JOC*Article*

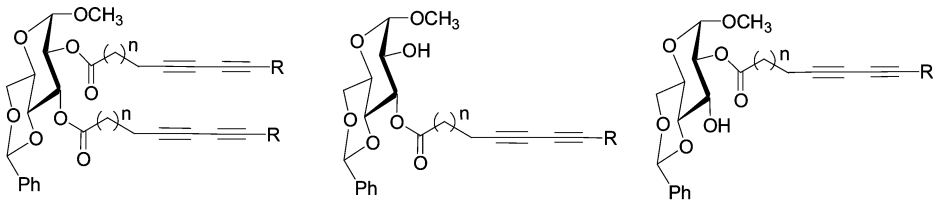
Synthesis and Self-Assembling Properties of Diacetylene-Containing Glycolipids

Xiaoping Nie and Guijun Wang*

Department of Chemistry, University of New Orleans, New Orleans, Louisiana 70148

gwang2@uno.edu

Received November 8, 2005



n=1, 2, 4, 6 R= alkyl or phenyl alkyl

Diacetylene-containing glycolipids are interesting molecules that have many potential applications. The polydiacetylenes formed by the cross-linking of the diacetylene lipids are new stimuli-responsive materials. In particular, diacetylene lipids that can form gels in aqueous solution are of great interest in designing functional biocompatible materials. We have synthesized a series of diacetylene-containing sugar lipids with different chain lengths, substituents, and positions of diyne and studied their self-assembling properties in several solvents including hexane, ethanol, and ethanol/water mixture. Among the 24 diacetylene-containing glycolipids synthesized, many of them exhibited excellent gelation properties in ethanol or ethanol/water mixture. Typically very long chain diacetylene lipids formed gels in ethanol and hexane. Shorter chain diacetylene lipids and compounds with one free hydroxyl group can form gels in aqueous solution. The position of the diyne and chain length affect the self-assembling properties significantly. The systematic study of the gelation properties for diacetylene lipids with different lipid chains can help us to understand the structure requirement for the desired physical properties. Optical microscopy studies showed that the molecules form interesting architectures such as tubules, rods, sheets, and belts. The resulting organogels can also be cross-linked and give different colored polymerized gels depending on their structures.

Introduction

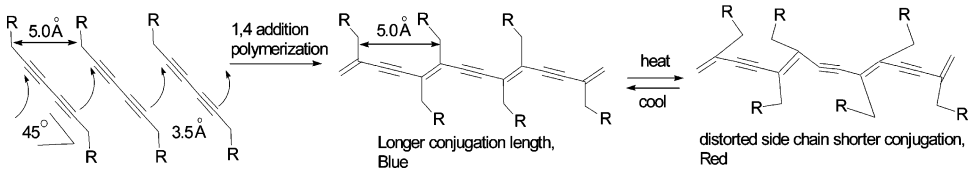
Polydiacetylenes (PDAs) are important conjugate polymers that have drawn great attention over the past few decades. PDAs exhibit a unique blue to red color transition in the presence of heat, mechanical stress, pH change, and binding to biological agents.[1−3] Extensive studies of polymerizable diacetylenes have been carried out in crystals,[4,5] thin films,[6,7] vesicles,[8,9] and at air−water interfaces.[10,11] The optical electronic properties and the unique color transitions of polydiacetylenes lend themselves to many applications in optical electronic devices, chemosensors, and biosensors.[12−16] To cross-link diacetylene groups, the monomer diacetylenes must be aligned at specific distances and

* Address correspondence to this author. Phone: 504 280-1258. Fax: 504 280-6860.

(1) Yuan, Z.; Lee, C.-W.; Lee, S.-H. *Angew. Chem., Int. Ed.* **2004**, *43*, 4197−4200.
(2) Rozner, S.; Kolusheva, S.; Cohen, Z.; Dowhan, W.; Eichler, J.; Jelinek, R. *Anal. Biochem.* **2003**, *319*, 96−104.
(3) Okada, S.; Peng, S.; Spevak, W.; Charych, D. *Acc. Chem. Res.* **1998**, *31*, 229−239.
(4) Ouyang, X.; Fowler, F. W.; Lauher, J. W. *J. Am. Chem. Soc.* **2003**, *125*, 12400−12401.
(5) Tachibana, H.; Kumai, R.; Hosaka, N.; Tokura, Y. *Chem. Mater.* **2001**, *13*, 155−158.
(6) Barentsen, H. M.; van Dijk, M.; Zuilhof, H.; Sudhölter, E. J. R. *Macromolecules* **2000**, *33*, 766−774.
(7) Mosley, D. W.; Sellmyer, M. A.; Daida, E. J.; Jacobson, J. M. *J. Am. Chem. Soc.* **2003**, *125*, 10532−10533.
(8) Ma, G.; Cheng, Q. *Langmuir* **2005**, *21*, 6123−6126
(9) Kolusheva, S.; Shahal, T.; Jelinek, R. *J. Am. Chem. Soc.* **2000**, *122*, 776−780.
(10) Niwa, M.; Shibahara, S.; Higashi, N. *J. Mater. Chem.* **2000**, 2647−2651.
(11) Ma, Z.; Li, J.; Li, H.; Jiang, L. *New J. Chem.* **2000**, 313−316.
(12) Kolusheva, S.; Shahal, T.; Jelinek, R. *J. Am. Chem. Soc.* **2000**, *122*, 776−780.
(13) Sarkar, A.; Okada, S.; Matsuzawa, H.; Matsuda, H.; Nakanishi, H. *J. Mater. Chem.* **2000**, 819−828.

10.1021/jo052317t CCC: $33.50
Published on Web 05/27/2006

SCHEME 1. The Topochemical Polymerization of Diacetylene and the Color Transition Mechanism



orientations to their neighbors. This strict topochemical requirement for polymerization can be used to probe the molecular aggregation structures of the monomers. It is generally accepted that the color transition is due to the conformation change of the PDA side chains (Scheme 1). The preparation of processable PDAs is important for the exploration of their further applications. Diacetylene-containing phospholipids are interesting molecules that can self-assemble and form tubules, nanotubules, and ribbons.[17−19] Membrane lipid mimetics have been used to achieve favorable alignment of diacetylene groups and form useful supramolecular structures including liposome, tubules, ribbons, and thin films.[20−22]

The self-assembling of small molecules to form supramolecular gels in organic solvent (organogels) or water (hydrogels) is an interesting phenomenon. These small molecules, which are termed as organogelators or hydrogelators, respectively, have great potential in preparing novel functional materials.[23−26] Biocompatible functional small molecule organogelators such as carbohydrates and amino acid derivatives are very interesting because they have potential applications in drug delivery, tissue engineering, and as biocompatible materials. Polysaccharides have been widely utilized in polymer gels for separation and immobilization of enzymes, etc. Some glycolipids and other small sugar derivatives have been found to be able to form gels in organic solvents and sometimes in water.[27−30] The formation of various supramolecular assemblies including liposomes, crystals, or gels in solvents can provide insight in understanding structure influences on the molecular self-assembling process. The advantages of forming supramolecular gels is that the structures of the gelators can be modified and synthesized readily, also the gels formed by noncovalent forces are reversible. Polymer gels have the advantage of being more stable but their structures are not flexible. Supramolecular gels such as organogels formed by a small molecule offer a direct and effective way of organizing molecular subunits in the gel state, cross-linking the diacetylene in the gel state can produce novel polydiacetylene gels. The gelation by small molecule has been barely used to prepare novel polydiacetylenes, and especially no systematic studies have been conducted. A few earlier studies have employed gelation in preparing polydiacetylenes, either involving a diacetylene dicholesteryl ester with two urethanes,[27,28] a diaminocyclohexane-based system,[29] or diacetylene-containing amides.[30]

The diacetylene-containing organogels may have interesting properties of color transition combined with gel−solution phase transition in response to external stimuli. These compounds can be useful in designing biosensors or chemosensors. Sugar-containing amphiphilic molecules are cell membrane mimics and are expected to be biocompatible. As part of our goal to discover carbohydrate-based stimuli-responsive functional materials that are useful in enzyme purification, protein and DNA immobilization, drug and gene delivery carriers, and as scaffolding material for tissue engineering, we have designed, synthesized, and tested a series of monosaccharide lipids containing diacetylene functional groups. Here we report the systematic synthesis and characterization of a series of diacetylene-containing monosaccharide lipids. Their self-assembling properties in hexane, ethanol, and an ethanol/water mixture are also studied. The synthesis can be carried out efficiently and we found several molecules with excellent gelation abilities for hexane and the ethanol/water mixture.

