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Synthesis and Characterizations of 3-*O*-Esters of *N*-Acetyl-D-Glucosamine Derivatives as Organogelators

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Abstract:

Carbohydrate derived low molecular weight organogelators are interesting compounds with many potential applications. Selective functionalization of the different hydroxyl substituents on D-glucose and D-glucosamine have resulted in small molecular gelators. Previously we have found that the C-2 acylated derivatives including esters, carbamates of 4,6-*O*-benzylidene protected glucose and glucosamine derivatives have shown remarkable applications as molecular gelators. In this research, in order to probe the structural influence of sugar derivatives towards molecular self-assemblies, we introduced acylation functional groups to the 3-hydroxyl group of a 4,6-*O*-benzylidene acetal protected *N*-acetyl glucosamine derivatives. A small library of fourteen ester derivatives were synthesized and characterized. The ester derivatives typically formed gels in pump oil and aqueous mixtures of dimethyl sulfoxide or ethanol. The resulting gels were characterized using optical microscopy, and rheology, etc. All alkyl ester derivatives were gelators for pump oil. A short chain ester derivative was able to form gels in a few different oils and the corresponding oil water mixtures phase selectively. The compound was also used to trap naproxen sodium and formed a stable co-gel. The controlled release of the drug from gel to aqueous phase was analyzed using UV-vis spectroscopy. These results show that the functionalization at 3-OH position of the N-acetyl glucosamine derivative is a feasible strategy in designing new classes of organogelators.

Keywords: Carbohydrate derivatives, organogelators, self-assembly, phase selective gelation

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Introduction:

Low molecular weight gelators (LMWGs) are interesting classes of compounds that have influenced many research fields.[1-3] The LMWGs form gels in organic solvents or aqueous solutions through non-covalent intermolecular forces such as hydrogen bonding, π-π stacking, van der Waals forces, etc.[2, 4, 5] The resulting gels are often termed supramolecular gels and the gel to solution transitions are reversible. There are many studies on the preparation of organogels and hydrogels from various components including amino acids, carbohydrates. Many carbohydrate derivatives have been found to be suitable LMWGs in different solvents; these have already been studied for a wide variety of applications in biomedical research, environmental sciences, and other research fields.[6-14] Those organogelators that are able to form gels in various oils, have intriguing applications for environmental sciences. These compounds have been explored for oil spill clean-ups and the phase selective oil gelation for other applications.[15-24] Several organogelators for oils were found useful for drug delivery studies[25-28] and they were also studied for food processing since organogel matrix can help reducing oxidative damage for entrapped agents.[29-31] Since carbohydrates are readily available and biocompatible, several sugar based organogelators have been studied for oil spill recovery.[10, 32-35] In addition to environmental applications, sugar based organogelators for oils have also found applications as optical devices and microreactors.[11, 35]

We have designed and synthesized effective carbohydrate based low molecular weight organogelators and hydrogelators using D-glucose and D-glucosamine as starting materials.[36] Selectively functionalization of the hydroxyl groups and amino group at C-2 positions especially led to several series of compounds that are effective organogelators for a wide range of solvents.[37-42] As shown in Figure 1, certain 4,6-*O*-benzylidene α-*O*-methyl-D-glucopyranoside derivatives

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with the general structures **1** and **2** are able to form gels. The dimeric esters **2** were not as effective gelators in aqueous solutions in comparison to the C-2 monoesters **1**, in which the 3-hydroxyl group is present. The 3-hydroxyl group participates in hydrogen bonding with other sugar derivatives and with solvents, which was important in organogelation process. However, when longer hydrocarbon chains were used for the esters, they were able to form gels in a few organic solvents, especially when there is an alkyne functional group present in the compounds. C-2 mono alkyl esters with the general structure of **1** require the presence of terminal alkyne group in order for them to form hydrogels. The glucosamine derivatives **3** are a class of effective LMWGs, forming gels in a series of polar solvents and aqueous mixtures. The amide derivatives **3** are more effective gelators than the corresponding esters **1**; more alkyl and aryl amide derivatives were found to be effective gelators. This was attributed to the hydrogen bonding capacity of the amido group in **3** in comparison to ester **1.**

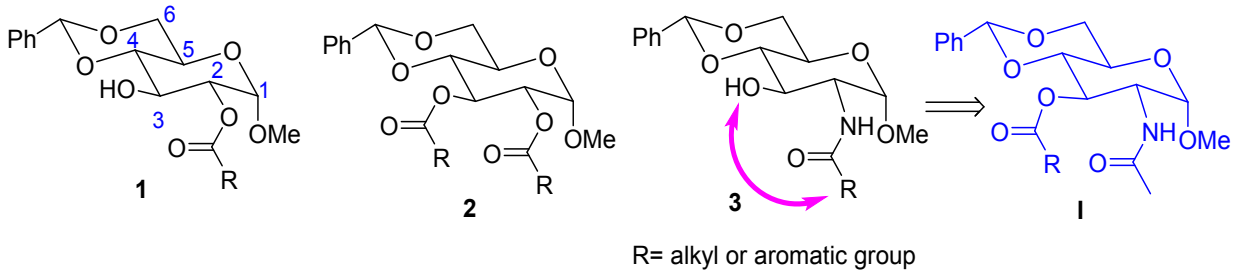

Figure 1. Structures of several classed of sugar derivatives.

Previously we have mostly focused on the synthesis and study of C-2 derivatives from 4,6-*O*-benzylidene α-*O*-methyl-D-glucopyranoside or glucosamine derivative (**1** and **3**).[41, 43] The crystal structure of a C-2 ester derivative exhibited intermolecular hydrogen bonding between the 3-hydroxyl group with ring oxygen.[39] The 3-hydroxyl group in the amides **3** also participates in

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hydrogen bonding in gelation as shown in an analog through NMR analysis,[44] especially in aqueous solution. Switching the acyl functional group from the C-2 position to the C-3 positon in amide **3** will lead to compounds **I**. These resulting compounds could be effective organic gelators. The intermolecular interactions in the structures are shown in Figure 2, with the 3-hydroxy group esterified, only the 2-NHAc can provide a hydrogen bond donor. Ester derivatives **I** contain suitable functional groups that can contribute to molecular self-assemblies and gelation in organic solvents. These compounds contain several types of intermolecular forces that may result in supramolecular gelation. These include van der Waals interactions and hydrophobic forces from the additional ester functions. Compound **4** was synthesized from *N*-acetyl glucosamine in two steps conveniently in high yield.[37, 43] It contains an acetamide functional group at the C-2 position, which can contribute to hydrogen bonding. Using this compound as the head group, through further functionalization at the 3-hydroxyl position, a series of compounds **I** can be obtained. As shown in Figure 2, after introducing an acyl functional group, the CLogP value changed from -0.39 for compound **4** to 2.58 for hexanoate derivative **I**, which indicates that the molecule will be more soluble in organic solvents. The functionalization of the C-3 hydroxyl group of compound **4** can be done via straightforward methods in one step. In addition, the ester derivatives can he hydrolyzed selectively over amide under alkaline conditions to afford chemical triggered gelators. The acyl derivative can also be cleaved using certain lipases to afford enzyme-triggered gelators.

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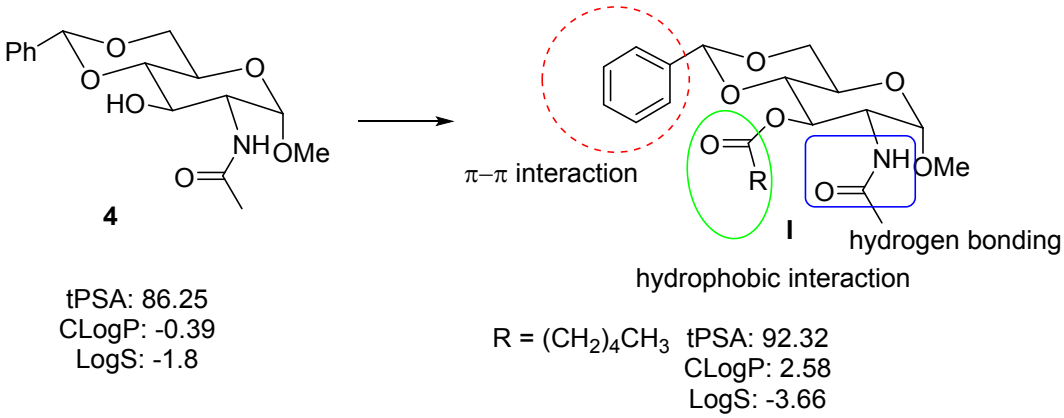

Figure 2. Rationalization of LMWGs design by esterification at 3-OH group.

Results and Discussion:

Synthesis of the 3-O-esters

In order to understand the structural influence towards gelation properties and produce sustainable functional organogelators, we synthesized and characterized a series of compounds **I**. The synthesis of these of 3-acyl derivatives is shown in Scheme 1.[43] Using a combinatorial approach, a small library of ester compounds was synthesized; these include short chain linear alkyl ester with 4, 5, 6, 7, 11 carbons, terminal chloro or acetylene substituted alkyl derivatives, cyclohexyl ester, and a few aromatic derivatives. The esterification using unhindered fatty acid or the corresponding acid chloride was typically carried out at room temperature, and for certain aromatic derivatives such as the 4-bromobenzoate the reaction requires heating and longer reaction times. The 3-posistion of the compound **4** is sterically hindered, therefore two equivalents of acid chlorides were necessary to obtain good yields. After these compounds were synthesized, we tested their gelation properties in a panel of organic solvents, the results are shown in Table 1. Hexane and water were included in the screen, and all compounds were insoluble in water and hexane at 20 mg/mL.

