JOC The Journal of Organic Chemistry

Article

pubs.acs.org/joc

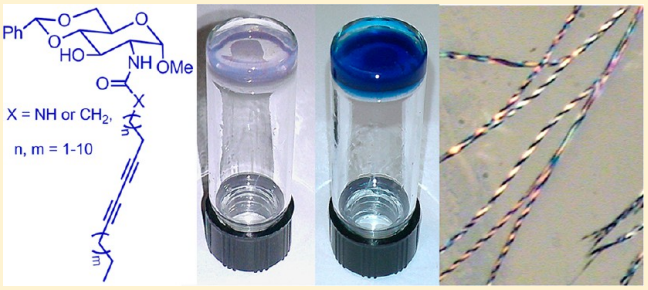
Preparation and Self-Assembly Study of Amphiphilic and Bispolar Diacetylene-Containing Glycolipids

Guijun Wang,* Navneet Goyal, Hari P. R. Mangunuru, Hao Yang, Sherwin Cheuk, and Puram V. Narasimha Reddy

Department of Chemistry and Biochemistry, Old Dominion University, Norfolk, Virginia 23529, United States

Supporting Information

ABSTRACT: Diacetylene-containing glycolipids are a unique class of compounds that are able to self-assemble and form ordered supramolecular structures. Polymerizable diacetylene glycolipids that can function as low molecular weight gelators are particularly interesting molecules which can lead to stimuli-responsive smart materials. To discover efficient organogelators with built-in functionality that may be useful in sensing local environmental changes, we have synthesized a series of novel diacetylene-containing amide and urea derivatives using D-glucosamine as the starting material. Both amphiphilic and dipolar glycolipids were synthesized, and these compounds are effective gelators for several organic solvents and aqueous solutions. The resulting gels can be cross-linked under 6 W UV light to produce blue or purple polydiacetylene gels. The cross-linked gels obtained from urea derivatives are generally dark blue and exhibit blue to red color transitions upon heating. Compared to the urea derivatives, the analogous diacetylene amides produced blue to deep purple polymerized gels, depending on the structures of the gelators. The morphologies of the gels were characterized by optical microscopy and scanning electron microscopy. Typically, self-assembled fibrous networks were observed. The synthesis and characterization of these polymerizable gelators and their UV−vis absorption upon polymerization are reported.



INTRODUCTION

Low molecular weight gelators (LMWGs) are small molecules that can self-assemble and form three-dimensional supramolecular structures that allow the trapping or immobilization of solvents. Because of the collective weak noncovalent interactions, the resulting gels by LMWGs are reversible and often referred to as supramolecular gels or physical gels. Depending on the solvents, they can be defined as organogels for organic solvents and hydrogels for water. LMWGs have gained a considerable amount of interest due in part to their connection with supramolecular chemistry and potential applications as advanced soft materials in biomedical and materials research.[1−5] Supramolecular gels are reversible, and many functional groups can be incorporated into the gelators to afford new materials with desired properties.[6,7] For instance, organogelators have been explored as optical electronic devices and found applications in semiconductors and photovoltaic cells.[2,8,9] They have also been explored as sequester agents for oil and chemical spill cleanup.[10−12] Moreover, supramolecular hydrogels have been explored more and more for biomedical applications, as matrixes for cell growth, enzyme immmolization, drug delivery, and tissue engineering.[11−15]

The structures of organogelators and hydrogelators encompass a broad range of functional groups. Carbohydrates, especially monosaccharides, contain chiral centers that can be functionalized specifically to produce advanced self-assembling materials.[16] When used as templates for gelators, they are also more likely to produce biocompatible gels and possess potential biomedical applications.[17−25] For example, sugar-based hydrogelators have been used to prepare semiwet peptide/protein arrays that are compatible with enzyme assays and the screening of enzyme inhibitors[5,24] and for wound healing.[25]

We have been working on the design and synthesis of effective organogelators from carbohydrates and have obtained a considerable amount of insight on how to functionalize monosaccharide derivatives as LMWGs, especially using compounds **1** and **2** as the templates.[26−31] The gelation properties of various acyl derivatives of the two headgroups have been systematically studied in our lab, and several types of small molecule hydro/organogelators (**3**−**6**) are shown in Figure 1. The D-glucosamine headgroup **2** is especially useful in preparing molecular gelators for polar solvents and aqueous mixtures, with most of the compounds forming gels at concentrations well below 1.0 wt %.[28] The amino group can contribute to hydrogen bonding in the self-assembly of the gelators. The significance of these systems lies in the creation of useful molecular architectures from the self-assembling network of small sugar molecules.

Received: July 14, 2014
Published: December 9, 2014

DOI: 10.1021/jo501568u
J. Org. Chem. 2015, 80, 733−743

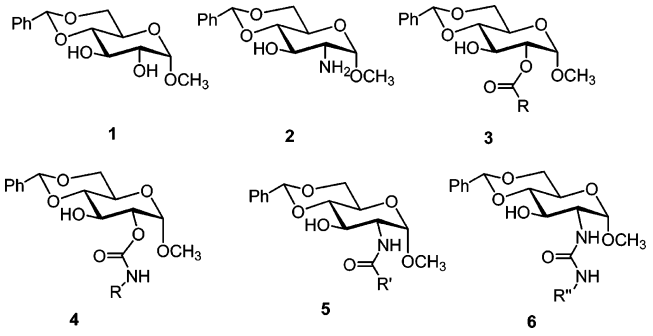


Figure 1. Structures of sugar headgroups and their derivatives as hydro/organogelators.

Stimuli-responsive supramolecular gels often exhibit phase transitions upon ligand binding, UV irradiation, enzymatic treatment, pH changes, etc.[4,12,32−35] These systems have potential applications as functional smart materials. Among these, photoresponsive gels, including styrene derivatives, azobenzenes, spyropyrans, and chromene-based systems have been studied most extensively.[2,8,34,36−39] Polydiacetylenes (PDAs) are interesting materials exhibiting typically blue to red color transitions in response to environmental changes and binding to biomolecules. They also have nonlinear optical properties and show other important optical effects.[40−44] PDAs are usually prepared by polymerization of properly aligned diacetylenes through 1,4-addition under UV light treatment. Diacetylene-containing supramolecular gels can be cross-linked and afford gel-like materials with color transition function, which can be used to monitor environmental changes such as changes of temperature, solvents, and binding agents.[42,45−52]

We have previously studied a series of diacetylene-containing glycolipids using 4,6-benzylidene methyl α-D-glucopyranoside **1** as the headgroup. A small library of glycolipids was synthesized and screened (Figure 2). The majority of the 2-monoacylated

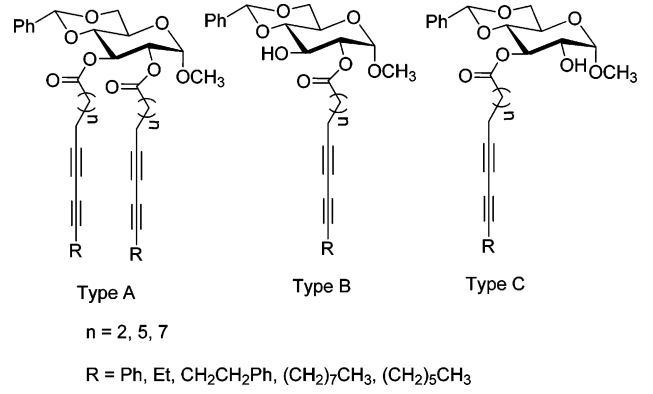


Figure 2. Structures of several types of diacetylene-containing lipids: diester A and monoesters B and C.

derivatives were effective low molecular weight gelators for ethanol and ethanol aqueous mixtures.[30] The topochemical polymerization mode of diacetylenes implies that the morphology of the cross-linked diacetylenes is the same as that before polymerization. Therefore, this is a good strategy for the preparation of stable PDA gels because it should enhance or maintain the gelation properties due to similar molecular packing modes of the monomers but with more covalent linkages.

We are interested in obtaining efficient gels that are responsive to local chemical and physical environmental changes such as light irradiation and change of solvents or other reagents and temperature, etc., and can find applications as smart materials or biosensors or chemosensors. To obtain potential functional LMWGs that are light-responsive and to understand the structure and gelation property correlations of D-glucosamine derivatives, we synthesized and studied the self-assembling properties of a series of diacetylene-containing D-glucosamine derivatives. These include amphiphilic derivatives with structures similar to the type B esters (Figure 2), and bispolar derivatives with two headgroups. These novel diacetylene sugar derivatives are expected to form unique supramolecular structures that can lead to light-responsive diacetylene gels.

RESULTS AND DISCUSSION

We synthesized a series of diacetylene-containing compounds using the D-glucosamine headgroup **2** as shown in Schemes 1 and 2. Here we prepared monoacyl chain derivatives **7**−**9** which can be viewed as analogues to the type B ester gelators. In comparison to the diacetylene ester derivatives from glucose, the synthesis of various derivatives using glucosamine derivative **2** is more straightforward and generally has high yields because the 2-acylation is much more selective. Besides the mono-diacetylene glycolipids **7**−**9**, we also synthesized a few bispolar derivatives with two polar headgroups at each end. The dimeric systems (**10**, **11**) are interesting compounds with higher polarities that may produce different self-assembling morphologies and properties and result in more interesting materials.