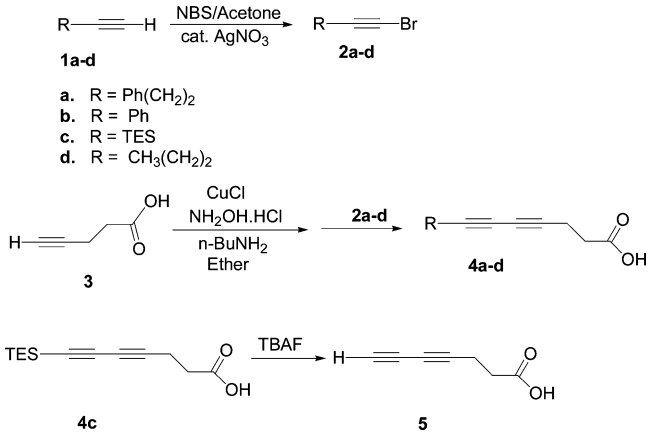
Results and Discussions

Synthesis of Diacetylene Fatty Acids. To synthesize a series of diacetylene-containing sugar lipids, the most straightforward method is esterification of free hydroxyl groups on the sugar with a diacetylene-containing fatty acid. The diacetylene acyl compounds can be prepared by coupling reactions of two acetylene-containing entities. Some long-chain diacetylene-containing fatty acids are also commercially available. The synthesis of diacetylene fatty acids is shown in Scheme 2. Treating the alkynes **1a**−**d** with NBS and silver nitrate afforded alkynyl bromides **2a**−**d** in almost quantitative yield. The bromo acetylenes **2a**−**d** were then coupled with terminal alkynes under a modified Cadiot−Chodkiewicz reaction condition,[31] using butylamine, hydroxylamine, and cuprous chloride to give the diacetylene-containing fatty acids **4a**−**d** in high yields. Terminal diacetylene fatty acid **5** can be prepared from fatty acid **4c** in 90% yield by removal of the TES group with TBAF.

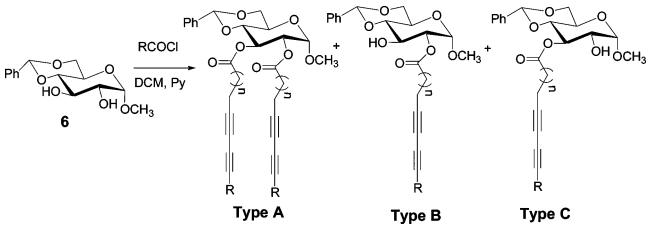
Synthesis of Diacetylene Lipids. To understand the structure influence of diacetylene the lipid tails on the gelation process, we synthesized a series of compounds with the same headgroup with either two acyl chains or one acyl chain. We can obtain

(14) Lu, Y.; Yang, Y.; Sellinger, A.; Lu, M.; Huang, J.; Fan, H.; Haddad, R.; Lopez, G.; Burns, A. R.; Sasaki, D. Y.; Shelnutt, J.; Brinker, C. J. *Nature* **2001**, *410*, 913−917.
(15) Charych, D.; Nagy, J.; Spevak, W.; Bednarski, M. *Science* **1993**, *261*, 585−588.
(16) Gill, I.; Ballesteros, A. *Angew. Chem., Int. Ed.* **2003**, *42*, 3264−3267.
(17) Georger, J. H.; Singh, A.; Price, R. R.; Schnur, J. M.; Yager, P.; Schoen, P. E. *J. Am. Chem. Soc.* **1987**, *109*, 6169−6175
(18) Thomas, B. N.; Lindemann, C. M.; Corcoran, R. C.; Cotant, C. L.; Kirsch, J. E.; Persichini, P. J. *J. Am. Chem. Soc.* **2002**, *124*, 1227−1233.
(19) Spector, M. S.; Singh, A.; Messersmith, P. B.; Schnur, J. M. *Nano Lett.* **2001**, *1*, 375−378.
(20) Wang, G.; Hollingsworth, R. I. *Langmuir* **1999**, *15*, 6135−6138.
(21) Wang, G.; Hollingsworth, R. I. *Adv. Mater.* **2000**, *12*, 871−874.
(22) Wang, G.; Hollingsworth, R. I. *Langmuir* **1999**, *15*, 5, 3062−3069.
(23) Terech, P.; Weiss, R. G. *Chem. Rev.* **1997**, *97*, 3133−3159.
(24) Abdallah, D. J.; Weiss, R. G. *Adv. Mater.* **2000**, *12*, 1237−1247.
(25) Si, C.; Huang, Z.; Kilic, S.; Xu, J.; Enick, R. M.; Beckman, E. J.; Carr, A. J.; Melendez, R. E.; Hamilton, A. D. *Science* **1999**, *289*, 1540−1543.
(26) Estroff, L. A.; Hamilton, A. D. *Chem. Rev.* **2004**, *104*, 1201−1217.
(27) Inoue, K.; Ono, Y.; Kanekiyo, Y.; Hanabusa, K.; Shinkai, S. *Chem. Lett.* **1999**, *5*, 429−430.
(28) Tamaoki, N.; Shimada, S.; Okada, Y.; Belaissaoui, A.; Kruk, G.; Yase, K.; Matsuda, H. *Langmuir* **2000**, *16*, 7545−7547.
(29) Nagasawa, J.; Kudo, M.; Hayashi, S.; Tamaoki, N. *Langmuir* **2004**, *20*, 7907−7916.
(30) George, M.; Weiss, R. G. *Chem. Mater.* **2003**, *15*, 2879−2888.
(31) Marino, J. P.; Nguyen, H. N. *J. Org. Chem.* **2002**, *67*, 6841−6844.

SCHEME 2. Synthesis of Diacetylene-Containing Fatty Acids



SCHEME 3. Synthesis of Diacetylene-Containing Lipids Type A, Type B, and Type C



the relationship of alkyl chain lengths and positions of diacetylene groups with their gelation and polymerization properties. The synthesis is shown in Scheme 3. The diacetylene acids **4a**−**d** and **5** were converted to the corresponding acid chlorides by treating them with oxalyl chloride in dichloromethane. Esterification of sugar headgroup **6** with diacetylene-containing acid chlorides can give the desired diacetylene-containing lipids. The strategy is to synthesize three types of lipids **A**, **B**, and **C** in a one-pot reaction and isolate them by flash chromatography. When 0.75 equiv of sugar headgroups were used, the 2-monoesters type **B** were obtained as major products, type **A** and type **C** were minor products. The structures of type **A** compounds are shown in Figure 1 (for type **B** and type **C**, the compounds with the same numbers have the same fatty acyl structures). Screening for their gelation properties in various solvents would allow us to find promising gelators. The advantage of this strategy is that we can build up a small library quickly and investigate their structure activity relationship.

The compounds with excellent gelation properties can be resynthesized in good yields and larger quantities under optimized reaction condition. To synthesize only the **A** compound, we just need to use slightly more than 2 equiv of acid; to obtain type **B** product only, slightly more than 1 equiv of acid can be used and the reaction can be done under kinetic controlled conditions to maximize the yield; to synthesize type **C** product only, a protecting group that is bulky and has good selectivity at the 2-position can be used, and after esterification at the 3-positions, the protecting group can be removed.

Gelation Properties Studies. The preliminary gel testing results are shown in Table 1. The compounds showing positive gelation properties are highlighted in bold. Several diesters (type **A** compounds) can form gels in ethanol; the longest chain compound **7A** is the most efficient one that forms gels at a concentration of 7 mg/mL (∼1 wt %). Compound **8A** is two carbons shorter; it formed stable translucent gels in ethanol at 0 °C at a similar concentration. The rigid phenyl acetylene derivative **13A** also formed gels in ethanol. In a water and ethanol mixture, compound **11A** formed unstable gels (precipitated after hours of standing) at 10 mg/mL, and the others precipitated out of solution. The diesters typically do not form gels in hexane. The 2-esters (type **B** compounds) are not gelators for hexane or ethanol; however, most of them formed stable gels in ethanol/water mixture at a very low concentration (<10 mg/mL, 1wt %). We expect that they can gelate another aqueous mixture with soluble organic solvents as well. The phenyl ethylene substituted diyne **14B** formed gels in ethanol at a higher concentration. It is worth mentioning that compound **13B** formed stable transparent gels in ethanol/water at a concentration as low as 2.5 mg/mL (0.3 wt %). The 3-esters (type **C** series) showed versatile gelating abilities, forming gels in hexane, ethanol, and an ethanol/water mixture. The majority of type **C** compounds formed stable gels in an ethanol/water mixture, the most effective one is **13C**. The phenyl ethylene-containing compound **14C** is an excellent gelator for hexane (2 mg/mL) and a good gelator for ethanol; the long chain compounds **7C**, **8C**, and **9C** formed gels in hexane, and they also formed gels in ethanol at higher concentrations.

