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Versatile and self-assembling urea-linked neosaccharides from sugar aminoalcohols



Dipartimento di Scienze Chimiche, Università di Napoli "Federico II", Complesso Universitario Monte S. Angelo, Via Cintia 4, I-80126 Napoli, Italy

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ABSTRACT

The increasing interest in urea compounds as self-assembling molecules, ion transporters and organocatalysts prompted several efforts towards synthetic urea-linked glycomimetics. In this frame we studied in details a novel two steps dimerization reaction of sugar vicinal aminoalcohol building blocks, opening a synthetic path to a series of urea-linked neosaccharides. Glucosamine neodisaccharide possessing an oxazolidinone–urea–oxazolidinone system could be transformed into both cyclic and higher linear neosaccharides. Furthermore, a series of six urea-linked glucosamine and galactosamine neodisaccharides was tested for self-assembling properties by measuring NMR spectra at different temperatures and concentrations as well as by gelation of several organic solvents.

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1. Introduction

Carbohydrates are involved in a myriad of biological processes that involve the recognition of glycans by specific receptors. The study of such interactions *in vivo* and *in vitro* as well as their exploitation for the development of carbohydrate-based functional materials is a 'hot topic' nowadays.¹ However, a clear drawback of natural occurring oligosaccharides is their metabolic instability in biological systems. For this reason, the study of carbohydrate mimics (glycomimetics)—molecules resembling carbohydrates but with some different properties (e.g., recognized but not hydrolyzed by a glycosidase)—has become a research area of great interest.² Much effort has been spent on the development of practicable ways to the synthesis of glycomimetics, which can serve as functional materials or as biochemical and biomedical tools.³

Among glycomimetics, attention has been mainly focused on the attainment of compounds—termed pseudosaccharides—having the acid-labile glycosidic bonds substituted with non-acetal linkages.⁴ Oligosaccharide mimics with linkages between monosaccharides not involving the anomeric position are termed neosaccharides. Pseudo- and neosaccharides with several kinds of linkages (thioether, amine, amide, olefin, etc.) have been reported. In the last decade urea-linked glycomimetics captured an increasing share of interest⁵ due to the occurrence of these linkages in natural antibiotics, such as glycocinnamoyl-spermidines.⁶ Furthermore, several urea compounds have recently staged a remarkable re-emergence in several fields of chemistry, after being almost ignored during 20th century. This renaissance is mainly associated with the exploitation of urea compounds as powerful, geometrically ordered hydrogen-bond donors and acceptors for the design of self-assembling supramolecular structures, ion transporters and organocatalysts, as well as coordinating molecules for promoting several reactions in metallation chemistry.⁷

Most urea-linked pseudosaccharides have been obtained by the reaction of glycosyl amines with unstable glycosyl isocyanates or their more stable synthetic equivalents, such as Steyermark's glycosyl-1,2-oxazolidinone or glycosyl trichloroacetamides.⁸ Glycosyl amines were also used in a Curtius rearrangement in the presence of sugar carboxylic acids to afford urea-linked pseudosaccharides.⁹ Urea-linked neosaccharides have been also reported, by two different synthetic routes. The first was based on the acid-catalyzed addition of water to diglycosyl-carbodiimides, obtained in turn by a tandem Staudinger/aza-Wittig reaction of a protected azide with a sugar isocyanate in the presence of triphenylphosphine.¹⁰ Alternatively, urea-linked neosaccharides were obtained by coupling sugar isocyanates with aminosugars.¹¹

Very recently, we reported the conversion of glucosamine 2,3aminoalcohol **1** into symmetric *N*,*N*'-urea-linked neodisaccharide





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^{*} Corresponding author. Tel.: +39 (0)81674153; fax: +39 (0)81674393; e-mail address: ebedini@unina.it (E. Bedini).

 $^{^\}dagger$ Present address: Novartis Farma S.p.A., Lg. Umberto Boccioni 1, I-21040 Origgio (VA), Italy.

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2 by slightly modifying¹² the reaction conditions usually employed for the closure of an oxazolidinone cycle (Scheme 1a).¹³ It is worth noting that a few scattered examples can be found in the literature on the formation of *N*,*N'*-urea-linked dimers from sugar building blocks, as byproducts of diverse reactions (Scheme 1b).¹⁴ This is usually attributed to adventitious hydrolysis of intermediate isocyanates or synthetic equivalents thereof by moisture, followed by addition of the resulting amine to another isocyanate molecule. Nonetheless, no study on the dependence of neodisaccharide formation on reaction conditions was conducted.

In this work we studied the dependence of urea-linked dimer versus oxazolidinone monomer species formation on several reaction conditions, starting from **1** or other sugar vicinal aminoalcohols. The obtained urea-linked neodisaccharides were demonstrated to be very versatile scaffolds for the synthesis of higher linear and cyclic neosaccharides and for the attainment of neosaccharide derivatives possessing self-assembling properties.



Fig. 1. Sugar vicinal aminoalcohols on which urea-linked dimerization was tested.



Scheme 1. Examples of urea-linked neosaccharide dimers as reaction byproducts.

2. Results and discussion

2.1. Synthesis of neosaccharides

The urea-linked dimerization reaction was investigated on the sugar vicinal aminoalcohols depicted in Fig. 1. They were obtained through standard literature procedures from commercially available carbohydrates. $^{15-19}$

The standard conditions used in carbohydrate chemistry to protect a vicinal aminoalcohol moiety as an oxazolidinone uses excess 4-nitrophenyl chloroformate (NPCC) in the presence of NaHCO₃ in H₂O–CH₃CN at 0 °C for 3 h, producing a mixture of the desired oxazolidinone and uncyclized carbamate. The latter could be converted into the former by an additional step with Amberlyst IR-120 Na⁺ ion-exchange resin.^{13b} We investigated the dependence on temperature and time of the reaction on glucosamine aminoalcohol **1**. The exclusive formation of oxazolidinone **9** could be obtained at 40 °C (Table 1, entry 1), whereas a lower reaction temperature (entries 5 and 6) afforded only uncyclized carbamate **8** (Scheme 2). By increasing the reaction time from 30 min to 2–3 h,

Table 1Uncyclized carbamate 8 versus oxazolidinone 9 formation from 1

| Entry ^a | Т | Time | 9 / 8 ^b |
|--------------------|-------|--------|----------------------------------|
| 1 | 40 °C | 30 min | 100:0 |
| 2 | 20 °C | 3 h | 19:81 |
| 3 ^c | 0 °C | 3 h | 17:83 |
| 4 | 0 °C | 2 h | 6:94 |
| 5 | 0 °C | 50 min | 0:100 |
| 6 | 0 ° C | 30 min | 0:100 |

 a Reactions conducted with NPCC (5 equiv) and NaHCO_3 (5 equiv) in 3:2 v/v CH_3CN/H_2O.

^b Percent molar ratio determined by ¹H NMR analysis of the crude mixture after extractive work-up.

^c Ref. 13b reaction conditions.

In the presence of a strong base, such as NaH, compound **8** (or analogously **10**) could be rapidly converted into oxazolidinone **9** through isocyanate **15**, in accordance with similar known transformations.^{13c,d,20} In the absence of NPCC in the reaction mixture, only this pathway can operate. Consistently, when the reaction was conducted on pure uncyclized carbamates **8** and **10**, oxazolidinone species **9** (Table 2, entry 7) and **13** (Table 3, entries 7 and 8) were obtained exclusively. On the contrary, when excess NPCC was present in the reaction mixture, isocyanate **16** could also be formed. An intramolecular nucleophilic addition cannot occur in **16**, whereas oxazolidinone **9** could act as external nucleophile to form a dimer, that could easily react further—again through an isocyanate species—to give the final product **2**. Oxazolidinone **9** can



Scheme 2. Reagents and conditions: (a) see Table 1; (b) see Table 2; (c) NPCC, NaHCO₃, 3:2 v/v CH₃CN/H₂O, 0 °C, 30 min; (d) see Table 3.

a mixture of oxazolidinone and uncyclized carbamate products was obtained at both 0 °C and 20 °C (entries 2–4). After a simple extractive work-up of the reaction conducted at 0 °C for 30 min (entry 6), the obtained mixture of 8 and excess NPCC was treated with sodium hydride in DMF. Depending on the conditions used, column chromatography of the crude reaction mixture afforded the expected oxazolidinone 9 and/or two other products (2 and 3), that were fully characterized by ¹H and ¹³C NMR spectroscopy as well as MALDI-MS. In particular, a peak at 715 m/z ([M+Na⁺]) in the MALDI-MS spectrum, together with the downfield shift of the H-2 and H-3 signals (δ 3.99 and 4.94 ppm, respectively) and the presence in the ¹³C NMR spectrum of two signals at δ 150.4 and 150.0 ppm—with the first one approximately of double intensity in comparison with the second—suggested the urea-linked dimeric structure for compound 2. The structure was confirmed by a detailed comparison of NMR data with those arising from molecular mechanics and dynamics calculations.¹²

The effect of the temperature on the formation of urea-linked dimer **2** was first investigated. Once it was found that a temperature of 30 °C was the best choice (Table 2, entries 1–4), the effect of the concentration of **8** was studied (entries 3, 5, 6), revealing that it is highly determinant for the attainment of **2** in high yields. Similar results were obtained by searching the optimal reaction conditions for the synthesis of urea-linked galactosamine dimer **11** from aminoalcohol **4** via NaH induced rearrangement of uncyclized carbamate **10** in DMF in the presence of excess NPCC (Scheme 2 and Table 3).

The high dependence of the dimerization process on the concentration parameter as well as on the presence of excess NPCC in the reaction mixture could be explained by the proposed mechanism for the formation of urea-linked neodisaccharide (Scheme 3). Table 2

Table 3

Screening of reaction conditions for urea-linked glucosamine neosaccharide **2** synthesis

| Entry ^a | Т | [8] | 2 ^b | 3 ^b | 9 ^b |
|--------------------|--------|--------|-----------------------|-----------------------|-----------------------|
| 1 | −30 °C | 220 mM | | 41% | |
| 2 | 0 °C | 220 mM | 51% | 7% | |
| 3 | 30 °C | 220 mM | 62% | 26% | |
| 4 | 50 °C | 220 mM | 21% | | |
| 5 | 30 °C | 72 mM | 97% | | |
| 6 | 30 °C | 24 mM | 17% | | 55% |
| 7 ^c | 0 °C | 220 mM | | | 91% |

^a Reaction conducted on crude **8** with NaH (5 equiv) in the presence of excess NPCC (approx. 4 equiv) unless otherwise stated.

^b Isolated yield.

