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A Urea-Linked Glucosamine Dimer as a Building Block for the Synthesis of Linear and Cyclic Neosaccharides

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A novel urea-linked glucosamine dimer was obtained through a modification of the standard oxazolidinone closure reaction on a 2,3-amino alcohol monomer and fully characterized by NMR spectroscopy and by molecular mechanics and dynamics techniques. A mechanism was proposed for the dimerization reaction that was based on the formation of a 2,3-bis[(*p*-nitrophenoxy)carbonyl] intermediate. Chemoselective manipulations on the orthogonal protecting group pattern of the dimer – especially on its unprecedented oxazolidinone–urea–oxazolidinone system – gave an alcohol building block that was useful for access to higher linear and cyclic neosaccharides. The conformational features and 3D-characterization of a novel carbamate-linked neodisaccharide macrocycle was accomplished through molecular mechanics and dynamics calculations.

Introduction

Oligosaccharides and glycoconjugates play a central role in many biological processes, including cellular recognition phenomena. For this reason, the synthesis of biologically relevant carbohydrates is a topic of wide interest in sugar chemistry.[1] In the last decade, increasing effort was also dedicated to obtaining sugar mimics. These molecules, usually termed glycomimetics, resemble carbohydrates but have some structural differences.[2] They are very interesting compounds because they can be recognized in biological processes involving carbohydrates, but show a different response due to the structural modification.

Recently, researchers have focused their synthetic efforts on the obtainment of compounds – termed pseudosaccharides – having the acid-labile glycosidic bonds substituted with non-acetal linkages. Among these compounds, urea-linked pseudosaccharides captured an increasing share of interest in the last decade[3] due to the occurrence of these linkages in natural antibiotics such as glycocinnamoylspermidines[4] as well as their potential application in the field of aminoglycosides.[5] Most urea-linked pseudosaccharides have a tether involving at least one anomeric position, and are typically obtained from unstable glycosyl isocyanates by reaction with an amine.[3a,3d,3e,3g] Very recently, alternative methods were developed that employ the reaction of Steyermark's glycosyl-1,2-oxazolidinone[3h] or glycosyl trichloroacetamides with an amine.[3k] Sugar carboxylic acids were also used in the Curtius rearrangement,[3j] in the presence of a nucleophile, to afford both carbamato- and urea-linked pseudosaccharides. A particular area of interest in glycomimetics is that of neosaccharides, which are oligosaccharides linked together without using the anomeric centre.[6] To the best of our knowledge, urea-linked neosaccharides have seldom been reported,[3b,3f,3j,3k] and have been synthesized according to only two methods. The first was based on the acid-catalysed addition of water to diglycosylcarbodiimides, which were in turn synthesized by the Staudinger/aza-Wittig reaction of a protected azide with a sugar isothiocyanate in the presence of triphenylphosphane (Scheme 1a).[3b] Alternatively, neosaccharides have been obtained by coupling of per-*O*-acetylated sugar isocyanates with amino sugars (Scheme 1b).[3f] Herein, we report a method of accessing a novel class of neosaccharides starting from an unprecedented urea-linked glucosamine dimer obtained from amino alcohol **1** through a modification of the known[7] oxazolidinone closure reaction.

Results and Discussion

Glucosamine Dimerization

The standard conditions used to protect a 2,3-amino alcohol sugar derivative as its oxazolidinone uses excess 4-nitrophenyl chloroformate (NPCC) at 0 °C for 3 h, producing a mixture of the desired oxazolidinone and uncyclized carbamate that is converted into the fully protected material by an additional step with Amberlyst IR-120 Na ion-exchange resin.[7b] We studied the dependence of the reaction of **1** – available from *N*-acetyl glucosamine in three standard steps – [8] on the temperature of the reaction. By con-

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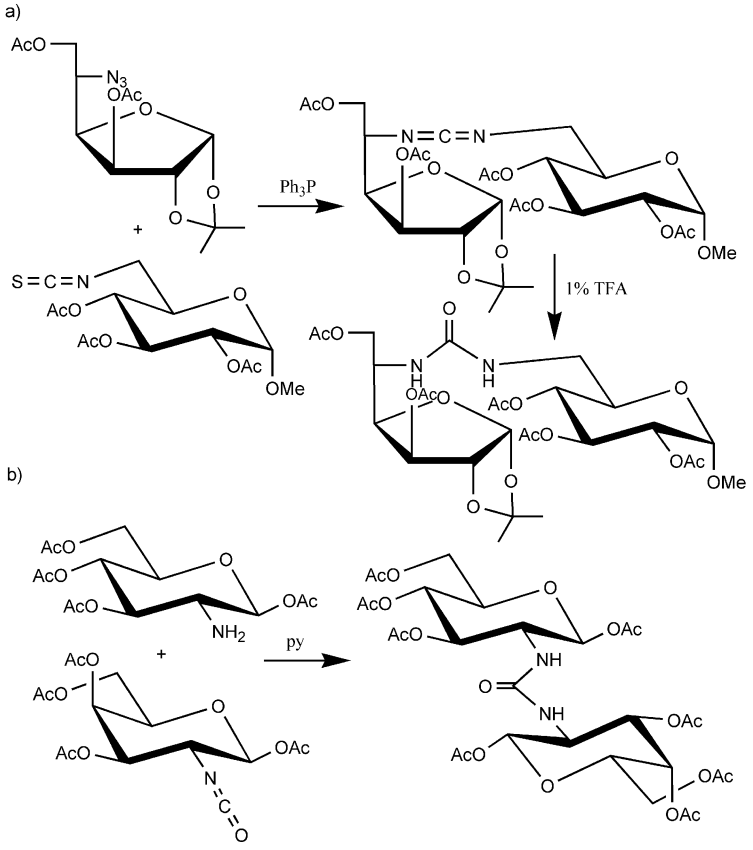


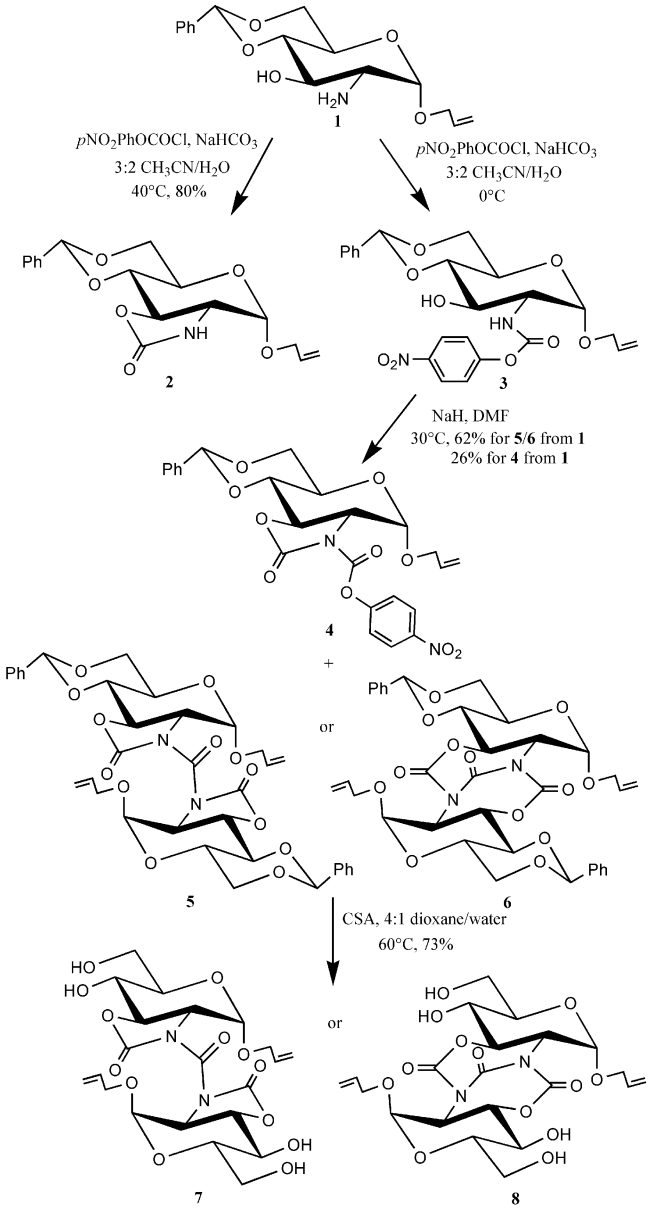
Scheme 1. Literature examples of urea-linked neosaccharide synthesis.

ducting the reaction at 40 °C, no uncyclized carbamate **3** was detected by ^{1}H NMR analysis of the crude mixture, and 2,3-oxazolidinone **2** was recovered in 80% isolated yield. In contrast, at 0 °C, only uncyclized carbamate **3** was obtained when the reaction was conducted for short times (Scheme 2 and Table 1). Compound **3** was recovered by simple extraction and then treated with sodium hydride in *N*,*N*-dimethylformamide (DMF) at 30 °C. No oxazolidinone **2** was recovered, whereas a new compound was isolated as the major product (62% yield over two steps) together with *N*-aryloxycarbonyl-oxazolidinone **4** (26% from **1**).

^{1}H NMR spectra of the unknown compound presented a single set of carbinolic signals, with those from H-2 and H-3 downfield shifted at δ = 3.99 and 4.94 ppm, respectively. The ^{13}C NMR spectrum was characterized by two signals at δ = 150.4 and 150.0 ppm, with the first signal intensity approximately double that of the second. The MALDI-MS spectrum gave a [M + Na$^+$] peak at *m*/*z* = 715. According to these data, a C_2-symmetric dimeric structure could be hypothesized, with two 2,3-oxazolidinone-protected glucosamines linked by an ureido bridge (see **5**). An alternative, less probable hypothesis could be a structure with two glucosamines linked by both an ureido and two carbamate bridges (see **6**). To assign an unequivocal structure to the new compound, the benzylidene rings were cleaved with CSA in dioxane/water to afford the water-soluble tetraol **7/8** (73% yield), which was subjected to detailed NMR analysis and molecular mechanics and dynamics calculations to discriminate between the two possible structures and, in addition, to evaluate the conformational behavior of the novel neosaccharide in aqueous solution.

Ring conformations have been defined by the analysis of $^3J_{H,H}$ coupling constants obtained from one-dimensional ^{1}H NMR and two dimensional DQF-COSY spectra, and supported by analysis of the inter-residual NOE contacts present in the T-ROESY spectrum. GlcN residues were found in the $^4C_1$ chair conformation in which carbon atoms C-4 and C-1 are, respectively, above and below the plane defined by carbons C-2, C-3, C-5, and the intra-ring oxygen O-5. Due to the symmetry of the spectra it was not possible to distinguish between potential intra and inter-residual NOE contacts. Moreover, the pattern of NOEs were those typical of an α-configured glucopyranose residue and not indicative of any particular spatial contact between the two symmetric units.

On the other hand, the dependence of long range coupling constants on dihedral angles is well known, and the general behavior is described by the Karplus equation in six-membered rings. A number of empirical correlations between the magnitude of these coupling constants and the geometric features of the chemical structure have been established; these studies have concluded that $^3J_{C,H}$ coupling is most significantly affected.[9] Taking into account the dif-



Scheme 2. Synthesis of urea-linked neodisaccharide from amino alcohol **1**.

Table 1. Oxazolidinone **2** versus uncyclized carbamate **3** formation from **1** with NPCC (5 equiv.) and $NaHCO_3$ (5 equiv.) in 2:3 (v/v) H_2O/CH_3CN.