Different functional group and chain length significantly influence the gelating properties. The triethylsilyl-substituted diacetylene lipids **12A**−**C** are not gelators for any of the solvents tested. Perhaps the bulky TES groups prevent the effective packing of the lipid tails and increase both disorders in the molecules and solubilities in the solvents. The compounds **11A**−**C** have the shortest chains in their series, and they are extremely light sensitive compared to other analogues. These make the testing and sample preserving more difficult. These compounds have terminal acetylene hydrogens, and the lipid tails have the least steric hindrance, thus increasing the chance of random polymerization. In studies to use these compounds for potential applications such as making sensors or enzyme immobilizations, compounds **11** and **12** are not likely to be good choices. For an ethanol/water solution, compounds **7B**, **13B**, and **13C** showed superior gelation properties. They can be used in forming stimuli-responsive systems in future studies.

The gels can be polymerized by treating them with 254 nm UV light, using a 4 W or 6W TLC UV lamp. The color of the polymerized gels depends on the structures of the gelators. Compound **7C** contains a very long chain diacetylene fatty acyl group. The hexane and ethanol gels both turned blue after shinning UV light on them for less than a minute. The stable blue gels turned red after heating; the color transition is reversible for many cycles when the heating temperature is below 70 °C. We noticed the red started disappearing as soon as the heat source was removed; usually it turned completely back to dark blue-purple within a few minutes when the gels were cooled in the air. Generally the gels are more robust after polymerization. Figure 2 shows the hexane gels of compound **7C** and the color transition of the polymerized gels. Other compounds give different colored polymerized gels. A more detailed study will be reported in a future communication.

Optical Microscopy Studies. The self-assembled aggregates of the long chain diacetylene lipids were studied with an optical microscope. Some examples of the images are shown in Figure 3. Most of the gels are polymerizable readily and they need to be protected from light to prevent unwanted polymerization. The ethanol gels of compound **7A** (Figure 3a) formed long rods

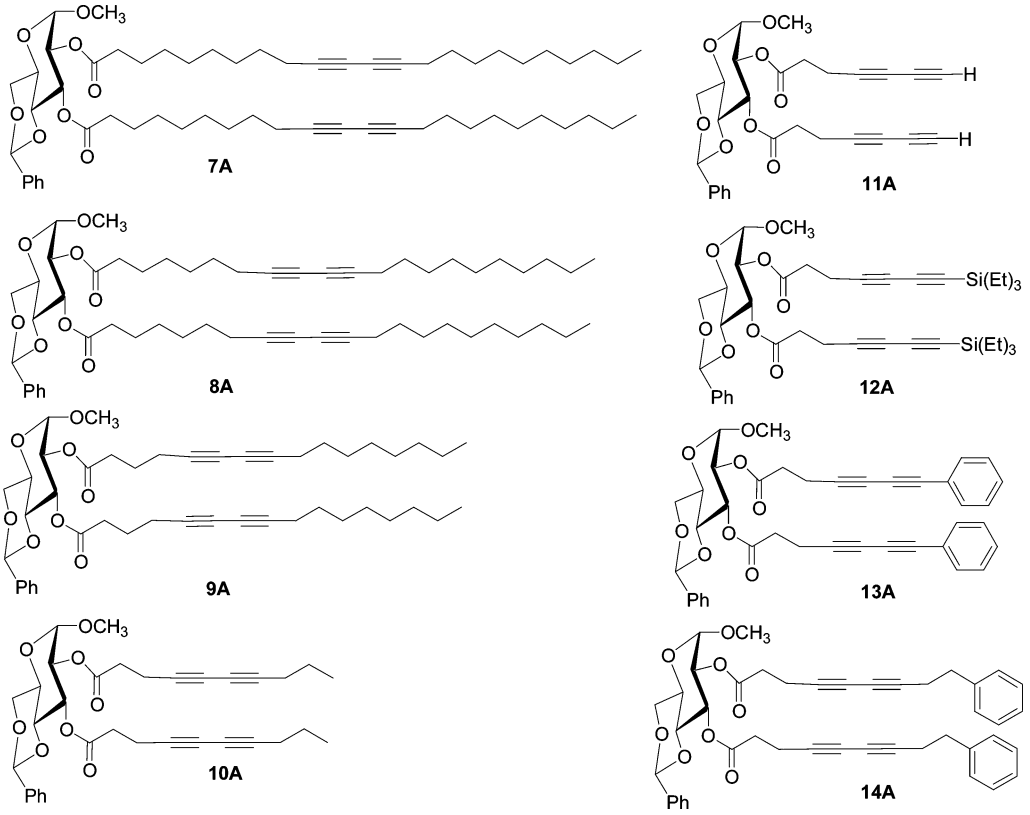


FIGURE 1. Structures of compounds synthesized: type **A** compounds are shown, type **B** and **C** are analogues with only one fattyl acyl chain.

TABLE 1. Gelation Properties of Type A Compounds in Hexane, Ethanol, and Ethanol/Water (1:1 v/v) Mixture[a]

compds	hexane	ethanol	ethanol/H_2O
7A	S	**G 7, G* 5**	P
8A	S	**G* 7**	P
9A	S	S	P
10A	P	S	P
11A	I	C	**Gp 10**
12A	S	S	P
13A	P	**G 15**	P
14A	P	P	P
7B	S	P	**G 5**
8B	S	S	**G10, G* 5**
9B	P	S	P
10B	P	S	**G 6**
11B	I	S	**G 7**
12B	S	S	P
13B	I	C	**G 2.5**
14B	I	**G 30**	**G 12**
7C	**G 11**	**G 13**	P
8C	**G 8**	S	**G 10, G* 5**
9C	**G 13**	**G 35**	**G 10**
10C	P	S (G 47)	**G 15**
11C	I	**G 28**	**G 14**
12C	P	S	P
13C	I	**G 20**	**G 2.5**
14C	**G 2**	**G 10**	P

[a] G: stable gel at room temperature. G*: stable gel at 0 °C. Gp: loose gel with some precipitation. C: crystallized when cool. P: precipitation. S: soluble. The numbers in the table stand for the gelation concentration of the compounds (mg/mL) in specific solvents. For those without numbers, typically 30 mg/mL concentrations were used.

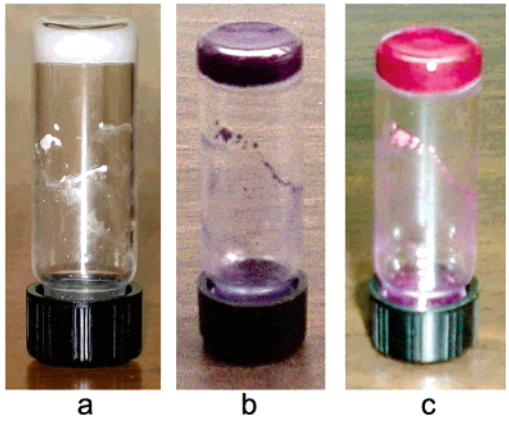


FIGURE 2. Photographs of the gels formed by compound **7C** in hexane (11 mg/mL): (a) a stable white gel after cooling to room temperature; (b) a deep blue-purple gel formed by treating the gels with a UV lamp; and (c) the blue gels in part b turned red after heating.

or tubules, and the self-assembled structures appeared to be solid rods rather than flat with a diameter of around 2 μm and length above 80 μm. Some tubules have diameters <1 μm and much longer lengths. The gels are harder to polymerize with a 6 W UV lamp. These reflect the packing order of tubules or rods that may need stronger UV energy to cross-link them. The ethanol gels of compound **8A** (Figure 3b−d) showed flatter structure features—they formed flat belts with a soft round turn, and the flat belts generally form loops and have a width of approximately 4 μm (Figure 3b). Larger flat sheets up to 7 μm wide can also be observed after longer periods of gelation. The gels can be polymerized with a 6 W UV lamp, turning red after UV irradiation. The air-dried gels also can be cross-linked by UV irradiation; the flat loop assemblies turned red but maintained the same shape after polymerization at the light microscope resolution (Figure 3c,d). The hexane gels of compound