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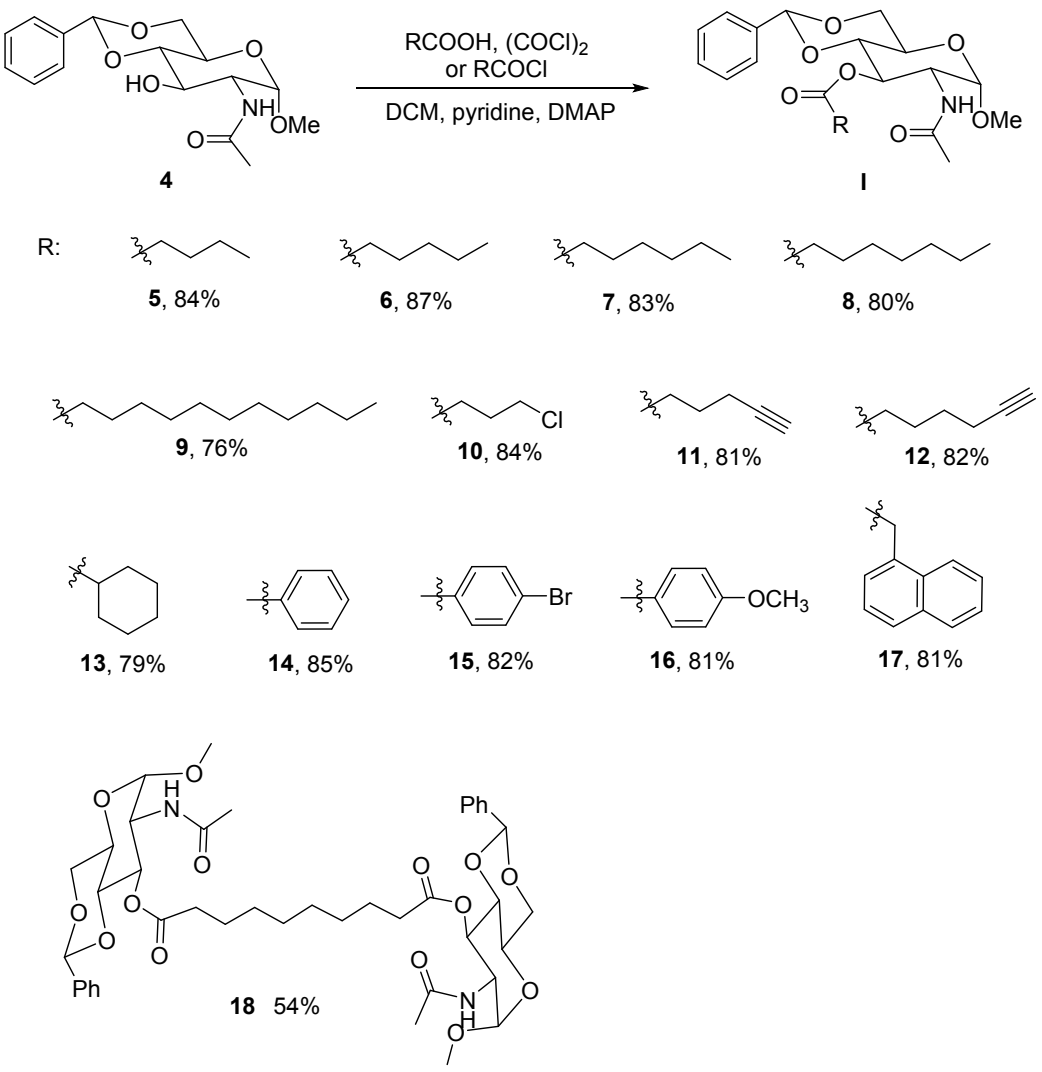

Scheme 1. Synthesis of 3-ester derivatives **5-18**.

Gelation properties of the synthesized esters

As shown in Table 1, interestingly all eleven aliphatic ester derivatives prepared in this study were able to form gels in pump oil (VWR® vacuum pump oil #19), and only one aromatic containing derivative was effective for the oil. A majority of the alkyl esters showed gelation properties for a mixture of water and DMSO or water and ethanol. Short chain linear aliphatic esters containing 6 to 8 carbon chains are the most versatile gelators, forming gels in at least six different solvents.

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These include compounds **6-8** with six to eight straight carbon chains, and compounds **11-12** containing 6 and 7 carbon chain with terminal acetylene. Compound **9** contains longer alkyl chain, it formed gels in pump oil with the lowest MGC of the entire series, 4.0 mg/mL. A dimeric ester compound **18** was also synthesized and studied, it showed effective gelation in seven of the tested solvents, which indicates that formation of dimeric derivatives containing two sugar units is a feasible method in achieving molecular self-assemblies. The hexanoate compound **6** was an effective gelator for seven solvents too and at lower concentrations than compound **18**. Compound **6** was selected and tested for several other oils and it formed stable gels in mineral oil (4.0 mg/mL) and engine oil (6.7 mg/mL) too, besides pump oil. The gels were mostly opaque for aqueous mixtures with polar solvents, and transparent for pump oil. Some photos of the gels are shown in Figure 3.

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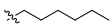
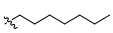
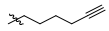
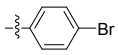
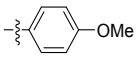
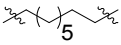
Table 1. Gelation properties of the synthesized compounds.

No.	R:	Pump oil	Tol	i-PrOH	EtOH	EtOH: H_2O (1:1)	EtOH: H_2O (1:2)	DMSO:H_2O (1:1)	DMSO:H_2O (1:2)	EG	Glycerol
5		G 6.7 c	S	S	S	S	G 6.7 o	G 5.0 o	G 5.0 o	P	S
6		G 4.0 c	S	S	S	G 10.0 o	G 3.3 o	G 5.0 o	G 5.0 o	G 10.0 o	G 20.0 o
7		G 20.0 c	S	S	S	G 20.0 o	G 20.0 o	G 10.0 o	G 20.0 o	G 10.0 o	P
8		G 20.0 c	S	S	S	G 6.7 o	G 6.7 o	G 5.0 o	G 5.0 o	G 20.0 o	P
9		G 4.0 c	S	S	S	G 2.8 o	P	P	P	G 20.0 o	P
10		G 10.0 c	S	P	S	S	P	P	P	S	S
11		G 10.0 c	S	P	S	G 20.0 o	G 20.0 o	G 20.0 o	G 20.0 o	S	G 20.0 o
12		G 10.0 o	S	P	P	G 20.0 o	G 20.0 o	G 20.0 o	G 20.0 o	S	G 20.0 o
13		G 10.0 c	S	S	S	P	P	G 10.0 o	G 10.0 o	S	P
14		G 6.7 o	P	P	S	P	P	P	P	G 20.0 o	P
15		I	G 20.0 o	P	G 20.0 o	I	I	P	I	P	P
16		S	S	P	S	P	I	P	G 20.0 o	P	P
17		I	P	P	P	I	I	I	I	I	I
18		G 10.0 c	G 20.0 c	G 20.0 o	G 20.0 o	G 6.7 o	I	G 10.0 o	G 10.0 o	P	P

G, gel at room temperature, the numbers are the corresponding minimum gelation concentrations (MGCs) in mg/mL; C for clear or transparent; T, translucent; O, opaque; UG, unstable gel; I, insoluble; P, crystallize or precipitate; S, soluble at ~20.0 mg/mL; Pump oil, VWR® vacuum pump oil #19; Tol, toluene; EG, ethylene glycol.

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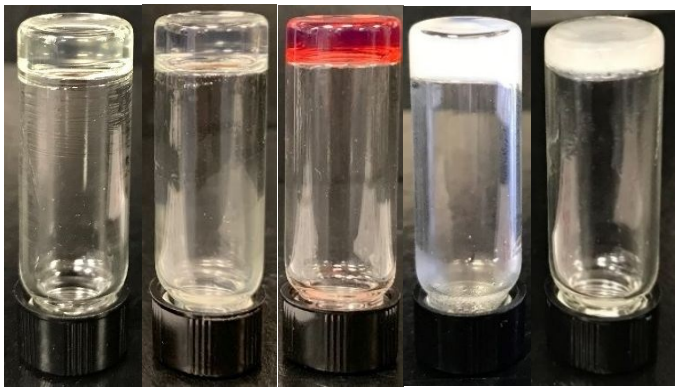
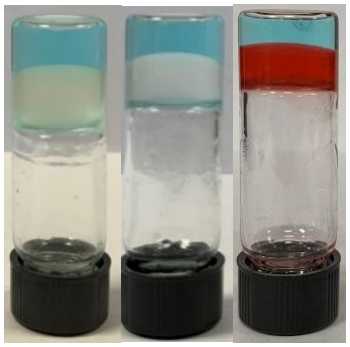


a b c d e

Figure 3. An transparent gel formed by **6** at a) 4.0 mg/mL in pump oil; b) 4.0 mg/mL in mineral oil and c) 6.7 mg/mL in engine oil; d) an opaque gel formed by **8** in DMSO/H_2O (v/v 1:1) at 5.0 mg/mL; e) an opaque gel formed by **15** in toluene at 20.0 mg/mL.

The compound **6** was then tested for phase selective gelation of oil and water mixtures. As shown in Figure 4, the gelator was effective in selective gelation for the oil phase in presence of aqueous phase, which contained copper sulfate to give the blue color for easy visualization of layers. The oil gels were strong enough to hold the weight of the aqueous phases for all three samples.



a b c

Figure 4. The phase selective gelation by compound **6** in oil and water ($CuSO_4$ solution) mixture: a) Compound **6** (4.0 mg) in pump oil (1 mL) and water (1 mL). b) Compound **6** (3.0 mg) in mineral oil (0.75 mL) and water (0.75 mL). c) Compound **6** (4.0 mg) in engine oil (0.6 mL) and water (0.6 mL).