Entry	*T* [°C]	Time [min]	**2/3**[a]
1	40	30	100:0
2	20	180	19:81
3	0	180	17:83
4	0	120	6:94
5	0	50	0:100
6	0	30	0:100

[a] Percent molar ratio determined by ^1H NMR analysis of the crude mixture.

ferences in the spatial orientation of the bridges with respect to the sugar moieties in **7** and in **8**, long range coupling constants $^3J_{C,H}$ across the carbonyl of these groups were determined from two different NMR experiments: J-HMBC and HSQMBC. The former provides cross peaks J-scaled in the carbon dimension, and can be used for determination of CH long-range coupling constants via splitting in *F*1,[10] whereas the latter technique provides cross peaks J-scaled in *F*2.[11] Relevant data obtained from these experiments are presented in Table 2. To check which structure (**7** or **8**) best match these data, both were constructed and subjected to extensive molecular mechanics and molecular dynamics calculations with Amber* force field, followed by the calculation of weighted averages heteronuclear long-range coupling constants; the results were then compared to the experimental values. The whole conformation of structure **7** is essentially defined by the relative orientation of the two sugar moieties around the ureido bridge, and a key step was the definition of the geometry around the partial double bonds of this group. Several maps were calculated, taking into account the possible orientations of the allylic groups (not shown) and different orientations of the 2,3-oxazolidinone-glucosamines with respect to the ureido bridge. The resulting adiabatic energy maps are displayed in Figure 1. These surfaces provided a rough estimation of the conformational states that could be adopted. It was ob-

Table 2. Experimental and theoretical values for selected $^3J_{C,H}$ coupling constants [Hz] of structures **7** and **8**.

Coupling constant	**7/8** (NMR data)	**7** (MD data)[a]	**8** (MD data)[a]
$^3J_{CO\ ureido,\ H-2}$	1.6/1.7[b]	1.6	5.1
$^3J_{CO\ carbamate,\ H-2}$	absent	0.9	6.5
$^3J_{CO\ carbamate,\ H-3}$	absent	0.9	7.7

[a] The values correspond to the weighted average $^3J_{C,H}$ coupling constant calculated from the molecular dynamics simulation. [b] The two values correspond to the $^3J_{C,H}$ coupling constants obtained from HSQMBC and J-HMBC experiments, respectively.

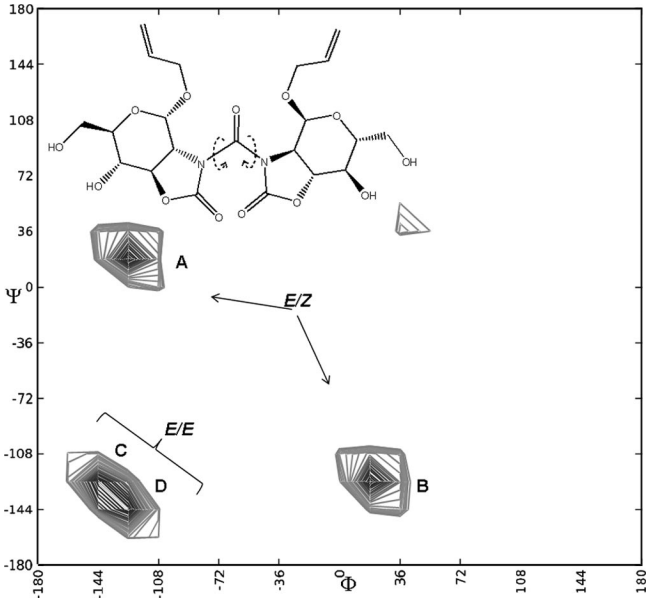


Figure 1. Relaxed energy maps for the symmetric dihedral angles around the partial double bond of the ureido bridges in **7**.

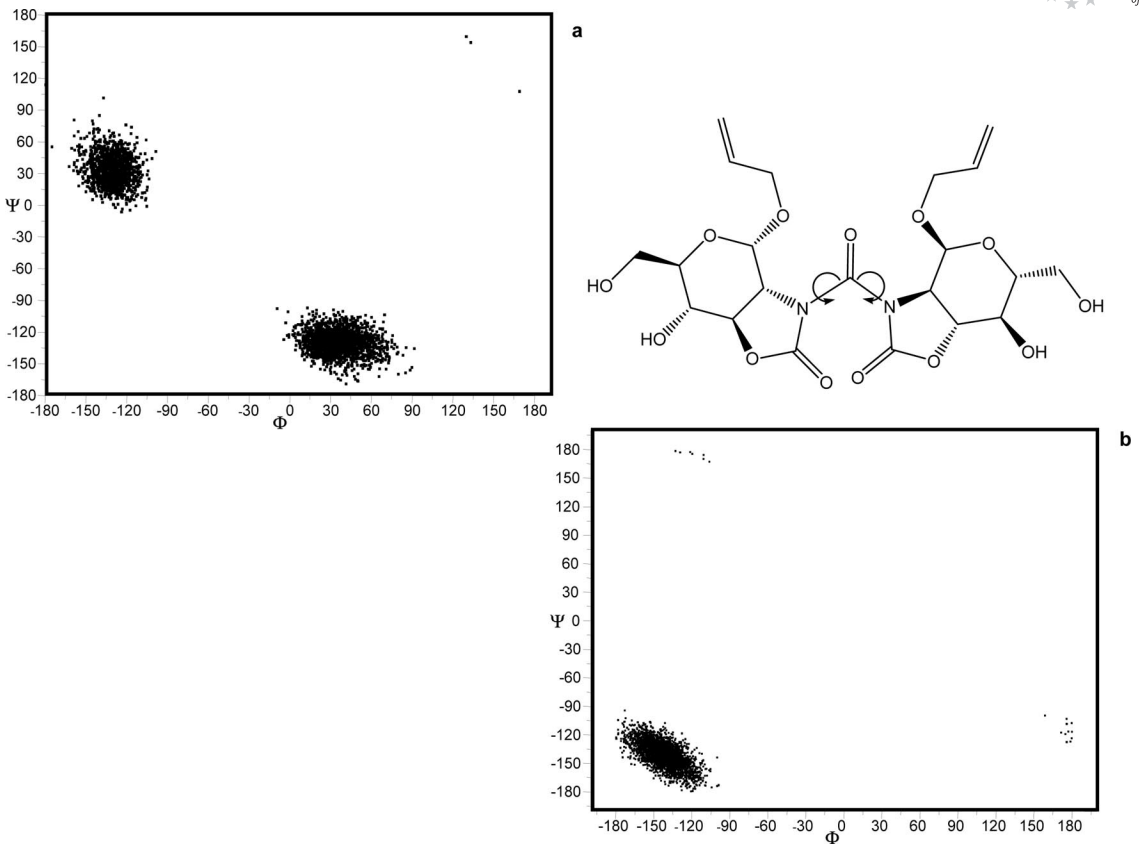


Figure 2. Scatter plots of Φ versus Ψ values of **7** starting from minima (a) A/B and (b) C/D obtained from molecular mechanics calculations.

served that the energy maps covered a large area, representing a high number of conformational states. The lowest energy regions were located around two symmetric groups of energy minima separated by a low energy barrier (below 2 kJ/mol): minima A/B located around 18/–128 and –128/18, respectively, corresponding to symmetric isomers with *E*,*Z* and *Z*,*E* geometry around the partial double bond of the ureido bridge, and minima C/D located around –144/–130 and –130/–144, respectively, corresponding to *E*,*E* disposition around the partial ureido double bond. The conformational space available for the regions was then investigated by molecular dynamics simulations. Computational models were generated using the two groups of energy minima obtained with the molecular mechanics approach. The Φ/Ψ scatter plots of the torsion angles for both minima A/B and C/D are displayed in Figure 2.

The simulation confirmed the existence, for A/B, of a compact energy-well located in the region spanning the two minima and predicted by the molecular mechanics calculations; for minima C/D, during the molecular dynamics simulation an oscillation between the two predicted values was observable starting from both C and D minima, as confirmed by the analysis of the scatter plot. It is worth noting that no interconversion between the two groups of minima was observed. A further examination of these data provided other useful information. Ensemble average inter-proton

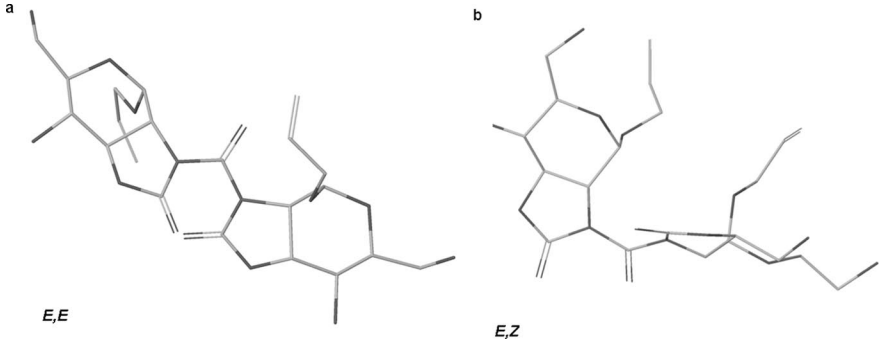
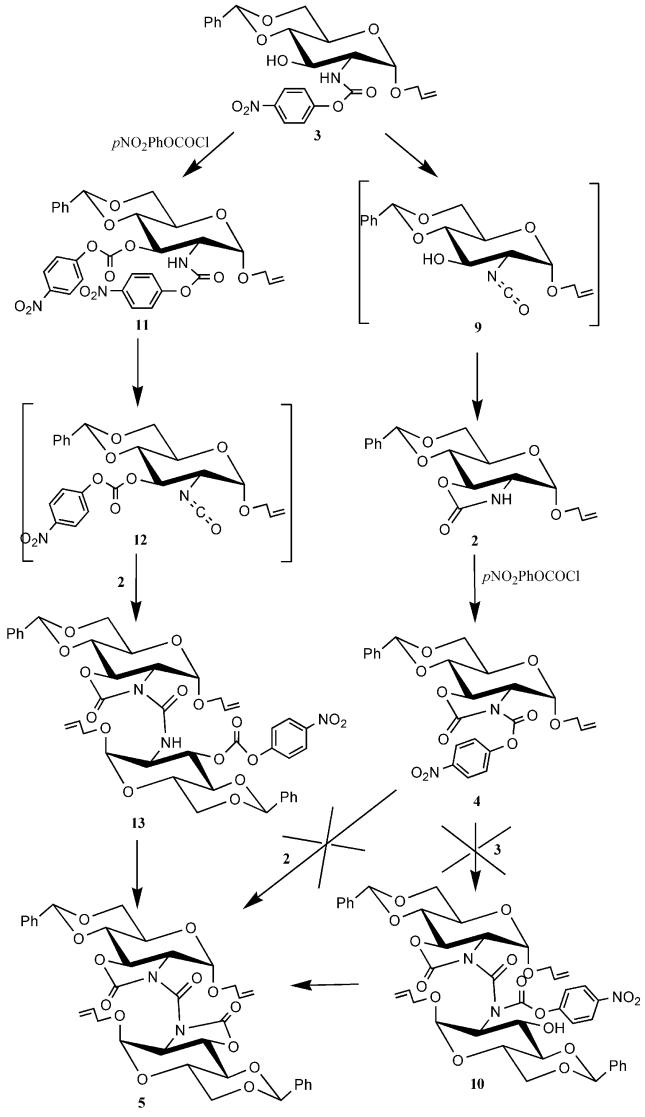


Figure 3. View of representative structures of **7** with (a) *E*,*E* and (b) *E*,*Z* disposition around the ureido bridge.

distances were extracted and translated into predicted NOEs by a full-matrix relaxation approach. The predicted NOEs were then compared to those experimentally collected to assess the reliability of the simulation data, and the corresponding average distances obtained for the simulation from <r-6> values were compared to those collected experimentally. A satisfactory agreement was observed between the calculated and the experimental values (data not shown). Average-weighted $^3J_{C,H}$ coupling constants were then calculated for the lowest energy families corresponding to the local minima A/B and C/D (Table 2). The experimental values were in agreement with the conformations adopted by both families, and also confirmed that, in both cases, the predicted coupling constant for H-2 and H-3 with oxazolidinone carbonyl was close to zero. Snapshots of the most representative conformers of **7** corresponding to the two groups of minima are depicted in Figure 3. *E*,*Z*/*Z*,*E* and *E*,*E* conformers adopted conformations with different shapes. Conformers with *E*,*E* geometry assumed a more extended shape in which a significant cleft was observable. On the other side, conformers with a *E*,*Z* geometry adopted a more constricted spatial disposition that was characterized by a contracted structure with an 'L'-shaped conformation corresponding to a quasi-perpendicular disposition of the sugar moieties.

