A Family of Hydrogels Based on Ureido-Linked Aminopolyol-Derived Amphiphiles and Bolaamphiphiles: Synthesis, Gelation under Thermal and Sonochemical Stimuli, and Mesomorphic Characterization

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Abstract: This article describes the systematic preparation of a novel family of carbohydrate amphiphiles and bolaamphiphiles in which hydrophilic and hydrophobic units are connected via a ureido or bis(ureido) moiety. The sugar core is derived from aminopolyols such as D-glucamine (**1**), *N*-methyl-D-glucamine (**2**), or the sugar-like species tris(hydroxymethyl)aminomethane (**3**). The *O*-unprotected derivatives behave as self-organizing nonionic surfactants with good water gelation ability, which can be induced under thermal or ultrasound-driven stimuli. In addition, some derivatives of **1** and **2**, and rarely **3** also formed lyotropic liquid crystals with lamellar or hexagonal structures that exhibit low-temperature transitions.

Keywords: amino sugars · amphiphiles · gels · liquid crystals · self-assembly

Introduction

Molecular aggregation and self-assembly leading to supramolecular structures such as plaques, fibers, as well as lamellar or columnar arrangements represent dominant research topics in modern chemistry. Prominent architectures in soft matter are exemplified by both gels[1] and liquid-crystalline phases,[2] which can be tailored for multiple and varied applications. Their design, however, and the search for specific properties are still far from being a mature discipline. Structural elements such as complementary shape and directional intermolecular interactions are often viewed as the driving forces that lead ultimately to stacking options and alignment preferences.

With these premises in mind and in view of our previous experience of the preparation and transformation of carbohydrate-based ureas,[3] we recently embarked on the synthesis and characterization of amphiphilic and bolaamphiphilic[4] structures that combine a polar carbohydrate moiety and a long-chain fragment through one or more urea linkages. Protection of the sugar hydroxy groups, for instance, by *O*-acylation, increases the lipophilicity, whereas incorporation of another carbohydrate fragment in the place of a hydrocarbon chain increases the hydrophilic character. The diversity of such glycoconjugates is summarized in Figure 1.

Conceptually, one or more of the above structural elements has already been explored in the construction of different supramolecular structures by the self-assembly of low-molecular-weight compounds. Thus, amphiphiles containing sugars as well as cyclic and acyclic polyols as polar heads often exhibit liquid-crystalline phases.[5] Our choice of introducing a ureido group to connect polar and nonpolar moieties follows a well-established rationale. It was demonstrated more than five decades ago that urea-type hydrogen bonds are capable of stabilizing gelator assemblies.[6] For ureas, the energies of hydrogen-bonding interactions are calculated to be 37.3 kJ mol^{-1} for the ribbon structure and 44.8 kJ mol^{-1} for a chain arrangement, although London dispersion forces also contribute to the stability of intermolecu-

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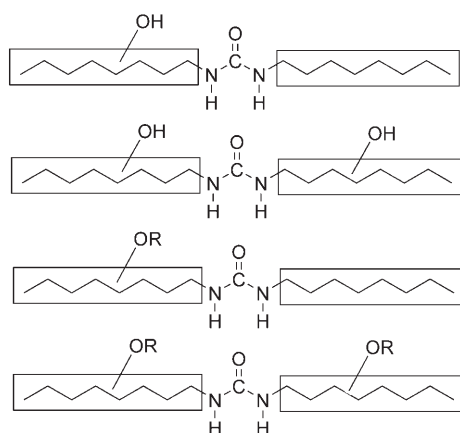y de los Materiales, Escuela de Ingenierías Industriales-UEX
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Figure 1. Schematic and simplified representation of amphiphiles and bo-laamphiphiles that combine protected and unprotected carbohydrate and long-chain hydrocarbons through a ureido spacer.

lar interactions, especially in longer-chain ureas.[7] Moreover, the self-association of ureas involving two hydrogen bonds is much stronger than that of amides or urethanes and the resulting assemblies are often insoluble materials. Therefore, it is not surprising that ureido linkages have largely been exploited as molecular constituents of low-molecular-mass organogels (LMOGs), oligomers, and foldamers.[7a,8,9] In addition, the urea moiety represents an attractive isosteric replacement of the peptide linkage and there have been numerous studies on oligoureas and ureidopeptoids that are capable of generating stable hydrogen-bonded structures that mimic the secondary structural motifs present in proteins.[10] Such peptidomimetics show promising perspectives for drug discovery and biomedical therapies because of their resistance to protease degradation.

In contrast, urea–carbohydrate hybrids have received minimal attention[3] and, in this context, and as mentioned above (Figure 1), we wanted to move from the conventional synthesis of sugar–iso(thio)cyanates and –(thio)ureas functionalized by discrete alkyl and aryl groups to structures resembling glycolipids, susceptible to self-organization and with a diverse range of specific properties (amphiphilic, bolaamphiphilic, mesogenic, nonionic surfactant, etc.). To this end, two readily available sugar aminopolyols, D-glucamine (**1**) and N-methyl-D-glucamine (**2**), were chosen as polar structural elements that can be further linked through a ureido group at a nonanomeric position. This latter aspect is particularly noteworthy as, unlike the corresponding glycosylamines, these aminopolyols are expected to exhibit resistance to hydrolytic cleavage or degradation. In the search for more simplified models, a non-carbohydrate aminopolyol, tris(hydroxymethyl)aminomethane (TRIS, **3**), was also envisaged as a polar scaffold.

While this manuscript was in preparation, Hamilton and co-workers reported the use of per-O-acetylated D-glucamine in the preparation of a series of non-fluorous hydrogen-bonding bis(ureas) capable of dissolving in CO₂ (by virtue of the interactions between this substance and the
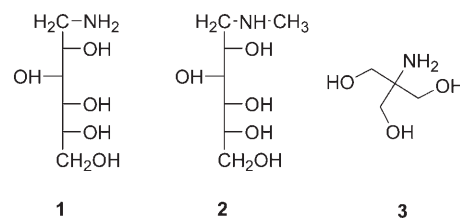
acetyl groups acting as CO_2-philic arms) and subsequently forming fibrillar foams.[11] This study, however, focuses on more amphiphilic substances, paying attention to unprotected derivatives at the sugar moiety and assessing the propensity for self-organization and aggregation in the search for more biodegradable materials. Such results are comprehensively shown in this article and complement current studies by other groups. It is gratifying to see how sugar aminoalditols, which have long been confined to the rich history of carbohydrate chemistry,[12] could now enjoy a further renaissance as precursors of novel synthetic and bioactive materials.

Results and Discussion

Synthesis of isocyanates and monoureas: A straightforward route to unprotected urea-based amphiphiles involves the condensation of aminopolyols with long-chain isocyanates. To this end, a preliminary screening of different heterocumulenes featuring flexible and rigid structures, as well as variable degrees of hydrophobicity, was carried out. Thus, monoureas have been generated from octyl isocyanate (**4**), dodecyl isocyanate (**5**), and 4-(octyloxy)phenyl isocyanate (**6**). Bifunctional derivatives suitable for the construction of the corresponding bis(ureas) were likewise envisaged. These include decane-1,10-diyl diisocyanate (**7**), 1,4-phenylene diisocyanate (**8**), and 4,4′-methylenediphenylene isocyanate (**9**). Note that neither compound **6** nor **7** were commercially available, although both could be satisfactorily prepared in yields in excess of 80% from 4-(octyloxy)aniline and 1,10-diaminodecane, respectively.

The synthesis of isocyanates is invariably challenging because it rests largely upon the use of phosgene and its derivatives,[13] although more environmentally benign and less hazardous processes have also emerged.[14] Isocyanates **6** and **7** were obtained as oils by using either a commercially and safer solution of phosgene in toluene or, better yet, with solid triphosgene,[15] which provides cleaner reactions. In addition, the range of isocyanates was expanded to 2,3,4,5,6-penta-O-acetyl-1-deoxy-1-isocyanato-D-glucitol (**10**), a valuable chiral precursor that can be employed in the construction of O-protected derivatives and bolaform ureas (see below). Compound **10** has recently been prepared in our laboratories from penta-O-acetylated D-glucamine hydrobromide by using both $COCl_2$ in toluene solution and triphosgene.[3, 16]
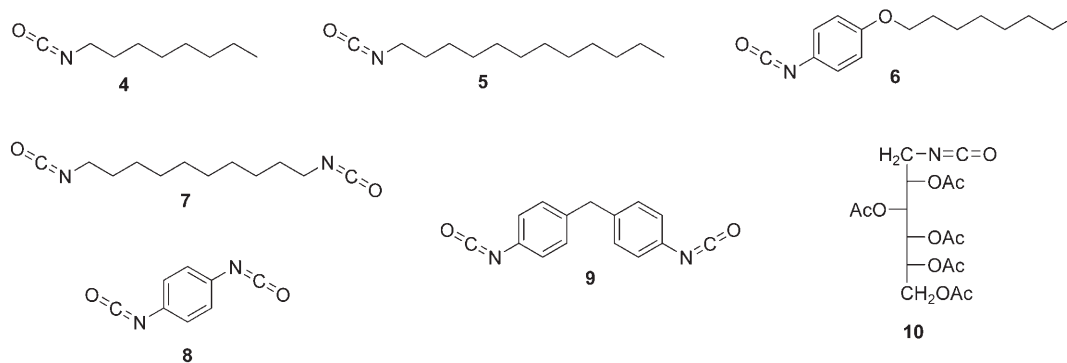
The reactions of aminopolyols **1–3** with isocyanates **4–6** gave rise to a series of asymmetrically substituted monoureas (**11–19**) with different structural variations of the head- and tail-group moieties (Scheme 1).

These condensations can easily be carried out in dioxane/water under vigorous agitation. Under these experimental conditions, monoureas **11–19** precipitated quickly and the free hydroxy groups remained unaffected as the electrophilic isocyanato group targets selectively the nitrogen atom of the aminopolyol. Alternatively, such monoureas can be generated by adding the isocyanate to a pyridine solution of the aminopolyol and subsequently pouring the reaction mixture into ice/water. This strategy was especially convenient for *N*-methyl-D-glucamine-based ureas (e.g., **14–16**) as the intro-

duction of a lateral methyl substituent at the nitrogen atom hinders the attack on the carbon atom of the isocyanate. Therefore, in aqueous dioxane, hydrolysis of the isocyanate competes with the attack of the amino group, thereby decreasing the isolated yields.

Peracetylated sugars exhibit enhanced lipophilicity and extraordinary solubility in numerous organic solvents. Such derivatives were prepared by direct condensation of sugar isocyanate **10** with the corresponding amines leading to ureas **20–22** (Scheme 2). This procedure thus complements the conventional acylation of the unprotected derivatives avoiding the use of the more expensive and irritant isocyanates.
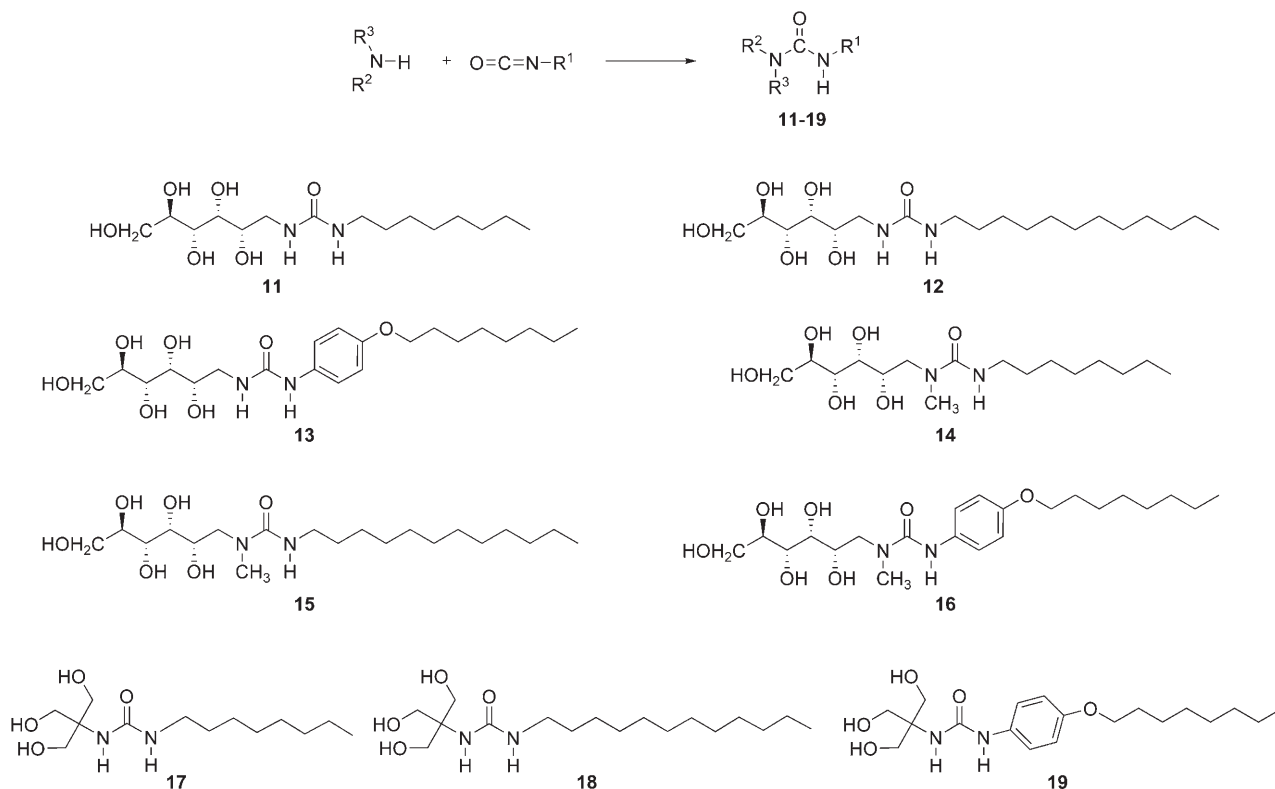
Scheme 1. Synthesis of *O*-unprotected aminopolyol-based ureido derivatives
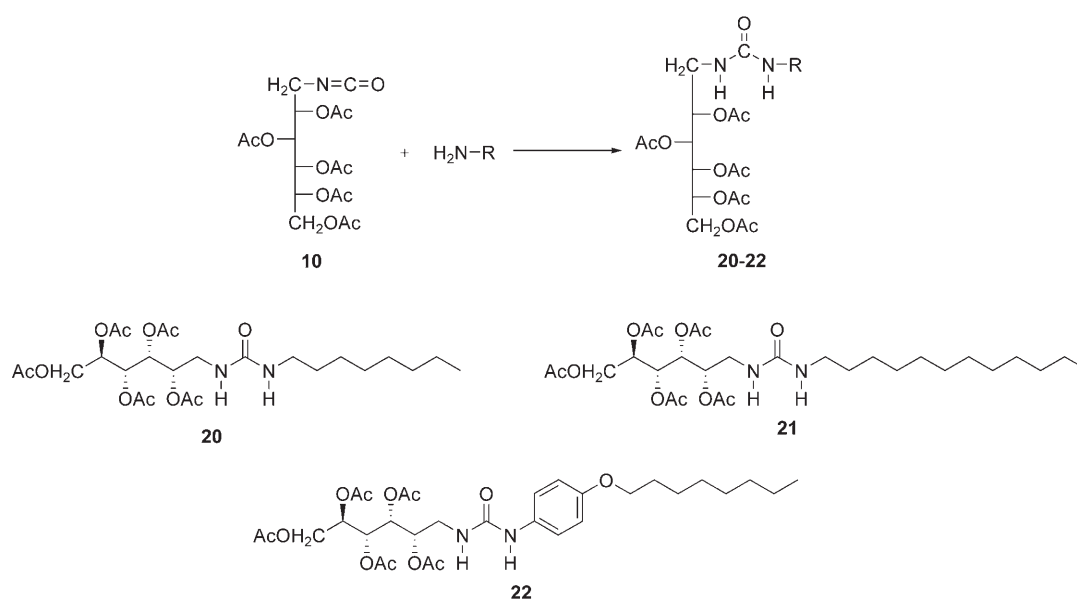
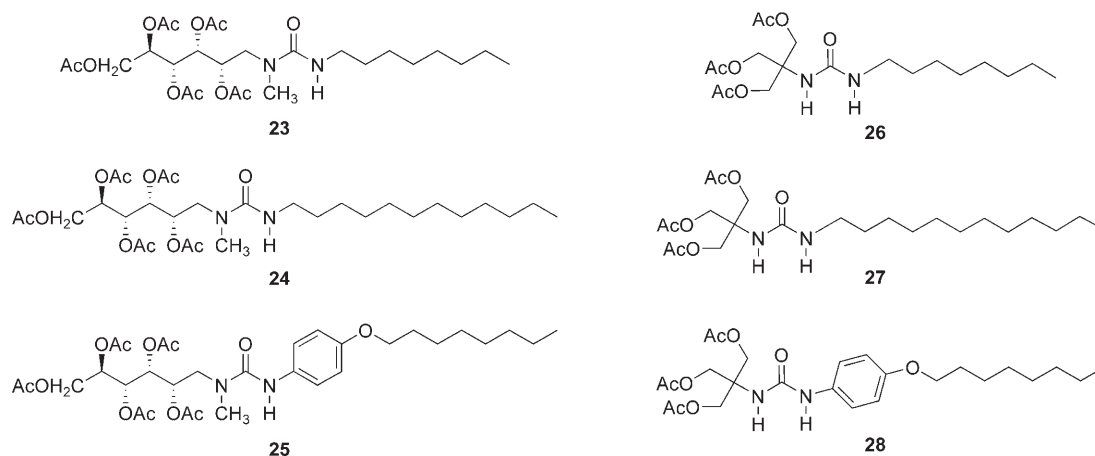Scheme 2. Formation of per-*O*-acetylated monoureas from isocyanate **10**.