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Gel morphology characterizations

The optical micrographs of several representative dried gels are shown in Figure 5. The morphology of the most versatile gelator compound **6** in different solvents are shown in Fig. 5A and 5B. The gel in DMSO/H_2O (*v* 1:2) formed uniform long and curved fibrous assemblies (Fig. 5A) with estimated diameter of 0.5 μm and several hundred microns in lengths, the fibers or tubules are curved and birefringent. The gel in EtOH/H_2O (*v* 1:1) formed long and uniform fibers (Fig. 5B). And increasing water content to EtOH:H_2O (*v* 1:2) the morphologies are very similar to those of compound **6** in EtOH/H_2O (*v* 1:1). The octanoate derivative compound **8** showed similar gelation properties, it formed gels in six tested solvents. The morphologies of some of these dried gels are shown in Figs 5C, D, and E. The gel of compound **8** in DMSO/H_2O (*v* 1:2) at 5.0 mg/mL showed similar fibrous morphologies (Fig. 5C) to compound **6** (Fig. 5A), and similar diameters. The DMSO/H_2O (*v* 1:1) gel however also formed uniform fibrous assemblies, but much thinner widths in the fibers or tubules (Fig. 5D) in comparison with Fig. 5B. The EtOH/H_2O (*v/v* 1:2) gel also showed uniform fibrous feature with thin diameters (Fig. 5E). The gel of compound **9** in EtOH/H_2O (*v/v* 1:1) at 2.8 mg/mL showed uniform birefringent fibrous or tubular assemblies (Fig. 5F). One interesting observation is that if the gelators are more efficient, e.g. forming gels at lower concentrations, the morphologies are typically long and narrow fibers. But when they are not very efficient such as forming gels at higher MGCs such as 20 mg/mL, they usually form wider or larger tubules and sometimes planar sheets. For example the gel formed by compound **12** in EtOH/H_2O (*v/v* 1:1) at 20.0 mg/mL showed planar sheets like features, these also showed liquid crystal like optical images (Fig. 5G). The toluene gel of compound **15** formed bundles of fibers rather than individual fibers, the morphology was not uniform as the others (Fig. 5H). And the ethanol gel of

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compound **15** exhibited more rigid rod like structures, the dried gels contain both fibers and crystalline planar sheets (Fig. 5I).

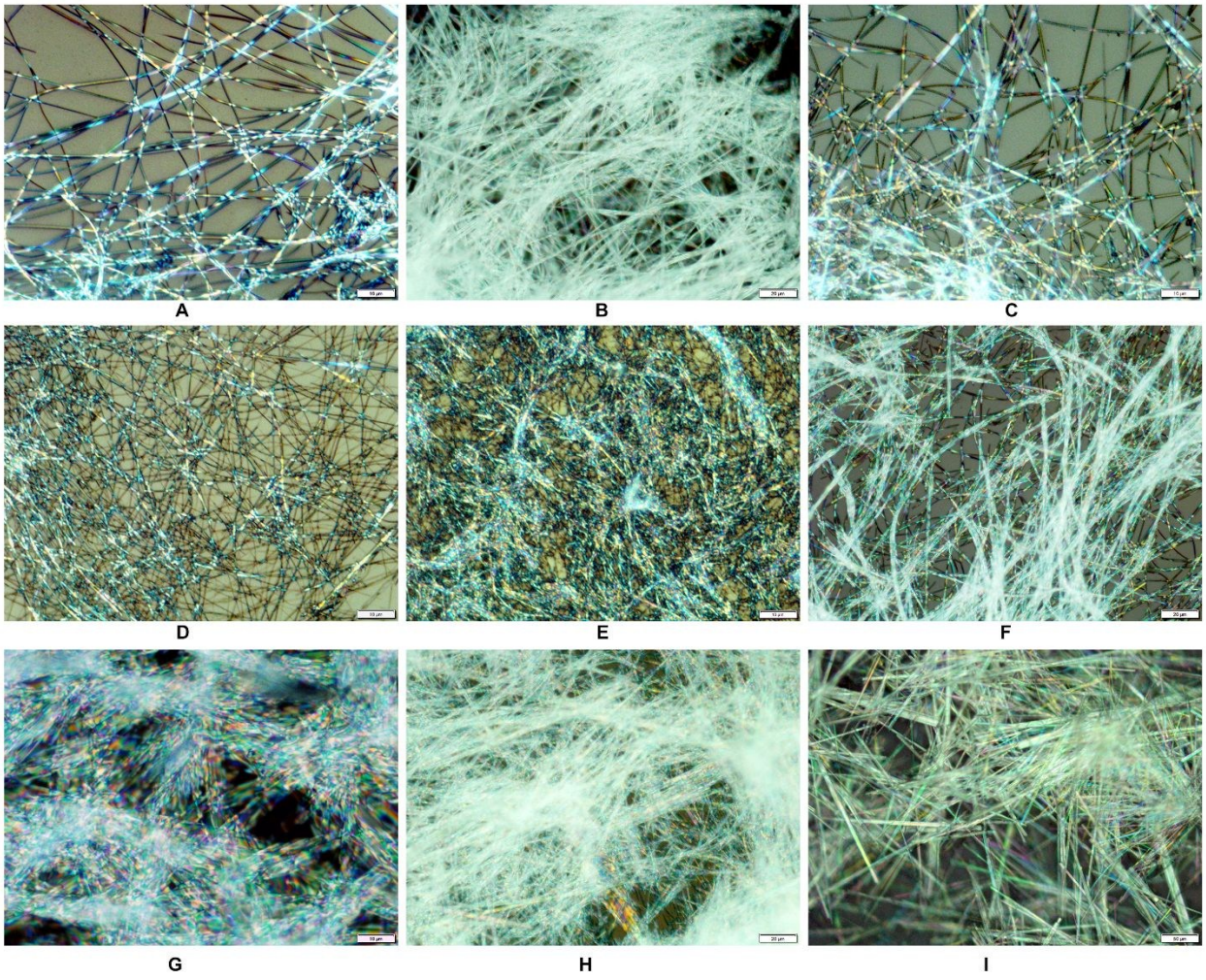

Figure 5. Optical micrographs of the gels formed by several compounds in different solvents. A) compound **6** in DMSO/H_2O (*v* 1:2) at 5.0 mg/mL; B) compound **6** in EtOH/H_2O (*v/v* 1:1) at 10.0 mg/mL; C) compound **8** in DMSO/H_2O (*v* 1:2) at 5.0 mg/mL; D) compound **8** in DMSO/H_2O (*v* 1:1) at 5.0 mg/mL; E) compound **8** in EtOH/H_2O (*v/v* 1:2) at 6.7 mg/mL; F) compound **9** in EtOH/H_2O (*v/v* 1:1) at 2.8 mg/mL; G) compound **12** in EtOH/H_2O (*v/v* 1:1) at 20.0 mg/mL; H) compound **15** in toluene at 20.0 mg/mL; I) compound **15** in ethanol at 20.0 mg/mL.

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Rheological properties of the gels

The rheological properties of gels formed by compounds **6**, **7** and **8** in mixed solvents of water with DMSO or water with ethanol are shown in Figure 6a. And the rheological properties for the oil gels are shown in Figure 6b. For all the tested gels, their storage moduli *G's* are greater than the loss moduli *G″s*, indicating that the gels have viscoelastic properties and are stable gels. For the gels in aqueous mixtures, the compound **8** in DMSO/H_2O (*v* 1:1) at 5.0 mg/mL concentration had the highest values of *G′* and *G″* and it was the strongest gel among all the tested samples. And the gel formed by compound **6** in DMSO/H_2O (*v* 1:2) had the largest *G′*/*G″* values. We also carried out the amplitude sweep experiment for these gels, and the results are shown in the SI Figures S1-S8.

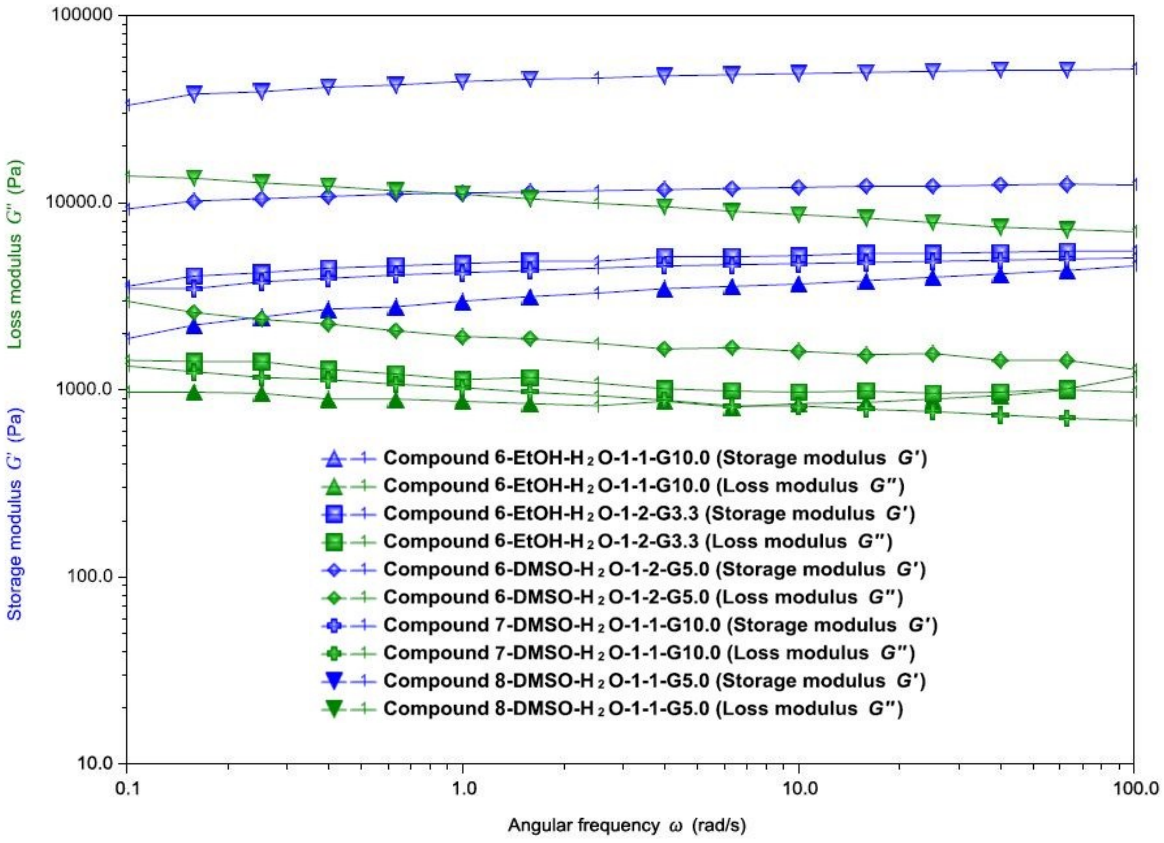

Figure 6a. Rheological properties of the gels formed by compound **6** (EtOH/H_2O, *v* 1:1, 10.0 mg/mL), compound **6** (EtOH/H_2O, *v* 1:2, 3.3 mg/mL), compound **6** (DMSO/H_2O, *v* 1:2, 5.0

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mg/mL), compound **7** (DMSO/H_2O, *v* 1:1, 10.0 mg/mL) and compound **8** (DMSO/H_2O, *v* 1:1, 5.0 mg/mL). Applied strain was 1% for all the samples.