^c Reaction conducted on pure **8** without NPCC.

| Screening | of reaction | conditions | for | urea-linked | galactosamine | neosaccharide | 11 |
|-----------|-------------|------------|-----|-------------|---------------|---------------|----|
| synthesis | | | | | | | |

| Entry ^a | Т | [10] | 11 ^b | 12 ^b | 13 ^b |
|--------------------|-------|--------|-----------------|-----------------|-----------------|
| 1 | 0 °C | 220 mM | 9% | 42% | 14% |
| 2 | 30 °C | 220 mM | 30% | 43% | |
| 3 | 50 °C | 220 mM | 43% | 27% | |
| 4 | 70 °C | 220 mM | 42% | 27% | |
| 5 | 30 °C | 650 mM | 78% | 13% | |
| 6 | 30 °C | 72 mM | 33% | 46% | |
| 7 ^c | 0 °C | 650 mM | | | 65% |
| 8 ^c | 30 °C | 650 mM | | | 68% |

^a Reaction conducted on crude **10** with NaH (5 equiv) in the presence of excess NPCC (approx. 4 equiv) unless otherwise stated.

^b Isolated yield.

^c Reaction conducted on pure **10** without NPCC.



Scheme 3. Proposed mechanism for the formation of products of Table 2.

give also addition on NPCC, thus affording **3**, that could not convert into dimer 2, as demonstrated by mixing pure 3 and 9 under dimerization conditions. No urea-linked neodisaccharide formation was detected in this case. Furthermore, by treating pure 9 with NaH in DMF, no dimer species were detected again. It is worth noting that alternative mechanisms for the formation of **2**, relying upon the adventitious hydrolysis of intermediate isocyanates 15 and/or 16 by moisture, followed by dimerization through addition of the resulting amine to another isocyanate molecule, cannot be ruled out. However, when oxazolidinone 9 was mixed with pure compound 14-obtained in turn from 8 by reaction with DMAP and excess NPCC in DMF at 5 °C---in the presence of NaH in DMF at 30 °C, neodisaccharide 2 was obtained exclusively (95% isolated yield) and neither residual oxazolidinone **9** nor **3** could be found. This strongly suggested that, even in the presence of adventitious partial hydrolysis of isocyanate species, the proposed mechanism is active in the formation of neodisaccharide 2.

In accordance with the proposed mechanism, concentration is a key parameter for glucosamine and galactosamine neodisaccharides (**2** and **11**, respectively) versus monomer species (**3**, **9** and **12**, **13**, respectively) formation. Indeed, the intramolecular oxazolidinone closure reaction affording the monomer species was favoured in dilute solutions, whereas higher concentrations allowed the prevalent formation of dimer species (see Tables 2 and 3).

Having optimized the dimerization conditions for glucosamine and galactosamine building blocks 1 and 4, the study was then expanded to other sugar aminoalcohols. Allosamine 5 and mannosamine 6 were treated with NaHCO3 and NPCC in CH3CN-water at 0°C for a short time to give crude carbamates 18 and 19, respectively. Surprisingly, their treatment with NaH in DMF in the presence of excess NPCC under the temperature and concentration conditions already optimized for glucosamine and galactosamine species, did not furnished any neodisaccharide product. Only oxazolidinones 20 and **21** were obtained²¹ (Scheme 4), thus suggesting that a *trans* configuration of the vicinal aminoalcohol moiety is essential for dimerization. This is probably due to a stereoelectronic effect, that decreases the C-N partial double bond character in the strained trans-configured oxazolidinone ring, and in turn increases the nucleophilic strength of the nitrogen atom. On the contrary, in the cisconfigured oxazolidinones **20** and **21** the higher C–N partial double bond character, due to a more favourable stereoelectronic feature, decreases the nucleophilic strength of the nitrogen atom, that is not able to attack the isocyanate or NPCC species, thus affording neither urea-linked dimer nor N-aryloxycarbonyl-oxazolidinone. Dimerization was then tested on disaccharide 7 possessing a 2,3-GlcNaminoalcohol moiety. Its trans configuration allowed the dimerization reaction furnishing neotetrasaccharide 23 in 35% unoptimized yield together with a minor amount of disaccharide 24.

Glucosamine and galactosamine dimers 2 and 11 were very versatile scaffolds, that could be suitably manipulated to enlarge the chemical diversity of these urea-linked neosaccharides. Indeed, a broad number of modifications on their structure were possible (Scheme 5). Benzylidene rings were useful for phase-tagging the neosaccharides. They could be hydrolytically removed to give water-soluble neosaccharide **25** (73%).¹² Benzylidene rings could also be cleaved under reductive conditions with Et₃SiH/TFA in the presence of 4 Å molecular sieves to give symmetrical diol 26 (54%). The regioselectivity of benzylidene opening was demonstrated by a downfield shift (δ 5.42 ppm) of H-4 signal in ¹H NMR spectrum of acetylated derivative 27. Diol 26 could be employed as a glycosyl acceptor to further access higher neooligosaccharides. For example, **26** was coupled with donor **28**²² to give stereoselectively α, α -linked neotetrasaccharide 29 in good yield (82%), in spite of the low nucleophilicity of the 4-hydroxy group in several GlcN acceptors,²³ as well as the high rate of glycosyl donor leaving group release in some reported fucosylations.²² It is worth noting that the obtained fucosylated neosaccharide could be a useful building block en route to the synthesis of a urea-linked dimeric Lewis A mimic.

Desymmetrization of **2** was possible by mild hydrolysis $(14:6:1:1 v/v/v/v CHCl_3/1,4-dioxane/H_2O/Et_3N at rt)^{12}$ of only one oxazolidinone ring, preserving the urea linkage. The obtained al-cohol **30** (81%) was employed as a glycosyl acceptor to again access higher neooligosaccharides, such as neotrisaccharide **31**. Alternatively, **30** could be treated with DBU in DMF to give carbamate-linked macrocycle **32**. By conducting the hydrolysis of the oxazolidinone-urea-oxazolidinone system of **2** with an increased amount of Et₃N (6:2:1 v/v/v 1,4-dioxane/H₂O/Et₃N) at higher temperatures (80 °C), both oxazolidinone rings of **2** could be cleaved, but the ureido linkage still remained intact (signal at δ 159.1 ppm in ¹³C NMR spectrum), thus affording symmetrical diol **33** in 76% yield.

Similarly, galactosamine neodisaccharide diol **34** was obtained in 64% yield from **11** (Scheme 6). The chemical diversity of this series of urea-linked neosaccharides was further increased by the derivatization of glucosamine and galactosamine diols **33** and **34** with ether-linked appendages at position 3. Treatment of **33** and **34** with 1-bromoundecane in the presence of NaH and NaI in DMF afforded neodisaccharides **35** and **36**, respectively (56–66%), bearing two long-chain hydrocarbon moieties. Analogously, a methyl or a benzyl group could be installed (compounds **37** and **38**).



Scheme 4. Reagents and conditions: (a) NPCC, NaHCO₃, 3:2 v/v CH₃CN/H₂O, 0 °C, 30 min; (b) NaH, NPCC, DMF, 30 °C, 45 min, 26% for 20 from 5, 50% for 21 from 6, 35% for 23 from 7, 13% for 24 from 7.



Scheme 5. Reagents and conditions: (a) CSA, 4:1 v/v 1,4-dioxane/H₂O, 60 °C, 4 h, 73%;¹² (b) Et₃SiH, TFA, AW-300 4 Å MS, CH₂Cl₂, 0 °C, overnight, 54%; (c) Ac₂O, py, rt, overnight, 97%; (d) **28**, TMSOTf, 1:1 v/v CH₂Cl₂/THF, -30 °C, 90 min, 82% for **29**, 76% for **31**; (e) 14:6:1:1 v/v/v/v CHCl₃/1,4-dioxane/H₂O/Et₃N, rt, 3 days, 81%;¹² (f) DBU, DMF, 50 °C, overnight, 43%;¹² (g) 6:2:1 v/v/v 1,4-dioxane/H₂O/Et₃N, 80 °C, overnight, 76%; (h) 1-bromoundecane, NaH, NaI, DMF, 0 °C, overnight, 66%.



 $\begin{array}{l} \textbf{Scheme 6.} Reagents and conditions: (a) 6:2:1 v/v/v 1.4-dioxane/H_2O/Et_3N, 80 °C, 2 \\ days, 64%; (b) 1-bromoundecane, NaH, NaI, DMF, 0 °C, overnight, 56%; (c) BnBr, NaH, DMF, 0 °C, 7 h, 61%. \\ \end{array}$

2.2. Self-association properties

Compounds **33–38** presented a RNHCONHR urea system that could form aggregates via geometrically ordered intermolecular hydrogen bonding interactions. The self-association behaviour of these ureas was characterized in solution by ¹H NMR spectroscopy in CDCl₃. Spectra were measured at different temperatures and the chemical shifts of the urea NH moieties were plotted against the temperature (Fig. 2). The upfield shifts showed with increasing temperature are a signature of hydrogen bonding.



Fig. 2. ¹H NMR chemical shift of urea N–H protons of **33–38** in $CDCl_3$ ([*C*]=10 mM) plotted against temperature.

More details on the self-association behaviour of 33-38 were obtained by measuring the chemical shifts of the urea NH moieties at different concentrations (Fig. 3a). With the exception of benzyland methyl-appended compounds 37 and 38 exhibiting a concentration-insensitive NH chemical shift, a downfield shift with increasing neodisaccharide concentration was observed. This implies that intermolecular hydrogen bonds were formed between urea functions of neighbouring neodisaccharides and they became stronger as the concentration increased. This effect was particularly marked for galactosamine neodisaccharide 34, that covered a chemical shift range of approx. 0.35 ppm, whereas the range for compounds **33**, **35** and **36** not exceeded 0.1 ppm.²⁴ At lower concentrations the chemical shifts reached a horizontal plateau, indicating that neodisaccharides were unassociated at such concentrations. No plateau was observed at the higher concentrations. This suggests that self-association did not reach equilibrium even in saturated solutions, that is a typical behaviour of ureas aggregated with a low association constant.²⁵ This could be due to the aliphatic nature of our ureas, and, in the case of neodisaccharides 33 and 34, also to the presence of two hydroxyls, that could form intramolecular five- and seven-membered hydrogen



Fig. 3. (a)¹ H NMR chemical shift of urea N–H protons in CDCl₃ at 298 K plotted against concentration of **33–38**; (b) ¹H NMR chemical shift of hydroxyl protons in CDCl₃ at 298 K plotted against concentration of **33** and **34**.

bonds with an adjacent urea NH, especially at lower concentrations.²⁶ Consistently, the plot of chemical shift of the hydroxyl proton against the concentration of **33** and **34** showed again a horizontal plateau at lower concentrations, whereas a downfield shift was observed with increasing neodisaccharide concentration (Fig. 3b).

The self-association behaviour of urea-linked neodisaccharides was tested for organogelation ability. Indeed, the presence of selfcomplementary, geometrically ordered intermolecular interactions enforcing the self-assembly is one of the general principles guiding gelator design. Furthermore, the not too close association between the urea functions could facilitate the dispersion of the neosaccharide assemblies in the solvent, thus enabling the organogelation process.²⁷ Moreover, some sugar derivatives possessing a 4,6-O-benzylidene protecting group exhibited good properties as low molecular weight gelators.^{28,29} The ability of neodisaccharides **33–38** to behave as organogelators was screened in nine solvents by the test tube inversion method. Three different stimuli were employed to trigger the gelation: thermic, ultrasonic and combined thermic-ultrasonic. The critical gelation concentration of neodisaccharides was determined from the minimum amount of gelator required to induce gel formation. The observed organogelation abilities are summarized in Table 4.