The secondary aminopolyol **2** cannot be converted into its isocyanate and, moreover, our attempts to transform **3** into the corresponding isocyanate were also unsuccessful. Accordingly, per-*O*-acetylated monoureas **23–28** were obtained by acetylation of **14–19** in pyridine at 0°C affording oily or solid products that were further purified by chromatographic methods.
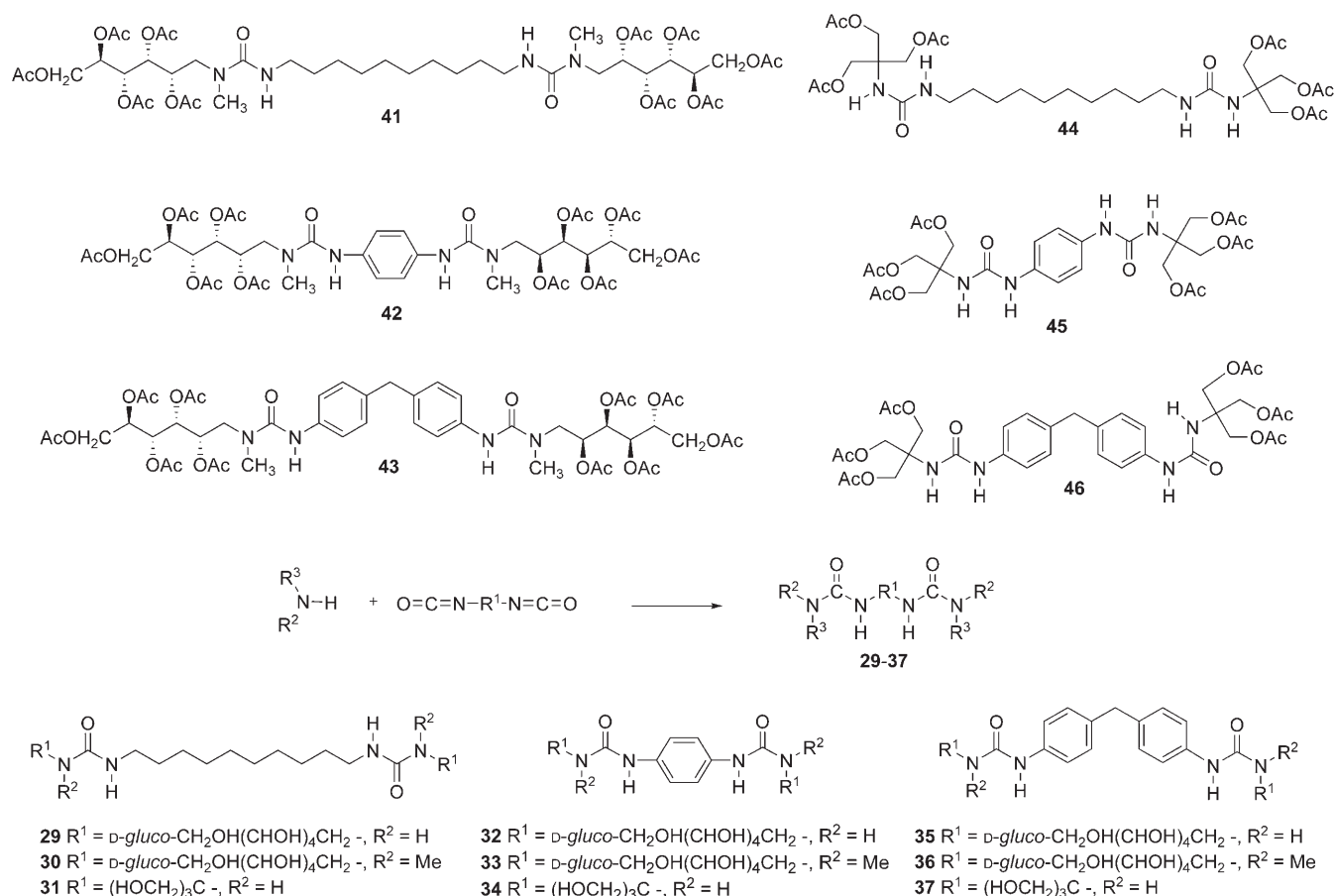
Formation of bis(ureas): As mentioned previously, carbohydrate and carbohydrate-like bolaamphiphiles can also be obtained by the reaction of aminopolyols **1–3** with diisocyanates **7–9** in dioxane/water leading to insoluble products (Scheme 3). The alternative protocol in pyridine solution took place with the formation of unwanted side-products and was ruled out. Three series of structurally analogous bolaamphiphiles (**29–31**, **32–34**, and **35–37**), which combine flexible and rigid, aliphatic and aromatic spacers, were thus readily available.

By following the above methodology for monoureas, chiral bolaforms with D-*gluco* configurations could be generated by condensation of D-glucamine isocyanate **10** with the corresponding diamines, which again avoids the use of diisocyanates (Scheme 4).
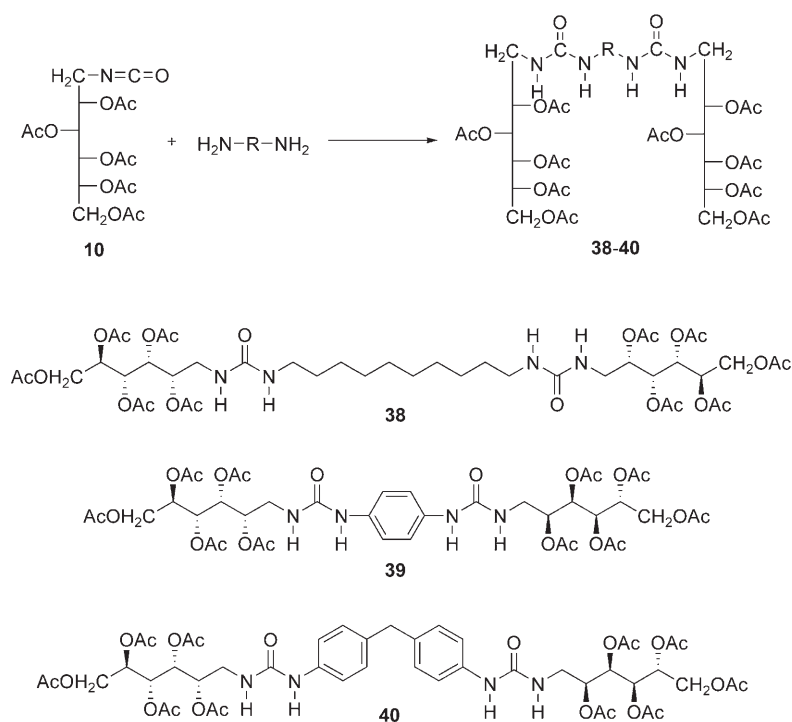
These transformations occurred readily in CH_2Cl_2 solutions at room temperature and were essentially complete within 10–15 min. Per-*O*-acetylated *N*-methyldiureas arising from **2** (compounds **41–43**) as well as those derived from aminopolyol **3** (compounds **44–46**) were prepared by acetylation (acetic anhydride, pyridine) of the corresponding unprotected derivatives.

Structural characterization of ureas: Spectroscopic elucidation, combustion analyses, and/or mass spectral data fully agree with the proposed structures for the above ureido derivatives. Among the diagnostic signals, isocyanates **6** and **7** show a strong IR absorption at about 2270 cm^{-1} and a ^{13}C

Scheme 3. Formation of bolaamphiphilic structures 29–37.

29 R^1 = D-gluco-CH$_2$OH(CHOH)$_4$CH$_2$ -, R^2 = H
30 R^1 = D-gluco-CH$_2$OH(CHOH)$_4$CH$_2$ -, R^2 = Me
31 R^1 = (HOCH$_2$)$_3$C -, R^2 = H

32 R^1 = D-gluco-CH$_2$OH(CHOH)$_4$CH$_2$ -, R^2 = H
33 R^1 = D-gluco-CH$_2$OH(CHOH)$_4$CH$_2$ -, R^2 = Me
34 R^1 = (HOCH$_2$)$_3$C -, R^2 = H

35 R^1 = D-gluco-CH$_2$OH(CHOH)$_4$CH$_2$ -, R^2 = H
36 R^1 = D-gluco-CH$_2$OH(CHOH)$_4$CH$_2$ -, R^2 = Me
37 R^1 = (HOCH$_2$)$_3$C -, R^2 = H

Scheme 4. Preparation of O-protected bis(ureas) 38–40.

NMR resonance at $\delta \approx 122$ ppm, which are typical of the isocyanato group. All of the ureas synthesized also exhibit characteristic IR absorptions at about 1650 and 1580 cm^{-1} (amide I and II bands) for the ureido moiety.[17]

The symmetrical derivatives 29–46 possess a C_2-symmetry axis and thus display simplified ^{1}H and ^{13}C NMR spectra that facilitate their interpretation. The diastereotopic protons of the N–CH$_2$ group of the bis-(ureas) derived from 1 and 2 lie in the range $\delta = 3.4$–3.2 and 3.2–3.0 ppm, respectively. In stark contrast, the protons of the N–CH$_2$ group of the poly-methylene side-chain appear as one signal at $\delta \approx 3.0$ ppm. The urea carbonyl groups resonate at $\delta \approx 156$–159 ppm. The skeletons derived from structures 1

and **2** show a signal from the carbon atom linked to the nitrogen at $\delta \approx 40$ and ≈ 49 ppm, respectively, whereas the signals of the remaining carbon atoms are shifted downfield, in the range $\delta = 72$–68 ppm, in agreement with the expected values for acyclic polyhydroxyalkyl chains.[3, 18]

In addition, it should also be mentioned that the relatively low optical rotations measured for the chiral derivatives are consistent with the presence of acyclic sugar moieties.[3]

Gelation properties: Having established simple and reliable methodologies for the construction of amphiphiles and bolaamphiphiles with multiple hydroxy and peracetyl groups, we were interested in studying the gelation ability of such low-molecular-mass molecules. A gelator, usually at a low concentration, self-assembles to form a three-dimensional network in which the solvent molecules are immobilized. At first glance, one could anticipate that an amphiphilic structure having an appropriate head group with long and/or hydrophobic chains is sufficient for the formation of detergency or soft solid-like materials. But, as noted by Terech and Weiss in their seminal review on the subject,[1b] it is not usually possible to predict in advance if a molecule will form a gel in a given solvent as this property depends on a subtle balance of different noncovalent intermolecular interactions. A recent study has shown that dendritic amphiphiles exhibit an unusual decrease in the critical micelle concentration (cmc) as the chain length increases; the longer homologues did not form micelles.[19,20]

We first observed the enhanced hygroscopicity of bis-(ureas) such as **29** and **30**. These substances are insoluble in a wide range of organic solvents (from methanol and ethanol to dichloromethane, benzene, and *n*-hexane), and attempts to purify them by recrystallization from water resulted in foaming and gel formation. This suggests that unprotected mono- and bis(ureas) might immobilize water molecules. Supramolecular hydrogels consist of water-soluble cross-linked polymers that can modify their degree of swelling, among other properties, in response to external stimuli such as changes in temperature, pH, or ionic strength. They are attractive materials that have found application as matrices for artificial enzymes, tissue engineering, biomineralization, or biocompatible scaffolds for wound healing.[21]

The gelation properties of the ureido amphiphiles and bolaamphiphiles were evaluated in various solvents, with the emphasis on water, by the inverted tube method. Mixtures of ureas at 1 wt% in a given solvent were heated (oil bath) until complete dissolution, if possible. The solutions were cooled to room temperature and gelation was observed visually. Positive results were considered to have been obtained when gels exhibited no gravitational flow over a period of several hours, even days. The process can be repeated, thereby demonstrating the thermoreversibility of the sol–gel transformation (Table 1).

In general, amphiphilic ureas are good hydrogelators, as evidenced in the cases of D-glucamine derivatives with long alkyl or oxyalkyl chains, even in the presence of an aromatic bridge. However, the presence of a methyl substituent on

Table 1. Gelation properties of *O*-unprotected ureas in different solvents at a concentration of 1 wt% unless otherwise specified.[a]

Compound	H$_2$O	EtOH	MeOH	CHCl$_3$	Benzene	DMSO
11	G[b]	P	P	I	I	S
12	G	P	P	I	I	S
13	G	P	P	I	I	S
14	S	S	S	P	P	S
15	G[b]	S	S	P	P	S
16	S	S	S	G[c]	G[c]	S
17	G	S	S	I	S	S
18	I	P	P	P	P	S
19	I	S	S	P	P	S
29	G	I	I	I	I	G[d]
30	G[e]	P	P	I	I	S
31	P	P	P	I	I	S
32	P	P	P	I	I	S
33	S	I	P	I	I	S
34	P	I	I	P	I	S
35	P	I	I	I	I	S
36	S	P	I	I	I	S
37	P	I	P	I	I	S

[a] G: Formation of stable gel; S: soluble after cooling; I: insoluble or partially soluble at the boiling point of the solvent; P: precipitates upon cooling. [b] Stable gel formed after sonication at room temperature. [c] Precipitates at 1 wt%, gel forms at 2 wt% and at 1 wt% with ultrasound at room temperature. [d] Soluble at 1 wt%, gelation at 3 wt%. [e] Soluble at 1 wt% on heating, gel forms at 2 wt% and at 1 wt% with ultrasound at room temperature.

the ureido moiety causes a dramatic change in the gelation ability, presumably by decreasing the number of hydrogen-bond-forming units. Compounds **14** and **16** are soluble on heating, although gelation at 1 wt% could only be observed for the longer dodecyl derivative **15**. For the tris(hydroxymethyl)aminomethane series, only **17** behaves as a hydrogelator under these experimental conditions, whereas **18** and **19** with longer chains and a smaller head group are insoluble. A similar trend was observed for bolaamphiphilic bis-(ureas); gelation occurs for compound **29** derived from D-glucamine as well as for its *N*-methyl-D-glucamine counterpart **30**, the latter at 2 wt% only. The remaining substances are either soluble in boiling water or precipitate upon cooling without forming gels.

Recent years have witnessed the emergence of a salient phenomenon: The ability of certain compounds to gel liquids under ultrasonic waves.[22,23] In this study, compounds that exhibited gelation ability on heating also gave stable hydrogels when heating and prolonged sonication (at 35 kHz, ultrasonic bath) were employed. Notably, monoureas **11** and **15** afforded hydrogels at room temperature. The bis(ureido) derivative **30** also promoted water gelation at room temperature under sonication, and ultrasound decreased the amount of urea required for this purpose (1 wt%) compared with under purely thermal conditions (2 wt%).

The unprotected ureas are in most cases insoluble or form precipitates in polar and apolar organic solvents. Compound **16** bearing an octyloxyphenyl unit and a lateral methyl group at the urea linkage, which precipitates in chloroform and benzene, gave more viscous solutions leading ultimately

to organogels at 2 wt % and, remarkably, at 1 wt % when such mixtures were sonicated at room temperature.

Molecular aggregation under ultrasound is still poorly understood. Further experiments suggest that multiple hydrogen-bonding interactions cause the precipitation of the compounds when the system is cooled without perturbation, whereas ultrasonic waves could partially disrupt hydrogen-bonding, which would facilitate the formation of the gel network.[23b, 24, 25] This conjecture also implies that ultrasonic effects can be restricted to supramolecular aggregates having weak intermolecular interactions.

SEM images of the as-prepared hydrogels (see the Supporting Information) reveal different micron-sized architectures, and although a molecular pattern cannot be inferred from such images, it is logical to assume that networking in aqueous solution is mainly due to hydrogen bonding and hydrophobic interactions, whereas π-stacking could be equally relevant with aromatic derivatives.

The self-organization of the corresponding per-*O*-acetyl mono- and bis(ureas) will be reported elsewhere, however, preliminary screenings reveal that most are insoluble in water, although **26** and **27** derived from **3** are soluble. They dissolve in benzene or toluene solutions, with the exception of **38**, **39**, **45**, and **46**, which precipitate upon cooling. Both protected and unprotected ureas are highly soluble in DMSO, gelation being observed in the case of **29** at a rather modest concentration of 3 wt %.

Mesomorphic behavior: Conventional surfactants aggregate in solution to form micelles because of the hydrophobic effect.[26] At high concentrations, micelles become ordered, forming lyotropic liquid crystals. Such mesophases are induced by the presence of a solvent and are characteristic of small molecules having hydrophilic and lipophilic termini.[27] This behavior has been previously studied in a series of linear nonionic urea surfactants derived from decyl and dodecyl ureas, the intermolecular hydrogen-bonding by the urea moiety being the dominant factor in determining the solid-state thermal behavior and crystal solubility boundary.[28] In this study, the surfactant properties of the amphiphilic molecules could be further assessed by means of surface-pressure–molecular-area isotherms and estimations of the critical micelle concentrations, as shown in the Supporting Information.

Visual observation of the samples between crossed-polarizing filters revealed the formation of just two types of liquid-crystalline textures, lamellar and hexagonal (Figure 2).