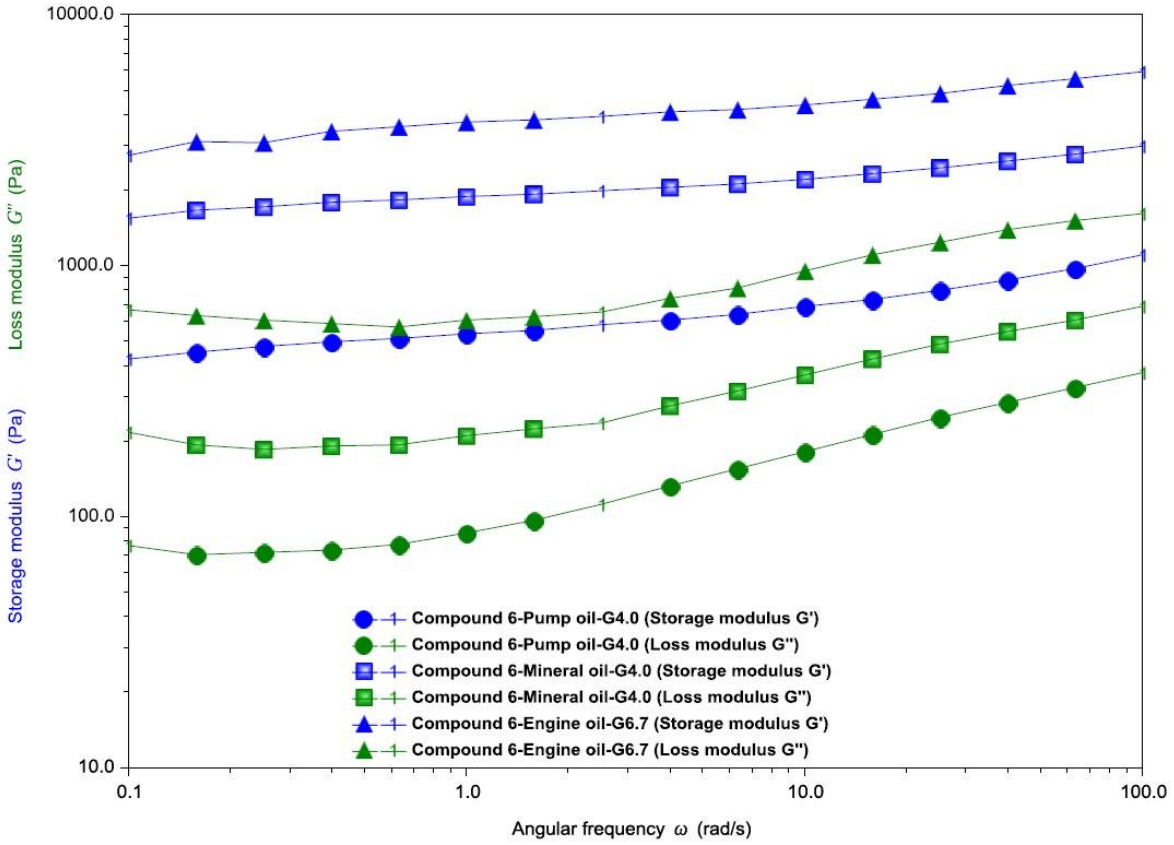

Figure 6b. Rheological properties of the gels formed by compound **6** in pump oil (4.0 mg/mL), mineral oil (4.0 mg/mL), and engine oil (6.7 mg/mL). Applied strain was 1% for all the samples.

Thermal stability

To further test the relative thermal stability, the melting points for a few DMSO:H_2O (v/v 1:1) gels formed by compounds **5**-**8** with different alkyl chain length were measured. As shown in Table 2, the melting points of gels with the same concentration range increased with an increase of the chain length. At 10.0 mg/mL concentrations for the four gelators, compound **8** with the longest

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chain had the highest melting points, and compound **5** with the shortest chain had the lowest middle-melting points among the four gelators. This trend is understandable that when increasing the hydrophobic chain, the intermolecular interactions increases and enhance the gelation. The gels formed by compound **7** in different concentrations were also tested, and the melting points increased when the concentration of the gels increased. At higher concentrations the gels were more stable, though the change in temperature is not huge, which indicates that concentration only plays a limited role in the gel stability, however, the structures of the gelation make much bigger differences towards stability.

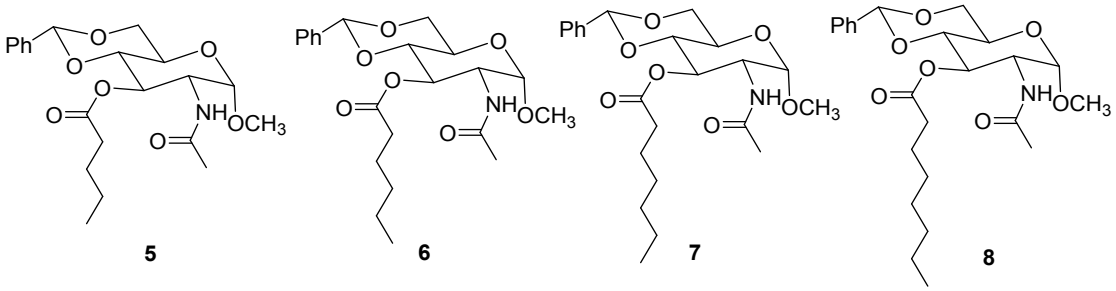

Table 2. The melting point range for some of the gels in DMSO:H_2O (v/v 1:1).

Compound number	G-C (mg/mL)	G-C (mM)	T_1 (°C)	T_2 (°C)	T_3 (°C)
5	10.0	24.6	48.7	55.4	60.7
6	10.0	23.7	53.6	67.2	77.6
7	10.0	23.0	56.2	83.5	99.4
7	15.0	34.5	62.4	89.0	103.4
7	20.0	46.0	65.7	94.3	108.4
8	10.0	22.3	58.7	87.6	102.3

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G-C: gelation concentration. T_1: initial melting temperature when liquid was first seen. T_2: temperature when the gel is half melted. T_3: the temperature of the entire gel turned into a colorless liquid and the ball reached the bottom of the tube.

Characterization of gelator structures using NMR spectroscopy

To elucidate the structural influences towards molecular self-assembly, we carried out the study of ^{1}H NMR spectroscopy at different temperatures for compounds **6** and **15**. The ^{1}H NMR spectra of compound **15** showed shifts in some of the signals when the temperature was increased (SI Figure S12 and S13). From 30 to 55 °C, the acetyl NH signal of compound **15** shifted from 5.84 to 5.80 ppm and the anomeric signal shifted from 4.77 to 4.78 ppm. There were also small shifts observed in the acetal (5.57 to 5.55 ppm) and OCH_3 (3.44 to 3.45 ppm) signals. These results suggest that the NH protons participate in hydrogen bonding interactions, which contribute to the molecular packing necessary for gelation.

The ^{1}H NMR spectra of compound **6** are shown in Figure 7. The amide N-H signal showed the most obvious shift among all signals, from 5.81 ppm shifted upfield to 5.77 ppm upon heating from 30 to 55 °C, which indicates that the amide hydrogen bonding is important among the different compounds. Other signals didn't show significant changes, the anomeric proton and the OCH_3 both slightly shifted downfield by 0.01 ppm at higher temperature, which indicate that the intramolecular hydrogen bonding between the NH with OCH_3 slightly enhances while intermolecular hydrogen bonding decreases. In oil and other non-polar solvents, the intermolecular hydrogen bonding among the gelator molecules plays an important role towards the gel stability and strength.