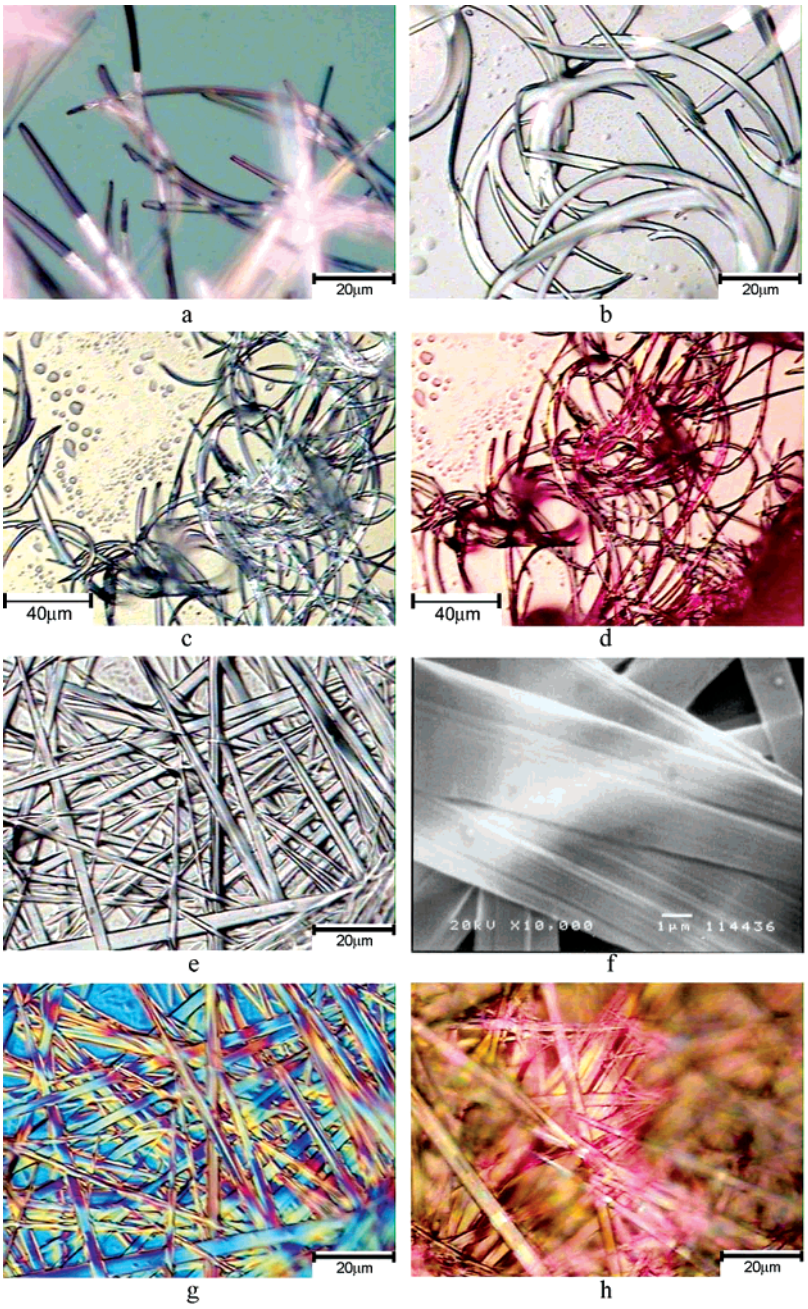


FIGURE 3. Optical micrographs of the gels formed by several compounds: (a) **7A** in ethanol, 10 mg/mL; (b and c) **8A** in ethanol, 10 mg/mL; (d) polymerized **8A**, with the same sample as in c (note that the flat belts turned red and maintained the same shape after treating with UV light); (e−h) **9C** in hexane, 10 mg/mL−(e) a bright field image, (f) a scanning electron micrograph, (g) the polarized image of part e, and (h) prepared from UV treated gels, the gels appeared pink in bulk, the red regions show the polymerized tubules also maintained similar shapes as before crosslinking.

9C formed longer straight fibers that can also be polymerized easily (Figure 3e−h). Some of the larger flat tubules are composed of a bundle of smaller fibers as shown in the SEM image (Figure 3f), and the tubular structures exhibited birefringence under polarized light (Figure 3g), which reflects the chiral molecular structure and the liquid crystal properties of the assemblies. The hexane gels of **9C** turned pink after UV treatment, and the partially cross-linked long flat tubules are shown in Figure 3h. The general morphology of the straight cylinders remnained the same as well.

The morphologies of supramolecular assemblies of diacetylene aldonamides were reported in early studies by O'Brien and co-worker and Fuhrhop and co-workers.[32,33] The transmission electron micrographs (TEM) of assemblies of diacetylenic galactonamide showed that the tubular and helical morphologies remained the same before and after polymerization.[32] When the molecular assemblies prevent the topochemical polymerization, a change of morphology was observed for some diacetylene gluconamides.[33] The optical micrographs of the several tested diacetylene sugar lipids in this study have shown that the morphologies were retained before and after polymerization. A further detailed morphology study with high-resolution

(32) Frankel, D. A.: O'Brien, D. F. *J. Am. Chem. Soc.* **1991**, *113*, 7436−7437.

(33) Fuhrhop, J.-H.; Blumtritt, P.; Lehmann, C.; Luger, P. *J. Am. Chem. Soc.* **1991**, *113*, 7436−7439.

electron microscopes will be reported in a future communication. We are also studying the applications of the compounds forming robust gels in enzyme immobilizations.

Conclusions

We have synthesized and characterized a series of diacetylene-containing sugar lipids. These compounds were synthesized by straightforward reactions with excellent yields. Among the 24 compounds synthesized and isolated, several compounds are excellent gelators for hexane, ethanol, and an ethanol/water solution. The gels are polymerizable to give polydiacetylene gels. The self-assembling properties and the ease of polymerization are determined by their structures. The diesters (type **A**) are generally good gelators for ethanol; 2-monoesters (type **B**) are excellent gelators for an ethanol/water mixture; and 3-monoesters (type **C**) are more versatile organogelators, they can form gels in hexane, ethanol, and an ethanol/water mixture. The lipid chain structures also affect the gelation properties significantly. The long chain diacetylene lipids with over 16 carbons showed good gelation abilities in several solvents, the middle ones with a total 6 to 10 carbons have a similar trend of activity for polar solvents but are less effective for hexane. The diacetylene lipids containing a benzene ring in the chains are excellent organogelators for hexane, ethanol, and an water/ethanol mixture. These studies showed systematically the properties of structures relating to their self-assembling properties in several solvents. The abilities of these molecules to form gels in polar organic solvents and aqueous solutions can lend them to potential applications in forming stimuli-responsive gels that can be used as chemosensors or biosensors.

Experimental Section

General Procedure for the Synthesis of Diynoic Acid (4a−d) Copper(I) chloride (25 mg, 0.25 mmol) was added to a 30% *n*-$BuNH_2$ aqueous solution (20 mL) at room temperature, which resulted in the formation of a blue solution. A few crystals of hydroxylamine hydrochloride were added to discharge the blue color. 4-Pentynoic acid (490 mg, 5 mmol) was then added to the solution and the reaction mixture was cooled with an ice−water bath. Bromoalkyne (6 mmol) in diethyl ether (10 mL) was added dropwise to the cooled reaction mixture. Occasionally adding a small amount of hydroxylamine hydrochloride was necessary to keep the color of the reaction light yellow. After the addition of bromoalkyne (usually 15−30 min), the cooling bath was removed. The reaction mixture was stirred at room temperature for another 2 h during which more crystals of hydroxylamine hydrochloride were added whenever the reaction mixture started to turn blue or green. The reaction was quenched and adjusted to pH ∼2 by adding 2 N HCl. The reaction mixture was extracted with ethyl acetate five times. The combined organic layer was dried over sodium sulfate and concentrated under reduced pressure. The crude product was further purified by recrystallization (EtOAc/hexane). The following are the data for the synthesized diacetylene acids.

9-Phenylnonan-4,6-diynoic acid (4a): 92%, colorless crystal, mp 109−111 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.29−7.27 (m, 2H), 7.21−7.17 (m, 3H), 2.82 (t, 2H, J = 7.3 Hz), 2.61−2.55 (m, 4H), 2.52 (t, 2H, J = 7.8 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 177.7, 140.0, 128.4, 128.3, 126.4, 77.3, 74.9, 66.1, 65.6, 34.5, 32.8, 21.3, 14.8; HRMS calcd for $C_{15}H_{14}O_2$ + H 227.1072, found 227.1067.

7-Phenylheptan-4,6-diynoic acid (4b): 96%, colorless crystals, mp 135−137 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.47−7.45 (m, 2H), 7.35−7.27 (m, 3H), 2.67 (d, 2H, J = 3.9 Hz), 2.66 (d, 2H, J = 3.9 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.5, 132.5, 130.0, 128.3, 121.7, 81.7, 75.5, 73.9, 65.9, 32.7, 15.2; HRMS calcd for $C_{13}H_{10}O_2$ + H 199.0759, found 199.0767.