The mesomorphic behavior of amphiphilic molecules containing polyhydroxy moieties and alkyl chains has also been studied in detail.[29] Although general rules cannot always be established, liquid-crystalline phases emerge from a balance of the volume fraction of the two incompatible philic parts and the molecular shape.[5g] Single-chain compounds usually form smectic phases, whereas the presence of two lipophilic parts leads to cylindrical aggregates that result in hexagonal columnar phases. Additional chains increase the interface
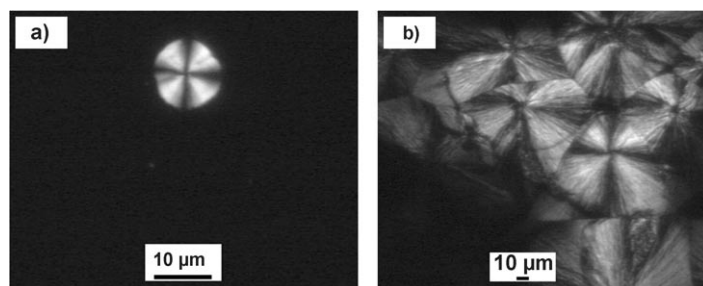

Figure 2. Typical textures observed for binary water/amphiphile systems under polarized light: lamellar (e.g., **15**, left) and hexagonal (e.g., **13**, right).

curvature to produce globular aggregates arranged in cubic lattices. These effects are also observed on increasing the hydrophilic parts, which leads to columnar and cubic structures with the hydrophobic chains on the inner sides. As expected, the driving force for the formation of the liquid-crystal phase is the generation of intermolecular hydrogen-bonding between hydroxy groups and the segregation of hydrophobic chains and sugar head groups.[30]

Table 2 summarizes the type of phase formed for each compound and the temperature at which it is formed. Ureas derived from aminopolyol **3** showed in general little or no

Table 2. Liquid-crystal phases observed for *O*-unprotected ureido amphiphiles.

Compound	Parent sugar	Mesophase	Temperature [°C]
11	**1**	–[a]	–
14	**2**	lamellar	29
12	**1**	hexagonal	120
15	**2**	lamellar	31
13	**1**	hexagonal	120
16	**2**	hexagonal	60
29	**1**	hexagonal	160
30	**2**	hexagonal	60
32	**1**	–[a]	–
33	**2**	lamellar	37
35	**1**	–[a]	–
36	**2**	lamellar[b]	25
37	**3**	lamellar[c]	37

[a] No liquid-crystal formation was observed. [b] Observation at 25 °C in the absence of water. [c] No mesophase was detected with other ureas derived from TRIS (**3**), such as **17**, **18**, and **34**.

activity. The rest of the compounds are grouped, for comparative purposes, in pairs according to the fatty chain length, with the second compound in each pair having a methyl group that is missing in the first compound. Thus, as a general trend, surfactants lacking the methyl substituent need a higher temperature than those of methylated derivatives for the liquid-crystal phase to occur.

FULL PAPER

Conclusion

We have described a convenient and reliable protocol for the synthesis of unprotected and peracetylated amphiphilic and bolaamphiphilic ureido sugars derived from aminopolyols. The *O*-unprotected derivatives act as highly efficient hydrogelators, with ultrasound stimulating gelation in most cases at room temperature and at a low critical concentration of 1 wt%. The gelation capability can chiefly be ascribed to hydrogen-bonding between the urea groups and van der Waals interactions between the long alkyl chains. Furthermore, it has been shown that some amphipathic structures bearing D-glucamine or *N*-methyl-D-glucamine unprotected chains can also form lyotropic liquid-crystalline phases. These findings consistently point to facile strategies en route to novel carbohydrate-based materials. In addition, owing to both the chelating and coordinating properties of the urea linkage, these compounds have good prospects in catalysis and organocatalysis, which are currently being explored.

Experimental Section

General methods: See the Supporting Information for a detailed description of the methods employed in product purification, structural characterization, and the assessment of surfactant properties.

General procedures for the preparation of isocyanates—Method A: The amine derivative (1.0 mmol) was added to a cooled solution of pyridine (0.32 mL) in anhydrous CH$_2$Cl$_2$ (10 mL) and the reaction mixture was vigorously stirred at 0 °C for 30 min. Then, a solution of phosgene in toluene (1.93 M, 1.1 mL/amino group, 2.0 mmol/amino group) was added dropwise and the resulting mixture was stirred at that temperature for a further 2 h. This solution was subsequently washed with 0.5 N HCl (2× 5 mL), brine (1×5 mL), and distilled water, dried over anhydrous MgSO$_4$, and evaporated to dryness.

Method B: Triphosgene (1.35 g, 4.6 mmol) was added to a mixture of the amine (4.6 mmol) in CH$_2$Cl$_2$ (50 mL) and a saturated solution of NaHCO$_3$ (30 mL). The resulting mixture was stirred vigorously at 0 °C for 30 min. The organic layer was separated and washed with brine and distilled water, dried (MgSO$_4$), and evaporated to dryness.

4-(Octyloxy)phenyl isocyanate (6): This derivative was obtained from 4-(octyloxy)aniline in yields of 83 (Method A) and 84% (Method B) after purification of the resulting oil by column chromatography (EtOAc/hexane, 1:10); ^{1}H NMR (400 MHz, CDCl$_3$): δ = 7.02 (d, $J_{o,m}$ = 9.0 Hz, 2H; 2-H, 6-H, Ar), 6.84 (d, $J_{o,m}$ = 9.0 Hz, 2H; 3-H, 5-H, Ar), 3.94 (t, 2H; CH_2-O), 1.80 (m, 2H; CH_2-CH$_2$-O), 1.46 (m, 2H; -CH_2-(CH$_2$)$_2$-O-), 1.36 (m, 8H; CH$_2$), 0.92 ppm (t, 3H; CH$_3$); ^{13}C NMR (100 MHz, CDCl$_3$): δ = 157.0 (C-4, Ar), 125.7 (C-1, Ar), 125.6 (C-2, C-6, Ar), 124.1 (NCO), 115.4 (C-3, C-5, Ar), 68.4 (C-1), 31.8 (C-2), 29.4, 29.3 (C-4, C-5, C-6), 26.1 (C-3), 22.7 (C-7), 14.1 ppm (C-8); IR (Nujol): $\tilde{v}$ = 2928 (CH$_3$), 2856 (CH$_2$), 2272 (NCO), 1523, 1458, 829 (Ar), 1245 (C−O), 1106, 1028 cm^{-1} (C−O); HRMS (CI): *m/z* calcd for C$_{15}$H$_{22}$NO$_2$: 248.1650; found: 248.1648.

Decamethylene diisocyanate (7): Obtained as above in yields of 80.5 (Method A) and 75% (Method B) on purification of the resulting oil by column chromatography (EtOAc/hexane, 1:10); ^{1}H NMR (400 MHz, CDCl$_3$): δ = 3.30 (t, 4H; CH_2-NCO), 1.38 (m, 4H; CH_2-CH$_2$-NCO), 1.32 (m, 4H; CH_2-(CH$_2$)$_2$-NCO), 1.31 ppm (m, 8H; CH$_2$); ^{13}C NMR (100 MHz, CDCl$_3$): δ = 122.0 (NCO), 43.0 (2C; C-1, C-10), 31.3 (2C; C-2, C-9), 29.3, 28.9 (4C; C-4, C-5, C-6, C-7), 26.5 ppm (2C; C-3, C-8); IR (Nujol): $\tilde{v}$ = 2930, 2856 (CH$_2$), 2273 (NCO), 1468 cm^{-1} (CH$_2$); LR-MS (CI): *m/z* (%): 227 (20) [*M*+3H]$^+$, 199 (100), 182 (45), 173 (29), 84 (35).

General procedures for the preparation of ureas—Method A: A solution of the isocyanate (4.0 mmol for monoisocyanates or 2.0 mmol for diisocyanates) in dioxane (0.6 mL/mmol) was added to a solution of D-glucamine (**1**), *N*-methyl-D-glucamine (**2**), or TRIS (**3**) (4.1 mmol) in water (2 mL), and the mixture was stirred at room temperature for 2 h. The resulting solid was filtered, washed successively with cold water, ethanol, and diethyl ether, and dried under vacuum.

Method B: The isocyanate (4.0 mmol for isocyanates or 2.0 mmol for diisocyanates) was added to a solution of D-glucamine (**1**), *N*-methyl-D-glucamine (**2**), or TRIS (**3**) (4.1 mmol) in pyridine (15 mL), and the mixture was vigorously stirred for 15 min. Then, it was poured into ice/water (120 mL) and the mixture was kept at 0 °C for 24 h. In most cases a solid appeared, which was filtered, washed with cold water, ethanol, and diethyl ether, and dried. In the absence of a precipitate, the solution was evaporated to dryness and the residue washed and dried as above.

N-(1-Deoxy-D-glucitol-1-yl)-N′-octylurea (11): Prepared from D-glucamine and octyl isocyanate (**4**) in a yield of 58% (Method A) and recrystallized from MeOH; m.p. 159–160 °C; $[\alpha]_D$ = −1.2, $[\alpha]_{578}$ = −1.0, $[\alpha]_{546}$ = −1.6, $[\alpha]_{436}$ = −2.4° (*c* = 1.0 in pyridine); ^{1}H NMR (400 MHz, [D$_6$]DMSO): δ = 6.00 (t, $J_{NH\text{-}CH2}$ = 5.6 Hz, 1H; N*H*-CH$_2$), 5.77 (t, $J_{NH,H1}$ = $J_{NH,H1'}$ = 5.4 Hz, 1H; N*H*-H1,1′), 4.80 (d, $J_{2\text{-}OH}$ = 3.6 Hz, 1H; 2-OH), 4.44 (d, $J_{5\text{-}OH}$ = 6.4 Hz, 1H; 5-OH), 4.36 (d, $J_{4\text{-}OH}$ = 5.2 Hz, 1H; 4-OH), 4.32 (t, $J_{6\text{-}OH} \approx J_{6'\text{-}OH}$ = 5.4 Hz, 1H; 6-OH), 4.28 (d, $J_{3\text{-}OH}$ = 6.4 Hz, 1H; 3-OH), 3.58 (m, 1H; 2-H), 3.54 (m, 2H; 3-H, 6-H), 3.46 (m, 1H; 5-H), 3.36 (m, 2H; 4-H, 6′-H), 3.20 (ddd, $J_{1,1'}$ = 13.2, $J_{1,2}$ = 4.0, $J_{NH,1}$ = 5.4 Hz, 1H; 1-H), 2.95 (m, 3H; 1-H′, CH_2-NH), 1.32 (q, 2H; CH_2-CH$_2$-NH), 1.24 (m, 10H; CH$_2$), 0.85 ppm (t, 3H; CH$_3$); ^{13}C NMR (100 MHz, [D$_6$]DMSO): δ = 158.6 (C=O, urea), 72.7 (C-5), 72.1 (C-2), 71.5 (C-3), 69.6 (C-4), 63.4 (C-6), 42.5 (C-1), 39.8 (C-1′), 31.3 (C-6′), 30.1 (C-2′), 28.8 (C-4′, C-5′), 26.5 (C-3′), 22.2 (C-7′), 14.0 ppm (C-8′); IR (KBr): $\tilde{v}$ = 3356, 3317 (OH, NH), 2923 (CH$_3$), 2844 (CH$_2$), 1610 (C=O, urea), 1580 (NH, urea), 1083 cm^{-1} (C−O); elemental analysis calcd (%) for C$_{15}$H$_{32}$N$_2$O$_6$: C 53.55, H 9.59, N 8.33; found: C 53.43, H 9.40, N 8.23.

N-(1-Deoxy-D-glucitol-1-yl)-N′-dodecylurea (12): Prepared from D-glucamine and dodecyl isocyanate (**5**) in a yield of 77% (Method A) and recrystallized from MeOH; m.p. 154–155 °C; $[\alpha]_D$ = −2.0, $[\alpha]_{578}$ = −1.2, $[\alpha]_{546}$ = −2.2, $[\alpha]_{436}$ = −3.2° (*c* = 1.0 in pyridine); ^{1}H NMR (400 MHz, [D$_6$]DMSO): δ = 6.00 (t, $J_{NH\text{-}CH2}$ = 5.6 Hz, 1H; N*H*-CH$_2$), 5.78 (t, $J_{NH,H1}$ = $J_{NH,H1'}$ = 5.2 Hz, 1H; N*H*-H1,1′), 4.80 (d, $J_{2\text{-}OH}$ = 4.8 Hz, 1H; 2-OH), 4.44 (d, $J_{5\text{-}OH}$ = 5.2 Hz, 1H; 5-OH), 4.37 (d, $J_{4\text{-}OH}$ = 5.6 Hz, 1H; 4-OH), 4.33 (t, $J_{6\text{-}OH}$ = $J_{6'\text{-}OH}$ = 5.6 Hz, 1H; 6-OH), 4.28 (d, $J_{3\text{-}OH}$ = 6.0 Hz, 1H; 3-OH), 3.58 (m, 1H; 2-H) 3.55 (m, 2H; 3-H, 6-H), 3.47 (m, 1H; 5-H), 3.38 (m, 2H; 4-H, 6′-H), 3.21 (ddd, $J_{1,1'}$ = 13.2, $J_{1,2}$ = 4.0, $J_{NH,1}$ = 5.2 Hz, 1H; 1-H), 2.95 (m, 3H; 1′-H, CH_2-NH), 1.33 (q, 2H; CH_2-CH$_2$-NH), 1.24 (m, 18H; CH$_2$), 0.85 ppm (t, 3H; CH$_3$); ^{13}C NMR (100 MHz, [D$_6$]DMSO): δ = 158.7 (C=O, urea), 72.7 (C-5), 72.1 (C-2), 71.5 (C-3), 69.6 (C-4), 63.4 (C-6), 42.5 (C-1), 39.8 (C-1′), 31.4 (C-10′), 30.1, 29.1, 28.9, 28.8 (C-2′, C-4′, C-5′, C-6′, C-7′, C-8′, C-9′), 26.5 (C-3′), 22.2 (C-11′), 14.0 ppm (C-12′); IR (KBr): $\tilde{v}$ = 3353 (NH, OH), 2919 (CH$_3$), 2848 (CH$_2$), 1613 (C=O, urea), 1581 (NH, urea), 1084 cm^{-1} (C−O); elemental analysis calcd (%) for C$_{19}$H$_{40}$N$_2$O$_6$: C 58.14, H 10.27, N 7.14; found: C 58.42, H 10.04, N 7.44.

N-(1-Deoxy-D-glucitol-1-yl)-N′-(4-octyloxyphenyl)urea (13): Prepared from D-glucamine and 4-(octyloxy)phenyl isocyanate (**6**) in a yield of 79% (Method A) and recrystallized from EtOH; m.p. 163–164 °C; $[\alpha]_D$ = −9.6, $[\alpha]_{578}$ = −10.6, $[\alpha]_{546}$ = −11.0, $[\alpha]_{436}$ = −20.0 (*c* = 1.0 in pyridine); ^{1}H NMR (400 MHz, [D$_6$]DMSO): δ = 8.41 (s, 1H; NH), 7.31 (d, $J_{o,m}$ = 8.8 Hz, 2H; 3-H, 5-H, Ar), 6.78 (d, $J_{o,m}$ = 8.8 Hz, 2H; 2-H, 6-H, Ar), 6.02 (t, $J_{NH,H1}$ = $J_{NH,H1'}$ = 5.2 Hz, 1H; N*H*-H1,1′) 4.82 (d, $J_{2\text{-}OH}$ = 4.4 Hz, 1H; 2-OH), 4.48 (d, $J_{5\text{-}OH}$ = 6.0 Hz, 1H; 5-OH), 4.41 (d, $J_{4\text{-}OH}$ = 5.6 Hz, 1H; 4-OH), 4.37 (t, $J_{6\text{-}OH}$ = $J_{6'\text{-}OH}$ = 5.6 Hz, 1H; 6-OH), 4.32 (d, $J_{3\text{-}OH}$ = 6.4 Hz, 1H; 3-OH), 3.86 (t, 2H; CH_2-O), 3.60 (m, 3H; 2-H, 3-H, 6-H), 3.49 (dddd, 1H; 5-H), 3.41 (m, 2H; 4-H, 6-H′), 3.31 (ddd, $J_{1,1'}$ = 13.2, $J_{1,2}$ = 4.0, $J_{NH,1}$ = 5.2 Hz, 1H; 1-H), 2.98 (dd, $J_{1,1'}$ = 13.2, $J_{1',2}$ = 7.2 Hz, 1H; 1′-H) 1.66 (q, 2H; CH_2-CH$_2$-O), 1.37 (q, 2H; -CH_2-(CH$_2$)$_2$-O-), 1.26 (m, 8H; CH$_2$), 0.85 ppm (t, 3H; CH$_3$); ^{13}C NMR (100 MHz, [D$_6$]DMSO): δ = 155.8 (C=O, urea), 153.4 (C-4, Ar), 133.7 (C-1, Ar), 119.3 (C-2, C-6, Ar), 114.5 (C-3, C-5, Ar) 72.2 (C-5), 72.0 (C-2), 71.5 (C-3), 70.0 (C-4), 67.6 (C−O), 63.5 (C-6), 42.3 (C-1), 31.4 (C-3′), 28.9, 28.8 (C-4′, C-5′, C-7′), 25.7 (C-6′), 22.2

(C-2′), 14.0 ppm (C-1′); IR (KBr): $\tilde{v} = 3512$ (OH), 3349 (NH), 2922 (CH$_3$), 2854 (CH$_2$), 1649 (C=O, urea), 1603 (aryl), 1579 (NH, urea), 1512 (Ar), 1248 (C–O, Ar), 1090 cm^{-1} (C–O); elemental analysis calcd (%) for C$_{21}$H$_{36}$N$_2$O$_7$: C 58.86, H 8.47, N 6.54; found: C 59.14, H 8.22, N 6.17.