Neodisaccharides **33–36** were able to form gels, whereas compounds **37** and **38** gave clear solutions or precipitates but no gel was observed. The ability of **33–36** to form organogels parallels their urea groups driven self-association behaviour observed in ¹H NMR spectra at different concentrations. Analogously, the inability of compounds **37** and **38** to act as organogelators finds a comparison with the absence of self-association showed in their ¹H NMR spectra at different concentrations. In the case of neodisaccharides **35** and **36**, van der Waals interactions between *n*-undecyl chains of neighbouring molecules could consolidate the self-aggregation process. Indeed, among screened compounds, galactosamine neodisaccharide **36** was able to induce gelation of the broadest variety of organic solvents, from the nonpolar toluene to the polar

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| Organogelation abilities of neodisaccharides 33–38 |

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| Solvent ^a | 33 ^b | 34 ^b | 35 ^b | 36 ^b | 37 ^b | 38 ^b |
|--------------------------------------|------------------------|------------------------|----------------------|------------------------|-----------------|-----------------|
| Acetone | G ^{c,d,e} (5) | S | Р | G ^{c,e} (2.5) | Р | S |
| Ethyl acetate | Р | Р | Р | G ^{ce} (1) | Р | Р |
| CH ₂ Cl ₂ | G ^e (5) | S | Р | S | Р | S |
| CHCl ₃ | G ^{c,e} (5) | S | G ^{c,e} (5) | S | S | S |
| THF | Р | S | G ^d (2.5) | S | Р | Р |
| CH₃CN | Р | S | Р | G ^{c,e} (3) | Р | S |
| Toluene | Р | Р | Р | $G^{c,e}(5)$ | Р | Р |
| CH₃OH | Р | G ^{c,d,e} (4) | Р | G ^{c,e} (2.5) | Р | S |
| (CH ₃) ₂ CHOH | Р | G ^{c,e} (4) | Р | $G^{c,e}(4)$ | Р | Р |

^a The solvent was dried before use on 4 Å molecular sieves.

^b P=precipitate at 5% wt/vol concentration; S=soluble at 5% wt/vol concentration; G=gelation (minimum gelator % wt/vol concentrations are indicated in parenthesis)

^c Gel formed upon slow cooling to rt after a thermic stimulus (60 °C, 60 s).

^d Gel formed upon standing at rt after an ultrasonic stimulus (37 kHz, 60 s).

 $^{\rm e}\,$ Gel formed upon slow cooling to rt after a combined thermic-ultrasonic stimulus (60 °C, 37 kHz, 60 s).

methanol and acetonitrile. This result ties in with the already reported higher ability of methyl 4,6-O-benzylidene α - and β -galactopyranosides to act as gelators when compared to their glucocounterparts.²⁸ Interestingly, glucosamine neodisaccharide **35** showed organogelation abilities somehow complementary to its galactosamine counterpart 36. Indeed, among the screened solvents, compound 35 revealed gelation properties exclusively in chloroform and THF, that were two of the three solvents not gelified by 36. It is also worth noting that the stimulus triggering the gelification process varied in dependence of the neodisaccharidesolvent couple under examination. Most gels were formed upon slow cooling after a conventional thermic stimulus at 60 °C, whereas the gelification process of **33** in CH₂Cl₂ and of **35** in THF required exclusively a combined thermic-ultrasonic stimulus consisting of an ultrasound irradiation at 60 °C. By submitting these two gelator-solvent systems to a thermic or ultrasound stimulus separately, precipitation was observed and no gel was obtained. A similar behaviour was recently reported for some ureafunctionalized guinacridone derivatives, that formed organogels exclusively after a thermic stimulus quickly followed by ultrasonic irradiation, inducing the formation of initial aggregates that spontaneously propagated to well-ordered clusters.³⁰

3. Conclusion

The reaction conditions influencing the urea-linked dimerization of sugar building blocks possessing a vicinal aminoalcohol moiety have been studied in detail. The dimerization process was demonstrated to be highly dependent on reaction temperature as well as on concentration and configuration of the starting sugar aminoalcohol. The obtained neodisaccharides were shown to be very versatile scaffolds for affording cyclic and higher linear neosaccharides. Furthermore, a series of six urea-linked glucosamine and galactosamine neodisaccharides was synthesized and their self-association properties were studied by measuring NMR spectra at different temperatures and concentrations. The four compounds showing self-association were able to induce gelation of several organic solvents at relatively low concentration. Depending on whether the neosaccharide possessed a gluco- or galacto-configuration as well as long-chain alkyl appendages or not, the organogelation abilities changed in terms of both the gelified solvent and the kind of stimulus triggering the process. This paves the way for preparing a larger library of neosaccharide derivatives, that in dependence of small structural variations, could be able to gelate solvents in a selective way and in response to a well-defined stimulus. However, more detailed information on the supramolecular assembly of the synthesized derivatives is needed in order to understand, which are the relationships between urea-linked neodisaccharide structure and environmental factors that allow the organogelation process. Further studies are therefore planned with this in mind. The results will be reported in due time.

4. Experimental section

4.1. General

¹H and ¹³C NMR spectra were recorded on Varian XL-200 (¹H NMR: 200 MHz, ¹³C NMR: 50 MHz), Bruker DRX-400 (¹H NMR: 400 MHz, ¹³C NMR: 100 MHz) and Varian INOVA 500 (¹H NMR: 500 MHz, ¹³C NMR: 125 MHz) instruments in CDCl₃ (internal standard, for ¹H: CHCl₃ at δ 7.26; for ¹³C: CDCl₃ at δ 77.0). I values are given in Hertz. MALDI-MS spectra were recorded on an Applied Biosystem Voyager DE-PRO MALDI-TOF mass spectrometer: compounds were dissolved in CH₃CN at a concentration of 0.1 mg/mL and 1 μ L of these solutions were mixed with 1 μ L of a 20 mg/mL solution of 2,5-dihydroxybenzoic acid in 7:3 CH₃CN/H₂O. Optical rotations were measured on a JASCO P-1010 polarimeter. Infrared spectra were measured on a Thermo Nicolet 5700 FT-IR spectrometer. Melting points were measured on a Gallenkamp melting point apparatus. Elemental analyses were performed on a Carlo Erba 1108 instrument. Centrifugations were performed with an Eppendorf 5804R centrifuge. Thermic, ultrasonic and combined thermic-ultrasonic stimuli triggering the organogelation processes were provided with an Elma Elmasonic S 30 H instrument. Analytical thin layer chromatographies (TLCs) were performed on aluminium plates precoated with Merck Silica Gel 60 F254 as the adsorbent. The plates were developed with 10% H₂SO₄ ethanolic solution and then heating to 130 °C. Column chromatographies were performed on Kieselgel 60 (63-200 mesh).

4.2. General procedure for aminoalcohol dimerization

Aminoalcohol (430 mg, 1.40 mmol) was suspended in 2:1 v/v water/CH₃CN (6.0 mL) and then cooled to 0 °C. NaHCO₃ (585 mg, 6.96 mmol) and then a solution of 4-nitrophenyl chloroformate (1.83 g, 6.80 mmol) in CH₃CN (4.0 mL) were added. After 30 min stirring at 0 °C, the mixture was diluted with ethyl acetate (300 mL) and washed with 1 M NaHCO₃. The organic layer was collected, dried over anhydrous Na₂SO₄ and concentrated to give a white gummy solid, that was dissolved in DMF (see Tables 2 and 3) and heated/cooled to the temperature indicated in Tables 2 and 3. NaH (60% dispersion in oil) (261 mg, 6.53 mmol) was then added portionwise to avoid sudden overheating. The yellow mixture was stirred for 45 min at the indicated temperature, then cooled to 0 °C and treated dropwise with water until production of gas ceased. The mixture was diluted with CH₂Cl₂ (150 mL) and washed with water. The organic layer was collected, dried over anhydrous Na₂SO₄, filtered and concentrated. The residue was subjected to flash-chromatography (6:1 to 2:3 v/v hexane/ethyl acetate).

4.3. Characterization data for aminoalcohol dimerization products

4.3.1. N,N'-Bis(1-O-allyl-4,6-O-benzylidene-2,3-N,O-carbonyl-2deoxy- α -D-glucopyranos-2-yl)urea (**2**). White powder. $[\alpha]_D^{22}$ +60 (c 0.9 in CH₂Cl₂). ν_{max} (powder) 2917, 1802, 1615, 1575, 1371, 1108, 1027 cm^{-1.1} H NMR (400 MHz, CDCl₃): δ 7.50–7.36 (10H, m, H–Ar), 5.89–5.81 (2H, m, OCH₂CH=CH₂), 5.61 (2H, s, CHPh), 5.53 (2H, d, $J_{1,2}$ 2.8, 1-H), 5.31 (2H, ddd, J_{vic} 17.3, ${}^4J_{H,H}$ 3.1, J_{gem} 1.3, trans OCH₂CH=CHH), 5.22 (2H, ddd, J_{vic} 10.4, ${}^4J_{H,H}$ 2.4, J_{gem} 1.3, cis OCH₂CH=CHH), 4.94 (2H, dd, $J_{3,2}$ 11.4, $J_{3,4}$ 10.0, 3-H), 4.31–4.25 (4H, m, 6a-H, OCHHCH=CH₂), 4.10–4.04 (4H, m, 4-H, OCHHCH=CH₂), 3.99 (2H, dd, $J_{2,3}$ 11.4, $J_{2,1}$ 2.8, 2-H), 3.96–3.88 (4H, m, 5-H, 6b-H). ¹³C NMR (100 MHz, CDCl₃): δ 150.4 (OCON), 150.0 (NCON), 136.4 (C_{ipso}), 132.3 (OCH₂CH=CH₂), 129.4, 128.4, 126.2 (C–Ar), 118.0 (OCH₂CH=CH₂), 101.4 (CHPh), 94.6 (C-1), 79.5, 74.0, 69.3, 68.4, 65.2, 61.0 (C-2, C-3, C-4, C-5, C-6, OCH₂CH=CH₂). MS (MALDI TOF): *m*/*z* 715.25 [M+Na]⁺. Anal. Calcd for C₃₅H₃₆N₂O₁₃: C, 60.09, H 5.24, N, 4.04. Found C, 60.49, H 5.09, N 3.97.