7-Triethylsilylheptan-4,6-diynoic acid (4c): 81%, colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.62−2.58 (m, 4H), 0.96 (t, 9H, J = 7.8 Hz), 0.59 (t, 6H, J = 7.8 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.3, 88.9, 82.2, 76.3, 66.5, 32.5, 14.8, 7.3, 4.2; HRMS calcd for $C_{13}H_{20}O_2Si$ + Na 259.1130, found 259.1121.

Decan-4,6-diynoic acid (4d): 92%, colorless crystal, mp 90−91 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 10.2−8.8 (br, 1H), 2.58 (t, 2H, J = 5.5 Hz), 2.57 (t, 2H, J = 5.5 Hz,), 2.20 (t, 2H, J = 7.1 Hz), 1.52 (tq, 2H, J = 7.1, 7.1 Hz), 0.96 (t, 3H, J = 7.1 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 177.6, 78.3, 74.5, 66.2, 65.0, 32.8, 21.7, 21.1, 14.8, 13.4; HRMS calcd for $C_{10}H_{12}O_2$ + Na 187.0735, found 187.0728.

Synthesis of Heptan-4,6-diynoic Acid (5). Under an atmosphere of nitrogen TBAF (1 M solution in THF, 10.5 mL) was added dropwise to a solution of 7-triethylsilylheptan-4,6-diynoic acid **4c** (1.65 g, 7.0 mmol) in THF (20 mL) at 0 °C. After being stirred at room temperature for 3 h, the reaction was quenched and adjusted to pH ∼2 by adding 2 N HCl. The reaction mixture was extracted with ethyl acetate five times. The combined organic layer was dried over sodium sulfate and concentrated under reduced pressure. The crude product was purified by chromatography (hexane/EtOAc/MeOH 82:17:1) to afford compound **5** as colorless crystals (0.74 g, 90%), mp 87−88 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.23 (br, 1H), 2.63−2.53 (m, 4H), 1.98 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.9, 75.6, 68.0, 65.54, 65.48, 32.5, 14.6; MS HRMS calcd for $C_7H_6O_2$ + H, 123.0446, found 123.0450.

General Procedure for Esterification of (+)-(4,6-*O*-Benzylidiene)methyl-α-D-glucopyranoside. Oxalyl chloride (2 mL) was added to the solution of carboxylic acid (1.5 mmol) in dry DCM (5 mL). The reaction mixture was stirred at room temperature overnight under the protection of a drying tube of $CaCl_2$. When crude NMR showed the reaction finished, the reaction mixture was evaporated under reduced pressure followed by coevaporation with hexane twice. The residue was dissolved with dry DCM (9 mL) under the protection of a drying tube of $CaCl_2$, and sugar (1.0 mmol) was added followed by the addition of 3 mL of pyridine. The reaction mixture was stirred at room temperature until TLC showed the esterification was complete (usually 24 h was enough). DCM (150 mL) was added to the reaction mixture. The resulting solution was washed with water and brine and dried with sodium sulfate. Silica gel chromatography (hexane and ethyl acetate from 20/1 to 5/1) gave diester and monoester as well.

Reaction of (+)-(4,6-*O*-Benzylidiene)methyl-α-D-glucopyranoside with 10,12-Tricosadiynoic Chloride, Total Yield 71%. Compound 7A: 4%, colorless crystal, mp 43−44 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.42−7.41 (m, 2H), 7.33−7.32 (m, 3H), 5.59 (t, 1H, J = 9.8 Hz), 5.49 (s, 1H), 4.93 (d, 1H, J = 3.9 Hz), 4.90 (dd, 1H, J = 9.7, 3.9 Hz), 4.30−4.27 (m, 1H), 3.93−3.89 (m, 1H), 3.75 (dd, 1H, J = 10.7, 9.8 Hz), 3.63 (t, 1H, J = 9.8 Hz), 3.39 (s, 3H), 2.33−2.18 (m, 12H), 1.59−1.41 (m, 12H), 1.37−1.14 (m, 44H), 0.86 (t, 6H, J = 6.8 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.2, 172.4, 136.9, 129.0, 128.1, 126.1, 101.5, 97.6, 79.3, 77.5, 71.4, 68.8, 68.6, 65.3, 65.2, 62.3, 55.3, 34.2, 34.0, 31.8, 29.4, 29.2, 29.0, 28.8, 28.7, 28.4, 28.3, 25.0, 24.8, 22.6, 19.1, 14.1; HRMS calcd for $C_{60}H_{90}O_8$ + H 939.6714, found 939.6685.

Compound 7B: 56%, semisolid, ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.48−7.46 (m, 2H), 7.36−7.34 (m, 3H), 5.53 (s, 1H), 4.93 (d, 1H, J = 3.9 Hz), 4.78 (dd, 1H, J = 9.8, 3.9 Hz), 4.27 (dd, 1H, J = 9.8, 3.9 Hz), 4.16 (dd, 1H, J = 8.8, 9.8 Hz), 3.85−3.79 (m, 1 H), 3.74 (dd, 1H, J = 10.7, 9.8 Hz), 3.54 (dd, 1H, J = 9.8, 8.8 Hz), 3.37 (s, 3 H), 2.40−2.36 (m, 2 H), 2.21 (t, 4H, J = 6.8 Hz), 1.65−1.58 (m, 2 H), 1.52−1.45 (m, 4 H), 1.40−1.17 (m, 22H), 0.86 (t, 3H, J = 6.8 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.4, 137.0, 129.2, 128.2, 126.2, 101.9, 97.5, 81.3, 77.5, 73.3, 68.7, 68.5, 65.3, 65.1, 61.9, 55.3, 33.9, 31.8, 29.5, 29.4, 29.2, 29.0, 28.7, 28.6, 28.3, 28.2, 24.7, 22.6, 19.1, 14.0; HRMS calcd for $C_{37}H_{54}O_7$ + H 611.3948, found 611.3955.

Compound 7C: 11%, colorless crystal, mp 91−93 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.46−7.43 (m, 2H), 7.36−7.34 (m, 3H), 5.50 (s, 1H), 5.34 (t, 1H, J = 9.8 Hz), 4.81 (d, 1H, J = 3.8 Hz), 4.31 (dd, 1H, J = 9.9, 4.7 Hz), 3.88−3.82 (m, 1H), 3.76 (t, 1H, J = 9.9 Hz), 3.71−3.64 (m, 1H), 3.59 (t, 1H, J = 9.6 Hz), 3.48 (s, 3H), 2.37 (t, 2H, J = 7.4 Hz), 2.27−2.19 (m, 4H), 1.68−1.57 (m, 2H), 1.54−1.42 (m, 4H), 1.40−1.11 (m, 22H), 0.87 (t, 3H, J = 6.6 Hz); ^{13}C NMR (62.5 MHz, $CDCl_3$) δ 173.8, 137.0, 129.2, 128.2, 126.1, 101.4, 100.1, 78.7, 77.6, 72.0, 71.8, 68.9, 65.3, 65.2, 62.7, 55.5, 34.4, 31.9, 29.5, 29.4, 29.3, 29.0, 28.8, 28.7, 28.3, 28.2, 25.0, 22.6, 19.1, 14.1; HRMS calcd for $C_{37}H_{54}O_7$ + H 611.3948, found 611.3966.

Reaction of (+)-(4,6-*O*-Benzylidiene)methyl-α-D-glucopyranoside with 8,10-Heneicosadiynoic Chloride, Total Yield 90%. Compound 8A: 20%, colorless crystal, mp 36−37 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42−7.39 (m, 2H), 7.35−7.30 (m, 3 H), 5.58 (t, 1H, J = 9.8 Hz), 5.48 (s, 1H), 4.92 (d, 1H, J = 3.9 Hz), 4.89−4.86 (m, 1H), 4.28 (dd, 1H, J = 9.8, 4.9 Hz), 3.90 (dt, 1H, J = 9.8, 4.9 Hz), 3.75 (t, 1H, J = 9.8 Hz), 3.62 (t, 1H, J = 9.8 Hz), 3.38 (s, 3H), 2.37−2.20 (m, 10H), 2.13 (t, 2H, J = 6.8 Hz), 1.62−1.23 (m, 48H), 0.85 (t, 6H, J = 6.8 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.0, 172.3, 136.9, 129.0, 128.2, 126.1, 101.5, 97.6, 79.2, 77.6, 77.1, 77.0, 71.4, 68.8, 68.6, 65.4, 65.2, 65.1, 62.3, 55.3, 34.2, 34.0, 31.8, 29.5, 29.4, 29.2, 29.0, 28.8, 28.4, 28.3(2), 28.27, 28.0, 27.9, 24.8, 24.6, 22.6, 19.1(2), 19.0, 14.1; HRMS calcd for $C_{56}H_{82}O_8$ + H 883.6088, found 883.6080.

