Available online at www.sciencedirect.com
SCIENCE DIRECT
Carbohydrate Research 341 (2006) 705–716
Carbohydrate RESEARCH

Synthesis and characterization of monosaccharide lipids as novel hydrogelators

Guijun Wang,* Sherwin Cheuk, Kristopher Williams, Vibha Sharma, Lousi Dakessian and Zeus Thorton

Department of Chemistry, University of New Orleans, New Orleans, LA 70148, USA

Received 20 September 2005; received in revised form 18 December 2005; accepted 10 January 2006
Available online 17 February 2006

Abstract—Self-assembly of small molecules is a useful strategy for forming functional supramolecular structures. Three new series of methyl α-D-glucopyranoside derivatives, including esters and carbamates, have been synthesized and characterized. Several of these compounds are excellent hydrogelators and formed interesting self-assembled network structures, including birefringent fibers and tubules. The gelation properties depend on the acyl chain length and the headgroup structures. Small molecule sugar-based hydrogelators have potential applications in drug delivery and enzyme immobilization.

Keywords: Monosaccharides; Lipids; Self-assembly; Hydrogelators; Organogelators

1. Introduction

Carbohydrates are abundant natural products and readily available chiral compounds. They contain all of the important elements necessary to prepare highly functional and synthetically flexible units, but they are the most complex and structurally dense of all naturally occurring materials. Attempts to overcome this complexity and integrate the rich functionality and the chirality of carbohydrates into structural units that self-assemble into grand architectures are very important to advance carbohydrate chemistry. Soft materials formed by carbohydrates and lipids are biocompatible and have potential uses in many biomedical areas and as biodegradable materials.

Small molecule self-assembly through non-covalent forces can afford interesting soft materials, such as hydrogels or organogels. Low molecular weight organogelators (LMWOs) are small molecules that can form gels in organic solvents or water.[1–3] The gelation processes are typically reversible because of the non-covalent interactions between the molecules. These molecules have potential applications in forming liquid crystalline materials, as templates for synthesizing other novel materials, and as matrices for separating peptides and amino acids.[4,5] Polymer hydrogels are useful for drug delivery, tissue engineering, enzyme immobilization, and controlled release of other biological agents.[6a,b,7a,b] Polysaccharide gels have been widely utilized for DNA and protein purification and enzyme immobilization. Supramolecular hydrogels are formed by LMWOs in water through non-covalent forces. They are a interesting new class of soft materials that also have important applications in biomaterials and pharmaceutical research.[8–10] These self-assembled supramolecular gels have the advantage that the monomers are easy to prepare and the resulting materials can have tunable physical properties. Small molecules can be synthesized and purified to give materials with a single molecular weight, as compared to polymers, which have a distribution of molecular weights. Their structure can also be readily modified to introduce functional groups that can give rise to desired physical properties. Reversible physical gelation may also have the advantage of

* Corresponding author. Tel.: +1 504 280 1258; fax: +1 504 280 6860; e-mail: gwang2@uno.edu

0008-6215/$ - see front matter © 2006 Elsevier Ltd. All rights reserved.
doi:10.1016/j.carres.2006.01.023

entrapping biomolecules in the matrix, without affecting the properties of the entrapped agents. The non-covalent interactions between the molecules make the gels easier to dissolve or break down than polymer gels, thus allowing the entrapped substances to be separated readily.

Low molecular weight hydrogelators have a variety of structures, including, but not limited to, ureas,[11,12] saccharides,[13a,b,14–16] amino acids,[17,18,19a–d,20–22] nucleotides,[23] nucleosides,[24] and other structural classes.[25–29] Many of them were discovered by serendipity, while some were discovered by rational design or combinatorial chemistry.[8,16] Several examples of existing hydrogelators (**1**–**3**) are shown in Figure 1. Mono-urea serine derivative **1** can form gels in pure water at a concentration of 0.8–1 wt %.[12] The hydrogen bonds between the urea moiety allow the molecules to self-assemble into a one-dimensional array and the short alkyl group provides flexibility. The short chain glucose and galactose amino acid lipids **2** and **3** were discovered by combinatorial chemistry and shown to be effective hydrogelators.[8,16] They can be used to immobilize enzymes and form protein microarrays. From an examination of the structures of small molecule hydrogelators, the common features of good hydrogelators that are apparent is a rigid region that can form hydrogen-bonding interactions, and a flexible short alkyl chain that will allow the molecules to interact with each other through hydrophobic forces.

Because of the great potential of hydrogelators, we are interested in discovering new biocompatible hydrogelators with straightforward structures, which will render large-scale synthesis more feasible. Carbohydrates are ideal starting materials because they are abundant natural chiral compounds with multiple sites available for functionalization. The creation of novel functional biocompatible materials from carbohydrates is important for the advancement of carbohydrate chemistry and biomaterials research. Chirality in supramolecular structures may be useful in molecular recognition with other chiral compounds. These functional materials have potential applications in drug delivery, tissue engineering, and as biocompatible materials. As part of our efforts to discover novel functional biocompatible materials, we designed and synthesized a series of D-glucose-based lipids and found that they are excellent gelators in water and other solvents.

Many glycolipids and other small sugar derivatives can form gels in organic solvents, but less frequently in water. Compound **4** is a simple and commercially available glucose derivative, which can form gels in organic solvents but not in water.[9] Modifying its structure by introducing short alkyl chains could potentially lead to good gelators in water or organic solvents. The structures of three molecular classes, (**A**, **B**, and **C**, Fig. 2) depending on the positions of functionalization, are shown in Figure 2. Inspired by the structures of hydrogelators **1**–**3**, we envisioned the incorporation of short chain fatty acyl unit to the 2 or 3-hydroxyl groups via ester or carbamate linkages (**B** and **C**) could potentially lead to small molecule hydrogelators and the diester or dicarbamate **A** could be potential organogelators. The hydroxyl groups and amide groups can provide hydrogen-bonding interactions. The incorporation of terminal acetylene groups may reduce the acyl chain packing order and therefore increase solubility to some extent. It can also be used as a group that allows further structural modification.

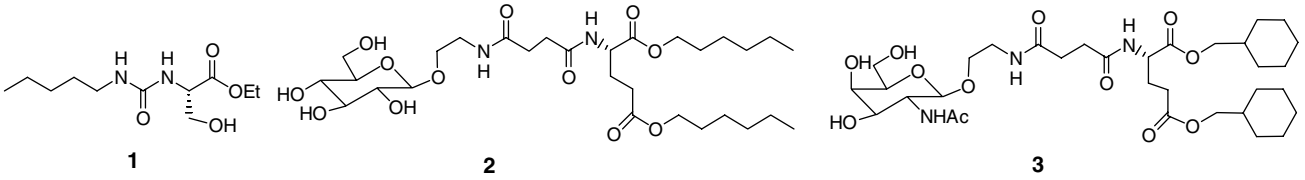


Figure 1. Structures of some hydrogelators (**1**–**3**).

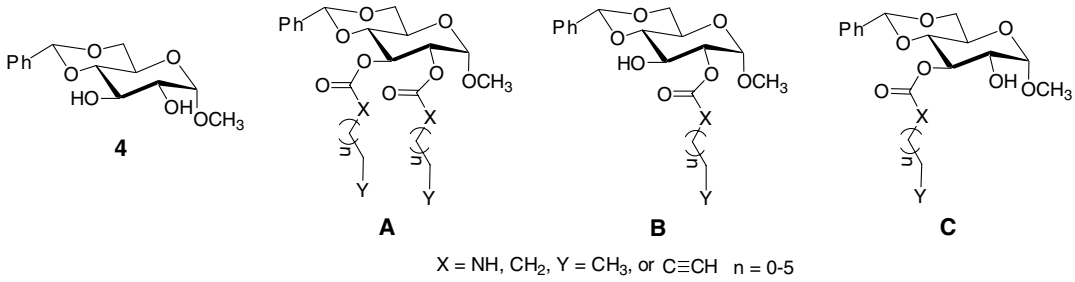


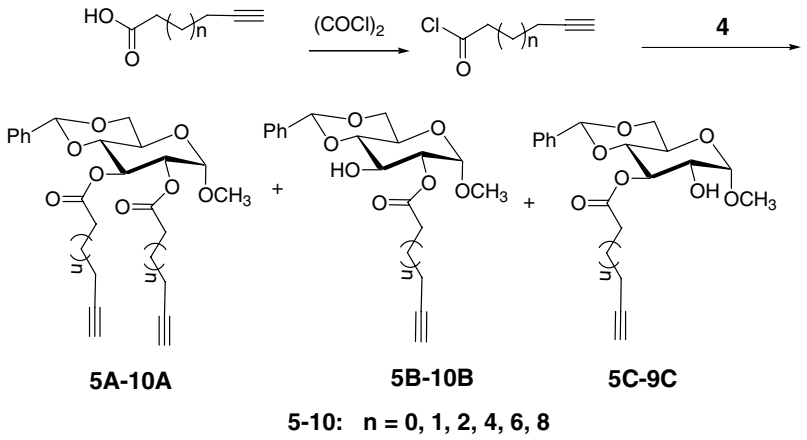
Figure 2. Structures of the designed hydrogelators.

2. Results and discussion

To synthesize the designed compounds efficiently, reactions were carried out in one-pot to produce the three products **A**, **B**, and **C**, which were then isolated by chromatography. This way, a small library of compounds was synthesized rapidly. The screening of these compounds will quickly give us information about structural influences on gelation properties. The structure–gelation properties obtained here can be used to design other effective gelators.

Compound **4** was synthesized readily by treating methyl α-D-glucopyranoside with dimethoxylbenzylidene acetal and a catalytic amount of *p*-toluenesulfonic acid (PTSA) in dimethyl formamide (DMF). Compounds **A**, **B**, and **C** were synthesized by esterification of the hydroxyl groups on the monosaccharide derivative **4** by the corresponding acid chlorides (Scheme 1). By controlling the ratio of the acid and the diol, three products were obtained in this reaction. We found that when using about 2 equiv of acid, typically two products were obtained: the diester **A** and the 2-*O*-monoester **B** although in theory only the diester **A** should be obtained. When the acid was used in 1–1.3 equiv relative to the diol, mainly the 2-*O*-monoester (compound **B**) was obtained, together with small amount of **A** and **C** as well. It is known that esterification generally favors the introduction of the acyl group at the 2-position of a glucose derivative. If the acyl group is not bulky, then esterification at 3-*O* is also observed. The 2-*O*-monoester is probably the kinetic product and is formed first, the 3-*O*-monoester is also formed in a small amount, and either product can react further to give the diester. Because we use less acylating agent comparing to the diol in the headgroup, this reduces the amount of diester. Therefore, we can obtain all three products in one-pot. These esters can be separated by flash chromatography on silica gel using a gradient of solvent systems (hexane/ethyl acetate from 95:5 to 75:25). We synthesized a series of these glucose derivatives and tested their gelation properties in several solvents. These include some acetylene containing lipids with the general structures of **5A**–**10A**, **5B**–**10B**, and **5C**–**9C**.