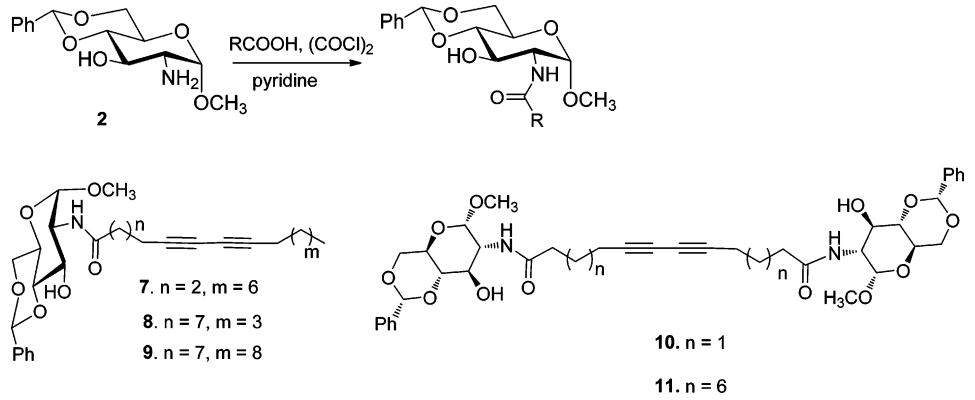
After obtaining these compounds, we screened their gelation properties in a series of solvents, and the results are shown in Table 1. Nearly all compounds synthesized here are effective gelators for ethanol at concentrations less than 20 mg/mL except compound **7**, which is soluble in ethanol. Although most of the compounds do not gel or dissolve in water or hexane or water/DMSO mixtures, several compounds were able to gel water/ethanol mixtures. Most of the compounds are efficient gelators for toluene, ethanol, and 2-propanol. Among these compounds, amide **9** is the most efficient gelator, forming gels in ethanol and 2-propanol at 0.8 and 3.0 mg/mL, respectively. The bispolar compounds **10**, **11**, and **16** were as effective as or better than the monomeric derivatives.

The rheology properties of gels formed by compounds **7**, **8**, **9**, and **13** were characterized and are shown in Figure 3. For all four compounds, the storage modulus G' is greater than the loss modulus G'' at all tested frequencies. This is an indication of the gel's elastic properties.[53,54] The storage modulus for compound **8** is about 2500 Pa, which is the strongest among these compounds. For the ureas, the ratio of the G'/G'' is 3.2−4.0, which is the largest among the four compounds. This is probably due to the very strong aryl stacking and urea hydrogen bonding which result in strong intermolecular interactions.

After the gelation screening, we selected several gels formed by mono-tail lipids and bispolar compounds and exposed them to a 6 W TLC illuminating UV lamp at 254 nm. Figure 4 shows the photographs of the gels formed by the amide **9** and urea **15** before and after polymerization. A visible color change usually indicates that polymerization has taken place. Typically, the gels formed by monomeric glycolipids cross-linked in less than 30 s upon treatment with UV light, the colors changed from colorless or white opaque to deep blue. The bispolar glycolipids are more resistant toward UV irradiation; typically it takes

DOI: 10.1021/jo501568u
J. Org. Chem. 2015, 80, 733−743

Scheme 1. Structures of Diacetylene-Containing Amide Derivatives Synthesized



Scheme 2. Structures of Diacetylene-Containing Urea Derivatives Synthesized

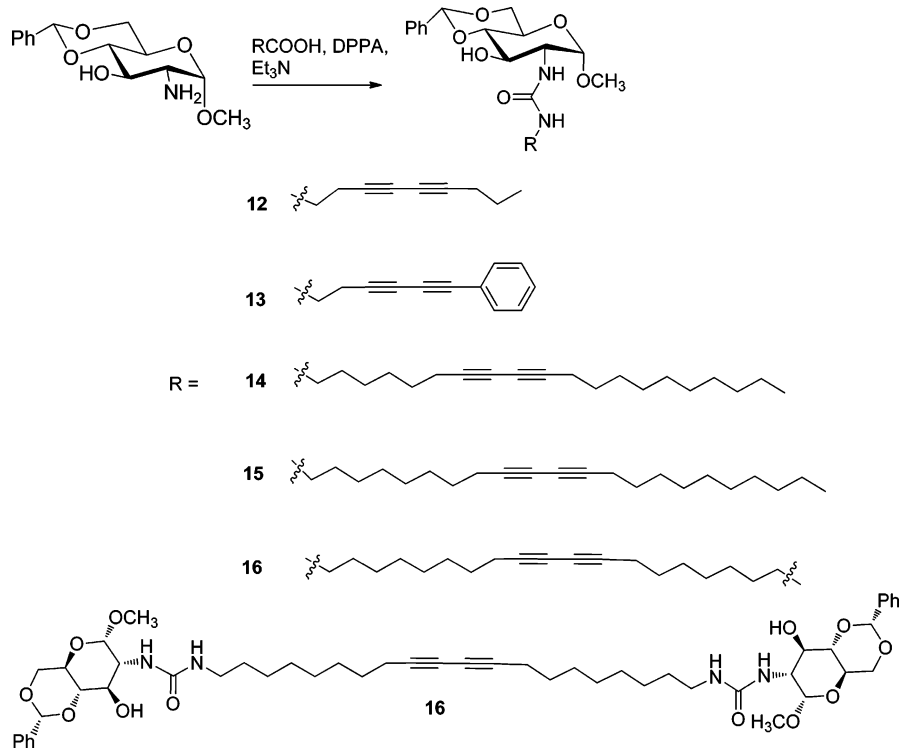


Table 1. Gelation Properties of the Diacetylene-Containing Amide and Urea Derivatives of D-Glucosamine[a]

compound	hexane	toluene	EtOH	iPr-OH	H_2O:EtOH (2:1)	water	H_2O:DMSO (2:1)
7	I	G 20	S	S	G 1.0	I	I
8	I	G 10	G 20.0	G 20	G 1.6	I	C
9	I	G 10	G 0.8	G 3.0	C	I	I
10	I	I	G 10.0	G 10	G 2.5	I	I
11	I	G 20	G 3.0	G 4.0	C	I	I
12	I	G 5	G 5.0	G 10	G 2.5	I	I
13	I	G 10	G 5.0	G 5.0	G 2.5	I	I
14	I	G 20	G 5.0	S	I	I	I
15	I	G 5.0	G 5.0	S	I	I	I
16	I	G 10	G 1.0	G 6.6	I	I	I

[a]G, gel at room temperature; the numbers are the corresponding minimum gelation concentrations (MGCs) in mg/mL. I, insoluble. C, crystallize or precipitate. S, soluble at ~20 mg/mL.

longer time (3 min or more) to see the gel changing color to light blue. This relative stability of the dimeric compounds under UV treatment can be attributed to their structures. The diacetylene groups are somewhat shielded due to the presence of the polar headgroups at each end. In the monomers, interdigitation of the diacetylene chains can take place which

DOI: 10.1021/jo501568u
J. Org. Chem. 2015, 80, 733−743

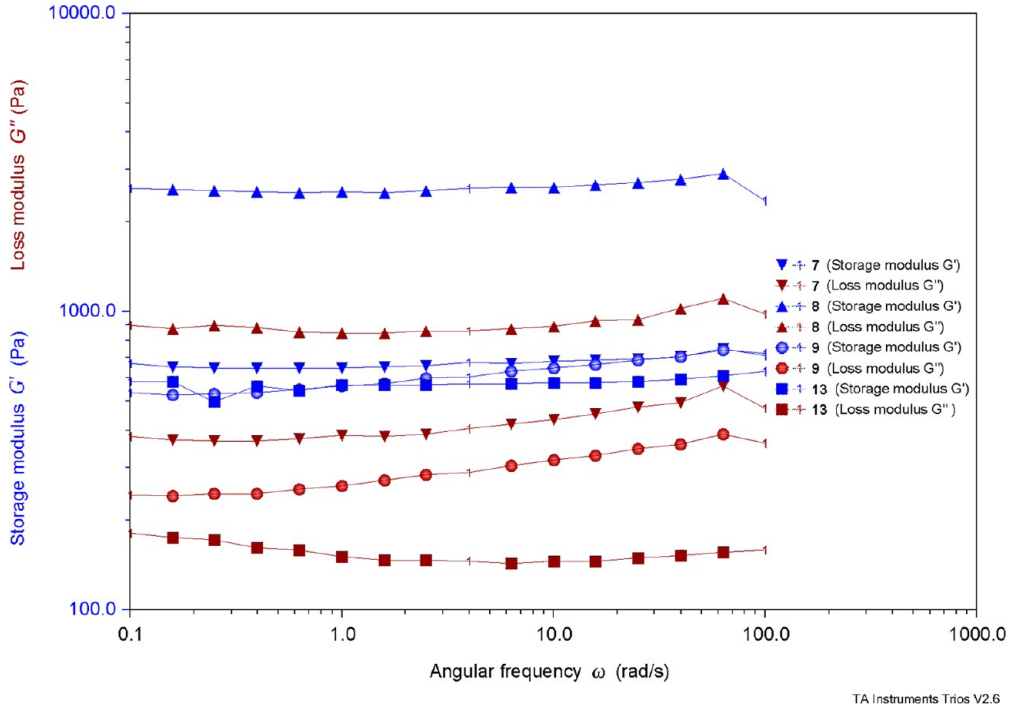


Figure 3. Rheology properties of several gels. Compound **7**, 3.0 mg/mL in ethanol–water (v/v = 1:2); compound **8**, 1.6 mg/mL in ethanol–water (v/v = 1:2); compound **9**, 2.0 mg/mL in ethanol; compound **13**, 2.5 mg/mL in ethanol–water (v/v = 1:2).

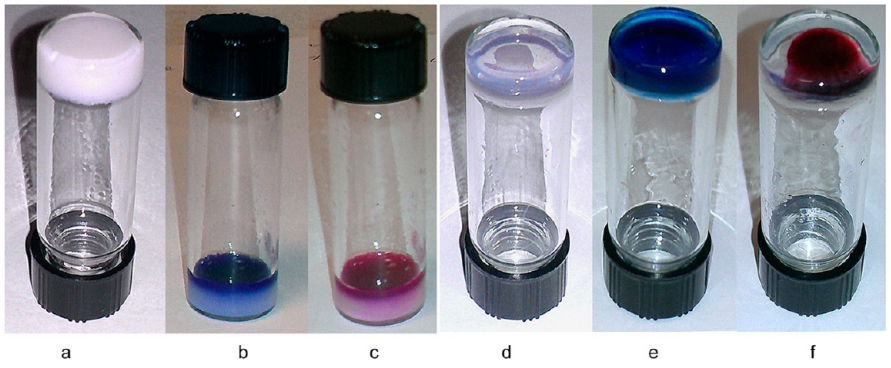


Figure 4. Gels formed by compounds **9** and **15** and their responses to UV treatment. (a) An opaque gel formed by compound **9** in ethanol at 1.5 mg/mL. (b) The gel in vial a was treated with UV irradiation for 7 min through the top of the vial. (c) The gel in vial b turned purple-red when heating at 70 °C in a water bath. (d) A transparent gel formed by compound **15** in ethanol at 5 mg/mL. (e) The gel in vial d was treated with UV light for 2 min. (f) The re-formed gel after heating the blue gel in vial e and then cooling to rt.

allows the feasible alignment of the diacetylene groups. Among these series of compounds, compound **13** has the phenyl group attached to the diyne rather than alkyl group. The gels formed by this compound are difficult to polymerize with the UV lamp; after 10 min of irradiation, no visible change of gel color was observed. However, the readiness of polymerization of most of the diacetylene derivatives indicates a facile packing order feasible for polymerization.

