = 2.6$ Hz, 1 H, 6-H_B), 5.18 (t, $J_{3,4} \approx J_{2,3}$ 9.6 Hz, 1 H, 3-H_A), 5.16 (t, $J_{3,4} \approx J_{2,3}$ 9.5 Hz, 1 H, 3-H_B), 5.13 (t, $J_{4,5} \approx J_{3,4}$ 9.6, 1 H, 4-H_A), 5.11 (t, $J_{4,5} \approx J_{3,4}$ 9.5, 1 H, 4-H_B), 5.03 (d, $J_{2,NH} = 9.1$ Hz, 1 H, NH), 5.01 (d, $J_{2,NH} = 9.0$ Hz, 1 H, NH), 4.30 (dd, $J_{5,6} = 4.5$ Hz, $J_{6,6'} = 11.7$ Hz, 1 H, 6-H_A), 4.27 (dd, $J_{6,7} = 4.5$ Hz, $J_{7,7'} = 12.6$ Hz, 1 H, 7-H_B), 4.14 (dd, $J_{6,7'} = 7.6$ Hz, $J_{7,7'} = 11.8$ Hz, 1 H, 7′-H_B), 4.12 (dd, $J_{5,6} = 2.0$ Hz, $J_{6,6'} = 12.7$ Hz, 1 H, 6′-H_A), 4.00 (m, $J_{2,NH} \approx J_{1,2} \approx J_{2,3}$ 10.1, 2 H, 2-H_A and 2-H_B), 3.86 (dd, $J_{4,5} = 9.8$ Hz, $J_{5,6} = 1.9$ Hz, 1 H, 5-H_B), 3.83 (dc, $J_{4,5} = 9.6$ Hz, $J_{5,6} = 2.2$ Hz, $J_{5,6} = 4.4$ Hz, 1 H, 5-H_A), 2.14, 2.11, 2.09, 2.08, 2.06, 2.05, 2.04, 2.02, 2.01 (s, 9 x 3 H, OAc) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 171.53$, 171.45, 170.63, 170.57, 170.35, 169.54, 169.45 (C=O, acetates), 169.27 (2×C=O, acetates), 155.97 (C=O, urea), 93.09 (C-1_A), 92.89 (C-1_B), 73.12 (C-3_B), 72.97 (C-5_B), 72.63 (C-3_A and C-5_A), 67.96 (C-4_A), 66.96 (C-4_B), 66.50 (C-6_B), 62.43 (C-7_B), 61.65 (C-6_A), 54.32 (C-2_A, C-2_B), 20.79 (3 OAc), 20.61 (6 OAc) ppm. HRMS-FAB ($C_{32}H_{44}N_2O_{21}Na$ $[M + Na]^+$): calcd. for 815.2329; found 815.2335.

***N*,*N*′-Bis(2,3,4,5,6-tetra-*O*-acetyl-1-deoxy-D-glucitol-1-yl)urea (43):** From **19** and **30** the title compound **43** was obtained (40%). M.p. 133–135 °C. $[\alpha]_{D}^{20} = +32.8$. $[\alpha]_{578}^{20} = +33.2$. $[\alpha]_{546}^{20} = +36.2$. $[\alpha]_{436}^{20} = +70.6$ ($c = 0.5$, $CHCl_3$). IR (KBr): $\tilde{\nu} = 3403$, 3348 (NH, crystallization H_2O), 1744 (C=O), 1649 (C=O), 1567 (NH), 1221 (C–O–C), 1050 (C–O) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): $\delta = 5.49$ (dd, $J_{3,4} = 4.4$ Hz, $J_{4,5} = 6.7$ Hz, 2 H, 4-H), 5.36 (dd, $J_{2,3} = 5.4$ Hz, $J_{3,4} = 4.6$ Hz, 2 H, 3-H), 5.06 (m, 4 H, 2-H, 5-H), 4.90 (t, 2 H, NH), 4.27 (dd, $J_{5,6} = 3.2$ Hz, $J_{6,6'} = 12.4$ Hz, 2 H, 6-H), 4.13 (dd, $J_{5,6'} = 5.6$ Hz, $J_{6,6'} = 12.4$ Hz, 1 H, 6′-H), 3.47 (dt, $J_{1,1'} = 13.7$ Hz, $J_{1,2} = 6.3$ Hz, 2 H, 1-H), 3.25 (dt, $J_{1,1'} = 12.6$ Hz, $J_{1,2} = 6.8$ Hz, 2 H, 1-H), 2.13, 2.10, 2.09, 2.08, 2.05 (s, 10×3 H, OAc) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 170.63$, 170.54, 170.30, 169.86 (C=O, acetates), 157.22 (C=O, urea), 71.03 (C-2), 69.17 (C-4), 68.72 (C-5, C-3), 61.50 (C-6), 40.33 (C-1), 20.75, 20.67, 20.52 (CH_3, acetates) ppm. $C_{33}H_{48}N_2O_{21}\cdot 2H_2O$ (844.77): calcd. C 46.92, H 6.20, N 3.32; found C 47.36, H 6.43, N 2.74. HRMS-FAB ($C_{33}H_{48}N_2O_{21}Na$ $[M + Na]^+$): calcd. for 831.2640; found 831.2662.