N-(1-Deoxy-D-glucitol-1-yl)-N-methyl-N′-octylurea (14): Prepared from N-methyl-D-glucamine and octyl isocyanate (**4**) in yields of 14 (Method A) and 91% (Method B), and recrystallized from EtOAc; m.p. 116–117°C; $[\alpha]_D = +9.6$, $[\alpha]_{578} = +10.2$, $[\alpha]_{546} = +12.0$, $[\alpha]_{436} = +20.6$ ($c = 1.0$ in pyridine); ^{1}H NMR (400 MHz, [D$_6$]DMSO): $\delta = 6.20$ (t, $J_{NH-CH2} = 5.2$ Hz, 1H; N*H*-CH$_2$), 4.96 (d, $J_{2-OH} = 4.8$ Hz, 1H; 2-OH), 4.48 (d, $J_{5-OH} = 5.2$ Hz, 1H; 5-OH), 4.43 (m, 2H; 3-OH, 4-OH), 4.33 (t, $J_{6-OH} \approx J_{6'-OH} = 5.6$ Hz, 1H; 6-OH), 3.71 (dddd, $J_{2-OH} = 4.8$, $J_{1,2} = 4.0$, $J_{1',2} = 8.0$, $J_{2,3} = 3.6$ Hz, 1H; 2-H), 3.55 (ddd, $J_{6-OH} = 5.6$, $J_{5,6} = 2.8$, $J_{6,6'} = 11.2$ Hz, 1H; 6-H), 3.49 (m, 2H; 3-H, 5-H), 3.42 (ddd, $J_{3,4} = 2.0$, $J_{4-OH} = 5.0$, $J_{4,5} = 8.0$ Hz, 1H; 4-H), 3.35 (ddd, $J_{6-OH} = 5.6$, $J_{5,6'} = 6.0$, $J_{6,6'} = 11.2$ Hz, 1H; 6'-H), 3.27 (dd, $J_{1,1'} = 14.8$, $J_{1,2} = 4.8$ Hz, 1H; 1-H), 3.12 (dd, $J_{1,1'} = 14.8$, $J_{1',2} = 8.0$ Hz, 1H; 1′-H), 2.97 (q, 2H; C*H*$_2$-NH), 2.80 (s, 3H; CH$_3$-N) 1.37 (q, 2H; C*H*$_2$-CH$_2$-NH), 1.24 (m, 10H; CH$_2$), 0.85 ppm (t, 3H; CH$_3$) ppm; ^{13}C NMR (100 MHz, [D$_6$]DMSO): $\delta = 158.7$ (C=O, urea), 72.4 (C-5), 72.1 (C-3), 71.4 (C-4), 69.1 (C-2), 63.3 (C-6), 51.6 (C-1), 40.1 (C-1′), 35.3 (CH$_3$-N), 31.3 (C-6′), 30.0 (C-2′), 28.8 (C-4′, C-5′), 26.5 (C-3′), 22.2 (C-7′), 14.0 ppm (C-8′); IR (KBr): $\tilde{v} = 3432$ (OH), 3375 (NH), 2926 (CH$_3$), 2852 (CH$_2$), 1632 (C=O, urea), 1583 (NH, urea), 1096 cm^{-1} (C–O); elemental analysis calcd (%) for C$_{16}$H$_{34}$N$_2$O$_6$: C 54.84, H 9.78, N 7.99; found: C 54.79, H 9.57, N 7.84.

N-(1-Deoxy-D-glucitol-1-yl)-N-methyl-N′-dodecylurea (15): Prepared from N-methyl-D-glucamine and dodecyl isocyanate (**5**) in yields of 74 (Method A) and 82% (Method B), and recrystallized from EtOAc; m.p. 120–121°C; $[\alpha]_D = +7.8$, $[\alpha]_{578} = +8.8$, $[\alpha]_{546} = +10.4$, $[\alpha]_{436} = +17.6$ ($c = 1.0$ in pyridine); ^{1}H NMR (400 MHz, [D$_6$]DMSO): $\delta = 6.20$ (t, $J_{NH-CH2} = 5.4$ Hz, 1H; N*H*-CH$_2$), 4.96 (d, $J_{2-OH} = 4.8$ Hz, 1H; 2-OH), 4.49 (d, $J_{5-OH} = 5.2$ Hz, 1H; 5-OH), 4.43 (m, 2H; 3-OH, 4-OH), (t, $J_{6-OH} \approx J_{6'-OH} = 5.6$ Hz, 1H; 6-OH), 3.71 (dddd, $J_{2-OH} = 4.8$, $J_{1,2} = 4.0$, $J_{1',2} = 8.0$, $J_{2,3} = 3.6$ Hz, 1H; 2-H), 3.55 (ddd, $J_{6-OH} = 5.6$, $J_{5,6} = 2.8$, $J_{6,6'} = 11.2$ Hz, 1H; 6-H), 3.49 (m, 2H; 3-H, 5-H), 3.42 (m, 1H; 4-H), 3.35 (ddd, $J_{6-OH} = 5.6$, $J_{5,6'} = 6.0$, $J_{6,6'} = 11.2$ Hz, 1H; 6′-H), 3.29 (dd, $J_{1,1'} = 14.8$, $J_{1,2} = 4.8$ Hz, 1H; 1-H), 3.13 (dd, $J_{1,1'} = 14.8$, $J_{1',2} = 8.0$ Hz, 1H; 1′-H), 2.97 (q, 2H; C*H*$_2$-NH), 2.80 (s, 3H; CH$_3$-N) 1.37 (q, 2H; C*H*$_2$-CH$_2$-NH), 1.24 (m, 18H; CH$_2$), 0.85 ppm (t, 3H; CH$_3$); ^{13}C NMR (100 MHz, [D$_6$]DMSO): $\delta = 158.7$ (C=O, urea), 72.4 (C-5), 72.1 (C-2), 71.4 (C-3), 69.1 (C-4), 63.3 (C-6), 51.6 (C-1), 40.1 (C-1′), 35.3 (CH$_3$-N), 31.4 (C-10′), 30.0, 29.1, 28.9, 28.8 (C-2′, C-4′, C-5′, C-6′, C-7′, C-8′, C-9′), 26.5 (C-3′), 22.1 (C-11′), 14.0 ppm (C-12′); IR (KBr): $\tilde{v} = 3431$ (OH), 3372 (NH), 2920 (CH$_3$), 2851 (CH$_2$), 1630 (C=O, urea), 1583 (NH, urea), 1101 cm^{-1} (C–O); elemental analysis calcd (%) for C$_{20}$H$_{42}$N$_2$O$_6$: C 59.08, H 10.41, N 6.89; found: C 59.38, H 10.12, N 6.65.

N-(1-Deoxy-D-glucitol-1-yl)-N-methyl-N′-(4-octyloxyphenyl)urea (16): Prepared from N-methyl-D-glucamine and 4-(octyloxy)phenyl isocyanate (**6**) in a yield of 66% (Method A), and recrystallized from EtOAc; m.p. 121–122°C; $[\alpha]_D = +7.8$, $[\alpha]_{578} = +8.4$, $[\alpha]_{546} = +9.8$, $[\alpha]_{436} = +22.6$ ($c = 1.0$ in pyridine); ^{1}H NMR (400 MHz, [D$_6$]DMSO): $\delta = 8.28$ (s, 1H; NH), 7.26 (d, $J_{o,m} = 8.8$ Hz, 2H; 2-H, 6-H, aryl), 6.79 (d, $J_{o,m} = 8.8$ Hz, 2H; 3-H, 5-H, aryl), 5.17 (d, $J_{2-OH} = 4.0$ Hz, 1H; 2-OH), 4.54 (m, 2H; 3-OH, 4-OH), 4.50 (d, $J_{5-OH} = 4.8$ Hz, 1H; 5-OH), 4.37 (t, $J_{6-OH} \approx J_{6'-OH} = 5.6$ Hz, 1H; 6-OH), 3.87 (t, 2H; C*H*$_2$-O), 3.82 (dddd, $J_{2-OH} = 4.0$, $J_{1,2} = 4.0$, $J_{1',2} = 8.0$, $J_{2,3} = 3.6$ Hz, 1H; 2-H), 3.63 (ddd, $J_{6-OH} = 5.6$, $J_{5,6} = 2.8$, $J_{6,6'} = 11.2$ Hz, 1H; 6-H), 3.57 (m, 2H; 3-H, 5-H), 3.51 (m, 1H; 4-H), 3.44 (ddd, $J_{6-OH} = 5.6$, $J_{5,6'} = 6.0$, $J_{6,6'} = 11.2$ Hz, 1H; 6′-H), 3.41 (dd, $J_{1,1'} = 14.8$, $J_{1,2} = 4.8$ Hz, 1H; 1-H), 3.28 (dd, $J_{1,1'} = 14.8$, $J_{1',2} = 8.0$ Hz, 1H; 1′-H), 2.93 (s, 3H; CH$_3$-N), 1.67 (q, 2H; C*H*$_2$-CH$_2$-O), 1.38 (q, 2H; -C*H*$_2$-(CH$_2$)$_2$-O-), 1.27 (m, 8H; CH$_2$), 0.86 ppm (t, 3H; CH$_3$); ^{13}C NMR (100 MHz, [D$_6$]DMSO): $\delta = 156.3$ (C=O, urea), 153.8 (C-4, Ar), 133.6 (C-1, Ar), 121.2 (C-2, C-6, Ar), 114.2 (C-3, C-5, Ar), 72.1 (C-5), 71.9 (C-2), 71.4 (C-3), 69.4 (C-4), 67.5 (C-1′), 63.3 (C-6), 51.8 (C-1), 35.5 (CH$_3$-N), 31.3 (C-3′), 28.8, 28.7 (C-4′, C-5′, C-7′), 25.6 (C-6′), 22.1 (C-2′), 14.0 ppm (C-8′); IR (KBr): $\tilde{v} = 3399$ (NH, OH), 2920 (CH$_3$), 2852 (CH$_2$), 1620 (C=O, urea), 1548 (NH, urea), 1515, 1413 (Ar), 1249 (C–O, Ar), 1079 cm^{-1} (C–O); elemental analysis calcd (%) for C$_{22}$H$_{38}$N$_2$O$_7$: C 59.71, H 8.65, N 6.33; found: C 59.81, H 8.74, N 6.40.

N-[Tris(hydroxymethyl)methyl]-N′-octylurea (17): Prepared from **3** and octyl isocyanate (**4**) in yield of 67 (Method A) and 59% (Method B), and

recrystallized from EtOAc; m.p. 145–146°C; ^{1}H NMR (400 MHz, [D$_6$]DMSO): $\delta = 6.45$ (t, $J_{NH-CH2} = 5.6$ Hz, 1H; N*H*-CH$_2$), 5.71 (s, 1H; N*H*-C), 5.09 (t, $J_{OH-H} = 5.6$ Hz, 3H; OH), 3.40 (d, $J_{OH-H} = 5.6$ Hz, 6H; C*H*$_2$-OH), 2.93 (q, 2H; C*H*$_2$-NH), 1.33 (q, 2H; C*H*$_2$-CH$_2$-NH), 1.24 (m, 10H; CH$_2$), 0.86 ppm (t, 3H; CH$_3$); ^{13}C NMR (100 MHz, [D$_6$]DMSO): $\delta = 159.1$ (C=O, urea), 61.4 (3C; CH$_2$OH), 60.6 (C-NH), 39.7 (C-1′), 31.3 (C-6′), 29.9 (C-2′), 28.8 (C-4′, C-5′), 26.5 (C-3′), 22.2 (C-7′), 14.0 ppm (C-8′) ppm; IR (KBr): $\tilde{v} = 3368$, 3240 (OH, NH), 2921 (CH$_3$), 2855 (CH$_2$), 1654 (C=O, urea), 1564 (NH, urea), 1048 cm^{-1} (C–O); elemental analysis calcd (%) for C$_{13}$H$_{28}$N$_2$O$_4$: C 56.50, H 10.21, N 10.14; found: C 56.70, H 10.23, N 10.07.

N-[Tris(hydroxymethyl)methyl]-N′-dodecylurea (18): Prepared from **3** and dodecyl isocyanate (**5**) in yields of 25 (Method A) and 42% (Method B), and recrystallized from EtOAc; m.p. 148-149°C; ^{1}H NMR (400 MHz, [D$_6$]DMSO): $\delta = 6.44$ (t, $J_{NH-CH2} = 6.0$ Hz, 1H; N*H*-CH$_2$), 5.71 (s, 1H; NH-C), 5.09 (t, $J_{OH-H} = 5.6$ Hz, 3H; OH), 3.40 (d, $J_{OH-H} = 5.6$ Hz, 6H; C*H*$_2$-OH), 2.93 (q, 2H; C*H*$_2$-NH), 1.32 (q, 2H; C*H*$_2$-CH$_2$-NH), 1.24 (m, 18H; CH$_2$), 0.85 ppm (t, 3H; CH$_3$); ^{13}C NMR (100 MHz, [D$_6$]DMSO): $\delta = 159.1$ (C=O, urea), 61.4 (3C; CH$_2$OH), 60.5 (C-NH), 40.1 (C-1′), 31.4 (C-10′), 29.8, 29.1, 28.9, 28.8 (C-2′, C-4′, C-5′, C-6′, C-7′, C-8′, C-9′), 26.5 (C-3′), 22.2 (C-11′), 14.0 ppm (C-12′); IR (KBr): $\tilde{v} = 3372$, 3240 (OH, NH), 2917 (CH$_3$), 2850 (CH$_2$), 1654 (C=O, urea), 1565 (NH, urea), 1120 cm^{-1} (C–O); elemental analysis calcd (%) for C$_{17}$H$_{36}$N$_2$O$_4$: C 61.41, H 10.91, N 8.43; found: C 61.75, H 11.06, N 8.28.

N-[Tris(hydroxymethyl)methyl]-N′-(4-octyloxyphenyl)urea (19): Prepared from **3** and 4-(octyloxy)phenyl isocyanate (**6**) in yields of 54 (Method A) and 53% (Method B), and recrystallized from EtOAc; m.p. 150-151°C; ^{1}H NMR (400 MHz, [D$_6$]DMSO): $\delta = 8.71$ (s, 1H; NH-Ar), 7.22 (d, $J_{o,m} = 8.8$ Hz, 2H; 2-H, 6-H, aryl), 6.78 (d, $J_{o,m} = 8.8$ Hz, 2H; 3-H, 5-H, aryl), 5.91 (s, 1H; NH-C), 4.92 (t, $J_{OH-H} = 5.6$ Hz, 3H; OH), 3.86 (t, 2H; C*H*$_2$-O), 3.52 (d, $J_{OH-H} = 5.6$ Hz, 6H; C*H*$_2$-OH), 1.66 (q, 2H; C*H*$_2$-CH$_2$-O), 1.37 (q, 2H; C*H*$_2$-(CH$_2$)$_2$-O-), 1.27 (m, 8H; CH$_2$), 0.86 ppm (t, 3H; CH$_3$); ^{13}C NMR (100 MHz, [D$_6$]DMSO): $\delta = 156.2$ (C=O, urea), 153.4 (C-4, Ar), 133.4 (C-1, Ar), 119.5 (C-2, C-6, Ar), 114.5 (C-3, C-5, Ar), 67.6 (C-1′), 61.1 (3C; CH$_2$-OH), 60.7 (C-NH), 31.3 (C-3′), 28.8, 28.7 (C-4′, C-5′, C-7′), 25.6 (C-6′), 22.1 (C-2′), 14.0 ppm (C-8′); IR (KBr): $\tilde{v} = 3368$, 3226 (OH, NH), 2937 (CH$_3$), 2867 (CH$_2$), 1675 (C=O, urea), 1606 (Ar), 1560 (NH, urea), 1511 (Ar), 1232, (Ar–O), 1125, 1021 cm^{-1} (C–O); elemental analysis calcd (%) for C$_{19}$H$_{32}$N$_2$O$_5$: C 61.93, H 8.75, N 7.60; found: C 62.28, H 8.77, N 7.84.

General preparation of per-O-acetylated ureas derived from D-glucamine: A stoichiometric amount of amine (3.0 mmol for monoamine derivatives and 1.5 mmol for diamines) was added to a solution of isocyanate **10** (1.25 g, 3.0 mmol) in CH$_2$Cl$_2$ (15 mL). The reaction mixture was vigorously stirred at room temperature for 15 min and then evaporated to dryness.