Compound 8B: 63%, colorless crystal, mp 56−57 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.48−7.46 (m, 2H), 7.39−7.33 (m, 3 H), 5.52 (s, 1H), 4.93 (d, 1H, J = 3.9 Hz), 4.77 (dd, 1H, J = 9.8, 3.9 Hz), 4.27 (dd, 1H, J = 9.8, 3.9 Hz), 4.15 (t, 1H, J = 9.8 Hz), 3.82 (dt, 1H, J = 9.8, 4.9 Hz), 3.73 (t, 1H, J = 9.8 Hz), 3.53 (t, 1H, J = 9.8 Hz), 3.37 (s, 3H), 2.37 (t, 2H, J = 7.8 Hz), 2.22−2.18 (m, 4H), 1.69−1.56 (m, 2H), 1.41−1.23 (m, 22H), 0.84 (t, 3H, J = 6.8 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.3, 137.0, 129.2, 128.3, 126.3, 101.9, 97.5, 81.4, 77.1, 76.7, 73.4, 68.8, 68.6, 65.4, 65.1, 62.0, 55.3, 33.9, 31.8, 29.5, 29.4, 29.2, 29.0, 28.8, 28.4, 28.3, 28.28, 28.0, 24.7, 22.6, 19.1, 19.0, 14.1; HRMS calcd for $C_{35}H_{50}O_7$ + H 583.3635, found 583.3642.

Compound 8C: 7%, colorless crystal, mp 76−78 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46−7.39 (m, 2H), 7.36−7.30 (m, 3H), 5.47 (s, 1H), 5.32 (t, 1H, J = 9.8 Hz), 4.78 (d, 1H, J = 3.9 Hz), 4.28 (dd, 1H, J = 9.8, 4.9 Hz), 3.88−3.82 (m, 1H), 3.73 (t, 1H, J = 9.8 Hz), 3.64 (dd, 1H, J = 9.8, 3.9 Hz), 3.56 (t, 1H, J = 9.8 Hz), 3.45 (s, 3H), 2.34 (t, 2H, J = 6.8 Hz), 2.22 (t, 2H, J = 6.8 Hz), 2.14 (t, 2H, J = 6.8 Hz), 1.64−1.56 (m, 2H), 1.52−1.45 (m, 2H), 1.42−1.14 (m, 20H), 0.87 (t, 3H, J = 6.8 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.7, 137.0, 129.0, 128.2, 126.1, 101.5, 100.1, 78.7, 77.6, 72.0, 71.8, 68.9, 65.3, 65.2, 62.7, 55.5, 34.3, 31.8, 29.7, 29.5, 29.4, 29.3, 29.1, 28.8, 28.4(2), 24.9, 22.7, 19.2, 19.1, 14.1; HRMS calcd for $C_{35}H_{50}O_7$ + H 583.3635, found 583.3641.

Reaction of (+)-(4,6-*O*-Benzylidiene)methyl-α-D-glucopyranoside with 5,7-Hexadecadiynoic Chloride, Total Yield 92%. Compound 9A: 19%, colorless crystal, mp 43−45 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45−7.39 (m, 2H), 7.38−7.31 (m, 3H), 5.58 (t, 1H, J = 9.8 Hz), 5.49 (s, 1H), 4.94 (d, 1H, J = 3.9 Hz), 4.90−4.86 (m, 1H), 4.29 (dd, 1H, J = 9.8, 4.9 Hz), 3.90 (dt, 1H, J = 9.8, 4.9 Hz), 3.78−3.72 (m, 1H), 3.62 (t, 1H, J = 9.8 Hz), 3.39 (s, 3H), 2.54−2.35 (m, 4H), 2.31 (t, 2H, J = 6.8 Hz), 2.27−2.18 (m, 6H), 1.84−1.74 (m, 4H), 1.53−1.45 (m, 4H), 1.40−1.17 (m, 20H), 0.86 (t, 6H, J = 6.8 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.2, 171.7, 136.9, 129.1, 128.2, 126.2, 101.6, 97.6, 79.3, 78.2, 78.0, 75.8, 75.6, 71.6, 68.8, 66.4, 66.2, 65.0, 62.3, 55.4, 32.8, 32.7, 31.8, 29.1, 29.1, 28.9, 28.3, 23.7, 23.4, 22.7, 19.2, 18.5, 18.4, 14.1; HRMS calcd for $C_{46}H_{62}O_8$ + Na 765.4342, found 765.4354.

Compound 9B: semisolid, 66%, ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.49−7.46 (m, 2H), 7.38−7.35 (m, 3H), 5.53 (s, 1H), 4.93 (d, 1H, J = 3.9 Hz), 4.79 (dd, 1H, J = 9.8, 3.9 Hz), 4.27 (dd, 1H, J = 9.8, 4.9 Hz), 4.17−4.13 (m, 1 H), 3.82 (dt, 1H, J = 9.8, 4.9 Hz), 3.74 (t, 1H, J = 9.8 Hz), 3.53 (t, 1H, J = 9.8 Hz), 3.38 (s, 3 H), 2.52 (dd, 2H, J = 7.8, 6.8 Hz), 2.33 (t, 2H, J = 6.8 Hz), 2.21 (t, 2H, J = 6.8 Hz), 1.88−1.81 (m, 2H), 1.52−1.45 (m, 2H), 1.39−1.25 (m, 10H), 0.86 (dd, 3H, J = 6.8, 5.9 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.6, 137.0, 129.3, 128.3, 126.3, 102.0, 97.5, 81.4, 78.1, 75.7, 73.5, 68.8, 68.6, 66.3, 65.0, 62.0, 55.4, 32.8, 31.8, 29.6, 29.0, 28.8, 28.2, 23.4, 22.6, 19.1, 18.4, 14.0; HRMS calcd for $C_{30}H_{40}O_7$ + H 513.2852, found 513.2853.

Compound 9C: 7%, colorless crystal, mp 93−95 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44−7.41 (m, 2H), 7.37−7.32 (m, 3H), 5.47 (s, 1H), 5.31 (t, 1H, J = 9.8 Hz), 4.78 (d, 1H, J = 3.9 Hz), 4.29 (dd, 1H, J = 10.7, 4.9 Hz), 3.87−3.81 (m, 1H), 3.76−3.70 (m, 1H), 3.64 (dd, 1H, J = 3.91 Hz), 3.56 (t, 1H, J = 9.8 Hz), 3.45 (s, 3H), 2.48 (dd, 2H, J = 7.8, 6.8 Hz), 2.27 (t, 2H, J = 6.8 Hz), 2.21 (t, 2H, J = 6.8 Hz), 1.86−1.79 (m, 2 H), 1.52−1.45 (m, 2 H), 1.38−1.23 (m, 10H), 0.89 (dd, 3H, J = 6.8, 5.9 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.0, 137.0, 129.1, 128.2, 126.1, 101.5, 100.2, 78.7, 78.0, 72.3, 71.8, 68.9, 66.1, 62.7, 55.6, 33.2, 31.8, 29.2, 29.1, 28.8, 28.3, 23.8, 22.7, 19.2, 18.5, 14.1; HRMS calcd for $C_{30}H_{40}O_7$ + H 513.2852, found 513.2848.

Reaction of (+)-(4,6-*O*-Benzylidiene)methyl-α-D-glucopyranoside with Heptan-4,6-diynoic Acid Chloride, Total Yield 96%. Compound 10A: 20%, colorless crystal, mp 72−73 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42−7.40 (m, 2H), 7.35−7.31 (m, 3H), 5.58 (t, 1H, J = 9.7 Hz), 5.49 (s, 1H), 4.94 (d, 1H, J = 3.7 Hz), 4.90 (dd, 1H, J = 9.7, 3.7 Hz), 4.28 (dd, 1H, J = 10.2, 4.8 Hz), 3.93−3.87 (m, 1H), 3.75 (t, 1H, J = 10.3 Hz), 3.64 (t, 1H, J = 9.6 Hz), 3.39 (s, 3H), 2.57−2.50 (m, 8H), 2.22−2.15 (m, 4H), 1.56−1.45 (m, 4H), 0.97−0.92 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.9, 170.4, 136.9, 129.0, 128.2, 126.1, 101.5, 97.6, 79.1, 78.4, 78.2, 74.9, 74.6, 71.8, 69.3, 68.3, 66.3, 66.0, 65.2, 62.3, 55.5, 33.0, 21.8, 21.1, 15.2, 13.5; HRMS calcd for $C_{34}H_{38}O_8$ + H 575.2645, found 575.2633.