1,3,4,6-tetra-O-acetyl-2-deoxy-2-ureido-α-D-glucopyranose (44): To a solution of **11** (4.28 g, 10.0 mmol) in water (40 mL) was added silver cyanate (1.90 g, 12.7 mmol). The mixture was stirred at 40–50 °C and then the solid was collected by filtration, and washed with water, ethanol and diethyl ether to give **44** (0.97 g, 25%). M.p. 204–206 °C. $[\alpha]_{D}^{19} = +118.8$. $[\alpha]_{578}^{19} = +123.7$. $[\alpha]_{546}^{19} = +139.8$. $[\alpha]_{436}^{19} = +230.4$. $[\alpha]_{365}^{19} = +345.8$ ($c = 1.0$, H_2O). [ref.[59] m.p. 202 °C. $[\alpha]_D = 115$ ($c = 1$, H_2O)]. IR (KBr): $\tilde{\nu} = 3492$, 3367 (NH), 1758 (C=O, ester), 1660 (C=O, urea), 1555 (NH), 1220 (C–O–C, ester), 1008 (C–O) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): $\delta = 6.19$ (d, $J_{1,2} = 3.6$ Hz, 1 H, 1-H), 6.00 (d, $J_{NH,2} = 9.2$ Hz, 1 H, NH), 5.26 (t, $J_{2,3} \approx J_{3,4}$ 10.0 Hz, 1 H, 3-H), 5.20 (t, $J_{3,4} \approx J_{4,5}$ 9.6 Hz, 1 H, 4-H), 5.13 (2 H,s, NH_2), 4.24 (dd, $J_{1,2} = 3.6$ Hz, 1 H, 2-H), 4.24 (dd, $J_{5,6} = 3.4$ Hz, $J_{6,6'} = 10.6$ Hz, 1 H, 6-H), 4.05 (dd, $J_{5,6} = 1.6$ Hz, $J_{6,6'} = 12.4$ Hz, 1 H, 6′-H), 4.03 (m, $J_{5,6'} = 1.8$ Hz, $J_{4,5} = 10.0$ Hz, 1 H, 5-H), 2.19, 2.10, 2.06, 2.05 (s, 4×3 H, OAc) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 171.32$, 170.72, 169.17 (C=O, acetates), 158.52 (C=N), 91.01 (C-1), 70.78 (C-3), 69.72 (C-5), 67.57 (C-4), 61.56 (C-6), 51.71 (C-2), 20.95, 20.74, 20.65, 20.50 (CH_3, acetates) ppm.