As shown in Figure 4, the gel formed by urea **15** is prone to UV cross-linking; it turned to dark blue color after only 10 s of UV treatment. The transparent nature of the gel also makes polymerization facile. The blue gel turned to red color upon heating in a water bath at 70 °C but turned deep red when heating further, and the gel re-formed upon cooling. This indicated that only partial polymerization had occurred during the UV treatment. The same phenomenon was observed after three cycles of heating and cooling, which indicated that the remaining unpolymerized diacetylene lipids are still very efficient gelators. For amide **9**, it formed an opaque gel, and only the top layers could be cross-linked easily. Under longer periods of UV irradiation, more samples turned blue, the thermoresponse was similar to that of urea **15**, but the pink-red colored gel (Figure 4c) turned orange-red upon heating until the unpolymerized white part of the gel melted. The mixture re-formed the gel upon cooling. Only partial polymerization occurred and the remaining diacetylene lipids are very efficient in gelation.

In general, the polymerized gels were more stable, as indicated by higher melting point ranges measured by the dropping ball method. We selected four compounds representative of each series; these include the amides **9**, **11** and ureas **14**, **16**. The gels from the monoamide **9** and urea **14** were treated with UV light for 5 min total, and the gels from the bisamide **11** and bisurea **16** were treated for 10 min total. The melting points of the gels before and after UV exposure of the four compounds are shown in Table 2. The cross-linked

DOI: 10.1021/jo501568u
J. Org. Chem. 2015, 80, 733–743

Table 2. Melting Point Range[a] of the Gels before and after UV Irradiation

compound	gel EtOH (mg/mL)	melting range before UV (°C)	melting range after UV (°C)	melting temperature increase (°C)
9	2.0	45–52–59	57–64–77	12–12–18
11	5.0	52–73–77	68–78–93	16–5–16
14	10.0	39–47–53	55–72–80	16–15–27
16	2.0	43–51–60	64–67–79	21–16–19

[a]The melting range was recorded as the temperature of the gel beginning to melt and when the ball moved to the center of the gel and to the bottom of the gel.

gels showed enhanced thermal stability, and the gel-to-sol transition temperatures increased upon polymerization with an average of 15–20 °C. The moderate increase indicated that the cross-linking of the diacetylenes did not change the overall gel morphology or packing substantially.

The morphologies of the gel matrix were also studied here. Very interesting and unique morphologies were formed in the gel phase when observed under an optical microscope. Diacetylene lipids are known to form lipid tubules, and the diacetylene derivatives synthesized here are also able to form similar tubular structures depending on the structure of the lipids. Some of the monomers formed helical fibers with marked pitches and handedness. This observation is expected because the compounds are chiral. They prefer to have a certain orientation or twisting during the assembly process and give helical types of morphologies. Several examples are shown in Figure 5 for diacetylene amide **9**, which formed remarkable helical structures which can be cross-linked.

The gel formed by compound **9** in ethanol was observed directly on a glass slide. The morphology of the gel aggregates includes tubules and helices (Figure 5a), twisted ribbons (Figure 5b), and double stranded helical ropes (Figure 5c). Upon treatment with UV light (254 nm) for 1 min, the gels turned to purple-blue color, and the morphology of the gels was similar to that prior to polymerization, with helices and bundles of helices and tubules (Figure 5d–f). However, it is clear that these helical fibers or tubules were polymerized, as they are purple colored tubules or fibers. The double stranded helical ropes can also be cross-linked, but it seems that there were partial polymerizations on areas of the helices (Figure 5f). This observation indicates that the polymerization of diacetylene gels occurred through a topochemical reaction and maintained similar packing compared to that of the unpolymerized diacetylenes.

Figure 6 shows the fibrous assemblies formed by several other derivatives. In contrast to amide analogue **9**, the urea derivatives with similar chain lengths showed different morphology, as shown in Figure 6a,b. Compound **15** formed a narrower fibrous network, with a continuous and soft appearance and more branching. The gels can be polymerized, and the partially polymerized thin fibrous networks exhibited dark blue or purple color. The dimeric compounds have shown more uniform gel surface, and the fibrous assemblies also appeared to be different compared to the monomers. The fibrous assemblies appeared to have certain symmetry orders.

Besides the optical micrographs, we also characterized the assemblies of the gel networks with field emission electron microscopy. The scanning electron micrographs for the four compounds are shown in Figures 7–9. At low magnification, the monoamide **9** formed long fibrous assemblies, and the fibers seemed to form bundles or clusters with over 30 μm in lengths (Figure 7a,c). At high magnification, the fibrous or tubular rods (Figure 7b,d) appear to have a certain twist or helical structure on some of the fibers. The cylindrical fibers have an average diameter of about 80 nm. The dimer amide **11** showed somewhat different morphology, as shown in Figure 8. The fibers appear to be smaller in diameters and also have more branching than the monomers. At higher resolution, it is pretty clear that the fibrous rods are about half the diameter of those formed by compound **9**, estimated at only 20–40 nm (Figure 8b,d). These agree with the OM results in that the diamide formed fibers thinner than those of the monoamide.

For the urea derivatives, mono-urea **15** formed fibrous networks that seemed to be shorter in length and more circular or connected between the fibers (Figure 9a,c); the individual fibers are estimated to have diameters of about 30–40 nm

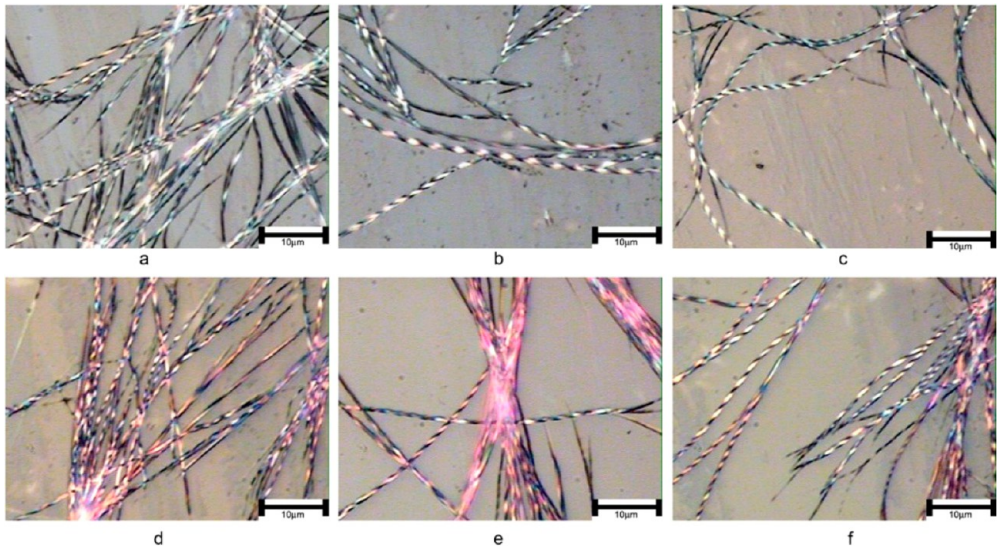


Figure 5. Optical micrographs of a gel formed by compound **9** in ethanol at 0.8 mg/mL. (a–c) Before treatment of the gel with UV light. (d–f) After irradiation with UV light for 1 min.

DOI: 10.1021/jo501568u
J. Org. Chem. 2015, 80, 733–743

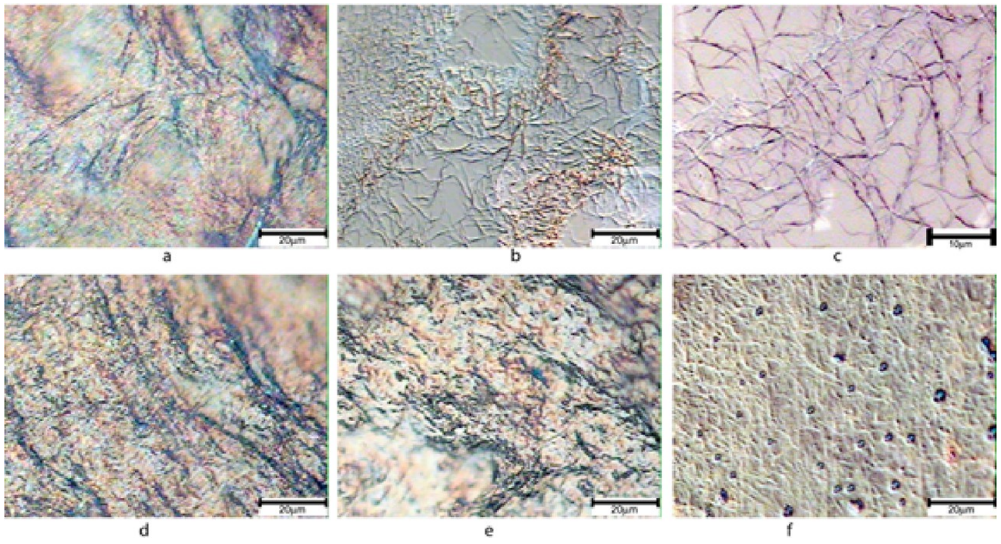


Figure 6. Optical micrographs of several ethanol gels. (a–c) Gels of compound **15** at 5 mg/mL. (d) Gels of compound **11** at 3 mg/mL. (e, f) Gels of compound **16** at 2 mg/mL.