N-(2,3,4,5,6-Penta-O-acetyl-1-deoxy-D-glucitol-1-yl)-N′-octylurea (20): This substance was synthesized from **10** and octylamine in a yield of 85% as a homogeneous oil that was further purified by preparative chromatography (EtOAc/hexane, 3:1); $[\alpha]_D = +10.5$, $[\alpha]_{578} = +12.6$, $[\alpha]_{546} = +13.8$, $[\alpha]_{436} = +25.0$, $[\alpha]_{365} = +40.5$ ($c = 1.0$ in CHCl$_3$); ^{1}H NMR (400 MHz, CDCl$_3$): $\delta = 5.48$ (dd, $J_{3,4} = 4.8$, $J_{4,5} = 6.4$ Hz, 1H; 4-H), 5.35 (t, $J_{2,3} = J_{3,4} = 4.8$ Hz, 1H; 3-H), 5.04 (m, 2H; 2-H, 5-H), 4.65 (br s, 2H; N*H*-CH$_2$, N*H*-H-1,1′), 4.27 (dd, $J_{5,6} = 3.6$, $J_{6,6'} = 12.4$ Hz, 1H; 6-H), 4.13 (dd, $J_{5,6'} = 5.6$, $J_{6,6'} = 12.4$ Hz, 1H; 6′-H), 3.50 (dd, $J_{1,1'} = 14.8$, $J_{1,2} = 5.4$ Hz, 1H; 1-H), 3.23 (dd, $J_{1,1'} = 14.8$, $J_{1',2} = 5.2$ Hz, 1H; 1′-H), 3.15 (t, 2H; C*H*$_2$-NH), 2.13, 2.11, 2.10, 2.08, 2.05 (s, 15H; OAc), 1.49 (q, 2H; C*H*$_2$-CH$_2$-NH), 1.29 (m, 10H; CH$_2$), 0.88 ppm (t, 3H; CH$_3$); ^{13}C NMR (100 MHz, CDCl$_3$): $\delta = 170.3$, 170.0, 169.6, 169.5 (5C; acetates), 157.6 (C=O, urea), 70.7 (C-2), 68.9 (C-4), 68.5 (C-3), 68.4 (C-5), 61.1 (C-6), 40.4 (C-1′), 40.1 (C-1), 31.5 (C-6′), 29.7 (C-2′), 28.9 (C-4′, C-5′), 26.5 (C-3′), 22.3 (C-7′), 20.5, 20.4, 20.2 (5C; acetates), 13.7 ppm (C-8′); IR (Nujol): $\tilde{v} = 3374$ (NH), 2928 (CH$_3$), 2856 (CH$_2$), 1748 (C=O, acetate), 1641 (C=O, urea), 1569 (NH, urea), 1219 (C–O–C, ester), 1049 cm^{-1} (C–O); HRMS (CI): m/z calcd for C$_{25}$H$_{43}$N$_2$O$_{11}$: 547.2867; found: 547.2857.

N-(2,3,4,5,6-Penta-O-acetyl-1-deoxy-D-glucitol-1-yl)-N′-dodecylurea (21): Prepared from **10** and dodecylamine in a yield of 80% as a homogeneous oil, which was further purified by preparative chromatography (EtOAc/

hexane, 3:1); $[\alpha]_D = +10.3$, $[\alpha]_{578} = +10.3$, $[\alpha]_{546} = +12.3$, $[\alpha]_{436} = +21.3$, $[\alpha]_{365} = +33.2$ ($c = 1.0$ in CHCl$_3$); ^{1}H NMR (400 MHz, CDCl$_3$): $\delta = 5.49$ (dd, $J_{3,4} = 4.8$, $J_{4,5} = 6.4$ Hz, 1H; 4-H), 5.36 (t, $J_{2,3} = J_{3,4} = 4.8$ Hz, 1H; 3-H), 5.05 (m, 2H; 2-H, 5-H), 4.72 (brs, 2H; NH-CH$_2$, NH-H-1,1′), 4.28 (dd, $J_{5,6} = 3.6$, $J_{6,6'} = 12.4$ Hz, 1H; 6-H), 4.13 (dd, $J_{5,6'} = 5.6$, $J_{6,6'} = 12.4$ Hz, 1H; 6′-H), 3.50 (dd, $J_{1,1'} = 14.8$, $J_{1,2} = 4.6$ Hz, 1H; 1-H), 3.23 (dd, $J_{1,1'} = 14.8$, $J_{1',2} = 5.4$ Hz, 1H; 1′-H), 3.15 (t, 2H; CH_2-NH), 2.13, 2.11, 2.10, 2.09, 2.05 (s, 15H; OAc), 1.48 (q, 2H; CH_2-CH$_2$-NH), 1.26 (m, 18H; CH$_2$), 0.88 ppm (t, 3H; CH$_3$); ^{13}C NMR (100 MHz, CDCl$_3$): $\delta = 170.7$, 170.6, 170.3, 169.9 (5 C; acetates), 157.9 (C=O, urea), 71.1 (C-2), 69.3 (C-4), 68.9 (C-3), 68.8 (C-5), 61.5 (C-6), 40.8 (C-1′), 40.4 (C-1), 31.9 (C-10′), 29.7, 29.6, 29.4 (C-2′, C-4′, C-5′, C-6′, C-7′, C-8′, C-9′), 26.9 (C-3′), 22.7 (C-11′), 20.9, 20.8, 20.7, 20.6 (5 C; acetates), 14.1 ppm (C-12′); IR (Nujol): $\tilde{\nu} = 3376$ (NH), 2926 (CH$_3$), 2854 (CH$_2$), 1752 (C=O, acetate), 1639 (C=O, urea), 1571 (NH, urea), 1221 (C−O−C, ester), 1050 cm^{-1} (C−O) cm^{-1}; HRMS (CI): m/z calcd for C$_{29}$H$_{51}$N$_2$O$_{11}$: 603.3493; found: 603.3513.

N-(2,3,4,5,6-Penta-O-acetyl-1-deoxy-D-glucitol-1-yl)-N′-(4-octyloxyphenyl)urea (22): Prepared from **10** and 4-octyloxyaniline in a yield of 95% as a solid that was purified by preparative chromatography (EtOAc/hexane, 3:1); m.p. 113–114°C; $[\alpha]_D = +9.1$, $[\alpha]_{578} = +10.5$, $[\alpha]_{546} = +12.5$, $[\alpha]_{436} = +20.4$ ($c = 1.0$ in CHCl$_3$); ^{1}H NMR (400 MHz, CDCl$_3$): $\delta = 7.20$ (d, $J_{o,m} = 8.8$ Hz, 2H; 2-H, 6-H, Ar), 6.83 (d, $J_{o,m} = 8.8$ Hz, 2H; 3-H, 5-H, Ar), 6.74 (s, 1H; NH-Ar), 5.51 (dd, $J_{3,4} = 4.8$, $J_{4,5} = 6.4$ Hz, 1H; 4-H), 5.37 (t, $J_{2,3} = J_{3,4} = 4.8$ Hz, 1H; 3-H), 5.11 (m, 2H; 2-H, 5-H), 5.05 (t, $J_{NH-H1} = J_{NH-H1'} = 6.0$ Hz, 1H; NH-H1,1′), 4.27 (dd, $J_{5,6} = 3.6$, $J_{6,6'} = 12.4$ Hz, 1H; 6-H), 4.10 (dd, $J_{5,6'} = 5.6$, $J_{6,6'} = 12.4$ Hz, 1H; 6′-H), 3.91 (t, 2H; CH$_2$-O-) 3.50 (ddd, $J_{NH-H1} = 6.0$, $J_{1,1'} = 14.8$, $J_{1,2} = 4.6$ Hz, 1H; 1-H), 3.23 (ddd, $J_{NH-H1'} = 6.0$, $J_{1,1'} = 14.8$, $J_{1',2} = 5.4$ Hz, 1H; 1′-H), 2.12, 2.07, 2.06, 2.02 (s, 15H; OAc), 1.76 (q, 2H; -CH$_2$-CH$_2$-O-), 1.44 (q, 2H; CH_2-(CH$_2$)$_2$-O-), 1.31 (m, 8H; CH$_2$), 0.89 ppm (t, 3H; CH$_3$); ^{13}C NMR (100 MHz, CDCl$_3$): $\delta = 170.7$, 170.4, 170.2, 169.9, 169.8 (5 C; acetates), 156.5 (C=O, urea), 156.2 (C-4, Ar), 130.6 (C-1, Ar), 124.5 (C-2, C-6, Ar), 115.1 (C-3, C-5, Ar), 70.9 (C-2), 69.0 (C-4), 68.8 (C-3), 68.7 (C-5), 68.3 (C-1′), 61.4 (C-6), 40.1 (C-1), 31.8 (C-6′), 29.3, 29.2 (C-5′, C-4′, C-2′), 26.0 (C-3′), 22.6 (C-7′), 20.8, 20.7, 20.5 (5 C; acetates), 14.0 ppm (C-8′); IR (KBr): $\tilde{\nu} = 3414$, 3375 (NH), 2926 (CH$_3$), 2860 (CH$_2$), 1745, 1742, (C=O, acetate), 1681 (C=O, urea), 1543 (NH, urea), 1505 (Ar), 1222 (C−O−C, ester), 1027 cm^{-1} (C−O); elemental analysis calcd (%) for C$_{31}$H$_{46}$N$_2$O$_{12}$: C 58.29, H 7.26, N 4.39; found: C 58.10, H 7.15, N 4.22.

General preparation of per-O-acetylated ureas derived from N-methyl-D-glucamine: Acetic anhydride (35 mL) was slowly added to a solution of the corresponding unprotected urea (4.0 mmol) in pyridine (15 mL). The reaction mixture was stirred at 0°C for 24 h and then it was poured into ice/water (200 mL). The solution was subsequently extracted with CH$_2$Cl$_2$ (3×100 mL) and washed successively with 2 N HCl (3×100 mL), a saturated solution of NaHCO$_3$ (2x100 mL), and distilled water (2×100 mL), dried (MgSO$_4$), and evaporated to dryness.

N-(2,3,4,5,6-Penta-O-acetyl-1-deoxy-D-glucitol-1-yl)-N-methyl-N′-octylurea (23): Prepared, according to the above procedure from **14** in a yield of 69% as a homogeneous oil that was further purified by preparative chromatography (EtOAc/hexane, 3:1); $[\alpha]_D = +5.3$, $[\alpha]_{578} = +5.8$, $[\alpha]_{546} = +6.5$, $[\alpha]_{436} = +11.3$ ($c = 1.0$ in CHCl$_3$); ^{1}H NMR (400 MHz, CDCl$_3$): $\delta = 5.45$ (dd, $J_{3,4} = 4.8$, $J_{4,5} = 6.4$ Hz, 1H; 4-H), 5.32 (dd, $J_{2,3} = 6.4$, $J_{3,4} = 4.8$ Hz, 1H; 3-H), 5.20 (ddd, $J_{1,2} = 7.6$, $J_{1',2} = 4.4$, $J_{2,3} = 6.4$ Hz, 1H; 2-H), 5.03 (ddd, $J_{4,5} = 6,4$, $J_{5,6} = 3.2$, $J_{5,6'} = 5.8$ Hz, 1H; 5-H), 4.70 (brs, 1H; NH), 4.30 (dd, $J_{5,6} = 3.2$, $J_{6,6'} = 12.4$ Hz, 1H; 6-H), 4.12 (dd, $J_{5,6'} = 5.8$, $J_{6,6'} = 12.4$ Hz, 1H; 6′-H), 3.61 (dd, $J_{1,1'} = 14.6$, $J_{1,2} = 7.6$ Hz, 1H; 1-H), 3.36 (dd, $J_{1,1'} = 14.6$, $J_{1',2} = 4.4$ Hz, 1H; 1′-H), 3.15 (m, 2H; CH_2-NH), 2.87 (s, 3H; CH$_3$-N), 2.14, 2.09, 2.08, 2.07, 2.05 (s, 15H; OAc), 1.48 (q, 2H; CH_2-CH$_2$-NH), 1.27 (m, 10H; CH$_2$), 0.88 ppm (t, 3H; CH$_3$); ^{13}C NMR (100 MHz, CDCl$_3$): $\delta = 170.5$, 170.3, 169.9, 169.8 (5 C; acetates), 158.0 (C=O, urea), 69.9 (C-2), 69.2 (C-4), 68.9 (C-3), 68.8 (C-5), 61.4 (C-6), 48.7 (C-1), 41.0 (C-1′), 35.3 (CH$_3$-N), 31.8 (C-6′), 30.2 (C-2′), 29.3, 29.2 (C-4′, C-5′), 26.9 (C-3′), 22.6 (C-7′), 20.8, 20.7, 20.6, 20.5 (5 C; acetates), 14.0 ppm (C-8′); IR (Nujol): $\tilde{\nu} = 3370$ (NH), 2927 (CH$_3$), 2855 (CH$_2$), 1748 (C=O, acetate), 1642 (C=O, urea), 1536 (NH, urea), 1220 (C−O−C, ester), 1049 cm^{-1} (C−O); HRMS (CI): m/z calcd for C$_{26}$H$_{45}$N$_2$O$_{11}$: 561.3023; found: 561.3028.

N-(2,3,4,5,6-Penta-O-acetyl-1-deoxy-D-glucitol-1-yl)-N-methyl-N′-dodecylurea (24): Prepared from **15** in a yield of 70%; the resulting oil was purified by preparative chromatography (EtOAc/hexane, 3:1); $[\alpha]_D = +5.0$, $[\alpha]_{578} = +5.8$, $[\alpha]_{546} = +6.6$, $[\alpha]_{436} = +13.0$ ($c = 1.0$ in CHCl$_3$); ^{1}H NMR (400 MHz, CDCl$_3$): $\delta = 5.45$ (dd, $J_{3,4} = 4.8$, $J_{4,5} = 6.4$ Hz, 1H; 4-H), 5.32 (dd, $J_{2,3} = 6.4$, $J_{3,4} = 4.8$ Hz, 1H; 3-H), 5.20 (ddd, $J_{1,2} = 7.6$, $J_{1',2} = 4.4$, $J_{2,3} = 6.4$ Hz, 1H; 2-H), 5.03 (ddd, $J_{4,5} = 6,4$, $J_{5,6} = 3.2$, $J_{5,6'} = 5.8$ Hz, 1H; 5-H), 4.69 (brs, 1H; NH), 4.30 (dd, $J_{5,6} = 3.2$, $J_{6,6'} = 12.4$ Hz, 1H; 6-H), 4.12 (dd, $J_{5,6'} = 5.8$, $J_{6,6'} = 12.4$ Hz, 1H; 6′-H), 3.61 (dd, $J_{1,1'} = 14.6$, $J_{1,2} = 7.6$ Hz, 1H; 1-H), 3.36 (dd, $J_{1,1'} = 14.6$, $J_{1',2} = 4.4$ Hz, 1H; 1′-H), 3.19 (dt, 2H; CH_2-NH), 2.86 (s, 3H; CH$_3$-N), 2.13, 2.09, 2.08, 2.07, 2.05 (s, 15H; OAc), 1.49 (q, 2H; CH_2-CH$_2$-NH), 1.28 (m, 10H; CH$_2$), 0.88 ppm (t, 3H; CH$_3$); ^{13}C NMR (100 MHz, CDCl$_3$): $\delta = 170.4$, 170.2, 169.8, 169.7 (5 C; acetates), 158.0 (C=O, urea), 69.8 (C-2), 69.2 (C-4), 68.9 (C-3), 68.7 (C-5), 61.3 (C-6), 48.6 (C-1), 41.0 (C-1′), 35.2 (CH$_3$-N), 31.8 (C-10′), 30.1, 29.5, 29.3, 29.2 (C-2′, C-4′, C-5′, C-6′, C-7′, C-8′, C-9′), 26.8 (C-3′), 22.6 (C-11′), 20.7, 20.6, 20.5, 20.4 (5 C; acetates), 14.1 ppm (C-12′); IR (Nujol): $\tilde{\nu} = 3375$ (NH), 2927 (CH$_3$), 2854 (CH$_2$), 1748 (C=O, acetate), 1642 (C=O, urea), 1537 (NH, urea), 1220 (C−O−C, ester), 1050 cm^{-1} (C−O); HRMS (CI): m/z calcd for C$_{30}$H$_{53}$N$_2$O$_{11}$: 617.3649; found: 617.3611.

N-(2,3,4,5,6-Penta-O-acetyl-1-deoxy-D-glucitol-1-yl)-N-methyl-N′-(4-octyloxyphenyl)urea (25): Prepared from **16** in a yield of 60%; the resulting solid was purified by preparative chromatography (EtOAc/hexane, 3:1); m.p. 109–110°C; $[\alpha]_D = +5.8$, $[\alpha]_{578} = +7.2$, $[\alpha]_{546} = +8.2$, $[\alpha]_{436} = +13.8$ ($c = 1.0$ in CHCl$_3$); ^{1}H NMR (400 MHz, CDCl$_3$): $\delta = 7.30$ (d, $J_{o,m} = 9.2$ Hz, 2H; 2-H, 6-H, Ar), 6.82 (d, $J_{o,m} = 9.2$ Hz, 2H; 3-H, 5-H, Ar), 6.73 (s, 1H; NH-Ar), 5.48 (dd, $J_{3,4} = 4.8$, $J_{4,5} = 6.4$ Hz, 1H; 4-H), 5.37 (dd, $J_{2,3} = 6.4$, $J_{3,4} = 4.8$ Hz, 1H; 3-H), 5.25 (ddd, $J_{1,2} = 7.6$, $J_{1',2} = 4.4$, $J_{2,3} = 6.4$ Hz, 1H; 2-H), 5.04 (ddd, $J_{4,5} = 6,4$, $J_{5,6} = 3.2$, $J_{5,6'} = 5.8$ Hz, 1H; 5-H), 4.31 (dd, $J_{5,6} = 3.2$, $J_{6,6'} = 12.4$ Hz, 1H; 6-H), 4.12 (dd, $J_{5,6'} = 5.8$, $J_{6,6'} = 12.4$ Hz, 1H; 6′-H), 3.91 (t, 2H; CH_2-O-), 3.70 (dd, $J_{1,1'} = 14.6$, $J_{1,2} = 7.6$ Hz, 1H; 1-H), 3.43 (dd, $J_{1,1'} = 14.6$, $J_{1',2} = 4.4$ Hz, 1H; 1′-H), 3.00 (s, 3H; CH$_3$-N), 2.13, 2.11, 2.10, 2.05, 2.03 (s, 15H; OAc), 1.75 (q, 2H; CH_2-CH$_2$-O-), 1.44 (q, 2H; CH_2-(CH$_2$)$_2$-O-), 1.32 (m, 8H; CH$_2$), 0.89 ppm (t, 3H; CH$_3$); ^{13}C NMR (100 MHz, CDCl$_3$): $\delta = 170.6$, 170.5, 170.1, 169.9, 169.8 (5 C; acetates), 155.3 (C=O, urea and C-4, Ar), 132.0 (C-1, Ar), 122.0 (C-2, C-6, Ar), 114.7 (C-3, C-5, Ar), 70.1 (C-2), 69.3 (C-4), 68.9 (C-3), 68.8 (C-5), 68.3 (C-1′), 61.4 (C-6), 49.0 (C-1), 35.9 (CH$_3$-N), 31.8 (C-6′), 29.3, 29.2 (C-5′, C-4′, C-2′), 26.0 (C-3′), 22.6 (C-7′), 20.8, 20.7, 20.5 (5 C; acetates), 14.1 ppm (C-8′); IR (KBr): $\tilde{\nu} = 3408$ (NH), 2924 (CH$_3$), 2860 (CH$_2$), 1748, 1729, (C=O, acetate), 1657 (C=O, urea), 1541 (NH, urea), 1512 (Ar), 1243 (C−O−C, ester), 1049 cm^{-1} (C−O); elemental analysis calcd (%) for C$_{32}$H$_{48}$N$_2$O$_{12}$: C 58.88, H 7.41, N 4.29; found: C 58.56, H 7.51, N 4.37.