For structural comparison purposes, we also synthesized the short-chain carbamate analogs **11A**–**12C** (Fig. 3). They were synthesized via similar methods as mentioned above using the corresponding isocyanates and isolated by flash chromatography. The carbamates



Scheme 1. The synthesis of target compounds that are designed to be gelators.

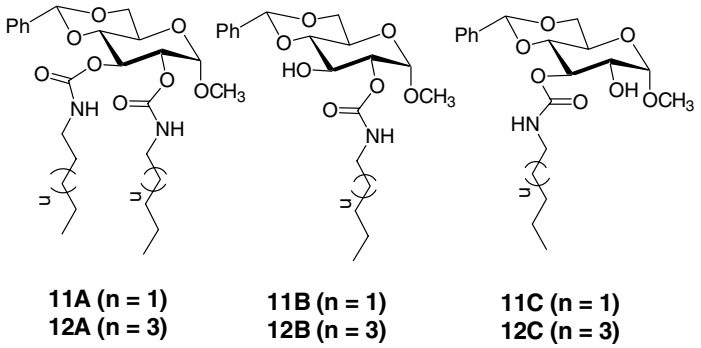


Figure 3. Structures of carbamate derivatives that are potential hydrogelators.

contain additional hydrogen bonding sites, which might also contribute to gelation in water.

The gelation properties of all compounds synthesized are given in Table 1. All compounds without free hydroxyl groups (**5A**–**12A**) are insoluble in water. The shorter chain diester (**5A**) formed gels in hexane and ethanol. The longest chain diester (**10A**) also formed gels in ethanol. The dicarbamates are not gelators in the solvents tested. Compounds with one free hydroxyl group exhibited versatile gelation properties in hexane and water but they are soluble in ethanol (Table 1). Typically the gels in pure water are opaque; an example is shown in Figure 4a. The reason that these gels are not transparent is probably due to the partial solubility of these compounds in pure water. For some samples, partial crystallization also led to opaque gels. In an ethanol/water mixture, the gels formed by the carbamate **11B** are transparent at low concentrations (Fig. 4b), but translucent at higher concentrations. The gel to solution transition temperatures were estimated for compounds **5B**, **6B**, **7B**, and **12B** in pure water at a concentration of 10 mg/mL (80–99, 78–93, 84–94, and 99–105 °C, respectively).

In addition to the results shown in Table 1, the 2-heptynoic ester **7B** also gelates water/alcohol mixtures and water/DMF mixtures. The carbamate **12B** formed a stable gel in water at 4 mg/mL. Other monochain carbamates did not form stable gels in pure water. However, they form stable gels in a mixture of water and polar organic solvents. Both **11C** and **12C** are able to gelate a 1:1 mixture of DMSO/water (v/v) at about 10 mg/mL. Compound **11B** also formed stable transparent gels in 1:2 (v/v) ethanol water mixture at a concentration of 1.4 mg/mL (Fig. 4b). Compounds **11B** and **12B** can form stable opaque gels in a 1:5 mixture of DMSO/water (v/v) at concentrations of 3 and 4 mg/mL, respectively. Notably, DMSO is a solvent often used to dissolve water insoluble drugs to deliver them through skin.

Table 1. Gelation properties of compounds **5A**–**12C** in hexane, water and ethanol[a,b]

Compound	Hexane	Water	Ethanol
5A	G 5	I	G 20
6A	G 15	I	P
7A	P	I	P
8A	G 21	I	P
9A	S	I	S
10A	S	I	G 20
11A	P	I	S
12A	P	I	S
5B	Gp 10	G 4	S
6B	Gp 10	G 7	S
7B	Gp 5	G 7	S
8B	P	Gp 10	S
9B	P	P	S
10B	P	I	S
11B	P	P	S
12B	P	G 4	S
5C	G 3	G 7	S
6C	G 3	G 7	S
7C	G 3	G 8	S
8C	P	Gp 10	S
9C	Gp 20	P	S
11C	G 4	P	S
12C	P	G 17	S

[a] G, gel at room temperature; Gp, unstable gel; P, precipitation; S, soluble (~20 mg/mL).

[b] The numbers after the description letter represent the concentrations for gelation in mg/mL.

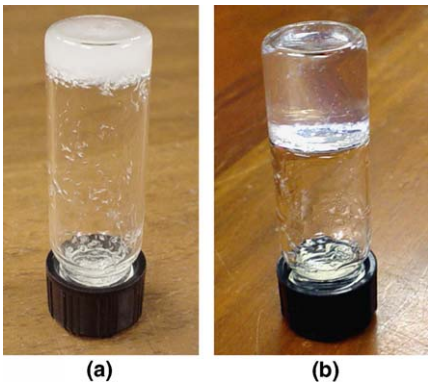


Figure 4. (a) Opaque gels formed by compound **6B** in water (10 mg/mL); (b) clear gels formed by compound **11B** in ethanol/water (1:2 v/v, 1.4 mg/mL).

Optical and electronic microscopy studies showed that these gelators typically form long fibers, tubules, or rods. Representative images are shown in Figure 5. The more effective gelators usually formed very long fibers that are birefringent. Based on the optical micrographs, the fibers that resulted from the water gels generally showed crystal-like structures. They polarize light into a gradient of different colors (Fig. 5e). These properties indicate some liquid-crystal properties and confirm that the gels can have localized order in their packing modes. Some tubules contain nested helices in their center (Fig. 5h). The scanning electronic micrographs (SEMs) indicated an intertwined fibrous assembly. We also observed that larger tubules are composed of a bundle of smaller fibers (Fig. 5b and g). These fibers are potentially useful in forming a functional drug delivery matrix and in the separation of biological molecules. The compounds with excellent gelation properties can be synthesized selectively in high yields by different methods. Their applications and the detailed characterization of molecular order will be reported in the future.

3. Conclusion

In summary, we have synthesized and characterized several series of methyl α-D-glucopyranoside derivatives. These compounds were synthesized by a one-pot reac-

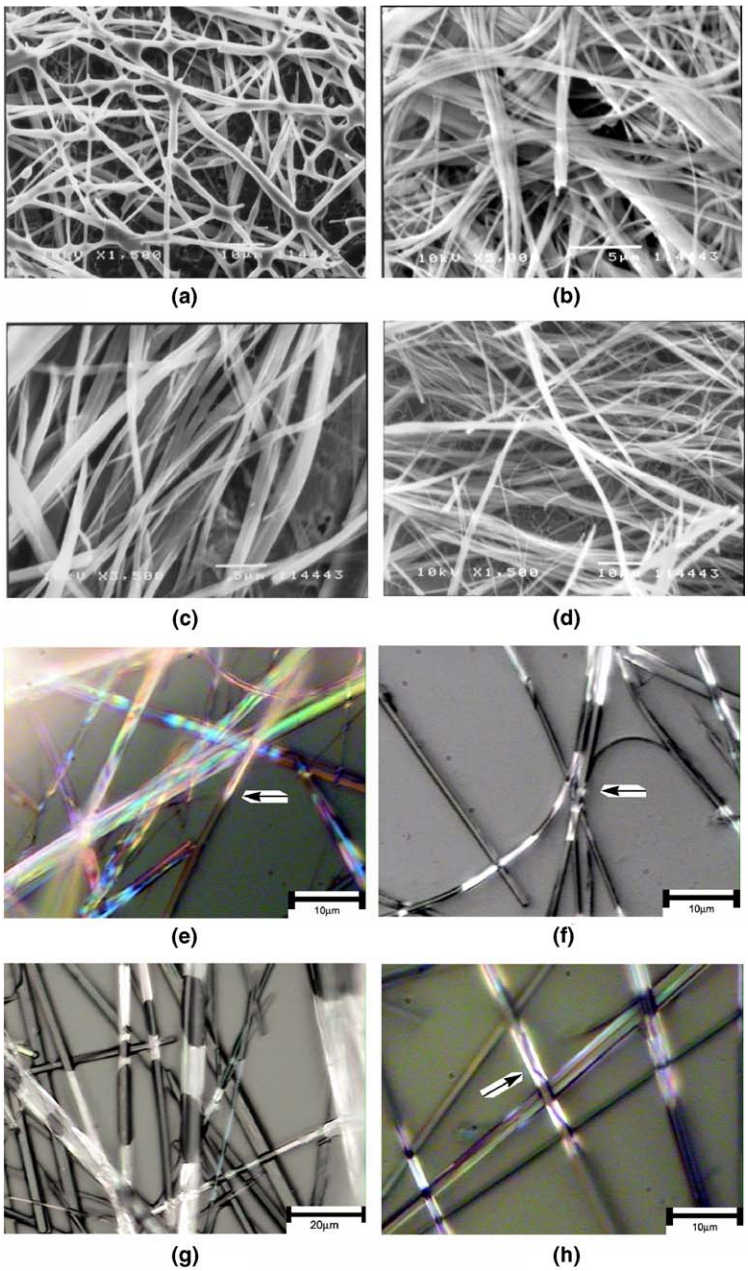


Figure 5. The scanning electron micrographs (a–d) and optical micrographs (e–h) of dried gels from water (a–f) and hexane (g–h). The numbers following are concentrations of gelators in mg/mL. (a) **5B**, 5; (b) **6B**, 10; (c) **7B**, 10; (d) **6C**, 10; (e) **5B**, 5; (f) **7C**, 10; (g) **5C**, 5; (h) **6C**, 5; (e) is obtained under crossed polarizer and (f)–(h) are bright field images.

tion and separated by chromatography. They are excellent gelators in hexane, ethanol, and water. The short-chain monoesters that contain 5–7 carbon chains are versatile gelators for both water and hexane. The hydrogen bonding of the free hydroxyl groups with water and other molecules is important for their self-assembly properties. The diesters without free hydroxyl groups cannot form gels in water, but they can form gels in hexane and ethanol. Perhaps π–π stacking among the gelators and hydrophobic interactions of the molecules with hexane contributed to the gelation properties observed. The monocarbamates that contain 5–7 carbon chains are also excellent gelators for water and organic solvents. The reversible physical gelation in water or water/DMSO mixture can be useful in applications such as enzyme immobilization and drug delivery. The correlation between structures and gelation properties of these molecules may be utilized in designing other effective hydrogelators. Supramolecular hydrogels formed by small sugar derivatives can be used in enzyme purification, protein and DNA immobilization, and as scaffolding material for tissue engineering.