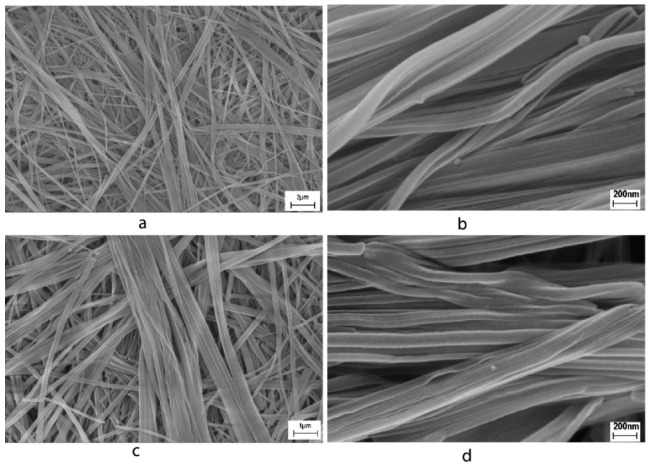


Figure 7. Field emission scanning electron micrographs of gels formed by compound **9**. Images a and b are without UV treatment. Images c and d are after treating with UV for 1 min.

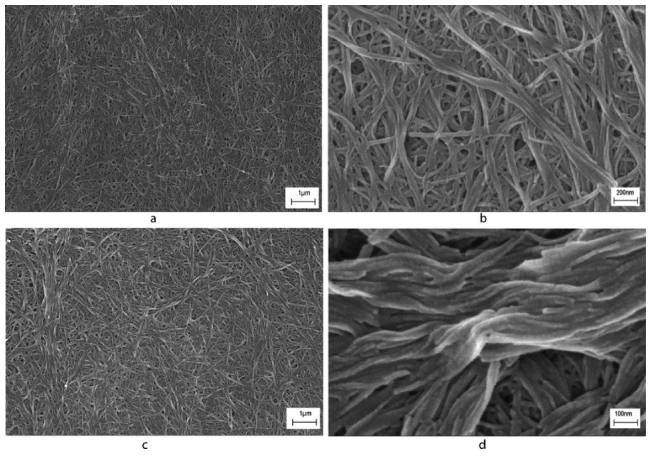


Figure 8. Field emission scanning electron micrographs of gels formed by compound **11** in ethanol at 3.0 mg/mL. Images a and b are without UV treatment. Images c and d are after treating with UV for 1 min.

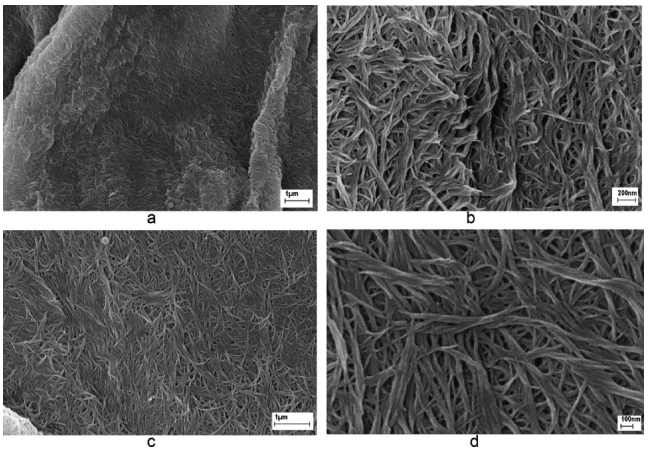


Figure 9. Field emission scanning electron micrographs of gels formed by compound **15** in ethanol at 5 mg/mL. Images a and b are without UV treatment. Images c and d are after treating with UV for 1 min.

(Figure, 9b,d). These thin sheet-like fibers are highly intertwined with the neighboring fibers. The bisurea derivative **16** formed interesting morphology (Figure 10), with somewhat tubular or rod shape, and then assembled together into a flower-like network with more connecting points. Figure 10d shows that the tubules are more uniform, with about 20 nm in diameter, and the tubular fibers bundled together to form rope-like assemblies. However, there is a clear difference between the mono-urea and bisurea in morphologies, which reflects that the molecular structure differences in turn control the assembly structure macroscopically.

Because these diacetyelene-containing gels can also be useful as optical sensors, we further characterized the absorption spectra of the gels formed by four selected compounds, as shown in Figures S1–S4, Supporting Information. The ethanol gel formed by monoamide **9** can be easily polymerized with a UV lamp. The absorption intensities increased with longer UV exposure; however, the absorption maxima maintained the same wavelength with two main absorptions at λ_{max} = 578 and 616 nm. The spectrum started blue-shifting at 35 °C, A_{578} and A_{616} started to decrease, and A_{540} started growing. The

DOI: 10.1021/jo501568u
J. Org. Chem. 2015, 80, 733–743

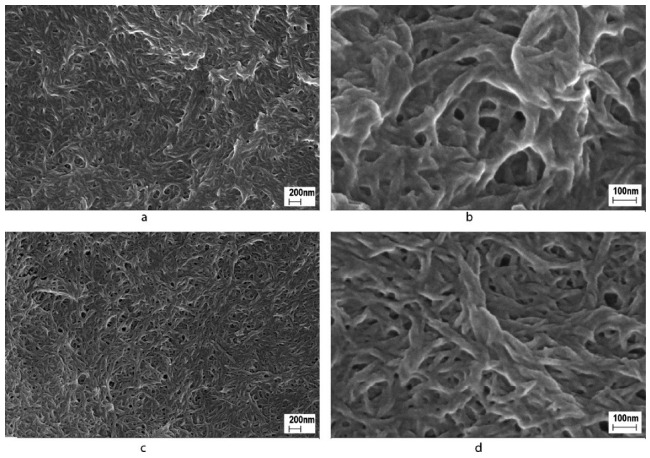


Figure 10. Field emission scanning electron micrographs of gels formed by compound **16** in ethanol at 1.2 mg/mL. Images a and b are without UV treatment. Images c and d are after treating with UV for 1 min.

absorption spectra are similar for 40 °C and 50 °C, with A_{540} continuing to increase in intensity and A_{616} weakening further. At 60 °C, the A_{616} signal cannot be recognized anymore, and A_{540} is almost equal to A_{578}. When the polymerized gel of compound **9** was heated to above 60 °C, the gel turned red and A_{540} was the strongest peak. The UV spectra of the polymerized gel formed by the bispolar amide **11** show two main absorption bands at 550 and 580 nm, and they are relatively insensitive to heating below 60 °C, as there is almost no change in the spectra (Figure S2, Supporting Information) except that A_{580} slowly decreased and A_{550} slowly increased. At 60 °C, A_{550} became stronger than A_{580}. When heating above 60 °C, the peak at 550 nm shifted to 526 nm and A_{580} decreased significantly.

The mono-urea derivative **15** and bisurea derivative **16** also showed similar absorption spectra (Figures S3 and S4, Supporting Information) which are significantly different from their amide analogues. Both of the urea gels were dark blue-purple upon UV irradiation, and their responses to heating were also similar. The absorption spectra of the gel of mono-urea **15** spanned from 500 to 700 nm, with almost continuous absorptions. The spectrum did not change much upon heating at below 50 °C, but gradually A_{500} increased and A_{650} decreased when heated to 60 °C or so. Upon heating at above 60 °C, part of the gel turned red-purple and the main absorption band appeared at 550 nm.

The gel formed by bisurea **16** is more difficult to cross-link in comparison to the mono-urea derivatives, possibly due to the rigidity of the molecule because the diacetylene-containing chains are not as freely packed as in the monomer case. After 5 min of UV irradiation, the absorptions are at 606 and 662 nm. The sample was also more resistant to heat than the amides, as the spectra had no significant changes with incubation up to 45 °C. At 50 °C, a new signal at 524 nm started appearing, and the other two bands were blue-shifted to 592 and 654 nm with the A_{654} being the strongest peak. At 60 °C, the intensities of A_{520}, A_{592}, and A_{654} are almost equal. When it was heated at above 60 °C, A_{592} and A_{654} decreased significantly, and A_{524} became the strongest. The absorption at 654 nm was not converted to