4.3.2. Allvl 4.6-O-benzvlidene-2.3-N.O-carbonvl-2-deoxv-2-(p-nitrophenoxycarbonylamino)- α -*D*-glucopyranoside (3). White powder. $[\alpha]_{D}^{22}$ +64.7 (*c* 1.0 in CH₂Cl₂). ν_{max} (powder) 2896, 1797, 1742, 1521, 1344, 1218, 997 cm⁻¹. ¹H NMR (400 MHz, CDCl₃): δ 8.29 (2H, d, *J*_{3',2'} 9.1, 2× 3'-H pNO₂-Ar), 7.51-7.38 (7H, m, H-Ar benzylidene, 2× 2'-H pNO₂-Ar), 5.92-5.84 (1H, m, OCH₂CH=CH₂), 5.64 (1H, s, CHPh), 5.63 (1H, d, J_{1.2} 2.7, 1-H), 5.32 (1H, br d, J_{vic} 17.2, trans OCH₂CH= CHH), 5.22 (1H, br d, J_{vic} 10.3, cis OCH₂CH=CHH), 4.90 (1H, t, J_{3,2}=J_{3,4} 11.0, 3-H), 4.33-4.27 (2H, m, 6a-H, OCHHCH=CH₂), 4.14-4.08 (2H, m, 4-H, OCHHCH=CH₂), 4.05 (1H, dd, J_{2.3} 11.0, J_{2.1} 2.7, 2-H), 3.95–3.89 (2H, m, 5-H, 6b-H). ¹³C NMR (100 MHz, CDCl₃): δ 154.3, 145.8 (2Cipso), 150.3, 148.9 (2 NCOO), 136.2 (Cipso benzylidene), 132.7 (OCH₂CH=CH₂), 129.3, 128.4, 126.1, 125.4, 122.2 (C-Ar), 118.8 (OCH₂CH=CH₂), 101.5 (CHPh), 95.5 (C-1), 79.5, 74.0, 69.7, 68.4, 65.4, 60.9 (C-2, C-3, C-4, C-5, C-6, OCH₂CH=CH₂). MS (MALDI TOF): unstable. Anal. Calcd for C24H22N2O10: C, 57.83, H 4.45, N, 5.62. Found C, 57.70, H 4.40, N 5.56.

4.3.3. Allyl 2-amino-4,6-O-benzylidene-2,3-N,O-carbonyl-2-deoxy- α -D-glucopyranoside (**9**). White powder. $[\alpha]_D^{22} + 33$ (c 0.3 in CH₂Cl₂). ν_{max} (powder) 2885, 1842, 1745, 1100, 1030, 968 cm⁻¹. ¹H NMR (400 MHz, CDCl₃): δ 7.51–7.36 (5H, m, H–Ar), 5.95–5.87 (1H, m, OCH₂CH=CH₂), 5.62 (1H, s, CHPh), 5.35 (1H, ddd, *J*_{vic} 17.2, ⁴*J*_{H,H} 3.0, *J*_{gem} 1.5, *trans* OCH₂CH=CHH), 5.28 (1H, dd, *J*_{vic} 10.4, *J*_{gem} 1.5, *cis* OCH₂CH=CHH), 5.15 (1H, d, *J*_{1,2} 2.9, 1-H), 5.07 (1H, br s, NH), 4.84 (1H, dd, *J*_{3,2} 11.3, *J*_{3,4} 10.2, 3-H), 4.32–4.26 (2H, m, 6a-H, OCHHCH= CH₂), 4.12–4.06 (2H, m, 4-H, OCHHCH=CH₂), 3.93–3.87 (2H, m, 5-H, 6b-H), 3.74 (1H, dd, *J*_{2,3} 11.3, *J*_{2,1} 2.9, 2-H). ¹³C NMR (125 MHz, CDCl₃): δ 159.1 (NCOO), 136.5 (*C*_{ipso}), 132.8 (OCH₂CH=CH₂), 129.2, 128.3, 126.2 (C–Ar), 118.5 (OCH₂CH=CH₂), 101.4 (CHPh), 95.5 (C-1), 80.1, 75.6, 69.1, 68.5, 65.5, 59.5 (C-2, C-3, C-4, C-5, C-6, OCH₂CH= CH₂). MS (MALDI TOF): *m*/*z* 334.16 [M+H]⁺. Anal. Calcd for C₁₇H₁₉NO₆: C, 61.26, H 5.75, N, 4.20. Found C, 61.06, H 5.58, N 4.11.

4.3.4. N,N'-Bis(1-O-allyl-4,6-O-benzylidene-2,3-N,O-carbonyl-2*deoxy*- α -*D*-galactopyranos-2-yl)urea (11). White powder. [α]_D²² +45 (c 0.5 in CH₂Cl₂). v_{max} (powder) 2902, 1810, 1620, 1581, 1385, 1096, 1019 cm⁻¹. ¹H NMR (400 MHz, CDCl₃): δ 7.54–7.37 (10H, m, H–Ar benzylidene), 5.86–5.78 (2H, m, OCH₂CH=CH₂), 5.64 (2H, s, CHPh), 5.60 (2H, d, J_{1,2} 2.6, 1-H), 5.25 (2H, dd, J_{vic} 17.1, J_{gem} 1.3, trans OCH₂CH=CHH), 5.15 (2H, dd, J_{vic} 10.5, J_{gem} 1.3, cis OCH₂CH=CHH), 4.89 (2H, dd, J_{3,2} 12.2, J_{3,4} 2.3, 3-H), 4.64–4.58 (4H, m, 2-H, 4-H), 4.35 (2H, br d, Jgem 12.6, 6a-H), 4.22 (2H, dd, Jgem 13.0, Jvic 5.1, OCHHCH=CH₂), 4.15 (2H, br d, Jgem 12.6, 6b-H), 4.08 (2H, dd, Jgem 13.0, Jvic 5.1, OCHHCH=CH₂), 3.70 (2H, br s, 5-H). ¹³C NMR (100 MHz, CDCl₃): δ 150.6 (OCON), 149.1 (NCON), 137.0 (C_{ipso}), 133.1 (OCH₂CH=CH₂), 129.3, 128.3, 126.2 (C-Ar), 117.9 (OCH₂CH=CH₂), 100.4 (CHPh), 95.2 (C-1), 73.4, 71.7, 69.9, 69.4, 63.4, 55.5 (C-2, C-3, C-4, C-5, C-6, OCH₂CH=CH₂). MS (MALDI TOF): *m*/*z* 715.08 $[M+Na]^+$. Anal. Calcd for $C_{35}H_{36}N_2O_{13}$: C, 60.09, H 5.24, N, 4.04. Found C, 59.79, H 5.42, N 3.92.

4.3.5. Allyl 4,6-O-benzylidene-2,3-N,O-carbonyl-2-deoxy-2-(p-nitrophenoxycarbonylamino)- α -D-galactopyranoside (**12**). White powder. ν_{max} (powder) 2919, 1839, 1735, 1522, 1344, 1220, 1113, 1025 cm⁻¹. [α]_D²² +55.3 (*c* 2.0 in CH₂Cl₂). ¹H NMR (400 MHz, CDCl₃): δ 8.30 (2H, d, $J_{3',2'}$ 7.0, 2× 3'-H pNO₂—Ar), 7.54—7.37 (7H, m, benzylidene, 2× 2'-H pNO₂—Ar), 5.91—5.84 (1H, m, OCH₂CH=CH₂), 5.72 (1H, d, $J_{1,2}$ 2.8, H-1), 5.67 (1H, s, CHPh), 5.30 (1H, dd, J_{vic} 17.2, *J*_{gem} 1.5, *trans* OCH₂CH=C*H*H), 5.22 (1H, dd, *J*_{vic} 10.4, *J*_{gem} 1.5, *cis* OCH₂CH=C*H*H), 4.88 (1H, dd, *J*_{3,2} 12.1, *J*_{3,4} 2.5, 3-H), 4.70 (1H, dd, *J*_{2,3} 12.1, *J*_{2,1} 2.8, 2-H), 4.68 (1H, d, *J*_{4,3} 2.5, 4-H), 4.37 (1H, dd, *J*_{gem} 12.7, *J*_{6a,5} 1.1, 6a-H), 4.30 (1H, dd, *J*_{gem} 12.9, *J*_{vic} 6.5, OCHHCH=CH₂), 4.18 (1H, dd, *J*_{gem} 12.7, *J*_{6b,5} 1.7, 6b-H), 4.14 (1H, dd, *J*_{gem} 12.9, *J*_{vic} 6.5, OCHHCH=CH₂), 3.76 (1H, br s, 5-H). ¹³C NMR (100 MHz, CDCl₃): δ 154.4 (*C*_{ipso}), 150.2, 148.9 (2 NCOO), 145.8 (*C*_{ipso}), 136.8 (*C*_{ipso}) benzylidene), 133.1 (OCH₂CH=CH₂), 129.3, 128.3, 126.1, 125.4, 122.1 (C−Ar), 118.5 (OCH₂CH=CH₂), 100.3 (CHPh), 96.1 (C−1), 73.5, 71.6, 69.8, 69.6, 63.6, 55.4 (C-2, C-3, C-4, C-5, C-6, OCH₂CH=CH₂). MS (MALDI TOF): unstable. Anal. Calcd for C₂₄H₂₂N₂O₁₀: C, 57.83, H 4.45, N, 5.62. Found C, 57.47, H 4.61, N 5.44.

4.3.6. Allyl 2-amino-4,6-O-benzylidene-2,3-N,O-carbonyl-2-deoxy- α -*D*-galactopyranoside (13). White powder. ν_{max} (powder) 2910, 1772, 1117, 1020, 1006 cm⁻¹. $[\alpha]_D^{22}$ +120 (c 0.4 in CH₃CN). ¹H NMR (500 MHz, CDCl₃): § 7.52-7.36 (5H, m, H-Ar), 5.95-5.87 (1H, m, OCH₂CH=CH₂), 5.64 (1H, s, CHPh), 5.33 (1H, br d, Jvic 17.0, trans OCH₂CH=CHH), 5.26 (1H, d, J_{NH,2} 2.0, NH), 5.25 (1H, d, J_{vic} 10.5, cis OCH₂CH=CHH), 5.05 (1H, br s, H-1), 4.81 (1H, dd, J_{3,2} 12.0, J_{3,4} 2.5, 3-H), 4.61 (1H, br s, 4-H), 4.39 (1H, dd, J_{2.3} 12.0, J_{2.NH} 2.0, 2-H), 4.33 (1H, br d, Jgem 12.5, 6a-H), 4.29 (1H, dd, Jgem 13.5, Jvic 5.5, OCHHCH= CH₂), 4.17–4.11 (2H, m, 6b-H, OCHHCH=CH₂), 3.69 (1H, br s, 5-H). ¹³C NMR (125 MHz, CDCl₃): δ 158.8 (NCOO), 137.0 (C_{ipso}), 133.1 (OCH₂CH=CH₂), 129.2, 128.2, 126.2 (C-Ar), 118.2 (OCH₂CH=CH₂), 100.3 (CHPh), 96.1 (C-1), 75.0, 72.1, 70.0, 69.1, 63.7, 53.3 (C-2, C-3, C-4, C-5, C-6, OCH₂CH=CH₂). MS (MALDI TOF): *m*/*z* 334.07 [M+H]⁺. Anal. Calcd for C₁₇H₁₉NO₆: C, 61.26, H 5.75, N, 4.20. Found C, 61.00, H 5.92, N 4.02.