The same molecular mechanics and dynamics calculations protocol was also used to characterize the structure **8**. Average-weighted $^3J_{C,H}$ coupling constants (Table 2) were calculated from the molecular dynamics simulation and compared with the experimental results. These data establish that – as expected – only **7** was in agreement with experimental data. The formation of **8** was excluded because the calculated data were in discordance with those measured in the NMR experiments. In fact, in the case of **8**, predictable and strong cross-peaks between the carbonyl of the ureido bridge with H-2 and H-3 as well as of the carbonyl of carbamate groups with H-2 should have been visible due to their high long-range heteronuclear coupling constant.



Scheme 3. Proposed mechanism for the formation of **5**.

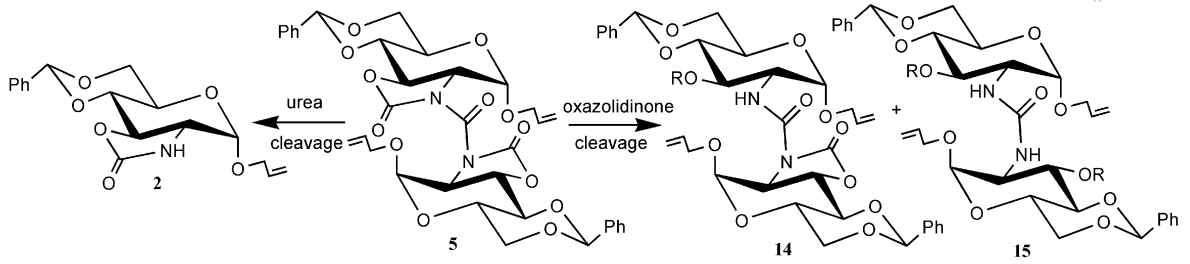
Mechanism Investigation

The dimerization process of amino alcohol **1** into **5** is strictly dependent on the presence of excess NPCC in the reaction mixture. Indeed, uncyclized carbamate **3** was recovered pure by column chromatography (87% yield from **1**) and then subjected to NaH/DMF treatment. No dimer **5** was detected in this case. The reaction produced oxazolidinone **2** exclusively in 91% yield, in accordance with similar known transformations.[7d,8,12] On the basis of this result, a mechanism was hypothesized in which, after the initial formation of oxazolidinone **2** through the reactive isocyanate **9**, *N*-aryloxycarbonyl-oxazolidinone **4** is produced and then coupled to **3** (Scheme 3).

Nonetheless, by mixing pure **3** and **4** in the presence of NaH in DMF, no dimer species were detected. Moreover, by treating pure **2** under dimerization conditions in the presence of excess NPCC, only compound **4** was recovered together with starting oxazolidinone. These results suggested that this pathway had to be discarded. Instead, the formation of derivative **11** was proposed as a pathway that operates in competition with oxazolidinone formation. Compound **11** could then be converted into isocyanate **12**, which, unlike **9**, cannot undergo the intramolecular reaction. On the contrary, it can be subjected to nucleophilic addition by oxazolidinone **2** to form a dimer that could easily react further to give the final product **5**. Indeed, when pure compound **11**[13] was mixed with **2** in the presence of excess NaH, dimer **5** was obtained exclusively (95% isolated yield). However, a more in-depth study is in progress to develop the details of the proposed mechanism.

Chemoselective Reactions on the Oxazolidinone–Urea–Oxazolidinone System

A case study of selective reactions on the oxazolidinone–urea–oxazolidinone system of dimer **5** was then pursued. To the best of our knowledge, this system is unprecedented.



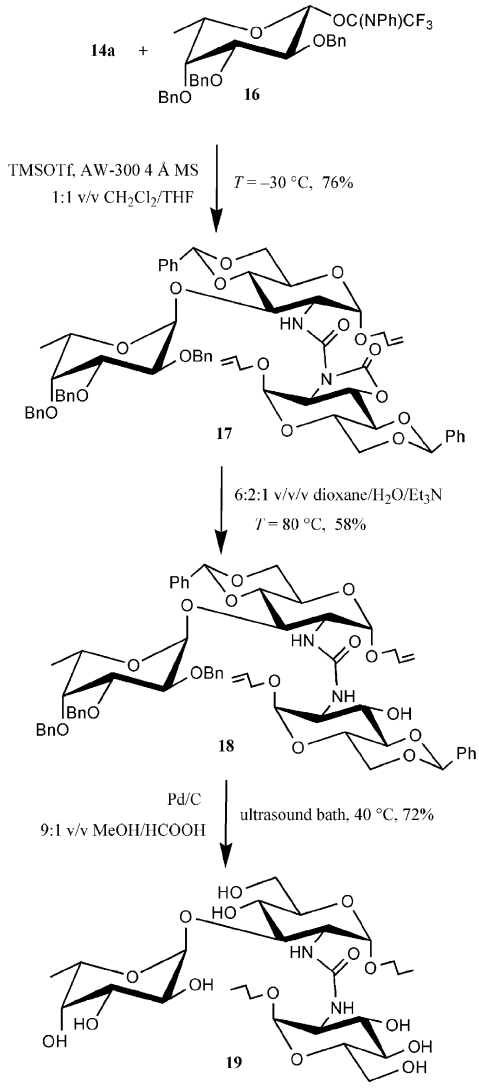
Scheme 4. Chemoselective cleavage of the oxazolidinone–urea–oxazolidinone system **5**.

Table 3. Chemoselective cleavage of the oxazolidinone–urea–oxazolidinone system **5**.

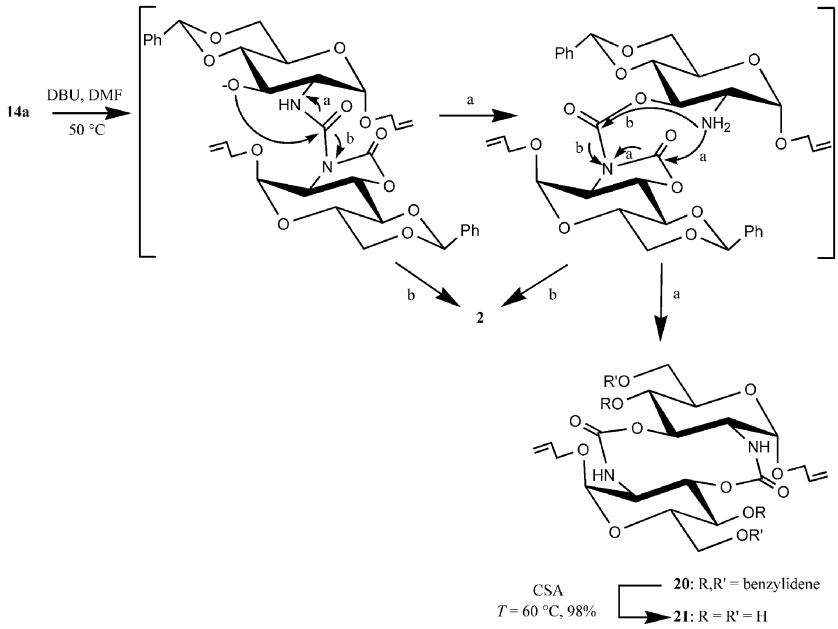
Entry	Reaction conditions	Products[a]
1	LiOH, H_2O_2, 7:2 v/v THF/H_2O, –40 °C to 0 °C, 15 min	**2** (42%), **14a** R = H (20%)
2	LiOH, LiCl, 3:1 v/v THF/H_2O, 0 °C, 75 min	**2** (41%), **14a** R = H (33%), **15a** R = H (21%)
3	NaOMe, 9:1 v/v CH_2Cl_2/MeOH, –60 °C, 40 min	**14b** R = COOMe (34%), **15b** R = COOMe (34%)
4	14:6:1 v/v/v $CHCl_3$/MeOH/Et_3N, room temp., 2 d	**15b** R = COOMe (54%)
5	14:6:1:1 v/v/v/v $CHCl_3$/1,4-dioxane/H_2O/Et_3N, room temp., 2 d	**14a** R = H (81%)
6	6:2:1 v/v/v 1,4-dioxane/H_2O/Et_3N, 80 °C, 14 h	**15a** R = H (76%)

[a] Isolated yield.

Mild conditions were sought for the chemoselective cleavage of one or both oxazolidinone rings with respect to the ureido bridge (Scheme 4). Solvolysis of **5** was conducted under several conditions, as indicated in Table 3. Reaction conditions employed for the chemoselective deprotection of *N*-acetyl-2,3-*N*,*O*-oxazolidinone of glucosamine[14] gave unsatisfactory results on **5** (entries 1–3). Interestingly, chemoselective cleavage of one or both carbamates with respect to the ureido bridge was accomplished by employing mild Et_3N-mediated hydrolysis or methanolysis. The C_2-symmetric urea-linked neodisaccharide **15a** was obtained in 76% yield by reaction of **5** in 6:2:1 (v/v/v) 1,4-dioxane/H_2O/Et_3N at 80 °C (entry 6). A very interesting compound – alcohol **14a** – was obtained in 81% yield by reaction in 14:6:1:1 (v/v/v/v) $CHCl_3$/1,4-dioxane/H_2O/Et_3N (entry 5). This compound could be used as a glycosyl acceptor to access higher neooligosaccharides. For example, a glycosylation reaction between **14a** and donor **16**[15] afforded neotrisaccharide **17** (76%), which was deprotected in two steps (Scheme 5). A chemoselective cleavage of the residual oxazolidinone ring was possible under the conditions developed above. Indeed, hydrolysis in 6:2:1 (v/v/v) dioxane/water/Et_3N gave alcohol **18** (58%). A subsequent transfer hydrogenation under Perlin conditions[16] furnished water-soluble urea-linked neotrisaccharide **19** in 72% yield. Alcohol **14a** was a useful building block that could also be used to access the first representative example of a novel class of carbamate-linked macrocyclic analogues of cyclodextrins.[3j,3k,17] Indeed, when treated with 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) in DMF, **14a** gave carbamate-linked macrocycle **20** in 43% yield (51% based on recovered starting material; Scheme 6). The detection of oxazolidinone **2** as the sole by-product in the crude reaction mixture suggested that the mechanism could proceed through attack of the alcoholate ion on the ureido carbonyl group, giving the macrocycle **20** after a subsequent rearrangement of the amine intermediate (path a,a) or could lead directly to the oxazolidinone **2**



Scheme 5. Synthesis of neotrisaccharide **19**.



Scheme 6. Synthesis of carbamate-linked cyclic neodisaccharide **21**.

(path b). The latter compound could also be obtained through the amine intermediate (paths a, b). Benzylidene cleavage of **20** with CSA in 4:1 (v/v) 1,4-dioxane/water at 60 °C afforded the water-soluble macrocycle **21** (98%). Its NMR characterization indicated a symmetric dimeric structure in which glucosamine residues were found in the $^4C_1$ chair conformation, as defined by the analysis of $^3J_{H,H}$ coupling constants. The ^{1}H NMR spectra in 9:1 (v/v) H_2O/D_2O allowed the *anti* orientation of the amide NH protons with respect to H-2 to be defined.[18]

Actually, the amide proton showed a large vicinal coupling constant ($^3J_{H,NH}$ = 9.5 Hz) with H-2 of GlcN, which restricts the torsion angle to ±162°, as calculated from the Karplus equation.[9] Taking into account the C_2-symmetry of the molecule, the *trans* disposition of the amide protons in relation to the H-2 atoms and the $^1C_4$ chair conformation, two possible low energy structures were built that differed in the relative orientation of the NH and C=O bonds (structures here named as *syn* and *anti* species).