Compound 10B: 65%, colorless crystal, mp 110−111 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.49−7.46 (m, 2H), 7.38−7.34 (m, 3H), 5.52 (s, 1H), 4.93 (d, 1H, J = 3.7 Hz), 4.79 (dd, 1H, J = 9.6, 3.7 Hz), 4.27 (dd, 1H, J = 9.9, 4.5 Hz), 4.15 (dd, 1H, J = 9.6, 9.4 Hz), 3.85−3.79 (m, 1H), 3.72 (dd, 1H, J = 10.2, 9.9 Hz), 3.53 (dd, 1H, J = 9.4, 9.2 Hz), 3.38 (s, 3H), 2.64−2.53 (m, 4H), 2.19 (t, 2H, J = 7.0 Hz), 1.56−1.47 (m, 2H), 0.95 (t, 3H, J = 7.4 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.3, 137.0, 129.3, 128.4, 126.3, 102.0, 97.5, 81.3, 78.4, 74.7, 73.9, 68.9, 68.6, 66.3, 65.1, 62.0, 55.5, 33.0, 21.8, 21.2, 15.2, 13.5; HRMS calcd for $C_{24}H_{28}O_7$ + H 429.1913, found 429.1917.

Compound 10C: 11%, colorless crystal, mp 155−157 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43−7.41 (m, 2H), 7.36−7.32 (m, 3H), 5.48 (s, 1H), 5.31 (t, 1H, J = 9.7 Hz), 4.78 (d, 1H, J = 3.7 Hz), 4.28 (dd, 1H, J = 10.1, 4.6 Hz), 3.87−3.81 (m, 1H), 3.73 (t, 1H, J = 10.2 Hz), 3.68−3.62 (m, 1H), 3.57 (t, 1H, J = 9.6 Hz), 3.44 (s, 3H), 2.63−2.53 (m, 4H), 2.21−2.16 (m, 2H), 1.55−1.46 (m, 4 H), 0.95 (t, 1H, J = 7.3 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.6, 137.0, 129.0, 128.3, 126.2, 101.5, 100.1, 78.6, 78.1, 74.9, 72.7, 71.7, 68.9, 66.1, 65.2, 62.7, 55.6, 33.1, 21.7, 21.1, 15.2, 13.5; HRMS calcd for $C_{24}H_{28}O_7$ + H 429.1913, found 429.1914.

Reaction of (+)-(4,6-*O*-Benzylidiene)methyl-α-D-glucopyranoside with Heptan-4,6-diynoic Acid Chloride, Total Yield 95%. Compound 11A: 11%, colorless crystal, mp 120−121 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42−7.40 (m, 2H), 7.36−7.32 (m, 3H), 5.59 (t, 1H, J = 9.7 Hz), 5.49 (s, 1H), 4.95 (d, 1H, J = 3.7 Hz), 4.91 (dd, 1H, J = 9.7, 3.7 Hz), 4.29 (dd, 1H, J = 10.2, 4.8 Hz), 3.91 (dt, 1H, J = 9.8, 4.7 Hz), 3.75 (t, 1H, J = 10.3 Hz), 3.65 (t, 1H, J = 9.6 Hz), 3.39 (s, 3H), 2.60−2.52 (m, 8H), 1.98 (s, 1H), 1.95 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.7, 170.2, 136.9, 129.1, 128.3, 126.2, 101.6, 97.5, 79.1, 76.0, 75.8, 71.9, 69.4, 68.8, 68.1, 65.5, 65.4, 62.3, 55.5, 32.6, 15.0; HRMS calcd for $C_{28}H_{26}O_7$ + H 491.1706, found 491.1701.

Compound 11B: 61%, colorless crystal, mp 172−174 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.48−7.46 (m, 2H), 7.36−7.34 (m, 3H), 5.50 (s, 1H), 4.92 (d, 1H, J = 3.7 Hz), 4.78 (dd, 1H, J = 9.6,

3.7 Hz), 4.25 (dd, 1H, J = 9.9, 4.5 Hz), 4.12 (dd, 1H, J = 9.6, 9.4 Hz), 3.83−3.77 (m, 1H), 3.72 (dd, 1H, J = 10.2, 9.9 Hz), 3.49 (dd, 1H, J = 9.4, 9.2 Hz), 3.37 (s, 3H), 2.86 (br, 1H), 2.64−2.53 (m, 4H), 1.99 (s, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.0, 136.9, 129.2, 128.3, 126.2, 101.9, 97.4, 81.2, 75.7, 73.8, 68.7, 68.4, 68.0, 65.4, 61.9, 55.4, 32.5, 14.9; HRMS calcd for $C_{21}H_{22}O_7$ + H 387.1444, found 387.1435.

Compound 11C: 23%, colorless crystal, mp >250 °C dec; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43−7.41 (m, 2H), 7.37−7.32 (m, 3H), 5.48 (s, 1H), 5.32 (t, 1H, J = 9.7 Hz), 4.79 (d, 1H, J = 3.8 Hz), 4.28 (dd, 1H, J = 10.1, 4.7 Hz), 3.87−3.81 (m, 1H), 3.73 (t, 1H, J = 10.2 Hz), 3.65 (dd, 1H, J = 9.6, 3.8 Hz), 3.57 (dd, 1H, J = 9.6, 9.5 Hz), 3.44 (s, 3H), 2.64−2.54 (m, 4H), 2.25 (br, 1H), 1.94 (s, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.3, 137.0, 129.1, 128.3, 126.2, 101.5, 100.1, 78.6, 76.0, 72.8, 71.7, 68.9, 68.2, 65.4, 65.2, 62.7, 55.5, 32.8, 15.4; HRMS calcd for $C_{21}H_{22}O_7$ + H 387.1444, found 387.1439.

Reaction of (+)-(4,6-*O*-Benzylidiene)methyl-α-D-glucopyranoside with 7-Triethylsilylheptan-4,6-diynoic Chloride, Total Yield 95%. Compound 12A: 19%, colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43−7.40 (m, 2H), 7.36−7.31 (m, 3H), 5.58 (t, 1H, J = 9.8 Hz), 5.50 (s, 1H), 4.96 (d, 1H, J = 3.9 Hz), 4.91 (dd, 1H, J = 9.8, 3.9 Hz), 4.28 (dd, 1H, J = 10.7, 4.9 Hz), 3.90 (dt, 1H, J = 9.8, 4.9 Hz), 3.75 (t, 1H, J = 9.8 Hz), 3.65 (t, 1H, J = 9.8 Hz), 3.40 (s, 3H), 2.62−2.50 (m, 8 H), 0.96 (t, 9H, J = 7.8 Hz), 0.95 (t, 9H, J = 7.8 Hz), 0.59 (t, 6H, J = 7.8 Hz), 0.58 (t, 6H, J = 7.8 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.8, 170.3, 136.9, 129.1, 128.2, 126.1, 101.3, 97.5, 89.1, 89.0, 82.1, 82.0, 79.1, 76.7, 76.4, 71.9, 69.4, 68.8, 66.5, 66.4, 62.3, 55.5, 32.7(2), 29.7, 15.2, 7.3, 4.2; HRMS calcd for $C_{40}H_{54}O_8Si_2$ + H 719.3436, found 719.3436.

Compound 12B: 61%, colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.48−7.44 (m, 2H), 7.37−7.33 (m, 3H), 5.51 (s, 1H), 4.92 (d, 1H, J = 3.9 Hz), 4.78 (dd, 1H, J = 9.8, 3.9 Hz), 4.30 (br, 1H), 4.26 (dd, 1H, J = 9.8, 3.9 Hz), 4.13 (t, 1H, J = 9.8 Hz), 3.80 (dt, 1H, J = 9.8, 4.9 Hz), 3.72 (t, 1H, J = 9.8 Hz), 3.51 (t, 1H, J = 9.8 Hz), 3.38 (s, 3H), 2.63−2.53 (m, 4 H), 0.96 (t, 9H, J = 7.8 Hz), 0.58 (t, 6H, J = 7.8 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.1, 136.8, 129.2, 128.2, 126.2, 101.9, 97.4, 88.9, 82.0, 81.2, 76.4, 73.8, 68.7, 68.4, 66.3, 61.9, 32.5, 15.0, 7.2, 4.0; HRMS calcd for $C_{27}H_{36}O_7Si$ + H 501.2309, found 501.2301.