4. Experimental

4.1. General methods and materials

4.1.1. Materials and instrumentation. Chemicals were usually purchased from Aldrich, and VWR; the acetylene containing fatty acids were purchased from GFS Chemicals. Optical microscope images were recorded by Olympus BX60 microscope and CCD camera. The samples were prepared as thin slices of gels placed on a cleaned glass slide, the gels were left to air dry to remove excess solvent. NMR spectra were recorded using 400–500 MHz Varian NMR spectrometers. IR data were recorded using Bruker Tensor 27 with direct sample observation (no KBr pellets). SEM images were obtained using JEOL Model 5410. Melting points were measured using Fisher–Jones melting point apparatus, the melting points are uncorrected.

4.1.2. Gelation testing. About 3–4 mg of the sample was placed in a small vial with a cap, 0.1 mL solvent was initially added to the vial. The mixture was then heated or sonicated until homogeneous, then left standing for 15 min. The solubility of these compounds in different solvents are recorded as I (insoluble), S (soluble), P (cool down crystallized or precipitated), G (stable gel), and Gp (unstable gel). The vials containing gels were inverted and when no solvent flowed it was recorded as G, otherwise as Gp. Serial dilution was performed on gels to find the minimum gelation concentration (mg/mL).

4.2. General synthesis methods

4.2.1. General procedure for the synthesis of compounds 5A–10C. One equivalent of acid was dissolved in anhydrous CH_2Cl_2, and 3 equiv of oxalyl chloride were added to the solution. The reaction mixture was stirred under anhydrous conditions for 4–8 h, then was concentrated on a rotary evaporator to remove the solvent and residual oxalyl chloride. The acid chloride thus obtained was then re-dissolved in anhydrous CH_2Cl_2, 1 equiv of methyl 4,6-*O*-benzylidene-α-D-glucopyranoside was added to the solution. The mixture was stirred for 5 min, and about 5 equiv of anhydrous pyridine was added. The reaction mixture was left stirring at room temperature for 24 h after which the solvent was removed and the residue was taken up in EtOAc or CH_2Cl_2. The organic phase was then washed with 5% sodium bicarbonate solution once, and water 3–4 times. The combined organic phase was dried with Na_2SO_4 overnight. The solvent was removed and the product mixture was then separated by flash chromatography using a gradient of solvent systems (hexane/EtOAc). The three isomers were isolated; the isolated yield of diester is 10–20%, the O2-monoester is 40–70%, and the O3-monoester is ~10%.

4.2.2. General procedure for the synthesis of compounds 11A–12C. 1.33 equiv of the corresponding isocyanate was dissolved in CH_2Cl_2. One equivalent of compound **4** was then added to the stirred isocyanate solution. Sometimes, a small amount of Et_3N (1–2 drops) was be added to the mixture. After stirring at room temperature for 24–48 h, the solution was concentrated and purified by chromatography on silica gel with a gradient solvent system (hexane/acetone from 19:1 to 3:1).

4.3. Characterization data for new compounds

The following sections detail the characterization of these compounds, including their melting points, major IR absorptions, ^{1}H and ^{13}NMR spectroscopy data and high-resolution mass spectrometry data. The protons on the sugar headgroup were labeled based on the positions to which they attached. The isolated yields from the one-pot reactions are not optimized, and the diol headgroup and the acid ratio in moles are given for each series. In the ^{1}H NMR data below, the abbreviation 'app t' is used to describe the multiplicity of signals coupled to two magnetically inequivalent hydrogens in which both coupling constants are of the same magnitude.

4.4. Compounds 5A–C

The diol and acid ratio used was ~1:1, total yield 54.4%.

4.4.1. Methyl 4,6-*O*-benzylidene-2,3-di-*O*-(4-pentynoyl)-α-D-glucopyranoside (5A). White crystals, mp 104.0–105.8 °C; yield 6.6%; IR (cm^{-1}) 3299, 2937, 2869, 2119, 1747, 1371, 1152, 1124, 1098, 1053, 994, 919, 736, 699; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38–7.46 (m, 2H, Ar-H), 7.30–7.36 (m, 3H, Ar-H), 5.60 (app t, 1H, $J_{2,3} = J_{3,4}$ 9.8 Hz, H-3), 5.48 (s, 1H, PhC*H*), 4.90–4.95 (m, 2H, H-1, H-2), 4.29 (dd, 1H, $J_{5,6e}$ 4.9, $J_{6e,6a}$ 9.8 Hz, H-6_{eq}), 3.91 (dt, 1H, $J_{5,6e}$ 4.9, $J_{4,5} = J_{5,6a}$ 9.8 Hz, H-5), 3.76 (app t, 1H, $J_{5,6a} = J_{6e,6a}$ 9.8 Hz, H-6_{ax}), 3.65 (app t, 1H, $J_{2,3} = J_{3,4}$ 9.8 Hz, H-4), 3.39 (s, 3H, OCH_3), 2.40–2.63 (m, 8H, $2 \times CH_2CH_2$), 1.97 (t, 1H, J 2.9 Hz, $CH_2C{\equiv}CH$), 1.86 (m, 1H, J 2.9 Hz, $CH_2C{\equiv}CH$); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 171.0, 170.4, 136.8, 129.0, 128.1, 126.1, 101.4, 97.4, 82.2, 82.0, 79.0, 71.6, 69.2, 69.1, 68.7, 62.2, 55.3, 33.13, 33.07, 14.3, 14.2; HR ESIMS calcd for $C_{24}H_{27}O_8$ $[M+H]^+$ 443.1706, found 443.1710.

4.4.2. Methyl 4,6-*O*-benzylidene-2-*O*-(4-pentynoyl)-α-D-glucopyranoside (5B). White crystals, mp 71.8–73.5 °C; yield, 35.6%; IR (cm^{-1}) 3495, 3287, 2933, 2866, 1743, 1379, 1150, 1124, 1094, 1061, 988, 918, 738, 700; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43–7.50 (m, 2H, Ar-H), 7.31–7.37 (m, 3H, Ar-H), 5.53 (s, 1H, PhC*H*), 4.93 (d, 1H, $J_{1,2}$ 3.9 Hz, H-1), 4.81 (dd, 1H, $J_{1,2}$ 3.9, $J_{2,3}$

9.8 Hz, H-2), 4.27 (dd, 1H, $J_{5,6e}$ 4.9, $J_{6e,6a}$ 9.8 Hz, H-6_{eq}), 4.18 (app t, 1H, $J_{2,3} = J_{3,4}$ 9.8 Hz, H-3), 3.83 (dt, 1H, $J_{5,6e}$ 4.9, $J_{4,5} = J_{5,6a}$ 9.8 Hz, H-5), 3.74 (app t, 1H, $J_{5,6a} = J_{6e,6a}$ 9.8 Hz, H-6_{ax}), 3.56 (app t, 1H, $J_{2,3} = J_{3,4}$ 9.8 Hz, H-4), 3.37 (s, 3H, OCH_3), 2.62 (t, 2H, $J = 7.3$ Hz, CH_2CO), 2.51 (m, 2H, CH_2C≡CH), 2.30 (s, broad, OH), 2.00 (t, 1H, J 2.9 Hz, CH$_2$C≡CH); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 171.3, 136.8, 129.1, 128.2, 126.2, 101.8, 97.3, 82.3, 81.1, 73.7, 69.2, 68.6, 68.2, 61.9, 55.2, 33.0, 14.2; HR ESIMS calcd for $C_{22}H_{33}NO_7$ $[M+H]^+$ 363.1444, found 363.1432.

4.4.3. Methyl 4,6-*O*-benzylidene-3-*O*-(4-pentynoyl)-α-D-glucopyranoside (5C). White crystals, mp 174.0–175.8 °C; yield 12.2%; IR (cm^{-1}) 3566, 3306, 2872, 1746, 1371, 1178, 1122, 1096, 1072, 1058, 1003, 731, 669, 651; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39–7.44 (m, 2H, Ar-H), 7.30–7.36 (m, 3H Ar-H), 5.47 (s, 1H, PhCH), 5.33 (app t, 1H, $J_{2,3} = J_{3,4}$ 9.8 Hz, H-3), 4.79 (d, 1H, $J_{1,2}$ 3.9 Hz, H-1), 4.29 (dd, 1H, $J_{5,6e}$ 4.9, $J_{6e,6a}$ 9.8 Hz, H-6_{eq}), 3.85 (dt, 1H, $J_{5,6e}$ 4.9, $J_{4,5} = J_{5,6a}$ 9.8 Hz, H-5), 3.73 (app t, 1H, $J_{5,6a} = J_{6e,6a}$ 9.8 Hz, H-6_{ax}), 3.66 (dd, 1H, $J_{1,2}$ 3.9, $J_{3,4}$ 9.8 Hz, H-2), 3.57 (app t, 1H, $J_{2,3} = J_{3,4}$ 9.8 Hz, H-4), 3.45 (s, 3H, OCH_3), 2.62 (t, 2H, $J = 7.3$ Hz, CH_2CO), 2.49 (m, 2H, CH_2C≡CH), 1.86 (t, 1H, CH$_2$C≡CH), 1.66 (sb, OH); ^{13}C NMR ($CDCl_3$, 100 MHz), δ 171.1, 136.9, 129.0, 128.1, 126.2, 101.5, 100.0, 82.3, 78.6, 72.6, 71.7, 69.0, 68.9, 62.7, 55.6, 33.3, 14.4; HR ESIMS calcd for $C_{22}H_{33}NO_7$ $[M+H]^+$ 363.1444, found 363.1445.

4.5. Compounds 6A–C

The diol and acid ratio used was ~1:1, total yield 58.4%.