NMR-derived data and extensive molecular mechanics and dynamics calculations with Amber* force field in GB/SA water solvation model were used to distinguish between the two conformers. NMR-derived homonuclear $^3J_{H\text{-}2,NH}$ coupling constants and heteronuclear long-range $^3J_{C,H}$ coupling constants from the ureido bridge carbonyl with H-2 and H-3 atoms were compared with average-weighted coupling constants obtained from molecular dynamics simulation performed on both candidate conformers. The data al-

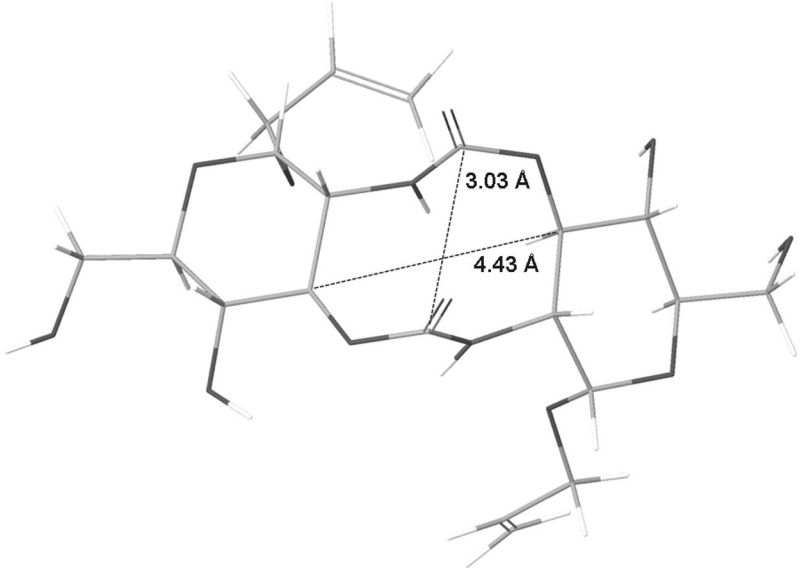


Figure 4. View of a representative conformer of **21**.

lowed us to demonstrate the exclusive existence of the *anti* species. In fact, a very satisfactory agreement was observed for the *anti* species between calculated and experimental values (Table 4), that were far from the experimental data in case of the *syn* species.

Table 4. Experimental and theoretical values for selected $^3J_{C,H}$ and $^3J_{H,H}$ coupling constants [Hz] of compound **21**.

Coupling constant	**21** (NMR data)	**21** *anti* (MD data)[a]	**21** *syn* (MD data)[a]
$^3J_{CO\ ureido,\ H\text{-}2}$	8.0	7.0	4.7
$^3J_{CO\ ureido,\ H\text{-}3}$	3.4	3.3	8.0
$^3J_{2,NH}$	9.5	9.8	6.1

[a] The values correspond to the weighted average $^3J_{C,H}$ and $^3J_{H,H}$ coupling constant calculated from the molecular dynamics simulation.

Molecular dynamics simulation also allowed us to estimate the conformational behavior of structure **21**. This cyclodextrin mimic possesses an elliptical cavity in which the major and minor axes have an average length of 4.43 and 3.03 Å, respectively (Figure 4).

Conclusions

In conclusion, the synthesis of a novel urea-tethered glucosamine neodisaccharide building block by dimerization of a simple 2,3-amino alcohol monomer through a modification of the standard oxazolidinone closure reaction has been reported. The dimer was fully characterized by NMR spectroscopy as well as by molecular mechanics and dynamics calculations. The behavior of the oxazolidinone–urea–oxazolidinone moiety of the dimer under mild solvolysis conditions was studied. The chemoselective cleavage of only one oxazolidinone afforded an alcohol building block that was used for the synthesis of a higher neoligosaccharide as well as a carbamate-bridged cyclic neosaccharide. The latter compound represents the first example of a novel class of cyclodextrin analogues. Its 3D-geometry was studied with both NMR spectroscopy and by using molecular mechanics and dynamics techniques. Work is in progress to apply the urea-dimerization approach to obtain a large family of linear and cyclic amino sugar neosaccharides as well as to develop these molecules as tools for carbohydrate-based supramolecular chemistry.

Experimental Section

General Remarks: ^{1}H and ^{13}C NMR spectra were recorded with Varian XL-200 (^{1}H: NMR 200 MHz, ^{13}C: NMR 50 MHz), Bruker DRX-400 (^{1}H NMR: 400 MHz, ^{13}C NMR: 100 MHz) or Varian INOVA 500 (^{1}H NMR: 500 MHz, ^{13}C NMR: 125 MHz) instruments in $CDCl_3$ ($CHCl_3$ as internal standard, ^{1}H NMR: $CHCl_3$ at δ = 7.26 ppm; ^{13}C NMR: $CDCl_3$ at δ = 77.0 ppm). Compounds **7**, **19** and **21** were analysed in D_2O [acetone as internal standard, ^{1}H: $(CH_3)_2CO$ at δ = 2.22 ppm; ^{13}C: $(CH_3)_2CO$ at δ = 31.0 ppm]. Extensive NMR analysis on compounds **7** and **21** were made with a Bruker-600 DRX (^{1}H NMR: 600 MHz, ^{13}C NMR: 150 MHz) instrument equipped with a cryo probe. Double quantum-filtered phase-sensitive COSY experiments were performed using spectral widths of either 3600 in both dimensions or data sets of 4096 × 256 points. Quadrature indirect dimensions were achieved through the States-TPPI method; spectra were processed by applying an unshifted Qsine function to both dimensions and the data matrix was zero-filled by a factor of two before Fourier transformation. Coupling constants were determined on a first order basis from high resolution 1D spectra or by 2D phase-sensitive DQF-COSY. TOCSY were performed with spinlock times from 20 to 100 ms, using data sets ($t1 \times t2$) of 4096 × 256 points. T-ROESY experiments were recorded using data sets ($t1 \times t2$) of 4096 × 256 points with mixing times of between 200 ms and 700 ms. Interproton distances were obtained by employing the isolated spin pair approximation as described.[19] In these homonuclear experiments, the data matrix was zero-filled in the $F1$ dimension to give a matrix of 4096 × 2048 points and was resolution-enhanced in both dimensions by a 90° shifted Qsine function before Fourier transformation. HSQC experiments were measured in the ^{1}H-detected mode via single quantum coherence with proton-decoupling in the ^{13}C domain, using data sets of 2048 × 256 points. In these heteronuclear experiments the data matrix was extended to 2048 × 1024 points using forward linear prediction extrapolation. Two different methods were used to measure long-range heteronuclear $^3J_{C,H}$ coupling constants: J-HMBC and HSQMBC. J-HMBC spectra were acquired using data sets of 4096 × 512 points transformed after zero filling to 4096 × 4096 complex points applying an unshifted cosine function to both $F1$ and $F2$ dimensions. The long-range coupling constant used for the evolution of long-range connectivities was varied from 2 to 10 Hz. For HSQMBC experiments, spectra were acquired with 8192 × 256 points transformed after zero filling to 16384 × 4096 complex points applying a cosine function to both $F1$ and $F2$ dimensions. Software TOPSPIN was used to measure homonuclear and heteronuclear coupling constants.

Positive MALDI-MS spectra were recorded with an Applied Biosystem Voyager DE-PRO MALDI-TOF mass spectrometer in the positive mode: compounds were dissolved in CH_3CN at a concentration of 1 mg/mL, and 1 μL of these solutions was mixed with 1 μL of a 20 mg/mL solution of 2,5-dihydroxybenzoic acid in 7:3 (v/v) CH_3CN/0.1 M trifluoroacetic acid. Analytical thin layer chromatography (TLC) was performed on aluminium plates precoated with Merck Silica Gel 60 F_{254} as the adsorbent. The plates were developed with 5% H_2SO_4 ethanolic solution and then heating to 130 °C. Flash chromatography was performed using Merck Kieselgel 60 (63–200 mesh).

Molecular Mechanics calculations were performed using the AMBER* force field as included in MacroModel 8.0. A dielectric constant of 80 was used. For each disaccharide structure, both Φ and Ψ were varied incrementally using a grid step of 18°, each (Φ, Ψ) point of the map was optimized using 2000 P.R. conjugate gradients. The Molecular Dynamics simulations were run by using the AMBER* force field; bulk water solvation was simulated by using MacroModel generalized Born GB/SA continuum solvent model. All simulations were performed at 300 K, structures were initially subjected to an equilibration time of 300 ps, then a 3000 ps molecular dynamic simulation was performed with a dynamic time-step of 1.5 fs, a bath constant (t) of 0.2 ps and the SHAKE protocol to the hydrogen bonds. Trajectory coordinates were sampled every picosecond, and a total of 3000 structures were collected for every simulation. Ensemble average-interproton distances were calculated using the NOEPROM program by applying the isolated spin pair approximation as described.[19] Coordinate extractions were performed with the program SuperMap, supplied with the NOEPROM package, and data was visualized with ORIGIN software.

Solvent-accessible surfaces were calculated with the Surface utility of Macromodel and with Molecular Surface displays of the Chem3D package.

Allyl 4,6-*O*-Benzylidene-2,3-*N*,*O*-carbonyl-2-deoxy-α-D-glucopyranoside (2): Compound **1** (95.4 mg, 0.310 mmol) was suspended in 2:1 (v/v) water/CH_3CN (1.12 mL) and then heated to 40 °C. $NaHCO_3$ (128 mg, 1.52 mmol) and then a solution of 4-nitrophenyl chloroformate (314 mg, 1.56 mmol) in CH_3CN (750 μL) were added. After 30 min stirring at 40 °C, the mixture was diluted with ethyl acetate (50 mL) and washed with 1 M $NaHCO_3$. The organic layer was collected, dried with anhydrous Na_2SO_4 and concentrated. Purification by flash chromatography (petroleum ether/ethyl acetate, 5:1 to 1:1 v/v) afforded **2** (82.3 mg, 80%) as a white powder. $[\alpha]_D$ = +33 (*c* = 0.3; CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.51–7.36 (m, 5 H, Ar-H), 5.91 (m, 1 H, OCH_2CH=CH_2), 5.62 (s, 1 H, C*H*Ph), 5.35 (ddd, J_{vic} = 17.2, $^4J_{H,H}$ = 3.0, J_{gem} = 1.5 Hz, 1 H, *trans* OCH_2CH=C*H*H), 5.28 (dd, J_{vic} = 10.4, J_{gem} = 1.5 Hz, 1 H, *cis* OCH_2CH=C*H*H), 5.15 (d, $J_{1,2}$ = 2.9 Hz, 1 H, 1-H), 5.07 (br. s, 1 H, NH), 4.84 (dd, $J_{3,2}$ = 11.3, $J_{3,4}$ = 10.2 Hz, 1 H, 3-H), 4.29 (m, 2 H, 6a-H, OC*H*HCH=CH_2), 4.09 (m, 2 H, 4-H, OC*H*HCH=CH_2), 3.90 (m, 2 H, 5-H, 6b-H), 3.74 (dd, $J_{2,3}$ = 11.3, $J_{2,1}$ = 2.9 Hz, 1 H, 2-H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 159.1 (N*C*OO), 136.5 (C_{ipso}), 132.8 (OCH_2CH=CH_2), 129.2, 128.3, 126.2 (C-Ar), 118.5 (OCH_2CH=CH_2), 101.4 (*C*HPh), 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, OCH_2CH=CH_2) ppm. MALDI TOF-MS: calcd. for $C_{17}H_{19}NO_6$ 333.12; found 334.16 $[M + H]^+$. $C_{17}H_{19}NO_6$ (333.12): calcd. C 61.26, H 5.75, N 4.20; found C 61.06, H 5.58, N 4.11.