Compound 12C: 15%, colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.49−7.30 (m, 5H), 5.48 (s, 1H), 5.31 (t, 1H, J = 9.8 Hz), 4.78 (d, 1H, J = 3.9 Hz), 4.28 (dd, 1H, J = 10.7, 4.9 Hz), 3.83 (dt, 1H, J = 9.8, 4.9 Hz), 3.73 (t, 1H, J = 10.7 Hz), 3.66 (dd, 1H, J = 9.8, 3.9 Hz), 3.57 (t, 1H, J = 9.8 Hz), 3.44 (s, 3 H), 3.16 (br, IH), 2.63−2.55 (m, 4H), 0.96 (t, 9H, J = 7.8 Hz), 0.58 (t, 6H, J = 7.8 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.4, 137.0, 129.1, 128.3, 126.2, 101.5, 100.1, 89.1, 81.9, 78.6, 76.8, 72.8, 71.6, 68.9, 66.3, 62.7, 55.6, 32.8, 15.0, 7.4, 4.2; HRMS calcd for $C_{27}H_{36}O_7Si$ + H 501.2309, found 501.2289.

Reaction of (+)-(4,6-*O*-Benzylidiene)methyl-α-D-glucopyranoside with 7-Phenylheptan-4,6-diynoic Chloride, Total Yield 95%. Compound 13A: 28%, colorless crystal, mp 132−133 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45−7.40 (m, 6H), 7.36−7.24 (m, 9H), 5.62 (t, 1H, J = 9.8 Hz), 5.51 (s, 1H), 4.98 (d, 1H, J = 3.9 Hz), 4.95 (dd, 1H, J = 9.8, 2.9 Hz), 4.29 (dd, 1H, J = 9.8, 4.9 Hz), 3.93 (dt, 1H, J = 9.8, 4.9 Hz), 3.76 (t, 1H, J = 9.8 Hz), 3.68 (t, 1H, J = 9.8 Hz), 3.41 (s, 3H), 2.69−2.59 (m, 8H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.8, 170.3, 136.8, 132.5, 132.4, 129.0(2), 128.8, 128.3, 128.2, 126.0, 121.7, 101.5, 97.5, 82.1, 81.8, 79.1, 75.5, 75.4, 74.0, 73.9, 71.9, 69.4, 68.8, 66.0, 65.8, 62.3, 55.5, 32.87, 32.83, 15.5; HRMS calcd for $C_{40}H_{34}O_8$ + H 643.2332, found 643.2333.

Compound 13B: 57% yield, colorless crystal, mp 141−142 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.49−7.43 (m, 4H), 7.38−7.24 (m, 6H), 5.53 (s, 1H), 4.96 (d, 1H, J = 2.9 Hz), 4.83 (dd, 1H, J = 9.8, 3.9 Hz), 4.28 (dd, 1H, J = 9.8, 3.9 Hz), 4.18 (t, 1H, J = 9.8 Hz), 3.83 (dt, 1H, J = 9.8, 4.9 Hz), 3.74 (t, 1H, J = 9.8 Hz), 3.54 (t, 1H, J = 9.8 Hz), 3.40 (s, 3H), 2.71−2.65 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.1, 136.9, 132.4, 129.3, 129.0, 128.34, 128.32, 126.2, 121.6, 102.0, 97.4, 81.9, 81.4, 77.3, 75.4, 74.0, 73.9, 68.8, 68.5, 65.9, 62.0, 55.4, 32.8, 15.5; HRMS calcd for $C_{27}H_{26}O_7$ + H 463.1757, found 463.1759.

Compound 13C: 10% yield, colorless crystal, mp 174−176 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45−7.41 (m, 4H), 7.36−7.24 (m, 6H), 5.49 (s, 1H), 5.35 (t, 1H, J = 9.8 Hz), 4.80 (d, 1H, J = 3.9 Hz), 4.29 (dd, 1H, J = 9.8, 3.9 Hz), 3.83 (dt, 1H, J = 9.8, 4.9 Hz), 3.74 (t, 1H, J = 9.8 Hz), 3.68 (dd, 1H, J = 9.8, 3.9 Hz), 3.59 (t, 1H, J = 9.8 Hz), 3.44 (s, 3H), 2.71−2.61 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.3, 136.9, 132.4, 129.0, 128.9, 128.2, 128.1, 126.0, 121.7, 101.3, 100.0, 82.1, 78.5, 75.2, 74.1, 72.7, 71.5, 68.7, 65.7, 62.6, 55.5, 32.8, 15.4; HRMS calcd for $C_{27}H_{26}O_7$ + H 463.1757, found 463.1759

Reaction of (+)-(4,6-*O*-Benzylidiene)methyl-α-D-glucopyranoside with 9-Phenylnonan-4,6-diynoic Chloride, Total Yield 52% (Unoptimized Yield). Compound 14A: 1% yield, semisolid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43−7.15 (m, 15H), 5.58 (t, 1H, J = 9.8 Hz), 5.49 (s, 1H), 4.94 (d, 1H, J = 2.9 Hz), 4.91 (dd, 1H, J = 9.8, 3.91 Hz), 4.29 (dd, 1H, J = 10.7, 4.9 Hz), 3.91 (dt, 1H, J = 10.7, 4.9 Hz), 3.75 (t, 1H, J = 10.7 Hz), 3.64 (t, 1H, J = 9.8 Hz), 3.38 (s, 3H), 2.81−2.74 (m, 4H), 2.57−2.45 (m, 12H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.9, 170.4, 140.1, 136.8, 129.0, 128.4, 128.3, 128.2, 126.4, 126.1, 101.5, 97.5, 79.1, 75.3, 75.0, 71.8, 69.2, 68.8, 66.1, 65.9, 65.7, 62.3, 55.4, 34.5, 32.9, 29.7, 21.3,15.1; HRMS calcd for $C_{44}H_{42}O_8$ + H 699.2958, found 699.2970

Compound 14B: 32% yield, semisolid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.51−7.49 (m, 2H), 7.40−7.35 (m, 3H), 7.31−7.28 (m, 2H), 7.23−7.18 (m, 3H), 5.53 (s, 1H), 4.94 (d, 1H, J = 3.9 Hz), 4.80 (dd, 1H, J = 9.8, 3.9 Hz), 4.28 (dd, 1H, J = 9.8, 4.9 Hz), 4.15 (t, 1H, J = 9.8 Hz), 3.83 (dt, 1H, J = 9.8, 4.9 Hz), 3.74 (t, 1H, J = 9.8 Hz), 3.52 (t, 1H, J = 9.8 Hz), 3.37 (s, 3H), 2.94 (br, 1H), 2.81 (t, 2H, J = 7.8 Hz), 2.63−2.51 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.1, 139.9, 136.9, 129.1, 128.2, 128.1, 128.0, 126.3, 126.2, 101.8, 97.3, 81.1, 77.2, 75.0, 73.7, 68.6, 68.3, 66.0, 65.6, 61.9, 55.3, 34.3, 32.7, 21.1, 15.0; HRMS calcd for $C_{29}H_{30}O_7$ + H 491.2070, found 491.2064.

Compound 14C: 19% yield, colorless crystal, mp 147−149 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46−7.45 (m, 2H), 7.38−7.35 (m, 3H), 7.31−7.27 (m, 2H), 7.23−7.17 (m, 3H), 5.50 (s, 1H), 5.35 (t, 1H, J = 9.8 Hz), 4.81 (d, 1H, J = 3.9 Hz), 4.31 (dd, 1H, J = 9.8, 4.9 Hz), 3.86 (dt, 1H, J = 9.8, 4.9 Hz), 3.75 (t, 1H, J = 9.8 Hz), 3.68 (dd, 1H, J = 9.8, 3.9 Hz), 3.59 (t, 1H, J = 9.8 Hz), 3.45 (s, 3 H), 2.80 (t, 2H, J = 7.8 Hz), 2.64−2.55 (m, 4H), 2.50 (t, 2H, J = 7.8 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.3, 139.9, 136.8, 128.8, 128.3, 128.1, 128.0, 126.2, 126.0, 101.2, 99.9, 78.4, 75.2, 72.5, 71.4, 68.6, 65.8, 65.6, 62.5, 55.4, 34.3, 32.8, 21.1, 15.0; HRMS calcd for $C_{29}H_{30}O_7$ + H 491.2070, found 491.2054

Acknowledgment. We thank the financial support from NSF grant no. 518283 and the assistance of acquiring SEM by AMRI at the University of New Orleans. We also thank the LSU chemistry department for providing lab space for us after Hurricane Katrina hit New Orleans so we could complete the manuscript submission and revision.

Supporting Information Available: Experimental procedure for compounds **2a**−**d**, **4a**−**d**, and **5**; ^{1}H and ^{13}C NMR spectra of compounds **2a**−**d, 4a**−**d**, **5**, and **7A**−**14C**, and 2D COSY spectrum of compound **10B**. This material is available free of charge via the Internet at http://pubs.acs.org.

JO052317T