N-[Tris(acetoxymethyl)methyl]-N′-octylurea (26): By following the above protocol for the acetylation of ureas derived from N-methyl-D-glucamine, the title compound was obtained from **17** in a yield of 76% yield as a solid that was further purified by preparative chromatography (EtOAc/hexane, 1:1); m.p. 121–122°C; ^{1}H NMR (400 MHz, CDCl$_3$): $\delta = 4.62$ (brs, 2H; NH-C, NH-CH$_2$), 4.43 (s, 6H; CH_2-OAc), 2.93 (t, 2H; CH_2-NH), 2.08 (s, 9H; OAc), 1.46 (q, 2H; CH_2-CH$_2$-NH), 1.28 (m, 10H; CH$_2$), 0.88 ppm (t, 3H; CH$_3$); ^{13}C NMR (100 MHz, CDCl$_3$): $\delta = 170.3$ (3 C; acetates), 156.9 (C=O, urea), 63.5 (3 C; CH$_2$OAc), 57.4 (C-NH), 40.6 (C-1′), 31.8 (C-6′), 30.0 (C-2′), 29.2 (C-4′, C-5′), 26.8 (C-3′), 22.6 (C-7′), 20.8 (3 C; acetates), 14.0 ppm (C-8′); IR(KBr): $\tilde{\nu} = 3360$, 3309 (NH), 2924 (CH$_3$), 2854 (CH$_2$), 1754, 1733 (C=O, acetates), 1627 (C=O, urea), 1571 (NH, urea), 1233 (C−O−C), 1043 cm^{-1} (C−O); elemental analysis calcd (%) for C$_{19}$H$_{34}$N$_2$O$_7$: C 56.70, H 8.51, N 6.96; found: C 56.75, H 8.48, N 6.95.

N-[Tris(acetoxymethyl)methyl]-N′-dodecylurea (27): Prepared by acetylation of **18** in a yield of 69% as a solid that was purified by preparative chromatography (EtOAc/hexane, 1:1); m.p. 127–128°C; ^{1}H NMR (400 MHz, CDCl$_3$): $\delta = 4.81$ (brs, 1H; NH-CH$_2$), 4.44 (s, 6H; CH_2-OAc), 4.34 (brs, 1H; NH-C), 3.09 (t, 2H; CH_2-NH), 2.09 (s, 9H; OAc), 1.47 (q, 2H; CH_2-CH$_2$-NH), 1.28 (m, 18H; CH$_2$), 0.88 ppm (t, 3H; CH$_3$); ^{13}C NMR (100 MHz, CDCl$_3$): $\delta = 170.6$ (3 C; acetates), 157.0 (C=O, urea), 63.3 (3 C; CH$_2$OAc), 57.1 (C-NH), 40.4 (C-1′), 31.8 (C-10′), 30.0, 29.5, 29.3 (C-2′, C-4′, C-5′, C-6′, C-7′, C-8′, C-9′), 26.8 (C-3′), 22.6 (C-11′), 20.8 (3 C; acetates), 14.0 ppm (C-12′); IR(KBr): $\tilde{\nu} = 3357$ (NH), 2921 (CH$_3$), 2852 (CH$_2$), 1754, 1733 (C=O, acetates), 1627 (C=O, urea), 1572 (NH,

urea), 1233 (C–O–C), 1042 cm^{-1} (C–O); elemental analysis calcd (%) for $C_{23}H_{42}N_2O_7$: C 60.24, H 9.23, N 6.11; found: C 60.21, H 9.42, N 6.10.

N-[Tris(acetoxymethyl)methyl]-N'-(4-octyloxyphenyl)urea (28): Prepared by acetylation of **19** in a yield of 77% as a solid that was further purified by preparative chromatography (EtOAc/hexane, 1:1); m.p. 125-126 °C; ^{1}H NMR (400 MHz, CDCl$_3$): $\delta = 7.14$ (d, $J_{o,m} = 8.8$ Hz, 2H; 2-H, 6-H, Ar), 6.94 (br s, 1H; NH-Ar), 6.84 (d, $J_{o,m} = 8.8$ Hz, 2H; 3-H, 5-H, Ar), 5.32 (br s, 1H; NH-C), 4.42 (s, 6H; CH$_2$-OAc), 3.90 (t, 2H; CH$_2$-O), 2.04 (s, 9H; OAc), 1.76 (q, 2H; CH$_2$-CH$_2$-O), 1.42 (q, 2H; CH$_2$-(CH$_2$)$_2$-O-), 1.31 (m, 8H; CH$_2$), 0.89 ppm (t, 3H; CH$_3$); ^{13}C NMR (100 MHz, CDCl$_3$): $\delta = 170.4$ (3C; acetates), 156.4 (C=O, urea), 155.6 (C-4, Ar), 130.3 (C-1, Ar), 124.0 (C-2, C-6, Ar), 115.0 (C-3, C-5, Ar), 68.2 (C-1′), 63.0 (CH$_2$-OAc), 57.0 (C-NH), 31.7 (C-6′), 37.6 (C-5′, C-4′, C-2′), 25.9 (C-3′), 22.5 (C-7′), 20.6 (3C; acetates), 14.0 ppm (C-8′); IR (KBr): $\tilde{\nu} = 3334$, 3274 (NH), 2921 (CH$_3$), 2853 (CH$_2$), 1754, 1737 (C=O, acetates), 1643 (C=O, urea), 1564 (NH, urea), 1513, 1478 (Ar), 1219 (C–O–C), 1049 cm^{-1} (C–O); elemental analysis calcd (%) for $C_{25}H_{38}N_2O_8$: C 60.71, H 7.74, N 5.66; found: C 60.57, H 7.54, N 5.66.

N,N′-Decamethylenebis[N″-(1-deoxy-D-glucitol-1-yl)urea] (29): Prepared from D-glucamine and diisocyanate **7** in a yield of 80% (Method A) and recrystallized from water; m.p. 160–161 °C; $[\alpha]_D = +5.6$, $[\alpha]_{578} = +6.4$, $[\alpha]_{546} = +7.8$, $[\alpha]_{436} = +15.2$, $[\alpha]_{365} = +25.2$ ($c = 1.0$ in pyridine); ^{1}H NMR (400 MHz, [D$_6$]DMSO): $\delta = 6.02$ (br s, 2H; NH-CH$_2$), 5.79 (br s, 2H; NH-H1,1′), 4.82 (br s, 2H; 2-OH), 4.47 (br s, 2H; 5-OH), 4.39 (br s, 2H; 4-OH), 4.36 (br s, 2H; 6-OH), 4.31 (br s, 2H; 3-OH), 3.53 (br s, 6H; 2-H, 3-H, 6-H), 3.46 (br s, 2H; 5-H), 3.40 (br s, 4H; 4-H, 6′-H), 3.19 (br s, 2H; 1-H), 2.93 (br s, 6H; 1′-H, CH$_2$-NH), 1.32 (br s, 4H; CH$_2$-CH$_2$-NH), 1.23 ppm (br s, 12H; CH$_2$); ^{13}C NMR (100 MHz, [D$_6$]DMSO): $\delta = 158.7$ (2C; urea), 72.7 (2C; C-5), 72.1 (2C; C-3), 71.6 (2C; C-4), 69.6 (2C; C-2), 63.5 (2C; C-6), 42.5 (2C; C-1), 40.0 (2C; C-1′, C-10′), 30.1 (2C; C-5′, C-6′), 29.2, 29.0 (4C; C-2′, C-4′ C-7′, C-9′), 26.5 ppm (2C; C-3′, C-8′); IR (KBr): $\tilde{\nu} = 3254$ (NH, OH), 2924, 2849 (CH$_2$), 1617 (C=O, urea), 1582 (NH, urea), 1085 cm^{-1} (C–O); elemental analysis calcd (%) for $C_{24}H_{50}N_4O_{12}$: C 49.13, H 8.59, N 9.55; found: C 48.82, H 8.85, N 9.42.

N,N′-Decamethylenebis[N″-(1-deoxy-D-glucitol-1-yl)-N″-methylurea] (30): Prepared from N-methyl-D-glucamine and diisocyanate **7** in yields of 98 (Method A) and 85% (Method B), and recrystallized from EtOH; m.p. 110–111 °C; $[\alpha]_D = +5.6$, $[\alpha]_{578} = +6.4$, $[\alpha]_{546} = +7.8$, $[\alpha]_{436} = +15.2$, $[\alpha]_{365} = +25.2$ ($c = 1.0$ in pyridine); ^{1}H NMR (400 MHz, [D$_6$]DMSO): $\delta = 6.20$ (t, 2H; NH), 4.97 (br s, 2H; 2-OH), 4.51 (br s, 2H; 5-OH), 4.46 (br s, 4H; 3-OH, 4-OH), 4.38 (br s, 2H; 6-OH), 3.70 (m, 2H; 2-H), 3.55 (m, 2H; 6-H), 3.52 (m, 4H; 3-H, 5-H), 3.45 (m, 2H; 4-H), 3.36 (dd, $J_{5,6'} = 6.0$, $J_{6,6'} = 11.2$ Hz, 2H; 6′-H), 3.30 (dd, $J_{1,1'} = 14.8$, $J_{1,2} = 4.8$ Hz, 2H; 1-H), 3.12 (dd, $J_{1,1'} = 14.8$, $J_{1',2} = 8.0$ Hz, 2H; 1′-H), 2.96 (q, 4H; CH$_2$-NH) 2.80 (s, 6H; CH$_3$-N), 1.37 (q, 4H; CH$_2$-CH$_2$-NH), 1.23 ppm (m, 12H; CH$_2$); ^{13}C NMR (100 MHz, [D$_6$]DMSO): $\delta = 158.9$ (2C; urea), 72.5 (2C; C-5), 72.1 (2C; C-3), 71.5 (2C; C-4), 69.2 (2C; C-2), 63.4 (2C; C-6), 51.7 (2C; C-1), 40.5 (2C; C-1′, C-10′), 35.4 (2C; CH$_3$-N), 30.0 (2C; C-5′, C-6′), 29.2, 29.0 (4C; C-2′, C-4′, C-7′, C-9′), 26.6 ppm (2C; C-3′, C-8′); IR (KBr): $\tilde{\nu} = 3450$ (OH), 3371 (NH), 2924 (CH$_3$), 2852 (CH$_2$), 1617 (C=O, urea), 1584 (NH, urea), 1096 cm^{-1} (C–O); elemental analysis calcd (%) for $C_{26}H_{54}N_4O_{12}$: C 50.80, H 8.85, N 9.11; found: C 50.49, H 8.46, N 9.42.

N,N′-Decamethylenebis{N″-[tris(hydroxymethyl)methyl]urea} (31): Prepared from aminopolyol **3** and diisocyanate **7** in yields of 61 (Method A) and 60% (Method B), and recrystallized from EtOH; m.p. 155–156 °C; ^{1}H NMR (400 MHz, [D$_6$]DMSO): $\delta = 6.45$ (t, 2H; NH), 5.70 (s, 2H; NH-C), 5.08 (t, $J_{OH-H} = 3.2$ Hz, 6H; OH), 3.40 (d, $J_{OH-H} = 3.2$ Hz, 12H; CH$_2$-OH), 2.93 (q, 4H; CH$_2$-NH), 1.33 (q, 4H; CH$_2$-CH$_2$-NH), 1.24 ppm (m, 12H; CH$_2$); ^{13}C NMR (100 MHz, [D$_6$]DMSO): $\delta = 159.1$ (2C; urea), 61.4 (6C; CH$_2$-OH), 60.7 (2C; C-NH), 39.9 (2C; C-1′, C-10′), 29.8 (2C; C-5′, C-6′), 29.1, 28.8 (4C; C-2′, C-4′, C-7′, C-9′), 26.5 ppm (2C; C-3′, C-8′); IR (KBr): $\tilde{\nu} = 3349$ (OH, NH), 2926, 2853 (CH$_2$), 1615 (C=O, urea), 1566 (NH, urea), 1024 cm^{-1} (C–O); elemental analysis calcd (%) for $C_{20}H_{42}N_4O_8$: C 51.49, H 9.07, N 12.01; found: C 51.93, H 9.09, N 11.96.

N,N′-(1,4-Phenylene)bis[N″-(1-deoxy-D-glucitol-1-yl)urea] (32): Prepared from D-glucamine and diisocyanate **8** in a yield of 82% (Method A) and recrystallized from water; m.p. 210–211 °C; ^{1}H NMR (400 MHz, [D$_6$]DMSO): $\delta = 8.42$ (s, 2H; NH-Ar), 7.20 (s, 4H; Ar), 6.03 (t, $J_{NH,H1} =$ $J_{NH,H1'} = 5.2$ Hz, 2H; NH-H1,1′), 4.83 (d, $J_{2-OH} = 2.8$ Hz, 2H; 2-OH), 4.49 (d, $J_{5-OH} = 6.0$ Hz, 2H; 5-OH), 4.10 (d, $J_{4-OH} = 5.6$ Hz, 2H; 4-OH), 4.37 (t, $J_{6-OH} = J_{6'-OH} = 5.6$ Hz, 2H; 6-OH), 4.32 (d, $J_{3-OH} = 5.6$ Hz, 2H; 3-OH), 3.55 (m, 6H; 2-H, 3-H, 6-H), 3.47 (m, 2H; 5-H), 3.32 (m, 4H; 4-H, 6′-H), 3.29 (ddd, $J_{1,1'} = 13.2$, $J_{1,2} = 4.0$, $J_{NH,H1} = 5.2$ Hz, 2H; 1-H), 2.98 ppm (ddd, $J_{1,1'} = 13.2$, $J_{1',2} = 7.2$, $J_{NH,H1'} = 5.2$ Hz, 2H; 1′-H); ^{13}C NMR (100 MHz, [D$_6$]DMSO): $\delta = 155.7$ (2C; urea), 134.4 (4C; C-1, C-4, Ar), 121.8 (8C; Ar), 72.1 (2C; C-5), 71.8 (2C; C-2), 71.5 (2C; C-3), 69.9 (2C; C-4), 63.4 (2C; C-6), 42.2 ppm (2C; C-1); IR (KBr): $\tilde{\nu} = 3519$ (OH), 3354 (NH), 2920 (CH$_2$), 1649, 1625 (C=O, urea), 1577 (NH, urea), 1404 (Ar), 1079 cm^{-1} (C–O); elemental analysis calcd (%) for $C_{20}H_{34}N_4O_{12}$: C 45.97, H 6.56, N 10.72; found: C 46.17, H 6.48, N 11.01.

N,N′-(1,4-Phenylene)bis[N″-(1-deoxy-D-glucitol-1-yl)-N″-methylurea] (33): Prepared from N-methyl-D-glucamine and diisocyanate **8** in a yield of 80% (Method A) and recrystallized from MeOH; m.p. 170–171 °C; $[\alpha]_D = +19.4$, $[\alpha]_{578} = +21.0$, $[\alpha]_{546} = +25.2$, $[\alpha]_{436} = +51.8$ ($c = 1.0$ in pyridine); ^{1}H NMR (400 MHz, [D$_6$]DMSO): $\delta = 8.34$ (s, 2H; NH), 7.23 (s, 4H; Ar), 5.25 (d, $J_{2-OH} = 3.2$ Hz, 2H; 2-OH), 4.80 (m, 4H; 3-OH, 4-OH), 4.52 (d, $J_{5-OH} = 5.2$ Hz, 2H; 5-OH), 4.39 (t, $J_{6-OH} = J_{6'-OH} = 5.6$ Hz, 2H; 6-OH), 3.80 (dddd, $J_{2-OH} = 3.2$, $J_{1,2} = 4.0$, $J_{1',2} = 8.0$, $J_{2,3} = 3.6$ Hz, 2H; 2-H), 3.61 (ddd, $J_{6-OH} = 5.6$, $J_{5,6} = 2.8$, $J_{6,6'} = 11.2$ Hz, 2H; 6-H), 3.57 (m, 4H; 3-H, 5-H), 3.49 (m, 2H; 4-H), 3.42 (ddd, $J_{6'-OH} = 5.6$, $J_{5,6'} = 6.0$, $J_{6,6'} = 11.2$ Hz, 2H; 6′-H), 3.37 (dd, $J_{1,1'} = 14.8$, $J_{1,2} = 4.8$ Hz, 2H; 1-H), 3.13 (dd, $J_{1,1'} = 14.8$, $J_{1',2} = 8.0$ Hz, 2H; 1′-H), 2.92 ppm (s, 6H; CH$_3$-N); ^{13}C NMR (100 MHz, [D$_6$]DMSO): $\delta = 156.3$ (2C; urea), 134.8 (2C; C-1, C-4, Ar), 119.9 (4C; Ar) 72.1 (2C; C-5), 71.9 (2C; C-2), 71.5 (2C; C-3), 69.4 (2C; C-4), 63.3 (2C; C-6), 51.9 (2C; C-1), 36.5 ppm (2C; CH$_3$-N); IR (KBr): $\tilde{\nu} = 3360$ (NH, OH), 2928 (CH$_2$), 1636 (C=O, urea), 1548 (NH, urea), 1515, 1404 (Ar), 1088 cm^{-1} (C–O); elemental analysis calcd (%) for $C_{22}H_{39}N_4O_{12}$: C 47.99, H 6.96, N 10.18; found: C 47.74, H 6.84, N 10.25.