1,3,4,6-Tetra-O-acetyl-2-deoxy-2-ureido-β-D-glucopyranose (45): To a solution of **12** (3.84 g, 10.0 mmol) in water (40 mL) was added silver cyanate (1.90 g, 12.7 mmol). The mixture was stirred at 40–50 °C. and then the solid was collected by filtration, and washed with water, ethanol and diethyl ether to give **45** (1.35 g, 35%). M.p. 204–206 °C. $[\alpha]_{D}^{22} = +32.0$. $[\alpha]_{578}^{22} = +33.2$. $[\alpha]_{546}^{22} = +38.0$. $[\alpha]_{436}^{22} = +65.8$ ($c = 0.5$, DMF). [ref.[60] m.p. 190–191 °C. $[\alpha]_D = 24.5$ ($c = 1.305$ g/100 mL, $CHCl_3$)]. IR (KBr): $\tilde{\nu} = 3486$, 3356 (NH), 1755 (C=O, ester), 1666 (C=O, urea), 1564 (NH), 1262, 1216 (C–O–C, ester), 1073, 1041 (C–O) cm^{-1}. ^1H NMR (400 MHz, $[D_6]DMSO$):

δ = 5.94 (d, $J_{NH,2}$ = 9.6 Hz, 1 H, NH), 5.75 (d, $J_{1,2}$ = 8.0 Hz, 1 H, 1-H), 5.63 (2 H,s, NH_2), 5.22 (t, $J_{2,3} \approx J_{3,4}$ 10.0 Hz, 1 H, 3-H), 4.85 (t, $J_{3,4} \approx J_{4,5}$ 9.6 Hz, 1 H, 4-H), 4.16 (dd, $J_{5,6}$ = 4.8 Hz, $J_{6,6'}$ = 12.8 Hz, 1 H, 6-H), 4.00 (m, $J_{5,6'}$ = 2.0 Hz, $J_{5,6}$ = 4.0 Hz 1 H, 5-H), 3.99 (dd, $J_{5,6}$ = 2.4 Hz, $J_{6,6'}$ = 11.2 Hz, 1 H, 6′-H), 3.79 (1 H, $J_{1,2} \approx J_{2,3} \approx J_{NH,2}$ 9.4 Hz, 1 H, 2-H), 2.04, 2.00, 1.97, 1.92 (s, 4×3 H, OAc) ppm. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.75 (d, $J_{1,2}$ = 8.8 Hz, 1 H, 1-H), 5.19 (t, $J_{2,3} \approx J_{3,4}$ 9.7 Hz, 1 H, 3-H), 5.14 (t, $J_{3,4} \approx J_{4,5}$ 9.4 Hz, 1 H, 4-H), 5.01 (d, $J_{NH,2}$ = 9.3 Hz, 1 H, NH), 4.65 (2 H,s, NH_2), 4.28 (dd, $J_{5,6}$ = 4.5 Hz, $J_{6,6'}$ = 12.5 Hz, 1 H, 6-H), 4.12 (dd, $J_{5,6}$ = 2.0 Hz, $J_{6,6'}$ = 12.4 Hz, 1 H, 6-H), 4.02 (1 H, $J_{1,2} \approx J_{2,3} \approx J_{NH,2}$ 9.0 Hz, 1 H, 2-H), 3.85 (ddd, $J_{5,6'}$ = 2.1 Hz, $J_{4,5}$ = 9.4 Hz, $J_{5,6}$ = 4.4 Hz 1 H, 5-H), 2.15, 2.10, 2.08, 2.04 (s, 3 H, OAc) ppm. ^{13}C NMR (100 MHz, [D$_6$]DMSO): δ = 171.02, 170.59, 170.26, 169.96 (C=O, acetates), 158.89 (C=O, urea), 93.32 (C-1), 73.55 (C-3), 72.28 (C-5), 69.25 (C-4), 62.55 (C-6), 53.88 (C-2), 21.59, 21.47, 21.41 (CH_3, acetates) ppm.

Acknowledgments

The authors thank the Ministerio de Ciencia y Tecnología (BQU2002–00015 and BQU2003–05956) and the Junta de Extremadura-Fondo Social Europeo (2PR02-A016) for financial support.

---

[1] M. E. Brown, M. D. Hollingsworth, *Nature* **1995**, *376*, 323–327.

[2] K. D. M. Harris, *Chem. Soc. Rev.* **1997**, *26*, 279–289.

[3] K. H. Choi, A. D. Hamilton, *Coord. Chem. Rev.* **2003**, *240*, 101–110.