4.5.1. Methyl 4,6-*O*-benzylidene-2,3-di-*O*-(5-hexynoyl)-α-D-glucopyranoside (6A). White crystals, mp 92.1–94.1 °C; yield 4.6%; IR (cm^{-1}) 3307, 3054, 2980, 2888, 2117, 1747, 1458, 1383, 1265, 1149, 1099, 1049, 964, 733, 703, 643; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39–7.46 (m, 2H, 2Ar-H), 7.30–7.37 (m, 3H, Ar-3CH), 5.59 (app t, 1H, $J_{2,3} = J_{3,4}$ 9.8 Hz, H-3), 5.49 (s, 1H, PhCH), 4.94 (d, 1H, $J_{1,2}$ 3.9 Hz, H-1), 4.89 (dd, 1H, $J_{1,2}$ 3.9, $J_{2,3}$ 9.8 Hz, H-2), 4.29 (dd, 1H, $J_{5,6e}$ 4.9, $J_{6e,6a}$ 9.8 Hz, H-6_{eq}), 3.91 (dt, 1H, $J_{5,6e}$ 4.9, $J_{4,5} = J_{5,6a}$ 9.8 Hz, H-5), 3.76 (app t, 1H, $J_{5,6a} = J_{6e,6a}$ 9.8 Hz, H-6_{ax}), 3.64 (app t, 1H, $J_{2,3} = J_{3,4}$ 9.8 Hz, H-4), 3.39 (s, 3H, OCH_3), 2.48 (m, 2H, CH_2CO), 2.44 (m, 2H, CH_2CO), 2.24 (dt, 2H, J 2.9, 6.8 Hz, CH_2C≡CH), 2.18 (dt, 2H, J 2.9, 6.8 Hz, CH_2C≡CH), 1.96 (t, 1H, J 2.9 Hz, CH$_2$C≡CH), 1.91 (t, 1H, J 2.9 Hz, CH$_2$C≡CH), 1.80 (m, 4H, 2 × CH$_2$CH_2CH$_2$); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 172.4, 171.7, 136.8, 129.0, 128.2, 126.0, 101.5, 97.5, 83.0, 82.9, 79.1, 71.5, 69.3, 69.1, 68.7, 62.2, 55.3, 32.65, 32.56, 23.6, 23.4, 17.6, 17.5; HR ESIMS calcd for $C_{26}H_{31}O_8$ $[M+H]^+$ 471.2019, found 424.2030.

4.5.2. Methyl 4,6-*O*-benzylidene-2-*O*-(5-hexynoyl)-α-D-glucopyranoside (6B). White crystals; mp 112.6–113.8 °C; yield 44.0%; IR (cm^{-1}) 3505, 3287, 2980, 2910, 1743, 1457, 1383, 1252, 1150, 1125, 1095, 1042, 985, 964, 917, 739, 702 and 657; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44–7.52 (m, 2H, 2Ar-H), 7.32–7.39 (m, 3H, 3Ar-H), 5.52 (s, 1H, PhCH), 4.93 (d, 1H, $J_{1,2}$ 3.9 Hz, H-1), 4.78 (dd, 1H, $J_{1,2}$ 3.9, $J_{2,3}$ 9.8 Hz, H-2), 4.27 (dd, 1H, $J_{5,6e}$ 4.9, $J_{6e,6a}$ 9.8 Hz, H-6_{eq}), 4.14 (app t, 1H, $J_{2,3} = J_{3,4}$ 9.8 Hz, H-3), 3.81 (dt, 1H, $J_{5,6e}$ 4.9, $J_{4,5} = J_{5,6a}$ 9.8 Hz, H-5), 3.73 (app t, 1H, $J_{5,6a} = J_{6e,6a}$ 9.8 Hz, H-6_{ax}), 3.53 (app t, 1H, $J_{2,3} = J_{3,4}$ 9.8 Hz, H-4), 3.37 (s, 3H, OCH_3), 2.59 (sb, 1H, OH), 2.54 (t, 2H, J 7.3 Hz, CH_2CO), 2.25 (m, 2H, CH_2C≡CH), 1.96 (m, 1H, CH$_2$C≡CH), 1.85 (quintet, 2H, J 7.3 Hz, CH$_2$CH_2CH$_2$); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 172.7, 136.9, 129.3, 128.3, 126.3, 102.0, 97.5, 83.1, 81.3, 73.5, 69.2, 68.8, 68.6, 61.9, 55.4, 32.7, 23.5, 17.6; HR ESIMS calcd for $C_{20}H_{25}O_7$ $[M+H]^+$ 377.1600, found 377.1588.

4.5.3. Methyl 4,6-*O*-benzylidene-3-*O*-(5-hexynoyl)-α-D-glucopyranoside (6C). White crystals, mp 138.5–139.2 °C; yield 9.8%; IR (cm^{-1}) 3662, 3466, 3299, 2937, 2842, 2119, 1747, 1371, 1266, 1152, 1124, 1098, 1053, 994, 919, 736, 699, 651; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39–7.47 (m, 2H, Ar-H), 7.30–7.38 (m, 3H, Ar-H), 5.48 (s, 1H, PhCH), 5.32 (app t, 1H, $J_{2,3} = J_{3,4}$ 9.8 Hz, H-3), 4.79 (d, 1H, $J_{1,2}$ 3.9 Hz, H-1), 4.29 (dd, 1H, $J_{5,6e}$ 4.9, $J_{6e,6a}$ 9.8 Hz, H-6_{eq}), 3.85 (dt, 1H, $J_{5,6e}$ 4.9, $J_{4,5} = J_{5,6a}$ 9.8 Hz, H-5), 3.73 (app t, 1H, $J_{5,6a} = J_{6e,6a}$ 9.8 Hz, H-6_{ax}), 3.64 (m, 1H, H-2), 3.57 (app t, 1H, $J_{2,3} = J_{3,4}$ 9.8 Hz, H-4), 3.45 (s, 3H, OCH_3), 2.50 (t, 2H, J 7.3 Hz, CH_2CO), 2.20 (m, 2H, CH_2C≡CH), 1.92 (t, 1H, J 2.9 Hz, CH$_2$C≡CH), 1.84 (quintet, 2H, J 7.3 Hz, CH$_2$CH_2CH$_2$); ^{13}C NMR ($CDCl_3$, 100 MHz), δ, 173.1, 136.9, 129.1, 128.2, 126.1, 101.5, 100.1, 83.3, 78.6, 72.2, 71.8, 69.0, 68.9, 62.7, 55.6, 33.0, 23.7, 17.6; HR ESIMS calcd for $C_{20}H_{25}O_7$ $[M+H]^+$ 377.1600, found 377.1592.

4.6. Compounds 7A–C

The diol and acid ratio used was 1:1, total yield 80.3%.

4.6.1. Methyl 4,6-*O*-benzylidene-2,3-di-*O*-(5-heptynoyl)-α-D-glucopyranoside (7A). White crystals, mp 64.0–66.0 °C; yield 12.8%; IR (cm^{-1}, film) 3305, 3055, 2987, 2940, 2869, 2117 (weak), 1745, 1421, 1266, 1053, 1021, 740, 705; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37–7.44 (m, 2H, Ar-H), 7.30–7.36 (m, 3H, Ar-H), 5.59 (app t, 1H, $J_{2,3} = J_{3,4}$ 9.8 Hz, H-3), 5.48 (s, 1H, PhCH), 4.93 (d, 1H, $J_{1,2}$ 3.9 Hz, H-1), 4.89 (dd, 1H, $J_{1,2}$ 3.9, $J_{2,3}$ 9.8 Hz, H-2), 4.29 (dd, 1H, $J_{5,6e}$ 4.9, $J_{6e,6a}$ 9.8 Hz, H-6_{eq}), 3.91 (dt, 1H, $J_{5,6e}$ 4.9, $J_{4,5} = J_{5,6a}$ 9.8 Hz, H-5), 3.75 (app t, 1H, $J_{5,6a} = J_{6e,6a}$ 9.8 Hz, H-6_{ax}), 3.63 (app

t, 1H, $J_{2,3} = J_{3,4}$ 9.8 Hz, H-4), 3.39 (s, 3H, OCH_3), 2.24–2.42 (m, 4H, 2 × CH_2CO), 2.19 (dt, 2H, *J* 2.9, 6.8 Hz, CH_2C≡CH), 2.09 (dt, 2H, *J* 2.9, 6.8 Hz, CH_2C≡CH) 1.93 (t, 1H, *J* 2.9 Hz, CH$_2$C≡C*H*), 1.89 (t, 1H, *J* 2.9 Hz, CH$_2$C≡C*H*), 1.70 (m, 4H, CH_2CH$_2$CO), 1.42–1.58 (m, 4H, CH_2CH$_2$C≡CH); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 172.7, 172.1, 136.8, 129.0, 128.2, 126.1, 101.5, 97.6, 83.8, 83.7, 79.2, 71.4, 68.8, 68.7, 68.6, 62.3, 55.4, 33.7, 33.5, 27.7, 27.5, 24.0, 23.9, 18.1, 18.0; HR ESIMS calcd for $C_{28}H_{35}O_8$ $[M+H]^+$ 499.2332, found 499.2320.

4.6.2. Methyl 4,6-*O*-benzylidene-2-*O*-(6-heptynoyl)-α-D-glucopyranoside (7B). White crystals, mp 58.0–59.0 °C; yield 48.9%; IR (cm^{-1}, film) 3596, 3305, 3055, 2987, 2938, 2869, 1739, 1421, 1266, 1059, 1039, 896, 740, 705; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44–7.50 (m, 2H, Ar-H), 7.32–7.39 (m, 3H, Ar-H), 5.52 (s, 1H, PhC*H*), 4.93 (d, 1H, $J_{1,2}$ 3.9 Hz, H-1), 4.78 (dd, 1H, $J_{1,2}$ 3.9, $J_{2,3}$ 9.8 Hz, H-2), 4.27 (dd, 1H, $J_{5,6e}$ 4.9, $J_{6e,6a}$ 9.8 Hz, H-6$_{eq}$), 4.14 (app t, 1H, $J_{2,3} = J_{3,4}$ 9.8 Hz, H-3), 3.82 (dt, 1H, $J_{5,6e}$ 4.9, $J_{4,5} = J_{5,6a}$ 9.8 Hz, H-5), 3.73 (app t, 1H, $J_{5,6a} = J_{6e,6a}$ 9.8 Hz, H-6$_{ax}$), 3.55 (app t, 1H, $J_{2,3} = J_{3,4}$ 9.8 Hz, H-4), 3.37 (s, 3H, OCH_3), 2.41 (t, 2H, *J* 7.3 Hz CH_2CO), 2.19 (dt, 2H, *J* 2.9, 7.3 Hz, CH$_2$CH_2C≡CH), 1.94 (t, 1H, *J* 2.9 Hz, CH$_2$C≡C*H*), 1.74 (quintet, 2H, *J* 7.3 Hz, CH_2CH$_2$CO), 1.56 (m, 2H, *J* 7.3, CH_2CH$_2$C≡CH); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 173.1, 136.9, 129.3, 128.3, 126.2, 102.0, 97.5, 83.9, 81.3, 73.4, 68.8, 68.7, 68.6, 61.9, 55.4, 33.5, 27.6, 23.9, 18.0; HR ESIMS calcd for $C_{21}H_{27}O_7$ $[M+H]^+$ 391.1757, found 391.1763.