Allyl 4,6-*O*-Benzylidene-2,3-*N*,*O*-carbonyl-2-deoxy-2-[(*p*-nitrophenoxy)carbonylamino]-α-D-glucopyranoside (4) and *N*,*N*′-Bis(1-*O*-allyl-4,6-*O*-benzylidene-2,3-*N*,*O*-carbonyl-2-deoxy-α-D-glucopyranos-2-yl)urea (5): Compound **1** (430 mg, 1.40 mmol) was suspended in 2:1 (v/v) water/CH_3CN (6.0 mL) and then cooled to 0 °C. $NaHCO_3$ (585 mg, 6.96 mmol) and then a solution of 4-nitrophenyl chloroformate (1.83 g, 6.80 mmol) in CH_3CN (4.0 mL) were added. After 45 min stirring at 0 °C, the mixture was diluted with ethyl acetate (300 mL) and washed with 1 M $NaHCO_3$. The organic layer was collected, dried with anhydrous Na_2SO_4 and concentrated to give a white gummy solid.

To obtain pure allyl 4,6-*O*-benzylidene-2-deoxy-2-[(*p*-nitrophenoxy)carbonylamino]-α-D-glucopyranoside (**3**) for analytical purposes, flash chromatography (petroleum ether/ethyl acetate, 15:1 to 2:1) was performed: $[\alpha]_D$ = +22.4 (*c* = 1.4; CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.25 (d, $J_{3',2'}$ = 8.8 Hz, 2 H, 2 × 3′-H *p*NO_2-Ar), 7.51–7.35 (m, 7 H, Ar-H benzylidene, 2 × 2′-H *p*NO_2-Ar), 5.94 (m, 1 H, OCH_2CH=CH_2), 5.58 (s, 1 H, C*H*Ph), 5.47 (d, $J_{H,NH}$ = 7.8 Hz, 1 H, NH), 5.35 (br. d, J_{vic} = 17.2 Hz, 1 H, *trans* OCH_2CH=C*H*H), 5.29 (br. d, J_{vic} = 10.4 Hz, 1 H, *cis* OCH_2CH=C*H*H), 5.00 (d, $J_{1,2}$ = 3.0 Hz, 1 H, 1-H), 4.30 (dd, J_{gem} = 10.2, $J_{6a,5}$ = 4.7 Hz, 1 H, 6a-H), 4.25 (dd, J_{gem} = 12.3, J_{vic} = 4.7 Hz, 1 H, OC*H*HCH=CH_2), 4.06 (dd, J_{gem} = 12.3, J_{vic} = 4.7 Hz, 1 H, OC*H*HCH=CH_2), 4.02 (m, 2 H, 2-H, 3-H), 3.89 (dt, $J_{5,4}$ = $J_{5,6b}$ = 10.2, $J_{5,6a}$ = 4.7 Hz, 1 H, 5-H), 3.78 (t, J_{gem} = $J_{6b,5}$ = 10.2 Hz, 1 H, 6b-H), 3.61 (t, $J_{4,3}$ = $J_{4,5}$ = 10.2 Hz, 1 H, 4-H), 2.58 (br. s, 1 H, OH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 155.7 (N*C*OO), 153.3, 145.1, 136.9 (3 × C_{ipso}), 133.1 (OCH_2CH=CH_2), 129.4, 128.4, 126.2, 125.1, 121.9 (C-Ar), 118.4 (OCH_2CH=CH_2), 102.0 (*C*HPh), 97.0 (C-1), 81.8, 70.2, 68.8, 68.7, 62.7, 55.7 (C-2, C-3, C-4, C-5, C-6, OCH_2CH=CH_2) ppm. MALDI TOF-MS: calcd. for $C_{23}H_{24}N_2O_9$ 472.15; found 495.28 $[M + Na]^+$. $C_{23}H_{24}N_2O_9$ (472.15): calcd. C 58.47, H 5.12, N 5.93; found C 58.30, H 5.01, N 5.85.

The crude gummy solid was dissolved in DMF (6.4 mL) and heated to 30 °C. NaH (60% dispersion in oil, 261 mg, 6.53 mmol) was then added portion-wise to avoid sudden overheating. The yellow mixture was stirred for 45 min at 30 °C, then cooled to 0 °C and treated dropwise with a little water until production of gas ceased. The mixture was diluted with CH_2Cl_2 (150 mL) and washed with water. The organic layer was collected, dried and concentrated. The residue was subjected to flash chromatography (hexane/ethyl acetate, 6:1 to 2:3) to give **4** (179 mg, 26%) as the first eluted compound, as white amorphous crystals. $[\alpha]_D$ = +64.7 (*c* = 1.0; CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.29 (d, $J_{3',2'}$ = 9.1 Hz, 2 H, 2 × 3′-H *p*NO_2-Ar), 7.51–7.38 (m, 7 H, benzylidene, 2 × 2′-H *p*NO_2-Ar), 5.88 (m, 1 H, OCH_2CH=CH_2), 5.64 (s, 1 H, C*H*Ph), 5.63 (d, $J_{1,2}$ = 2.7 Hz, 1 H, 1-H), 5.32 (br. d, J_{vic} = 17.2 Hz, 1 H, *trans* OCH_2CH=C*H*H), 5.22 (br. d, J_{vic} = 10.3 Hz, 1 H, *cis* OCH_2CH=C*H*H), 4.90 (t, $J_{3,2}$ = $J_{3,4}$ = 11.0 Hz, 1 H, 3-H), 4.30 (m, 2 H, 6a-H, OC*H*HCH=CH_2), 4.11 (m, 2 H, 4-H, OC*H*HCH=CH_2), 4.05 (dd, $J_{2,3}$ = 11.0, $J_{2,1}$ = 2.7 Hz, 1 H, 2-H), 3.92 (m, 2 H, 5-H, 6b-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 154.3, 145.8 (2 × C_{ipso}), 150.3, 148.9 (2 × N*C*OO), 136.2 (C_{ipso} benzylidene), 132.7 (OCH_2CH=CH_2), 129.3, 128.4, 126.1, 125.4, 122.2 (C-Ar), 118.8 (OCH_2CH=CH_2), 101.5 (*C*HPh), 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, OCH_2CH=CH_2) ppm. MALDI TOF-MS: unstable. $C_{24}H_{22}N_2O_{10}$ (498.13): calcd. C 57.83, H 4.45, N 5.62; found C 57.70, H 4.40, N 5.56.

Second eluted compound **5** (299 mg, 62%) was recovered as a white powder. $[\alpha]_D$ = +60 (*c* = 0.9; CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.50–7.36 (m, 5 H, Ar-H), 5.85 (m, 1 H, OCH_2CH=CH_2), 5.61 (s, 1 H, C*H*Ph), 5.53 (d, $J_{1,2}$ = 2.8 Hz, 1 H, 1-H), 5.31 (ddd, J_{vic} = 17.3, $^4J_{H,H}$ = 3.1, J_{gem} = 1.3 Hz, 1 H, *trans* OCH_2CH=C*H*H), 5.22 (ddd, J_{vic} = 10.4, $^4J_{H,H}$ = 2.4, J_{gem} = 1.3 Hz, 1 H, *cis* OCH_2CH=C*H*H), 4.94 (dd, $J_{3,2}$ = 11.4, $J_{3,4}$ = 10.0 Hz, 1 H, 3-H), 4.28 (m, 2 H, 6a-H, OC*H*HCH=CH_2), 4.07 (m, 2 H, 4-H, OC*H*HCH=CH_2), 3.99 (dd, $J_{2,3}$ = 11.4, $J_{2,1}$ = 2.8 Hz, 1 H, 2-H), 3.92 (m, 2 H, 5-H, 6b-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 150.4 (O*C*ON), 150.0 (N*C*ON), 136.4 (C_{ipso}), 132.3 (OCH_2CH=CH_2), 129.4, 128.4, 126.2 (C-Ar), 118.0 (OCH_2CH=CH_2), 101.4 (*C*HPh), 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, OCH_2CH=CH_2) ppm. MALDI TOF-MS: calcd. for $C_{35}H_{36}N_2O_{13}$ 692.22; found 715.25 $[M + Na]^+$. $C_{35}H_{36}N_2O_{13}$ (692.22): calcd. C 60.09, H 5.24, N 4.04; found C 60.49, H 5.09, N 3.97.

***N*,*N*′-Bis(1-*O*-allyl-2,3-*N*,*O*-carbonyl-2-deoxy-α-D-glucopyranos-2-yl)urea (7):** Compound **5** (44.7 mg, 64.6 μmol) was dissolved in 4:1 (v/v) 1,4-dioxane/water (1.2 mL) and then treated with (±)-camphor-10-sulfonic acid (35.0 mg, 151 μmol). After 4 h stirring at 60 °C, silica gel (500 mg) was added and the mixture was evaporated. The residue was subjected to flash chromatography (chloroform/methanol, 94:6 to 90:10) to afford **7** (24.3 mg, 73%) as a white powder. $[\alpha]_D$ = +134 (*c* = 0.8; H_2O). ^{1}H NMR (400 MHz, D_2O): δ = 5.86 (m, 1 H, OCH_2CH=CH_2), 5.54 (d, $J_{1,2}$ = 2.9 Hz, 1 H, 1-H), 5.32 (dd, J_{vic} = 17.3, J_{gem} = 1.1 Hz, 1 H, *trans* OCH_2CH=C*H*H), 5.25 (dd, J_{vic} = 10.5, J_{gem} = 0.8 Hz, 1 H, *cis* OCH_2CH=C*H*H), 4.81 (dd, $J_{3,2}$ = 12.0, $J_{3,4}$ = 10.0 Hz, 1 H, 3-H), 4.30 (dd, J_{gem} = 13.2, J_{vic} = 5.0 Hz, 1 H, OC*H*HCH=CH_2), 4.19 (dd, $J_{2,3}$ = 12.0, $J_{2,1}$ = 2.9 Hz, 1 H, 2-H), 4.11 (m, 2 H, 4-H, OC*H*HCH=CH_2), 3.86 (m, 2 H, 6a-H, 6b-H), 3.73 (m, 1 H, 5-H) ppm. ^{13}C NMR (50 MHz, D_2O): δ = 153.4 (O*C*ON), 149.8 (N*C*ON), 134.0 (OCH_2CH=CH_2), 118.8 (OCH_2CH=CH_2), 94.3 (C-1), 78.6 (C-3), 75.3 (C-5), 69.6 (OCH_2CH=CH_2), 67.9 (C-4), 60.6 (C-2), 60.4 (C-6) ppm. MALDI TOF-MS: calcd. for $C_{21}H_{28}N_2O_{13}$ 516.16; found 539.32 [M +

Na]$^+$. $C_{21}H_{28}N_2O_{13}$ (516.16): calcd. C 48.84, H 5.46, N 5.42; found C 48.77, H 5.28, N 5.35.