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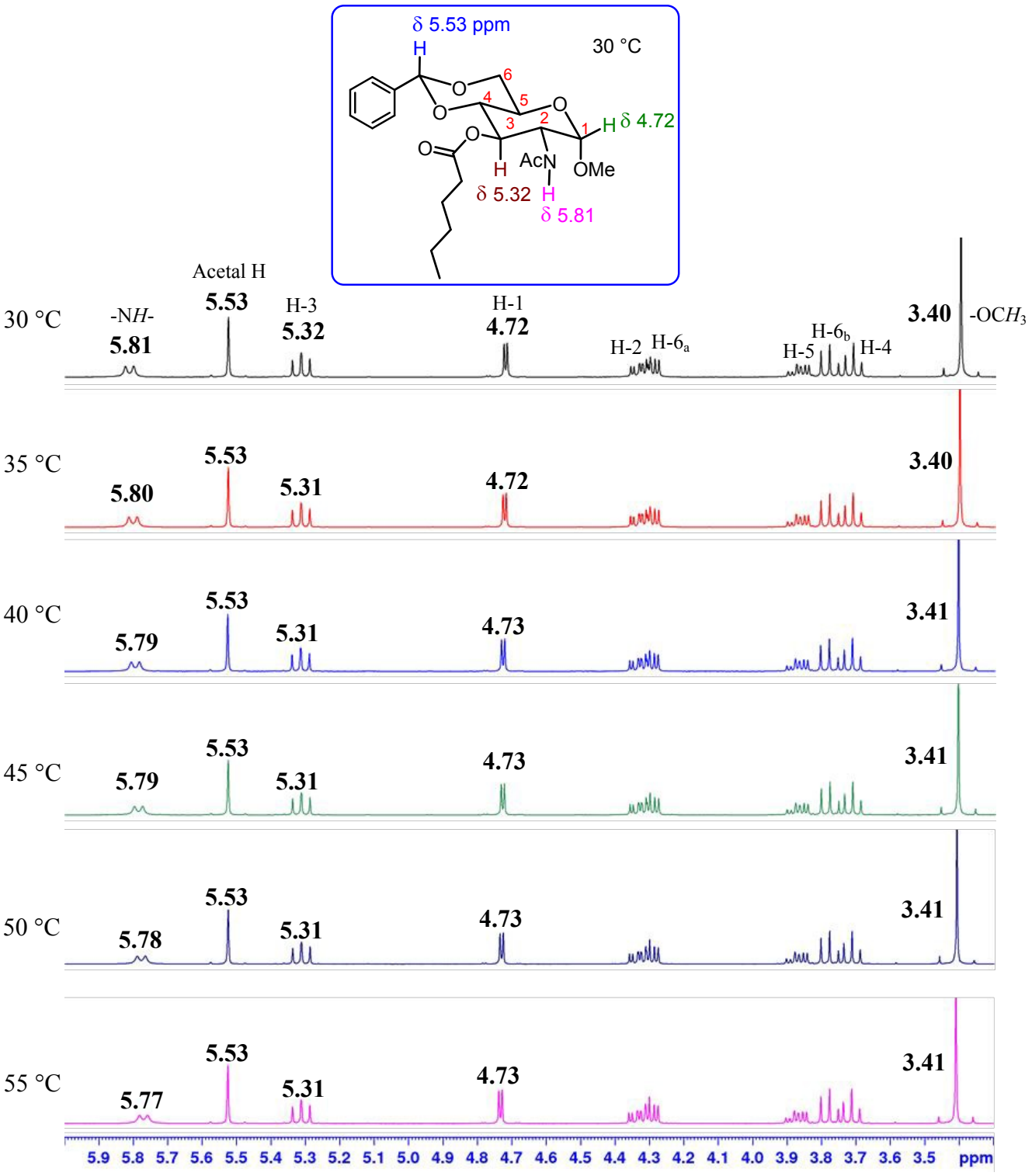

Figure 7. The ^{1}H NMR spectra (3.3 to 6.0 ppm) of compound **6** from 30 °C to 55 °C in $CDCl_3$ (10.0 mg/mL).

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Drug encapsulation and release

Compound **6** was also tested in a series of DMSO and water mixture by sequentially adding water to DMSO. It formed stable gels in DMSO:H_2O (v/v 1:3) at 5.0 mg/mL concentration (SI Figure Table S6.). This compound was used for the entrapping of a model drug naproxen and the release of naproxen from the co-gels at different time was monitored by UV-Vis spectroscopy. The UV-vis absorbance and release% over time are shown in Figure 8. About 50% of naproxen was released to the water phase during the first 10 h, and more slowly after that. About 75% was released to the aqueous phase at 48 h. The naproxen co-gels was also subjected to pH=10 solution and the gel was stable during the period of 48 hours, when naproxen release was monitored by UV-Vis spectroscopy. This is shown in Figure S19, the naproxen release speed was almost the same as using pH 7 water as shown in Figure 8. We tested the stability of the gel formed by compound **6** in DMSO:H_2O (v/v 1:3) at 5.0 mg/mL and treated the gels with stronger base solution (pH=14), the gel was stable for several hours but showed slow degradation over 10 hours (Figure S20). The results indicated that the gels were stable under mild alkaline conditions and should be suitable to use in presence of a wide pH range.

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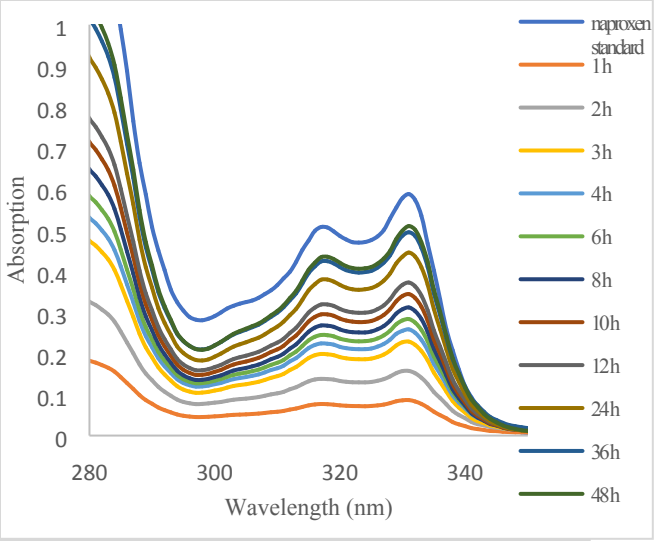

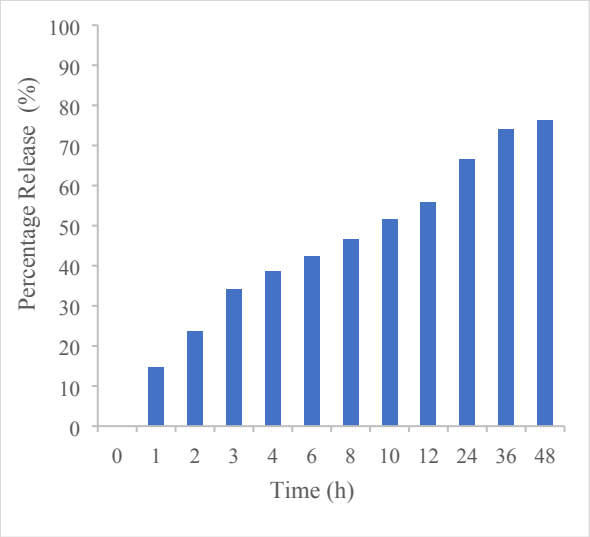

a b

Figure 8. Release of naproxen from gel to aqueous phase. a) UV spectra of naproxen timed release, the gel was formed by 7.5 mg of compound **6** in 1.5 mL DMSO:H_2O (v/v 1:3) with 0.3 mg of naproxen, then 1.5 mL of water (pH 7) was added to the top of the gel; naproxen control was prepared by dissolving 0.3 mg of naproxen in 3 mL of water (pH 7). b) The % release at different times based on the UV absorbance at 331 nm.

Conclusions

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In summary, a series of fourteen 3-*O*-ester derivatives of 2-acetamido-2-deoxy-4,6-*O*-benzylidene methyl-α-D-glucopyranoside were synthesized and characterized. All the ten synthesized alkyl ester derivatives were effective gelators for pump oil and many of them were found to be effective gelators for aqueous mixtures of ethanol and DMSO. In contrast, the aromatic ester derivatives did not perform well, only the benzoate derivative formed gels in oil and the p-bromobenzoate formed two organogels. The dimeric ester derivative **18** can be considered as covalently linking two monomer (compound **5**), the dimerization resulted in more gelation tendency in organic solvents. Optical microscopy studies showed that the gelators formed typically uniform fibrous network and some derivatives formed crystalline sheets. The rheological studies showed that the storage moduli *G's* for the gels were higher than the loss moduli *G"s* indicating the viscoelastic properties of the gels. The hexanote derivative **6** was able to encapsulate naproxen and form a co-gel, and the gelator showed sustained release of the trapped naproxen from gel to aqueous phase. In addition, the hexanoate compound **6** was also effective in phase selective gelation for several different oils in presence of aqueous phase. The ^{1}H NMR spectra of compound **6** at different temperature showed that the amide function played an important role in the intermolecular hydrogen bonding during molecular assembling. Since this new class of carbohydrate derived esters can be synthesized via straightforward methods from readily available starting materials, they could have many practical applications including oil spill cleanup. The systematic derivatization at the C-3 position of *N*-acetyl glucosamine derivatives led to a new class of low molecular weight organo and hydrogelators. The general structural features obtained from this series of compounds can be applied to other sugar derivatives and afford functional and versatile organogelators.

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Experimental Section

General method and materials

Reagents and solvents were used as they were received from the suppliers. All purification was conducted by flash chromatography using 230-400 mesh silica gel with a gradient of solvent systems. ^{1}H NMR and proton-decoupled ^{13}C NMR spectra were obtained with Bruker 400 MHz spectrometers in $CDCl_3$. The chemical shifts were reported using $CDCl_3$/d_6-DMSO calibrated at 7.26/2.50 ppm and 77.00/39.50 ppm respectively. Melting point measurements were carried out using a Fisher Jones melting point apparatus. Rheology experiment was done using a HR-2 Discovery Hybrid Rheometer from TA instrument and a 25 mm Peltier Plate. FTIR experiments were conducted using liquid or solid samples directly. The molecular mass was measured using LCMS on an Agilent 6120B Single Quad Mass Spectrometer coupled with LC1260 system and Shimazu LC 2030C system with LCMS 2030 Mass Spectrometer.

Optical microscopy

A small amount of the gels was placed on a clean glass slide and this was observed under an Olympus BX60M optical microscope and the Olympus DP73-1-51 high performance 17MP digital camera with pixel shifting and Peltier cooled. The imaging software for image capturing was CellSens 1.11. For aqueous DMSO mixtures, the gel was left air dried for a day or so, for other solvents the slides were observed directly.

Gelation test

About 2 mg of dried compound was placed in a 1 dram glass vial and the corresponding solvent was added to obtain a concentration of 20 mg/mL. The mixture was then heated until the solid was

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fully dissolved, sometimes sonication was needed to dissolve the sample, and then the solution was allowed to cool to room temperature and left standing for 30 minutes. If a stable gel formed (observed by inverting the vial), it was then serially diluted till the minimum gelation concentration (MGC), which is the concentration prior to unstable gelation, was obtained.