4.6.3. Methyl 4,6-*O*-benzylidene-3-*O*-(6-heptynoyl)-α-D-glucopyranoside (7C). White crystals, mp 124.0–125.0 °C; yield 18.6%; IR (cm^{-1}, film) 3305, 3054, 2987, 1741, 1422, 1266, 1057, 896, 740, 705; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30–7.44 (m, 5H, Ar-H), 5.47 (s, 1H, PhC*H*), 5.32 (app t, 1H, $J_{2,3} = J_{3,4}$ 9.8 Hz, H-3), 4.78 (d, 1H, $J_{1,2}$ 3.9 Hz, H-1), 4.28 (dd, 1H, $J_{5,6e}$ 4.9, $J_{6e,6a}$ 9.8 Hz, H-6$_{eq}$), 3.85 (dt, 1H, $J_{5,6e}$ 4.9, $J_{4,5} = J_{5,6a}$ 9.8 Hz, H-5), 3.73 (app t, 1H, $J_{5,6a} = J_{6e,6a}$ 9.8 Hz, H-6$_{ax}$), 3.64 (m, 1H, H-2), 3.57 (app t, 1H, $J_{2,3} = J_{3,4}$ 9.8 Hz, H-4), 3.45 (s, 3H, OCH_3), 2.39 (t, 2H, *J* 7.3 Hz, CH_2CO), 2.11 (dt, 2H, *J* 2.9, 6.8 Hz, CH$_2$CH_2C≡CH), 1.89 (t, 1H, *J* 2.9 Hz, CH$_2$C≡C*H*), 1.74 (quintet, 2H, *J* 7.3, CH_2CH$_2$CO), 1.51 (quintet, 2H, *J* 6.8 Hz, CH_2CH$_2$C≡CH); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 173.5, 136.9, 129.1, 128.2, 126.1, 101.5, 100.1, 84.0, 78.7, 72.1, 71.8, 68.9, 68.5, 62.7, 55.6, 33.8, 27.5, 24.0, 18.0; HR ESIMS calcd for $C_{21}H_{27}O_7$ $[M+H]^+$ 391.1757, found 391.1751.

4.7. Compounds 8A–C

The diol and acid ratio used was 1:1, yield 63.2%.

4.7.1. Methyl 4,6-*O*-benzylidene-2,3-di-*O*-(8-nonynoyl)-α-D-glucopyranoside (8A). White crystals, mp 63.8–65.0 °C; yield 9.6%; IR (cm^{-1}) 3307, 2937, 2862, 2115, 1745, 1458, 1266, 1151, 1126, 1095, 1051, 1021, 988, 916, 735, 699, 632; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38–7.44 (m, 2H, Ar-H), 7.30–7.36 (m, 3H, Ar-H), 5.58 (app t, 1H, $J_{2,3} = J_{3,4}$ 9.8 Hz, H-3), 5.48 (s, 1H, PhC*H*), 4.92 (d, 1H, $J_{1,2}$ 3.9 Hz, H-1), 4.88 (dd, 1H, $J_{1,2}$ 3.9, $J_{2,3}$ 9.8 Hz, H-2), 4.28 (dd, 1H, $J_{5,6e}$ 4.9, $J_{6e,6a}$ 9.8 Hz, H-6$_{eq}$), 3.91 (dt, 1H, $J_{5,6e}$ 4.9, $J_{4,5} = J_{5,6a}$ 9.8 Hz, H-5), 3.75 (app t, 1H, $J_{5,6a} = J_{6e,6a}$ 9.8 Hz, H-6$_{ax}$), 3.62 (app t, 1H, $J_{2,3} = J_{3,4}$ 9.8 Hz, H-4), 3.39 (s, 3H, OCH_3), 2.22–2.40 (m, 4H, 2 × CH_2CO), 2.16 (m, 2H, CH_2C≡CH), 2.09 (m, 2H, CH_2C≡CH), 1.89–1.94 (m, 2H, 2 × CH$_2$C≡C*H*), 1.46–1.65 (m, 8H, 2 × CH_2CH$_2$CO, 2 × CH_2CH$_2$C≡CH), 1.20–1.45 (m, 8H, 2 × CH_2CH_2CH$_2$CH$_2$CO); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 173.0, 172.3, 136.8, 129.0, 128.1, 126.0, 101.4, 97.6, 84.4, 84.3, 79.2, 71.3, 68.8, 68.6, 68.24, 68.18, 62.2, 55.3, 34.1, 33.9, 28.4, 28.3, 28.2, 28.1, 28.0, 24.8, 24.6, 18.2; HR ESIMS calcd for $C_{32}H_{43}O_8$ $[M+H]^+$ 555.2958, found 555.2957.

4.7.2. Methyl (*R*)-4,6-*O*-benzylidene-2-*O*-(8-nonynoyl)-α-D-glucopyranoside (8B). White crystals, mp 80.5–82.4 °C; yield 38.4%; IR (cm^{-1}) 3505, 3286, 2935, 2862, 1743, 1458, 1257, 1210, 1125, 1094, 1061, 1042, 986, 965, 916, 764, 745, 700, 674; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.44–7.52 (m, 2H, Ar-H), 7.32–7.40 (m, 3H, Ar-H), 5.52 (s, 1H, PhC*H*), 4.93 (d, 1H, $J_{1,2}$ 3.9 Hz, H-1), 4.78 (dd, 1H, $J_{1,2}$ 3.9, $J_{2,3}$ 9.8 Hz, H-2), 4.27 (dd, 1H, $J_{5,6e}$ 4.9, $J_{6e,6a}$ 9.8 Hz, H-6$_{eq}$), 4.15 (app t, 1H, $J_{2,3} = J_{3,4}$ 9.8 Hz, H-3), 3.82 (dt, 1H, $J_{5,6e}$ 4.9, $J_{4,5} = J_{5,6a}$ 9.8 Hz, H-5), 3.73 (app t, 1H, $J_{5,6a} = J_{6e,6a}$ 9.8 Hz, H-6$_{ax}$), 3.53 (app t, 1H, $J_{2,3} = J_{3,4}$ 9.8 Hz, H-4), 3.37 (s, 3H, OCH_3), 2.39 (t, 2H, *J* 7.8 Hz, CH_2CO), 2.16 (dt, 2H, *J* 2.9, 6.8 Hz, CH_2C≡CH), 1.92 (t, 1H, *J* 2.9 Hz, CH$_2$C≡C*H*), 1.64 (m, 2H, CH_2CH$_2$CO), 1.50 (m, 2H, CH_2CH$_2$C≡CH), 1.38–1.44 (m, 4H, CH_2CH_2CH$_2$CH$_2$CO); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 173.1, 136.8, 128.9, 128.0, 126.1, 101.6, 97.3, 84.2, 81.1, 73.2, 68.5, 68.2, 61.8, 60.1, 55.1, 33.7, 28.1, 28.0, 24.5, 18.0; HR ESIMS calcd for $C_{23}H_{31}O_7$ $[M+H]^+$ 419.2070, found 419.2046.

4.7.3. Methyl 4,6-*O*-benzylidene-3-*O*-(8-nonynoyl)-α-D-glucopyranoside (8C). White crystals, mp 97.6–99.0; yield 15.2%; IR (cm^{-1}) 3565, 3308, 2938, 2305, 1745, 1458, 1265, 1132, 1096, 1070, 1016, 984, 896, 734, 703; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.38–7.46 (m, 2H, Ar-H), 7.28–7.37 (m, 3H, Ar-H), 5.46 (s, 1H, s, 1H, PhC*H*), 5.31 (app t, 1H, $J_{2,3} = J_{3,4}$ 9.8 Hz, H-3), 4.78 (d, 1H, $J_{1,2}$ 3.9 Hz, H-1), 4.27 (dd, 1H, $J_{5,6e}$ 4.9, $J_{6e,6a}$ 9.8 Hz, H-6$_{eq}$), 3.84 (dt, 1H, $J_{5,6e}$ 4.9, $J_{4,5} = J_{5,6a}$ 9.8 Hz, H-5), 3.72 (app t, 1H, $J_{5,6a} = J_{6e,6a}$ 9.8 Hz, H-6$_{ax}$), 3.64 (dd, 1H, $J_{1,2}$ 3.9, $J_{2,3}$ 9.8 Hz, H-2), 3.55 (app t, 1H,

$J_{2,3} = J_{3,4}$ 9.8 Hz, H-4), 3.43 (s, 3H, OCH_3), 2.35 (t, 2H, J 7.3 Hz, CH_2CO), 2.08 (dt, 1H, J 2.9, 6.8 Hz, CH_2C≡CH), 1.91 (t, 1H, J 2.9 Hz, CH$_2$C≡CH), 1.61 (m, 2H, CH_2CH$_2$CO), 1.40 (m, 2H, CH_2CH$_2$C≡CH), 1.22–1.35 (m, 4H, CH_2CH_2CH$_2$CH$_2$CO); ^{13}C NMR (CDCl$_3$, 100 MHz) δ 173.6, 136.9, 128.9, 128.1, 126.0, 101.3, 100.1, 84.5, 78.6, 71.9, 71.7, 68.8, 68.2, 62.6, 55.5, 34.2, 28.2, 28.0, 24.8, 18.2; HR ESIMS calcd for $C_{23}H_{31}O_7$ $[M+H]^+$ 419.2070, found 419.2065.

4.8. Compounds 9A–C

The diol and acid ratio used was 1:1, total yield 80.3%.