Allyl 4,6-*O*-Benzylidene-2-deoxy-3-(*p*-nitrophenoxycarbonyl)-2-[(*p*-nitrophenoxy)carbonylamino]-α-D-glucopyranoside (11): Compound **1** (143 mg, 0.466 mmol) was treated as described above to give crude **3**, which was then dissolved in DMF (3.3 mL) and treated at 5 °C with DMAP (28.5 mg, 0.233 mmol). After 1 h stirring at 5 °C, the solution was diluted with CH_2Cl_2 (50 mL) and washed with 0.1 M HCl and water. The organic layer was collected, dried and concentrated. The residue was subjected to column chromatography (toluene/ethyl acetate, 12:1 to 9:1) to give **11** (68.4 mg, 23%) as white amorphous crystals. $[\alpha]_D$ = –15 (c = 0.9; CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.23 (d, $J_{3',2'}$ = 9.1 Hz, 2 H, 2 × 3′-H *p*NO_2-Ar), 8.20 (d, $J_{3',2'}$ = 9.1 Hz, 2 H, 2 × 3′-H *p*NO_2-Ar), 7.49–7.39 (m, 5 H, Ar-H benzylidene), 7.28 (d, $J_{2',3'}$ = 9.1 Hz, 2 H, 2 × 2′-H *p*NO_2-Ar), 7.27 (d, $J_{2',3'}$ = 9.1 Hz, 2 H, 2 × 2′-H *p*NO_2-Ar), 5.94 (m, 1 H, OCH_2CH=CH_2), 5.61 (d, $J_{H,NH}$ = 10.0 Hz, 1 H, NH), 5.59 (s, 1 H, C*H*Ph), 5.37 (br. d, J_{vic} = 17.2 Hz, 1 H, *trans* OCH_2CH=C*H*H), 5.32 (br. d, J_{vic} = 10.6 Hz, 1 H, *cis* OCH_2CH=C*H*H), 5.27 (t, $J_{3,2}$ = $J_{3,4}$ = 9.9 Hz, 1 H, 3-H), 5.05 (d, $J_{1,2}$ = 3.8 Hz, 1 H, 1-H), 4.35 (dd, J_{gem} = 10.3, $J_{6a,5}$ = 4.8 Hz, 1 H, 6a-H), 4.28 (m, 2 H, 2-H, OC*H*HCH=CH_2), 4.09 (dd, J_{gem} = 12.6, J_{vic} = 6.5 Hz, 1 H, OC*H*HCH=CH_2), 4.01 (dt, $J_{5,4}$ = $J_{5,6b}$ = 10.3, $J_{5,6a}$ = 4.8 Hz, 1 H, 5-H), 3.88 (t, $J_{4,3}$ = $J_{4,5}$ = 10.3 Hz, 1 H, 4-H), 3.83 (t, J_{gem} = $J_{6b,5}$ = 10.3 Hz, 1 H, 6b-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 155.3, 155.2, 145.5, 144.8 (4 × C_{ipso}), 152.9, 152.5 (N*C*OO, O*C*OO), 136.6 (C_{ipso} benzylidene), 132.7 (OCH_2CH=CH_2), 129.3–121.6 (C-Ar), 118.9 (OCH_2CH=CH_2), 101.8 (*C*HPh), 96.8 (C-1), 78.5, 76.3, 68.8, 68.6, 62.7, 54.2 (C-2, C-3, C-4, C-5, C-6, OCH_2CH=CH_2) ppm. MALDI TOF-MS: unstable. $C_{30}H_{27}N_3O_{13}$ (637.15): calcd. C 56.52, H 4.27, N 6.59; found C 56.38, H 4.19, N 6.50.

***N*-(1-*O*-Allyl-4,6-*O*-benzylidene-2,3-*N*,*O*-carbonyl-2-deoxy-α-D-glucopyranos-2-yl)-*N*′-(1-*O*-allyl-4,6-*O*-benzylidene-2-deoxy-α-D-glucopyranos-2-yl)urea (14a):** A solution of compound **5** (45.6 mg, 65.9 μmol) in chloroform (1.5 mL) was treated with water (110 μL), triethylamine (110 μL) and finally with 1,4-dioxane (660 μL). After 3 d stirring at room temp., the mixture was treated at 0 °C with some drops of 0.1 M HCl, then quickly diluted with dichloromethane (40 mL) and washed with water. The organic layer was collected, dried with anhydrous Na_2SO_4 and concentrated to give a residue, that, after flash chromatography (toluene/ethyl acetate, 6:1 to 2:1), afforded **14a** (35.6 mg, 81%) as a white powder. $[\alpha]_D$ = +81.4 (c = 1.0; CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.89 (d, $J_{H,NH}$ = 8.7 Hz, 1 H, NH), 7.51–7.36 (m, 10 H, Ar-H), 5.90 (m, 2 H, 2 × OCH_2CH=CH_2), 5.76 (d, $J_{1,2}$ = 2.8 Hz, 1 H, 1_A-H), 5.62 (s, 1 H, C*H*Ph), 5.56 (s, 1 H, C*H*Ph), 5.32 (dd, J_{vic} = 17.2, J_{gem} = 1.5 Hz, 1 H, *trans* OCH_2CH=C*H*H), 5.29 (dd, J_{vic} = 17.2, J_{gem} = 1.5 Hz, 1 H, *trans* OCH_2CH=C*H*H), 5.24 (dd, J_{vic} = 10.3, J_{gem} = 1.5 Hz, 1 H, *cis* OCH_2CH=C*H*H), 5.22 (dd, J_{vic} = 10.5, J_{gem} = 1.5 Hz, 1 H, *cis* OCH_2CH=C*H*H), 4.91 (d, $J_{1,2}$ = 3.8 Hz, 1 H, 1_B-H), 4.83 (dd, $J_{3,2}$ = 11.7, $J_{3,4}$ = 10.1 Hz, 1 H, 3_A-H), 4.26 (m, 4 H, $6a_A$-H, 3 × OC*H*HCH=CH_2), 4.16 (m, 2 H, 2_A-H, OC*H*HCH=CH_2), 4.04 (m, 3 H, 5_A-H, 5_B-H, $6a_B$-H), 3.91 (m, 4 H, 2_B-H, 3_A-H, 4_A-H, 4_B-H), 3.76 (d, J_{gem} = $J_{6,5}$ = 10.3 Hz, 1 H, $6b_A$-H), 3.59 (d, J_{gem} = $J_{6,5}$ = 9.9 Hz, 1 H, $6b_B$-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 154.9 (O*C*ON), 152.5 (N*C*ON), 137.0, 136.4 (2 × C_{ipso}), 133.2, 133.1 (2 × OCH_2CH=CH_2), 129.3–126.1 (C-Ar), 118.4, 118.3 (2 × OCH_2CH=CH_2), 102.0, 101.4 (2 × *C*HPh), 96.9, 96.5 (2 × C-1), 81.9, 79.8, 74.1, 70.5, 69.9, 68.9, 68.8, 68.5, 65.4, 62.6, 60.9 (C-2_A, C-3_A, C-3_B, C-4_A, C-4_B, C-5_A, C-5_B, C-6_A, C-6_B, 2 × OCH_2CH=CH_2), 54.7 (C-2_B) ppm. MALDI TOF-MS: calcd. for $C_{34}H_{38}N_2O_{12}$ 666.24; found 689.39 [M + Na]$^+$. $C_{34}H_{38}N_2O_{12}$ (666.24): calcd. C 61.25, H 5.75, N 4.20; found C 61.06, H 5.57, N 4.11.

***N*,*N*′-Bis(1-*O*-allyl-4,6-*O*-benzylidene-2-deoxy-α-D-glucopyranos-2-yl)urea (15a):** A solution of compound **5** (172 mg, 0.25 mmol) in 3:1 (v/v) 1,4-dioxane/water (8.0 mL) was treated with triethylamine (1.0 mL). After 14 h stirring at 80 °C, silica gel (1.25 g) was added. The mixture was immediately cooled to room temp. and concentrated. Flash chromatography (chloroform/methanol, 99:1 to 96:4) afforded **15a** (122 mg, 76%) as a white powder. $[\alpha]_D$ = +32 (c = 0.5; CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.50–7.34 (m, 5 H, Ar-H), 5.91 (m, 1 H, OCH_2CH=CH_2), 5.55 (s, 1 H, C*H*Ph), 5.32 (br. d, J_{vic} = 17.2 Hz, 1 H, *trans* OCH_2CH=C*H*H), 5.24 (br. d, J_{vic} = 10.4 Hz, 1 H, *cis* OCH_2CH=C*H*H), 4.88 (d, $J_{1,2}$ = 3.0 Hz, 1 H, 1-H), 4.26 (dd, J_{gem} = 9.9, $J_{6a,5}$ = 4.5 Hz, 1 H, 6a-H), 4.20 (dd, J_{gem} = 12.8, J_{vic} = 5.2 Hz, 1 H, OC*H*HCH=CH_2), 4.01 (dd, J_{gem} = 12.8, J_{vic} = 5.2 Hz, 1 H, OC*H*HCH=CH_2), 3.93 (m, 2 H, 2-H, 3-H), 3.83 (dt, $J_{5,4}$ = $J_{5,6b}$ = 9.9, $J_{5,6a}$ = 4.5 Hz, 1 H, 5-H), 3.74 (t, J_{gem} = $J_{6b,5}$ = 9.9 Hz, 1 H, 6b-H), 3.56 (t, $J_{4,3}$ = $J_{4,5}$ = 9.9 Hz, 1 H, 4-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 159.1 (N*C*ON), 137.2 (C_{ipso}), 133.4 (OCH_2CH=CH_2), 129.1, 128.2, 126.4 (C-Ar), 118.2 (OCH_2CH=CH_2), 102.0 (*C*HPh), 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, OCH_2CH=CH_2) ppm. MALDI TOF-MS: calcd. for $C_{33}H_{40}N_2O_{11}$ 640.26; found 641.39 [M + H]$^+$. $C_{33}H_{40}N_2O_{11}$ (640.26): calcd. C 61.86, H 6.29, N 4.37; found C 62.02, H 6.40, N 4.45.

***N*-(1-*O*-Allyl-4,6-*O*-benzylidene-2,3-*N*,*O*-carbonyl-2-deoxy-α-D-glucopyranos-2-yl)-*N*′-(1-*O*-allyl-4,6-*O*-benzylidene-2-deoxy-3-methoxycarbonyl-α-D-glucopyranos-2-yl)urea (14b) and *N*,*N*′-Bis(1-*O*-allyl-4,6-*O*-benzylidene-2-deoxy-3-methoxycarbonyl-α-D-glucopyranos-2-yl)urea (15b):** Compound **5** (32.3 mg, 46.7 μmol) was dissolved in CH_2Cl_2 (1.4 mL), cooled to –60 °C and treated with a 1.5 M solution of NaOMe in MeOH (155 mL). After 40 min stirring at –60 °C, sat. NH_4Cl (5 mL) was added. The mixture was immediately diluted with EtOAc (30 mL), warmed to room temp. and washed with water. The organic layer was collected, dried with anhydrous Na_2SO_4, filtered and concentrated to give a residue, that, after flash chromatography (toluene/ethyl acetate, 7:1 to 5:1), afforded, **14b** (11.5 mg, 34%) as the first eluted compound as a white powder. $[\alpha]_D$ = +66 (c = 0.5; CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.91 (d, $J_{H,NH}$ = 9.5 Hz, 1 H, NH), 7.49–7.34 (m, 10 H, Ar-H), 5.90 (m, 2 H, 2 × OCH_2CH=CH_2), 5.75 (d, $J_{1,2}$ = 2.8 Hz, 1 H, 1_A-H), 5.62 (s, 1 H, C*H*Ph), 5.52 (s, 1 H, C*H*Ph), 5.33 (dd, J_{vic} = 17.2, J_{gem} = 1.5 Hz, 1 H, *trans* OCH_2CH=C*H*H), 5.30 (dd, J_{vic} = 17.2, J_{gem} = 1.5 Hz, 1 H, *trans* OCH_2CH=C*H*H), 5.23 (m, 3 H, 3_B-H, 2 × *cis* OCH_2CH=C*H*H), 4.91 (d, $J_{1,2}$ = 3.7 Hz, 1 H, 1_B-H), 4.80 (dd, $J_{3,2}$ = 11.7, $J_{3,4}$ = 10.1 Hz, 1 H, 3_A-H), 4.36–4.21 (m, 6 H, 2_B-H, $6a_A$-H, $6a_B$-H, $6b_A$-H, 2 × OC*H*HCH=CH_2), 4.15 (dd, J_{gem} = 12.8, J_{vic} = 5.9 Hz, 1 H, OC*H*HCH=CH_2), 4.05 (m, 2 H, 4_A-H, OC*H*HCH=CH_2), 3.98 (td, $J_{5,6a}$ = $J_{5,6b}$ = 10.3, $J_{5,4}$ = 9.4 Hz, 1 H, 5_B-H), 3.90 (d, $J_{5,4}$ = 6.8 Hz, 1 H, 5_A-H), 3.87 (dd, $J_{2,3}$ = 11.7, $J_{2,1}$ = 2.8 Hz, 1 H, 2_A-H), 3.78 (t, $J_{6,5}$ = J_{gem} = 10.3 Hz, 1 H, $6b_B$-H), 3.76 (s, 3 H, OCH_3), 3.74 (t, $J_{4,3}$ = $J_{4,5}$ = 9.4 Hz, 1 H, 4_B-H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ = 155.3, 154.7, 151.8 (*C*OOCH_3, N*C*ON, O*C*ON), 136.9, 136.4 (2 × C_{ipso}), 133.1, 133.0 (2 × OCH_2CH=CH_2), 129.3, 129.1, 128.3, 128.2, 126.2, 126.1 (C-Ar), 118.5, 118.3 (2 × OCH_2CH=CH_2), 101.6, 101.4 (2 × *C*HPh), 97.0, 96.3 (C-1_A, C-1_B), 79.8, 79.2, 74.6, 74.0, 69.7, 69.0, 68.7, 68.5, 65.4, 62.9, 60.9, 55.2, 52.9 (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, 2 × OCH_2CH=CH_2, OCH_3) ppm. MALDI TOF-MS: calcd. for $C_{36}H_{40}N_2O_{14}$ 724.25; found 747.11 [M + Na]$^+$. $C_{36}H_{40}N_2O_{14}$ (724.25): calcd. C 59.66, H 5.56, N 3.87; found C 59.48, H 5.47, N 3.80.