4.3.7. Allyl 2-amino-4,6-O-benzylidene-2,3-N,O-carbonyl-2-deoxy- α -*D*-allopyranoside (**20**). White powder. ν_{max} (powder) 2904, 1764, 1705, 1355, 1220, 998 cm⁻¹. $[\alpha]_D^{22}$ +104 (*c* 0.8 in CH₃CN). ¹H NMR (500 MHz, CDCl₃): δ 7.51-7.33 (5H, m, H-Ar), 5.93-5.85 (1H, m, OCH₂CH=CH₂), 5.59 (1H, s, CHPh), 5.33 (1H, d, J_{vic} 17.0, trans OCH₂CH=CHH), 5.27-5.20 (2H, m, NH, cis OCH₂CH=CHH), 4.94–4.90 (2H, m, 1-H, 3-H), 4.37 (1H, dd, J_{gem} 10.5, J_{6a.5} 5.5, 6a-H), 4.25–4.19 (2H, m, 5-H, OCHHCH=CH₂), 4.00 (1H, dd, J_{gem} 13.0, J_{vic} 5.5, OCHHCH=CH₂), 3.95 (1H, t, J_{2,3}=J_{2,1} 5.5, 2-H), 3.82 (1H, dd, J_{gem} 10.5, $J_{6b,5}$ 3.5, 6b-H), 3.73 (1H, t, $J_{4,5}=J_{4,3}$ 10.0, 4-H). ¹³C NMR (125 MHz, CDCl₃): δ 160.1 (OCON), 137.2 (C_{ipso}), 132.9 (OCH₂CH= CH₂), 129.4, 128.3, 126.4, 125.4, 121.8 (C-Ar), 117.9 (OCH₂CH=CH₂), 102.7 (OCHPh), 94.8 (C-1), 75.5, 73.0, 68.9, 68.5, 59.9, 53.6 (C-2, C-3, C-4, C-5, C-6, OCH₂CH=CH₂). MS (MALDI TOF): *m*/*z* 334.26 [M+H]⁺. Anal. Calcd for C₁₇H₁₉NO₆: C, 61.26, H 5.75, N, 4.20. Found C, 60.88, H 5.84, N 4.07.

4.3.8. Methyl 2-amino-4,6-O-benzylidene-2,3-N,O-carbonyl-2deoxy-α-D-mannopyranoside (**21**). White powder. ν_{max} (powder) 2905, 1755, 1716, 1387, 1240, 1014 cm⁻¹. [α]_D²² -45 (c 0.4 in CH₃CN). ¹H NMR (400 MHz, CDCl₃): δ 7.50–7.36 (5H, m, H–Ar), 6.07 (1H, br s, NH), 5.59 (1H, s, CHPh), 4.78 (1H, s, 1-H), 4.76 (1H, t, *J*_{3,4}=*J*_{3,2} 7.7, 3-H), 4.36–4.31 (1H, m, 6a-H), 4.12 (1H, d, *J*_{2,3} 7.7, 2-H), 3.92 (1H, t, *J*_{4,5}=*J*_{4,3} 7.7, 4-H), 3.83–3.77 (2H, m, 5-H, 6b-H), 3.38 (3H, s, OCH₃). ¹³C NMR (125 MHz, CDCl₃): δ 159.0 (OCON), 136.8 (*C*_{ipso}), 129.2, 128.3, 126.1 (C–Ar), 101.9 (OCHPh), 98.0 (C-1), 78.7, 75.0, 68.8, 59.5, 56.4, 55.2 (C-2, C-3, C-4, C-5, C-6, OCH₃). MS (MALDI TOF): *m/z* 308.19 [M+H]⁺. Anal. Calcd for C₁₅H₁₇NO₆: C, 58.63, H 5.58, N, 4.56. Found C, 58.87, H 5.72, N 4.41.

4.3.9. *N*,*N*'-*Bis*[(2-*azido*-3,6-*di*-O-*benzy*]-2-*deoxy*-4-O-*p*-*methox*ybenzyl-α-*p*-glucopyranosyl)-(1→4)-1-O-allyl-6-O-benzyl-2,3-*N*,Ocarbonyl-2-*deoxy*-α-*p*-glucopyranos-2-yl]urea (**23**). Colourless oil. [α]_D² +35 (*c* 0.4 in CH₂Cl₂). ¹H NMR (500 MHz, CDCl₃): δ 7.40−7.26 (30H, m, H−Ar), 7.05 (4H, d, J_{vic} 8.0, H−Ar PMB), 6.81 (4H, d, J_{vic} 8.0, H−Ar PMB), 5.86−5.78 (2H, m, OCH₂CH=CH₂), 5.49 (2H, d, J₁₂ 2.5,

1_A-H), 5.41 (2H, d, J_{1,2} 3.5, 1_B-H), 5.27 (2H, d, J_{gem} 17.0, trans OCH₂CH=CHH), 5.19 (2H, d, Jgem 10.5, cis OCH₂CH=CHH), 4.91 (2H, t, J_{3.2}=J_{3.4} 9.5, 3_A-H), 4.86 (4H, s, OCH₂Ph PMB), 4.69 (2H, d, J_{gem} 10.0, OCHHPh), 4.56 (2H, d, Jgem 12.0, OCHHPh), 4.52 (2H, d, Jgem 11.5, OCHHPh), 4.50 (2H, d, Jgem 11.5, OCHHPh), 4.41 (2H, d, Jgem 10.0, OCHHPh), 4.37 (2H, t, J_{4,3}=J_{4,5} 9.5, 4_A-H), 4.32 (2H, d, J_{gem} 12.0, OCHHPh), 4.21 (2H, dd, Jgem 13.0, Jvic 5.5, OCHHCH=CH₂), 4.03 (2H, dd, Jgem 13.0, Jvic 5.5, OCHHCH=CH₂), 3.92 (2H, dd, J_{2.3} 9.5, J_{2.1} 2.5, 2_A-H), 3.88–3.67 (18H, m, 3_B-H, 4_B-H, 5_A-H, 5_B-H, 6a_A-H, 6b_A-H, OCH₃), 3.51 (2H, d, J_{gem} 10.0, 6a_B-H), 3.45 (2H, dd, J_{2,3} 10.0, J_{2,1} 3.5, 2_B-H), 3.37 (2H, d, J_{gem} 10.0, 6b_B-H). ¹³C NMR (125 MHz, CDCl₃): δ 159.3 (Cipso PMB) 150.4 (OCON), 149.0 (NCON), 137.9 (3Cipso Bn), 132.9 (OCH₂CH=CH₂), 130.2 (C_{inso} PMB), 129.6-127.3 (C-Ar), 117.8 (OCH₂CH=CH₂), 113.7 (C-Ar PMB), 96.3, 93.7 (C-1_A, C-1_B), 80.2, 75.4, 74.7, 74.6, 73.5, 73.4, 71.8, 71.6, 70.9, 70.3, 69.1, 68.1, 67.8, 63.2, 60.2, 55.3 (C-2_A, C-2_B, C-3_A, C-3_B, C-4_A, C-4_B, C-5_A, C-5_B, C-6_A, C-6_B, 30CH₂Ph, OCH₂Ph PMB, OCH₂CH=CH₂, OCH₃). MS (MALDI TOF): *m*/*z* 1693.36 [M+Na]⁺. Anal. Calcd for C₉₁H₉₈N₈O₂₃: C, 65.38, H 5.91, N, 6.70. Found C, 65.06, H 6.05, N 6.83.

4.3.10. Allyl (2-azido-3,6-di-O-benzyl-2-deoxy-4-O-p-methoxybenzyl- α -D-glucopyranosyl)-(1 \rightarrow 4)-2-amino-6-O-benzyl-2,3-N,Ocarbonyl-2-deoxy- α -D-glucopyranoside (24). Yellowish oil. $[\alpha]_D^{22}$ +40.1 (*c* 1.5 in CH₂Cl₂). ¹H NMR (500 MHz, CDCl₃): δ 7.38–7.26 (15H, m, H–Ar), 7.04 (2H, d, Jvic 8.5, H–Ar PMB), 6.81 (2H, d, Jvic 8.5, H–Ar PMB), 5.93–5.85 (1H, m, OCH₂CH=CH₂), 5.46 (1H, d, J_{1,2} 3.5, 1_B-H), 5.32 (1H, dd, Jgem 17.5, Jvic 1.5, trans OCH₂CH=CHH), 5.27-5.21 (2H, m, NH, cis OCH₂CH=CHH), 5.12 (1H, d, J_{1,2} 2.5, 1_A-H), 4.86 (2H, s, OCH₂Ph PMB), 4.81 (1H, dd, J_{3.2} 11.5, J_{3.4} 10.0, 3_A-H), 4.69 (1H, d, J_{gem} 10.5, OCHHPh), 4.55 (1H, d, Jgem 11.5, OCHHPh), 4.54 (1H, d, Jgem 10.0, OCHHPh), 4.51 (1H, d, Jgem 10.5, OCHHPh), 4.42 (1H, d, Jgem 10.0, OCHHPh), 4.36–4.31 (2H, m, 4_A-H, OCHHPh), 4.26 (1H, dd, Jgem 12.5, Jvic 5.0, OCHHCH=CH₂), 4.08 (1H, dd, Jgem 12.5, Jvic 5.0, OCHHCH=CH₂), 3.86–3.64 (10H, m, 2_A-H, 3_B-H, 4_B-H, 5_A-H, 5_B-H, 6a_A-H, 6b_A-H, OCH₃), 3.53 (1H, d, J_{gem} 11.0, J_{6a,5} 3.0, 6a_B-H), 3.45 (1H, dd, J_{2,3} 10.0, J_{2,1} 3.5, 2_B-H), 3.40 (1H, d, J_{gem} 11.0, 6b_B-H). ¹³C NMR (125 MHz, CDCl₃): δ 159.3, 159.0 (Cipso PMB, OCON), 137.9 (3Cipso Bn), 133.0 (OCH₂CH=CH₂), 130.2 (C_{inso} PMB), 129.6–127.3 (C-Ar), 118.2 (OCH₂CH=CH₂), 113.8 (C-Ar PMB), 96.2, 94.6 (C-1_A, C-1_B), 80.3, 79.2, 77.6, 75.4, 74.7, 73.5, 73.4, 72.0, 71.7, 70.9, 69.3, 68.3, 67.9, 63.3, 58.4, 55.3 (C-2_A, C-2_B, C-3_A, C-3_B, C-4_A, C-4_B, C-5_A, C-5_B, C-6_A, C-6_B, 3OCH₂Ph, OCH₂Ph PMB, OCH₂CH=CH₂, OCH₃). MS (MALDI TOF): *m*/*z* 823.28 [M+H]⁺. Anal. Calcd for C₄₅H₅₀N₄O₁₁: C, 65.68, H 6.12, N, 6.81. Found C, 65.39, H 7.00, N 6.69.