Phase selective gelation test for oil and water mixture: The test results of compound **6** in several oil and water mixtures are shown in Figure 5. General method: compound **6** (4.0 mg) was added to the mixture of 1 mL pump oil and 1 mL of copper sulfate solution. Then the sample vial was heated till all dissolve then was left cooling to rt, 10 minutes later, the pump oil gel was formed and strong enough to hold the aqueous phase. The other oils were tested similarly, so only the quantities of samples are given here: 3 mg of compound **6**, 0.75 mL of mineral oil and 0.75 mL of copper sulfate solution. For engine oil the time waiting for gelation was 1 hour, the gel was prepared using 4 mg of compound **6**, 0.6 mL of engine oil and 0.6 mL of copper sulfate solution.

Rheological analyses

The rheological behavior of the gel was investigated with an HR-2 Discovery hybrid rheometer from TA Instruments with TRIOS software. A sample (approximately 1mL of the gel) was placed on the steel plate of the rheometer. The cone geometry is a 25 mm Peltier plate with a gap of 100 μm. The experimental temperature was 25 °C, and the sample was subjected to amplitude sweep for oscillation strain from 0.125 to 100 %. A frequency sweep was then performed for the sample in the range of 0.1 to 100 rad/s for the angular frequency. The results were expressed as the storage modulus (G') and loss modulus (G'') as a function of angular frequency.

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Measurement of melting point ranges of gels

The gelator was dissolved in a small vial at the certain gelation concentration and heated to form the solution. The hot solution was transferred to an NMR tube or a narrow glass tube, where it was allowed to cool down to form the gel. A metal ball was placed on top of the gel. The NMR tube was immersed in an oil bath which was heated gradually. T_1 is the temperature of the initial melting at which liquid was first seen. T_2 is the temperature at which the gel is estimated to be half melted. And T_3 is the temperature at which the entire gel turned into a colorless liquid when the ball fell towards the bottom of the tube.

Naproxen release study

The gels were formed by adding 7.5 mg compound **6**, followed by 1.5 mL of DMSO:H_2O (v/v 1:3) containing 0.3 mg Naproxen. The mixture was heated and cooled to form a stable gel in a vial. Water (1.5 mL, pH = 7 or 10) was pipetted on top of the gel carefully. The aqueous phased was periodically transferred to a quartz cuvette and the UV-Vis spectrum was measured. The naproxen standard was prepared by dissolving 0.3 mg naproxen sodium in 3 mL of water (pH = 7). All measurements were carried out using Thermo Scientific™ Evolution™ 201 UV-Visible spectrophotometer.

Liquid chromatography-mass spectrometer (LC-MS) conditions

The molecular mass acquisition was performed using an Agilent 1260 Infinity LC system coupled to a G6120B single quadrupole mass spectrometer with an atmospheric pressure ionization electrospray (API-ES). The analytical column was an Agilent poroshell 120 EC-C18 4.6 mm × 50 mm column with 2.7 μm particle size. The mobile phase was 0.1% formic acid in acetonitrile/water (70/30, v/v) with ejection volume 5 μL and 8 minutes of total run time typically. The flow rate was

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0.40 mL/min and the column temperature set at 25 °C. The diode-array detector (DAD) was 254 nm. Agilent OpenLAB CDS ChemStation (Version C.01.05) was used for data processing. The ESI spray voltage was set at 4000 V, the source temperature was 350 °C and the nebulizer gas setting was 35 psi.

General procedure for the synthesis of compounds 5-18

To a suspension of **4** (100 mg, 0.313 mmol, 1 equiv) in CH_2Cl_2 (4 mL, anhydrous) at 0 °C was added pyridine and DMAP (6 mg, 0.047 mmol, 0.15 equiv) under nitrogen atmosphere and protected from moisture using a drying tube. The resulting mixture was stirred at 0 °C for about 30 minutes. Two equivalents of acyl chloride (commercially available or prepared *in situ* by treating the corresponding acid with oxalyl chloride) was then added drop-wise to the reaction mixture followed by stirring at room temperature for 6 hours unless otherwise stated. TLC (5% MeOH/CH_2Cl_2) and ^{1}H NMR spectrum of the reaction mixture indicated the complete consumption of the starting material to the desired product. The reaction was then quenched with satd. $NaHCO_3$ (aq. 5 mL) and the phases were then separated and the aqueous phases was further extracted with CH_2Cl_2 (15 mL x 2). The combined organic phases were dried with anhydrous Na_2SO_4, filtered and concentrated to afford the crude product, which was purified by column chromatography to obtain the desired product. The detailed synthesis for compound **5** and di-ester compound **18** are included only; and for all other compounds the amount of the reagents, yield, R_f value and characterization data of the products are listed respectively.

Synthesis of 3-*O*-pentanoyl 2-acetamido-2-deoxy-4,6-*O*-benzylidene methyl-α-D-glucopyranoside 5. Pyridine (0.12 mL, 1.55 mmol, 5 equiv) was added followed by DMAP (6.0

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mg, 0.047 mmol, 0.15 equiv) to a mixture of compound **4** (100 mg, 0.313 mmol, 1 equiv) in CH_2Cl_2 and the resulting mixture was stirred at 0 °C for about 30 minutes. Pentanoyl chloride (0.626 mmol, 2 equiv) in 1 mL of CH_2Cl_2 was then added drop wise and the reaction mixture was stirred for about 6 hours at room temperature. The product was obtained as a white solid (107 mg, 84%). R_f = 0.45 in 60% EtOAc/hexanes, m.p. 133.0-135.0 °C, ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.48-7.45 (m, 2H), 7.38-7.36 (m, 3H), 5.83 (d, J = 9.5 Hz, 1H), 5.55 (s, 1H), 5.34 (t, J = 10.0 Hz, 1H), 4.75 (d, J = 3.6 Hz, 1H), 4.38-4.30 (m, 2H), 3.93-3.87 (m, 1H), 3.81 (t, J = 10.1 Hz, 1H), 3.74 (t, J = 9.5 Hz, 1H), 3.43 (s, 3H), 2.34 (dt, J = 7.4, 2.9 Hz, 2H), 1.97 (s, 3H), 1.61-1.55 (m, 2H), 1.35-1.28 (m, 2H), 0.87 (t, J = 7.3 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 174.3, 169.9, 137.0, 129.0, 128.2, 126.1, 101.5, 99.1, 79.1, 69.9, 68.9, 62.8, 55.3, 52.6, 34.0, 27.1, 23.2, 22.1, 13.6. LC-MS (ESI+) cald $C_{21}H_{30}NO_7$ $[M + H]^+$ 408.2 found 408.2.

Synthesis of 3-*O*-hexanoyl 2-acetamido-2-deoxy-4,6-*O*-benzylidene methyl-α-D-glucopyranoside 6. Pyridine (0.12 mL, 1.55 mmol), DMAP (6.0 mg, 0.047 mmol), compound **4** (100 mg, 0.313 mmol, 1 equiv) and hexanoyl chloride (0.086 mL, 0.618 mmol, 2 equiv) were added similarly as above. The product was obtained as a white solid (114 mg, 87%). R_f = 0.55 in 60% EtOAc/hexanes, m.p. 142.0-144.0 °C, ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.38-7.36 (m, 2H), 7.29-7.26 (m, 3H), 5.73 (d, J = 9.4 Hz, 1H), 5.46 (s, 1H), 5.24 (t, J = 10.0 Hz, 1H), 4.65 (d, J = 3.6 Hz, 1H), 4.29-4.21 (m, 2H), 3.83-3.77 (m, 1H), 3.71 (t, J = 10.1 Hz, 1H), 3.64 (t, J = 9.4 Hz, 1H), 3.33 (s, 3H), 2.30-2.17 (m, 2H), 1.88 (s, 3H), 1.55-1.47 (m, 2H), 1.21-1.16 (m, 4H), 0.76 (t, J = 6.9 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 174.3, 169.9, 137.1, 129.0, 128.2, 126.1, 101.5, 99.1, 79.1, 68.9, 62.8, 55.3, 52.6, 34.3, 31.1, 24.7, 23.2, 22.2, 13.8. LC-MS (ESI+) cald $C_{22}H_{32}NO_7$ $[M + H]^+$ 422 found 422.

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Synthesis of 3-*O*-hepanoyl 2-acetamido-2-deoxy-4,6-*O*-benzylidene methyl-α-D-glucopyranoside 7. Pyridine (0.12 mL, 1.55 mmol, 5 equiv), DMAP (6.0 mg, 0.047 mmol, 0.15 equiv), compound **4** (100 mg, 0.313 mmol, 1 equiv) and Heptanoyl chloride (0.096 mL, 0.618 mmol, 2 equiv) were added were added similarly as above. The product was obtained as a white solid (112 mg, 83%). R_f = 0.6 in 60% EtOAc/hexanes, m.p. 137.0-139.0 °C, ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.47-7.41 (m, 2H), 7.37-7.32 (m, 3H), 5.82 (d, J = 9.4 Hz, 1H), 5.52 (s, 1H), 5.30 (t, J = 10.1 Hz, 1H), 4.72 (d, J = 3.6 Hz, 1H), 4.36-4.27 (m, 2H), 3.91-3.82 (m, 1H), 3.78 (t, J = 10.1 Hz, 1H), 3.71 (t, J = 9.5 Hz, 1H), 3.40 (s, 3H), 2.30 (dt, J = 7.4, 3.6 Hz, 2H), 1.95 (s, 3H), 1.58-1.53 (m, 2H), 1.31-1.18 (m, 6H), 0.84 (t, J = 6.7 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 174.3, 169.9, 137.0, 129.0, 128.2, 126.1, 101.5, 99.1, 79.1, 69.9, 68.9, 62.8, 55.3, 52.6, 34.3, 31.4, 28.6, 25.0, 23.2, 22.4, 14.0. LC-MS (ESI+) cald $C_{23}H_{34}NO_7$ $[M + H]^+$ 436 found 436.

