JOC The Journal of Organic Chemistry

pubs.acs.org/joc Article

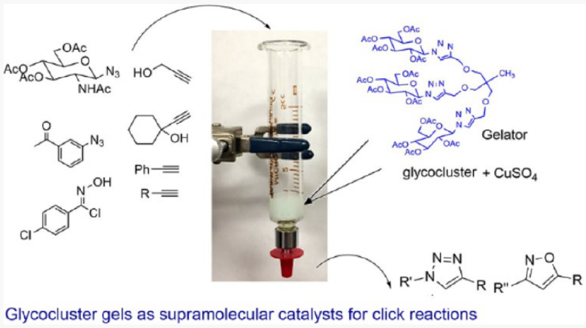
# Synthesis of Dendritic Glycoclusters and Their Applications for Supramolecular Gelation and Catalysis

Guijun Wang,* Dan Wang, Jonathan Bietsch, Anji Chen, and Pooja Sharma

Cite This: J. Org. Chem. 2020, 85, 16136−16156 Read Online

ACCESS | Metrics & More | Article Recommendations | Supporting Information

**ABSTRACT:** Glycoclusters with three, four, and six arms of glycosyl triazoles were designed, synthesized, and characterized. The self-assembling properties of these molecules and their catalytic activity as ligands in copper-catalyzed azide and alkyne cycloaddition (CuAAC) reactions were studied. The compounds with a lower number of branches exhibit excellent gelation properties and can function as supramolecular gelators. The resulting gels were characterized using optical microcopy and atomic force microscopy. The glycoconjugates containing six branches showed significant catalytic activity for copper sulfate mediated cycloaddition reactions. In aqueous solutions, 1 mol % of glycoclusters to substrates was efficient at accelerating these reactions. Several trimeric compounds were found to be capable of forming co-gels with the catalytically active hexameric compounds. Using the organogels formed by the glycoconjugates as supramolecular catalysts, efficient catalysis was demonstrated for several CuAAC reactions. The metallogels with $CuSO_4$ were also prepared as gel columns, which can be reused for the cycloaddition reactions several times. These include the preparation of a few glycosyl triazoles and aryl triazoles and isoxazoles. We expect that these sugar-based soft biomaterials will have applications beyond supramolecular catalysis for copper-catalyzed cycloaddition reactions. They may also be useful as ligands or gel matrixes for other metal-ion catalyzed organic reactions.



Glycocluster gels as supramolecular catalysts for click reactions

## ■ INTRODUCTION

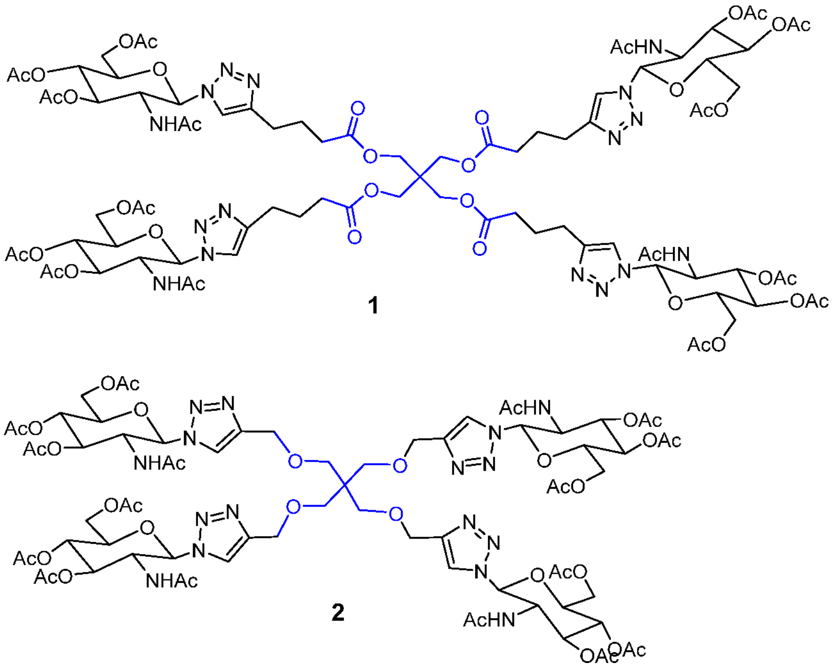
Carbohydrates contain a broad range of structural diversity, and they are produced from renewable resources. Monosaccharides and disaccharides are useful as templates and building blocks for the construction of molecular gelators, which can self-assemble and form 3-dimensional fibrous networks that immobilize solvents. Molecular gelators are also called supramolecular gelators or low molecular weight gelators (LMWGs). These compounds can self-assemble and form reversible supramolecular gels in organic solvents or water. The structures of these compounds can be designed to afford certain functional soft materials by including built-in noncovalent interactions that favor gelation and self-assembly.[1] Supramolecular gels have found a variety of applications including drug delivery, tissue engineering, enzyme immobilizations, pollutant removal, and catalysis.[1−4] Carbohydrate building blocks are useful for the preparation of functional glycoconjugates that exhibit a variety of different applications as advanced materials due to their biocompatibility and structural diversity. Carbohydrate-based gelators have also been designed and discovered for applications in several research fields and showed great promise for the discovery of novel soft biomaterials with desirable functions.[5] The functionalization of D-glucose and D-glucosamine have been systematically studied and resulted in suitable structure templates that can effect gelation properties.[1c,5] These common monosaccharides have been used extensively in many gelator designs, which have shown a variety of applications for oil spill cleanup, dye absorption, drug delivery and as other biomedical agents.[6−10]

Copper(I)-catalyzed azide alkyne cycloaddition (CuAAC) reactions, also called "click reactions", are very important in organic synthesis, pharmaceutical chemistry, and materials sciences.[11−14] Click chemistry has been shown to be a useful method for the construction of small and large sugar-based 1,2,3-triazole derivatives, which have had many applications in recent years.[15,16] For instance, click chemistry has been used to synthesize many glycoclusters and glycodendrimers,[17,18] such as pentaerythritol dendrimer derivatives[19] and glycoporphyrin-cored dendrimers containing 8, 12, 16, and 24 $\beta$-D-glucopyranose units at their peripheries.[20] Using a nonsymmetrical glycocluster core, unsymmetrical Janus glycodendrimers can be synthesized, which have been shown to be useful as lectin inhibitors.[21,22] Triazole-based glycoclusters

**Special Issue:** A New Era of Discovery in Carbohydrate Chemistry

**Received:** August 17, 2020
**Published:** December 10, 2020

https://dx.doi.org/10.1021/acs.joc.0c01978



1

2

**Figure 1.** Structures of two tetrameric glycoconjugates derived from pentaerythritol.

have received a great deal of interest over recent years. Some glycosyl triazoles have been converted to other derivatives with biological activities such as glycosidase inhibitors etc. Many multivalent glycoconjugates have been designed, synthesized, and studied for potential applications in biological systems.[23−26] In addition to biomedical applications, click chemistry is also useful for the construction of polymer-supported covalent catalysts and functional materials.[27]

Because of the importance of click reactions, many studies have been carried out to catalyze the cycloaddition reactions. Interestingly, triazole-containing compounds have been found to be suitable ligands to accelerate copper-catalyzed AAC reactions.[28−32] A series of tris-triazole methanol ligands, which were covalently immobilized, were found to be useful recyclable catalysts.[33] Some triazole-containing dendritic catalysts, which act as ligands for Cu(I) in click chemistry and other chemistry, have been found to be capable of forming reusable nanoreactors in water.[34,35] In the studies of screening the catalytic effects of various triazole containing ligands, different cycloaddition rates have been observed depending the alkyne starting material being used.[36,37]

Catalytically active supramolecular gelators that form gels through noncovalent intermolecular forces, while retaining their catalytic activity, are very attractive new materials.[4,38−40] Several systems have been reported to have useful catalytic properties, including proline-derived organogelators for catalysis of aldol reactions, aza-Henry reactions.[41,42] Gel media, such as copper-containing polymer gels, have been used for catalysis of click reactions.[43] A topical azide−alkyne cycloaddition reaction was also carried out using gels as catalysts.[44] A palladium carbene complex based low molecular weight gelator was found to be useful for catalyzing Michael additions.[45] A metal−metalloporphyrin gel was used as catalytic pocket for reactions using heterogeneous catalyst, leading to high chemo-/stereoselectivity.[46] Besides using gels, a reusable dendrimer was found to be an effective cocatalyst for CuAAC reactions using copper sulfate.[35]

In previous studies, we have found that the selective functionalization of D-glucose or D-glucosamine at different positions can produce effective molecular gelators. Several series of LMWGs and functional molecular assemblies have been discovered by introducing a triazole moiety into various sugar molecules. Many of these derivatives were found to effectively interact with organic solvents and solvent/water mixtures to form supramolecular gels.[47,48] We have found that trimeric and tetrameric glycoclusters are effective molecular gelators for a variety of organic solvents.[49] Catalytic gels are unique new materials for organic synthesis and new reaction processes. We envisioned that triazole based gelators may be able to catalyze copper-mediated cycloaddition reactions. Supramolecular self-assembly results in unique nanostructures that may have superior catalytic properties, mimicking enzymatic reactions.

## ■ RESULTS AND DISCUSSION

Previously, we have shown that the branched compounds with three or four sugar triazole units are effective gelators.[49] Using various peracetylated glucose and glucosamine units, we systematically studied the gelation properties of two main series of pentaerythritol derivatives. The two glucosamine-based tetramers with ester (**1**) and ether (**2**) linkages are shown in Figure 1. In addition, bistriazole-linked glucosamine-based macrocycles were found to be effective at catalyzing the copper sulfate mediated azide alkyne cycloaddition (CuAAC) reactions.[30] We envisioned that by arranging the triazole functional groups in more densely branched molecules, unique molecular architectures that can lead to different functions or improved catalytic properties can be created. In this study, we have synthesized a library of glycoclusters and analyzed their self-assembling properties, gelation properties, and applications as ligands for copper-catalyzed cycloaddition reactions. The structures of the multimeric alkyne derivatives **3−10** and the sugar azide building blocks **11−13** are shown in Figure 2. These include the trimesic acid derivatives **3−5**, tris-

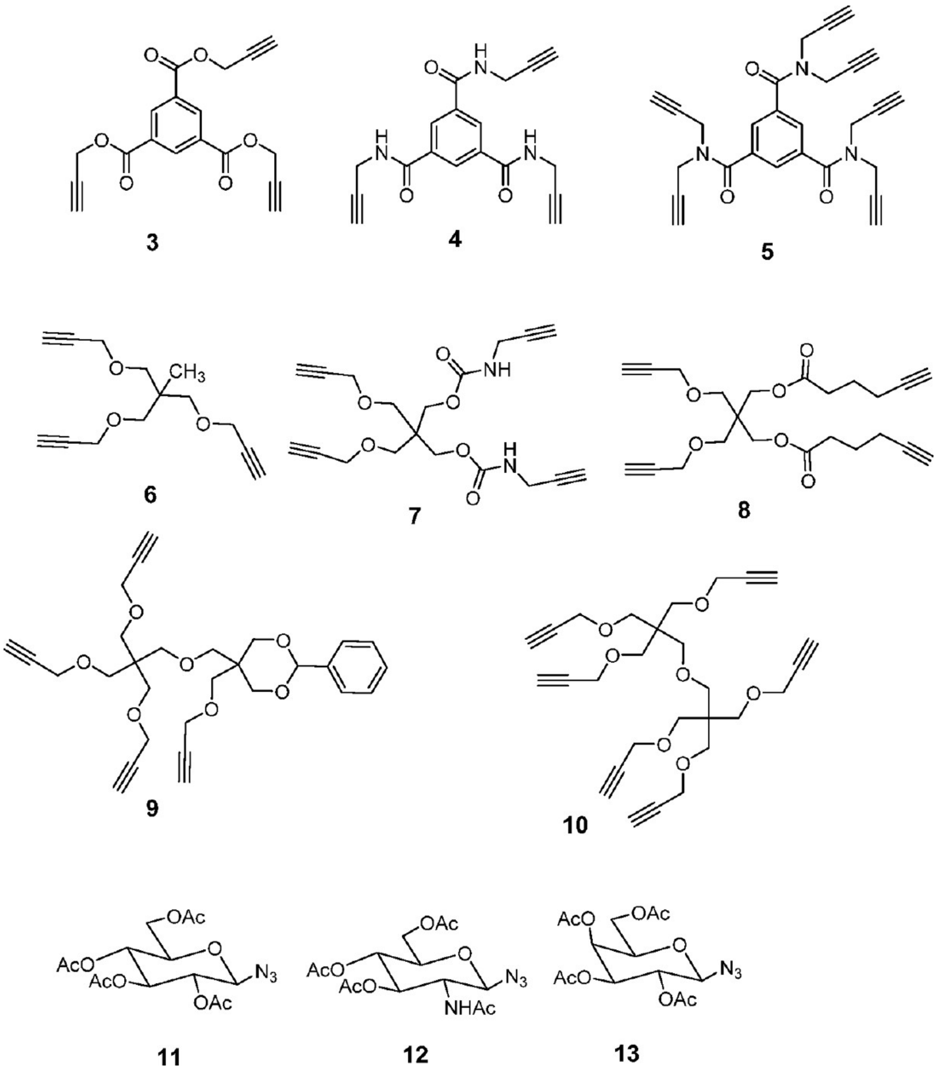


**Figure 2.** Structure of alkyne building blocks **3**−**10** and the sugar azides **11**−**13**.

(hydroxymethyl)ethane derivative **6**, pentaerythritol derivatives **7** and **8**, and dipentarerythritol derivatives **9** and **10**. The alkyne derivatives were synthesized in short steps from the corresponding alcohols by alkylation with propargyl chloride typically.

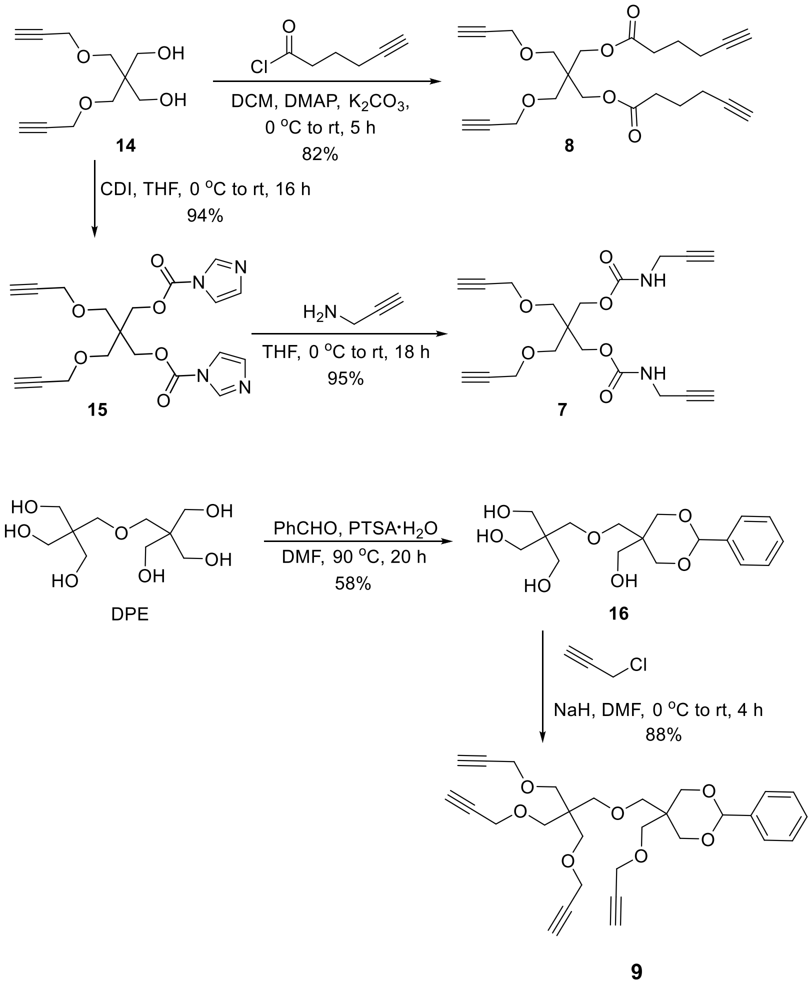
Scheme 1 shows the synthesis of the alkyne building blocks **7**−**9**. Starting from the dipropargyl diol **14**, esterification with the 5-hexynoyl chloride (prepared in situ from the corresponding acid) afforded the tetra-alkyne **8**. Alternatively, the diol **14** was converted to the imidazole carbonate intermediate **15** and followed by treatment with propargyl amine afforded the tetra-alkyne **7**. Compound **9** was synthesized from the dipentaerythritol (DPE), monobenzylidene acetal formation afforded the intermediate **16**, which was then converted to the compound **9** through $S_N2$ reactions.

Using CuAAC reactions, the alkyne building blocks with various numbers of acetylene arms, were utilized for the synthesis of trimeric, tetrameric, and hexameric glycoconjugates **17**−**33**, as shown in Figures 3 and 4.

**Self-Assembly and Molecular Gelation Properties.** After the glycoclusters were synthesized, their gelation properties were analyzed in several solvents and are listed in Table 1. The gels typically appeared translucent for these glycoclusters, and the photos of several representative gels are included in Figure 5. The gelation test results indicate that effective LMWGs were obtained through rational design of multimeric glycoconjugates. Using trimesic acid as the building block, the ester derivatives **17** and **18** were both effective gelators, forming gels in seven of the tested solvents. The glucose derivatives **17** formed gels in toluene, ethanol, 2-propanol, *n*-propanol, and ethanol−water mixtures. The glucosamine derivative **18** formed gels in similar solvents, but at relatively lower concentrations. With the trimeric ester derivatives, it seems that the glucosamine derivative was more effective. This is presumably due to the additional hydrogen-bonding ability of the amide functional group. The trimeric amide linked glucose derivative **19** only formed gels in ethanol and *n*-butanol, and the glucosamine derivative **20** only formed gels in *n*-propanol, *n*-butanol, and glycerol at 10 mg/mL. When comparing the amide-linked derivatives **19** and **20** to the ester-linked derivatives **17** and **18**, we can conclude that the ester linkage is more effective in the formation of supramolecular gels. The presence of three amide functional groups generates intermolecular interactions that are too strong and result in precipitation rather than gelation. The hexameric glycoclusters **21** and **22** were not gelators for most of the tested solvents.

The tris(hydroxymethyl)ethane derivatives **23** and **24**, which have three sugar triazole arms, formed gels in several solvents.

Scheme 1. Preparation of the Alkyne Building Blocks 7−9

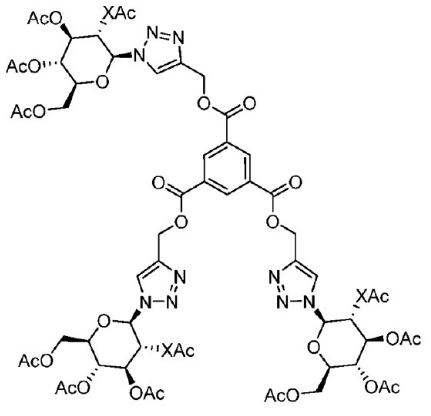


Both glucose and glucosamine derivatives were able to gelate a series of solvents at moderate concentrations. The pentaerythritol derivatives with the carbamate functional groups, **25** and **26**, were not effective gelators as compared to the ether-linked compound **2**, but the glucosamine derivative **26** was able to form gels in ethanol and *n*-butanol, making it a more efficient gelator than the glucose derivative **25**. The pentaerythritol derivatives **27** and **28** have half ester linkages and half ether linkages, so they can be considered as hybrids of compounds **1** and **2**. The glucose derivative **27** did not form gels in most of the solvents, while on the other hand, the glucosamine derivative **28** showed gelation properties in seven of the tested solvents, showing that it has similar gelation properties compared to compound **2**. Compounds **29**−**33** are derivatives synthesized from dipentaerythritol. The tetrameric glucosamine-based glycoconjugate **29** and the deprotected compound **30** were effective gelators for five and six of the selected solvents, respectively. In comparison, the glucosamine-based hexameric glycoconjugate **32** formed gels in five of the selected solvents, including ethanol and *n*-butanol. The D-glucose and D-galactose derivatives **31** and **33**, on the other hand, were not gelators for any of the tested solvents.