4.4. Allyl 4,6-O-benzylidene-2-deoxy-2-(p-nitro-phenox-ycarbonylamino)-3-O-(p-nitro-phenoxycarbonyl)- α -p-gluco-pyranoside (14)

Compound 1 (197 mg, 643 µmol) was suspended in 2:1 v/v water/CH₃CN (3.0 mL), cooled to 0 °C and treated with NaHCO₃ (268 mg, 3.19 mmol) and then with a solution of 4-nitrophenyl chloroformate (631 mg, 3.13 mmol) in CH₃CN (1.4 mL). After 30 min stirring at 0 °C, the mixture was diluted with ethyl acetate (100 mL) and washed with 1 M NaHCO₃. The organic layer was collected, dried over anhydrous Na₂SO₄ and concentrated. The obtained gummy solid was dissolved in DMF (3.3 mL), cooled to 0 °C and then treated with DMAP (28.5 mg, 233 µmol). After 1 h stirring at 0 °C, CH₂Cl₂ (50 mL) was added. The solution was washed with 0.1 M HCl and then with water. The organic layer was collected, dried over anhydrous Na₂SO₄, filtered and concentrated to give a residue, that was subjected to flash-chromatography (8:1 to 5:2 v/v n-hexane/ethyl acetate) to give 14 (102 mg, 25%) as amorphous white crystals. Mp 126–128 °C. $[\alpha]_D^{22}$ –15 (*c* 0.9 in CH₂Cl₂). *v*_{max} (powder) 1720, 1532, 1519, 1490, 1211 cm⁻¹.¹H NMR (400 MHz, CDCl₃): δ 8.21 (2H, d, $J_{3',2'}$ 9.1, 2× 3'-H pNO₂-Ar), 8.18 (2H, d, $J_{3',2'}$ 9.2, $2 \times 3'$ -H pNO₂—Ar), 7.50–7.25 (9H, m, benzylidene, $4 \times 2'$ -H pNO₂—Ar), 5.97–5.90 (1H, m, OCH₂CH=CH₂), 5.71 (1H, d, $J_{H,NH}$ 9.9, NH), 5.59 (1H, s, CHPh), 5.37 (1H, dd, J_{vic} 16.1, J_{gem} 1.4, trans OCH₂CH=CHH), 5.30 (1H, dd, J_{vic} 10.3, J_{gem} 1.4, cis OCH₂CH=CHH), 5.28 (1H, t, $J_{3,4}=J_{3,2}$ 10.0, 3-H), 5.06 (1H, d, $J_{1,2}$ 3.8, 1-H), 4.33–4.27 (2H, m, 6a-H, OCHHCH=CH₂), 4.14–4.08 (2H, m, 2-H, OCHHCH=CH₂), 4.01 (1H, dd, $J_{6b,5}$ 10.0, J_{gem} 4.8, 6b-H), 3.89 (1H, q, $J_{5,4}=J_{5,6a}=J_{5,6b}$ 10.0, 5-H), 3.83 (1H, t, $J_{4,5}=J_{4,3}$ 10.0, 4-H). ¹³C NMR (100 MHz, CDCl₃): δ 155.3, 155.2 (2C_{ipso}), 152.9, 152.5 (NCOO, OCOO), 145.6, 144.9 (2C_{ipso}), 136.6 (C_{ipso} benzylidene), 132.7 (OCH₂CH=CH₂), 129.3, 128.3, 126.1, 125.2, 121.8, 121.6 (C–Ar), 118.9 (OCH₂CH=CH₂), 101.8 (CHPh), 96.8 (C-1), 78.5, 76.3, 68.9, 68.6, 62.7, 54.2 (C-2, C-3, C-4, C-5, C-6, OCH₂CH=CH₂). MS (MALDI TOF): unstable. Anal. Calcd for C₃₀H₂₇N₃O₁₃: C, 56.52, H 4.27, N, 6.59. Found C, 56.26, H 4.43, N 6.31.

4.5. N,N'-Bis(1-O-allyl-6-O-benzyl-2,3-N,O-carbonyl-2-deoxy- α -D-glucopyranos-2-yl)urea (26)

Compound 2 (254.2 mg, 367 µmol) was coevaporated three times with anhydrous toluene (3 mL). The residue was dried, then mixed with freshly activated AW-300 4 Å molecular sieves and suspended in CH₂Cl₂ (10 mL) under Ar atmosphere. The mixture was cooled to 0 °C, treated with Et₃SiH (591 μ L, 3.67 mmol) and then with 3 M TFA in CH₂Cl₂ (1.43 mL, 4.51 mmol). After stirring overnight, the mixture was heated to rt, filtered on a Celite pad, diluted with CH₂Cl₂ (100 mL) and washed with 1 M NaHCO₃. The organic layer was collected, dried over anhydrous Na₂SO₄, filtered and concentrated. The obtained residue was subjected to flashchromatography (6:1 to 1:1 v/v n-hexane/ethyl acetate) to give **26** (138.8 mg, 54%) as a yellowish oil. $[\alpha]_D^{22}$ +64 (*c* 0.4 in CH₂Cl₂). ¹H NMR (400 MHz, CDCl₃): ô 7.37-7.30 (10H, m, H-Ar), 5.85-5.78 (2H, m, OCH₂CH=CH₂), 5.45 (2H, d, J_{1,2} 2.8, 1-H), 5.26 (2H, ddd, J_{vic} 17.2, ⁴J_{H,H} 3.1, J_{gem} 1.5, trans OCH₂CH=CHH), 5.16 (2H, ddd, J_{vic} 10.5, ⁴J_{H,H} 2.7, Jgem 1.4, cis OCH₂CH=CHH), 4.75 (2H, dd, J_{3,2} 11.9, J_{3,4} 9.9, 3-H), 4.64 (2H, d, Jgem 12.0, OCHHPh), 4.55 (2H, d, Jgem 12.0, OCHHPh), 4.19 (2H, dd, J_{gem} 13.2, J_{vic} 8.1, OCHHCH=CH₂), 4.12 (2H, t, J_{4.3}=J_{4.5} 9.9, 4-H), 4.03 (2H, dd, J_{gem} 13.2, J_{vic} 8.1, OCHHCH=CH₂), 3.89 (2H, dd, J_{2,3} 11.9, J_{2,1} 2.8, 2-H), 3.81 (2H, dd, Jgem 9.7, J_{6a,5} 6.0, 6a-H), 3.77-3.73 (2H, m, 5-H), 3.70 (2H, dd, Jgem 9.7, J_{6b,5} 4.2, 6b-H). ¹³C NMR (50 MHz, CDCl₃): δ 151.2 (OCON), 148.8 (NCON), 137.7 (Cipso), 133.1 (OCH₂CH=CH₂), 128.5, 127.9, 127.7 (C-Ar), 117.6 (OCH₂CH=CH₂), 93.8 (C-1), 77.4, 73.6, 72.9, 69.0, 68.7, 60.5, 60.0 (C-2, C-3, C-4, C-5, C-6, OCH₂Ph, OCH₂CH=CH₂). MS (MALDI TOF): m/z 719.14 $[M+Na]^+$. Anal. Calcd for $C_{35}H_{40}N_2O_{13}$: C, 60.34, H 5.81, N, 4.02. Found C, 60.00, H 5.94, N 3.96.

4.6. *N*,N'-Bis(4-O-acetyl-1-O-allyl-6-O-benzyl-2,3-*N*,O-carbonyl-2-deoxy-α-D-glucopyranos-2-yl)urea (27)

Compound **26** (9.8 mg, 14.1 µmol) was treated with pyridine (250 µL) and Ac₂O (250 µL). The solution was stirred overnight at rt, then diluted with CH₂Cl₂ (20 mL) and washed with 1 M HCl and then with water. The organic layer was collected, dried over anhydrous Na₂SO₄, filtered and concentrated to give **27** (10.7 mg, 97%) as a yellowish oil. $[\alpha]_{12}^{22}$ +85 (*c* 0.4 in CH₂Cl₂). ¹H NMR (400 MHz, CDCl₃): δ 7.34–7.29 (10H, m, H–Ar), 5.85–5.78 (2H, m, OCH₂CH=CH₂), 5.50 (2H, d, *J*_{1,2} 2.8, 1-H), 5.42 (2H, t, *J*_{4,3}=*J*_{4.5} 9.9, 4-H), 5.26 (2H, ddd, *J*_{vic} 17.2, ⁴*J*_{H.H} 3.0, *J*_{gem} 1.5, *trans* OCH₂CH=CHH), 5.19 (2H, dd, *J*_{vic} 10.5, *J*_{gem} 1.3, *cis* OCH₂CH=CHH), 4.81 (2H, dd, *J*_{3.2} 11.7, *J*_{3.4} 10.3, 3-H), 4.61 (2H, dd, *J*_{gem} 12.0, OCHHPh), 4.48 (2H, d, *J*_{gem} 12.0, OCHHPh), 4.21 (2H, dd, *J*_{gem} 13.1, *J*_{vic} 5.9, OCHHCH=CH₂), 4.05 (2H, dd, *J*_{gem} 13.1, *J*_{vic} 5.9, OCHHCH=CH₂), 4.05 (2H, dd, *J*_{gem} 13.1, *J*_{vic} 5.9, OCHHCH=CH₂), 4.05 (2H, dd, *J*_{2.3} 11.7, *J*_{2.1} 2.8, 2-H), 3.87 (2H, dt, *J*_{5.4} 9.4, *J*_{5.6a}=*J*_{5.6b} 3.5, 5-H), 3.60–3.55 (4H, m, 6a-H, 6b-H), 1.98 (6H, s, COCH₃). ¹³C NMR (125 MHz, CDCl₃): δ 169.1 (COCH₃), 150.3 (OCON), 148.6 (NCON), 137.5 (C_{ipso}), 132.8

(OCH₂CH=CH₂), 128.4, 128.0, 127.9 (C–Ar), 118.0 (OCH₂CH=CH₂), 93.7 (C-1), 75.1, 73.6, 71.2, 69.3, 68.1, 67.4, 60.0 (C-2, C-3, C-4, C-5, C-6, OCH₂Ph, OCH₂CH=CH₂), 23.7 (COCH₃). MS (MALDI TOF): m/z 803.20 [M+Na]⁺. Anal. Calcd for C₃₉H₄₄N₂O₁₁: C, 59.99, H 5.68, N, 3.59. Found C, 59.70, H 5.90, N 3.46.