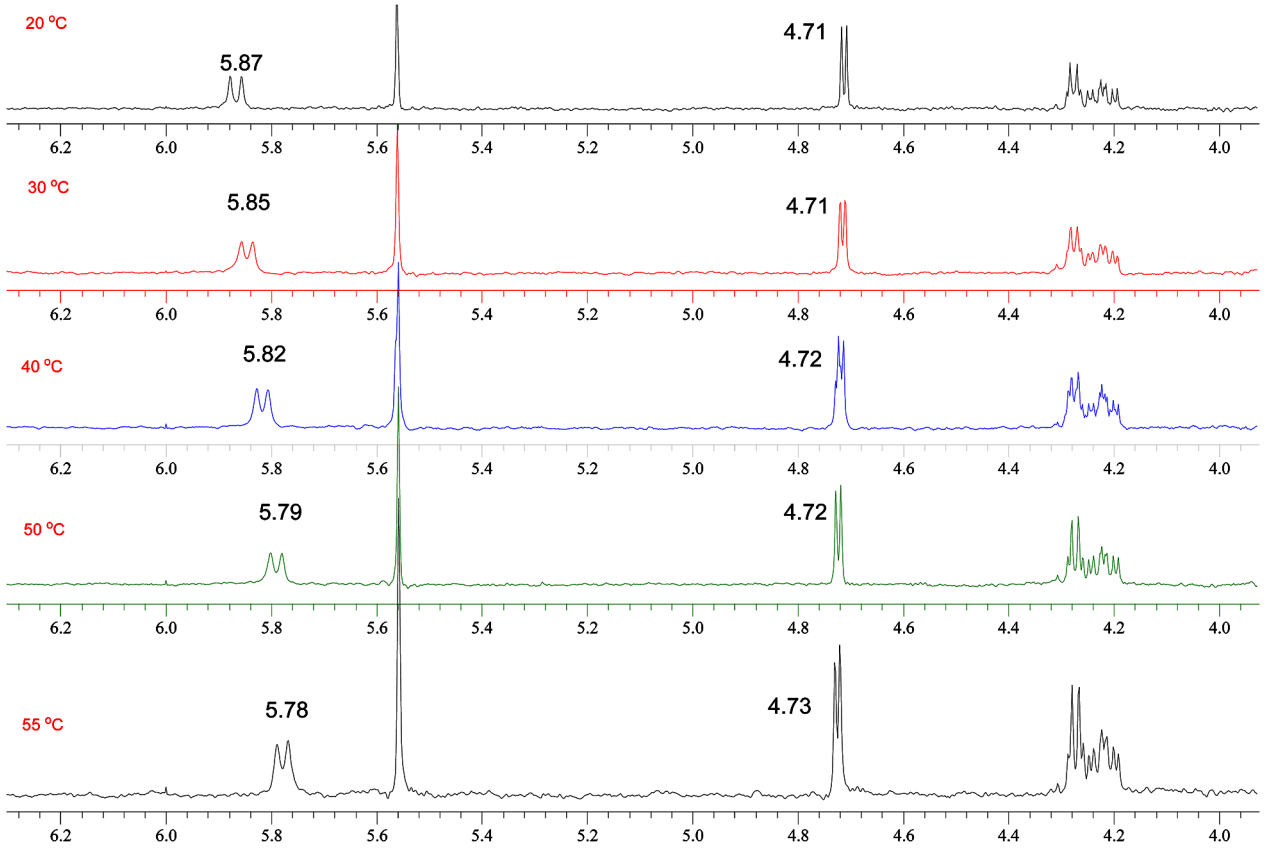


Figure 11. Temperature dependence study of compound **9** from 20 °C to 55 °C. Note that the NH bond absorption shifted gradually from 5.87 to 5.78 ppm at 55 °C.

DOI: 10.1021/jo501568u
J. Org. Chem. 2015, 80, 733−743

shorter wavelength, implying that the dark blue color of the gel was more resistant to heating.

We also studied the hydrogen bonding effect of amide **9** using NMR spectroscopy in $CDCl_3$. As shown in Figure 11, the amide bond NH peak shifted to lower frequencies upon increasing temperatures, with a significant amount of upfield shift from 5.87 ppm at 20 °C to 5.78 ppm at 55 °C. This indicated that intermolecular hydrogen bonding between the gelator molecules decreased at higher temperature, which led to absorptions at lower frequencies. Also a small downfield shift from 4.71 to 4.73 ppm for the anomeric proton was observed. At 40 °C, two sets of the anomeric signals appeared at this position, and this became one set of doublets again at 50 °C (see Figure S8, Supporting Information). The slight downfield shift of the anomeric proton absorption at higher temperatures may be due to the different conformations of the amide bond with the anomeric oxygen and intramolecular hydrogen bonding. The decreased intermolecular hydrogen bonding of the amides at higher temperature led to the slight decrease of shielding for the anomeric position and thus a shift to slightly higher frequencies. A similar but smaller change is also observed for the methoxy signal, which also shifted slightly downfield similarly, from 3.40 ppm at 20 °C to 3.41 ppm at 55 °C, and at 40 °C, two peaks are observed at 3.40 and 3.41 ppm (Figure S9, Supporting Information).

The clear trend of temperature dependence of the NH bond in glucosamine derivative **9** indicates that hydrogen bonding is an important driving force for gelation in organic solvents. From this study and our previous studies using glucosamine derivatives, we can see that the headgroup **2** is a very effective scaffold for constructing self-assembled glycolipids which may be efficient organogelators or hydrogelators. The 4,6-benzylidene acetal protective group on glucosamine, which leads to a relatively rigid conformation of the sugar ring, and the hydrogen bonding from the amino group at the 2-position are important factors that lead to effective gelators. It seems that various functional groups can be introduced at the 2-position without losing gelation tendencies. The glucosamines are good templates for installing various functional groups to obtain advanced functional materials. The presence of amino groups is desirable in designing suitable sugar-based LMWGs. It is anticipated that other monosaccharides or disaccharides with suitable functionalizations may also be effective LMWGs as long as the various intermolecular interactions are considered.

CONCLUSIONS

In summary, we have synthesized and characterized a series of diacetylene-containing glycolipids using protected D-glucosamine as the headgroup. The self-assembling properties of these compounds were studied in several solvents. Among the 10 amide- and urea-linked glycolipids, a majority of them are effective organogelators for ethanol, toluene, and ethanol–water mixture. Optical and electronic microscopy studies have shown that typically these gelators form long fibers or tubules and sometimes planar sheets, and the fibers are generally birefringent. The long chain amide of 10,12-tricosadiynoic acid **9** formed helices, which are also polymerizable. The ^{1}H NMR spectroscopy study of compound **9** indicated that hydrogen bonding was an important driving force for gelation in organic solvent. The ethanol gels formed by two amides and two ureas were also characterized after UV treatment. Typically, the thermal stability increased upon cross-linking the gels. The field emission SEM study and OM study both confirmed that polymerization did not affect the morphology of the gel networks, or at least no obvious changes of morphologies occurred at their detection limits. The color transitions versus temperature of the UV-treated gels were also studied by UV–vis spectroscopy. The monoamide and mono-ureas were far more amenable to polymerization than the bisamides and bisureas, and the UV absorptions of the ureas gave similar patterns, which have many absorption bands from 550 to 700 nm. The amides typically showed peaks around 550 and 620 nm. The color transitions were monitored at different temperatures, and typically a visible change could be detected. These color transition properties of the polydiacetylene gels can be used to predict changes in their immediate environment, such as in the event of binding to a biological agent. The ureas give UV bands at wavelengths much longer than those of the amides, which reflects that the urea functional groups help the molecules to assemble in a very organized manner and result in longer conjugation lengths of the product PDAs. Though both amides and ureas performed similarly as gelators, their spectral properties are quite different. These properties are useful in designing diacetylene gel materials that can polymerize and give strong UV absorptions at longer wavelengths and for applications where such materials are desired. These polymerized gels may be useful as sensors for their interaction with other molecules.

EXPERIMENTAL SECTION

General Methods and Materials. Diacetylene-containing fatty acids were purchased from GFS Chemicals. High resolution mass spectrometry data were measured on the Q-TOF. The ionization technique used was ESI (electrospray ionization) in ES+ mode. Melting points were measured using a Fisher-Jones melting point apparatus. Scanning electron microscopy was performed using a field emission scanning electron microscope (FESEM), model LEO 1530VP.

Melting Point Measurement of the Gels. For the melting points of before and after polymerization, quartz NMR tubes were used as the containers of gels for the dropping ball method. The steel ball has an average weight of 128 mg. The gels were exposed to a 6 W TLC illuminating lamp at both 254 and 365 nm for either 5 min for the monolipids or 10 min total for the bispolar lipids. In general, a compound was dissolved in a small vial and then transferred to the NMR tube using a pipet while it was still warm. The NMR tube was then sonicated and cooled until a stable gel was re-formed. Then a steel ball was gently placed on top of the gel surface using a magnetic bar. The tube was immersed in a water bath controlled by a stirring hot plate. The temperatures when the ball starts dropping (at initial melting), when it travels to the middle of the gel, and when it reaches the bottom of the gel were recorded by reading the thermometer in the water bath.

Rheological Analysis. The rheology experiment was performed on a TA Instruments HR-2 Discovery hybrid rheometer, operating in oscillatory mode, with a 25 mm stainless steel parallel plate geometry. A Peltier temperature controller was set to maintain 25 °C during the measurement. The gels were transferred to the Peltier plate center, the gel samples were analyzed immediately with a gap of 100 μm, and dynamic frequency sweep was performed from 0.1 to 100 rad/s with 5% strain.

Synthesis of Compounds 7–16. Compound 7: 4,6-*O*-Benzylidene methyl α-D-2-deoxy-2-glucosamine 2-(5,7-hexadecadiynoyl amide). The glucosamine headgroup **2** (100 mg, 0.355 mmol) was dissolved in anhydrous dichloromethane (DCM, 5 mL) and was cooled to 0 °C, and then pyridine (42 mg, 0.53 mmol) was added to the reaction mixture. Then 5,7-hexadecadiynoic acid chloride was prepared by treating the acid (85 mg, 0.342 mmol) with oxalyl chloride (47 mg, 0.376 mmol) in about 3 mL anhydrous DCM and a drop of DMF and stirring for 1 h. This acid chloride was added to the

DOI: 10.1021/jo501568u
J. Org. Chem. 2015, 80, 733–743

flask, the mixture was stirred for 5 h at room temperature, and the flask was covered with aluminum foil and protected from moisture with a nitrogen balloon and a drying tube filled with calcium chloride. After the reaction was complete as indicated by TLC and ^{1}H NMR spectroscopy, the reaction was stopped and diluted with 20 mL of DCM, and the mixture was then washed with 5 mL of water twice and brine once. The organic phase was dried over sodium sulfate, and the solvent was removed using a rotoevaporator to give the crude product. The product was then purified using flash chromatography on silica gel with a gradient solvent system of hexane:dichloromethane:methanol, and the polarity was increased gradually to obtain the best separation . The R_f value was 0.4 in hexane:DCM:MeOH (4.5:4.5:1). During all steps of reaction, workup, and purification, to prevent polymerization, caution was taken to protect the samples from exposure to light, and products were stored in the refrigerator. The purified product was obtained as a white solid (0.152 g, 0.297 mmol) in 87% yield, mp 149.0−150.0 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46−7.54 (m, 2H), 7.32−7.41 (m, 3H), 5.97 (d, 1H, J = 8.4 Hz), 5.55 (s, 1H), 4.71 (d, 1H, J = 4.0 Hz), 4.24−4.30 (m, 1H), 4.16−4.24 (m, 1H), 3.84−3.92 (m, 1H), 3.71−3.83 (m, 2H), 3.57 (t, 1H, J = 9.0 Hz), 3.40 (s, 3H), 3.28 (d, 1H, J = 3.3 Hz), 2.28−2.40 (m, 4H), 2.24 (t, 2H, J = 7.0 Hz), 1.84 (q, 2H, J = 7.0 Hz), 1.51 (q, 2H, J = 7.1 Hz), 1.18−1.43 (m, 10H), 0.86 (t, 3H, $J \cong$ 6.8 Hz). ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.4, 137.1, 129.1, 128.2, 126.3, 101.8, 98.8, 82.0, 78.1, 76.0, 70.5, 68.8, 66.3, 65.0, 62.3, 55.3, 53.9, 34.9, 31.7, 29.1, 29.0, 28.8, 28.2, 23.8, 22.6, 19.1, 18.4, 14.1. HRMS calcd for $C_{30}H_{42}NO_6$ $[M + H]^+$ 512.3012, found 512.2999.