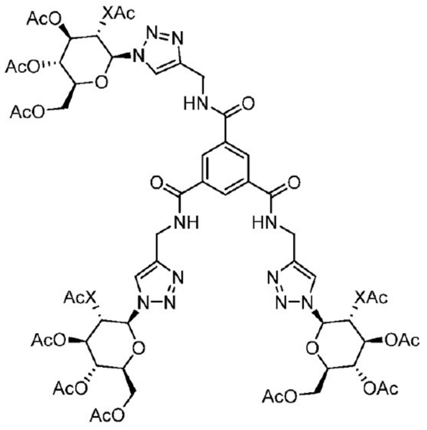
The organogels formed by these clusters in alcohols appeared mostly transparent or translucent. The morphologies of several gels are characterized using an optical microscope, as shown in Figure 6. The gel of compound **18** in DMSO/$H_2O$ (v/v 1:2) showed a uniform fibrous network (Figure 6a) and in *n*-butanol showed smooth filmlike gels with some fibrous network distributed on top of the film (Figure 6b). Compound **32** in DMSO/$H_2O$ (v/v 1:2) appeared to have a similar thin film type of morphology, but with an interesting circular arrangement of fibrous assemblies (Figure 6c). The gel also showed similar smooth filmlike features in *n*-butanol but with long and twisted fibrous networks mixed on the gel surface (Figure 6d).

We also characterized the molecular assemblies of several gels by AFM, and a few representative phase images are shown in Figure 7. The gel of compound **18** in *n*-BuOH at 4.0 mg/mL exhibited a braided thin fibrous network (Figure 7a,b). The fibers appeared uniform and have a diameter of ∼50 nm. The gel formed by compound **26** in *n*-butanol at 10 mg/mL, which is more concentrated than the MGC, appeared as a thin, porous fishnet-type of morphology, which is composed of interconnected thin fibers. A different region of the gel showed long and thin thread of fibers with an estimated diameter of 20 nm (Figure 7d). The gel of compound **28** in ethanol showed more uniform fibrous assembly (Figure 7e). The gel of hexamer compound **32** in *n*-butanol at 5.0 mg/mL showed a more smooth filmlike surface composed of small fibers (Figure 7f).

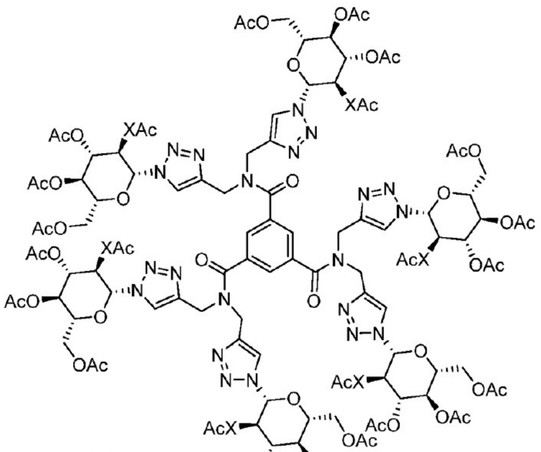
**Application of the Supramolecular Dendritic Glycoclusters in Triazole Synthesis.** In this study, we investigated the rate acceleratory effects of a series of triazole-linked glucosamine/glucose derivatives as ligands in copper-catalyzed



**17**, X = O
**18** X = NH



**19**, X = O
**20**, X = NH



**21**, X = O
**22**, X = NH

**Figure 3.** Structures of the synthesized glycoconjugates **17**−**22** with a trimesic acid core structure.

azide−alkyne cycloaddition (CuAAC) reactions. The selection of the reactions using *N*-acetyl glucosamine azide **12** with phenyl acetylene and 1-octyne was based on our previous studies that these reactions typically require longer reaction time without added ligands.[30] The results for the click reaction of azide **12** with phenyl acetylene are shown in Table 2; the reactions were monitored by $^1$H NMR spectroscopy, and the summarized spectra are included in Figures S1−S3. The conversions were calculated using $^1$H NMR integration of the product **34** versus the starting material **12**. For instance, the signals for the anomeric proton doublet at 4.8 and a triplet at 5.1 ppm are distinctive and separated from the product's anomeric signal at 6.05 ppm and a triplet 5.4 ppm (Figure S1), so they can be used for the calculation.

As shown in Table 2, we screened all 17 glycoclusters **17**−**33** that were synthesized and included the fully symmetrical pentaerythritol derived tetramers **1** and **2**. All of the glycoclusters showed significant reaction rate acceleration in comparison to the control experiments without the addition of ligands. We found that at 5 h the two ester-linked trimesic acid derivatives **17** and **18** were able to help the reaction reach 100% conversion. The amide-linked glucose derivative **19** and glucosamine derivative **20** were less effective, showing only 79% and 72% conversion at 5 h, respectively. In contrast, upon increasing the number of triazole branches, hexamers **21** and **22** were both very effective at catalyzing the CuAAC reactions, reaching 100% conversions within 2 h, with isolated yields of 95% and 93%, respectively. The glucose derivative **21** was slightly faster than the glucosamine derivative at 1 h, reaching 93% conversion, versus 89% conversion for hexamer **22**. From the results of these six glycoclusters, the trend is clear that the hexamer clusters are much more effective catalysts for the CuAAC reactions than the corresponding trimeric clusters.

The cluster derivatives based off the pentaerythritol building blocks showed a catalytic trend similar to that of our previous research. The tetraether compound **2** was a more efficient gelator than the tetraester compound **1** and was also found to be more efficient at accelerating the reaction. In the presence of the tetraether **2**, the azide **12** was fully converted to compound **34** in 3 h. This same reaction using the tetraester **1** only achieved 85% conversion at 5 h. The trimeric glycocluster **24** was less effective in comparison to tetramer **2** as well. The trimer glucose derivative **23** was not as efficient as the glucosamine derivative, and the reaction using 1 mol % **23** reached 28% conversion at 1 h and 64% conversion at 4 h. The two hybrid ether and carbamate-linked glycoconjugates **25**−**26** showed very similar results, reaching 100% conversion at 6 h. However, the hybrid ether and ester linked compounds **27**−**28** have different effects for the CuAAC reaction. The glucosamine derivative **28** was found to be more effective, reaching

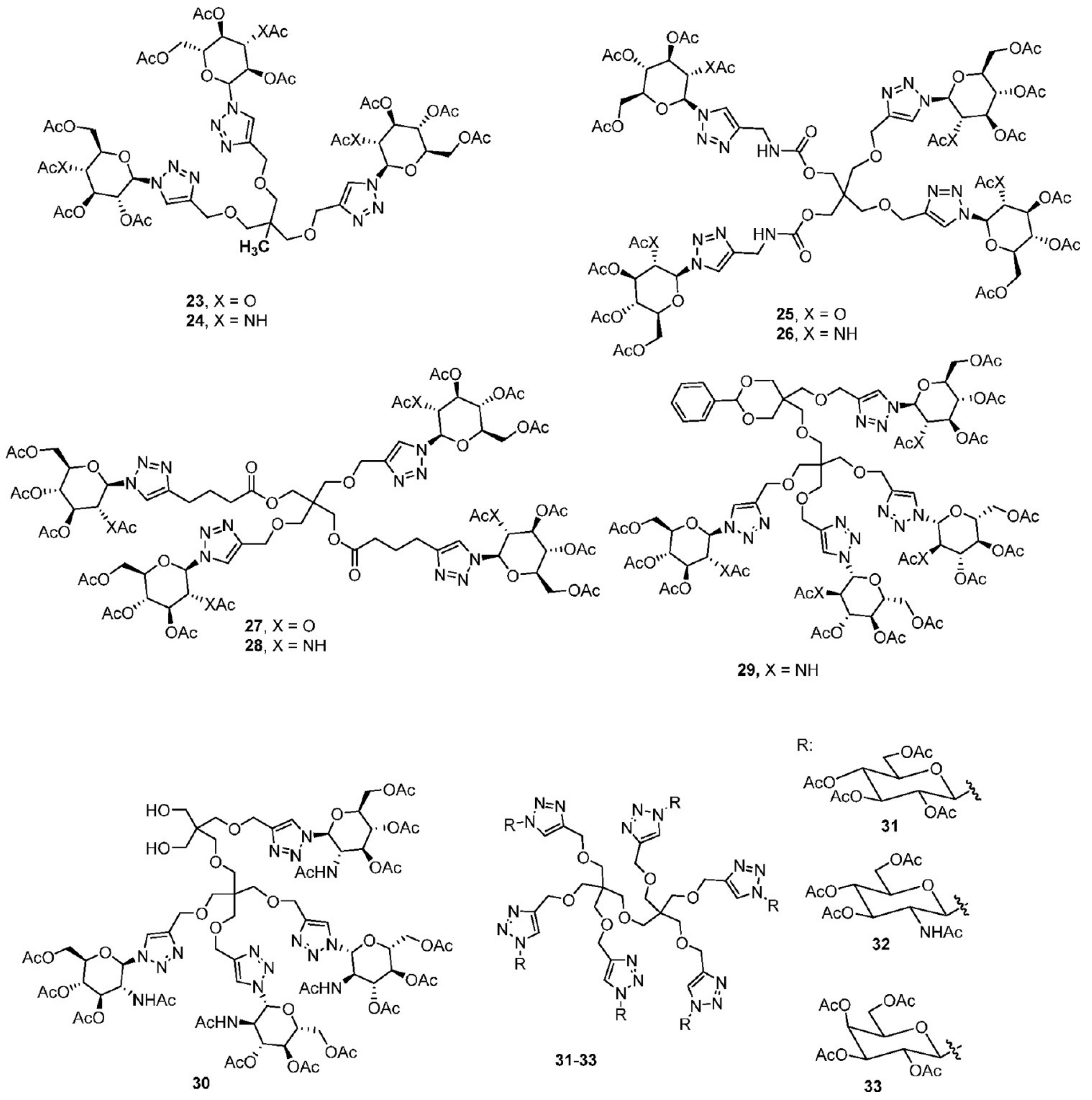


**Figure 4.** Structures of the synthesized glycoconjugates **23**−**33** from pentaerythritol and dipentaerythritol building blocks.

83% conversion at 1 h, and the reaction was worked up at 6 h and an isolated yield of 92% was obtained for the product **34**. The tetrameric glycoclusters **29** and **30** derived from dipentaerythritol had catalytic effects comparable to other tetrameric glycoclusters. We found the that most efficient catalyst for the click reaction was the hexameric glucose derivative **31**; using 1 mol % of the ligand, the reaction reached 100% conversion after 30 min. With compound **31** reduced to 0.5 mol %, the reaction reached full conversion at 1 h. The hexamer galactose and glucosamine derivatives **32**−**33** also showed good activities for the reactions, reaching 100% conversion within 2 h. These studies showed that hexameric derivatives were more efficient ligands for copper catalyzed cycloaddition reactions.

With the phenyl acetylene substrate analysis results, we have observed an interesting correlation where the degree of conjugation increases the catalytic activity. The hexamers are generally more effective than trimers and tetramers. We also screened the catalytic effects of selected glycoclusters for the 1-octyne cycloaddition reaction with compound **12**. The results are shown in Table 3 and Figures S4−S8. For the 1-octyne substrate, the effectiveness of the glycoclusters for the reaction followed a similar trend. We found that hexamers are generally more effective in comparison to others, but several tetrameric derivatives were also quite efficient. The most efficient ligand for 1-octyne was the tetrameric glycocluster **29**. The reaction reached 100% conversion at 2 h, and the hexameric clusters were also quite efficient for the reactions, typically reaching full conversion within 2−3 h. The other effective compounds are the mixed pentaerythritol glucose derivatives **25** and **27**. The reaction almost reached full conversion at 4 h. The hexamer glucose and galactose derivatives **31**, **33**, and glucosamine derivative **22** also reached close to full conversion within 3 h. It was noticed that for different alkyne substrates, the performance of the glycoclusters was quite different, with certain ligands being more favorable than the others.

To look at the glycocluster's catalytic versatility, we decided to screen a reaction utilizing a different azide substate. The reaction of 3-acetylphenyl azide **36** with phenyl acetylene was selected for the test reaction, and the results are shown in

Table 1. Gelation Properties of the Glycoconjugates Synthesized[a]

| cluster | Tol | EtOH | *i*-PrOH | *n*-PrOH | *n*-BuOH | glycerol | EtOH/$H_2O$ (1:2) | EtOH/$H_2O$ (1:1) | DMSO/$H_2O$ (1:2) | DMSO/$H_2O$ (1:1) |
|---|---|---|---|---|---|---|---|---|---|---|
| **17** | $G_T$ 20.0 | $G_T$ 10.0 | $G_T$ 10.0 | $G_T$ 10.0 | $G_T$ 10.0 | S | I | $G_T$ 10.0 | I | $G_O$ 10.0 |
| **18** | S | $G_T$ 6.7 | P | $G_T$ 4.0 | $G_T$ 4.0 | S | $G_T$ 5.0 | $G_T$ 6.7 | $G_T$ 2.8 | $G_T$ 4.0 |
| **19** | P | Gc 6.7 | P | P | Gc* 6.7 | S | P | P | P | P |
| **20** | I | P | P | $G_O$ 10.0 | $G_O$ 10.0 | $G_O$ 20.0 | P | P | P | P |
| **21** | P | P | P | P | P | P | P | P | P | P |
| **22** | I | P | P | P | P | $G_T$ 20.0 | P | P | P | P |
| **23** | Gc 10.0 | $G_T$* 20.0 | $G_T$ 20.0 | $G_T$ 20.0 | $G_T$ 10.0 | $G_C$20.0 | $G_T$ 10.0 | $G_T$ 20.0 | $G_T$ 10.0 | $G_T$ 10.0 |
| **24** | I | P | $G_T$ 10.0 | $G_T$ 20.0 | $G_T$ 20.0 | $G_C$ 20.0 | $G_T$ 10.0 | P | $G_T$ 20.0 | $G_T$ 20.0 |
| **25** | I | P | P | P | P | $G_O$ 20.0 | P | P | P | P |
| **26** | I | $G_T$ 20.0 | P | P | $G_O$ 5.0 | $G_O$ 20.0 | P | P | P | P |
| **27** | P | P | P | P | P | $G_C$ 10.0 | P | P | P | P |
| **28** | I | $G_T$ 10.0 | $G_T$ 10.0 | $G_T$ 20.0 | $G_T$ 20.0 | $G_C$10.0 | P | P | $G_T$ 20.0 | $G_T$ 20.0 |
| **29** | I | P | $G_T$* 20.0 | $G_T$ 10.0 | $G_T$ 10.0 | $G_T$ 20.0 | $G_T$* 20.0 | P | P | P |
| **30** | I | P | $G_T$ 10.0 | $G_T$ 10.0 | $G_T$ 10.0 | $G_T$ 20.0 | P | P | $G_T$ 10.0 | $G_T$ 20.0 |
| **31** | S | S | P | P | P | P | P | P | P | P |
| **32** | I | $G_T$ 10.0 | P | P | $G_T$ 5.0 | $G_T$ 20.0 | $G_T$ 20.0 | P | $G_T$ 10.0 | P |
| **33** | S | S | P | P | P | P | P | P | P | P |

[a] G, gel at room temperature; the numbers are the corresponding minimum gelation concentrations (MGCs) in mg/mL; G*, unstable gel or partial gel; C, clear or transparent; T, translucent; O, opaque; I, insoluble; P, crystallize or precipitate; S, soluble at ~20.0 mg/mL. All tested samples were insoluble in hexanes, insoluble, or precipitated in water. Compound **17** also formed a translucent gel in triethylene glycol at 10.0 mg/mL.

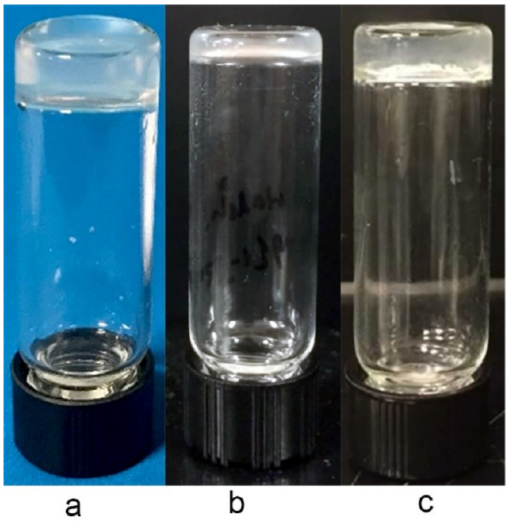


**Figure 5.** Translucent gels formed by compound **18** in (a) DMSO/$H_2O$ (v/v 1:2) at 2.8 mg/mL, (b) compound **30** in 2-propanol at 10 mg/mL, and (c) compound **32** in *n*-butanol at 5.0 mg/mL.

Table 4 and Figures S9−S12. We found that the tetramers **27** and **29** and the hexamers **21**−**22** and **31**−**33** were all effective for this reaction, reaching 100% conversion in less than 2 h. The pentaerythritol derivatives were slightly more effective than trimesic derivatives, showing more conversion at 1 h. The trimeric derivatives **17** and **18** were shown to be less effective; however, they were able to accelerate the reaction to almost full conversion at 3 h. The control reaction only using copper sulfate/sodium ascorbate was much slower, only reaching about 40% at 3 h and 50% conversion at 6 h.

**Synthesis of Triazoles Catalyzed by the Cluster Ligand.** After finding that all hexameric clusters are more effective ligands for the copper-catalyzed reactions, we selected the hexamer glucose derivative **31** (0.5 mol %) to run the click reactions at a larger scale of 300 mg of sugar azide **12** with phenyl acetylene and 1-octyne, and the reactions reached 100% conversions within 3 h and afforded isolated yields of 93% for **34** and 95% for **35**. This indicated that the conditions used in the screening reactions can be scaled up to larger scale reactions though reaction time was longer than small scale screening.

The scope of the substrates was also extended to include a few other alkynes, 5-phenyl-1-pentyne **A3**, 1-ethynylcyclohexan-1-ol **A4**, and 6-chloro-1-hexyne **A5**, as shown in Scheme 2. Using 1 mol % of the hexameric glucosyl conjugate **31**, the reactions of the sugar azide **12** with alkynes **A3** and **A4** reached 100% conversion within 2 h based on the $^1H$ NMR monitoring (Figure S13). The reactions of the 3-acetylphenyl azide **36** with **A4** and **A6** also reached full conversion within 1 h (Figure S14). The $^1H$ NMR of isolated click reaction products are included in Figure S15.

**Catalysis of the Glycoclusters in Gel Form and in Solution Form.** From the above three set of screening reactions, we found that in general the hexameric derivatives performed better as a ligand for the CuAAC reactions. These compounds, however, were not effective gelators, with the exception of the glucosamine derivative **32**, which formed several gels in alcohol and alcohol water mixtures. To explore the effect of supramolecular assemblies, on catalysis, several copper metallogels were created and the gels were used to catalyze various click reactions. We found that gels formed using compound **32** were able to accelerate the click reaction, although the gels were not stable after adding reagents and solvents. A combination of the stronger trimer gelators with more catalytically active hexamer clusters can allow us to obtain stronger supramolecular gels with superior catalytic properties. We were interested in finding out whether the reactions carried out in or on gels are faster than those done in mixtures of solutions.