4.8.1. Methyl 4,6-*O*-benzylidene-2,3-di-*O*-(10-undecynoyl)-α-D-glucopyranoside (9A). White solid, mp 43.0–44.9 °C; yield 14.3%; IR (cm^{-1}) 3289, 2931, 2857, 2115, 1746, 1138, 1458, 1378, 1312, 1260, 1151, 1125, 1096, 917, 738, 698, 630; ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.38–7.46 (m, 2H, Ar-H), 7.29–7.35 (m, 3H, Ar-H), 5.58 (app t, 1H, $J_{2,3} = J_{3,4}$ 9.8 Hz, H-3), 5.48 (s, 1H, PhCH), 4.92 (d, 1H, $J_{1,2}$ 3.9 Hz, H-1), 4.88 (dd, 1H, $J_{1,2}$ 3.9, $J_{2,3}$ 9.8 Hz, H-2), 4.28 (dd, 1H, $J_{5,6e}$ 4.9, $J_{6e,6a}$ 9.8 Hz, H-6$_{eq}$), 3.90 (dt, 1H, $J_{5,6e}$ 4.9, $J_{4,5} = J_{5,6a}$ 9.8 Hz, H-5), 3.75 (app t, 1H, $J_{5,6a} = J_{6e,6a}$ 9.8 Hz, H-6$_{ax}$), 3.62 (app t, 1H, $J_{2,3} = J_{3,4}$ 9.8 Hz, H-4), 3.38 (s, 3H, OCH_3), 2.18–2.37 (m, 4H, 2 × CH_2CO), 2.09–2.18 (m, 4H, 2 × CH_2C≡CH), 1.89–1.92 (m, 2H, 2 × CH$_2$C≡CH), 1.40–1.62 (m, 8H, 2 × CH_2CH$_2$CO, 2 × CH_2CH$_2$C≡CH), 1.10–1.40 (m, 16H, 2 × (CH_2)$_4$-CH$_2$CH$_2$CO); ^{13}C NMR (CDCl$_3$, 100 MHz) δ 173.1, 172.4, 136.9, 129.0, 128.1, 126.0, 101.4, 97.6, 84.6, 79.3, 71.3, 68.8, 68.5, 68.1, 62.3, 55.3, 34.2, 34.0, 29.0, 28.9, 28.82, 28.77, 28.6, 28.3, 25.0, 24.8, 18.3; HR ESIMS calcd for $C_{36}H_{51}O_8$ $[M+H]^+$ 611.3584, found 611.3581.

4.8.2. Methyl 4,6-*O*-benzylidene-2-*O*-(10-undecynoyl)-α-D-glucopyranoside (9B). White solid, mp 71.0–73.5 °C; yield 55.5%; IR (cm^{-1}) 3522, 3308, 2934, 2859, 2115, 1743, 1458, 1381, 1314, 1266, 1150, 1123, 1093, 1059, 1041, 987, 917, 735, 701, 639; ^{1}H NMR (CDCl$_3$, 400 MHz) δ 7.44–7.52 (m, 2H, Ar-H), 7.32–7.40 (m, 3H, Ar-H), 5.54 (s, 1H, PhCH), 4.94 (d, 1H, $J_{1,2}$ 3.9 Hz, H-1), 4.79 (dd, 1H, $J_{1,2}$ 3.9, $J_{2,3}$ 9.8 Hz, H-2), 4.28 (dd, 1H, $J_{5,6e}$ 4.9, $J_{6e,6a}$ 9.8 Hz, H-6$_{eq}$), 4.17 (app t, 1H, $J_{2,3} = J_{3,4}$ 9.8 Hz, H-3), 3.83 (dt, 1H, $J_{5,6e}$ 4.9, $J_{4,5} = J_{5,6a}$ 9.8 Hz, H-5), 3.75 (app t, 1H, $J_{5,6a} = J_{6e,6a}$ 9.8 Hz, H-6$_{ax}$), 3.55 (app t, 1H, $J_{2,3} = J_{3,4}$ 9.8 Hz, H-4), 3.38 (s, 3H, OCH_3), 2.39 (t, 2H, J 7.8 Hz, CH_2CO), 2.16 (dt, 2H, J 2.9, 6.8 Hz, CH_2C≡CH), 1.91 (t, 1H, J 2.9 Hz, CH$_2$C≡CH), 1.63 (m, 2H, CH_2CH$_2$CO), 1.49 (m, 2H, CH_2CH$_2$C≡CH), 1.18–1.42 (m, 8H, (CH_2)$_4$CH$_2$CH$_2$CO); ^{13}C NMR (CDCl$_3$, 100 MHz) δ, 173.5, 136.9, 129.3, 128.3, 126.3, 102.0, 97.6, 84.7, 81.4, 73.3, 68.8, 68.6, 68.1, 61.9, 55.4, 34.0, 29.0, 28.8, 28.6, 28.3, 24.8, 18.3; HR ESIMS Calcd for $C_{25}H_{35}O_7$ $[M+H]^+$ 447.2383, found 447.2369.

4.8.3. Methyl 4,6-*O*-benzylidene-3-*O*-(10-undecynoyl)-α-D-glucopyranoside (9C). Off white solid, mp 93.8–95.0 °C; yield 10.5%; IR (cm^{-1}) 3466, 3299, 2937, 2119, 1747, 1371, 1266, 1152, 1124, 1098, 1053, 994, 919, 736, 699, 651; ^{1}H NMR (CDCl$_3$, 400 MHz) δ 7.39–7.45 (m, 2H, Ar-H), 7.30–7.35 (m, 3H, Ar-H), 5.47 (s, 1H, s, 1H, PhCH), 5.31 (app t, 1H, $J_{2,3} = J_{3,4}$ 9.8 Hz, H-3), 4.78 (d, 1H, $J_{1,2}$ 3.9 Hz, H-1), 4.28 (dd, 1H, $J_{5,6e}$ 4.9, $J_{6e,6a}$ 9.8 Hz, H-6$_{eq}$), 3.85 (app t, 1H, $J_{5,6e}$ 4.9, $J_{4,5}$ 9.8, $J_{5,6a}$ 10.7 Hz, H-5), 3.73 (app t, 1H, $J_{5,6a}$ 10.7, $J_{6e,6a}$ 9.8 Hz, H-6$_{ax}$), 3.64 (dd, 1H, $J_{1,2}$ 3.9, $J_{2,3}$ 9.8 Hz, H-2), 3.56 (app t, 1H, $J_{2,3} = J_{3,4}$ 9.8 Hz, H-4), 3.45 (s, 3H, OCH_3), 2.35 (t, 2H, J 7.8 Hz, CH_2CO), 2.13 (dt, 1H, J 2.9, 6.8 Hz, CH_2C≡CH), 1.91 (t, 1H, J 2.9 Hz, CH$_2$C≡CH), 1.60 (m, 2H, CH_2CH$_2$CO), 1.46 (m, 2H, CH_2CH$_2$C≡CH), 1.12–1.36 (m, 8H, (CH_2)$_4$CH$_2$CH$_2$CO); ^{13}C NMR (CDCl$_3$, 100 MHz) δ 173.9, 137.0, 129.0, 128.2, 126.1, 101.4, 100.1, 84.7, 78.7, 72.0, 71.8, 68.9, 68.1, 62.7, 55.6, 34.3, 29.0, 28.8, 28.6, 28.4, 25.0, 18.3; HR ESIMS calcd for $C_{25}H_{35}O_7$ $[M+H]^+$ 447.2383, found 447.2398.

4.9. Compounds 10A–C

The diol and acid ratio used was 2:1, isomer **C** was not isolated, total yield 73.8%.

4.9.1. Methyl 4,6-*O*-benzylidene-2,3-di-*O*-(12-tridecynoyl)-α-D-glucopyranoside (10A). White solid, mp 49.9–51.8 °C; yield 58.7%; IR (cm^{-1}) 3305, 2926, 2856, 2115, 1744, 1367, 1183, 1124, 1097, 1054, 870, 742, 631; ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.38–7.46 (m, 2H, Ar-H), 7.29–7.37 (m, 3H, Ar-H), 5.58 (app t, 1H, $J_{2,3} = J_{3,4}$ 9.8 Hz, H-3), 5.48 (s, 1H, PhCH), 4.92 (d, 1H, $J_{1,2}$ 3.9 Hz, H-1), 4.88 (dd, 1H, $J_{1,2}$ 3.9, $J_{2,3}$ 9.8 Hz, H-2), 4.28 (dd, 1H, $J_{5,6e}$ 4.9, $J_{6e,6a}$ 9.8 Hz, H-6$_{eq}$), 3.91 (dt, 1H, $J_{5,6e}$ 4.9, $J_{4,5} = J_{5,6a}$ 9.8 Hz, H-5), 3.75 (app t, 1H, $J_{5,6a} = J_{6e,6a}$ 9.8 Hz, H-6$_{ax}$), 3.62 (app t, 1H, $J_{2,3} = J_{3,4}$ 9.8 Hz, H-4), 3.38 (s, 3H, OCH_3), 2.28 (m, 4H, 2 × CH_2CO), 2.15 (m, 4H, 2 × CH_2C≡CH), 1.89–2.02 (m, 2H, 2 × CH$_2$C≡CH), 1.42–1.64 (m, 8H, 2 × CH_2CH$_2$CO, 2 × CH_2CH$_2$C≡ CH), 1.02–1.42 (m, 24H, 2 × (CH_2)$_6$CH$_2$CH$_2$CO); ^{13}C NMR (CDCl$_3$, 100 MHz) δ 173.2, 172.4, 136.9, 129.0, 128.1, 126.0, 101.4, 97.6, 84.7, 79.3, 71.3, 68.8, 68.5, 68.0, 62.3, 55.3, 34.2, 34.0, 29.4(m), 29.2, 29.0(m), 28.7, 28.4, 25.0, 24.8, 18.3; HR ESIMS calcd for $C_{40}H_{59}O_8$ $[M+H]^+$ 667.4210, found 667.4203.

4.9.2. Methyl 4,6-*O*-benzylidene-2-*O*-(12-tridecynoyl)-α-D-glucopyranoside (10B). White crystals, mp 77.0–78.0 °C; yield 15.1%; IR (cm^{-1}) 3478, 3305, 2929, 2856, 2115, 1737, 1376, 1174, 1122, 1094, 1058, 872,

743, 634; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.44–7.52 (m, 2H, Ar-H), 7.32–7.40 (m, 3H, Ar-H), 5.53 (s, 1H, PhC*H*), 4.94 (d, 1H, $J_{1,2}$ 3.9 Hz, H-1), 4.78 (dd, 1H, $J_{1,2}$ 3.9, $J_{2,3}$ 9.8 Hz, H-2), 4.28 (dd, 1H, $J_{5,6e}$ 4.9, $J_{6e,6a}$ 9.8 Hz, H-6_{eq}), 4.16 (app t, 1H, $J_{2,3} = J_{3,4}$ 9.8 Hz, H-3), 3.83 (dt, 1H, $J_{5,6e}$ 4.9, $J_{4,5} = J_{5,6a}$ 9.8 Hz, H-5), 3.75 (app t, 1H, $J_{5,6a} = J_{6e,6a}$ 9.8 Hz, H-6_{ax}), 3.55 (app t, 1H, $J_{2,3} = J_{3,4}$ 9.8 Hz, H-4), 3.38 (s, 3H, OC*H*$_3$), 2.38 (t, 2H, *J* 7.8 Hz, C*H*$_2$CO), 2.15 (dt, 2H, *J* 2.9, 6.8 Hz, C*H*$_2$C≡CH), 1.91 (t, 1H, *J* 2.9 Hz, CH$_2$C≡C*H*), 1.62 (m, 2H, C*H*$_2$CH$_2$CO), 1.49 (m, 2H, C*H*$_2$CH$_2$C≡CH), 1.12–1.40 (m, 12H, (C*H*$_2$)$_6$CH$_2$CH$_2$CO); ^{13}C NMR ($CDCl_3$, 100 MHz) δ, 173.6, 136.9, 129.3, 128.3, 126.3, 102.0, 97.6, 84.7, 81.4, 73.4, 68.8, 68.6, 68.0, 62.0, 55.4, 34.1, 29.3, 29.2, 20.0, 28.7, 28.4, 24.9, 18.3; HR ESIMS calcd for $C_{27}H_{39}O_7$ $[M+H]^+$ 475.2696, found 475.2695.