Compound **8**: 4,6-*O*-Benzylidene methyl α-D-2-deoxy-2-glucosamine 2-(10,12-octadecadiynoyl amide). The compound was synthesized with the same method as used for the synthesis of **7**. The starting materials were compound **2** (100 mg, 0.355 mmol), pyridine (42 mg, 0.53 mmol), 10,12-octadecadiynoic acid (95 mg, 0.344 mmol), and oxalyl chloride (48 mg, 0.378 mmol). Product was a white crystalline solid (0.154 g, 0.285 mmol) in 83% yield. The R_f value was 0.5 in hexane:DCM:MeOH (4.5:4.5:1). Mp 151.0−153.0 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.46−7.54 (m, 2H), 7.33−7.40 (m, 3H), 5.85 (d, 1H, J = 8.8 Hz), 5.56 (s, 1H), 4.72 (d, 1H, J = 3.7 Hz), 4.26−4.31 (m, 1H), 4.19−4.26 (m, 1H), 3.86−3.93 (m, 1H), 3.73−3.83 (m, 2H), 3.55−3.62 (m, 1H), 3.40 (s, 3H), 3.15 (d, 1H, J = 3.3 Hz), 2.19−2.29 (m, 6H), 1.59−1.65 (m, 2H), 1.46−1.56 (m, 4H), 1.22−1.42 (m, 12H), 0.89 (t, 3H, J = 7.1 Hz). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 174.7, 137.1, 129.1, 128.2, 126.3, 101.9, 98.8, 82.1, 77.6, 77.4, 70.8, 68.7, 68.1, 65.3, 62.3, 55.3, 54.0, 36.6, 31.0, 29.1, 29.0, 28.9, 28.7, 28.2, 28.0, 25.5, 22.1, 19.1, 13.8. HR ESIMS calcd for $C_{32}H_{46}NO_6$ $[M + H]^+$ 540.3325, found 540.3308.

Compound **9**: 4,6-*O*-Benzylidene methyl α-D-2-deoxy-2-glucosamine 2-(10,12-tricosadiynoyl amide). The compound was synthesized with the same method as used for the synthesis of **7**. The starting materials were compound **2** (75 mg, 0.267 mmol), pyridine (32 mg, 0.53 mmol), 10,12-octadecadiynoic acid (95 mg, 0.274 mmol), and oxalyl chloride (38 mg, 0.301 mmol). The R_f value was 0.43 in hexane:DCM:MeOH (4.5:4.5:1). The product was obtained as white crystals (0.135 g, 0.221 mmol) in 83% yield, mp 144.0−144.5 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.48−7.53 (m, 2H), 7.33−7.39 (m, 3H), 5.84 (d, 1H, J = 8.4 Hz), 5.57 (s, 1H), 4.72 (d, 1H, J = 3.7 Hz), 4.20−4.31 (m, 2H), 3.86−3.94 (m, 1H), 3.74−3.84 (m, 2H), 3.56−3.62 (m, 1H), 3.41 (s, 3H), 3.12 (d, 1H, J = 3.7 Hz), 2.20−2.29 (m, 6H), 1.60−1.69 (m, 2H), 1.46−1.55 (m, 4H), 1.20−1.42 (m, 22H), 0.88 (t, 3H, $J \cong$ 6.8 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.7, 137.1, 129.1, 128.2, 126.3, 101.9, 98.8, 82.1, 77.6, 77.4, 70.9, 68.8, 65.3, 65.2, 62.3, 55.3, 54.0, 36.6, 31.8, 29.5, 29.4, 29.3, 29.1, 29.0, 28.9, 28.8, 28.7, 28.3, 28.2, 25.5, 22.6, 19.2, 19.1, 14.1. HRMS calcd for $C_{37}H_{56}NO_6$ $[M + 1]^+$ 610.4108, found 610.4108.

Compound **10**: 4,6-*O*-Benzylidene methyl α-D-2-deoxy-2-glucosamine 2-(5,7-dodecadiyndioyl amide). The compound was synthesized with a method similar to that used for the synthesis of **7**, the main difference being the solvent system used for purification; a more polar (with an increasing amount of methanol) solvent was used here. The starting materials were compound **2** (100 mg, 0.355 mmol), pyridine (56 mg, 0.71 mmol), 5,7-dodecadiyndioic acid (40 mg, 0.179 mmol), and oxalyl chloride (45 mg, 0.358 mmol). Product **10** R_f value was 0.6 in hexane:DCM:MeOH (4:4:2). The product was obtained as a light yellow solid (0.111 g, 0.148 mmol) in 83% yield, mp 153.0−155.0 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.92 (d, 2H, J = 8.4 Hz), 7.42−7.48 (m, 4H), 7.34−7.40 (m, 6H), 5.60 (s, 2H), 5.15 (d, 2H, J = 5.9 Hz, OH), 4.62 (d, 2H, J = 3.7 Hz), 4.13−4.21 (m, 2H), 3.80−3.88 (m, 2H), 3.71−3.79 (m, 2H), 3.56−3.71 (m, 4H), 3.46 (t, 2H, J = 9.2 Hz), 3.29 (s, 6H), 2.30 (t, 4H, J = 7.0 Hz), 2.22 (t, 4H, J = 7.3 Hz), 1.63−1.73 (m, 4H); ^{13}C NMR (100 MHz, DMSO) δ 171.7, 137.7, 128.8, 128.0, 126.4, 100.8, 98.6, 81.9, 77.7, 68.0, 67.3, 65.5, 62.4, 54.8, 54.0, 34.0, 24.0, 17.9. HRMS calcd for $C_{40}H_{49}N_2O_{12}$ $[M + 1]^+$ 749.3286, found 749.3278.

Compound **11**: 4,6-*O*-Benzylidene methyl α-D-2-deoxy-2-glucosamine 2-(10,12-docosadiyndioyl diamide). The compound was synthesized with a method similar to that used for the synthesis of **7**, the main difference being the solvent system for purification. A more polar (with increasing amount of methanol) solvent was used here. The starting materials were compound **2** (100 mg, 0.355 mmol), pyridine (56 mg, 0.712 mmol), 10,12-docosadiyndioic acid (60 mg, 0.165 mmol), and oxalyl chloride (23 mg, 0.182 mmol). Product compound **11** R_f value was 0.5 in hexane:DCM:MeOH (4:4:2). The product was obtained as a white solid (0.114 g, 0.128 mmol) in 78% yield, mp 168.0−169.5 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45−7.52 (m, 4H), 7.31−7.38 (m, 6H), 5.90 (d, 2H, J = 8.8 Hz), 5.54 (s, 2H), 4.71 (d, 2H, J = 3.7 Hz), 4.24−4.29 (m, 2H), 4.16−4.24 (m, 2H), 3.84−3.92 (m, 2H), 3.71−3.82 (m, 4H), 3.54−3.61 (m, 2H), 3.39 (s, 6H), 3.32 (d, 2H, J = 2.9 Hz, OH), 2.17−2.28 (m, 8H), 1.57−1.67 (m, 4H), 1.44−1.54 (m, 4H), 1.21−1.41 (m, 16H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.6, 137.1, 129.1, 128.2, 126.3, 101.8, 98.8, 82.0, 77.4, 70.6, 68.8, 65.3, 62.3, 55.3, 54.0, 36.5, 29.1, 29.0, 28.8, 28.6, 28.2, 25.5, 19.1. HRMS Calcd for $C_{50}H_{69}N_2O_{12}$ $[M + 1]^+$889.4851, found 889.4857.

Compound **12**: 4,6-*O*-Benzylidene methyl α-D-2-deoxy-2-glucosamine 2-(nona-3,5-diyn-1-yl)urea. The deca-4,6-diynoic acid (50 mg, 0.304 mmol) was dissolved in 5 mL of THF at room temperature, the flask was kept in a dark environment and protected from light by covering with aluminum foil, and then Et_3N (0.065 mL, 0.466 mmol) and DPPA (0.101 mL, 0.419 mmol) were added to the reaction mixture. The reaction was stirred at 60 °C for 2 h after which the isocyanate formed, the flask was cooled to room temperature, the glucosamine headgroup **2** (65 mg, 0.231 mmol) was added, and the reaction mixture was then stirred at room temperature for 6 h. After the reaction was complete as indicated by TLC and ^{1}H NMR spectroscopy, the reaction mixture was concentrated on a rotoevaporator, the residue was taken up in 20 mL of DCM and 10 mL of water, and the aqueous phase was extracted with 15 mL of DCM twice. The combined organic phase was dried over sodium sulfate, and the crude product was obtained after the solvent was removed on a rotoevaporator. It was purified using flash chromatography on silica gel with a gradient solvent system starting with hexane and DCM and then DCM and methanol. The R_f value was 0.4 in DCM:MeOH (95:5). The product was obtained as a white solid (92 mg, 0.208 mmol) in 90% yield, mp 173.0−175.0 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.47−7.52 (m, 2H), 7.32−7.40 (m, 3H), 5.56 (s, 1H), 5.08−5.16 (m, 1H), 4.91 (d, 1H, J = 8.1 Hz), 4.72 (d, 1H, J = 3.3 Hz), 4.24−4.31 (m, 1H), 3.85−3.96 (m, 2H), 3.73−3.83 (m, 2H), 3.55−3.63 (m, 2H), 3.41 (s, 3H), 3.25−3.40 (m, 2H), 2.42−2.51 (m, 2H), 2.23 (t, 2H, J = 7.0 Hz), 1.49−1.59 (m, 2H), 0.98 (t, 3H, J = 7.3 Hz). ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.4, 137.1, 129.2, 128.3, 126.3, 101.9, 99.2, 82.0, 78.3, 74.6, 71.5, 68.8, 66.8, 65.1, 62.2, 55.3, 39.1, 21.7, 21.1, 20.9, 13.5. HRMS Calcd for $C_{24}H_{31}N_2O_6$ $[M + H]^+$ 443.2179, found 443.2182.