In order to validate that these gels can be used as matrices for catalysis, the cogels were prepared using the combination of trimeric gelators with the effective hexameric catalysts which were not gelators. After screening several mixtures using gelators, we found that in a 2:1 molar ratio, the gelator **17** was

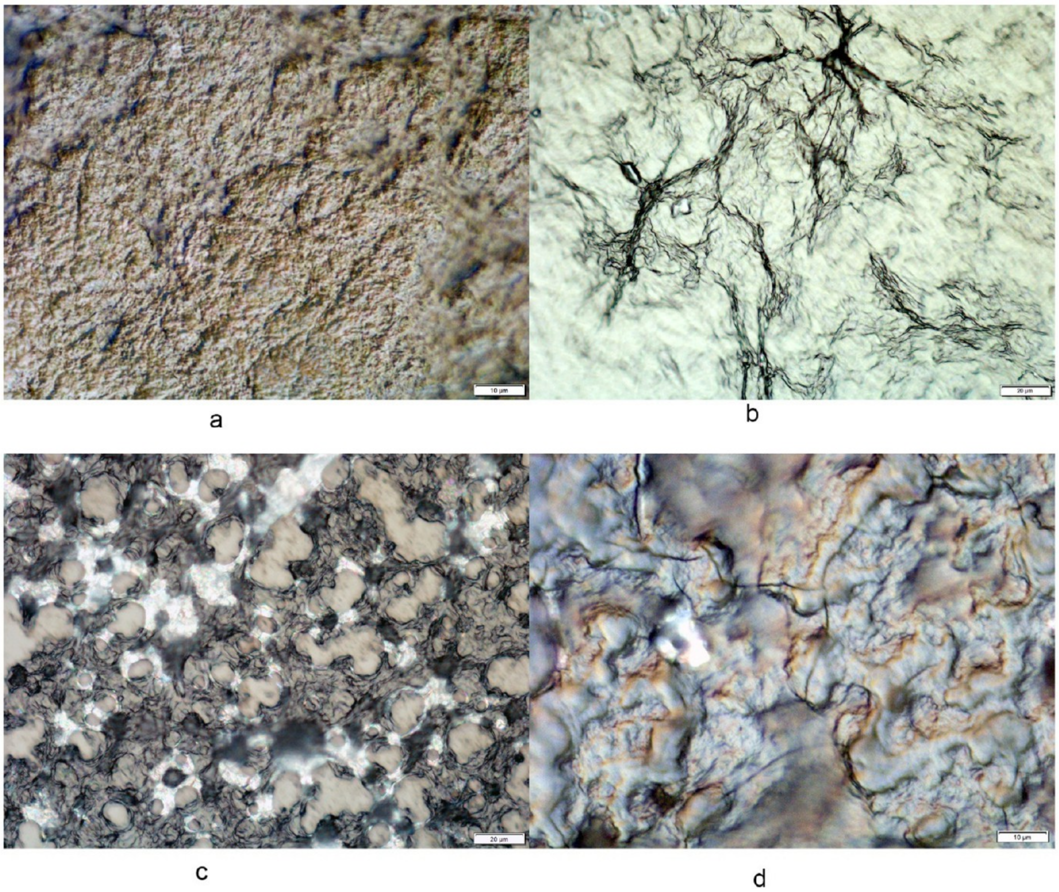


**Figure 6.** (a) Optical micrographs of the gels formed by several compounds. Compound **18** in DMSO/$H_2O$ (v/v 1:2) at 4.0 mg/mL; (b) compound **18** in *n*-BuOH at 4.0 mg/mL; (c) compound **32** in DMSO/$H_2O$ (v/v 1:2) at 10.0 mg/mL, (d) compound **32** in *n*-BuOH at 5.0 mg/mL.

able to form a co-gel with catalyst **21**, and the trimer gelator **24** was able to form a co-gel with the hexamer **33**. The photos of the cogels are included in the Figure S16. The two trimer compounds showed better gelation properties in the appropriate solvents. The prepared cogels were used to test for the same click reactions. The results are shown in Table 5 entries 1−4. The reactants for these reactions are identical to those shown in Table 1; however, these reactions were carried out without stirring. Only gentle swirling of the vials in a shaker was applied so the gels did not degrade. A control experiment was set up the same way except that the gelator was added to the mixture directly and the reaction mixture appeared as a slurry. The reactants and reagents were added on top of the gel or the control reaction mixture. We found that the reactions were significantly faster in the gel phase versus control mixture solution. At 4 h, both gels were able to accelerate the reactions to completion. The reactions were stopped at 8 h, and the isolated yields indicated the effectiveness of the gel-catalyzed reaction compared to the regular solution phased homogeneous mixtures. The results are shown in Table 5 and Figures S16−S18. For both cogels, the gels were more efficient for accelerating the reactions. This indicated that the glycocluster was a more effective catalyst in the gel form than in the slurry form, indicating that self-assembled microstructures can be used to catalyze the reactions.

**Using Gel Columns for Copper-Catalyzed Cycloaddition Reactions.** *Gel Column I Formed by Gelator 18.* To further explore the applications of the gelators for catalysis, several different gelator and cluster combinations were analyzed in order to form stable gels or cogels that can also be used as stationary-phase catalysts. After extensive experimental screening, the gel formed by compound **18** in ethanol−water mixture was selected for the gel column experiment, and this has shown good stability and reusability. As shown in Figure 8, the gel was formed inside the column (syringe), and then the cycloaddition reaction for compound **36** with phenyl acetylene was used as the test reaction (Scheme 3). After the stable gel was formed, the reagents were added on top the gel matrix and allowed to elute slowly through the gel. After the elution finished, the gel was washed with the solvents. The combined filtrate was collected under the gel column and analyzed by $^1$H NMR, which indicated 100% conversion of the azide to the product **37** without byproduct (Figure S19). The same procedure was repeated six times, and the gel was stable after that cycle; the gel was further eluted with ethanol to collect the product adsorbed on to the gel matrix, with an overall yield of 93%. This copper-containing gel column was efficient at catalyzing the cycloaddition reactions and can be utilized as a reusable catalyst. The product obtained was pure and without the need of further purification since the catalysts were immobilized in the gel column.

The gel formed by compound **18** was also prepared and transferred to a scintillation vial, and the same click reaction was performed in a biphase format rather than passing through a gel-column. The reaction was repeated five times, and the gel

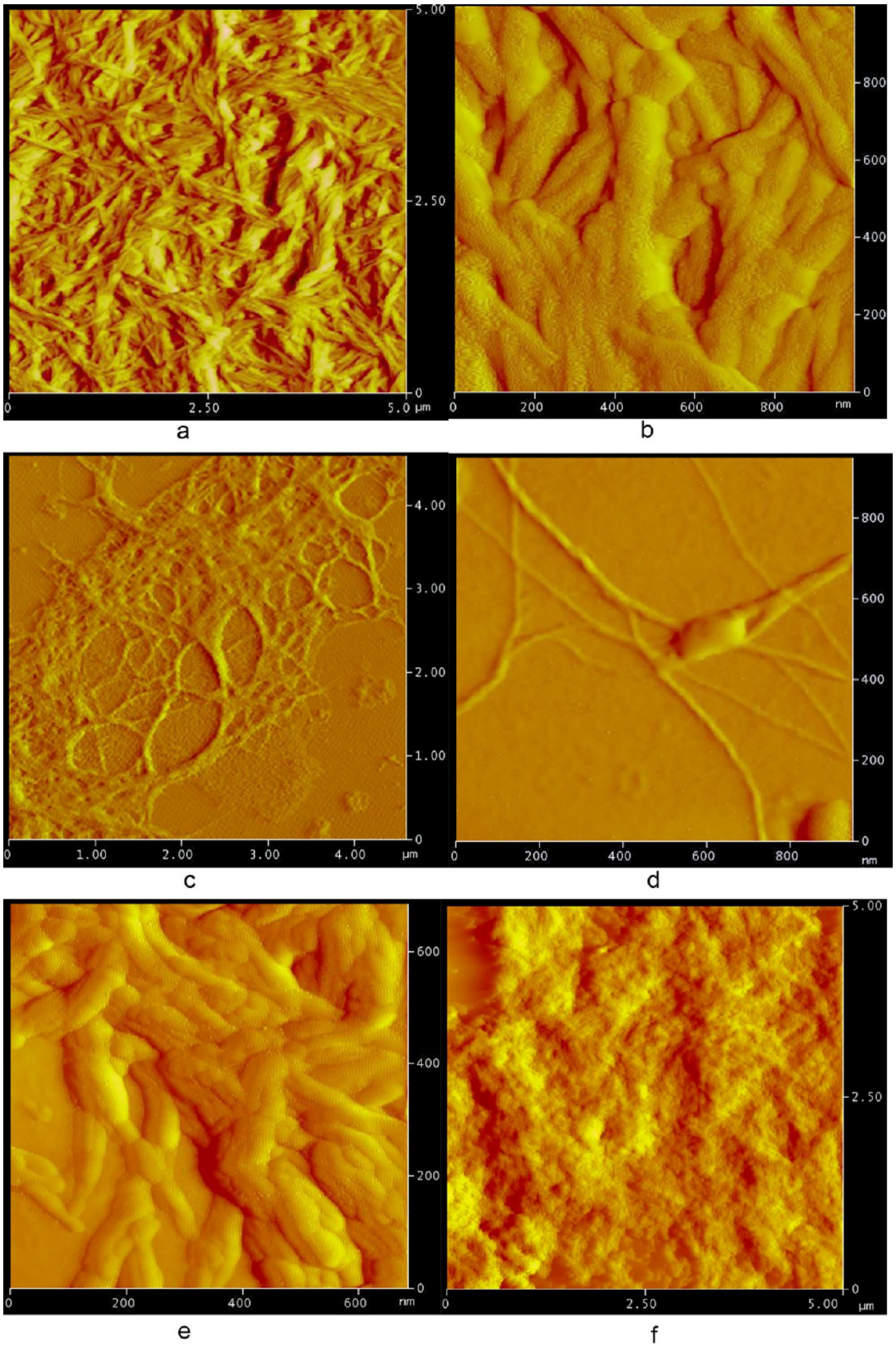
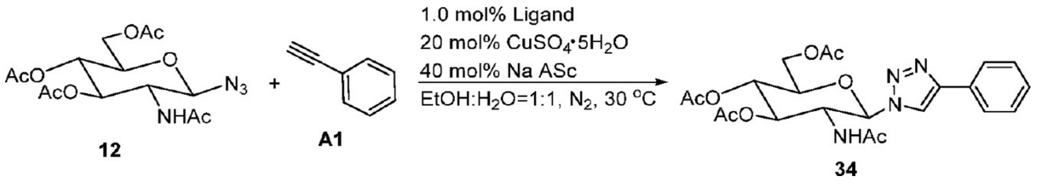


**Figure 7.** AFM images for the gels formed by several compounds. (a, b) compound **18** in *n*-BuOH at 4.0 mg/mL; (c, d) compound **26** in *n*-BuOH at 10.0 mg/mL; (e) compound **28** in ethanol at 10.0 mg/mL; (f) compound **32** in *n*-BuOH at 5.0 mg/mL.

was stable after the fifth cycle for the same reaction; the total product was obtained in 89% yield (Figure S20).

*Gel Column II Catalyzed Reactions.* Since the hexameric glycoconjugates are typically more effective ligands for copper catalysts, to further explore the gelator−cluster catalyst systems, we did several gelation tests using different combinations of the trimers with hexamers. In order for the gels to be reused, the components of the gel need to have certain stability in the eluting solvent. Several monotriazole-based gelators were used to form stable gels with the hexameric clusters; however, the resulting gel columns became unstable after elution with ethanol/water solvent. Various mixtures of trimeric and hexameric glycoconjugates were tested to search for a more stable co-gel system, capable of holding up when flushed with solvent. After several experiments, we found the trimer cluster compound **23** and the hexamer **31** can form a stable co-gel in ethanol−water mixtures. This gel was prepared and transferred to a glass syringe (gel column **II**) and used for several reactions.

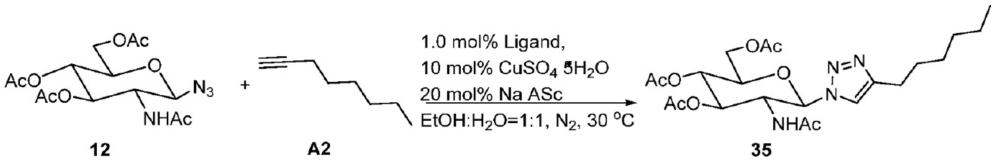
Table 2. Catalytic Effects of Monomeric and Multimeric Triazole Derivatives in Click Reactions[a]



| entry PhC≡CH | compd | ligand (mol %) | time (h), conversion (%) | time (h), conversion (%) | isolated yields (%) |
|---|---|---|---|---|---|
| 1 | control | none | 24, 50 | | |
| 2 | **1** | 1.0 | 5, 83 | | |
| 3 | **2** | 1.0 | 3, 100 | | |
| 4 | **17** | 1.0 | 5, 100 | | |
| 5 | **18** | 1.0 | 5, 100 | | |
| 6 | **19** | 1.0 | 5, 79 | | |
| 7 | **20** | 1.0 | 5, 72 | | |
| 8 | **21** | 1.0 | 1, 93 | 2, 100 | 95 |
| 9 | **22** | 1.0 | 1, 89 | 2, 100 | 93 |
| 10 | **23** | 1.0 | 1, 41 | 5, 64 | |
| 11 | **24** | 1.0 | 4, 68 | 7, 85 | |
| 12 | **25** | 1.0 | 4, 73 | 6, 100 | |
| 13 | **26** | 1.0 | 4, 79 | 6, 100 | |
| 14 | **27** | 1.0 | 4, 74 | 6, 82 | |
| 15 | **28** | 1.0 | 1, 50 | 5, 100 | 92 |
| 16 | **29** | 1.0 | 4, 84 | 7, 100 | |
| 17 | **30** | 1.0 | 4, 95 | | |
| 18 | **31** | 1.0 | 1, 100 | | |
| 19 | **32** | 1.0 | 1, 90 | 2, 100 | |
| 20 | **33** | 1.0 | 2, 100 | | 95 |

[a] Typical conditions: sugar azide 1.0 equiv, 50 mg or 40 mg scale; 2.0 mL of solvent was used for all entries, phenyl acetylene (1.2 equiv to the azide), sodium ascorbate was 2 equiv of the corresponding $CuSO_4 \cdot 5H_2O$, all ratios in % are mol %, using carousel at 30 °C under $N_2$. The percent conversion is based on NMR integration. The information presented in Tables 3 and 4 was gathered similarly with different substrates.

Table 3. Catalytic Effects of Triazole Derivatives in Click Reaction with 1-Octyne

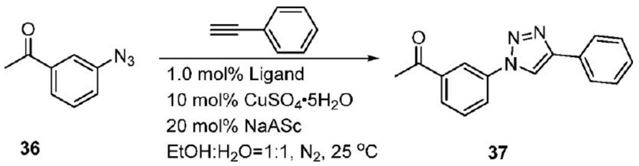


| entry | compd | cluster (mol %) | conversion (%) (2 h) | conversion (%) (4 h) | isolated yield (%) |
|---|---|---|---|---|---|
| 1 | **2** | 1.0 | 72 | 92 | |
| 2 | **17** | 1.0 | 29 | 44 | |
| 3 | **18** | 1.0 | 23 | 38 | |
| 4 | **19** | 1.0 | 46 | 76 | |
| 5 | **22** | 1.0 | 87 | 100 (3 h) | 97 |
| 6 | **23** | 1.0 | 62 | 81 (3 h) | |
| 7 | **24** | 1.0 | 56 | 68 | |
| 8 | **25** | 1.0 | 78 | 98 | |
| 9 | **26** | 1.0 | 63 | 85 (3 h) | |
| 10 | **27** | 1.0 | 77 | 95 | |
| 11 | **28** | 1.0 | 38 | 48 | |
| 12 | **29** | 1.0 | 100 | | |
| 13 | **30** | 1.0 | 75 | 90 | |
| 14 | **31** | 1.0 | 98 | | |
| 15 | **32** | 1.0 | 83 | 100 (3 h) | |
| 16 | **33** | 1.0 | 51 | 95 | 93 |

The gel column **II** was used for the reaction of sugar azide **12** with propargyl alcohol **A6** to synthesize the triazole **12-A6**, and the gel column was stable and effective for the reaction in two cycles at least (Figure S23) and afforded isolated yields of 90% and 88% in the first and second cycles. At the end of the second reaction, the gel was stable and could be reused for another reaction.

Another gel column II was also prepared and was used for the click reactions of the sugar azide **13** with propargyl alcohol and 1-ethynylcyclohexan-1-ol (Scheme 4). The gel was

Table 4. Catalytic Effects of Selected Glycoclusters for Click Reaction of 3-Acetylphenyl Azide



| entry | compd | ligand (mol %) | conversion (%) (0.5 h) | conversion (%) (1 h) | conversion (%) (2 h) | conversion (%) (3 h) |
|---|---|---|---|---|---|---|
| 1 | N/A | | | | 37 | |
| 2 | **17** | 1.0 | 18 | | | 89 |
| 3 | **18** | 1.0 | 14 | | | 93 |
| 4 | **19** | 1.0 | 34 | 72 | 100 | |
| 5 | **22** | 1.0 | 40 | 70 | 100 | |
| 6 | **27** | 1.0 | | | 100 | |
| 7 | **29** | 1.0 | | | 100 | |
| 8 | **31** | 1.0 | 36 | 87 | 100 | |
| 9 | **32** | 1.0 | 35 | 83 | 100 | |
| 10 | **33** | 1.0 | 28 | 82 | 100 | |

Scheme 2. Alkyne Structures and the Triazoles Synthesized Using Cluster Ligand

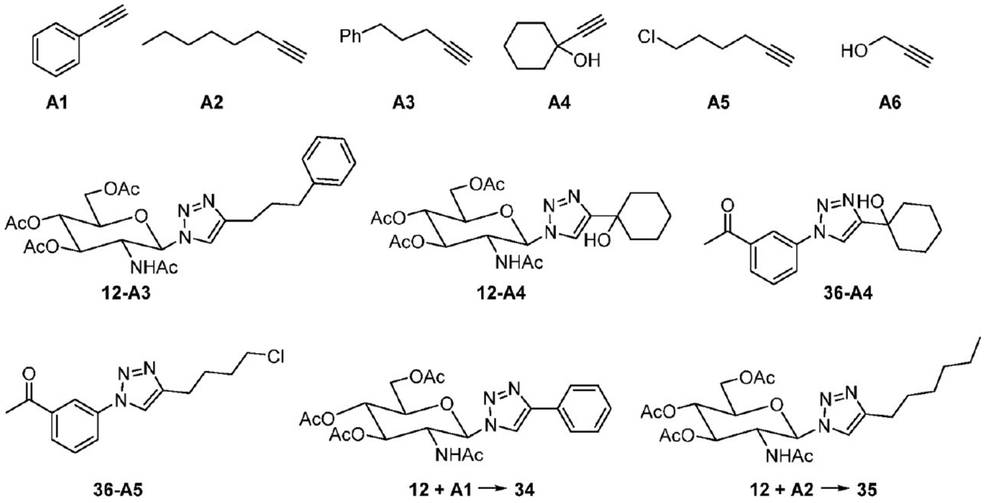
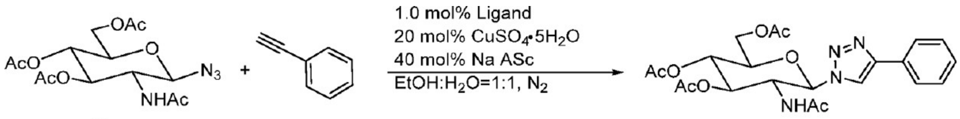


Table 5. Comparison of the Gel versus Solution for Click Reaction for Compound 34



12

34

| entry | gelator and amount in mol | state | conversion (%) (0.5 h) | conversion (%) (0.5 h) | conversion (%) (0.5 h) | yield (%) |
|---|---|---|---|---|---|---|
| 1 | **21**, 1.0%; **17**, 2.0% | gel | 33 | 76 | 95 | 93 |
| 2 | **21**, 1.0%; **17**, 2.0% | control | 27 | 53 | 63 | 69 |
| 3 | **33**, 1.0%; **24**, 2.0% | gel | 31 | 90 | 100 | 91 |
| 4 | **33**, 1.0%; **24**, 2.0% | control | 23 | 61 | 92 | 87 |

prepared by heating the mixture of trimer **23** with hexamer **31** together in EtOH/$H_2O$ (v/v 1:1). The gel column is shown in Figure 9. This gel column II was able to catalyze the synthesis of compound **13-A6** in 92% yield in the first cycle. In the second cycle, different alkyne was added to the same gel column, and the product **13-A4** was obtained in 89% yield (Figure S24).

**Synthesis of Isoxazoles Using Gel-Columns.** Using the same procedure as shown in Figure 8a, another gel-column **I** was prepared using compound **18**. The cycloaddition reaction (Scheme 5) of the 4-chlorophenyl chloroxime **38** and phenyl acetylene was carried out. The reactants, NaAsc together with $NaHCO_3$, were added to the gel column, and the reaction mixture was eluted through the gel column. The product isoxazole **39** was obtained by collecting the filtrate from the gel column with full conversion; however, the gel became unstable after washing with solvent. The total collected filtrate was concentrated, and the pure product was obtained by chromatography in 94% yield (Supporting Information Figure S21).