4.7. N,N'-Bis[(4-O-(2,3,4-tri-O-benzyl- α -L-fucopyranosyl)-1-O-allyl-6-O-benzyl-2,3-N,O-carbonyl-2-deoxy- α -D-glucopyranos-2-yl]urea (29)

A mixture of 27 (20.5 mg, 29.4 µmol) and 28 (74.5 mg, 123 µmol) was coevaporated three times with anhydrous toluene (2 mL). The residue was dried, mixed with freshly activated AW-300 4 Å molecular sieves and suspended in 1:1 v/v CH₂Cl₂/THF (2.0 mL) under Ar atmosphere. The mixture was stirred at -30 °C for 15 min. A 10.4 mg/mL solution of TMSOTf in CH_2Cl_2 (130 µL, 6.1 µmol) was then added. The mixture was stirred for 90 min at -30 °C. A drop of Et₃N was then added. The mixture was filtered over a Celite pad and concentrated. The residue was subjected to column chromatography (8:1 to 3:1 v/v n-hexane/ethyl acetate) to give 29 (36.8 mg, 82%) as a white powder. $[\alpha]_{D}^{22}$ +0.2 (c 1.0 in CH₂Cl₂). ¹H NMR (400 MHz, CDCl₃): δ 7.40-7.26 (40H, m, H-Ar), 5.83-5.76 (2H, m, OCH₂CH=CH₂), 5.46 (2H, d, J_{1.2} 2.6, 1_{GlcN}-H), 5.24 (2H, dd, J_{vic} 17.2, Jgem 1.5, trans OCH2CH=CHH), 5.17 (2H, dd, Jvic 10.5, Jgem 1.5, cis OCH₂CH=CHH), 4.99 (2H, d, J_{1,2} 3.7, 1_{Fuc}-H), 4.96 (2H, d, J_{gem} 11.5, OCHHPh), 4.96 (2H, d, Jgem 11.7, OCHHPh), 4.79-4.73 (6H, m, 3GlcN-H, 2× OCHHPh), 4.65 (2H, d, Jgem 11.5, OCHHPh), 4.63 (2H, d, Jgem 11.6, OCHHPh), 4.47 (2H, d, Jgem 11.9, OCHHPh), 4.36 (2H, d, Jgem 11.9, OCHHPh), 4.22 (2H, t, J_{4,5}=J_{4,3} 9.7, 4_{GlcN}-H), 4.19–4.14 (4H, m, 5_{Fuc}-H, OCHHCH=CH₂), 4.07 (2H, dd, *J*_{2.3} 10.2, *J*_{2.1} 3.7, 2_{Fuc}-H), 4.02–3.94 (8H, m, 2_{GlcN}-H, 3_{Fuc}-H, 6a_{GlcN}-H, OCHHCH=CH₂), 3.84 (2H, d, J_{5.4} 9.7, 5_{GlcN}-H), 3.73 (2H, br s, 4_{Fuc}-H), 3.59 (2H, d, J_{gem} 10.7, 6b_{GlcN}-H), 1.19 (6H, d, $J_{6,5}$ 6.4, 6_{Fuc}-H). ¹³C NMR (100 MHz, CDCl₃): δ 150.9 (OCON), 148.6 (NCON), 138.6, 138.5, 138.3, 137.9 (4Cipso), 133.0 (OCH₂CH=CH₂), 128.4–127.4 (C-Ar), 117.7 (OCH₂CH=CH₂), 99.3 (C-1_{Fuc}), 93.5 (C-1_{GlcN}), 79.9, 77.6, 76.3, 75.7, 74.9, 74.4, 73.7, 73.3, 72.9, 72.7, 68.9, 67.3, 67.1, 60.3 (C-2_{Fuc}, C-2_{GlcN}, C-3_{Fuc}, C-3_{GlcN}, C-4Fuc, C-4GlcN, C-5Fuc, C-5GlcN, C-6GlcN, 40CH2Ph, 0CH2CH=CH2), 16.3 (C-6_{Fuc}). MS (MALDI TOF): m/z 1551.31 [M+Na]⁺. Anal. Calcd for C89H96N2O21: C, 69.88, H 6.33, N, 1.83. Found C, 69.69, H 6.44, N 1.80.

4.8. *N*,*N*'-Bis(1-O-allyl-4,6-O-benzylidene-2-deoxy-α-D-glucopyranos-2-yl)urea (33)

A solution of 2 (172 mg, 0.250 mmol) in 3:1 v/v 1,4-dioxane/ water (8.0 mL) was treated with triethylamine (1.0 mL). After overnight stirring at 80 $^{\circ}$ C, SiO₂ (1.25 g) was added. The mixture was immediately cooled to rt and concentrated. Flashchromatography (99:1 to 96:4 v/v CHCl₃/MeOH) afforded 33 (122 mg, 76%) as a white powder. $[\alpha]_D^{22}$ +32 (*c* 0.5 in CH₂Cl₂). ν_{max} (powder) 2920, 2849, 1643, 1583, 1055 cm⁻¹. ¹H NMR (400 MHz, CDCl₃): δ 7.50−7.34 (10H, m, H–Ar), 5.95–5.88 (2H, m, OCH₂CH= CH₂), 5.55 (2H, s, CHPh), 5.32 (2H, br d, J_{vic} 17.2, trans OCH₂CH= CHH), 5.27–5.21 (4H, m, NH, *cis* OCH₂CH=CHH), 4.88 (2H, d, *J*_{1,2} 3.0, 1-H), 4.26 (2H, dd, Jgem 9.9, J6a, 5 4.5, 6a-H), 4.20 (2H, dd, Jgem 12.8, Jvic 5.2, OCHHCH=CH₂), 4.01 (2H, dd, *J_{gem}* 12.8, *J_{vic}* 5.2, OCHHCH=CH₂), 3.95–3.91 (4H, m, 2-H, 3-H), 3.83 (2H, dt, *J*_{5.4=}*J*_{5.6b} 9.9, *J*_{5.6a} 4.5, 5-H), 3.74 (2H, t, J_{gem}=J_{6b,5} 9.9, 6b-H), 3.64 (2H, br s, OH), 3.56 (2H, t, J_{4,3}=J_{4,5} 9.9, 4-H). ¹³C NMR (100 MHz, CDCl₃): δ 159.1 (NCON), 137.2 (Cipso), 133.4 (OCH2CH=CH2), 129.1, 128.2, 126.4 (C-Ar), 118.2 (OCH₂CH=CH₂), 102.0 (CHPh), 97.5 (C-1), 82.2, 71.5, 68.9, 68.8, 62.6, 55.7 (C-2, C-3, C-4, C-5, C-6, OCH₂CH=CH₂). MS (MALDI TOF): *m*/*z* 641.39 [M+H]⁺. Anal. Calcd for C₃₃H₄₀N₂O₁₁: C, 61.86, H 6.29, N, 4.37. Found C, 62.02, H 6.40, N 4.45.

4.9. N,N'-Bis(1-O-allyl-4,6-O-benzylidene-2-deoxy- α -D-galactopyranos-2-yl)urea (34)

A solution of **11** (74.8 mg, 0.108 mmol) in 3:1 v/v 1,4-dioxane/ water (3.6 mL) was treated with triethylamine (450 µL). After two days stirring at 80 °C, SiO₂ (600 mg) was added. The mixture was immediately cooled to rt and concentrated to give a residue, that was subjected to flash-chromatography (99:1 to 98:2 v/v CHCl₃/ MeOH) to afford **34** (44.2 mg, 64%) as a white powder. $[\alpha]_{D}^{22}$ +126.1 (c 2.0 in acetone). v_{max} (powder) 2905, 1653, 1601, 1250, 1014 cm⁻¹. ¹H NMR (500 MHz, CDCl₃): δ 7.52–7.35 (10H, m, H–Ar), 5.90–5.83 (2H, m, OCH₂CH=CH₂), 5.56 (2H, s, CHPh), 5.27 (2H, br d, *Ivic* 17.0, trans OCH₂CH=CHH), 5.19 (2H, br d, Jvic 10.0, cis OCH₂CH=CHH), 5.01 (2H, d, J_{1.2} 3.5, 1-H), 4.92 (2H, br s, NH), 4.26 (2H, d, J_{gem} 11.0, 6a-H), 4.23–4.20 (4H, m, 2-H, 4-H), 4.18 (2H, dd, Jgem 13.0, Jvic 5.0, OCHHCH=CH₂), 4.07 (2H, d, J_{gem} 11.0, 6a-H), 4.00 (2H, dd, J_{gem} 13.0, Jvic 5.0, OCHHCH=CH₂), 3.88 (2H, td, J_{3.2}=J_{3.0H} 8.0, J_{3.4} 3.5, 3-H), 3.69 (2H, br s, 5-H), 3.39 (2H, br s, OH). ¹³C NMR (100 MHz, CDCl₃): δ 159.6 (NCON), 137.8 (Cipso), 133.6 (OCH₂CH=CH₂), 128.9, 128.0, 126.4 (C-Ar), 117.6 (OCH₂CH=CH₂), 101.1 (CHPh), 98.0 (C-1), 75.6, 69.2, 69.0, 68.5, 63.0, 51.4 (C-2, C-3, C-4, C-5, C-6, OCH₂CH=CH₂). MS (MALDI TOF): *m*/*z* 641.13 [M+H]⁺. Anal. Calcd for C₃₃H₄₀N₂O₁₁: C, 61.86, H 6.29, N, 4.37. Found C, 61.53, H 6.37, N 4.29.

4.10. *N*,*N*'-Bis(1-O-allyl-4,6-O-benzylidene-2-deoxy-3-O-*n*-un-decyl-α-D-glucopyranos-2-yl)urea (35)

A solution of 33 (29.9 mg, 46.7 µmol) in DMF (1.0 mL) was cooled to 0 °C. It was treated with 1-bromoundecane (52 µL, 0.234 µmol). NaH (60% dispersion in oil) (9.5 mg, 236 µmol) and finally with NaI (3.5 mg, 23.0 µmol). After overnight stirring at 0 °C, some drops of water were added. The mixture was diluted with CH₂Cl₂ (25 mL) and washed with water. The organic layer was collected, dried over anhydrous Na₂SO₄, filtered and concentrated. The residue was subjected to flash-chromatography (99:1 to 98:2 v/v CH₂Cl₂/ MeOH). The product was further purified by dissolving it into CH₂Cl₂ (1.0 mL) and then adding *n*-hexane dropwise. The obtained precipitate was collected by centrifugation (4 °C, 6000 rpm, 10 min), giving pure **35** (29.4 mg, 66%) as a white powder. $[\alpha]_{D}^{22}$ +16 (c 0.5 in CH₂Cl₂). v_{max} (powder) 2914, 2851, 1629, 1588, 1371, 1080, 983 cm⁻¹. ¹H NMR (500 MHz, CDCl₃): δ 7.49–7.36 (10H, m, H–Ar), 5.95-5.87 (2H, m, OCH₂CH=CH₂), 5.57 (2H, s, CHPh), 5.32 (2H, d, J_{vic} 17.0, trans OCH₂CH=CHH), 5.22 (2H, d, J_{vic} 10.0, cis OCH₂CH= CHH), 5.07 (2H, br s, NH), 4.90 (2H, d, J_{1.2} 4.0, 1-H), 4.27 (2H, dd, J_{gem} 10.0, *J*_{6a,5} 4.5, 6a-H), 4.19 (2H, dd, *J*_{gem} 12.5, *J*_{vic} 5.5, OCHHCH=CH₂), 3.98 (2H, dd, Jgem 12.5, Jvic 5.5, OCHHCH=CH2), 3.87-3.80 (8H, m, 2-Н, 5-Н, 6b-Н, ОСНН(СН₂)₉СН₃), 3.67-3.59 (6Н, m, 3-Н, 4-Н, $OCHH(CH_2)_9CH_3$), 1.62–1.54 (8H, m, 4× $OCH_2(CHH)_9CH_3$), 1.26–1.17 $(28H, m, 14 \times OCH_2(CHH)_9CH_3), 0.88 (6H, t, J_{vic} 6.0, OCH_2(CH_2)_9CH_3).$ ¹³C NMR (125 MHz, CDCl₃): δ 158.0 (NCON), 137.4 (C_{ipso}), 133.5 (OCH₂CH=CH₂), 128.9, 128.2, 126.0 (C-Ar), 117.9 (OCH₂CH=CH₂), 101.2 (CHPh), 98.1 (C-1), 82.3, 78.0, 72.8, 69.0, 68.7, 62.9, 54.7 (C-2, C-3, C-4, C-5, C-6, OCH₂CH=CH₂, OCH₂(CH₂)₉CH₃), 31.9, 30.3, 29.7-29.3, 26.0, 22.7 (OCH₂(CH₂)₉CH₃), 14.1 (OCH₂(CH₂)₉CH₃). MS (MALDI TOF): *m*/*z* 971.38 [M+Na]⁺. Anal. Calcd for C₅₅H₈₄N₂O₁₁: C, 69.59, H 8.92, N, 2.95. Found C, 69.37, H 8.86, N 2.90.