4.10. Compounds 11A–C

The diol and isocyanoate ratio used was 3:4, total yield 97.9%.

4.10.1. Methyl 4,6-*O*-benzylidene-2,3-di-*O*-(pentyl-carbamoyl)-α-D-glucopyranoside (11A). Semisolid; yield 10.7%; IR (cm^{-1}, film) 3444, 3055, 2987, 2934, 1731, 1519, 1422, 1266, 1053, 896, 731 and 706; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42–7.45 (m, 2H, 2Ar-*H*), 7.30–7.34 (m, 3H, 3Ar-*H*), 5.48 (s, 1H, PhC*H*), 5.37 (app t, 1H, $J_{2,3} = J_{3,4}$ 9.8 Hz, H-3), 4.95 (m, 1H, N*H*), 4.91 (d, 1H, $J_{1,2}$ 3.9 Hz, H-1), 4.78 (dd, 1H, $J_{1,2}$ 3.9, $J_{2,3}$ 9.8 Hz, H-2), 4.67 (m, 1H, N*H*), 4.27 (dd, 1H, $J_{5,6e}$ 4.9, $J_{6e,6a}$ 10.7 Hz, H-6_{eq}), 3.89 (dt, 1H, $J_{5,6e}$ 4.9, $J_{4,5} = J_{5,6a}$ 9.8 Hz, H-5), 3.75 (app t, 1H, $J_{5,6a}$ 9.8, $J_{6e,6a}$ 10.7 Hz, H-6_{ax}), 3.59 (app t, 1H, $J_{2,3} = J_{3,4}$ 9.8 Hz, H-4), 3.39 (s, 3H, OC*H*$_3$), 3.06–3.16 (m, 4H, 2 × C*H*$_2$NH), 1.44 (m, 4H, 2 × C*H*$_2$CH$_2$NH), 1.26–1.30 (m, 4H, CH$_2$C*H*$_2$C*H*$_2$CH$_3$), 1.22–1.26 (m, 4H, CH$_2$C*H*$_2$C*H*$_2$CH$_3$), 0.87 (t, 3H, *J* 6.8, CH$_2$C*H*$_3$), 0.83 (t, 3H, *J* 6.8, CH$_2$C*H*$_3$); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 155.5, 155.4, 136.9, 128.9, 128.0, 126.1, 101.4, 98.3, 71.9, 69.9, 68.8, 62.3, 55.2, 41.0, 40.4, 29.9, 29.4, 28.9, 28.7, 22.3, 22.1, 13.8; HR ESIMS calcd for $C_{26}H_{41}N_2O_8$ $[M+H]^+$ 509.2863, found 509.2850.

4.10.2. Methyl 4,6-*O*-benzylidene-2-*O*-(pentyl-carbamoyl)-α-D-glucopyranoside (11B). White needles, mp 147.5–148.5 °C; yield 59.6%; IR (cm^{-1}, film) 3442, 3055, 2987, 2935, 2872, 1726, 1518, 1266, 1094, 993, 740, 705; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46–7.49 (m, 2H, 2Ar-*H*), 7.33–7.37 (m, 3H, 3Ar-*H*), 5.54 (s, 1H, PhC*H*), 4.96 (d, 1H, $J_{1,2}$ 3.9 Hz, H-1), 4.91 (m, 1H, CON*H*), 4.71 (dd, 1H, $J_{1,2}$ 3.9, $J_{2,3}$ 9.8 Hz, H-2), 4.28 (dd, 1H, $J_{5,6e}$ 4.9, $J_{6e,6a}$ 9.8 Hz, H-6_{eq}), 4.12 (app t, 1H, $J_{2,3} = J_{3,4}$ 9.8 Hz, H-3), 3.82 (dt, 1H, $J_{5,6e}$ 4.9, $J_{4,5} = J_{5,6a}$ 9.8 Hz, H-5), 3.75 (app t, 1H, $J_{5,6a} = J_{6e,6a}$ 9.8 Hz, H-6_{ax}), 3.56 (app t, 1H, $J_{2,3}$, $J_{3,4}$ 9.8 Hz, H-4), 3.41 (s, 3H, OC*H*$_3$), 3.16 (quartet, 2H, *J* 6.8, C*H*$_2$NH), 1.56 (br s, 1H, O*H*), 1.49 (quintet, 2H, *J* 6.8 Hz, C*H*$_2$CH$_2$NH), 1.23–1.33 (m, 4H, CH$_2$C*H*$_2$C*H*$_2$CH$_3$), 0.88 (t, 3H, *J* 6.8, CH$_2$C*H*$_3$); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 155.8, 136.9, 129.0, 128.1, 126.2, 126.1, 101.8, 98.1, 73.9, 68.6, 68.4, 62.0, 55.1, 40.9, 31.6, 30.0, 29.5, 28.8, 28.7, 26.7, 26.5, 22.4, 13.9; HR ESIMS calcd for $C_{20}H_{30}NO_7$ $[M+H]^+$ 396.2022, found 396.2014.

4.10.3. Methyl 4,6-*O*-benzylidene-3-*O*-(pentyl-carbamoyl)-α-D-glucopyranoside (11C). White solid, mp 183.0–185.0 °C; yield 27.6%; IR (cm^{-1}, film) 3448, 3054, 2987, 2929, 1725, 1422, 1266, 896, 739, 705; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43–7.46 (m, 2H, 2Ar-*H*), 7.32–7.36 (m, 3H, 3Ar-*H*), 5.47 (s, 1H, Ph-acetal-C*H*), 5.13 (app t, 1H, $J_{2,3} = J_{3,4}$ 9.8 Hz, H-3), 4.70–4.85 (m, 2H, H-2, N*H*), 4.28 (dd, 1H, $J_{5,6e}$ 4.9, $J_{6e,6a}$ 9.8 Hz, H-6_{eq}), 3.86 (dt, 1H, $J_{5,6e}$ 4.9, $J_{4,5} = J_{5,6a}$ 9.8 Hz, H-5), 3.73 (app t, 1H, $J_{5,6a}$, $J_{6e,6a}$ 9.8 Hz, H-6_{ax}), 3.63 (m, 1H, H-2), 3.54 (app t, 1H, $J_{2,3}$, $J_{3,4}$ 9.8 Hz, H-4), 3.44 (s, 3H, OC*H*$_3$), 3.15 (quartet, 2H, *J* 6.8, C*H*$_2$NH), 1.47 (quintet, 2H, *J* 6.8 Hz, C*H*$_2$CH$_2$NH), 1.22–1.30 (m, 4H, m, 4H, CH$_2$C*H*$_2$C*H*$_2$CH$_3$), 0.85 (t, 3H, *J* 6.8, CH$_2$C*H*$_3$). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 156.7, 137.0, 129.0, 128.1, 126.2, 101.5, 100.3, 78.7, 73.1, 72.2, 68.9, 62.6, 55.5, 41.1, 29.3, 28.7, 22.2, 13.8; HR ESIMS calcd for $C_{20}H_{30}NO_7$ $[M+H]^+$ 396.2022, found 396.2014.

4.11. Compounds 12A–C

The diol and isocyanate ratio used was 3:4, total yield 71.5%.

4.11.1. Methyl 4,6-*O*-benzylidene-2,3-di-*O*-(heptyl-carbamoyl)-α-D-glucopyranoside (12A). White amorphous solid, mp 98.5–101.0 °C; yield 5.1%; IR (cm^{-1}) 3443, 2929, 2859, 2360, 2341, 1732, 1519, 1374, 1185, 1097, 1053, 745, 669; ^{1}H NMR ($CDCl_3$, 400 MHz) 7.43–7.46 (m, 2H, 2Ar-H), 7.30–7.34 (m, 3H, 3Ar-*H*), 5.48 (s, 1H, Ph-acetal-C*H*), 5.37 (app t, 1H, $J_{2,3} = J_{3,4}$ 9.8 Hz, H-3), 4.95 (m, 1H, N*H*), 4.91 (d, 1H, $J_{1,2}$ 3.9 Hz, H-1), 4.79 (dd, 1H, $J_{1,2}$ 3.9, $J_{2,3}$ 9.8 Hz, H-2), 4.67 (t, *J* 4.9 Hz, 1H, N*H*), 4.27 (dd, 1H, $J_{5,6e}$ 4.9, $J_{6e,6a}$ 9.8 Hz, H-6_{eq}), 3.90 (dt, 1H, $J_{5,6e}$ 4.9, $J_{4,5} = J_{5,6a}$ 9.8 Hz, H-5), 3.75 (app t, 1H, $J_{5,6a}$, $J_{6e,6a}$ 9.8 Hz, H-6_{ax}), 3.59 (app t, 1H, $J_{2,3}$, $J_{3,4}$ 9.8 Hz, H-4), 3.39 (s, 3H, OC*H*$_3$), 3.07–3.16 (m, 4H, 2 × C*H*$_2$NH), 1.43 (m, 4H, 2 × C*H*$_2$CH$_2$NH), 1.20–1.28 (m, 16H, 2 × (C*H*$_2$)$_4$CH$_3$), 0.85 (m, 6H, 2 × CH$_2$C*H*$_3$); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 155. 5, 155.4, 137.0, 128.9, 128.1, 126.2, 101.4, 98.3, 79.4, 75.5, 72.0, 69.9, 68.8, 62.3, 55.2, 45.8, 41.1, 40.5, 31.7, 31.6, 30.3, 29.8, 29.7, 29.4, 29.0, 28.9,

26.8, 26.6, 22.5, 14.0; HR ESIMS calcd for $C_{30}H_{49}N_2O_8$ $[M+H]^+$ 565.3489, found 565.3494.