Using gel column II, the isoxazole reaction using compound **38** was carried out by eluting through the gel column (Figure

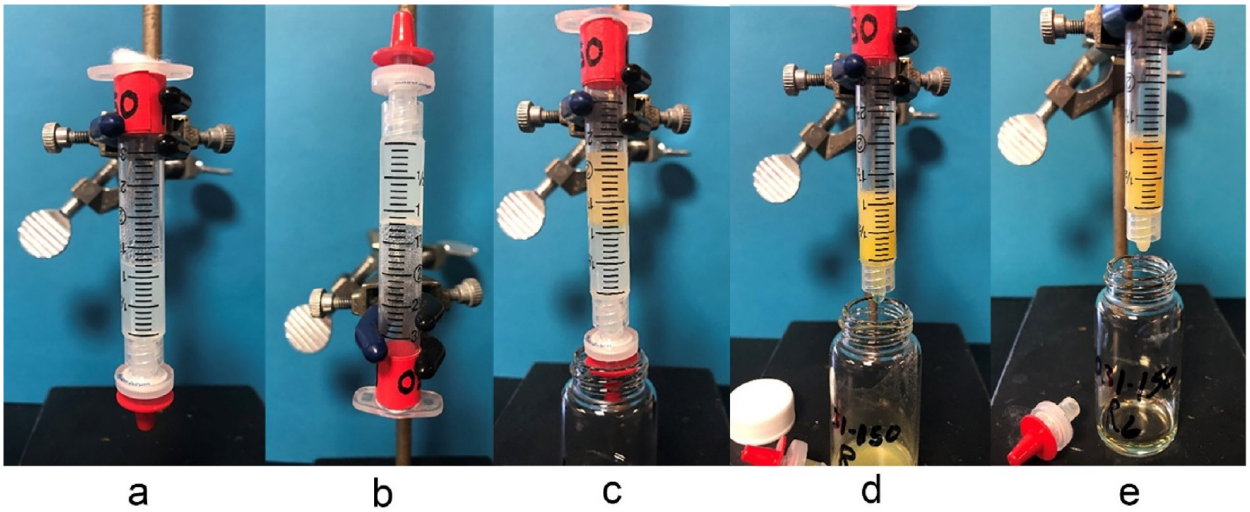
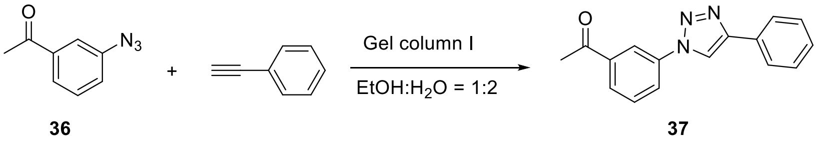
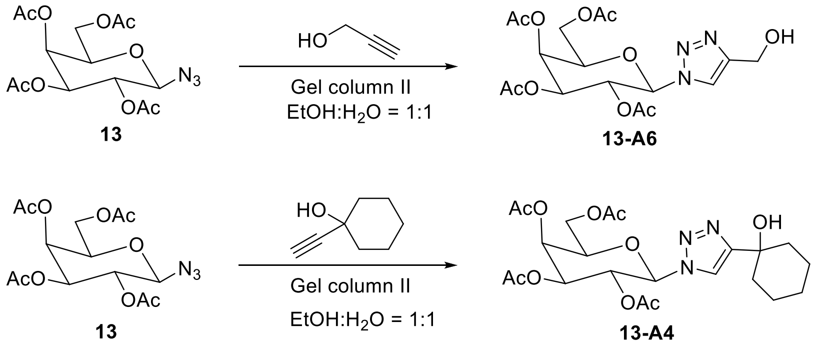


**Figure 8.** (a) Gel column (I) made of compound **18** (10.0 mg, 0.007 mmol) containing $CuSO_4$ pentahydrate (6.0 mg, 0.022 mmol) in 1.5 mL of $EtOH/H_2O$ (v/v, 1:2); (b) reversed gel column to show the stability of gel; (c) reaction mixture was added on top of gel column: phenyl acetylene (30 μL, 0.27 mmol), 3-acetyl phenyl azide (35.0 mg, 0.22 mmol), NaAsc (9.0 mg, 0.044 mmol) dissolved in 1.0 mL of $EtOH/H_2O$ (v/v, 1:2); (d) after the elution of the reaction mixture; (e) at the end of the sixth round of elution.

**Scheme 3. Synthesis of Triazole 37 on Gel Column I**



**Scheme 4. Synthesis of Triazoles 13-A4 and 13-A6 Using Gel Column II**



S25) similar to that described in Figure 9, except for the reagent for the reaction with the addition of $NaHCO_3$. To show the recyclability of the gel column, two separate isoxazole syntheses were carried out on the same gel column. The first cycle of reagents loaded to the gel was chloroxime **38** and propargyl alcohol. The isoxazole compound **40** was obtained by collecting the filtrate in 93% yield. After rinsing with solvent, the same gel column II was reused for another cycle using phenyl acetylene as the substrate, the filtrate was collected and worked up to afford compound **39** in 92% yield (Figure S26). Therefore, the cogels formed by the combination of a trimer with a hexamer afforded stable gels and effective, reusable gel catalysts.

## ■ CONCLUSIONS

Three main series of branched and dendritic glycoconjugates containing protected glucose and glucosamine triazole moieties have been designed and synthesized through click chemistry. The self-assembling properties of these compounds were analyzed in several polar organic solvents. Many compounds with three or four triazole branches were effective gelators, forming gels in at least one of the tested solvents. In contrast, the glycoclusters with six triazole sugar branches were not as effective as gelators, with only the glucosamine derivatives being able to form gels. The glucose and galactose analogues were not found to be gelators. The gels showed typically fibrous or thin film networks based on AFM characterizations. These glycoconjugates were also studied for their effects at accelerating CuAAC reactions of sugar azide with phenyl acetylene and 1-octyne. We found that for phenyl acetylene, all glycoclusters synthesized in this study showed certain rate acceleration, with the hexameric glycoclusters being far superior to the others. The hexameric dipentaerythritol derivatives with glucose, glucosamine, and galactosyl triazoles **31**−**33** were the most effective ligands. The glucose derivative **31** was especially effective for the phenyl acetylene click reaction and was used for the synthesis of several triazole

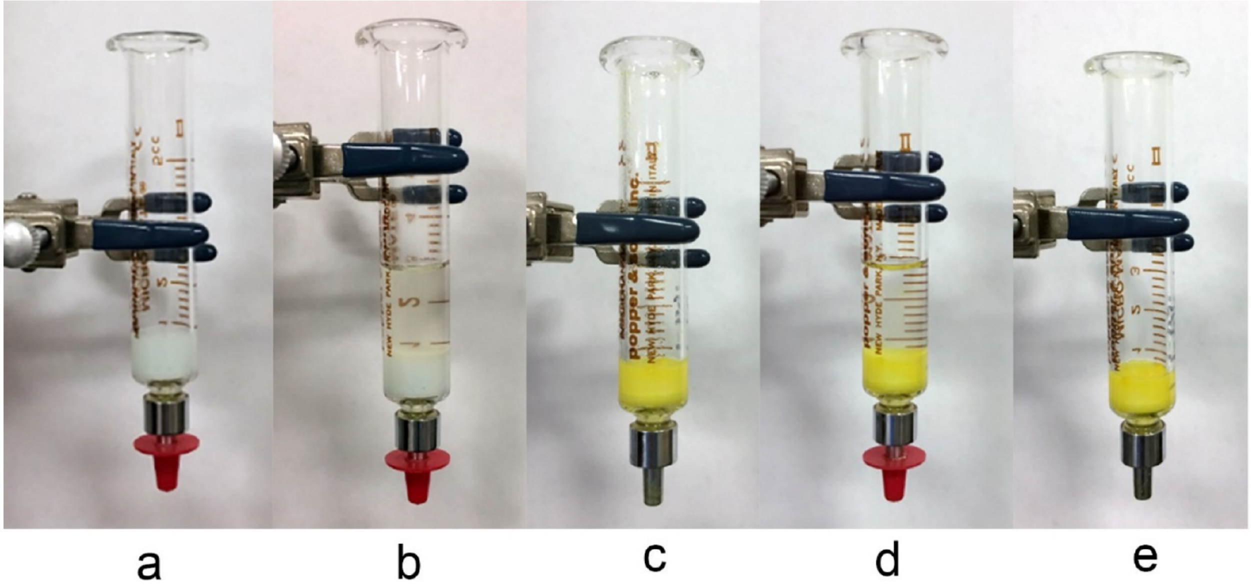
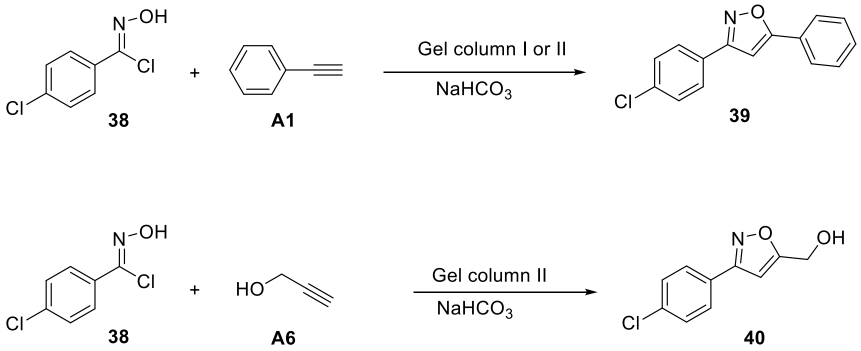


**Figure 9.** (a) Gel column II prepared by compound **23** (10.0 mg, 0.0074 mmol), **31** (5.0 mg, 0.0018 mmol), and $CuSO_4 \cdot 5H_2O$ (9.2 mg, 0.0186 mmol) in 0.8 mL of $EtOH/H_2O$ (v/v, 1:1); (b) after reaction mixture of the azide **13** (68.6 mg, 0.184 mmol) and propargyl alcohol (12.4 mg, 0.22 mmol), and NaAsc (14.8 mg, 0.074 mmol) dissolved in 2.0 mL were added $EtOH/H_2O$ (v/v, 1:1) was added to the gel; (c) after elution of the gel column in (b); (d) after addition reaction mixture, the same as in (b) except propargyl alcohol was replaced with 1-ethynyl-1-cyclohexanol (27.3 mg, 0.22 mmol); (e) after elution of the gel in (d).

**Scheme 5. Synthesis of Isoxazole Using the Gelator Catalyst**



derivatives, affording high yields in a short time. The hexameric derivatives, synthesized from trimesic acids **21**−**22** and some trimeric clusters, were also effective catalysts, reaching almost full conversion quickly, and the products were obtained in high yields. Interestingly, the performance of the glycoclusters was different for 1-octyne substrate in comparison to phenyl acetylene substrate. However, the general trend of a higher number of branches affording more effective ligands also follows. Using 3-acetylphenyl azide as the substrate, a similar trend was observed with all hexamers showing effectiveness for the reaction. Several gels were prepared and studied for their catalytic effects, and we found that the gels were able to accelerate the reactions more efficiently than in solution. Several click reactions were carried out using the stable copper sulfate gels formed by compound **18** and the cogels formed by a trimer with a hexameric cluster. These gels demonstrated effectiveness in catalyzing CuAAC reactions and for isoxazole synthesis; moreover, the gel columns can be reused for different substrates or for the same substrate but reusable for at least six cycles. The supramolecular gels from the current study can also be useful for other catalytic reactions where copper ions or other metal ions are used as the catalysts.

## ■ EXPERIMENTAL SECTION

Reagents and solvents were used as received from the suppliers. All purifications were conducted using flash column chromatography using 230−400 mesh silica gel with a gradient of solvent systems. $^1H$ NMR and proton-decoupled $^{13}C$ NMR spectra were obtained with a Bruker 400 MHz NMR spectrometer in $d_6$-DMSO, $D_2O$, or $CDCl_3$. The chemical shifts were reported using $CDCl_3/d_6$-DMSO as the internal standard at 7.26/2.50 and 77.00/39.50 ppm, respectively. 2D NMR experiments (HSQC, COSY) were also conducted using a 400 MHz Bruker NMR spectrometer to assist the proton and carbon signal assignment. Structural assignments were made with additional information from gCOSY, gHSQC, and gHMBC experiments. Melting point measurements were carried out using a Fisher Jones melting point apparatus. The molecular mass was measured using LCMS on an Agilent 6120B Single Quad mass spectrometer and LC1260 system. HRMS was acquired on a Bruker 10 Telsa APEX-Qe Fourier-transform ion cyclotron resonance mass spectrometer (FTICR-MS) with an Apollo II ion source using positive electrospray ionization. Optical micrographs were obtained using an Olympus BX60 M optical microscope and the Olympus DP73-1-51 high-performance 17MP digital camera with pixel shifting and Peltier cooled. The imaging software for image capturing was CellSens 1.11.

**Gelation Test.** Approximately 2 mg of the desired compound was placed in a 1-dram vial, and 0.1 mL of the gelation solvent or solution was transferred inside the vial to attain a concentration of 20 mg/mL. The vial was then heated until the gelator dissolved fully; sometimes, the mixture was sonicated to help with dissolving the compound and the mixture was allowed to cool for approximately 15 min or longer for the gel to form. After this period, if the solution was clear, this was recorded as soluble; if the solid reappeared, this was recorded as a precipitate; if the sample formed a gel, then the vial was inverted; if no solvent was flowing, this indicated that a stable gel was formed; otherwise, this was recorded as unstable gel. If gelation occurred, another 0.1 mL was added and the method was repeated until an unstable gel was formed. The minimum gelation concentration (MGC), the concentration prior to unstable gelation, was recorded.

**Atomic Force Microscopy.** The gels were prepared about 12 h before sample preparation. A same gel sample was transferred to a precleaned glass slide (1 × 5 in.) and allowed to air dry for 1 day or so before being observed under an atomic force microscope (AFM). AFM measurements were carried out using a Veeco Dimension 3100 atomic force microscope using tapping mode. The tips used were Nanosensors silicon AFM probes with a resonant frequency of 340−500 kHz and a force constant of 20−45 N m$^{-1}$.

**Synthesis of Alkyne Building Blocks 3−10.** *Synthesis of the Alkyne 3.*[50] Trimesic acid (0.5 g, 2.3 mmol, 1 equiv) was dissolved in 10 mL of DCM (anhydrous) in a 50 mL round-bottomed flask. Oxalyl chloride (0.91 mL, 10.35 mmol, 4.5 equiv) was added dropwise over a period of 10 min at 0 °C. A drop of DMF (anhydrous) was added to the reaction mixture, and the resulting solution was stirred under reflux in an oil bath for 12 h. Excess oxalyl chloride was removed under reduced pressure. The trimesic acyl chloride as a pale-yellow semisolid was used in the next step without further purification. Propargyl alcohol (0.91 mL, 16.2 mmol, 3.6 equiv) and triethyl amine (3.79 mL, 27 mmol, 6 equiv) were dissolved in 20 mL of DCM (anhydrous) and chilled to 0 °C. The above-prepared triacid chloride (1.20 g, 4.5 mmol, 1 equiv) was dissolved in 10 mL of DCM (anhydrous) and added dropwise over a period of 10 min at 0 °C. The resulting mixture was then allowed to warm to ambient temperature and stir for 24 h. Water (5 mL) was added to quench the reaction and extracted with DCM (15 mL × 3). The combined organic layers were dried over $Na_2SO_4$ (anhydrous), concentrated, and purified by column chromatography to obtain a gray solid (1.32 g, 86%) as the desired product: mp 99.0−101.0 °C; $^1$H NMR (400 MHz, $d_6$-DMSO) $\delta$ 8.67 (s, 3H), 5.05 (d, $J$ = 2.4 Hz, 6H), 3.67 (t, $J$ = 2.4 Hz, 3H); $^{13}$C{$^1$H} NMR (100 MHz, $d_6$-DMSO) $\delta$ 163.2, 133.9, 130.6, 78.5, 77.9, 53.4; LCMS (ESI/Quadrupole) $m/z$ $[M + H]^+$ calcd for $C_{18}H_{13}O_6$325.1, found 325.1.

*Synthesis of the Alkyne 4.*[51,52] Trimesic acid (0.50 g, 2.30 mmol, 1 equiv) was dissolved in 10 mL of DCM (anhydrous) in a 50 mL round-bottomed flask. Oxalyl chloride (0.91 mL, 10.35 mmol, 4.5 equiv) was added dropwise over a period of 10 min at 0 °C. A drop of DMF (anhydrous) was added to the reaction mixture, and the resulting solution was stirred under reflux in an oil bath for 12 h. Excess oxalyl chloride was removed under reduced pressure. The trimesic acid chloride as a pale-yellow semisolid was used in the next step without further purification. Propargyl amine (0.45 mL, 6.6 mmol, 3 equiv) and pyridine (1.10 mL, 13.2 mmol, 6 equiv) were dissolved in 10 mL of DCM (anhydrous) and chilled to 0 °C. The acid chloride thus prepared (0.60 g, 2.2 mmol, 1 equiv) was dissolved in 10 mL of DCM (anhydrous), added dropwise over a period of 10 min at 0 °C to the reaction mixture, and then allowed to warm to ambient temperature and stir for 24 h. Solvent was removed under reduced pressure, and the obtained residue was dissolved in ethyl acetate (50 mL) and washed with aqueous 2 N $H_2SO_4$ (5 mL) followed by water (5 mL) and saturated $NaHCO_3$ solution (5 mL). The organic layer was dried over anhydrous $Na_2SO_4$ (anhydrous), and the solvent was evaporated to yield a white solid (0.54 g, 74%) as the desired product: mp 267.4−270.9 °C; $^1$H NMR (400 MHz, $d_6$-DMSO) $\delta$ 9.15 (t, $J$ = 5.7 Hz, 3H), 8.44 (s, 3H), 4.10 (dd, $J$ = 5.7, 2.5 Hz, 6H), 3.14 (t, $J$ = 2.5 Hz, 3H); $^{13}$C{$^1$H} NMR (100 MHz, $d_6$-DMSO) $\delta$ 165.6, 134.9, 129.4, 81.5, 73.5, 29.2; LCMS (ESI/Quadrupole) $m/z$ $[M + H]^+$ calcd for $C_{18}H_{16}N_3O_3$ 322.1, found 322.0.

*Synthesis of the Alkyne 5.*[53] Trimesic acid (2.10 g, 10.0 mmol, 1 equiv) was dissolved in DCM (anhydrous, 40 mL) in a 50 mL round-bottomed flask, and the reaction mixture was cooled to 0 °C. Oxalyl chloride (3.81 mL, 45.0 mmol, 4.5 equiv) in 0.46 mL of DMF (anhydrous) was added to the reaction mixture over a period of 10 min. The reaction continued to stir for 4 h from 0 °C to room temperature and then the temperature was further increased to 50 °C in an oil bath for another 16 h. The reaction mixture became clear. The reaction mixture was concentrated under reduced pressure to give a crude acyl chloride as a solid and was used directly for the next step without purification. Pyridine (2.73 mL, 35.0 mmol, 3.5 equiv), $K_2CO_3$ (4.83 g, 35.0 mmol, 3.5 equiv), and 9 mL of DCM (anhydrous) were added to the above prepared acyl chloride in the given order. Dipropargylamine (3.63 mL, 35.0 mmol, 3.5 equiv) was added to the reaction mixture at 0 °C over a period of 10 min. The reaction was stirred at room temperature for 18 h. The reaction was quenched with $NaHCO_3$(3 mL, 5% aq) and extracted with DCM (20 mL × 3). Crude product was dried over $Na_2SO_4$ (anhydrous) and purified by column chromatography using eluent from pure hexanes to 20% EtOAc/hexanes to afford a white solid (3.52 g, 8.1 mmol, 81%) as the desired product ($R_f$ = 0.6 in 50% EtOAc/hexanes): $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.80 (m, 3H), 4.31 (br s, 12H), 2.32 (s, 6H); $^{13}$C{$^1$H} NMR (100 MHz, $CDCl_3$) $\delta$ 168.7, 135.8, 127.6, 77.4, 73.5, 38.1, 34.3; LCMS (ESI/Quadrupole) $m/z$ $[M + H]^+$ calcd for $C_{27}H_{22}N_3O_3$ 436, found 436.

*Synthesis of Alkyne 6.*[54] 1,1,1-Tris(hydroxymethyl)ethane (1.00 g, 8.5 mmol, 1 equiv) was added to a solution of NaH (1.36 g, 33.9 mmol, 4 equiv, 60 wt %) in anhydrous DMF (15 mL). After the solution was stirred at 0 °C for 0.5 h, propargyl chloride (3.6 mL, 33.9 mmol, 4 equiv, 70 w% in toluene) was added to the reaction mixture. The reaction mixture was stirred at room temperature for 1 h. The reaction mixture was quenched with water (3 mL). Workup was performed with EtOAc (10 mL x 3) and the combined organic layers were dried over $Na_2SO_4$ (anhydrous), concentrated and purified by column chromatography using eluent from 5% to 15% EtOAc/hexanes to give a light yellow liquid (1.61 g, 6.9 mmol, 83%) as the desired product ($R_f$ = 0.55 in 30% EtOAc/hexanes): $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 4.11 (d, $J$ = 2.4 Hz, 3H), 3.39 (s, 6H), 2.39 (t, $J$ = 2.4 Hz, 3H), 0.96 (s, 3H); $^{13}$C{$^1$H} NMR (100 MHz, $CDCl_3$) $\delta$ 80.1, 74.0 72.7, 58.6, 40.3. 17.3; LCMS (ESI/Quadrupole) $m/z$ $[M + H]^+$ calcd for $C_{14}H_{19}O_3$ 235, found 235.

*Synthesis of Intermediate 15.* 1,1′-Carbonyldiimidazole (2.292 g, 14.1 mmol, 3 equiv) was dissolved in 8 mL of anhydrous THF and added to a dried 50 mL round-bottomed flask. The reaction mixture was cooled to 0 °C. To the mixture, compound **14**[49,55] (1.00 g, 4.7 mmol, 1 equiv) was dissolved in 8 mL of anhydrous THF and added dropwise over 5 min. The resulting solution was warmed to room temperature and stirred overnight for 16 h. THF was removed under reduced pressure, leaving a white solid. The crude product was dissolved in 60 mL of DCM and washed with water (30 mL × 2). The organic layer was dried with $Na_2SO_4$ (anhydrous) and filtered, and solvent was removed under reduced pressure. The crude product was purified via column chromatography ($SiO_2$) using eluent from 20% to 80% EtOAc/hexanes to afford a white solid (1.763 g, 94%) as the desired product (compound **15**, $R_f$ = 0.25 in 60% EtOAc/hexanes): mp 113.0−115.0 °C; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 8.15−8.11 (m, 2H), 7.42−7.38 (m, 2H), 7.09−7.05 (m, 2H), 4.56 (s, 4H), 4.13 (d, $J$ = 2.4 Hz, 4H), 3.65 (s, 4H), 2.34 (t, $J$ = 2.4 Hz, 2H); $^{13}$C{$^1$H} NMR (100 MHz, $CDCl_3$) $\delta$ 148.3, 137.0, 130.9, 117.0, 78.7, 77.2, 75.2, 67.9, 66.4, 58.7, 43.9; HRMS (ESI/ICR) $m/z$ $[M + Na]^+$ calcd for $C_{19}H_{20}N_4O_6Na$ 423.1275, found 423.1274.