Compound **13**: 4,6-*O*-Benzylidene methyl α-D-2-deoxy-2-glucosamine 2-(6-phenylhexa-3,5-diyn-1-yl)urea. Compound **13** was synthesized by the same method as that described above for compound **12**. The starting materials and reagents used were 7-phenylhepta-4,6-diynoic acid (0.075 g, 0.378 mmol), Et_3N (0.078 mL, 0.569 mmol), DPPA (0.110 mL, 0.512 mmol), and compound **2** (80.0 mg, 0.284 mmol). The R_f value was 0.6 in DCM:MeOH (95:5). The product was obtained as a white solid (0.122 g, 0.256 mmol) with 90% yield, mp

DOI: 10.1021/jo501568u
J. Org. Chem. 2015, 80, 733−743

181.0−184.0 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45−7.51 (m, 4H), 7.26−7.38 (m, 6H), 5.55 (s, 1H), 5.22−5.29 (m, 1H), 5.03 (d, 1H, J = 8.1 Hz), 4.72 (d, 1H, J = 3.3 Hz), 4.24−4.31 (m, 1H), 3.86−3.97 (m, 2H), 3.70−3.83 (m, 3H), 3.55−3.62 (m, 1H), 3.40 (s, 3H), 3.28−3.43 (m, 2H), 2.53−2.58 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.5, 137.1, 132.5, 129.2, 129.1, 128.4, 128.3, 126.3, 121.6, 101.9, 99.2, 82.0, 81.96, 75.4, 74.0, 71.4, 68.8, 66.5, 62.2, 55.3, 39.0, 21.3. HRMS Calcd for $C_{27}H_{29}N_2O_6$ $[M + H]^+$ 477.2014, found 477.2026.

Compound **14**: 4,6-*O*-Benzylidene methyl α-D-2-deoxy-2-glucosamine 2-(icosa-7,9-diyn-1-yl)urea. Compound **14** was synthesized by the same method as that described above for compound **12**. The starting materials and reagents used were 8,10-heneicosadiynoic acid (21 mg, 0.066 mmol), Et_3N (0.02 mL, 0.13 mmol), DPPA (0.03 mL, 0.13 mmol), and glucosamine headgroup **2** (0. 015 g, 0.053 mmol). The R_f value was 0.6 in DCM:MeOH (95:5). The product was obtained as a white solid (25 mg, 0.42 mmol) with 79% yield, mp 164.0−165.5 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43−7.53 (m, 2H), 7.29−7.39 (m, 3H), 5.54 (s, 1H), 5.07−5.20 (m, 2H), 4.69 (d, 1H, J = 3.7 Hz), 4.22−4.30 (m, 1H), 4.18 (brs, 1H, OH), 3.81−4.00 (m, 2H), 3.71−3.81 (m, 2H), 3.54−3.63 (m, 1H), 3.37 (s, 3H), 2.98−3.22 (m, 2H), 2.22 (t, 4H, J = 7.0 Hz), 1.18−1.56 (m, 24H), 0.87 (t, 3H, J = 7.0 Hz). ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.0, 137.1, 129.1, 128.2, 126.3, 101.9, 99.4, 82.0, 77.7, 77.2, 71.2, 68.8, 65.4, 65.1, 62.3, 55.2, 55.1, 40.4, 31.8, 29.8, 29.5, 29.4, 29.2, 29.0, 28.9, 28.4, 28.3, 28.1, 26.3, 22.6, 19.1, 19.0, 14.1. HRMS Calcd for $C_{35}H_{53}N_2O_6$ $[M + H]^+$ 597.3904, found 597.3907.

Compound **15**: 4,6-*O*-Benzylidene methyl α-D-2-deoxy-2-glucosamine 2-(docosa-9,11-diyn-1-yl)urea. Compound **15** was synthesized by the same method as that described above for compound **12**. The starting materials and reagents used were 10,12-tricosadiynoic acid (148 mg, 0.43 mmol), Et_3N (0.12 mL, 0.86 mmol), DPPA (0.18 mL, 0.86 mmol), and glucosamine headgroup **2** (0.10 g, 0.355 mmol). The R_f value in DCM:MeOH (98:2) was 0.3. The product was obtained as a white solid (0.201 g, 0.322 mmol) with 91% yield, mp 164.0−166.0 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.47−7.54 (m, 2H), 7.32−7.40 (m, 3H), 5.56 (s, 1H), 4.83 (d, 1H, J = 7.7 Hz), 4.69−4.78 (m, 1H), 4.71 (d, 1H, J = 3.7 Hz), 4.22−4.33 (m, 1H), 3.84−4.00 (m, 2H), 3.72−3.83 (m, 2H), 3.55−3.63 (m, 1H), 3.40 (s, 3H), 3.08−3.22 (m, 2H), 2.24 (t, 4H, J = 7.0 Hz), 1.43−1.58 (m, 6H), 1.15−1.43 (m, 22H), 0.88 (t, 3H, J = 7.0 Hz). ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.8, 137.1, 129.2, 128.3, 126.3, 101.9, 99.2, 82.0, 77.6, 77.4, 71.6, 68.8, 65.3, 65.2, 62.2, 55.3, 40.1, 31.8, 29.9, 29.5, 29.4, 29.3, 29.1, 28.9, 28.8, 28.7, 28.3, 28.2, 26.7, 22.6, 19.2, 19.1, 14.1. HRMS Calcd for $C_{37}H_{56}N_2O_6$ $[M + H]^+$ 625.4217, found 625.4220.

Compound **16**: Bis-4,6-*O*-benzylidene methyl α-D-2-deoxy-2-glucosamine 2-ureado(icosa-9,11-diyn-1-yl)urea. Compound **16** was synthesized by a method similar to that described above for compound **12**. The starting materials and reagents were 10,12-docosadiyndioic acid (70 mg, 0.19 mmol), Et_3N (0.11 mL, 0.4 mmol), DPPA (0.16 mL, 0.4 mmol), and glucosamine headgroup **2** (136 mg, 0.483 mmol). The product R_f value was 0.3 in DCM:MeOH (95:5). The product was obtained as a white solid (90 mg, 0.098 mmol) with 51.5% yield, mp 146.0−147.5 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.42−7.48 (m, 4H), 7.34−7.40 (m, 6H), 6.05 (t, 2H, J = 5.1 Hz), 5.77 (d, 2H, J = 8.8 Hz), 5.60 (s, 2H), 5.19 (d, 2H, J = 5.1 Hz), 4.62 (d, 2H, J = 2.9 Hz), 4.16 (dd, 2H, J = 4.8, 9.9 Hz), 3.64−3.77 (m, 4H), 3.43−3.62 (m, 6H), 3.30 (s, 6H), 2.92−3.03 (m, 4H), 2.27 (t, 4H, J = 6.8 Hz), 1.39−1.49 (m, 4H), 1.18−1.39 (m, 20H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.9, 137.7, 128.8, 128.0, 126.3, 100.8, 99.5, 81.9, 78.0, 68.5, 68.0, 65.3, 62.4, 54.7, 54.5, 39.1, 29.9, 28.6, 28.4, 28.1, 27.7, 26.3, 18.2. HRMS Calcd for $C_{50}H_{71}N_4O_{12}$ $[M + H]^+$ 919.5068, found 919.5067.

■ ASSOCIATED CONTENT

Supporting Information

^{1}H and ^{13}C NMR spectra for compounds **7**−**16**, UV studies for compounds **9**, **11**, **15**, and **16**, NMR variable temperature study for compound **9**, and the general procedure for optical microscopy. This material is available free of charge via the Internet at http://pubs.acs.org.

■ AUTHOR INFORMATION

Corresponding Author

*E-mail: g1wang@odu.edu. Telephone: (757) 683-3781. Fax: (757) 683-4628.

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

We thank Dr. Weilie Zhou and Dr. Baobao Cao of Advanced Materials Institute at the University of New Orleans (UNO) for assistance with the scanning electron microscopy studies. We also thank the Chemistry Department of UNO and Old Dominion University. We are grateful to National Science Foundation for financial support (NSF CHE 1313633).

■ REFERENCES

(1) Most recent reviews: (a) Babu, S. S.; Praveen, V. K.; Ajayaghosh, A. *Chem. Rev.* **2014**, *114*, 1973−2129. (b) Yu, X.; Chen, L.; Zhang, M.; Yi, T. *Chem. Soc. Rev.* **2014**, *43*, 5346−5371.

(2) Yagai, S.; Kitamura, A. *Chem. Soc. Rev.* **2008**, *37*, 1520−1529.

(3) (a) Yu, L.; Ding, J. *Chem. Soc. Rev.* **2008**, *37*, 1473−1481. (b) Sangeetha, N. M.; Maitra, U. *Chem. Soc. Rev.* **2005**, *34*, 821−836.

(4) Lyon, L. A.; Meng, Z.; Singh, N.; Sorrell, C. D.; St. John, A. *Chem. Soc. Rev.* **2009**, *38*, 865−874.

(5) Zhao, F.; Ma, M. L.; Xu, B. *Chem. Soc. Rev.* **2009**, *38*, 883−891.

(6) Hirst, A. R.; Escuder, B.; Miravet, J. F.; Smith, D. K. *Angew. Chem., Int. Ed.* **2008**, *47*, 8002−8018.

(7) (a) Ajayaghosh, A.; Vijayakumar, C.; Varghese, R.; George, S. J. *Angew. Chem., Int. Ed.* **2006**, *45*, 456−460. (b) Ajayaghosh, A.; Praveen, V. K.; Vijayakumar, C.; George, S. J. *Angew. Chem., Int. Ed.* **2007**, *46*, 6260−6265.

(8) Yan, Q.; Luo, Z.; Cai, K.; Ma, Y.; Zhao, D. *Chem. Soc. Rev.* **2014**, *43*, 4199−4221.