4.11.2. Methyl 4,6-*O*-benzylidene-2-*O*-(heptyl-carbamoyl)-α-D-glucopyranoside (12B). Needle-like crystals, mp 131.6–133.0 °C; yield 43.0%; IR (cm^{-1}) 3437, 2929, 2658, 2360, 2481, 1723, 1519, 1376, 1093, 1058, 99.4, 874, 743, 697; ^1H NMR ($CDCl_3$, 400 MHz) 7.47–7.50 (m, 2H, 2Ar-H), 7.34–7.38 (m, 3H, 3Ar-H), 5.54 (s, 1H, Ph-acetal-C*H*), 4.95 (d, 1H, $J_{1,2}$ 3.9 Hz, H-1), 4.89 (m, 1H, N*H*), 4.71 (dd, 1H, $J_{1,2}$ 3.9, $J_{2,3}$ 9.8 Hz, H-2), 4.28 (dd, 1H, $J_{5,6e}$ 4.9, $J_{6e,6a}$ 9.8 Hz, H-6_{eq}), 4.12 (app t, 1H, $J_{2,3} = J_{3,4}$ 9.8 Hz, H-3), 3.83 (m, 1H, H-5), 3.75 (app t, 1H, $J_{5,6a}$, $J_{6e,6a}$ 9.8 Hz, H-6_{ax}), 3.56 (app t, 1H, $J_{2,3}$, $J_{3,4}$ 9.8 Hz, H-4), 3.41 (s, 3H, OCH_3), 3.17 (quartet, 2H, *J* 6.8 Hz, CH_2NH), 1.48 (m, 2H, CH_2CH$_2$NH), 1.20–1.28 (m, 8H, (CH_2)$_4$CH$_3$), 0.86 (t, *J* 6.8 Hz, 3H, CH$_2$CH_3); ^{13}C NMR ($CDCl_3$, 400 MHz) δ 155.8, 137.0, 129.2, 128.2, 126.3, 101.9, 98.1, 81.3, 73.9, 68.7, 62.0, 55.2, 41.1, 31.6, 29.6, 28.8, 26.6, 22.5, 14.0; HR ESIMS calcd for $C_{22}H_{33}NO_7$ $[M+H]^+$ 424.2335, found 424.2331.

4.11.3. Methyl 4,6-*O*-benzylidene-3-*O*-(heptyl-carbamoyl)-α-D-glucopyranoside (12C). White crystals, mp 181.5–182.5 °C; yield 23.4%; IR (cm^{-1}) 3558, 3446, 2925, 2859, 1726, 1516, 1372, 1180, 1096, 1071, 1057, 1000, 918, 873. ^1H NMR ($CDCl_3$, 400 MHz) 7.41–7.47 (m, 2H, 2Ar-*H*), 7.31–7.37 (m, 3H, 3Ar-*H*), 5.47 (s, 1H, Ph-acetal-C*H*), 5.13 (app t, 1H, $J_{2,3} = J_{3,4}$ 9.8 Hz, H-3), 4.73–4.83 (m, 2H, H-2, N*H*), 4.28 (dd, 1H, $J_{5,6e}$ 4.9, $J_{6e,6a}$ 9.8 Hz, H-6_{eq}), 3.85 (dt, 1H, $J_{5,6e}$ 4.9, $J_{4,5} = J_{5,6a}$ 9.8 Hz, H-5), 3.72 (app t, 1H, $J_{5,6a}$, $J_{6e,6a}$ 9.8 Hz, H-6_{ax}), 3.63 (m, 1H, H-2), 3.54 (app t, 1H, $J_{2,3}$, $J_{3,4}$ 9.8 Hz, H-4), 3.44 (s, 3H, OCH_3), 3.15 (quartet, 2H, *J* 6.8, CH_2NH), 1.47 (quintet, 2H, *J* 6.8 Hz, CH_2-CH$_2$NH), 1.22–1.30 (m, 8H, (CH_2)$_4$CH$_3$), 0.85 (t, 3H, *J* 6.8, CH$_2$CH_3); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 156.7, 137.0, 129.0, 128.1, 126.2, 101.6, 100.3, 78.8, 77.3, 76.6, 73.2, 72.2, 68.9, 62.6, 55.5, 41.1, 31.6, 29.7, 28.8, 26.6, 22.5, 14.0; HR ESIMS calcd for $C_{22}H_{33}NO_7$ $[M+H]^+$ 424.2335, found 424.2326.

Acknowledgements

We thank for the financial support provided by University of New Orleans start-up fund and NSF grant 518283. Special thanks to the Chemistry Department at Louisiana State University for providing laboratory space for us to complete the manuscript submission. We thank Dr. Steven Mullen at Mass Spectrometry Facility of UIUC for his assistance, and Dr. Weilie Zhou from AMRI at UNO with SEM for his assistance.

Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.carres.2006.01.023.

References

1. Reviews on organogelators: (a) Terech, P.; Weiss, R. G. *Chem. Rev.* **1997**, *97*, 3133–3159; (b) Abdallah, D. J.; Weiss, R. G. *Adv. Mater.* **2000**, *12*, 1237–1247.
2. Estroff, L. A.; Hamilton, A. D. *Chem. Rev.* **2004**, *104*, 1201–1217.
3. van Esch, J. H.; Feringa, B. L. *Angew. Chem., Int. Ed.* **2000**, *39*, 2263–2266.
4. (a) Abe, H.; Kikuchi, H.; Hanabusa, K. *Liq. Cryst.* **2003**, *30*, 1423–1431; (b) Jung, J. H.; Lee, S. H.; Yoo, J. S.; Yoshida, K.; Shimizu, T.; Shinkai, S. *Chem. Eur. J.* **2003**, *9*, 5307–5313.
5. Mizrahi, S.; Gun, J.; Kipervaser, Z. G.; Lev, O. *Anal. Chem.* **2004**, *76*, 5399–5404.
6. Reviews on hydrogels and applications: (a) Lee, K. Y.; Mooney, D. J. *Chem. Rev.* **2001**, *101*, 1680–1869; (b) Miyata, T.; Uragami, T.; Nakamae, K. *Adv. Drug Del. Rev.* **2002**, *54*, 79–98.
7. (a) Jen, A. C.; Wake, M. C.; Mikos, A. G. *Biotechnol. Bioeng.* **1996**, *50*, 357–364; (b) Fadnavis, N. W.; Sheelu, G.; Kumar, B. M.; Bhalerao, M. U.; Deshpande, A. A. *Biotechnol. Prog.* **2003**, *19*, 557–564.
8. Kiyonaka, S.; Sada, K.; Yoshimura, I.; Shinkai, S.; Kato, N.; Hamachi, I. *Nat. Mater.* **2004**, *3*, 58–64.
9. Tiller, J. C. *Angew. Chem., Int. Ed.* **2003**, *42*, 3072–3075.
10. Zhang, Y.; Yang, Z. M.; Yuan, F.; Gu, H. W.; Gao, P.; Xu, B. *J. Am. Chem. Soc.* **2004**, *126*, 15028–15029.
11. Estroff, L. A.; Addadi, L.; Weiner, S.; Hamilton, A. D. *Org. Biomol. Chem.* **2003**, *22*, 4124–4131.
12. Wang, G.; Hamilton, A. D. *Chem. Commun.* **2003**, *3*, 310–311.
13. (a) Gronwald, O.; Shinkai, S. *Chem. Eur. J.* **2001**, *7*, 4328–4334; (b) Luboradzki, R.; Gronwald, O.; Ikeda, M.; Shinkai, S.; Reinhoudt, D. N. *Tetrahedron* **2000**, *6*, 9595–9599.
14. Kobayashi, H.; Friggeri, A.; Koumoto, K.; Amaike, M.; Shinkai, S.; Reinhoudt, D. N. *Org. Lett.* **2002**, *4*, 1423–1426.
15. Gronwald, O.; Sakurai, K.; Luboradzki, R.; Kimura, T.; Shinkai, S. *Carbohydr. Res.* **2001**, *331*, 307–318.
16. Kiyonaka, S.; Shinkai, S.; Hamachi, I. *Chem. Eur. J.* **2003**, *9*, 976–983.
17. Luboradzkia, R.; Pakulski, Z. *Tetrahedron* **2004**, *60*, 4613–4616.
18. Bhuniya, S.; Park, S. M.; Kim, B. H. *Org. Lett.* **2005**, *7*, 1741–1744.
19. (a) Suzuki, M.; Nigawara, T.; Yumoto, M.; Kimura, M.; Shirai, H.; Hanabusa, K. *Org. Biomol. Chem.* **2003**, *22*, 4124–4131; (b) Suzuki, M.; Yumoto, M.; Kimura, M.; Shirai, H.; Hanabusa, K. A. *Chem.-Eur. J.* **2003**, *9*, 348–354; (c) Suzuki, M.; Owa, S.; Yumoto, M.; Kimura, M.; Shirai, H.; Hanabusa, K. *Tetrahedron Lett.* **2004**, *45*, 5399–5402; (d) Suzuki, M.; Sato, T.; Kurose, A.; Shirai, H.; Hanabusa, K. *Tetrahedron Lett.* **2005**, *46*, 2741–2745.
20. Menger, F. M.; Caran, K. L. *J. Am. Chem. Soc.* **2000**, *122*, 11679–11691.

21. Suzuki, M.; Yumoto, M.; Kimura, M.; Shirai, H.; Hanabusa, K. *Chem. Commun.* **2002**, *8*, 884–885.
22. Jokić, M.; Perić, B.; Tomišić, V.; Kojić-Prodić, B.; Žinić, M. *Chem. Eur. J.* **2001**, *7*, 3328–3341.
23. Iwaura, R.; Yoshida, K.; Masuda, M.; Yase, K.; Shimizu, T. *Chem. Mater.* **2002**, *14*, 3047–3053.
24. Park, S. M.; Lee, Y. S.; Kim, B. H. *Chem. Commun.* **2003**, *23*, 2912–2913.
25. Mukhopadhyay, S.; Maitra, U.; Krishnamoorthy, I. G.; Schmidt, J.; Talmon, Y. *J. Am. Chem. Soc.* **2004**, *126*, 15905–15914.
26. Heeres, A.; van der Pol, C.; Stuart, M.; Friggeri, A.; Feringa, B. L.; van Esch, J. *J. Am. Chem. Soc.* **2003**, *125*, 14252–14253.
27. van Bommel, K. J. C.; van der Pol, C.; Muizebelt, I.; Friggeri, A.; Heeres, A.; Meetsma, A.; Feringa, B. L.; van Esch, J. *Angew. Chem., Int. Ed.* **2004**, *43*, 1663–1667.
28. Zhou, S. L.; Matsumoto, S.; Tian, H. D.; Yamane, H.; Ojida, A.; Kiyonaka, S.; Hamachi, I. *Chem. Eur. J.* **2005**, *11*, 1130–1136.
29. Oda, R.; Huc, I.; Candau, S. J. *Angew. Chem., Int. Ed.* **1998**, *37*, 2689–2691.