N,N′-(1,4-Phenylene)bis{N″-[tris(hydroxymethyl)methyl]urea} (34): Prepared from aminopolyol **3** and diisocyanate **8** in a yield of 98% (Method A) and recrystallized from MeOH; m.p. 201–202 °C; ^{1}H NMR (400 MHz, [D$_6$]DMSO): $\delta = 8.73$ (s, 2H; NH-Ar), 7.19 (s, 4H; Ar) 5.91 (s, 2H; NH-C), 4.91 (t, $J_{OH-H} = 5.6$ Hz, 6H; OH), 3.40 ppm (d, $J_{OH-H} = 5.6$ Hz, 12H; CH$_2$-OH); ^{13}C NMR (100 MHz, [D$_6$]DMSO): $\delta = 156.1$ (2C; urea), 134.3 (2C; C-1, C-4, Ar), 118.5 (4C; Ar), 61.4 (6C; CH$_2$OH), 60.5 ppm (2C; C-NH); IR (KBr): $\tilde{\nu} = 3324$ (OH, NH), 2942 (CH$_2$), 1620 (C=O, urea), 1560 (NH, urea), 1514, 1403 (Ar), 1135 cm^{-1} (C–O); elemental analysis calcd (%) for $C_{16}H_{26}N_4O_8$: C 47.76, H 6.51, N 13.92; found: C 47.36, H 6.25, N 13.52.

4,4′-Methylene-N,N′-di(1,4-phenylene)bis[N″-(1-deoxy-D-glucitol-1-yl)-urea] (35): Prepared from D-glucamine and diisocyanate **9** in a yield of 74% (Method A) and recrystallized from water; m.p. 212–213 °C; $[\alpha]_D = +51.6$, $[\alpha]_{578} = +54.2$, $[\alpha]_{546} = +62.8$, $[\alpha]_{436} = +107.2$, $[\alpha]_{365} = +169.0$ ($c = 1.0$ in pyridine); ^{1}H NMR (400 MHz, [D$_6$]DMSO): $\delta = 8.54$ (s, 2H; NH-Ar), 7.27 (d, $J_{o,m} = 8.6$ Hz, 4H; 3-H, 5-H, Ar), 7.03 (d, $J_{o,m} = 8.6$ Hz, 4H; 2-H, 6-H, Ar), 6.09 (t, $J_{NH,H1} = J_{NH,H1'} = 5.2$ Hz, 2H; NH-H1,1′), 4.83 (d, $J_{2-OH} = 4.0$ Hz, 2H; 2-OH), 4.49 (d, $J_{5-OH} = 5.6$ Hz, 2H; 5-OH), 4.42 (d, $J_{4-OH} = 5.6$ Hz, 2H; 4-OH), 4.37 (t, $J_{6-OH} \approx J_{6'-OH} = 5.6$ Hz, 2H; 6-OH), 4.32 (d, $J_{3-OH} = 6.4$ Hz, 2H; 3-OH), 3.74 (s, 2H; CH$_2$ bridge) 3.60 (m, 6H; 2-H, 3-H, 6-H), 3.49 (m, 2H; 5-H), 3.42 (m, 4H; 4-H, 6′-H), 3.31 (ddd, $J_{1,1'} = 13.2$, $J_{1,2} = 4.0$, $J_{NH,1} = 5.2$ Hz, 2H; 1-H), 2.98 ppm (ddd, $J_{1,1'} = 13.2$, $J_{1',2} = 7.2$, $J_{NH,1'} = 5.2$ Hz 2H; 1′-H); ^{13}C NMR (100 MHz, [D$_6$]DMSO): $\delta = 155.6$ (2C; urea), 138.5 (2C; C-1, Ar), 134.3 (2C; C-4, Ar), 128.8 (4C; C-2, C-6, Ar), 117.8 (4C; C-3, C-5, Ar) 72.1 (2C; C-5), 71.9 (2C; C-2), 71.5 (2C; C-3), 67.0 (2C; C-4), 63.5 (2C; C-6), 42.2 (2C; C-1), 39.8 ppm (CH$_2$ bridge); IR (KBr): $\tilde{\nu} = 3402$ (OH), 3341 (NH), 2931 (CH$_2$), 1674, 1631 (C=O, urea), 1594 (NH, urea), 1556 (Ar), 1086 cm^{-1} (C–O); elemental analysis calcd (%) for $C_{27}H_{40}N_4O_{12}$: C 52.93, H 6.58, N 9.15; found: C 52.89, H 6.60, N 8.95.

4,4′-Methylene-N,N′-di(1,4-phenylene)bis[N″-(1-deoxy-D-glucitol-1-yl)-N″-methylurea] (36): Prepared from N-methyl-D-glucamine and diisocyanate **9** in a yield of 80% (Method A) and recrystallized from EtOH; m.p. 149–150 °C; $[\alpha]_D = +13.6$, $[\alpha]_{578} = +15.0$, $[\alpha]_{546} = +16.4$, $[\alpha]_{436} = +32.6$ ($c = 1.0$ in pyridine); ^{1}H NMR (400 MHz, [D$_6$]DMSO): $\delta = 8.42$ (s, 2H; NH), 7.28 (d, $J_{o,m} = 8.0$ Hz, 4H; 3-H, 5-H, Ar), 7.04 (d, $J_{o,m} = 8.0$ Hz, 4H; 2-H, 6-H, Ar), 5.22 (d, $J_{2-OH} = 4.0$ Hz, 2H; 2-OH), 4.55 (m, 4H; 3-OH, 4-OH),

4.51 (d, $J_{5\text{-OH}} = 5.2$ Hz, 2H; 5-OH), 4.38 (t, $J_{6\text{-OH}} = 5.6$ Hz, 2H; 6-OH), 3.81 (dddd, $J_{2\text{-OH}} = 4.0$, $J_{1,2} = 4.0$, $J_{1',2} = 8.0$, $J_{2,3} = 3.6$ Hz, 2H; 2-H), 3.77 (s, 2H; CH$_2$ bridge), 3.62 (ddd, $J_{6\text{-OH}} = 5.6$, $J_{5,6} = 2.8$, $J_{6,6'} = 11.2$ Hz, 2H; 6-H), 3.58 (m, 4H; 3-H, 5-H), 3.50 (m, 2H; 4-H), 3.43 (dd, $J_{6',\text{OH}} = 5.6$, $J_{5,6'} = 6.0$, $J_{6,6'} = 11.2$ Hz, 2H; 6'-H), 3.40 (dd, $J_{1,1'} = 14.8$, $J_{1,2} = 4.8$ Hz, 2H; 1-H), 3.30 (dd, $J_{1,1'} = 14.8$, $J_{1',2} = 8.0$ Hz, 2H; 1'-H), 2.92 ppm (s, 6H; CH$_3$-N); ^{13}C NMR (100 MHz, [D$_6$]DMSO): $\delta = 156.2$ (2C; urea), 138.6 (2C; C-1, Ar), 134.9 (2C; C-4, Ar), 128.6 (4C; C-2, C-6, Ar), 119.9 (4C; C-3, C-5, Ar) 72.1 (2C; C-5), 71.9 (2C; C-2), 71.5 (2C; C-3), 69.4 (2C; C-4), 63.4 (2C; C-6), 51.9 (2C; C-1), 39.8 (CH$_2$ bridge), 35.5 ppm (2C; CH$_3$-N); IR (KBr): $\tilde{v} = 3304$ (NH, OH), 2907 (CH$_2$), 1656 (C=O, urea), 1594 (aryl), 1536 (NH, urea), 1411 (Ar), 1078 cm^{-1} (C−O); HRMS (FAB): m/z calcd for C$_{29}$H$_{44}$N$_4$O$_{12}$Na: 663.2853; found: 663.2882; elemental analysis calcd (%) for C$_{29}$H$_{44}$N$_4$O$_{12}$: C 54.37, H 6.92, N 8.74; found: C 54.30, H 6.49, N 9.05.

4,4′-Methylene-N,N′-di(1,4-phenylene)bis{N″-[tris(hydroxymethyl)-methyl]urea} (37): Prepared from aminopolyol **3** and diisocyanate **9** in a yield of 92% (Method A) and recrystallized from EtOH; m.p. 196–197°C; ^{1}H NMR (400 MHz, [D$_6$]DMSO): $\delta = 8.82$ (s, 2H; NH-Ar), 7.19 (d, $J_{o,m} = 8.0$ Hz, 4H; 3-H, 5-H, Ar), 7.02 (d, $J_{o,m} = 8.0$ Hz, 4H; 2-H, 6-H, Ar), 5.95 (s, 2H; NH-C), 4.89 (t, $J_{\text{OH-H}} = 5.6$ Hz, 6H; OH), 3.75 (s, 2H; CH$_2$ bridge), 3.53 ppm (d, $J_{\text{OH-H}} = 5.6$ Hz, 12H; CH_2-OH); ^{13}C NMR (100 MHz, [D$_6$]DMSO): $\delta = 155.9$ (2C; urea), 138.2 (2C; C-1, Ar), 134.4 (2C; C-4, Ar), 128.8 (4C; C-2, C-6, Ar), 117.9 (4C; C-3, C-5, Ar), 61.0 (6C; CH_2OH), 60.7 (2C; C-NH), 39.8 ppm (CH$_2$ bridge); IR (KBr): $\tilde{v} = 3325$ (OH, NH), 2932 (CH$_2$), 1620 (C=O, urea), 1546 (NH, urea), 1510, 1411 (Ar), 1134 cm^{-1} (C−O); elemental analysis calcd (%) for C$_{23}$H$_{32}$N$_4$O$_8$: C 56.09, H 6.55, N 11.38; found: C 56.44, H 6.19, N 11.22.

N,N′-Decamethylenebis[N″-(2,3,4,5,6-penta-O-acetyl-1-deoxy-D-glucitol-1-yl)urea] (38): By following the general acetylation procedure, the title substance was obtained from isocyanate **10** and 1,10-diaminodecane in a yield of 87%, which was further purified by preparative chromatography (EtOAc/hexane, 5:1); m.p. 71–72°C; $[\alpha]_D = +15.8$, $[\alpha]_{578} = +17.4$, $[\alpha]_{546} = +19.8$, $[\alpha]_{436} = +34.4$ ($c = 1.0$ in CHCl$_3$); ^{1}H NMR (400 MHz, CDCl$_3$): $\delta = 5.49$ (dd, $J_{3,4} = 4.8$, $J_{4,5} = 6.4$ Hz, 2H; 4-H), 5.35 (t, $J_{2,3} = J_{3,4} = 4.8$ Hz, 2H; 3-H), 5.06 (m, 4H; 2-H, 5-H), 4.98 (t, $J_{\text{NH-CH2}} = 6.4$ Hz, 2H; NH-CH$_2$), 4.80 (t, $J_{\text{NH-H1}} = J_{\text{NH-H1'}} = 6.0$ Hz, 2H; NH-H-1,1′), 4.28 (dd, $J_{5,6} = 3.6$, $J_{6,6'} = 12.4$ Hz, 2H; 6-H), 4.13 (dd, $J_{5,6'} = 5.6$, $J_{6,6'} = 12.4$ Hz, 2H; 6′-H), 3.48 (ddd, $J_{\text{NH-H1}} = 6.0$, $J_{1,1'} = 14.8$, $J_{1,2} = 5.4$ Hz, 2H; 1-H), 3.24 (ddd, $J_{\text{NH-H1'}} = 6.0$, $J_{1,1'} = 14.8$, $J_{1',2} = 5.2$ Hz, 2H; 1′-H), 3.14 (br s, 4H; CH_2-NH), 2.13, 2.10, 2.08, 2.05 (s, 30H; OAc), 1.48 (q, 4H; CH_2-CH$_2$-NH), 1.28 ppm (m, 12H; CH$_2$); ^{13}C NMR (100 MHz, CDCl$_3$): $\delta = 170.6$, 170.5, 170.3, 169.9, (10C; acetates), 157.8 (2C; urea), 71.1 (2C; C-2), 69.2 (2C; C-4), 68.8 (2C; C-3), 68.7 (2C; C-5), 61.5 (2C; C-6), 40.5 (2C; C-1′, C-10′), 40.3 (2C; C-1), 29.9, 29.1, 28.9 (6C; C-2′, C-4′, C-5′, C-6′, C-7′, C-9′), 26.6 (C-3′, C-8′), 20.9, 20.7, 20.5 ppm (10C; acetates); IR (KBr): $\tilde{v} = 3350$ (NH), 2931 (CH$_2$), 1752 (C=O, acetate), 1660 (C=O, urea), 1561 (NH, urea), 1222 (C−O−C, ester), 1050 cm^{-1} (C−O); HRMS (FAB): m/z calcd for C$_{44}$H$_{70}$N$_4$O$_{22}$Na: 1029.4379; found: 1029.4398.

N,N′-(1,4-Phenylene)bis[N″-(2,3,4,5,6-penta-O-acetyl-1-deoxy-D-glucitol-1-yl)urea] (39): Prepared from isocyanate **10** and 1,4-phenylenediamine in a yield of 93% as a solid that was further purified by preparative chromatography (EtOAc/Et$_2$O, 5:1); m.p. 106–107°C; $[\alpha]_D = +17.5$, $[\alpha]_{578} = +17.5$, $[\alpha]_{546} = +21.1$ ($c = 1.0$ in CHCl$_3$); ^{1}H NMR (400 MHz, CDCl$_3$): $\delta = 7.30$ (s, 4H; Ar), 7.04 (s, 2H; NH-Ar), 5.64 (br s, 2H; NH-H1,1′), 5.52 (dd, $J_{3,4} = 4.8$, $J_{4,5} = 6.4$ Hz, 2H; 4-H), 5.38 (t, $J_{2,3} = J_{3,4} = 4.8$ Hz, 2H; 3-H), 5.17 (ddd, $J_{1,2} = 4.6$, $J_{1',2} = 5.2$, $J_{2,3} = 4.8$ Hz, 2H; 2-H), 5.07 (ddd, $J_{4,5} = 6.4$, $J_{5,6} = 3.6$, $J_{5,6'} = 5.6$ Hz, 2H; 5-H), 4.29 (dd, $J_{5,6} = 3.6$, $J_{6,6'} = 12.4$ Hz, 2H; 6-H), 4.12 (dd, $J_{5,6'} = 5.6$, $J_{6,6'} = 12.4$ Hz, 2H; 6′-H), 3.47 (ddd, $J_{\text{NH-H1}} = 6.0$, $J_{1,1'} = 14.8$, $J_{1,2} = 4.6$ Hz, 2H; 1-H), 3.36 (ddd, $J_{\text{NH-H1'}} = 6.0$, $J_{1,1'} = 14.8$, $J_{1',2} = 5.2$ Hz, 2H; 1′-H), 2.13, 2.09, 2.05, 2.02 ppm (s, 30H; OAc); ^{13}C NMR (100 MHz, CDCl$_3$): $\delta = 170.7$, 170.5, 170.2, 169.9 (5C; C=O, acetates), 156.5 (2C; urea), 134.4 (2C; C-1, C-4, Ar), 122.1 (4C; Ar), 70.9 (2C; C-2), 69.2 (2C; C-4), 69.0 (2C; C-3), 68.7 (2C; C-5), 61.4 (2C; C-6), 39.33 (2C; C-1), 20.8, 20.7, 20.5 ppm (10C; acetates); IR (KBr): $\tilde{v} = 3380$ (NH), 2970 (CH$_2$), 1750 (C=O, acetate), 1660 (C=O, urea), 1564 (NH, urea), 1515, 1435 (Ar), 1220 (C−O−C, ester), 1030 cm^{-1} (C−O); elemental anal-

ysis calcd (%) for C$_{40}$H$_{54}$N$_4$O$_{22}$: C 50.95, H 5.77, N 5.94; found: C 50.56, H 5.93, N 5.71.