(9) (a) Ajayaghosh, A.; Praveen, V. K.; Vijayakumar, C. *Chem. Soc. Rev.* **2008**, *37*, 109−122. (b) Dastidar, P. *Chem. Soc. Rev.* **2008**, *37*, 2699−2715.

(10) Jadhav, S. R.; Vemula, P. K.; Kumar, R.; Raghavan, S. R.; John, G. *Angew. Chem., Int. Ed.* **2010**, *49*, 7695−7698.

(11) Zhao, F.; Ma, M. L.; Xu, B. *Chem. Soc. Rev.* **2009**, *38*, 883−891.

(12) Zhou, S. L.; Matsumoto, S.; Tian, H. D.; Yamane, H.; Ojida, A.; Kiyonaka, S.; Hamachi, I. *Chem.—Eur. J.* **2005**, *11*, 1130−1136.

(13) Bowerman, C. J.; Nilsson, B. L. *J. Am. Chem. Soc.* **2010**, *132*, 9526−9527.

(14) Gao, Y.; Kuang, Y.; Guo, Z.-F.; Guo, Z.; Krauss, I. J.; Xu, B. *J. Am. Chem. Soc.* **2009**, *131*, 13576−13577.

(15) Bhuniya, S.; Seo, Y. J.; Kim, B. H. *Tetrahedron Lett.* **2006**, *47*, 7153−7156.

(16) Vemula, P. K.; John, G. *Acc. Chem. Res.* **2008**, *41*, 769−782.

(17) (a) Vemula, P. K.; Cruikshank, G. A.; Karp, J. M.; John, G. *Biomaterials* **2009**, *30*, 383−393. (b) Wang, W.; Wang, H.; Ren, C.; Wang, J.; Tan, M.; Shen, J.; Yang, Z.; Wang, P. G.; Wang, L. *Carbohydr. Res.* **2011**, *346*, 1013−1017.

(18) Liao, S. W.; Yu, T.-B.; Guan, Z. *J. Am. Chem. Soc.* **2009**, *131*, 17638−17646.

(19) Yang, Z.; Liang, G.; Wang, L.; Xu, B. *J. Am. Chem. Soc.* **2006**, *128*, 3038−3043.

(20) Shome, A.; Debnath, S.; Das, P. K. *Langmuir* **2008**, *24*, 4280−4288.

(21) (a) Wu, D.-Q.; Wang, T.; Lu, B.; Xu, X.-D.; Cheng, S.-X.; Jiang, X.-J.; Zhang, X.-Z.; Zhuo, R.-X. *Langmuir* **2008**, *24*, 10306−10312. (b) Yang, Z.; Liang, G.; Xu, B. *Soft Matter* **2007**, *3*, 515−520.

(22) Saez, J. A.; Escuder, B.; Miravet, J. F. *Tetrahedron* **2010**, *66*, 2614−2618.

(23) Jung, J. H.; Rim, J. A.; Cho, E. J.; Lee, S. J.; Jeong, I. Y.; Kameda, N.; Masuda, M.; Shimizu, T. *Tetrahedron* **2007**, *63*, 7449−7456.

(24) Kiyonaka, S.; Sada, K.; Yoshimura, I.; Shinkai, S.; Kato, N.; Hamachi, I. *Nat. Mater.* **2004**, *3*, 58−64.

DOI: 10.1021/jo501568u
J. Org. Chem. 2015, 80, 733−743

(25) Yang, Z.; Liang, G.; Xu, B. *Acc. Chem. Res.* **2008**, *41*, 315−326.
(26) Wang, G.; Cheuk, S.; Williams, K.; Sharma, V.; Dakessian, L.; Thorton, Z. *Carbohydr. Res.* **2006**, *341*, 705−716.
(27) Wang, G.; Yang, H.; Cheuk, S.; Coleman, S. *Beilstein J. Org. Chem.* **2011**, *7*, 234−242.
(28) Goyal, N.; Cheuk, S.; Wang, G. *Tetrahedron* **2010**, *66*, 5962−5971.
(29) Wang, G.; Cheuk, S.; Yang, H.; Goyal, N.; Reddy, P. V. N.; Hopkinson, B. *Langmuir* **2009**, *25*, 8696−8705.
(30) Nie, X.; Wang, G. *J. Org. Chem.* **2006**, *71*, 4734−4741.
(31) Cheuk, S.; Stevens, E. D.; Wang, G. *Carbohydr. Res.* **2009**, *344*, 417−425.
(32) Schneider, J. P.; Pochan, D. J.; Ozbas, B.; Rajagopal, K.; Pakstis, L.; Kretsinger, J. *J. Am. Chem. Soc.* **2002**, *124*, 15030−15037.
(33) (a) Kar, T.; Debnath, S.; Das, D.; Shome, A.; Das, P. K. *Langmuir* **2009**, *25*, 8639−8648. (b) Komatsu, H.; Matsumoto, S.; Tamaru, S.; Kaneko, K.; Ikeda, M.; Hamachi, I. *J. Am. Chem. Soc.* **2009**, *131*, 5580−5585. (c) Chen, Q.; Lv, Y.; Zhang, D.; Zhang, G.; Liu, C.; Zhu, D. *Langmuir* **2010**, *26*, 3165−3168. (d) He, Y.; Bian, Z.; Kang, C.; Cheng, Y.; Gao, L. *Chem. Commun.* **2010**, *46*, 3532−3534.
(34) Chen, Q.; Feng, Y.; Zhang, D.; Zhang, G.; Fan, Q.; Sun, S.; Zhu, D. *Adv. Funct. Mater.* **2010**, *20*, 36−42.
(35) (a) Hendrickson, G. R.; Smith, M. H.; South, A. B.; Lyon, L. A. *Adv. Funct. Mater.* **2010**, *20*, 1697−1712. (b) Huang, Y.; Liao, F.; Zheng, W.; Liu, X.; Wu, X.; Hong, X.; Tsang, S. C. *Langmuir* **2010**, *26*, 3106−3114.
(36) Rao, K. V.; Datta, K. K. R.; Eswaramoorthy, M.; George, S. J. *Angew. Chem., Int. Ed.* **2011**, *50*, 1179−1184.
(37) Zhao, Y.-L.; Stoddart, J. F. *Langmuir* **2009**, *25*, 8442−8446.
(38) He, B.; Zeng, J.; Nie, Y.; Ji, L.; Wang, R.; Li, Y.; Wu, Y.; Li, L.; Wang, G.; Luo, X.; Zhang, Z.; Gu, Z. *Macromol. Biosci.* **2009**, *9*, 1169−1175.
(39) Sako, Y.; Takaguchi, Y. *Biomol. Chem.* **2008**, *6*, 3843−3847.
(40) Sun, X.; Chen, T.; Huang, S.; Li, L.; Peng, H. *Chem. Soc. Rev.* **2010**, *39*, 4244−4257.
(41) (a) Assali, M.; Cid, J.-J.; Fernandez, I.; Khiar, N. *Chem. Mater.* **2013**, *25*, 4250−4261. (b) Neabo, J. R.; Tohoundjona, K. I. S.; Morin, J.-F. *Org. Lett.* **2011**, *13*, 1358−1361.
(42) Fujita, N.; Sakamoto, Y.; Shirakawa, M.; Ojima, M.; Fujii, A.; Ozaki, M.; Shinkai, S. *J. Am. Chem. Soc.* **2007**, *129*, 4134−4135.
(43) Filhol, J.-S.; Deschamps, J.; Dutremez, S. G.; Boury, B.; Barisien, T.; Legrand, L.; Schott, M. *J. Am. Chem. Soc.* **2009**, *131*, 6976−6988.
(44) Schott, M. *J. Phys. Chem. B* **2006**, *110*, 15864−15868.
(45) Jung, S. H.; Lee, H.; Han, W. S.; Jung, J. H. *J. Nanosci. Nanotechnol.* **2011**, *11*, 2113−2120.
(46) (a) Aoki, K.; Kudo, M.; Tamaoki, N. *Org. Lett.* **2004**, *6*, 4009−4012. (b) Wang, J.; Yang, G.; Jiang, H.; Zou, G.; Zhang, Q. *Soft Matter* **2013**, *9*, 9785−9791.
(47) Haridas, V.; Sharma, Y. K.; Creasey, R.; Sahu, S.; Gibson, C. T.; Voelcker, N. H. *New J. Chem.* **2011**, *35*, 303−309.
(48) Dautel, O. J.; Robitzer, M.; Lère-Porte, J.-P.; Serein-Spirau, F.; Moreau, J. J. E. *J. Am. Chem. Soc.* **2006**, *128*, 16213−16223.
(49) Hsu, L.; Cvetanovich, G. L.; Stupp, S. I. *J. Am. Chem. Soc.* **2008**, *130*, 3892−3899. (b) Stone, D. A.; Hsu, L.; Wheeler, N. R.; Wilusz, E.; Zukas, W.; Wnek, G. E.; Korley, L. T. J. *Soft Matter* **2011**, *7*, 2449−2455.
(50) Rondeau-Gagne, S.; Neabo, J. R.; Desroches, M.; Larouche, J.; Brisson, J.; Morin, J.-F. *J. Am. Chem. Soc.* **2013**, *135*, 110−113.
(51) Tamaoki, N.; Shimada, S.; Okada, Y.; Belaissaoui, A.; Kruk, G.; Yase, K.; Matsuda, H. *Langmuir* **2000**, *16*, 7545−7547.
(52) (a) Nagasawa, J.; Kudo, M.; Hayashi, S.; Tamaoki, N. *Langmuir* **2004**, *20*, 7907−7916. (b) Nagasawa, J.; Yoshida, M.; Tamaoki, N. *Eur. J. Org. Chem.* **2011**, 2247−2255.
(53) Bieser, A. M.; Tiller, J. C. *J. Phys. Chem. B* **2007**, *111*, 13180−13187.
(54) Ryan, D. M.; Anderson, S. B.; Nilsson, B. L. *Soft Matter* **2010**, *6*, 3220−3231.

DOI: 10.1021/jo501568u
J. Org. Chem. 2015, 80, 733−743