*Synthesis of Alkyne 7.* Compound **15** (100 mg, 0.25 mmol, 1 equiv) was dissolved in THF (2 mL) and added to a dried and nitrogen-flushed 50 mL round-bottomed flask. The reaction mixture was cooled to 0 °C via an ice bath, and propargyl amine (40 $\mu$L, 0.625 mmol, 2.5 equiv) was then added dropwise. The reaction was warmed to room temperature and stirred for 18 h. THF was removed under reduced pressure, the remaining solid was dissolved in EtOAc (10 mL), followed by an aqueous workup using DI water (10 mL × 2) and EtOAc (10 mL × 1) was carried out. The organic layers were then treated with $Na_2SO_4$(anhydrous) and filtered, and solvent was removed under reduced pressure. The crude product was purified via column chromatography using eluent from pure hexanes to 60% EtOAc/hexanes. A clear liquid (88.4 mg, 95%) was obtained as the desired product ($R_f$ = 0.45 in 45% EtOAc/hexanes): $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 4.99 (s, 2H), 4.15 (s, 4H), 4.11 (d, $J$ = 2.3 Hz, 4H), 3.96 (d, $J$ = 2.6 Hz, 4H), 3.51 (s, 4H), 2.41 (t, $J$ = 2.3 Hz, 2H), 2.25 (t, $J$ = 2.6 Hz, 2H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) $\delta$ 155.7, 79.7, 79.6, 74.5, 71.6, 68.5, 64.1, 58.7, 43.6, 30.8; HRMS (ESI/ICR) $m/z$ $[M + Na]^+$ calcd for $C_{19}H_{22}N_2O_6Na$ 397.1370, found 397.1367.

*Synthesis of Alkyne **8**.* 5-Hexynoic acid (0.172 mL, 1.56 mmol, 2.2 equiv) was dissolved in 2 mL of anhydrous DCM with one drop of DMF in a dried and nitrogen-flushed 50 mL round-bottomed flask. The temperature was decreased to 0 °C, and oxalyl chloride (0.146 mL, 1.70 mmol, 2.4 equiv) was added to the reaction mixture. The reaction stirred at 0 °C for 10 min and then warmed to room temperature for 3 h. Compound **14** (150 mg, 0.71 mmol, 1 equiv), $K_2CO_3$ (294 mg, 2.14 mmol, 3 equiv), and DMAP (8.7 mg, 0.071 mmol, 0.1 equiv) were dissolved in 3 mL of anhydrous DCM in a dried and nitrogen-flushed round-bottomed flask. The temperature was reduced to 0 °C, and the crude acid chloride was added dropwise. The reaction was then warmed to room temperature and the reaction stirred for 5 h. The reaction was quenched with 0.5 mL $NaHCO_3$ (5% aq). The reaction mixture then underwent an aqueous workup using DCM (20 mL × 2) and DI water (20 mL × 2). The organic layers were combined, dried with $Na_2SO_4$, and filtered, and solvent was removed under reduced pressure, leaving a light-yellow oil. The crude product was purified via column chromatography ($SiO_2$) using eluent from pure hexanes to 25% EtOAc/hexanes. A clear liquid (231.7 mg, 82%) was obtained as the desired product ($R_f$ = 0.5 in 20% EtOAc/hexanes): $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 4.11 (d, $J$ = 2.4 Hz, 6H), 3.39 (s, 6H), 2.39 (t, $J$ = 2.4 Hz, 3H), 0.96 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) $\delta$ 80.1, 74.0, 72.7, 58.6, 40.3, 17.3; HRMS (ESI/ICR) $m/z$ $[M + Na]^+$ calcd for $C_{23}H_{28}O_6Na$ 423.1778, found 423.1778.

*Synthesis of Compound **16**.* Dipentaerythritol (2.0 g, 7.85 mmol, 2 equiv) was dried by coevaporation with toluene (5 mL × 2) followed by addition of benzaldehyde (413 mg, 3.93 mmol, 1 equiv), PTSA monohydrate (137.5 mg, 0.80 mmol, 0.2 equiv), and 15 mL of anhydrous DMF. The mixture was stirred for 20 h at 90 °C under nitrogen. The reaction mixture was cooled to room temperature and then quenched by addition of saturated $NaHCO_3$ solution (5 mL). The solvent was removed under vacuum to afford the crude product, which was purified by column chromatography using eluent from pure DCM to 8% MeOH/DCM to afford a white solid as compound **16** (774 mg, 2.26 mmol, 58%). When 1 equiv of the dipentaerytritol (2.0 g, 7.85 mmol, 1 equiv), benzaldehyde (827 mg, 7.85 mmol, 1 equiv), and PTSA monohydrate (137.5 mg, 0.80 mmol, 0.1 equiv) were added via a similar procedure the desired product **16** was obtained in 40% yield (1.08 g, 3.16 mmol, 40%) together with a significant amount of the dimeric benzylidene acetal. Compound **16** was obtained as a mixture of 1:1 stereoisomers, inseparable by flash chromatography ($R_f$ = 0.55 in 10% MeOH/DCM): mp 112.0−119.0 °C; $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 7.49−7.31 (m, 5 H), 5.42 (s, 1H), 4.71−4.53 (m, 1H), 4.23−4.16 (m, 3H), 3.98−3.88 (m, 2H), 3.87−3.77 (m, 2H), 3.69 (d, $J$ = 5.4 Hz, 1H), 3.61 (s, 1H), 3.47−3.35 (m, 7H), 3.29−3.25 (m, 2H), 3.17 (s, 1H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) $\delta$ 139.19, 139.16, 129.1, 128.5, 126.7, 126.6 101.2, 71.5, 71.1, 70.9, 70.2, 69.8, 69.5, 61.8, 61.5, 61.3, 60.4, 46.31, 46.30; HRMS (ESI/ICR) $m/z$ $[M + Na]^+$ calcd for $C_{17}H_{26}O_7Na$ 365.1571, found 365.1570.

*Synthesis of Alkyne **9**.* Compound **16** (100 mg, 0.29 mmol, 1 equiv) was added to a solution of NaH (52 mg, 60 wt % in mineral oil, 1.32 mmol, 4.5 equiv) in anhydrous DMF (3 mL) and cooled to 0 °C. Then propargyl chloride (0.10 mL, 1.32 mmol, 70 wt % in toluene, 4.5 equiv) was added to the reaction mixture. The reaction mixture was stirred at room temperature for 4 h at which time TLC indicated completion of reaction. The reaction was cooled to 0 °C and quenched with 1 mL of water. The solvent was removed, and the crude product was obtained by phase extraction of using water $H_2O$ (3 mL) and DCM (5 mL × 2). The organic layers were combined and dried over $Na_2SO_4$, solvent was removed, and the crude product was purified by flash chromatography using eluent from 2% to 30% EtOAc/hexanes to afford a light brown liquid as the desired product (127.1 mg, 0.26 mmol, 88%); this was a 1:1 mixture of stereoisomers: $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 7.52−7.44 (m, 2H), 7.41−7.30 (m, 3H), 5.44 (s, 1H), 4.22 (d, $J$ = 2.4 Hz, 1H), 4.18−4.09 (m, 8H), 3.95−3.86 (m, 3H), 3.76 (s, 1H), 3.58−3.50 (m, 7H), 3.41 (d, $J$ = 4.5 Hz, 2H), 3.28 (s, 1H), 2.50−2.41 (m, 4H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) $\delta$ 138.4, 128.9, 128.3, 126.13, 126.08, 101.82, 101.75, 80.1, 80.03, 79.99, 79.7, 74.6, 74.24, 74.15, 74.1, 71.0, 70.1, 70.01, 69.95, 69.8, 69.1, 69.0, 68.9, 58.8, 58.7, 45.2, 45.1, 39.0, 38.8; HRMS (ESI/ICR) $m/z$ $[M + Na]^+$ calcd for $C_{29}H_{34}O_7Na$ 517.2197, found 517.2197.

*Synthesis of Alkyne **10**.*[16,26] Dipentaerythritol (400 mg, 1.57 mmol, 1 equiv) was added to a solution of NaH (409 mg, 10.23 mmol, 6.5 equiv, 60 wt %) in anhydrous DMF (3 mL) and cooled to 0 °C. Then propargyl chloride (1.08 g, 10.23 mmol, 6.5 equiv, 70 w% in toluene) was added to the reaction mixture. The reaction mixture was stirred at room temperature for 5 h. The TLC test indicated that the reaction was completed. The reaction was quenched with $H_2O$ (1 mL) or $NH_4Cl$ solution. After removal of the solvent, 2 mL of water was added to the residue and the crude was extracted with DCM (10 mL × 3). The combined organic layers were dried over $Na_2SO_4$, and then the solvent was removed to obtain the crude product, which was purified by flash chromatography using eluent from 2% EtOAc/hexanes to 40% EtOAc/hexanes to afford the desired product as a light brown oil (688.6 mg, 1.43 mmol, 91%) ($R_f$ = 0.5 in 25% EtOAc/hexanes): $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 4.12 (d, $J$ = 2.4 Hz, 12H), 3.51 (s, 12H), 3.38 (s, 4H), 2.41 (t, $J$ = 2.4 Hz, 6H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) $\delta$ 80.2, 74.1, 69.8, 69.2, 58.7, 45.1; LCMS (ESI/Quadrupole) $m/z$ $[M + H]^+$ calcd for$C_{28}H_{35}O_7$ 483, found 483.

**General Procedure for the Synthesis of Triazole Products.** To a 50 mL round-bottomed flask, the sugar azide and alkyne were dissolved in *t*-BuOH/$H_2O$/THF (v/v/v = 1/1/1) or EtOH/$H_2O$ (v/v = 1/1). $CuSO_4$ or $CuSO_4$ pentahydrate and L-ascorbic acid sodium salt was added to the reaction mixture. The reaction was stirred for 6−36 h at room temperature or heated at 30 or 50 °C in an oil bath under $N_2$ atmosphere. Solvent was removed under reduced pressure to give the crude product. For some experiments, no phase−phase extraction workup protocol was performed, after solvent was removed, the crude product was directly loaded to the column for purification. For most of the experiments, workup was performed by DCM and water. The organic layers were then combined, dried with $Na_2SO_4$(anhydrous), and filtered, and the solvent was removed under reduced pressure. The crude product was purified by flash column chromatography ($SiO_2$) using pure DCM to 5−15% MeOH/DCM solvent system as the eluent to afford the desired triazole cluster compound. Only the amount of reagent, solvent, reaction conditions, and characterization of the final cluster products ($R_f$ value, melting point, $^1H$ and $^{13}C$ NMR, and mass spectra data) are provided for each experiment.

*Synthesis of Trimeric Triazole Linked Cluster **17**.* Sugar azide **11**[48] (125 mg, 0.335 mmol, 3.3 equiv), alkyne **3** (33 mg, 0.102 mmol, 1 equiv), $CuSO_4$ pentahydrate (15.3 mg, 0.061 mmol, 0.6 equiv), L-ascorbic acid sodium salt (24.1 mg, 0.122 mmol, 1.2 equiv), and 6 mL of solvent mixture of *t*-BuOH/$H_2O$/THF (v/v/v = 1/1/1) were used. The reaction mixture was stirred at room temperature for 24 h. The crude was purified by column chromatography with MeOH/DCM (1% to 3%) to afford a white solid (125 mg, 86%) as the desired product ($R_f$ = 0.2 in 2% MeOH/DCM): mp 216.0−218.0 °C; $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 8.83 (s, 3H, phenyl-H), 7.95 (s, 3H, triazole-H), 5.89 (d, $J$ = 8.8 Hz, 3H, H-1), 5.53−5.46 (m, 6H, $-CH_2O-$), 5.45−5.38 (m, 6H, H-2, H-3), 5.24 (t, $J$ = 9.8 Hz, 3H, H-4), 4.30 (dd, $J$ = 12.6, 4.9 Hz, 3H, $H_a$-6), 4.15 (dd, $J$ = 12.6, 1.8 Hz, 3H, $H_b$-6), 4.04−3.98 (m, 3H, H-5), 2.06 (s, 9H), 2.05 (s, 9H), 2.01 (s, 9H), 1.83 (s, 9H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) $\delta$ 170.5, 169.9, 169.3, 168.8, 164.5, 143.1, 135.1, 130.9, 122.7, 85.8 (C-1), 75.3 (C-5), 72.6 (C-3), 70.3 (C-2), 67.7 (C-4), 61.5 (C-6), 58.4

(−CH$_2$O−), 20.7, 20.50, 20.48, 20.1; HRMS (ESI/ICR) *m*/*z* [M + 2Na]$^{2+}$ calcd for [C$_{60}$H$_{69}$N$_9$O$_{33}$Na$_2$]$^{2+}$/2 744.6891, found 744.6904.

*Synthesis of Trimeric Triazole Linked Cluster **18**.* Sugar azide **12**[47] (189 mg, 0.495 mmol, 3.3 equiv), alkyne **3** (50 mg, 0.150 mmol, 1 equiv), CuSO$_4$ (14 mg, 0.090 mmol, 0.6 equiv) L-ascorbic acid sodium salt (36 mg, 0.180 mmol, 1.2 equiv), and 6 mL of solvent mixture of *t*-BuOH/H$_2$O/THF (v/v/v = 1/1/1) were used. The reaction mixture was stirred at room temperature for 24 h. Solvent was removed under reduced pressure, and the crude product was purified via column chromatography using eluent from pure DCM to 7% MeOH/DCM. A white solid (184 mg, 83%) was obtained as the desired product ($R_f$ = 0.4 in 5% MeOH/DCM): mp 246.0−248.0 °C; $^1$H NMR (400 MHz, $d_6$-DMSO) $\delta$ 8.65 (s, 3H, phenyl-H), 8.43 (s, 3H, triazole-H), 8.03 (d, *J* = 9.1 Hz, 3H, −N*H*−), 6.14 (d, *J* = 9.9 Hz, 3H, H-1), 5.48 (s, 6H, −C*H*$_2$O−), 5.35 (t, *J* = 9.7 Hz, 3H, H-3), 5.09 (t, *J* = 9.7 Hz, 3H, H-4), 4.64−4.53 (m, 3H, H-2), 4.27−4.20 (m, 3H, H-5), 4.18−4.11 (m, 3H, H$_a$-6), 4.09−4.02 (m, 3H, H$_b$-6), 2.01 (s, 9H), 1.99 (s, 9H), 1.94 (s, 9H), 1.55 (s, 9H, C*H*$_3$ in −NHAc); $^{13}$C{$^1$H} NMR (100 MHz, $d_6$-DMSO) $\delta$ 170.0, 169.5, 169.4, 169.2, 163.7, 141.7, 133.8, 130.8, 124.0, 84.7 (C-1), 73.4 (C-5), 72.2 (C-3), 68.0 (C-4), 61.7 (C-6), 58.4 (−CH$_2$O−), 52.1 (C-2), 22.2, 20.4, 20.3, 20.2; HRMS (ESI/ICR) *m*/*z* [M + 2Na]$^{2+}$ calcd for [C$_{60}$H$_{72}$N$_{12}$O$_{30}$Na$_2$]$^{2+}$/2 743.2131, found 743.2134.

*Synthesis of Trimeric Triazole Linked Cluster **19**.*[56] Sugar azide **11** (191 mg, 0.513 mmol, 3.3 equiv), alkyne **4** (50 mg, 0.157 mmol, 1 equiv), CuSO$_4$ (14 mg, 0.094 mmol, 0.6 equiv), L-ascorbic acid sodium salt (36 mg, 0.188 mmol, 1.2 equiv), and 6 mL of a solvent mixture of *t*-BuOH/H$_2$O/THF (v/v/v = 1/1/1) were used. The reaction mixture was stirred at room temperature for 24 h. An off-white solid (178 mg, 79%) was obtained as the desired product ($R_f$ = 0.4 in 5% MeOH/DCM): mp 165.0−167.0 °C; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.34 (t, *J* = 5.4 Hz, 3H, −N*H*−), 8.12 (s, 3H, triazole-H), 8.09 (s, 3H, phenyl-H), 5.94 (d, *J* = 9.4 Hz, 3H, H-1), 5.75 (t, *J* = 9.4 Hz, 3H, H-2), 5.43 (t, *J* = 9.4 Hz, 3H, H-3), 5.31 (t, *J* = 9.4 Hz, 3H, H-4), 4.84−4.70 (m, 6H, −C*H*$_2$NH−), 4.31 (dd, *J* = 12.7, 5.1 Hz, 3H, H$_a$-6), 4.13 (dd, *J* = 12.7, 1.9 Hz, 3H, H$_b$-6), 4.10−4.04 (m, 3H, H-5), 2.05 (s, 9H), 2.01 (s, 9H), 1.98 (s, 9H), 1.76 (s, 9H); $^{13}$C{$^1$H} NMR (100 MHz, CDCl$_3$) $\delta$ 170.5, 170.0, 169.44, 169.36, 166.1, 146.0, 134.5, 128.5, 121.5, 85.8 (C-1), 75.0 (C-5), 72.9 (C-3), 70.5 (C-2), 67.8 (C-4), 61.8 (C-6), 35.8 (−CH$_2$NH−), 20.60, 20.55, 20.1; LCMS (ESI/Quadrupole) *m*/*z* [M + H]$^+$ calcd for C$_{60}$H$_{73}$N$_{12}$O$_{30}$1440.4, found 1441.4.

*Synthesis of Trimeric Triazole Linked Cluster **20**.* Sugar azide **12** (286 mg, 0.769 mmol, 3.3 equiv), alkyne **4** (75 mg, 0.233 mmol, 1 equiv), CuSO$_4$ pentahydrate (35 mg, 0.140 mmol, 0.6 equiv), L-ascorbic acid sodium salt (55.4 mg, 0.280 mmol, 1.2 equiv), and 6 mL of solvent mixture of *t*-BuOH/H$_2$O/THF (v/v/v = 1/1/1) were used. The reaction mixture was stirred at room temperature for 24 h. A green precipitate was observed in the reaction mixture. The reaction mixture was filtered, and the precipitate was washed with DI water (10 mL) and DCM (10 mL). Light green solid (226 mg, 67%) was obtained as the desired product: mp 259.0−261.0 °C (sample turned brown at 180 °C and started melting at 259.0 °C); $^1$H NMR (400 MHz, $d_6$-DMSO) $\delta$ 9.35−9.14 (m, 3H, -N*H*-CH$_2$), 8.48 (s, 3H, phenyl-H), 8.16 (s, 3H, triazole-H), 8.05 (d, *J* = 8.8 Hz, 3H, −N*H*−), 6.10 (d, *J* = 9.7 Hz, 3H, H-1), 5.34 (t, *J* = 9.7 Hz, 3H, H-3), 5.07 (t, *J* = 9.7 Hz, 3H, H-4), 4.65−4.43 (m, 9H, H-2, −NHC*H*$_2$), 4.28−3.94 (m, 9H, H-5, H$_a$-6, H$_b$-6), 2.00 (s, 9H), 1.97 (s, 9H), 1.93 (s, 9H), 1.58 (s, 9H, C*H*$_3$ in −NHAc); $^{13}$C{$^1$H} NMR (100 MHz, $d_6$-DMSO) $\delta$ 169.9, 169.5, 169.4, 169.2, 165.3, 134.5, 128.8, 121.9, 84.5 (C-1), 73.3 (C-5), 72.3 (C-3), 67.9 (C-4), 61.7 (C-6), 52.0 (C-2), 34.8 (−NH-CH$_2$), 22.2, 20.4, 20.3, 20.1; HRMS (ESI/ICR) *m*/*z* [M + 2Na]$^{2+}$ calcd for [C$_{60}$H$_{75}$N$_{15}$O$_{27}$Na$_2$]$^{2+}$/2 741.7371, found 741.7379.