Second eluted compound **15b** (12.1 mg, 34%) was recovered as a white powder. $[\alpha]_D$ = +84.1 (c = 1.5; CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.46–7.35 (m, 5 H, Ar-H), 5.87 (m, 1 H, OCH_2CH=CH_2), 5.52 (s, 1 H, CHPh), 5.30 (br. d, J_{vic} = 17.2 Hz, 1 H, *trans* OCH_2CH=CHH), 5.23 (br. d, J_{vic} = 10.3 Hz, 1 H, *cis* OCH_2CH=CHH), 5.09 (t, $J_{3,2}$ = $J_{3,4}$ = 10.0 Hz, 1 H, 3-H), 4.90 (d, $J_{1,2}$ = 3.6 Hz, 1 H, 1-H), 4.85 (d, $J_{H,NH}$ = 9.6 Hz, 1 H, NH), 4.27 (dd, J_{gem} = 10.2, $J_{6a,5}$ = 4.8 Hz, 1 H, 6a-H), 4.18 (m, 2 H, 2-H, OCHHCH=CH_2), 4.00 (dd, J_{gem} = 12.8, J_{vic} = 6.1 Hz, 1 H, OCHHCH=CH_2), 3.91 (dt, $J_{5,4}$ = $J_{5,6b}$ = 9.9, $J_{5,6a}$ = 4.8 Hz, 1 H, 5-H), 3.75 (m, 5 H, 4-H, 6b-H, OCH_3) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 156.2, 155.9 ($COOCH_3$, NCON), 137.0 (C_{ipso}), 133.2 (OCH_2CH=CH_2), 129.1, 128.3, 126.2 (C-Ar), 118.2 (OCH_2CH=CH_2), 101.6 (CHPh), 97.6 (C-1), 79.1, 74.5, 68.8, 68.7, 62.9, 55.1, 53.4 (C-2, C-3, C-4, C-5, C-6, OCH_2CH=CH_2, OCH_3) ppm. MALDI TOF-MS: calcd. for $C_{37}H_{44}N_2O_{15}$ 756.27; found 779.38 $[M + Na]^+$. $C_{37}H_{44}N_2O_{15}$ (756.27): calcd. C 58.72, H 5.86, N 3.70; found C 58.50, H 5.68, N 3.65.

Alternatively, compound **15b** could be obtained by dissolving **5** (42.4 mg, 61.3 μmol) in chloroform (1.4 mL) and then treating it with methanol (0.6 mL) and triethylamine (0.1 mL). The solution was stirred at room temp. for two days. The reaction was quenched by adding a few drops of 0.1 M HCl. The mixture was immediately diluted with CH_2Cl_2 (25 mL) and washed with water. The organic layer was collected, dried and concentrated. Column chromatography (toluene/ethyl acetate, 7:1 to 5:1) of the residue afforded **15b** (24.9 mg, 54%).

***N*-[3-*O*-(2,3,4-Tri-*O*-benzyl-α-L-fucopyranosyl)-1-*O*-allyl-4,6-*O*-benzylidene-2-deoxy-α-D-glucopyranos-2-yl]-*N*′-(1-*O*-allyl-4,6-*O*-benzylidene-2,3-*N*,*O*-carbonyl-2-deoxy-α-D-glucopyranos-2-yl)urea (17):** A mixture of **14a** (39.0 mg, 58.6 μmol) and **16** (70.8 mg, 117 μmol) was coevaporated three times with toluene, the residue was dried and then mixed with freshly activated molecular sieves (AW-300, 4 Å), suspended under argon in 1:1 (v/v) CH_2Cl_2/THF (1.5 mL). The mixture was stirred at –30 °C for 15 min. A solution of TMSOTf in CH_2Cl_2 (24.6 mg/mL, 27.4 μL, 3.0 μmol) was then added. The mixture was stirred for 75 min at –30 °C, then a few drops of Et_3N were added. The mixture was filtered through a Celite pad and concentrated. The residue was subjected to column chromatography (toluene/ethyl acetate, 12:1 to 8:1) to give **17** (48.1 mg, 76%) as a colorless oil. $[\alpha]_D$ = +23.1 (c = 1.7; CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.08 (d, $J_{H,NH}$ = 10.0 Hz, 1 H, NH), 7.39–7.25 (m, 25 H, Ar-H), 5.86 (m, 1 H, OCH_2CH=CH_2), 5.69 (m, 2 H, 1_A-H, OCH_2CH=CH_2), 5.54 (s, 1 H, CHPh), 5.51 (s, 1 H, CHPh), 5.35 (d, $J_{1,2}$ = 3.6 Hz, 1 H, 1_C-H), 5.31 (dd, J_{vic} = 17.2, J_{gem} = 1.5 Hz, 1 H, *trans* OCH_2CH=CHH), 5.22 (dd, J_{vic} = 10.5, J_{gem} = 1.5 Hz, 1 H, *cis* OCH_2CH=CHH), 5.09 (dd, J_{vic} = 17.0, J_{gem} = 1.5 Hz, 1 H, *trans* OCH_2CH=CH_2), 5.06 (dd, J_{vic} = 10.5, J_{gem} = 1.5 Hz, 1 H, *cis* OCH_2CH=CH_2), 4.89 (d, J_{gem} = 11.5 Hz, 1 H, OCHHPh), 4.87 (d, $J_{1,2}$ = 3.5 Hz, 1 H, 1_B-H), 4.83 (d, J_{gem} = 11.7 Hz, 1 H, OCHHPh), 4.73 (d, J_{gem} = 11.6 Hz, 1 H, OCHHPh), 4.66 (d, J_{gem} = 11.7 Hz, 1 H, OCHHPh), 4.65 (t, $J_{3,4}$ = $J_{3,2}$ = 10.0 Hz, 1 H, 3_A-H), 4.56 (d, J_{gem} = 11.6 Hz, 1 H, OCHHPh), 4.55 (d, J_{gem} = 11.5 Hz, 1 H, OCHHPh), 4.35 (dt, $J_{2,3}$ = $J_{2,NH}$ = 10.0, $J_{2,1}$ = 3.5 Hz, 1 H, 2_B-H), 4.31–4.17 (m, 5 H, 2_A-H, $6a_A$-H, $6b_A$-H, OCH_2CH=CH_2), 4.12 (q, $J_{5,6}$ = 6.4 Hz, 1 H, 5_C-H), 4.05–3.72 (m, 11 H, 2_C-H, 3_B-H, 3_C-H, 4_A-H, 4_B-H, 5_A-H, 5_B-H, $6a_B$-H, $6b_B$-H, OCH_2CH=CH_2), 3.49 (d, $J_{4,3}$ = 2.0 Hz, 1 H, 4_C-H), 0.88 (d, $J_{6,5}$ = 6.4 Hz, 3 H, 6_C-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 154.9, 152.4 (OCON, NCON), 139.0, 138.6, 138.2, 137.3, 136.4 (3 × C_{ipso} Bn, 2 × C_{ipso} benzylidene), 133.4, 133.0 (2 × OCH_2CH=CH_2), 129.3–125.9 (C-Ar), 118.0, 117.9 (2 × OCH_2CH=CH_2), 101.6, 101.4 (2 × CHPh), 97.2, 96.6, 96.5 ($C\text{-}1_A$, $C\text{-}1_B$, $C\text{-}1_C$), 80.6, 79.8, 79.4, 77.9, 76.0, 74.7, 73.6, 73.3, 72.2, 71.7, 69.1, 69.0, 68.9, 68.5, 66.7, 65.1, 62.9, 61.2, 55.0 ($C\text{-}2_A$, $C\text{-}2_B$, $C\text{-}2_C$, $C\text{-}3_A$, $C\text{-}3_B$, $C\text{-}3_C$, $C\text{-}4_A$, $C\text{-}4_B$, $C\text{-}4_C$, $C\text{-}5_A$, $C\text{-}5_B$, $C\text{-}5_C$, $C\text{-}6_A$, $C\text{-}6_B$, 3 × OCH_2Ph, 2 × OCH_2CH=CH_2), 16.3 ($C\text{-}6_C$) ppm. MALDI TOF-MS: calcd. for $C_{61}H_{66}N_2O_{16}$ 1082.44; found 1105.21 $[M + Na]^+$. $C_{61}H_{66}N_2O_{16}$ (1082.44): calcd. C 67.64, H 6.14, N 2.59; found C 67.48, H 6.00, N 2.50.