Synthesis of 3-*O*-octanoyl 2-acetamido-2-deoxy-4,6-*O*-benzylidene methyl-α-D-glucopyranoside 8. Pyridine (0.12 mL, 1.55 mmol, 5 equiv), DMAP (6.0 mg, 0.047 mmol, 0.15 equiv), compound **4** (100 mg, 0.313 mmol, 1 equiv) and Octanoyl chloride (0.11 mL, 0.618 mmol, 2 equiv) were added similarly as above. The product was obtained as a white solid (111 mg, 80%). R_f = 0.6 in 60% EtOAc/hexanes, m.p. 128.0-130.0 °C, ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.48-7.45 (m, 2H), 7.38-7.35 (m, 3H), 5.82 (d, J = 9.6 Hz, 1H), 5.55 (s, 1H), 5.34 (t, J = 10.1 Hz, 1H), 4.75 (d, J = 3.6 Hz, 1H), 4.38-4.30 (m, 2H), 3.93-3.87 (m, 1H), 3.81 (t, J = 10.2 Hz, 1H), 3.74 (t, J = 9.4 Hz, 1H), 3.43 (s, 3H), 2.39-2.27 (m, 2H), 1.98 (s, 3H), 1.63-1.56 (m, 2H), 1.29-1.23 (m, 8H), 0.87 (t, J = 7.0 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 174.3, 169.9, 137.1, 129.0, 128.2, 126.1, 101.5, 99.1, 79.1, 69.9, 68.9, 62.8, 55.3, 52.6, 34.3, 31.6, 28.93, 28.87, 25.0, 23.2, 22.6, 14.0. LC-

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MS (ESI+) cald $C_{24}H_{36}NO_7$ $[M + H]^+$ 450 found 450.

Synthesis of 3-*O*-dodecanoyl 2-acetamido-2-deoxy-4,6-*O*-benzylidene methyl-α-D-glucopyranoside 9. Pyridine (0.12 mL, 1.55 mmol, 5 equiv), DMAP (6.0 mg, 0.047 mmol, 0.15 equiv), compound **4** (100 mg, 0.313 mmol, 1 equiv) and Lauroyl chloride (0.626 mmol, 2 equiv) were added similarly as above. The product was obtained as a white solid (120 mg, 76%). R_f = 0.6 in 60% EtOAc/hexanes, m.p. 96.0-98.0 °C, ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.47-7.40 (m, 2H), 7.37-7.30 (m, 3H), 5.81 (d, J = 9.5 Hz, 1H), 5.53 (s, 1H), 5.31 (t, J = 10.0 Hz, 1H), 4.72 (d, J = 3.7 Hz, 1H), 4.37-4.27 (m, 2H), 3.91-3.83 (m, 1H), 3.80 (t, J = 10.1 Hz, 1H), 3.71 (t, J = 9.4 Hz, 1H), 3.40 (s, 3H), 2.34-2.25 (m, 2H), 1.95 (s, 3H), 1.61-1.52 (m, 2H), 1.34-1.14 (m, 16H), 0.88 (t, J = 6.9 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 174.3, 169.9, 137.1, 129.0, 128.2, 126.1, 101.5, 99.1, 79.1, 69.9, 68.9, 62.8, 55.3, 52.6, 34.3, 31.9, 29.59, 29.57, 29.4, 29.3, 29.2, 29.0, 25.0, 23.2, 22.7, 14.1. LC-MS (ESI+) cald $C_{28}H_{44}NO_7$ $[M + H]^+$ 506 found 506.

Synthesis of 3-*O*-4'-chlorobutanoyl 2-acetamido-2-deoxy-4,6-*O*-benzylidene methyl-α-D-glucopyranoside 10. Pyridine (0.12 mL, 1.55 mmol, 5 equiv), DMAP (6.0 mg, 0.047 mmol, 0.15 equiv), compound **4** (100 mg, 0.313 mmol, 1 equiv) and 4-Chlorobutyryl chloride (0.07 mL, 0.626 mmol, 2 equiv) were added similarly as above. The product was obtained as an off-white solid (111 mg, 84%). R_f = 0.5 in 60% EtOAc/hexanes, m.p. 129.0-131.0 °C, ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.47-7.41 (m, 2H), 7.38-7.32 (m, 3H), 5.79 (d, J = 9.6 Hz, 1H), 5.53 (s, 1H), 5.31 (t, J = 10.0 Hz, 1H), 4.71 (d, J = 3.7 Hz, 1H), 4.39-4.28 (m, 2H), 3.91-3.84 (m, 1H), 3.79 (t, J = 10.1 Hz, 1H), 3.72 (t, J = 9.5 Hz, 1H), 3.52 (t, J = 6.2 Hz, 2H), 3.41 (s, 3H), 2.54-2.47 (m, 2H), 2.08-2.00 (m, 2H), 1.96 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 173.0, 170.0, 136.9, 129.1, 128.2, 126.1,

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101.6, 99.0, 79.0, 70.5, 68.9, 62.8, 55.3, 52.4, 43.7, 31.3, 27.7, 23.2. LC-MS (ESI+) cald $C_{20}H_{27}ClNO_7$ $[M + H]^+$ 428 found 428.

Synthesis of 3-*O*-5'-hexynoyl 2-acetamido-2-deoxy-4,6-*O*-benzylidene methyl-α-D-glucopyranoside 11. Pyridine (0.12 mL, 1.55 mmol, 5 equiv), DMAP (6.0 mg, 0.047 mmol, 0.15 equiv), compound **4** (100 mg, 0.313 mmol, 1 equiv) and 5-hexynoyl chloride (0.626 mmol, 2 equiv) were added similarly as above. The product was obtained as a white solid (105 mg, 81%). R_f = 0.3 in 60% EtOAc/hexanes, m.p. 162.0-164.0 °C, ^{1}H NMR (d_6-DMSO, 400 MHz) δ 7.95 (d, J = 9.4 Hz, 1H), 7.41-7.32 (m, 5H), 5.65 (s, 1H), 5.18 (t, J = 10.2 Hz, 1H), 4.67 (d, J = 3.5 Hz, 1H), 4.27-4.16 (m, 2H), 3.85-3.76 (m, 2H), 3.75-3.67 (m, 1H), 3.36 (s, 3H), 2.76 (t, J = 2.6 Hz, 1H), 2.40-2.27 (m, 2H), 2.14 (dt, J = 7.1, 2.6 Hz, 2H), 1.82 (s, 3H), 1.71-1.58 (m, 2H); ^{13}C NMR (d_6-DMSO, 100 MHz) δ 171.7, 169.6, 137.3, 128.8, 128.0, 126.0, 100.3, 98.8, 83.5, 78.8, 71.6, 69.4, 67.8, 62.6, 54.9, 51.2, 32.3, 23.7, 22.2, 16.8. LC-MS (ESI+) cald $C_{22}H_{28}NO_7$ $[M + H]^+$ 418, found 418.

Synthesis of 3-*O*-6'-heptynoyl 2-acetamido-2-deoxy-4,6-*O*-benzylidene methyl-α-D-glucopyranoside 12. Pyridine (0.12 mL, 1.55 mmol, 5 equiv), DMAP (6.0 mg, 0.047 mmol, 0.15 equiv), compound **4** (100 mg, 0.313 mmol, 1 equiv) and 6-heptynoyl chloride (0.626 mmol, 2 equiv) were added similarly as above. The product was obtained as a white solid (111 mg, 82%). R_f = 0.45 in 60% EtOAc/hexanes, m.p. 159.0-161.0 °C, ^{1}H NMR (d_6-DMSO, 400 MHz) δ 7.94 (d, J = 9.4 Hz, 1H), 7.39-7.34 (m, 5H), 5.64 (s, 1H), 5.17 (t, J = 9.6 Hz, 1H), 4.67 (d, J = 3.5 Hz, 1H), 4.27-4.16 (m, 2H), 3.84-3.76 (m, 2H), 3.75-3.67 (m, 1H), 3.36 (s, 3H), 2.72 (t, J = 2.6 Hz, 1H), 2.34-2.18 (m, 2H), 2.08 (dt, J = 7.0, 2.6 Hz, 2H), 1.82 (s, 3H), 1.60-1.50 (m, 2H), 1.44-1.34 (m,

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2H); ^{13}C NMR (d_6-DMSO, 100 MHz) δ 172.0, 169.6, 137.3, 128.8, 128.0, 126.0, 100.3, 98.9, 84.0, 78.8, 71.2, 69.3, 67.8, 62.6, 54.9, 51.2, 33.0, 27.0, 23.7, 22.3, 17.3. LC-MS (ESI+) cald $C_{23}H_{30}NO_7$ $[M + H]^+$ 432.2 found 432.2.

Synthesis of 3-*O*-cyclohexanoyl 2-acetamido-2-deoxy-4,6-*O*-benzylidene methyl-α-D-glucopyranoside 13. Pyridine (0.12 mL, 1.55 mmol, 5 equiv), compound **4** (100 mg, 0.313 mmol, 1 equiv) and Cyclohexanecarbonyl chloride (0.2 mL, 1.24 mmol, 4 equiv) were added similarly as above. Then the reaction mixture was stirred for about 90 minutes at 0 °C. The product was obtained as a white solid (106 mg, 79%). R_f = 0.22 in 50% EtOAc/hexanes. m.p. 175.0-177.0 °C, ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.47 (m, 2H), 7.39-7.35 (m, 3H), 5.80 (d, J = 9.6 Hz, 1H), 5.55 (s, 1H), 5.34 (t, J = 10.0 Hz, 1H), 4.74 (d, J = 3.6 Hz, 1H), 4.40-4.31 (m, 2H), 3.92-3.86 (m, 1H), 3.81 (t, J = 10.1 Hz, 1H), 3.74 (t, J = 9.6 Hz, 1H), 3.43 (s, 3H), 2.35 (tt, J = 11.1, 3.6 Hz, 1H), 1.97 (s, 3H), 1.86 (m, 2H), 1.76-1.72 (m, 2H), 1.65-1.61 (m, 1H), 1.50-1.37 (m, 2H), 1.33-1.20 (m, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 176.5, 169.9, 137.1, 129.0, 128.2, 126.1, 101.4, 99.1, 79.2, 69.6, 68.9, 62.9, 55.3, 52.6, 43.1, 28.93, 28.87, 25.7, 25.3, 25.2, 23.2. LC-MS (ESI+) cald $C_{23}H_{32}NO_7$ $[M + H]^+$ 434.2 found 434.2.