[4] a) R. K. Castellano, C. Nuckolls, J. Rebek Jr., *J. Am. Chem. Soc.* **1999**, *121*, 11156–11163; b) Y. L. Cho, D. M. Rudkevich, A. Shivanyuk, K. Rissanen, J. Rebek Jr., *Chem. Eur. J.* **2000**, *6*, 3788–3796.

[5] a) P. Terech, R. G. Weiss, *Chem. Rev.* **1997**, *97*, 3133–3160; b) J. van Esch, S. De Feyter, R. M. Kellogg, S. De Schryver, B. L. Feringa, *Chem. Eur. J.* **1997**, *3*, 1238–1243; c) L. A. Estroff, A. D. Hamilton, *Angew. Chem.* **2000**, *112*, 3589–3592; *Angew. Chem. Int. Ed.* **2000**, *39*, 3447–3450; d) M. de Loos, J. van Esch, R. M. Kellogg, B. L. Feringa, *Angew. Chem.* **2001**, *113*, 633–636; *Angew. Chem. Int. Ed.* **2001**, *40*, 613–616; e) M. Kölbel, F. M. Menger, *Langmuir* **2001**, *17*, 4490–4492; f) U. Beginn, B. Tartsch, *Chem. Commun.* **2001**, 1924–1925; g) S.-I. Tamaru, S.-Y. Uchino, M. Takeuchi, M. Ikeda, T. Hatano, S. Shinkai, *Tetrahedron Lett.* **2002**, *43*, 3751–3755; h) G. Wang, A. D. Hamilton, *Chem. Commun.* **2003**, 310–311; i) P. Babu, N. M. Sangeetha, P. Vijayakumar, U. Mitra, K. Rissanen, A. R. Raju, *Chem. Eur. J.* **2003**, *9*, 1922–1932; j) S. J. George, A. Ajayaghosh, *Chem. Eur. J.* **2005**, *11*, 3217–3227.

[6] M. George, G. Tan, V. T. John, R. G. Weiss, *Chem. Eur. J.* **2005**, *11*, 3243–3254 and references cited therein.

[7] M. Avalos, R. Babiano, P. Cintas, J. L. Jiménez, J. C. Palacios, J. Fuentes, *J. Chem. Soc., Perkin Trans. 1* **1990**, 495–501.

[8] S. Omoto, T. Shomura, H. Suzuki, S. Inouye, *J. Antibiot.* **1979**, *32*, 436–441.

[9] a) M. Ichimura, T. Koguchi, T. Yasuzawa, F. Tomita, *J. Antibiot.* **1987**, *40*, 723–726; b) T. Yasuzawa, M. Yoshida, M. Ichimura, K. Shirahata, H. Sano, *J. Antibiot.* **1987**, *40*, 727–731.

[10] G. A. Ellestad, D. B. Cosulich, R. W. Broschard, J. M. Martin, M. P. Kunstmann, G. O. Morton, J. E. Lancaster, W. Fulmor, F. M. Lovell, *J. Am. Chem. Soc.* **1978**, *100*, 2515–2524.

[11] N. Tewari, V. K. Tiwari, R. C. Misrha, R. P. Tripathi, A. K. Srivastava, R. Ahmad, R. Srivastava, B. S. Srivastava, *Bioorg. Med. Chem.* **2003**, *11*, 2911–2922.

[12] a) R. R. Herr, H. K. Jahnke, A. D. Argoudelis, *J. Am. Chem. Soc.* **1967**, *89*, 4808–4809; b) P. F. Wiley, D. L. McMichael, J. M. Koert, V. H. Wiley, *J. Antibiot.* **1976**, *29*, 1218–1225.

[13] Ch. F. Hammer, R. A. Loranger, P. S. Schein, *J. Org. Chem.* **1981**, *46*, 1521–1531.

[14] For a review on N-nitrosoureas as anticancer drugs, see: C. T. Gnewuch, G. Sosnovsky, *Chem. Rev.* **1997**, *97*, 829–1013.