4.11. *N*,*N*'-Bis(1-O-allyl-4,6-O-benzylidene-2-deoxy-3-O-*n*-un-decyl-α-D-galactopyranos-2-yl)urea (36)

A solution of **34** (43.8 mg, 68.4 μ mol) in DMF (750 μ L) was cooled to 0 °C. It was then treated with 1-bromoundecane (54.3 μ L, 258 μ mol), NaH (60% dispersion in oil) (10.3 mg, 257 μ mol) and finally with NaI (5.1 mg, 33.1 μ mol). After overnight stirring at 0 °C, some drops of water were added. The mixture was diluted with CH₂Cl₂ (25 mL), heated to rt and washed with water. The organic

layer was collected, dried over anhydrous Na₂SO₄, filtered and concentrated to give a residue, that was subjected to flashchromatography (5:1 to 1:2 v/v *n*-hexane/ethyl acetate) to afford **36** (36.1 mg, 56%) as a white powder. $[\alpha]_D^{22}$ +92 (*c* 0.9 in CH₂Cl₂). $\nu_{\rm max}$ (powder) 2912, 2849, 1643, 1584, 1258, 1013 cm⁻¹. ¹H NMR (500 MHz, CDCl₃): δ 7.52-7.32 (10H, m, H-Ar), 5.85-5.77 (2H, m, OCH₂CH=CH₂), 5.55 (2H, s, CHPh), 5.21 (2H, d, J_{vic} 17.0, trans OCH₂CH=CHH), 5.13-5.07 (6H, m, 1-H, NH, cis OCH₂CH=CHH), 4.30-4.25 (4H, m, 4-H, 6a-H), 4.14-4.07 (6H, m, 2-H. 6b-H. OCHHCH=CH₂), 3.96 (2H, dd, Jgem 13.0, Jvic 6.5, OCHHCH=CH₂), 3.65 (2H, br s, 5-H), 3.62-3.56 (4H, m, 3-H, OCHH(CH₂)₉CH₃), 3.46 (2H, q, J_{gem}=J_{vic} 7.0, OCHH(CH₂)₉CH₃), 1.59-1.53 (6H, m, 3× OCH₂(CHH)₉CH₃), 1.28–1.19 (30H, m, 15× OCH₂(CHH)₉CH₃), 0.88 (6H, t, J_{vic} 6.7, OCH₂(CH₂)₉CH₃). ¹³C NMR (50 MHz, CDCl₃): δ 158.8 (NCON), 137.9 (Cinso), 133.7 (OCH2CH=CH2), 128.8, 128.0, 126.3 (C-Ar), 117.7 (OCH₂CH=CH₂), 101.0 (CHPh), 98.0 (C-1), 75.9, 73.1, 69.6, 69.1, 68.8, 62.9, 50.3 (C-2, C-3, C-4, C-5, C-6, OCH₂CH=CH₂, OCH₂(CH₂)₉CH₃), 31.9, 29.9–29.3, 26.0, 22.7 (OCH₂(CH₂)₉CH₃), 14.1 $(OCH_2(CH_2)_9CH_3)$. MS (MALDI TOF): m/z 971.16 $[M+Na]^+$. Anal. Calcd for C₅₅H₈₄N₂O₁₁: C, 69.59, H 8.92, N, 2.95. Found C, 69.30, H 8.81, N 2.89.

4.12. N,N'-Bis(1-O-allyl-3-O-benzyl-4,6-O-benzylidene-2-deoxy- α -D-galactopyranos-2-yl)urea (37)

A solution of 34 (46.1 mg, 72.0 µmol) in DMF (470 µL) was cooled to 0 °C. The solution was treated with benzvl bromide (171 uL. 1.44 mmol) and then with NaH (60% dispersion in oil) (16.2 mg, 404 umol). The mixture was stirred at 0 °C for 6 h. then treated with some drops of water, diluted with CH₂Cl₂ (25 mL) and heated to rt. The organic layer was washed with water, collected, dried over filtered and anhydrous Na₂SO₄, concentrated. Flashchromatography (99:1 to 98:2 v/v CH₂Cl₂/MeOH) afforded 37 (35.4 mg, 60%) as a white powder. $[\alpha]_{D}^{22} + 117.4 (c \ 1.0 \ in \ CH_2Cl_2)$. ν_{max} (powder) 2940, 1630, 1576, 1244, 1051, 995 cm⁻¹. ¹H NMR (500 MHz, CDCl₃): δ 7.54-7.22 (20H, m, H-Ar), 5.86-5.78 (2H, m, OCH₂CH=CH₂), 5.44 (2H, s, CHPh), 5.20 (2H, d, J_{vic} 18.0, trans OCH₂CH=CHH), 5.11 (2H, d, Jvic 10.5, cis OCH₂CH=CHH), 5.08 (2H, d, J_{1,2} 3.5, 1-H), 5.06 (2H, br s, NH), 4.51 (4H, br s, CH₂Ph), 4.30 (2H, br s, 2-H), 4.24 (2H, d, Jgem 12.0, 6a-H), 4.14-4.09 (4H, m, 4-H, OCHHCH=CH₂), 3.99 (2H, d, Jgem 12.0, 6b-H), 3.95 (2H, dd, Jgem 12.5, Jvic 6.0, OCHHCH=CH₂), 3.61 (2H, br d, J_{3,2} 11.0, 2-H), 3.57 (2H, s, 5-H). ¹³C NMR (100 MHz, CDCl₃): δ 158.4 (NCON), 138.5, 137.9 (C_{ipso}), 133.7 (OCH₂CH=CH₂), 128.8-126.3 (C-Ar), 117.7 (OCH₂CH=CH₂), 101.1 (CHPh), 98.0 (C-1), 75.7, 73.2, 70.8, 69.5, 68.8, 62.9, 50.2 (C-2, C-3, C-4, C-5, C-6, OCH₂CH=CH₂, OCH₂Ph). MS (MALDI TOF): *m*/*z* 843.18 [M+Na]⁺. Anal. Calcd for C₄₇H₅₂N₂O₁₁: C, 68.76, H 6.38, N, 3.41. Found C, 68.42, H 6.53, N 3.32.

4.13. *N*,*N*'-Bis(1-O-allyl-4,6-O-benzylidene-2-deoxy-3-O-methyl- α -D-galactopyranos-2-yl)urea (38)

A solution of **34** (38.9 mg, 60.8 µmol) in DMF (400 µL) was cooled to 0 °C and treated with CH₃I (75.8 µL, 1.22 mmol) and then with NaH (60% dispersion in oil) (6.8 mg, 170 µmol). After 7 h stirring at 0 °C, some drops of water were added. The mixture was diluted with CH₂Cl₂ (25 mL) and heated. The organic layer was washed with water, collected, dried over anhydrous Na₂S₂O₄, filtered and concentrated. The residue was subjected to flash-chromatography (99:1 to 98:2 v/v CH₂Cl₂/MeOH) to give **38** (24.6 mg, 61%) as a white powder. $[\alpha]_{D}^{D^2}$ +122.7 (*c* 2.0 in CH₂Cl₂). ν_{max} (powder) 2915, 1639, 1585, 1258, 1050, 1015 cm⁻¹. ¹H NMR (500 MHz, CDCl₃): δ 7.54–7.32 (10H, m, H–Ar), 5.88–5.80 (2H, m, OCH₂CH=CH₂), 5.57 (2H, s, CHPh), 5.24 (2H, dd, *J_{vic}* 17.0, *J_{gem}* 1.0, *trans* OCH₂CH=CHH), 5.16–5.09 (6H, m, 1-H, NH, *cis* OCH₂CH=CHH), 4.34 (2H, d, *J*_{4,3} 3.0, 4–H), 4.26 (2H, dd, *J_{gem}* 12.0, *J*_{6a,5} 1.5, 6a-

H), 4.21 (2H, br s, 2-H), 4.13 (2H, dd, J_{gem} 13.0, J_{vic} 5.5, OCHHCH= CH₂), 4.07 (2H, dd, J_{gem} 12.0, $J_{6b,5}$ 1.0, 6b-H), 3.99 (2H, dd, J_{gem} 13.0, J_{vic} 5.5, OCHHCH=CH₂), 3.65 (2H, br s, 5-H), 3.55 (2H, dd, $J_{3,2}$ 10.5, $J_{3,4}$ 3.0, 3-H), 3.44 (6H, s, OCH₃). ¹³C NMR (125 MHz, CDCl₃): δ 158.6 (NCON), 137.8 (C_{ipso}), 133.6 (OCH₂CH=CH₂), 128.8, 128.1, 126.4 (C-Ar), 117.7 (OCH₂CH=CH₂), 101.0 (CHPh), 97.9 (C-1), 72.3, 69.5, 68.9, 62.8, 56.7, 50.2 (C-2, C-3, C-4, C-5, C-6, OCH₂CH=CH₂, OCH₃). MS (MALDI TOF): m/z 691.09 [M+Na]⁺. Anal. Calcd for C₃₅H₄₄N₂O₁₁: C, 62.86, H 6.63, N, 4.19. Found C, 62.72, H 6.69, N 4.15.

4.14. General procedure for ¹H NMR titration

A measured amount of CDCl₃, that was freshly dried over 4 Å molecular sieves, was added to a weighed amount of neosaccharide (**36–41**) in a NMR tube. ¹H NMR data were collected at 298 K and 500 MHz. A further measured amount of solvent was added and, after mixing, the ¹H NMR spectrum was recorded again. The procedure was iterated until signal to noise ratio obtained after 32 scans was judged unsatisfactory.

4.15. General procedure for organogelation testing

The organogelation ability of the neosaccharide (**33–38**) was tested at a starting concentration of 5% wt/vol in a glass vial. Solvents used were dried over 4 Å molecular sieves. After a 60 s thermic (60 °C), ultrasonic (37 kHz) or combined thermicultrasonic (60 °C-37 KHz) stimulus, the vial was left standing for some minutes at rt and then inverted to check gel formation. Gelator-solvent couples that gave a positive response to the inversion test, were evaporated to dryness and the procedure was then repeated at a lower concentration. The process was iterated until no gel formation was observed. Minimum gelator concentration was recorded as the lowest gelator concentration for which an unstable gel (gel or part of the gel felt apart during inversion test) was formed.

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