*Synthesis of Hexameric Triazole Linked Cluster **21**.* Alkyne **5** (87 mg, 0.2 mmol, 1 equiv), sugar azide **11** (491.2 mg, 1.32 mmol, 6.6 equiv), CuSO$_4$ pentahydrate (60 mg, 0.24 mmol, 1.2 equiv, L-ascorbic acid sodium salt (95 mg, 0.48 mmol, 2.4 equiv), and 3 mL of ethanol/water mixture (v/v = 1/1) were used. The reaction mixture was stirred at room temperature for 30 h. The reaction mixture was then diluted with DCM (10 mL) and underwent a workup using DI water (10 mL) and DCM (10 mL × 2). The crude product was purified via column chromatography using eluent from pure DCM to 10% MeOH/DCM. A white solid (430 mg, 81%) was obtained as the desired product ($R_f$ = 0.35 in 3% MeOH/DCM): mp 165.7−166.8 °C; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.11−8.00 (m, 9H), 6.05−5.90 (m, 6H), 5.58 (t, *J* = 9.3 Hz, 6H), 5.53−5.41 (m, 6H), 5.35−5.23 (m, 6H), 4.84−4.64 (m, 6H), 4.60−4.43 (m, 6H), 4.36−4.26 (m, 6H), 4.23−4.00 (m, 12H), 2.12−1.98 (m, 54H), 1.92−1.80 (m, 18H); $^{13}$C{$^1$H} NMR (100 MHz, CDCl$_3$) $\delta$ 170.6, 170.1, 169.9, 169.4, 169.0, 168.9, 143.8, 143.3, 136.7, 127.5, 122.7, 122.3, 85.7, 75.1, 72.7, 70.7, 70.5, 67.9, 61.8, 43.6, 39.1, 20.7, 20.5, 20.2. HRMS (ESI/ICR) *m*/*z* [M + 2Na]$^{2+}$ calcd for [C$_{111}$H$_{135}$N$_{21}$O$_{57}$Na$_2$]$^{2+}$/2 1359.9048, found 1359.9023.

*Synthesis of Hexameric Triazole Linked Cluster **22**.* Alkyne **5** (65.3 mg, 0.15 mmol, 1.0 equiv), sugar azide **12** (390 mg, 10.5 mmol, 7.0 equiv), CuSO$_4$ pentahydrate (45.0 mg, 0.18 mmol, 1.2 equiv), L-ascorbic acid sodium salt (72 mg, 0.36 mmol, 2.4 equiv), and 6 mL of EtOH/water (v/v = 1/1) were used. The reaction mixture was stirred at room temperature for 24 h. Solvent was removed to give the crude product, which was worked up by DCM (10 mL × 3) and water (3 mL). The crude product was purified by column chromatography using eluent from pure DCM to 15% MeOH/DCM to give a white solid (301 mg, 0.11 mmol, 75%) as the desired product ($R_f$ = 0.2 in 10% MeOH/DCM): mp 210.0−213.2 °C; $^1$H NMR (400 MHz, $d_6$-DMSO) $\delta$ 8.33 (s, 6H), 8.06 (d, *J* = 8.4 Hz, 6H), 7.79 (s, 3H), 6.17−6.00 (m, 6H), 5.43−5.32 (m, 6H), 5.12 (t, *J* = 8.8 Hz, 6H), 4.84−4.43 (m, 12H), 4.41−4.00 (m, 24H), 2.06−1.88 (m, 54H), 1.64−1.54 (m, 18H); $^{13}$C{$^1$H} NMR (100 MHz, $d_6$-DMSO) $\delta$ 170.0, 169.6, 169.2, 136.4, 143.3, 85.0, 79.2, 78.9, 78.6, 73.4, 72.1, 68.0, 61.8, 52.2, 43.6, 22.2, 20.3, 20.2. HRMS (ESI/ICR) *m*/*z* [M + 2Na]$^{2+}$ calcd for [C$_{111}$H$_{141}$N$_{27}$O$_{51}$Na$_2$]$^{2+}$/2 calcd for 1356.9527, found 1356.9533.

*Synthesis of Trimeric Triazole Linked Cluster **23**.* Alkyne **6** (50 mg, 0.214 mmol, 1.0 equiv), sugar azide **11** (318 mg, 0.854 mmol, 4.0 equiv), CuSO$_4$ pentahydrate (32 mg, 0.128 mmol, 0.6 equiv), L-ascorbic acid sodium salt (51.4 mg, 0.257 mmol, 1.2 equiv), and 6 mL of EtOH/water (v/v = 1/1) were used. The reaction mixture was stirred at room temperature for 17 h. Solvent was removed to give the crude product, which was worked up by DCM (10 mL × 3) and water (3 mL). The crude product was purified by column chromatography using eluent from 1% MeOH/DCM to 5% MeOH/DCM to afford a white solid (255 mg, 0.188 mmol, 88%) as the desired product ($R_f$ = 0.18 in 2% MeOH/DCM): mp 121.0−122.5 °C; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.90 (s, 3H), 5.99 (d, *J* = 9.3 Hz, 3H), 5.53 (t, *J* = 9.4 Hz, 3H), 5.44 (t, *J* = 9.4 Hz, 3H), 5.37−5.28 (m, 3H), 4.67−4.55 (m, 6H), 4.32 (dd, *J* = 12.6, 5.0 Hz, 3H), 4.17 (dd, *J* = 12.6, 2.0 Hz, 3H), 4.11−4.04 (m, 3H), 3.42−3.30 (m, 6H), 2.08 (s, 9H), 2.04 (s, 9H), 2.03 (s, 9H), 1.81 (s, 9H), 0.92 (s, 3H). $^{13}$C{$^1$H} NMR (100 MHz, CDCl$_3$) $\delta$ 170.5, 170.0, 169.4, 168.8, 146.2, 121.2, 85.6, 75.0, 73.0, 72.9, 70.3, 67.9, 64.8, 61.6, 40.7, 20.63, 20.57, 20.5, 20.1, 17.5; HRMS (ESI/ICR) *m*/*z* [M + 2Na]$^{2+}$ calcd for [C$_{56}$H$_{75}$N$_9$O$_{30}$Na$_2$]$^{2+}$/2 calcd for 699.7202, found 699.7196.

*Synthesis of Trimeric Triazole Linked Cluster **24**.* Alkyne **6** (50 mg, 0.214 mmol, 1.0 equiv), sugar azide **12** (318 mg, 0.854 mmol, 4.0 equiv), CuSO$_4$ pentahydrate (32 mg, 0.128 mmol, 0.6 equiv), L-ascorbic acid sodium salt (51.4 mg, 0.257 mmol, 1.2 equiv), and 6 mL of EtOH/water (v/v = 1/1) were used. The reaction mixture was stirred at room temperature for 17 h. Solvent was removed to give the crude product, which was worked up by DCM (10 mL × 3) and water (3 mL). The crude product was purified by column chromatography using eluent from 1% MeOH/DCM to 5% MeOH/DCM to afford a white solid (245 mg, 0.180 mmol, 85%) as the desired product ($R_f$ = 0.18 in 5% MeOH/DCM): mp 150.0−152.5 °C; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.92 (s, 3H), 6.92 (d, *J* = 8.9 Hz, 3H), 6.18 (d, *J* = 9.8 Hz, 3H), 5.51 (t, *J* = 9.9 Hz, 3H), 5.32 (t, *J* = 9.7 Hz, 3H), 4.70−4.59 (m, 3H), 4.57−4.47 (m, 6H), 4.33 (dd, *J* = 12.7, 4.7 Hz, 3H), 4.23−4.16 (m, 3H), 4.14−4.07 (m, 3H), 3.27 (s, 6H), 2.10−2.00 (m, 27H), 1.72 (s, 9H), 0.87 (s, 3H); $^{13}$C{$^1$H} NMR (100 MHz, CDCl$_3$) $\delta$ 171.0, 170.7, 170.6, 169.4, 145.5, 122.2, 85.6, 75.0, 72.6, 72.5, 68.1, 64.2, 61.8, 53.5, 40.6, 22.7, 20.7, 20.64, 20.60, 17.5; HRMS (ESI/

ICR) *m*/*z* [M + 2Na]$^{2+}$ calcd for $[C_{56}H_{78}N_{12}O_{27}Na_2]^{2+}$/2 calcd for 698.2442, found 698.2453.

*Synthesis of Tetrameric Triazole Linked Cluster **25**.* Alkyne **7** (45 mg, 0.12 mmol, 1 equiv), sugar azide **11** (197 mg, 0.53 mmol, 4.4 equiv), $CuSO_4$ pentahydrate (24 mg, 0.10 mmol, 0.8 equiv), L-ascorbate sodium salt (38 mg, 0.19 mmol, 1.6 equiv), and 3 mL of *t*-BuOH/$H_2O$/THF (v/v/v = 1/1/1) were used. The reaction mixture was stirred at 30 °C in an oil bath for 24 h. Solvent was removed under reduced pressure. Crude product was purified via column chromatography using pure DCM to 15% MeOH/DCM. Product was further recrystallized in reagent alcohol. A white solid (161 mg, 72%) was obtained as the desired product ($R_f$ = 0.45 in 5% MeOH/DCM): mp 134.3−135.8 °C; $^1$H NMR (400 MHz, $CDCl_3$) δ 7.90 (s, 4H), 6.01 (d, *J* = 9.0 Hz, 2H), 5.92 (d, *J* = 8.8 Hz, 2H), 5.86−5.67 (br s, 2H), 5.24−5.61 (m, 12H), 4.67−4.54 (m, 4H), 4.52−4.27 (m, 8H), 4.25−3.99 (m, 12H), 3.42 (s, 4H), 2.12−2.00 (m, 36H), 1.92−1.80 (m, 12H); $^{13}$C{$^1$H} NMR (100 MHz, $CDCl_3$) δ 170.52, 170.50, 170.0, 169.9, 169.4, 169.1, 168.9, 156.3, 145.9, 145.7, 121.4, 120.9, 85.7, 85.6, 75.1, 75.0, 72.80, 72.75, 70.4, 70.3, 68.7, 67.9, 67.8, 64.7, 63.9, 61.7, 44.0, 36.5, 20.64, 20.61, 20.55, 20.52, 20.49, 20.13, 20.07; HRMS (ESI/ICR) *m*/*z* [M + 2Na]$^{2+}$ calcd for $[C_{75}H_{98}N_{14}O_{42}Na_2]^{2+}$/2 calcd for 956.2873, found 956.2881.

*Synthesis of Tetrameric Triazole Linked Cluster **26**.* Alkyne **7** (45 mg, 0.12 mmol, 1 equiv), sugar azide **12** (197 mg, 0.53 mmol, 4.4 equiv), $CuSO_4$ pentahydrate (24 mg, 0.10 mmol, 0.8 equiv), L-ascorbate sodium salt (38 mg, 0.19 mmol, 1.6 equiv), and 3 mL of *t*-BuOH/$H_2O$/THF (v/v/v = 1/1/1) were used. The reaction mixture was stirred at 30 °C in an oil bath for 32 h. Solvent was removed under reduced pressure. The crude product was purified via column chromatography using pure DCM to 8% MeOH/DCM. A white solid (191 mg, 85%) was obtained as the desired product ($R_f$ = 0.5 in 7.5% MeOH/DCM): mp 235.0−238.0 °C (sample turned brown at 215 °C, an melted at 235.0−238.0 °C); $^1$H NMR (400 MHz, $d_6$-DMSO) δ 8.26 (s, 2H), 8.16−7.97 (m, 6H), 7.79−7.62 (m, 2H), 6.16−6.07 (m, 4H), 5.36 (t, *J* = 9.7 Hz, 4H), 5.10 (dt, *J* = 9.7, 5.4 Hz, 4H), 4.72−4.41 (m, 8H), 4.30−3.92 (m, 20H), 3.48−3.37 (m, 4H), 2.06−1.91 (m, 36H), 1.62−1.55 (m, 12H); $^{13}$C{$^1$H} NMR (100 MHz, $d_6$-DMSO) δ 170.0, 169.5, 169.4, 169.3, 156.1, 145.3, 144.1, 122.6, 121.5, 84.62, 84.56, 73.4, 72.4, 68.9, 68.0, 64.2, 63.1, 61.7, 52.1, 43.6, 35.8, 22.3, 22.2, 20.4, 20.3, 20.3. HRMS (ESI/ICR) *m*/*z* [M + 2Na]$^{2+}$ calcd for $[C_{75}H_{102}N_{18}O_{38}Na_2]^{2+}$/2 calcd for 954.3193, found 954.3192.

*Synthesis of Tetrameric Triazole Linked Cluster **27**.* Alkyne **8** (50 mg, 0.13 mmol, 1 equiv), sugar azide **11** (213 mg, 0.57 mmol, 4.4 equiv), $CuSO_4$ pentahydrate (26 mg, 0.10 mmol, 0.8 equiv), L-ascorbate sodium salt (42 mg, 0.20 mmol, 1.6 equiv), and 3 mL of *t*-BuOH/$H_2O$/THF (v/v/v = 1/1/1) were used. The reaction mixture was stirred at 30 °C in an oil bath for 20 h. Solvent was removed under reduced pressure. Crude product was purified via column chromatography using pure DCM to 5% MeOH/DCM. A white solid (190.5 mg, 77%) was obtained as the desired product ($R_f$ = 0.55 in 5% MeOH/DCM): mp 104.2−106.5 °C; $^1$H NMR (400 MHz, $CDCl_3$) δ 8.02 (s, 2H), 7.69 (s, 2H), 6.02 (d, *J* = 9.3 Hz, 2H), 5.92 (d, *J* = 9.1 Hz, 2H), 5.56 (t, *J* = 9.4 Hz, 2H), 5.50−5.27 (m, 10H), 4.67−4.57 (m, 4H), 4.36−4.28 (m, 4H), 4.21−4.14 (m, 4H), 4.13−4.08 (m, 6H), 4.07−4.02 (m, 2H), 3.54−3.46 (m, 4H), 2.77 (dt, *J* = 7.5, 1.6 Hz, 4H), 2.37 (t, *J* = 7.4 Hz, 4H), 2.10−2.05 (m, 18H), 2.05−2.02 (m, 18H), 2.02−1.97 (m, 4H), 1.86 (s, 6H), 1.82 (s, 6H); $^{13}$C{$^1$H} NMR (100 MHz, $CDCl_3$) δ 172.7, 170.5, 170.5, 169.94, 169.88, 169.43, 169.38, 168.82, 168.75, 147.8, 145.5, 121.6, 119.5, 85.62, 85.56, 77.2, 75.0, 72.8, 72.7, 70.31, 70.27, 68.6, 67.8, 64.8, 62.7, 61.6, 43.6, 33.2, 24.8, 24.3, 20.60, 20.58, 20.55, 20.51, 20.50, 20.47, 20.1, 20.0. HRMS (ESI/ICR) *m*/*z* [M + 2Na]$^{2+}$ calcd for $[C_{79}H_{104}N_{12}O_{42}Na_2]^{2+}$/2 calcd for 969.3078, found 969.3078.

*Synthesis of Tetrameric Triazole Linked Cluster **28**.* Alkyne **8** (50 mg, 0.13 mmol, 1 equiv), sugar azide **12** (213 mg, 0.57 mmol, 4.4 equiv), $CuSO_4$ pentahydrate (26 mg, 0.10 mmol, 0.8 equiv), L-ascorbate sodium salt (42 mg, 0.20 mmol, 1.6 equiv), and 3 mL of *t*-BuOH/$H_2O$/THF (v/v/v = 1/1/1) were used. The reaction mixture was stirred at 30 °C in an oil bath for 24 h. The solvent was removed under reduced pressure. The crude product was purified via column chromatography using 5% MeOH/DCM to 7.5% MeOH/DCM. A white solid (198.6 mg, 81%) was obtained as the desired product ($R_f$ = 0.45 in 7.5% MeOH/DCM): mp 142.6−145.1 °C; $^1$H NMR (400 MHz, $CDCl_3$) δ 8.08 (s, 2H), 7.78 (s, 2H), 7.34 (d, *J* = 9.2 Hz, 2H), 7.02 (d, *J* = 9.2 Hz, 2H), 6.28−6.16 (m, 4H), 5.62−5.56 (m, 4H), 5.39−5.24 (m, 4H), 4.79−4.62 (m, 4H), 4.57 (s, 4H), 4.39−4.31 (m, 4H), 4.25−4.10 (m, 8H), 4.09−3.96 (m, 4H), 3.50−3.39 (m, 4H), 2.81−2.68 (m, 4H), 2.37−2.25 (m, 4H), 2.12−2.04 (m, 36H), 2.01−1.90 (m, 4H), 1.78−1.72 (m, 12H). $^{13}$C{$^1$H} NMR (100 MHz, $CDCl_3$) δ 172.7, 171.1, 170.9, 170.7, 170.6, 170.6, 170.53, 169.5, 169.4, 147.4, 145.0, 122.4, 120.6, 85.6, 85.6, 74.9, 72.8, 72.4, 68.3, 68.3, 68.2, 64.1, 62.8, 61.8, 53.5, 53.3, 43.5, 33.2, 24.6, 24.3, 22.8, 22.7, 20.7, 20.6, 20.6. HRMS (ESI/ICR) *m*/*z* [M + 2Na]$^{2+}$ calcd for $[C_{79}H_{108}N_{16}O_{38}Na_2]^{2+}$/2 calcd for 967.3397, found 967.3402.

*Synthesis of Tetrameric Triazole Linked Cluster **29**.* Alkyne **9** (100 mg, 0.20 mmol, 1.0 equiv), sugar azide **12** (332 mg, 0.89 mmol, 4.4 equiv), $CuSO_4$ pentahydrate (41 mg, 0.16 mmol, 0.8 equiv), L-ascorbic acid sodium salt (64 mg, 0.8 mmol, 1.6 equiv), and 3 mL of EtOH/$H_2O$ (v/v = 1/1) were added to a 50 mL round-bottomed flask. The reaction mixture was stirred at room temperature for 24 h. Solvent was removed to give the crude product. An aqueous workup was carried out using DCM (10 mL × 3) and DI water (10 mL). The crude product was purified by column chromatography using eluent from 1% MeOH/DCM to 6% MeOH/DCM to afford white solid (327 mg, 0.16 mmol, 82%) as the desired product ($R_f$ = 0.3 in 5% MeOH/DCM). The cluster contains 1:1 stereoisomers of the benzylidene acetal: mp 133.0−151.0 °C; $^1$H NMR (400 MHz, $d_6$-DMSO) δ 8.34−8.21 (m, 4H), 8.10−8.00 (m, 4H), 7.48−7.29 (m, 5H), 6.13 (d, *J* = 9.8 Hz, 4H), 5.47−5.32 (m, 5H), 5.10 (t, *J* = 9.7 Hz, 4H), 4.70−4.40 (m, 12H), 4.29−3.99 (m, 12H), 3.97−3.78 (m, 4H), 3.75−3.56 (m, 2H), 3.41 (s, 6H), 3.28−3.13 (m, 4H), 2.05−1.93 (m, 36H), 1.58 (s, 12H). $^{13}$C{$^1$H} NMR (100 MHz, $d_6$-DMSO) δ 169.9, 169.5, 169.4, 169.3, 144.3, 138.5, 128.6, 127.9, 126.1, 122.6, 100.7, 84.6, 73.4, 72.3, 68.9, 68.0, 64.1, 61.7, 52.0, 45.2, 22.2, 20.4, 20.3, 20.2. HRMS (ESI/ICR) *m*/*z* [M + 2Na]$^{2+}$ calcd for $[C_{85}H_{114}N_{16}O_{39}Na_2]^{2+}$/2 calcd for 1014.3607, found 1014.3601.

*Synthesis of Tetrameric Triazole Linked Cluster **30**.* Compound **29** (150 mg, 0.076 mmol, 1.0 equiv) was dissolved in acetic acid (3 mL, 66% aq). The reaction mixture was stirred at room temperature for 12 h. The mixture solvent was removed to give the crude product, which was purified by column chromatography using eluent from 1% MeOH/DCM to 6% MeOH/DCM to afford white solid (98 mg, 0.051 mmol, 68%) as the desired product ($R_f$ = 0.1 in 5% MeOH/DCM): mp 149.3−151.8 °C; $^1$H NMR (400 MHz, $d_6$-DMSO) δ 8.24 (s, 4H), 8.06 (d, *J* = 9.1 Hz, 4H), 6.17−6.07 (m, 4H), 5.37 (t, *J* = 9.8 Hz, 4H), 5.10 (t, *J* = 9.7 Hz, 4H), 4.67−4.55 (m, 4H), 4.52−4.43 (m, 8H), 4.29−4.11 (m, 12H), 4.11−4.03 (m, 4H), 3.43−3.35 (m, 12H), 2.05−1.92 (s, 36H), 1.62−1.55 (s, 12H); $^{13}$C{$^1$H} NMR (100 MHz, $d_6$-DMSO) δ 170.0, 169.5, 169.4, 169.3, 144.5, 144.4, 122.6, 122.4, 84.6, 79.2, 78.9, 78.6, 73.4, 72.3, 69.2, 68.0, 64.2, 61.7, 60.6, 52.0, 45.6, 45.2, 22.2, 20.4, 20.3, 20.2. HRMS (ESI/ICR) *m*/*z* [M + 2Na]$^{2+}$ calcd for $[C_{78}H_{110}N_{16}O_{39}Na_2]^{2+}$/2 calcd for 970.3450, found 970.3452.