[15] R. B. Silverman, *The Organic Chemistry of Drug Design and Drug Action*, Academic Press, San Diego, **1992**, pp. 251–254 and references cited therein.

[16] M. N. Schoorl, *Recl. Trav. Chim. Pays-Bas* **1903**, *22*, 31–77.

[17] a) M. H. Benn, A. S. Jones, *J. Chem. Soc.* **1960**, 3837–3841; b) A. S. Jones, G. W. Ross, *Tetrahedron* **1962**, *18*, 189–193.

[18] D. Plusquellec, F. Roulleau, E. Brown, *Tetrahedron Lett.* **1984**, *25*, 1901–1904.

[19] I. Goodman, *Adv. Carbohydr. Chem.* **1958**, *13*, 215–236 and references cited therein.

[20] M. Ávalos, R. Babiano, P. Cintas, J. L. Jiménez, J. C. Palacios, C. Valencia, *Tetrahedron* **1993**, *49*, 2655–2675.

[21] M. Avalos, R. Babiano, P. Cintas, J. L. Jiménez, J. C. Palacios, C. Valencia, *Tetrahedron* **1993**, *49*, 2676–2690.

[22] I. Maya, O. López, S. Maza, J. G. Fernández-Bolaños, J. Fuentes, *Tetrahedron Lett.* **2003**, *44*, 8539–8543.

[23] Y. Ichikawa, Y. Matsukawa, T. Nishiyama, M. Isobe, *Eur. J. Org. Chem.* **2004**, 586–591.

[24] S. Knapp, C. Jaramillo, B. Freeman, *J. Org. Chem.* **1994**, *59*, 4800–4804.

[25] a) Q. Liu, N. W. Luedtke, Y. Tor, *Tetrahedron Lett.* **2001**, *42*, 1445–1447; b) B. Piekarska-Bartoszewicz, A. Temeriusz, *Carbohydr. Res.* **1990**, *203*, 302–307.

[26] Y. Ichikawa, T. Nishiyama, M. Isobe, *Tetrahedron* **2004**, *60*, 2621–2627.

[27] J. Kovács, I. Pintér, A. Messmer, G. Töth, H. Duddeck, *Carbohydr. Res.* **1987**, *166*, 101–111.

[28] V. M. Díaz, C. Ortiz, J. Fuentes, J. M. García, *Carbohydr. Res.* **2000**, *326*, 161–175.

[29] C. Ukita, A. Hamada, M. Yoshida, *Chem. Pharm. Bull.* **1964**, *12*, 454–459.

[30] Y. Ichikawa, T. Nishiyama, M. Isobe, *J. Org. Chem.* **2001**, *66*, 4200–4205.

[31] For a recent review on the synthesis of ureas through phosgene substitutes, see:.-F. Bigi, R. Maggi, G. Sartori, *Green Chem.* **2000**, *2*, 140–148.

[32] E. Fischer, *Ber.* **1914**, *47*, 1377–1381.

[33] I. Píntér, J. Kovács, G. Tóth, *Carbohydr. Res.* **1995**, *273*, 99–108.

[34] Y. Ichikawa, T. Nishiyama, M. Isobe, *Synlett* **2000**, *9*, 1253–1256.

[35] D. Prosperi, S. Ronchi, L. Lay, A. Rencurosi, G. Russo, *Eur. J. Org. Chem.* **2004**, 395–405.

[36] J. C. Jochims, A. Seeliger, *Tetrahedron* **1965**, *21*, 2611–2616.

[37] a) A. Gómez, M. Gómez, A. Cert, U. Scheidegger, *Anal. Real Soc., Esp. Fis. Quim.* **1968**, *64*, 579–590; b) A. Gómez-Sánchez, P. Borrachero, J. Bellanato, *Carbohydr. Res.* **1984**, *135*, 101–116.

[38] R. Babiano, J. Fuentes, J. A. Galbis, *Carbohydr. Res.* **1986**, *154*, 280–288.

[39] R. C. G. Moggridge, A. Neuberger, *J. Chem. Soc.* **1938**, 745–750.

[40] M. Bergmann, L. Zervas, *Ber.* **1931**, *64*, 975–980.