***N*-[3-*O*-(2,3,4-Tri-*O*-benzyl-α-L-fucopyranosyl)-1-*O*-allyl-4,6-*O*-benzylidene-2-deoxy-α-D-glucopyranos-2-yl]-*N*′-(1-*O*-allyl-4,6-*O*-benzylidene-2-deoxy-α-D-glucopyranos-2-yl)urea (18):** A solution of compound **17** (36.6 mg, 33.8 μmol) in 3:1 (v/v) 1,4-dioxane/water (2.1 mL) was treated with triethylamine (260 μL). After 30 h stirring at 80 °C, silica gel (600 mg) was added. The mixture was immediately cooled to room temp. and concentrated. Flash chromatography (toluene/ethyl acetate, 6:1 to 2:1) afforded **18** (20.8 mg, 58%) as white amorphous crystals. $[\alpha]_D$ = –3 (c = 0.7; CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.40–7.27 (m, 25 H, Ar-H), 5.88 (m, 1 H, OCH_2CH=CH_2), 5.78 (m, 1 H, OCH_2CH=CH_2), 5.54 (s, 2 H, 2 × CHPh), 5.30 (dd, J_{vic} = 17.2, J_{gem} = 1.4 Hz, 1 H, *trans* OCH_2CH=CHH), 5.28 (d, $J_{1,2}$ = 3.1 Hz, 2 H, 1_A-H, 1_B-H), 5.23 (dd, J_{vic} = 10.4, J_{gem} = 1.4 Hz, 1 H, *cis* OCH_2CH=CHH), 5.17 (dd, J_{vic} = 17.2, J_{gem} = 1.4 Hz, 1 H, *trans* OCH_2CH=CH_2), 5.14 (dd, J_{vic} = 10.4, J_{gem} = 1.4 Hz, 1 H, *cis* OCH_2CH=CHH), 5.05 (br. s, 2 H, 2 × NH), 5.01 (d, $J_{1,2}$ = 3.8 Hz, 1 H, 1_C-H), 4.89 (d, J_{gem} = 11.5 Hz, 1 H, OCHHPh), 4.82 (d, J_{gem} = 11.9 Hz, 1 H, OCHHPh), 4.75 (s, 2 H, OCH_2Ph), 4.65 (d, J_{gem} = 11.5 Hz, 1 H, OCHHPh), 4.57 (d, J_{gem} = 11.9 Hz, 1 H, OCHHPh), 4.28 (dd, $J_{2,3}$ = 10.0, $J_{2,1}$ = 3.5 Hz, 1 H, 2_A-H), 4.23 (dd, $J_{2,3}$ = 10.0, $J_{2,1}$ = 3.5 Hz, 1 H, 2_B-H), 4.16 (dd, J_{gem} = 13.4, J_{vic} = 6.8 Hz, 1 H, OCHHCH=CH_2), 4.09–3.68 (m, 16 H, 2_C-H, 3_A-H, 3_B-H, 3_C-H, 4_A-H, 4_B-H, 5_A-H, 5_B-H, 5_C-H, $6a_A$-H, $6b_A$-H, $6a_B$-H, $6b_B$-H, 3 × OCHHCH=CH_2), 3.53 (d, $J_{4,3}$ = 2.0 Hz, 1 H, 4_C-H), 0.96 (d, $J_{6,5}$ = 6.4 Hz, 3 H, 6_C-H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ = 158.9 (NCON), 138.7, 138.5, 137.6, 137.3, 137.1 (3 × C_{ipso} Bn, 2 × C_{ipso} benzylidene), 133.7, 133.2 (2 × OCH_2CH=CH_2), 129.0–125.9 (C-Ar), 118.4, 117.9 (2 × OCH_2CH=CH_2), 101.7, 101.1 (2 × CHPh), 97.9, 97.4, 97.3 ($C\text{-}1_A$, $C\text{-}1_B$, $C\text{-}1_C$), 81.7, 81.5, 79.2, 79.1, 77.5, 74.9, 74.5, 73.7, 73.3, 71.8, 71.7, 68.8, 68.7, 68.6, 67.2, 63.0, 62.5, 55.6, 55.1 ($C\text{-}2_A$, $C\text{-}2_B$, $C\text{-}2_C$, $C\text{-}3_A$, $C\text{-}3_B$, $C\text{-}3_C$, $C\text{-}4_A$, $C\text{-}4_B$, $C\text{-}4_C$, $C\text{-}5_A$, $C\text{-}5_B$, $C\text{-}5_C$, $C\text{-}6_A$, $C\text{-}6_B$, 3 × OCH_2Ph, 2 × OCH_2CH=CH_2), 16.5 ($C\text{-}6_C$) ppm. MALDI TOF-MS: calcd. for $C_{60}H_{68}N_2O_{15}$ 1056.46; found 1078.61 $[M + Na]^+$. $C_{60}H_{68}N_2O_{15}$ (1056.46): calcd. C 68.17, H 6.48, N 2.65; found C 68.08, H 6.42, N 2.60.

***N*-(1-*O*-Allyl-3-*O*-α-L-fucopyranosyl-2-deoxy-α-D-glucopyranos-2-yl)-*N*′-(1-*O*-allyl-2-deoxy-α-D-glucopyranos-2-yl)urea (19):** A solution of **18** (10.0 mg, 9.5 μmol) in 9:1 (v/v) MeOH/HCOOH (500 μL) was treated with Pd/C (3 mg) under an Ar atmosphere. After 1 h in an ultrasound bath, the mixture was filtered through a Celite pad and concentrated. The residue was lyophilized to give pure **19** (4.2 mg, 72%) as a white foam. $[\alpha]_D$ = +37 (c = 0.3; H_2O). ^{1}H NMR (400 MHz, D_2O): δ = 5.04 (d, $J_{1,2}$ = 3.9 Hz, 1 H, 1-H), 4.89 (d, $J_{1,2}$ = 3.4 Hz, 1 H, 1-H), 4.82 (d, $J_{1,2}$ = 3.6 Hz, 1 H, 1-H), 4.34 (q, $J_{5,6}$ = 6.6 Hz, 1 H, 5_C-H), 3.88–3.40 (m, 19 H, 2_A-H, 2_B-H, 2_C-H, 3_A-H, 3_B-H, 3_C-H, 4_A-H, 4_B-H, 4_C-H, 5_A-H, 5_B-H, 6_A-H, 6_B-H, 2 × $OCH_2CH_2CH_3$), 1.62 (m, 4 H, 2 × $OCH_2CH_2CH_3$), 1.16 (d, $J_{6,5}$ = 6.6 Hz, 3 H, 6_C-H), 0.93 (t, J_{vic} = 7.4 Hz, 6 H, 2 × $OCH_2CH_2CH_3$) ppm. ^{13}C NMR (100 MHz, D_2O): δ = 160.1 (NCON), 100.0, 98.3 ($C\text{-}1_A$, $C\text{-}1_B$, $C\text{-}1_C$), 79.0, 72.6, 72.5, 70.9, 70.8, 70.7, 69.3, 68.9, 67.8, 61.4 ($C\text{-}2_C$, $C\text{-}3_A$, $C\text{-}3_B$, $C\text{-}3_C$, $C\text{-}4_A$, $C\text{-}4_B$, $C\text{-}4_C$, $C\text{-}5_A$, $C\text{-}5_B$, $C\text{-}5_C$, $C\text{-}6_A$, $C\text{-}6_B$, $OCH_2CH_2CH_3$), 55.0, 54.7 ($C\text{-}2_A$, $C\text{-}2_B$), 22.8 ($OCH_2CH_2CH_3$), 16.0 ($C\text{-}6_C$), 10.7 ($OCH_2CH_2CH_3$) ppm. MALDI TOF-MS: calcd. for $C_{25}H_{46}N_2O_{15}$

614.29; found 637.10 [M + Na]$^+$. $C_{25}H_{46}N_2O_{15}$ (614.29): calcd. C 48.85, H 7.54, N 4.56; found C 48.60, H 7.78, N 4.39.

1-*O*-Allyl-4,6-*O*-benzylidene Cyclic Neodisaccharide (20): Compound **14a** (36.8 mg, 55.2 μmol) was dissolved in DMF (2.0 mL) under an Ar atmosphere. The solution was treated with DBU (10.2 μL, 68.4 μmol) and then heated to 50 °C. After overnight stirring, the reaction was cooled to room temp., diluted with ethyl acetate (20 mL) and washed with 0.1 M HCl and then water. The organic layer was collected, dried with anhydrous Na_2SO_4, filtered and concentrated to give a residue, that, after flash chromatography (toluene/ethyl acetate, 6:1 to 2:1), afforded **20** (15.7 mg, 43%) as a white powder. $[\alpha]_D$ = +32 (c = 0.9; CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.49–7.33 (m, 5 H, Ar-H), 5.85 (m, 1 H, OCH_2CH=CH_2), 5.52 (s, 1 H, C*H*Ph), 5.28 (m, 3 H, 3-H, OCH_2CH=CH_2), 5.00 (d, $J_{H,NH}$ = 9.8 Hz, 1 H, NH), 4.92 (d, $J_{1,2}$ = 3.8 Hz, 1 H, 1-H), 4.29 (dd, J_{gem} = 10.2, $J_{6a,5}$ = 4.8 Hz, 1 H, 6a-H), 4.20 (dd, J_{gem} = 12.5, J_{vic} = 5.4 Hz, 1 H, OC*H*HCH=CH_2), 4.07 (dt, $J_{2,3}$ = $J_{H,NH}$ = 9.8, $J_{2,1}$ = 3.8 Hz, 1 H, 2-H), 3.99 (dd, J_{gem} = 12.5, J_{vic} = 5.4 Hz, 1 H, OC*H*HCH=CH_2), 3.94 (ddd, $J_{5,6b}$ = 10.3, $J_{5,4}$ = 9.6, $J_{5,6a}$ = 4.8 Hz, 1 H, 5-H), 3.77 (t, J_{gem} = $J_{6b,5}$ = 10.3 Hz, 1 H, 6b-H), 3.73 (t, $J_{4,3}$ = $J_{4,5}$ = 9.6 Hz, 1 H, 4-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 155.5 (O*C*ON), 136.8 (C_{ipso}), 132.7 (OCH_2*C*H=CH_2), 129.2, 128.2, 126.3 (C-Ar), 119.2 (OCH_2CH=*C*H_2), 101.8 (*C*HPh), 96.6 (C-1), 78.3, 75.1, 68.9, 68.8, 63.2, 56.4 (C-2, C-3, C-4, C-5, C-6, O*C*H_2CH=CH_2) ppm. MALDI TOF-MS: calcd. for $C_{34}H_{38}N_2O_{12}$ 666.24; found 689.37 [M + Na]$^+$. $C_{34}H_{38}N_2O_{12}$ (666.24): calcd. C 61.25, H 5.75, N 4.20; found C 61.08, H 5.66, N 4.11.

1-*O*-Allyl Cyclic Neodisaccharide (21): Compound **20** (36.0 mg, 54.1 μmol) was dissolved in 4:1 (v/v) 1,4-dioxane/water (1.0 mL) and then treated with (±)-camphor-10-sulfonic acid (31.1 mg, 134 μmol). After 4 h stirring at 60 °C, silica gel (500 mg) was added and the mixture was evaporated. The residue was subjected to flash chromatography (chloroform/methanol, 95:5 to 86:14) affording **21** (25.9 mg, 98%) as a white powder. $[\alpha]_D$ = +104 (c = 0.9; H_2O). ^{1}H NMR (400 MHz, D_2O): δ = 6.00 (m, 1 H, OCH_2CH=CH_2), 5.38 (d, J_{vic} = 17.2 Hz, 1 H, *trans* OCH_2CH=C*H*H), 5.28 (d, $J_{1,2}$ = 3.7 Hz, 1 H, *cis* OCH_2CH=C*H*H), 5.07 (d, $J_{1,2}$ = 3.7 Hz, 1 H, 1-H), 4.87 (dd, $J_{3,2}$ = 10.0, $J_{3,4}$ = 9.2 Hz, 1 H, 3-H), 4.25 (dd, J_{gem} = 12.7, J_{vic} = 5.5 Hz, 1 H, OC*H*HCH=CH_2), 4.15 (dd, $J_{2,3}$ = 10.0, $J_{2,1}$ = 3.7 Hz, 1 H, 2-H), 4.09 (dd, J_{gem} = 12.7, J_{vic} = 5.5 Hz, 1 H, OC*H*HCH=CH_2), 3.91–3.73 (m, 4 H, 4-H, 5-H, 6a-H, 6b-H) ppm. ^{13}C NMR (50 MHz, D_2O): δ = 158.6 (O*C*ON), 134.0 (OCH_2*C*H=CH_2), 119.1 (OCH_2CH=*C*H_2), 96.4 (C-1), 79.6, 72.4, 69.2, 67.3, 60.8, 55.8 (C-2, C-3, C-4, C-5, C-6, O*C*H_2CH=CH_2) ppm. MALDI TOF-MS: calcd. for $C_{20}H_{30}N_2O_{12}$ 490.18; found 513.00 [M + Na]$^+$. $C_{20}H_{30}N_2O_{12}$ (490.18): calcd. C 48.98, H 6.17, N 5.71; found C 48.78, H 6.04, N 5.61.

Supporting Information (see also the footnote on the first page of this article): Copies of ^{1}H and ^{13}C NMR spectra for all new compounds. Copies of HSQBMC spectra of compounds **7** and **21** as well as of J-HMBC spectrum of compound **7**.

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