*Synthesis of Hexameric Triazole Linked Cluster **31**.*[16] Alkyne **10** (31 mg, 0.065 mmol, 1.0 equiv), sugar azide **11** (140 mg, 0.40 mmol, 6.2 equiv), $CuSO_4$ pentahydrate (23 mg, 0.078 mmol, 1.2 equiv), L-ascorbic acid sodium salt (39.6 mg, 0.16 mmol, 2.4 equiv), and 4 mL of EtOH/water (v/v = 1/1) were used. The reaction mixture was stirred at 30 °C in an oil bath for 14 h. Solvent was removed to give the crude product, which was worked up by DCM (10 mL × 3) and water (3 mL). The crude product was purified by column chromatography using eluent 0.5% MeOH/DCM to 5% MeOH/DCM to afford a white solid (155 mg, 0.057 mmol, 89%) as the desired product ($R_f$ = 0.35 in 5% MeOH/DCM): mp 120.3−122.5 °C; $^1$H NMR (400 MHz, $CDCl_3$) δ 8.19 (s, 6H), 6.09 (d, *J* = 9.4 Hz, 6H), 5.62 (t, *J* = 9.3 Hz, 6H), 5.56−5.38 (m, 12H), 4.60 (q, *J* = 12.4 Hz, 12H), 4.32 (dd, *J* = 12.4, 4.7 Hz, 6H), 4.22−4.09 (m, 12H), 3.47 (s, 12H), 3.27 (s, 4H), 2.19−1.99 (m, 54H), 1.76 (s, 18H); $^{13}$C{$^1$H} NMR (100 MHz, $CDCl_3$) δ 170.5, 170.0, 169.5, 168.7, 146.0, 122.0, 85.5, 74.9, 73.0, 70.4, 69.0, 67.9, 64.9, 61.7, 45.6, 20.60, 20.57, 20.5, 20.0. HRMS (ESI/ICR) *m*/*z* $[M + 2Na]^{2+}$ calcd for $[C_{112}H_{148}N_{18}O_{61}Na_2]^{2+}/2$ calcd for 1383.4408, found 1383.4386.

*Synthesis of Hexameric Triazole Linked Cluster **32**.* Alkyne **10** (40 mg, 0.083 mmol, 1.0 equiv), sugar azide **12** (191 mg, 0.51 mmol, 6.2 equiv), $CuSO_4$ pentahydrate (25.5 mg, 0.10 mmol, 1.2 equiv), L-ascorbic acid sodium salt (39.6 mg, 0.20 mmol, 2.4 equiv), and 5 mL of EtOH/water (v/v = 1/1) were used. The reaction mixture was stirred at 50 °C in an oil bath for 7 h. Solvent was removed to give the crude product, which was worked up by DCM (10 mL × 3) and water (3 mL). The crude product was purified by column chromatography using eluent from 0.5% MeOH/DCM to 10% MeOH/DCM to afford white solid (191 mg, 0.07 mmol, 85%) as the desired product ($R_f$ = 0.6 in 10% MeOH/DCM): mp 180.2−182.8 °C; $^1H$ NMR (400 MHz, $d_6$-DMSO) $\delta$ 8.24 (s, 6H), 8.07 (d, *J* = 8.9 Hz, 6H), 6.13 (d, *J* = 9.8 Hz, 6H), 5.37 (t, *J* = 9.8 Hz, 6H), 5.10 (t, *J* = 9.7 Hz, 6H), 4.67−4.55 (m, 6H), 4.46 (s, 12H), 4.26−4.11 (m, 12H), 4.10−4.01 (m, 6H), 2.06−1.88 (s, 54H), 1.58 (s, 18H); $^{13}C\{^1H\}$ NMR (100 MHz, $d_6$-DMSO) $\delta$ 170.0, 169.6, 169.5, 169.3, 144.4, 122.6, 84.6, 73.5, 72.4, 69.0, 68.0, 64.1, 61.7, 52.1, 45.2, 22.2, 20.4, 20.2. HRMS (ESI/ICR) *m*/*z* $[M + 2Na]^{2+}$ calcd for $[C_{112}H_{154}N_{24}O_{55}Na_2]^{2+}/2$ calcd for 1380.4888, found 1380.4870.

*Synthesis of Hexameric Triazole Linked Cluster **33**.* Alkyne **10** (48.2 mg, 0.10 mmol, 1.0 equiv), sugar azide **13**[26] (231.0 mg, 0.62 mmol, 6.2 equiv), $CuSO_4$ pentahydrate (30 mg, 0.12 mmol, 1.2 equiv), L-ascorbic sodium salt (48 mg, 0.24 mmol, 2.4 equiv), and 4 mL of EtOH/water (v/v = 1/1). were used. The reaction mixture was stirred at room temperature for 24 h. Solvent was removed to give the crude product, which was worked up by DCM (10 mL × 3) and water (3 mL). The crude product was purified by column chromatography using eluent from 0.5% MeOH/DCM to 5% MeOH/DCM to afford a white solid (236.7 mg, 0.087 mmol, 87%) as the desired product ($R_f$ = 0.55 in 5% MeOH/DCM): mp 122.2−124.5 °C; $^1H$ NMR (400 MHz, $d_6$-DMSO) $\delta$ 8.27 (s, 6H), 6.24 (d, *J* = 9.2 Hz, 6H), 5.61 (t, *J* = 9.5 Hz, 6H), 5.50−5.39 (m, 12H), 4.57 (t, *J* = 6.0 Hz, 6H), 4.47 (s, 12H), 4.12 (dd, *J* = 11.6, 5.3 Hz, 6H), 4.01 (dd, *J* = 11.6, 7.1 Hz, 6H), 3.24 (s, 16H), 2.15 (s, 18H), 1.97 (s, 18H), 1.93 (s, 18H), 1.76 (s, 18H); $^{13}C\{^1H\}$ NMR (100 MHz, $d_6$-DMSO) $\delta$ 169.9, 169.8, 169.4, 168.4, 144.6, 123.2, 84.2, 72.9, 70.4, 68.7, 67.7, 67.2, 63.8, 61.4, 45.0, 20.4, 20.3, 20.2, 19.8. HRMS (ESI/ICR) *m*/*z* $[M + 2Na]^{2+}$ calcd for $[C_{112}H_{148}N_{18}O_{61}Na_2]^{2+}/2$ calcd for 1383.4408, found 1383.4401.

**Synthesis of Triazoles Using Cluster 31 as the Ligand.** The reactions of synthesizing triazoles **34** and **35** were carried out on a larger scale using a Radley 6 plus carousel reaction station equipped with a 250 mL round-bottom flask. For the synthesis of the triazoles **12-A3**, **12-A4**, **36-A4**, and **36-A5**, the reactions were carried out using the Radley 12 plus carousel reaction station equipped with 20 mL reaction tube.

*Synthesis of Sugar Triazole **34**.* To a carousel reaction 250 mL round-bottom flask, sugar azide **12** (300 mg, 0.806 mmol, 1 equiv) and glycoclusters **31** (10.9 mg, 0.004 mmol, 0.5 mol %) were dissolved in 7.5 mL of degassed EtOH. $CuSO_4$ pentahydrate (40.5 mg, 0.16 mmol, 0.2 equiv) dissolved in 7.5 mL of degassed $H_2O$ was added to the above solution followed by addition of L-ascorbic acid sodium salt (64.5 mg, 0.32 mmol, 0.4 equiv). Then phenyl acetylene (98 mg, 0.97 mmol, 1.2 equiv) was added. The mixture was stirred at 500 rpm at 30 °C under $N_2$. The reaction reached full converted in 2 h as indicated by $^1H$ NMR monitoring. Solvent was removed, and DCM (30 mL) was added to the crude, which was then washed with water (10 mL × 3) and dried over anhydrous $Na_2SO_4$, the solvent was removed, and the product was purified by column chromatography using eluent from pure DCM to 5% MeOH/DCM to give a white solid (355 mg, 0.750 mmol, 93%, $R_f$ = 0.45 in 5% MeOH/DCM) as the desired product.

*Synthesis of Sugar Triazole **35**.* To a 250 mL reaction flask, 1-octyne (106 mg, 0.97 mmol, 1.2 equiv) was dissolved in 7.5 mL of degassed EtOH; $CuSO_4$ pentahydrate (20.2 mg, 0.08 mmol, 0.1 equiv) dissolved in 7.5 mL of degassed $H_2O$ was added to above solution followed by adding sugar azide **12** (300 mg, 0.806 mmol, 1 equiv) and glycoclusters **31** (10.9 mg, 0.004 mmol, 0.5 mol %). Then sodium ascorbate (32.2 mg, 0.16 mmol, 0.2 equiv) was added. The mixture was stirred with 500 rpm at 30 °C under $N_2$. The reaction was completed in 3 h as indicated by $^1H$ NMR monitoring. Solvent was removed, and DCM (30 mL) was added to the reaction, fwhich was then washed with water (10 mL × 3), dried over anhydrous $Na_2SO_4$, concentrated, and purified by column chromatography using eluent from pure DCM to 5% MeOH/DCM to give a white solid (369 mg, 0.760 mmol, 95%, $R_f$ = 0.42 in 5% MeOH/DCM) as the desired product.

*Synthesis of Triazoles **12-A3**, **12-A4**, **36-A4**, and **36-A5** Using Cluster **31**.* These reactions were carried out using the Radley 12 plus carousel reaction station equipped with 20 mL reaction tube. The general procedure: Azide (80 mg, 1 equiv), alkyne (1.2 equiv), and compound **31** (0.01 equiv) were dissolved in 4 mL of solvent EtOH:$H_2O$ (v/v = 1/1) in a carousel reaction tube, followed by addition of $CuSO_4$ pentahydrate (0.1 equiv) and sodium ascorbate (0.2 equiv). The reaction mixture was stirred at 30 °C for 1−2 h under $N_2$ atmosphere. The reaction was monitored by $^1H$ NMR. When the reaction was completed, solvent was removed, followed by addition of $H_2O$ (1 mL), and extraction was performed with DCM (5 mL × 3) in a separatory funnel. The organic layers were dried over anhydrous $Na_2SO_4$. The residue obtained was purified by column chromatography to afford the desired product.

*Synthesis of Triazole **12-A3**.* The reaction was completed in 1 h. Compound **12** (80 mg, 0.22 mmol, 1 equiv), 5-phenyl-1-pentyne (37.2 mg, 0.26 mmol, 1.2 equiv), compound **31** (6.0 mg, 0.0022 mmol, 0.01 equiv), $CuSO_4$ pentahydrate (5.5 mg, 0.022 mmol, 0.1 equiv), and sodium ascorbate (8.8 mg, 0.044 mmol, 0.2 equiv) were used. The residue obtained was purified by column chromatography using eluent from pure DCM to 3% MeOH/DCM to afford a white solid (107 mg, 0.21 mmol, 95%) as the desired product ($R_f$ = 0.50 in 5% MeOH/DCM).

*Synthesis of Triazole **12-A4**.* The reaction was completed in 2 h. Compound **12** (80 mg, 0.22 mmol,1 equiv), cyclohexanol-1- ethynyl (32.0 mg, 0.26 mmol, 1.2 equiv), compound **31** (6.0 mg, 0.0022 mmol, 0.01 equiv), $CuSO_4$ pentahydrate (5.5 mg, 0.022 mmol, 0.1 equiv), and sodium ascorbate (8.8 mg, 0.044 mmol, 0.2 equiv) were used. The product was partially soluble in water and some was lost to aqueous phase; the isolated pure compound was obtained as a white solid (73 mg, 68%).

*Synthesis of Triazole **36-A4**.* The reaction was completed in 1 h. Compound **36** (80 mg, 0.50 mmol,1 equiv), cyclohexanol-1-ethynyl (74.0 mg, 0.60 mmol, 1.2 equiv), compound **31** (13.6 mg, 0.005 mmol, 0.01 equiv), $CuSO_4$ pentahydrate (12.5 mg, 0.05 mmol, 0.1 equiv), and sodium ascorbate (20.0 mg, 0.10 mmol, 0.2 equiv) were used. The residue obtained was purified by column chromatography using eluent from 10% EtOAc/hexanes to 50% EtOAc/hexanes to afford a white solid (136 mg, 0.48 mmol, 96%) as the desired product ($R_f$ = 0.45 in 60% EtOAc/hexanes).

*Synthesis of Triazole **36-A5**.* The reaction was completed in 1 h. Compound **36** (80 mg, 0.50 mmol, 1 equiv), 6-chloro-1-hexyne (69.6 mg, 0.60 mmol, 1.2 equiv), compound **31** (13.6 mg, 0.005 mmol, 0.01 equiv), $CuSO_4$ pentahydrate (12.5 mg, 0.05 mmol, 0.1 equiv), and sodium ascorbate (20.0 mg, 0.10 mmol, 0.2 equiv) were used. The residue obtained was purified by column chromatography using eluent from 10% EtOAc/hexanes to 50% EtOAc/hexanes to afford a white solid (124.6 mg, 0.45 mmol, 90%) as the desired product ($R_f$ = 0.60 in 60% EtOAc/hexanes).

**General Procedure for the Preparation of Cluster-Gel Catalyzed Reactions.** The different compounds that were gelators were tested for their performance as ligands for the copper-catalyzed click reactions. When using the combination of two compounds, a few monomeric triazole gelators were also tested for their gelation capacity with the hexamers. The gel-filled columns could be used once since the gel became unstable after passing through reaction mixtures, and although good yields were obtained by this procedure, the gel column was not stable for repeated uses. We further tested different combinations of the gelators with the hexameric clusters and found that the gelator compound **23** and cluster **31** were able to form stable gels in ethanol/water mixture. This was used for the catalyzing the click reactions.

**Gel Column I Preparation and Reactions Catalyzed by the Gel-Column.** Compound **18** (10 mg, 0.007 mmol, 0.03 equiv) was added to a 2 dram vial. EtOH/$H_2O$ (v/v 1:2, 1.5 mL) containing $CuSO_4$ pentahydrate (6 mg, 0.022 mmol, 0.1 equiv) was added, and the vial was gently heated until the solids were dissolved. The hot solution was then added to a 3 mL syringe (with plunger removed and a syringe filter/stopper attached). The syringe was then allowed to cool, and a stable gel formed at rt (Figure 8). The reaction of compound **36** with phenyl acetylene was carried out by the gelator-column.

*Synthesis of Compound **37** Using the Gel Column-I.* A solution of phenyl acetylene (0.030 mL, 0.27 mmol, 1.2 equiv), 3-acetylphenyl azide (35 mg, 0.22 mmol, 1 equiv), and sodium ascorbate (9 mg, 0.044 mmol, 0.2 equiv) dissolved in ethanol/DI water (1 mL) was added on top of the gel column. The reaction mixture was allowed to sit on top of the gel column for 1 h. The cap was then removed, and elution occurred over a 5 min period. After the elution was complete, 1 mL EtOH/$H_2O$ (v/v 1:1) was added to the top of the gel to push the compound off the gel column followed by 0.5 mL EtOH/$H_2O$ (v/v = 2/1), and 0.5 mL EtOH/$H_2O$ (v/v, 1/1) to prepare the column for the next round of reaction mixture. The eluent was collected in a scintillation vial, and solvent was removed under reduced pressure to yield a light yellow solid. $^1$H NMR indicated that full conversion to the desired product for each round without byproduct formation was reached. This procedure was repeated a total of six times, with the product obtained from each round obtained as follows: cycle 1, 24.1 mg; 2, 32.7 mg; 3, 33.3 mg; 4, 33.1 mg; 5, 32.7 mg; 6, 34.1 mg. The product was not very soluble in the eluting solvent which contains water; therefore, a fair amount of the product was trapped in the gel-column. After the end of the sixth round of addition, the column was flushed with pure EtOH (10 mL). and after drying of solvents and another 127.6 mg of product was obtained (Figure S19). The total final product was obtained in 93% yield (317.6 mg, 1.21 mmol), and the yield was calculated using the total amount of phenyl azide starting material: 35 mg × 6 = 210 mg, 1.30 mmol.

*Gel Catalysis in Biphase Form.* The gel formed by compound **18** was also prepared and transferred to a scintillation vial, and the same click reaction was performed in a biphase format rather than passing through a gel-column. The reaction was repeated 5 times, and the gel was stable after the fifth cycle. In a 2-dram vial, compound **18** (10 mg, 0.007 mmol, 0.03 equiv to one loading of the azide), 1.5 mL of EtOH/$H_2O$ (v/v = 1:2), and $CuSO_4$ pentahydrate (6 mg, 0.022 mmol, 0.1 equiv) were added and the mixture heated until all of the solids were dissolved. The hot solution was then added to a preheated scintillation vial. Upon cooling a stable gel formed. The following reaction mixture was added on top of the gel: a solution of phenyl acetylene (0.030 mL, 0.27 mmol, 1.2 equiv), 3-acetylphenyl azide (35 mg, 0.22 mmol, 1 equiv), and sodium ascorbate (9 mg, 0.044 mmol, 0.2 equiv) in 1 mL of EtOH/$H_2O$ (v/v 1:1). The reaction mixture was then placed in a shaker at 30 °C at 15 rpm. The reaction was found to be finished after 4 h. The reaction mixture was decanted, and the gel surface was washed with 1 mL of EtOH/$H_2O$ (v/v = 2/1). The same procedure was repeated five cycles, and the gel remained stable after throughout the experiment. After the fifth round, the gel was rinsed with pure ethanol (4 mL) overnight. The product obtained in each round was the desired product without the need for further purification, the crude $^1$H NMR spectra showed only the pure product (Figure S20). The yields obtained for the five cycles are 47.4, 43.7, 44.4, 42.3, and 40.3 mg; the final rinse 36.6 mg. The total final product was obtained in 89% yield (254.7 mg, 0.97 mmol).

**Gel Column II Preparation and Applications for Click Reaction.** *Preparation of Co-Gel Catalyst of Compounds **23** and **31** and the Synthesis of Triazoles.* Compounds **23** (10.0 mg, 0.0074 mmol, 4.0 mol % to azide) and **31** (5.0 mg, 0.00184 mmol, 1 mol % to azide) and $CuSO_4{\cdot}5H_2O$ (9.2 mg, 0.0186 mmol, 0.2 equiv) were dissolved in 0.8 mL of the mixture solvent of EtOH/$H_2O$ (v, 1:1) by heating, the hot solution was transferred to a syringe, and a gel was formed after 2 h at rt. This co-gel is called gel column II and shown in Figure 9a.

The gel column II was stored at room temperature for 12 h before being sued for the reaction. The mixture of galactose azide **13** (68.6 mg, 0.184 mmol, 1 equiv), propargyl alcohol **A6** (12.4 mg, 0.22 mmol, 1.2 equiv), and NaAsc (14.8 mg, 0.074 mmol, 0.2 equiv) in 2.0 mL of degassed EtOH/$H_2O$ (v/v, 1:1) was then added to the gel top. After 15 min, the stopper was removed to collect the filtrate without extra pressure, and the solution was not flowing much. After 3 h, extra pressure was applied using the plunger (glass) of the syringe and the reaction solution was pushed through the gel carefully in 0.5 h. The gel column was then rinsed by passing 2 mL of EtOH/$H_2O$ (v/v 1:1) through the column. The combined filtrate was tested by TLC, which indicated that the reaction had full conversion. Solvent was removed, and the crude was worked up with water (2 mL)/ DCM (10 mL × 2), dried over anhydrous $Na_2SO_4$, and concentrated to afford light yellow solid (72.6 mg, 0.17 mmol, 92%) as the desired product **13-A6** (Figure S24).

The same gel column II was left at rt overnight and reused for another cycle of reaction of the azide with a different alkyne to prepare compound **13-A4**: The mixture of galactose azide **13** (68.6 mg, 0.184 mmol, 1 equiv), 1-ethynyl-1-cyclohexanol **A4** (27.3 mg, 0.22 mmol, 1.2 equiv), and NaAsc (14.8 mg, 0.074 mmol, 0.2 equiv) in 2.0 mL of degassed EtOH/$H_2O$ (v/v, 1:1) was then added to the gel top. After 15 min, the stopper was removed to collect the filtrate with extra pressure using a plunger (glass) of the syringe. The reaction solution was passed through the gel slowly over 2 h. Gel was then washed with 2 mL of EtOH/$H_2O$ (v/v 1:1). The combined filtrate was tested by TLC, which indicated that the reaction had full conversion. Solvent was removed, and the crude was worked up with water (1 mL)/ DCM (5 mL × 2) and dried over anhydrous $Na_2SO_4$, concentrated to afford solid (70.3 mg, 0.164 mmol, 89%) compound **13-A4** (Figure S24).