[41] M. Avalos, R. Babiano, P. Cintas, J. L. Jiménez, J. C. Palacios, C. Valencia, *Tetrahedron* **1994**, *50*, 3273–3296.

[42] A. Bertho, A. Révész, *Justus Liebigs Ann. Chem.* **1953**, *581*, 163–167.

[43] C. Ortiz, J. L. Jiménez, J. M. García, J. Fuentes, *J. Carbohydr. Chem.* **1995**, *14*, 1133–1152.

[44] H. S. Isbell, H. J. Frush, *J. Org. Chem.* **1958**, *23*, 1309–1319.

[45] J. S. Norwick, N. A. Powell, T. M. Nguyen, G. Noronha, *J. Org. Chem.* **1992**, *57*, 7364–7366.

[46] a) M. Avalos, J. Fuentes, I. M. Gómez, J. L. Jiménez, J. C. Palacios, M. C. Ortiz, *Carbohydr. Res.* **1986**, *154*, 49–62; b) J. Fuentes, M. Avalos, J. L. Jiménez, J. C. Palacios, I. M. Gómez, *An. Quim.* **1985**, *81C*, 239–243.

[47] CCDC-278200 (for **30**) contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

[48] D. Horton, J. D. Wander, *J. Org. Chem.* **1974**, *39*, 1859–1863.

[49] S. Konstas, I. Photaki, L. Zervas, *Chem. Ber.* **1959**, *92*, 1288–1293.

[50] T. Ito, *Chem. Pharm. Bull.* **1964**, *12*, 499–501.

[51] P. Boullanger, M. Jouineau, B. Bouammali, D. Lafont, G. Descotes, *Carbohydr. Res.* **1990**, *202*, 151–164.

[52] a) C. M. Lee, W. D. Kumler, *J. Am. Chem. Soc.* **1961**, *83*, 4593–4596; b) C. M. Lee, W. D. Kumler, *J. Am. Chem. Soc.* **1961**, 4596–4600; c) C. M. Lee, W. D. Kumler, *J. Am. Chem. Soc.* **1962**, *84*, 565–571.

[53] R. Greenhalgh, M. Weinberger, *Can. J. Chem.* **1965**, *43*, 3340–3346.

[54] a) M. Avalos, J. L. Jiménez, J. C. Palacios, M. D. Ramos, J. A. Galbis, *Carbohydr. Res.* **1987**, *161*, 49–64; b) M. Avalos, P. Cintas, I. M. Gómez, J. L. Jiménez, J. C. Palacios, F. Rebolledo, *Carbohydr. Res.* **1989**, *187*, 1–14.

[55] M. Avalos, R. Babiano, P. Cintas, J. L. Jiménez, J. C. Palacios, G. Silvero, C. Valencia, *Tetrahedron* **1999**, *55*, 4377–4400.

[56] C. Foces-Foces, F. H. Cano, M. Bernabé, S. Penades, M. Martín-Lomas, *Carbohydr. Res.* **1984**, *135*, 1–11.

[57] J. Kovács, I. Pintér, A. Messmer, G. Töth, *Carbohydr. Res.* **1985**, *141*, 57–65.

[58] CCDC-276927 (for **40**) contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

[59] F. Micheel, W. Lengsfeld, *Chem. Ber.* **1956**, *89*, 1246–1253.

[60] W. H. Bromund, R. M. Herbst, *J. Org. Chem.* **1945**, *10*, 267–276.

[61] R. Babiano, C. Durán, J. Plumet, E. Román, E. Sánchez, J. A. Serrano, J. Fuentes, *J. Chem. Soc., Perkin Trans. 1* **1989**, 1923–1926.

[62] M. Avalos, R. Babiano, C. J. Durán, J. L. Jiménez, J. C. Palacios, *J. Chem. Soc., Perkin Trans. 2* **1992**, 2205–2215.

[63] M. Avalos, R. Babiano, P. Cintas, J. L. Jiménez, J. C. Palacios, C. Valencia, *Tetrahedron* **1993**, *49*, 2676–2690.

Received: August 5, 2005