Synthesis of 3-*O*-benzoyl 2-acetamido-2-deoxy-4,6-*O*-benzylidene methyl-α-D-glucopyranoside 14. Pyridine (0.12 mL, 1.55 mmol, 5 equiv), DMAP (6.0 mg, 0.047 mmol, 0.15 equiv), compound **4** (100 mg, 0.313 mmol, 1 equiv) and Benzoyl chloride (0.070 mL, 0.618 mmol, 2 equiv) were added similarly as above. The product was obtained as a white solid (112 mg, 85%). R_f = 0.45 in 60% EtOAc/hexanes, m.p. 194.0-196.0 °C, ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.05-8.03 (m, 2H), 7.59-7.54 (m, 1H), 7.47-7.42 (m, 4H), 7.34-7.31 (m, 3H), 5.89 (d, J = 9.6 Hz, 1H), 5.64-

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5.55 (m, 2H), 4.81 (d, J = 3.6 Hz, 1H), 4.54 (dt, J = 10.1, 3.6 Hz, 1H), 4.36 (dd, J = 10.2, 4.6 Hz, 1 H), 4.01-3.96 (m, 1H), 3.90 (t, J = 9.4 Hz, 1H), 3.86 (t, J = 10.2 Hz, 1H), 3.47 (s, 3 H), 1.89 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 170.0, 167.0, 137.0, 133.2, 129.9, 129.6, 129.0, 128.4, 128.2, 126.1, 101.5, 99.2, 79.4, 70.8, 69.0, 63.0, 55.4, 52.6, 23.2. LC-MS (ESI+) cald $C_{23}H_{26}NO_7$ $[M + H]^+$ 428.2 found 428.2.

Synthesis of 3-*O*-4'-bromobenzoyl 2-acetamido-2-deoxy-4,6-*O*-benzylidene methyl-α-D-glucopyranoside 15. Pyridine (3.0 mL), DMAP (6.0 mg, 0.047 mmol, 0.15 equiv), compound **4** (100 mg, 0.313 mmol, 1 equiv) and 4-Bromobenzoyl chloride (140 mg, 0.62 mmol, 2 equiv) were added similarly as above. Then the reaction mixture was stirred at 60 °C for about 9 hours. The product was obtained as a white solid (128 mg, 82%). R_f = 0.5 in 60% EtOAc/hexanes, m.p. 262.0-264.0 °C, ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.89 (d, J = 8.6 Hz, 2H), 7.58 (d, J = 8.6 Hz, 2H), 7.44-7.41 (m, 2H), 7.33-7.32 (m, 3H), 5.92 (d, J = 9.6 Hz, 1H), 5.57 (t, J = 9.6 Hz, 1H), 5.57 (s, 1H), 4.79 (d, J = 6.6 Hz, 1H), 4.55 (d, J = 3.6, 10.1 Hz, 1H), 4.35 (dd, J = 4.6, 10.1 Hz, 1H), 4.00-3.95 (m, 1H), 3.91-3.82 (m, 2H), 3.46 (s, 3H), 1.88 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 170.0, 166.2, 136.9, 131.8, 131.4, 129.1, 128.5, 128.4, 128.2, 126.1, 101.6, 99.2, 79.3, 71.2, 68.9, 63.0, 55.4, 52.5, 23.1. LC-MS (ESI+) cald $C_{23}H_{25}NO_7Br$ $[M + H]^+$ 506.1 found 506.1.

Synthesis of 3-*O*-4'-methoxybenzoyl 2-acetamido-2-deoxy-4,6-*O*-benzylidene methyl-α-D-glucopyranoside 16. Pyridine (2.0 mL), DMAP (6.0 mg, 0.047 mmol, 0.15 equiv), compound **4** (100 mg, 0.313 mmol, 1 equiv) and 4-Methoxy benzoyl chloride (0.08 mL, 0.626 mmol, 2 equiv) were added similarly as above. The product was obtained as a white solid (115 mg, 81%). R_f = 0.4 in 60% EtOAc/hexanes, m.p. 196.0-198.0 °C, ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.01-7.98 (m, 2H),

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7.45-7.42 (m, 2H), 7.34-7.31 (m, 3H), 6.93-6.90 (m, 2H), 5.91 (d, J = 9.5 Hz, 1H), 5.58 (s, 1H), 5.57 (t, J = 9.96 Hz, 1H), 4.81 (d, J = 3.6 Hz, 1H), 4.54-4.48 (m, 1H), 4.35 (dd, J = 10.1, 4.6 Hz, 1H), 4.00-4.95 (m, 1H), 3.91-3.83 (overlapping m and s, 5H), 3.46 (s, 3H), 1.88 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 170.0, 166.7, 163.6, 137.0, 132.0, 129.0, 128.2, 126.1, 121.9, 113.7, 101.5, 99.2, 79.4, 70.4, 69.0, 63.0, 55.42, 55.36, 52.8, 23.2. LC-MS (ESI+) cald $C_{24}H_{28}NO_8$ $[M + H]^+$ 458.2 found 458.2.

Synthesis of 3-*O*-[2-(1-naphthalenyl) acetyl] 2-acetamido-2-deoxy-4,6-*O*-benzylidene methyl-α-D-glucopyranoside 17. Pyridine (0.12 mL, 1.55 mmol, 5 equiv), DMAP (6.0 mg, 0.047 mmol, 0.15 equiv), compound **4** (100 mg, 0.313 mmol, 1 equiv) and 1-naphthalene acetyl chloride (0.626 mmol, 2 equiv) were added similarly as above. The product was obtained as a white solid (121 mg, 81%). R_f = 0.4 in 60% EtOAc/hexanes, m.p. 231.0-233.0 °C, ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.95 (d, J = 8.5 Hz, 1H), 7.83 (d, J = 8.1 Hz, 1H), 7.77 (d, J = 8.0 Hz, 1H), 7.46-7.34 (m, 9H), 5.73 (d, J = 9.5 Hz, 1H), 5.50 (s, 1H), 5.36 (t, J = 10.0 Hz, 1H), 4.72 (d, J = 3.6 Hz, 1H), 4.40-4.35 (m, 1H), 4.34-4.28 (m, 1H), 4.17-4.04 (m, 2H), 3.91-3.85 (m, 1H), 3.80 (t, J = 9.3 Hz, 1H), 3.75 (t, J = 8.6 Hz, 1H), 3.39 (s, 3H), 1.70 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 172.0, 170.0, 137.0, 133.8, 132.0, 130.1, 129.0, 128.6, 128.2, 128.1, 128.0, 126.4, 126.2, 125.7, 125.5, 123.7, 101.6, 99.0, 79.1, 70.5, 68.9, 62.8, 55.3, 52.5, 38.9, 23.0. LC-MS (ESI+) cald $C_{28}H_{30}NO_7$ $[M + H]^+$ 492.2 found 492.2.

Synthesis of di-ester compound 18. Pyridine (0.12 mL, 1.55 mmol, 5 equiv) was added followed by DMAP (6.0 mg, 0.047 mmol, 0.15 equiv) to a mixture of compound **4** (100 mg, 0.313 mmol, 1 equiv) in CH_2Cl_2 and the resulting mixture was stirred at 0 °C for about 30 minutes. Decanedioyl

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dichloride (0.141 mmol, 0.45 equiv) in 1 mL of CH_2Cl_2 was then added drop wise and the reaction mixture was stirred for about 12 hours at room temperature. The di-ester product was obtained as a white solid (62 mg, 54%). R_f = 0.6 in 5% MeOH/DCM, m.p. 215.0-217.0 °C, ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.45-7.40 (m, 4H), 7.36-7.31 (m, 4H), 5.88 (d, J = 9.5 Hz, 2H), 5.51 (s, 2H), 5.32 (t, J = 9.8 Hz, 2H), 4.72 (d, J = 3.6 Hz, 2H), 4.37-4.26 (m, 4H), 3.91-3.84 (m, 2H), 3.78 (t, J = 10.1 Hz, 2H), 3.71 (t, J = 9.5 Hz, 2H), 3.40 (s, 6H), 2.31-2.25 (m, 4H), 1.95 (s, 6H), 1.58-1.48 (m, 4H), 1.27-1.14 (m, 8H), 0.88; ^{13}C NMR ($CDCl_3$, 100 MHz) δ 174.2, 170.0, 137.1, 129.0, 128.2, 126.1, 101.5, 99.1, 79.1, 69.9, 68.9, 62.8, 55.4, 52.6, 34.2, 28.8, 28.7, 24.9, 23.2. LC-MS (ESI+) cald $C_{42}H_{57}N_2O_{14}$ $[M + H]^+$ 813.4 found 813.4.

Electronic supplementary information (ESI)

Preparation of acid chloride intermediates if not commercially available. Copies of ^{1}H and ^{13}C NMR spectra for compounds **5-18**, measurement of melting point ranges, rheological data and amplitude experiments, ^{1}H NMR spectra at varied temperatures for compounds **6** and **15**, FTIR spectra for compound **6** and **15**. Gelation test for water and DMSO mixture for compounds **6** and **8**, and the gel photos for naproxen co-gels and release profile at pH 10, photos for gel degradation at pH14.

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Fourteen glycolipids were synthesized, all alkyl esters were organogelators. The hexanoate was a phase-selective gelator for oil in water.