*Synthesis of **39** Using Gel Column I.* The gel column I formed by compound **18** was prepared as described above. This gel was used to catalyze the choroxime reaction with phenyl acetylene to compound **39**: A solution of phenyl acetylene (34 $\mu$L, 0.32 mmol, 1.2 equiv) and chloroxime **38** (50 mg, 0.26 mmol, 1 equiv) dissolved in 0.5 mL of ethanol, followed by a solution of sodium ascorbate (10 mg, 0.05 mmol, 0.2 equiv) and sodium bicarbonate (27 mg, 0.32, 1.2 equiv) dissolved in 0.5 mL of DI water to start the reaction. The reaction mixture was kept on top of the gel column for 30 min. The cap was then removed, and elution started slowly. After all of the reaction mixture had eluted, 1 mL of EtOH/$H_2O$ (v/v 1:1) was added to the gel column; however, the gel became unstable, and the gel column was then flushed with 2 mL of EtOH/$H_2O$ (v/v 2:1) and then 1 mL EtOH. The combined filtrate was sampled for $^1$H NMR, which indicated full conversion to the product (Supporting Information Figure S21). The crude product was then purified via column chromatography using 2−5% EtOAc/hexanes. The total final product **39** was obtained in 94% yield (62.5 mg, 0.25 mmol).

*Synthesis of **39** and **40** Using Gel Column II.* The gel column II was prepared as described (Figure S25). The mixture of compound **38** (34.8 mg, 0.18 mmol, 1 equiv), propargyl alcohol **A6** (12.4 mg, 0.22 mmol, 1.2 equiv), $NaHCO_3$ (30.2 mg, 0.36 mmol, 2 equiv), and sodium ascorbate (7.36 mg, 0.037 mmol, 0.2 equiv) in 2.0 mL of EtOH/$H_2O$ (v/v, 1:1) was added to the top of the gel column. After 15 min, the stopper was removed and filtrate was collected without added pressure but the mixture passed very slowly. After 3 h, pressure was applied using a plunger of the glass syringe, and the reaction solution was passed through the gel slowly in 0.5 h. Gel was then washed with 2 mL of EtOH/$H_2O$ (v/v 1:1). The combined filtrate was tested by TLC, which indicated that the reaction had full conversion. Solvent was removed, and the crude was worked up with water (1 mL)/ DCM (5 mL × 2), dried over anhydrous $Na_2SO_4$, and concentrated to afford yellow solid **40** (35.0 mg, 0.17 mmol, 93%).

The same gel column was then reused for the preparation of compound **39**. The mixture of compound **38** (34.8 mg, 0.18 mmol, 1 equiv), phenyl acetylene **A1** (22.4 mg, 0.22 mmol, 1.2 equiv), $NaHCO_3$ (30.2 mg, 0.36 mmol, 2 equiv), and sodium ascorbate (7.36

mg, 0.037 mmol, 0.2 equiv) in 2.0 mL of EtOH/$H_2O$ (v/v, 1:1) was added to the gel top. After 15 min, the stopper was removed to collect the filtrate with extra pressure using a plunger of the glass syringe. The reaction solution was passed through the gel slowly in 2 h. Gel was then washed with 2 mL of EtOH/$H_2O$ (v/v 1:1). The combined filtrate was tested by TLC, which indicated that the reaction was fully converted, and the crude was worked up with water (1 mL)/ DCM (5 mL × 2), dried over anhydrous $Na_2SO_4$, and concentrated to afford a light yellow solid **39** (42.2 mg, 0.17 mmol, 92%).

## ■ ASSOCIATED CONTENT

### Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acs.joc.0c01978.

> $^1$H and $^{13}$C NMR spectra for compounds **3−33**; 2D-COSY and HSQC NMR spectra for selected glycoconjugates and HRMS spectra ; stacked $^1$H NMR spectra for catalytic reaction monitoring and the detailed experimental conditions for reactions using gels and gel columns (PDF)
>
> Full range of HRMS spectra of compounds 17−18, 20−33 (PDF)

## ■ AUTHOR INFORMATION

### Corresponding Author

**Guijun Wang** − *Department of Chemistry and Biochemistry, Old Dominion University, Norfolk, Virginia 23529, United States;* orcid.org/0000-0001-7473-0004; Phone: (757) 683-3781; Email: g1wang@odu.edu; Fax: (757) 683-4628

### Authors

**Dan Wang** − *Department of Chemistry and Biochemistry, Old Dominion University, Norfolk, Virginia 23529, United States*

**Jonathan Bietsch** − *Department of Chemistry and Biochemistry, Old Dominion University, Norfolk, Virginia 23529, United States*

**Anji Chen** − *Department of Chemistry and Biochemistry, Old Dominion University, Norfolk, Virginia 23529, United States*

**Pooja Sharma** − *Department of Chemistry and Biochemistry, Old Dominion University, Norfolk, Virginia 23529, United States*

Complete contact information is available at: https://pubs.acs.org/10.1021/acs.joc.0c01978

### Notes

The authors declare no competing financial interest.

## ■ ACKNOWLEDGMENTS

We acknowledge financial support from the National Science Foundation (CHE No. 1818609) and Old Dominion University.

## ■ REFERENCES

(1) Terech, P.; Weiss, R. G. Low Molecular Mass Gelators of Organic Liquids and the Properties of Their Gels. *Chem. Rev.* **1997**, *97*, 3133−3160. (b) Estroff, L. A.; Hamilton, A. D. Water Gelation by Small Organic Molecules. *Chem. Rev.* **2004**, *104*, 1201−1217. (c) Du, X.; Zhou, J.; Shi, J.; Xu, B. Supramolecular Hydrogelators and Hydrogels: From Soft Matter to Molecular Biomaterials. *Chem. Rev.* **2015**, *115*, 13165−13307.

(2) Babu, S. S.; Praveen, V. K.; Ajayaghosh, A. Functional $\pi$-Gelators and Their Applications. *Chem. Rev.* **2014**, *114*, 1973−2129.

(3) Piepenbrock, M. O.; Lloyd, G. O.; Clarke, N.; Steed, J. W. Metal- and anion-binding supramolecular gels. *Chem. Rev.* **2010**, *110*, 1960−2004.

(4) Diaz Diaz, D.; Kuhbeck, D.; Koopmans, R. J. Stimuli-responsive gels as reaction vessels and reusable catalysts. *Chem. Soc. Rev.* **2011**, *40*, 427−448.

(5) (a) Datta, S.; Bhattacharya, S. Multifarious facets of sugar-derived molecular gels: molecular features, mechanisms of self-assembly and emerging applications. *Chem. Soc. Rev.* **2015**, *44*, 5596−5637. (b) Wang, G.; Goyal, N.; Mangunuru, H. P. R.; Yang, H.; Cheuk, S.; Reddy, P. V. N. Preparation and Self-assembly Study of Amphiphilic and Bispolar Diacetylene-containing Glycolipids. *J. Org. Chem.* **2015**, *80*, 733−743.

(6) Liu, M.; Ouyang, G.; Niu, D.; Sang, Y. Supramolecular gelatons: towards the design of molecular gels. *Org. Chem. Front.* **2018**, *5*, 2885−2900.

(7) Khayat, Z.; Zali-Boeini, H. Novel sugar-based azo dyes as multistimuli responsive supramolecular gelators and chemosensors. *Dyes Pigm.* **2018**, *159*, 337−344.

(8) Tsuzuki, T.; Kabumoto, M.; Arakawa, H.; Ikeda, M. The effect of carbohydrate structures on the hydrogelation ability and morphology of self-assembled structures of peptide-carbohydrate conjugates in water. *Org. Biomol. Chem.* **2017**, *15*, 4595−4600.

(9) Jadhav, S. R.; Vemula, P. K.; Kumar, R.; Raghavan, S. R.; John, G. Sugar-derived phase-selective molecular gelators as model solidifiers for oil spills. *Angew. Chem., Int. Ed.* **2010**, *49*, 7695−7698.

(10) Zhang, X.; Liu, J.; Gao, Y.; Hao, J.; Hu, J.; Ju, Y. Multi-stimuli-responsive hydrogels of gluconamide-tailored anthracene. *Soft Matter* **2019**, *15*, 4662−4668.

(11) Hein, J. E.; Fokin, V. V. Copper-catalyzed azide-alkyne cycloaddition (CuAAC) and beyond: new reactivity of copper(i) acetylides. *Chem. Soc. Rev.* **2010**, *39*, 1302−1315.

(12) Haldon, E.; Nicasio, M. C.; Perez, P. J. Copper-catalysed azide-alkyne cycloadditions (CuAAC): an update. *Org. Biomol. Chem.* **2015**, *13*, 9528−9550.

(13) Moses, J. E.; Moorhouse, A. D. The growing applications of click chemistry. *Chem. Soc. Rev.* **2007**, *36*, 1249−1262.

(14) Liang, L.; Astruc, D. The copper(I)-catalyzed alkyne-azide cycloaddition (CuAAC) "click" reaction and its applications. An overview. *Coord. Chem. Rev.* **2011**, *255*, 2933−2945.

(15) Tiwari, V. K.; Mishra, B. B.; Mishra, K. B.; Mishra, N.; Singh, A. S.; Chen, X. Cu-Catalyzed Click Reaction in Carbohydrate Chemistry. *Chem. Rev.* **2016**, *116*, 3086−3240.

(16) Figueredo, A. S.; Zamoner, L. O. B.; Rejzek, M.; Field, R. A.; Carvalho, I. Cluster glycosides and hetero-glycoclusters presented in alternative arrangements. *Tetrahedron Lett.* **2018**, *59*, 4405−4409.

(17) Chabre, Y. M.; Contino-Pepin, C.; Placide, V.; Shiao, T. C.; Roy, R. Expeditive Synthesis of Glycodendrimer Scaffolds Based on Versatile TRIS and Mannoside Derivatives. *J. Org. Chem.* **2008**, *73*, 5602−5605.

(18) Chittaboina, S.; Xie, F.; Wang, Q. One-pot synthesis of triazole-linked glycoconjugates. *Tetrahedron Lett.* **2005**, *46*, 2331−2336.

(19) Al-Mughaid, H.; Grindley, T. B. Synthesis of a Nona-valent Mannoside Glyco-dendrimer Based on Penta-erythritol. *J. Org. Chem.* **2006**, *71*, 1390−1398.

(20) Kushwaha, D.; Tiwari, V. K. Click Chemistry Inspired Synthesis of Glycoporphyrin Dendrimers. *J. Org. Chem.* **2013**, *78*, 8184−8190.

(21) Percec, V.; Leowanawat, P.; Sun, H.-J.; Kulikov, O.; Nusbaum, C. D.; Tran, T. M.; Bertin, A.; Wilson, D. A.; Peterca, M.; Zhang, S.; Kamat, N. P.; Vargo, K.; Moock, D.; Johnston, E. D.; Hammer, D. A.; Pochan, D. J.; Chen, Y.; Chabre, Y. M.; Shiao, T. C.; Bergeron-Brlek, M.; Andre, S.; Roy, R.; Gabius, H.-J.; Heiney, P. A. Modular Synthesis of Amphiphilic Janus Glycodendrimers and Their Self-Assembly into Glycodendrimersomes and Other Complex Architectures with Bioactivity to Biomedically Relevant Lectins. *J. Am. Chem. Soc.* **2013**, *135*, 9055−9077.

(22) Zhang, S.; Xiao, Q.; Sherman, S. E.; Muncan, A.; Ramos Vicente, A. D. M.; Wang, Z.; Hammer, D. A.; Williams, D.; Chen, Y.; Pochan, D. J.; Vertesy, S.; Andre, S.; Klein, M. L.; Gabius, H.-J.;

Percec, V. Glycodendrimersomes from Sequence-Defined Janus Glycodendrimers Reveal High Activity and Sensor Capacity for the Agglutination by Natural Variants of Human Lectins. *J. Am. Chem. Soc.* **2015**, *137*, 13334−13344.

(23) Cecioni, S.; Imberty, A.; Vidal, S. Glycomimetics versus Multivalent Glycoconjugates for the Design of High Affinity Lectin Ligands. *Chem. Rev.* **2015**, *115*, 525−561.

(24) Chabre, Y. M.; Roy, R. Multivalent glycoconjugate syntheses and applications using aromatic scaffolds. *Chem. Soc. Rev.* **2013**, *42*, 4657−4708.

(25) Lundquist, J. J.; Toone, E. J. The Cluster Glycoside Effect. *Chem. Rev.* **2002**, *102*, 555−578.

(26) Rajaram, H.; Palanivelu, M. K.; Arumugam, T. V.; Rao, V. M.; Shaw, P. N.; McGeary, R. P.; Ross, B. P. 'Click' assembly of glycoclusters and discovery of a trehalose analogue that retards A$\beta$40 aggregation and inhibits A$\beta$40-induced neurotoxicity. *Bioorg. Med. Chem. Lett.* **2014**, *24*, 4523−4528.

(27) Fernandes, A. E.; Jonas, A. M.; Riant, O. Application of CuAAC for the covalent immobilization of homogeneous catalysts. *Tetrahedron* **2014**, *70*, 1709−1731.

(28) Michaels, H. A.; Zhu, L. Ligand-Assisted, Copper(II) Acetate-Accelerated Azide-Alkyne Cycloaddition. *Chem. - Asian J.* **2011**, *6*, 2825−2834.

(29) Lim, M.; Lee, H.; Kang, M.; Yoo, W.; Rhee, H. Azide-alkyne cycloaddition reactions in water via recyclable heterogeneous Cu catalysts: reverse phase silica gel and thermoresponsive hydrogels. *RSC Adv.* **2018**, *8*, 6152−6159.

(30) Chen, A.; Samankumara, L. P.; Dodlapati, S.; Wang, D.; Adhikari, S.; Wang, G. Syntheses of Bis-Triazole Linked Carbohydrate Based Macrocycles and Their Applications for Accelerating Copper Sulfate Mediated Click Reaction. *Eur. J. Org. Chem.* **2019**, *2019*, 1189−1194.

(31) Araujo, M.; Diaz-Oltra, S.; Escuder, B. Triazolyl-Based Molecular Gels as Ligands for Autocatalytic 'Click' Reactions. *Chem. - Eur. J.* **2016**, *22*, 8676−8684.

(32) Karan, C. K.; Sau, M. C.; Bhattacharjee, M. A copper(II) metal-organic hydrogel as a multifunctional precatalyst for CuAAC reactions and chemical fixation of CO2 under solvent free conditions. *Chem. Commun. (Cambridge, U. K.)* **2017**, *53*, 1526−1529.

(33) Ozkal, E.; Oezcubukcu, S.; Jimeno, C.; Pericas, M. A. Covalently immobilized tris(triazolyl)methanol-Cu(I) complexes: highly active and recyclable catalysts for CuAAC reactions. *Catal. Sci. Technol.* **2012**, *2*, 195−200.

(34) Wang, D.; Deraedt, C.; Ruiz, J.; Astruc, D. Magnetic and Dendritic Catalysts. *Acc. Chem. Res.* **2015**, *48*, 1871−1880.

(35) Deraedt, C.; Pinaud, N.; Astruc, D. Recyclable Catalytic Dendrimer Nanoreactor for Part-Per-Million CuI Catalysis of "Click" Chemistry in Water. *J. Am. Chem. Soc.* **2014**, *136*, 12092−12098.

(36) Zhang, X.; Liu, P.; Zhu, L. Structural determinants of alkyne reactivity in copper-catalyzed azide-alkyne cycloadditions. *Molecules* **2016**, *21*, 1697.

(37) Kislukhin, A. A.; Hong, V. P.; Breitenkamp, K. E.; Finn, M. G. Relative Performance of Alkynes in Copper-Catalyzed Azide-Alkyne Cycloaddition. *Bioconjugate Chem.* **2013**, *24*, 684−689.

(38) Fang, W.; Zhang, Y.; Wu, J.; Liu, C.; Zhu, H.; Tu, T. Recent Advances in Supramolecular Gels and Catalysis. *Chem. - Asian J.* **2018**, *13*, 712−729.

(39) Hawkins, K.; Patterson, A. K.; Clarke, P. A.; Smith, D. K. Catalytic Gels for a Prebiotically Relevant Asymmetric Aldol Reaction in Water: From Organocatalyst Design to Hydrogel Discovery and Back Again. *J. Am. Chem. Soc.* **2020**, *142*, 4379−4389.

(40) Dawn, A. Supramolecular gel as the template for catalysis, inorganic superstructure, and pharmaceutical crystallization. *Int. J. Mol. Sci.* **2019**, *20*, 781.

(41) Rodriguez-Llansola, F.; Escuder, B.; Miravet, J. F. Switchable performance of an L-proline-derived basic catalyst controlled by supramolecular gelation. *J. Am. Chem. Soc.* **2009**, *131*, 11478−11484.

(42) Escuder, B.; Rodriguez-Llansola, F.; Miravet, J. F. Supramolecular gels as active media for organic reactions and catalysis (review). *New J. Chem.* **2010**, *34*, 1044−1054.

(43) He, Y.; Bian, Z.; Kang, C.; Cheng, Y.; Gao, L. Chiral binaphthylbisbipyridine-based copper(I) coordination polymer gels as supramolecular catalysts. *Chem. Commun. (Cambridge, U. K.)* **2010**, *46*, 3532−3534.

(44) Krishnan, B. P.; Sureshan, K. M. Topochemical azide-alkyne cycloaddition reaction in gels: Size-tunable synthesis of triazole-linked polypeptides. *J. Am. Chem. Soc.* **2017**, *139*, 1584−1589.

(45) Tu, T.; Assenmacher, W.; Peterlik, H.; Weisbarth, R.; Nieger, M.; Dotz, K. H. An air-stable organometallic low-molecular-mass gelator: synthesis, aggregation, and catalytic application of a palladium pincer complex. *Angew. Chem., Int. Ed.* **2007**, *46*, 6368−6371.

(46) Zhang, W.; Dynes, J. J.; Hu, Y.; Jiang, P.; Ma, S. Porous metal-metalloporphyrin gel as catalytic binding pocket for highly efficient synergistic catalysis. *Nat. Commun.* **2019**, *10*, 1−8.

(47) Mangunuru, H. P. R.; Yerabolu, J. R.; Wang, G. Synthesis and study of N-acetyl D-glucosamine triazole derivatives as effective low molecular weight gelators. *Tetrahedron Lett.* **2015**, *56*, 3361−3364.

(48) Mangunuru, H. P. R.; Yerabolu, J. R.; Liu, D.; Wang, G. Synthesis of a series of glucosyl triazole derivatives and their self-assembling properties. *Tetrahedron Lett.* **2015**, *56*, 82−85.

(49) Chen, A.; Wang, D.; Bietsch, J.; Wang, G. Synthesis and characterization of pentaerythritol derived glycoconjugates as supramolecular gelators. *Org. Biomol. Chem.* **2019**, *17*, 6043−6056.

(50) Chen, G.; Kumar, J.; Gregory, A.; Stenzel, M. H. Efficient synthesis of dendrimers via a thiol-yne and esterification process and their potential application in the delivery of platinum anti-cancer drugs. *Chem. Commun. (Cambridge, U. K.)* **2009**, 6291−6293.

(51) Haridas, V.; Sharma, Y. K.; Naik, S. Multi-tier dendrimers with an aromatic core. *Eur. J. Org. Chem.* **2009**, *2009*, 1570−1577.

(52) Weyrauch, J. P.; Hashmi, A. S. K.; Schuster, A.; Hengst, T.; Schetter, S.; Littmann, A.; Rudolph, M.; Hamzic, M.; Visus, J.; Rominger, F.; Frey, W.; Bats, J. W. Cyclization of propargylic amides: mild access to oxazole derivatives. *Chem. - Eur. J.* **2010**, *16*, 956−963.

(53) Chabre, Y. M.; Giguere, D.; Blanchard, B.; Rodrigue, J.; Rocheleau, S.; Neault, M.; Rauthu, S.; Papadopoulos, A.; Arnold, A. A.; Imberty, A.; Roy, R. Combining Glycomimetic and Multivalent Strategies toward Designing Potent Bacterial Lectin Inhibitors. *Chem. - Eur. J.* **2011**, *17*, 6545−6562.

(54) Gragert, M.; Schunack, M.; Binder, W. H. Azide/alkyne-"Click"-reactions of encapsulated reagents: toward self-healing materials. *Macromol. Rapid Commun.* **2011**, *32*, 419−425.

(55) Ortega-Munoz, M.; Perez-Balderas, F.; Morales-Sanfrutos, J.; Hernandez-Mateo, F.; Isac-Garcia, J.; Santoyo-Gonzalez, F. Click Multivalent Heterogeneous Neoglycoconjugates - Modular Synthesis and Evaluation of Their Binding Affinities. *Eur. J. Org. Chem.* **2009**, *2009*, 2454−2473.

(56) Haridas, V.; Sharma, Y. K.; Sahu, S.; Verma, R. P.; Sadanandan, S.; Kacheshwar, B. G. Designer peptide dendrimers using click reaction. *Tetrahedron* **2011**, *67*, 1873−1884.