4,4′-Methylene-N,N′-di(1,4-phenylene)bis[N″-(2,3,4,5,6-penta-O-acetyl-1-deoxy-D-glucitol-1-yl)urea] (40): Prepared from isocyanate **10** and 4,4′-methylenedianiline in a yield of 88% as a solid that was purified by preparative chromatography (EtOAc/Et$_2$O, 5:1); m.p. 106–107°C; $[\alpha]_D = +19.0$, $[\alpha]_{578} = +20.2$, $[\alpha]_{546} = +24.0$, $[\alpha]_{436} = +40.4$ ($c = 1.0$ in CHCl$_3$); ^{1}H NMR (400 MHz, CDCl$_3$): $\delta = 7.18$ (d, $J_{o,m} = 8.2$ Hz, 4H; 3-H, 5-H, Ar), 7.03 (d, $J_{o,m} = 8.2$ Hz, 4H; 2-H, 6-H, Ar), 6.91 (s, 2H; NH-Ar), 5.51 (dd, $J_{3,4} = 4.8$, $J_{4,5} = 6.4$ Hz, 2H; 4-H), 5.38 (t, $J_{2,3} = J_{3,4} = 4.8$ Hz, 2H; 3-H), 5.28 (t, $J_{\text{NH-H1}} = J_{\text{NH-H1'}} = 6.0$ Hz, 2H; NH-H-1,1′), 5.13 (ddd, $J_{1,2} = 4.6$, $J_{1',2} = 5.2$, $J_{2,3} = 4.8$ Hz, 2H; 2-H), 5.05 (ddd, $J_{4,5} = 6.4$, $J_{5,6} = 3.6$, $J_{5,6'} = 5.6$ Hz, 2H; 5-H), 4.28 (dd, $J_{5,6} = 3.6$, $J_{6,6'} = 12.4$ Hz, 2H; 6-H), 4.12 (dd, $J_{5,6'} = 5.6$, $J_{6,6'} = 12.4$ Hz, 2H; 6′-H), 3.82 (s, 2H; CH$_2$ bridge), 3.55 (ddd, $J_{\text{NH-H1}} = 6.0$, $J_{1,1'} = 14.8$, $J_{1,2} = 4.6$ Hz, 2H; 1-H), 3.35 (ddd, $J_{\text{NH-H1'}} = 6.0$, $J_{1,1'} = 14.8$, $J_{1',2} = 5.2$ Hz, 2H; 1′-H), 2.12, 2.08, 2.07, 2.05, 2.01 ppm (s, 30H; OAc); ^{13}C NMR (100 MHz, CDCl$_3$): $\delta = 170.8$, 170.2, 169.9 (10C; acetates), 156.0 (2C; C=O, urea), 136.7 (2C; C-1, Ar), 136.5 (2C; C-4, Ar), 129.3 (4C; C-2, C-6, Ar), 120.7 (4C; C-3, C-5, Ar), 70.9 (2C; C-2), 69.2 (2C; C-4), 69.0 (2C; C-3), 68.8 (2C; C-5), 61.5 (2C; C-6), 40.0 (3C; C-1, CH$_2$ bridge), 20.8, 20.7, 20.6, 20.5 ppm (10C; acetates); IR (KBr): $\tilde{v} = 3386$ (NH), 2960 (CH$_2$), 1750 (C=O, acetate), 1655 (C=O, urea), 1600 (Ar), 1548 (NH, urea), 1512 (Ar), 1219 (C−O−C, ester), 1045 cm^{-1} (C−O); HRMS (FAB): m/z calcd for C$_{47}$H$_{60}$N$_4$O$_{22}$Na: 1055.3597; found: 1055.3620.

N,N′-Decamethylenebis[N″-(2,3,4,5,6-penta-O-acetyl-1-deoxy-D-glucitol-1-yl)-N″-methylurea] (41): Prepared by acetylation of the unprotected derivative **30** in a yield of 41%. Further purification by preparative chromatography (EtOAc/MeOH, 1:1) gave the pure material; m.p. 68–69°C; $[\alpha]_D = +7.6$, $[\alpha]_{578} = +7.6$, $[\alpha]_{546} = +9.0$, $[\alpha]_{436} = +16.6$ ($c = 1.0$ in CHCl$_3$); ^{1}H NMR (400 MHz, CDCl$_3$): $\delta = 5.45$ (dd, $J_{3,4} = 4.8$, $J_{4,5} = 6.4$ Hz, 2H; 4-H), 5.32 (dd, $J_{2,3} = 6.4$, $J_{3,4} = 4.8$ Hz, 2H; 3-H), 5.20 (ddd, $J_{1,2} = 7.6$, $J_{1',2} = 4.4$, $J_{2,3} = 6.4$ Hz, 2H; 2-H), 5.03 (ddd, $J_{4,5} = 6,4$, $J_{5,6} = 3.2$, $J_{5,6'} = 5.8$ Hz, 2H; 5-H), 4.70 (br s, 2H; NH), 4.30 (dd, $J_{5,6} = 3.6$, $J_{6,6'} = 12.4$ Hz, 2H; 6-H), 4.12 (dd, $J_{5,6'} = 5.6$, $J_{6,6'} = 12.4$ Hz, 2H; 6′-H), 3.60 (dd, $J_{1,1'} = 14.8$, $J_{1,2} = 5.4$ Hz, 2H; 1-H), 3.36 (dd, $J_{1,1'} = 14.8$, $J_{1',2} = 5.2$ Hz, 2H; 1′-H), 3.19 (t, 4H; CH_2-NH), 2.86 (s, 6H; CH$_3$-N), 2.13, 2.09, 2.08, 2.05 (s, 30H; OAc), 1.49 (q, 4H; CH_2-CH$_2$-NH), 1.27 ppm (m, 12H; CH$_2$); ^{13}C NMR (100 MHz, CDCl$_3$): $\delta = 170.6$, 170.3, 170.0, 169.9 (10C; acetates), 158.1 (2C; C=O, urea), 70.0 (2C; C-2), 69.3 (2C; C-4), 69.0 (2C; C-3), 68.9 (2C; C-5), 61.5 (2C; C-6), 48.8 (2C; C-1), 41.1 (2C; C-1′, C-10′), 35.6 (2C; CH$_3$-N), 30.3 (2C; C-2′, C-9′), 29.5, 29.4 (4C; C-4′, C-5′, C-6′, C-7′), 26.9 (2C; C-3′, C-8′), 20.9, 20.8, 20.7, 20.6 ppm (10C; acetates); IR (KBr): $\tilde{v} = 3435$ (NH), 2937 (CH$_3$), 2855 (CH$_2$), 1752 (C=O, acetate), 1642 (C=O, urea), 1540 (NH, urea), 1218 (C−O−C, ester), 1049 cm^{-1} (C−O); HRMS (FAB): m/z calcd for C$_{46}$H$_{74}$N$_4$O$_{22}$Na: 1057.4692; found: 1057.4730.

N,N′-(1,4-Phenylene)bis[N″-(2,3,4,5,6-penta-O-acetyl-1-deoxy-D-glucitol-1-yl)-N″-methylurea] (42): Prepared by acetylation of urea **33** in a yield of 60% as a solid that was further purified by preparative chromatography (EtOAc/hexane, 8:1); m.p. 116–117°C; $[\alpha]_D = +9.2$, $[\alpha]_{578} = +7.9$, $[\alpha]_{546} = +10.8$, $[\alpha]_{436} = +18.8$ ($c = 1.0$ in CHCl$_3$); ^{1}H NMR (400 MHz, CDCl$_3$): $\delta = 7.35$ (s, 4H; Ar), 6.83 (br s, 2H; NH-Ar), 5.48 (dd, $J_{3,4} = 4.8$, $J_{4,5} = 6.4$ Hz, 2H; 4-H), 5.36 (t, $J_{2,3} = J_{3,4} = 4.8$ Hz, 2H; 3-H), 5.25 (ddd, $J_{1,2} = 4.6$, $J_{1',2} = 5.2$, $J_{2,3} = 4.8$ Hz, 2H; 2-H), 5.04 (ddd, $J_{4,5} = 6.4$, $J_{5,6} = 3.6$, $J_{5,6'} = 5.6$ Hz, 2H; 5-H), 4.31 (dd, $J_{5,6} = 3.6$, $J_{6,6'} = 12.4$ Hz, 2H; 6-H), 4.13 (dd, $J_{5,6'} = 5.6$, $J_{6,6'} = 12.4$ Hz, 2H; 6′-H), 3.71 (ddd, $J_{\text{NH-H1}} = 6.0$, $J_{1,1'} = 14.8$, $J_{1,2} = 4.6$ Hz, 2H; 1-H), 3.43 (ddd, $J_{\text{NH-H1'}} = 6.0$, $J_{1,1'} = 14.8$, $J_{1',2} = 5.2$ Hz, 2H; 1′-H), 3.01 (s, 6H; CH$_3$-N), 2.14, 2.11, 2.10, 2.06, 2.03 ppm (s, 30H; OAc); ^{13}C NMR (100 MHz, CDCl$_3$): $\delta = 170.5$, 170.3, 169.9, 169.8, 169.7 (10C; acetates), 155.5 (2C; C=O, urea), 134.4 (2C; C-1, C-4, Ar), 120.5 (4C; Ar), 69.9 (2C; C-2), 69.0 (2C; C-4), 68.8 (2C; C-3), 68.6 (2C; C-5), 61.2 (2C; C-6), 48.8 (2C; C-1), 35.6 (2C; CH$_3$-N), 20.6, 20.5, 20.4 ppm (10C; acetates); IR (KBr): $\tilde{v} = 3402$ (NH), 2964 (CH$_2$), 1748 (C=O, acetate), 1656 (C=O, urea), 1545 (NH, urea), 1517, 1408 (Ar), 1219 (C−O−C, ester), 1044 cm^{-1} (C−O); elemental analysis calcd (%) for C$_{42}$H$_{58}$N$_4$O$_{22}$: C 51.96, H 6.02, N 5.77; found: C 51.46, H 6.14, N 5.49.

4,4′-Methylene-*N*,*N*′-di(1,4-phenylene)bis[*N*″-(2,3,4,5,6-penta-*O*-acetyl-1-deoxy-D-glucitol-1-yl)-*N*″-methylurea] (43): Prepared by acetylation of compound **36** in a yield of 51%. The resulting solid was further purified by preparative chromatography (EtOAc/hexane, 8:1); m.p. 111–112 °C; $[\alpha]_D = +7.4$, $[\alpha]_{578} = +7.0$, $[\alpha]_{546} = +8.8$, $[\alpha]_{436} = +17.2$ ($c = 1.0$ in CHCl$_3$); ^{1}H NMR (400 MHz, CDCl$_3$): $\delta = 7.33$ (d, $J_{o,m} = 8.2$ Hz, 4H; 3-H, 5-H, Ar), 7.07 (d, $J_{o,m} = 8.2$ Hz, 4H; 2-H, 6-H, Ar), 6.81 (s, 2H; NH-Ar), 5.47 (dd, $J_{3,4} = 4.8$, $J_{4,5} = 6.4$ Hz, 2H; 4-H), 5.36 (t, $J_{2,3} = J_{3,4} = 4.8$ Hz, 2H; 3-H), 5.25 (ddd, $J_{1,2} = 4.6$, $J_{1′,2} = 5.2$, $J_{2,3} = 4.8$ Hz, 2H; 2-H), 5.03 (ddd, $J_{4,5} = 6.4$, $J_{5,6} = 3.6$, $J_{5,6′} = 5.6$ Hz, 2H; 5-H), 4.30 (dd, $J_{5,6} = 3.6$, $J_{6,6′} = 12.4$ Hz, 2H; 6-H), 4.12 (dd, $J_{5,6′} = 5.6$, $J_{6,6′} = 12.4$ Hz, 2H; 6′-H), 3.87 (s, 2H; CH$_2$ bridge), 3.71 (dd, $J_{1,1′} = 14.8$, $J_{1,2} = 4.6$ Hz, 2H; 1-H), 3.42 (dd, $J_{1,1′} = 14.8$, $J_{1′,2} = 5.2$ Hz, 2H; 1′-H), 3.00 (s, 6H; CH$_3$-N), 2.14, 2.10, 2.05, 2.03 ppm (s, 30H; OAc); ^{13}C NMR (100 MHz, CDCl$_3$): $\delta = 170.6$, 170.1, 170.0, 169.9 (10C; acetates), 155.6 (2C; C=O, urea), 137.1 (2C; C-1, Ar), 136.1 (2C; C-4, Ar), 129.2 (4C; C-2, C-6, Ar), 120.1 (4C; C-3, C-5, Ar), 70.1 (2C; C-2), 69.3 (2C; C-4), 68.9 (2C; C-3), 68.8 (2C; C-5), 61.4 (2C; C-6), 49.0 (2C; C-1), 40.6 (CH$_2$ bridge), 20.9, 20.8, 20.7, 20.6, 20.5 ppm (10C; acetates); IR (KBr): $\tilde{\nu} = 3414$ (NH), 2932 (CH$_3$), 1749 (C=O, acetate), 1665 (C=O, urea), 1595 (NH, urea), 1518 (Ar), 1219 (C−O−C, ester), 1045 cm^{-1} (C−O); HRMS (FAB): m/z calcd for C$_{49}$H$_{64}$N$_4$O$_{22}$Na: 1083.3910; found: 1083.3904.

N,N′-Decamethylenebis{*N*″-[tris(acetoxymethyl)methyl]urea} (44): Prepared by acetylation of the unprotected derivative **31** in a yield of 74% yield as a solid that was recrystallized from ethyl acetate; m.p. 131–132 °C; ^{1}H NMR (400 MHz, [D$_6$]DMSO): $\delta = 5.98$ (br s, 2H; N*H*-CH$_2$), 5.73 (s, 2H; N*H*-C), 4.25 (s, 12H; C*H*$_2$-OAc), 2.93 (q, 4H; C*H*$_2$-NH), 2.01 (s, 18H; OAc), 1.33 (q, 4H; C*H*$_2$-CH$_2$-NH), 1.23 ppm (m, 12H; CH$_2$); ^{13}C NMR (100 MHz, [D$_6$]DMSO): $\delta = 170.2$, (6C; acetates), 157.2 (2C; C=O, urea), 62.9 (6C; *C*H$_2$-OAc), 55.9 (2C; *C*-NH), 39.0 (2C; C-1′, C-10′), 29.9 (2C; C-5′, C-6′), 29.1 (2C; C-4′, C-7′), 28.9 (2C; C-2′, C-9′), 26.5 (2C; C-3′, C-8′), 20.7 ppm (6C; acetates); IR (KBr): $\tilde{\nu} = 3355$ (NH), 2926, 2855 (CH$_2$), 1753 (C=O, acetate), 1628 (C=O, urea), 1572 (NH, urea), 1233 (C−O−C), 1044 cm^{-1} (C−O); HRMS (FAB): m/z calcd for C$_{32}$H$_{54}$N$_4$O$_{14}$Na: 741.3534; found: 741.3572.

N,N′-(1,4-Phenylene)bis{*N*″-[tris(acetoxymethyl)methyl]urea} (45): Prepared by acetylation of urea **34** in a yield of 46% as a solid that was recrystallized from MeOH; m.p. 125–126 °C; ^{1}H NMR (400 MHz, [D$_6$]DMSO): $\delta = 8.38$ (s, 2H; NH-Ar), 7.22 (s, 4H; Ar), 6.24 (s, 2H; NH-C), 4.33 (s, 12H; C*H*$_2$-OAc), 2.05 ppm (s, 18H; OAc); ^{13}C NMR (100 MHz, [D$_6$]DMSO): $\delta = 170.1$ (6C; acetates), 154.5 (2C; C=O, urea), 134.0 (2C; C-1, C-4, Ar), 118.6 (4C; Ar), 61.9 (6C; *C*H$_2$-OAc), 56.2 (2C; *C*-NH), 20.6 ppm (6C; acetates); IR (KBr): $\tilde{\nu} = 3334$ (NH), 1747 (C=O, acetates), 1650 (C=O, urea), 1574 (NH, urea), 1511 (Ar), 1219 (C−O−C), 1048 cm^{-1} (C−O); elemental analysis calcd (%) for C$_{28}$H$_{38}$N$_4$O$_{14}$: C 51.37, H 5.85, N 8.56; found: C 51.06, H 5.81, N 8.59.

4,4′-Methylene-*N*,*N*′-di(1,4-phenylene)bis{*N*″-[tris(acetoxymethyl)-methyl]urea} (46): Prepared by acetylation of the unprotected derivative **37** in a yield of 70% yield as a solid that was recrystallized from EtOH; m.p. 143–144 °C; ^{1}H NMR (400 MHz, [D$_6$]DMSO): $\delta = 8.46$ (s, 2H; NH-Ar), 7.24 (d, $J_{o,m} = 8.4$ Hz, 4H; 3-H, 5-H), 7.05 (d, $J_{o,m} = 8.2$ Hz, 4H; 2-H, 6-H), 6.29 (s, 2H; N*H*-C), 4.32 (s, 12H; C*H*$_2$-OAc), 3.76 (s, 2H; CH$_2$ bridge), 2.04 ppm (s, 18H; OAc); ^{13}C NMR (100 MHz, [D$_6$]DMSO): $\delta = 170.2$ (6C; acetates), 154.5 (2C; C=O, urea), 137.8 (2C; C-1, Ar), 134.9 (2C; C-4, Ar), 128.9 (4C; C-2, C-6, Ar), 118.1 (4C; C-3, C-5, Ar), 62.6 (6C; *C*H$_2$-OAc), 56.2 (2C; *C*-NH), 39.8 (CH$_2$ bridge), 20.7 ppm (6C; acetates); IR (KBr): $\tilde{\nu} = 3333$ (NH), 1741 (C=O, acetates), 1649 (C=O, urea), 1603 (Ar), 1551 (NH, urea), 1512 (Ar), 1231 (C−O−C), 1046 cm^{-1} (C−O); elemental analysis calcd (%) for C$_{35}$H$_{44}$N$_4$O$_{14}$: C 56.45, H 5.95, N 7.52; found: C 56.07, H 5.70, N 7.46.

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