Clickable Amphiphilic Triblock Copolymers

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ABSTRACT: Amphiphilic polymers have recently garnered much attention due to their potential use in drug delivery and other biomedical applications. A modular synthesis of these polymers is extremely desirable, because it offers precise individual block characterization and increased yields. We present here for the first time a modular synthesis of poly(oxazoline)–poly(siloxane)–poly(oxazoline) block copolymers that have been clicked together using the copper-catalyzed azide–alkyne cycloaddition reaction. Various click methodologies for the synthesis of these polymers have been carefully evaluated and optimized. The approach using copper nanoparticles was found to be the most optimal among the methods evaluated. Furthermore, these results were extended to allow for a reactive Si—H group-based siloxane middle block to be successfully clicked. This enables the design of more complex amphiphilic block copolymers that have additional functionality, such as stimuli responsiveness, to be synthesized via a simple hydrosilylation reaction. © 2012 Wiley Periodicals, Inc. J Polym Sci Part A: Polym Chem 000: 000–000, 2012

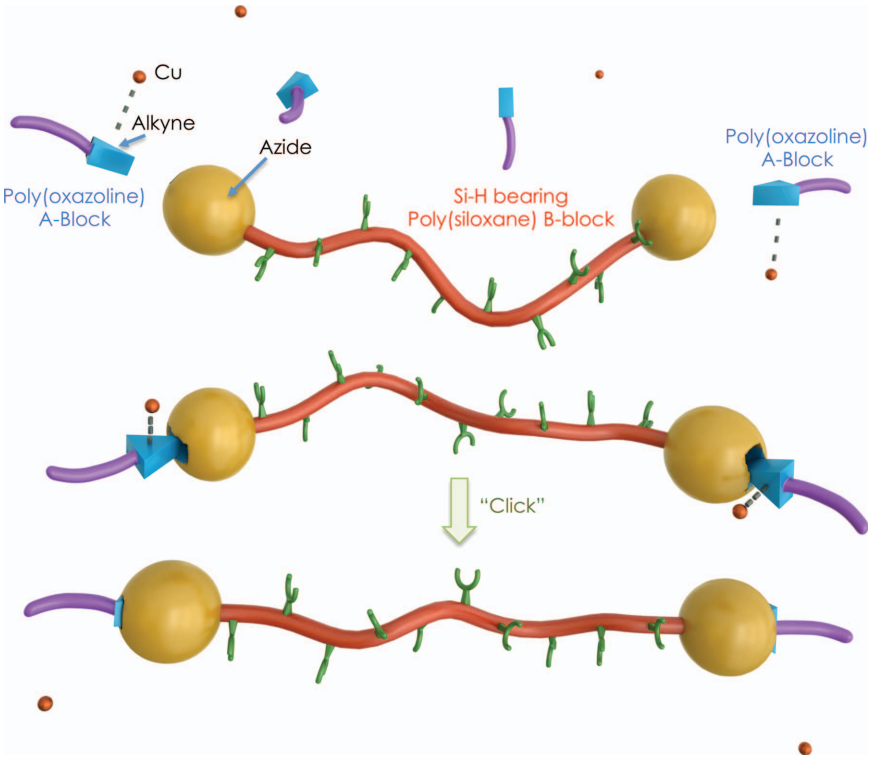
KEYWORDS: click chemistry; self-assembly; triblock copolymers

INTRODUCTION Self-assembly on the nanoscale is a key property that nature relies on to generate biological membranes. These membranes provide a structural framework via a microenvironment and a functional framework by incorporation of channels, receptors, and pumps. By exploiting hydrophobic–hydrophilic interactions, these membranes assemble into bilayers and other structures. If we hope to mimic the principles of natural nanoarchitectures, the self-assembling membrane is a critical component. Recently, a plethora of polymeric systems has successfully exploited self-assembly for the purposes of drug delivery,[1] biomedical coatings,[2] virus-assisted gene delivery,[3] and nanoreactors.[4] These are amphiphilic diblock or triblock copolymers that self-assemble into micelles, worm-like micelles, tubular structures, membranes, or vesicles in a suitable solvent.[5]

Recently, click chemistry has found considerable use in polymer–polymer conjugation via the copper-catalyzed azide–alkyne cycloaddtion (CuAAC) reaction.[6] Click-based conjugation allows for the modular synthesis of block copolymer architectures with well-defined block lengths and end-groups. This allows for systematic investigation of the effect of a single parameter variation on the self-assembling properties of the macromolecular system. For example, by using individually well-characterized hydrophobic and hydrophilic blocks, the effect of the hydrophilic block length on the self-assembling properties could be studied. This exquisite level of control allows for sophisticated scientific exploration and will enable the understanding of the underlying structure–function relationships that influence the physics of self-assembly in these macromolecules.

Although there are myriad block copolymer architectures, the ABA triblock copolymer is particularly attractive from a self-assembly standpoint due to its inherent ability to form vesicular structures, albeit with high hydrophobic to hydrophilic ratios.[7] From a biomedical perspective, the pseudopolypeptide architecture offered by poly(oxazoline) is particularly attractive and was chosen as the hydrophilic A-block.[8] Poly(siloxane)s, especially those that contain at least one methyl group, exhibit very low-glass transition temperatures and are mostly liquids at room temperatures, due to the partial ionic character of the Si—CH_3 bond.[9] Furthermore, poly(siloxane)s have very low-surface energy and are extremely hydrophobic; thus, they were chosen as the B-block. This ABA block copolymer system has been studied by our group and others using a macroinitiation-based synthesis scheme and has been shown to possess interesting biomedical and self-assembling properties.[10–14] However, macroinitiation-based schemes suffer from low yields and poor repeatability. To increase yield and enable accurate molecular weight control of the hydrophilic blocks, we envisioned that a modular click-based approach would be superior. In this work, we report for the first time a facile and versatile click-based

Additional Supporting Information may be found in the online version of this article.

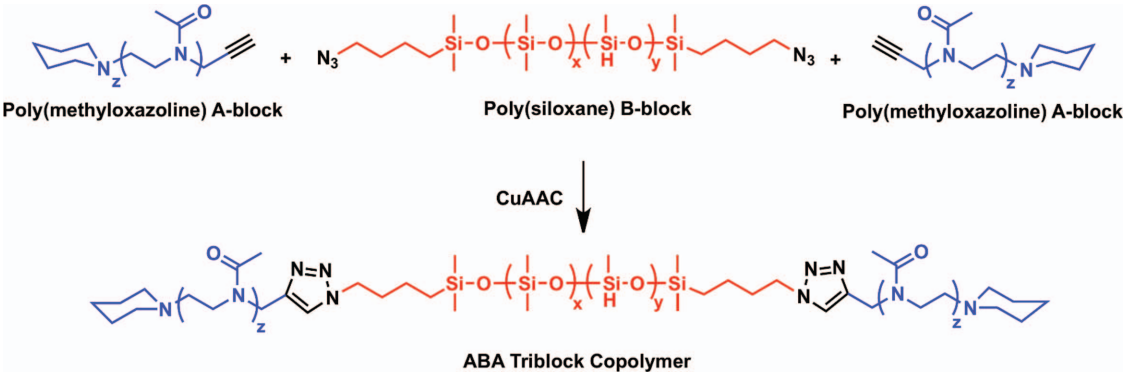


SCHEME 1 Schematic view of our click-based triblock copolymer synthesis. The A-blocks bear an alkyne terminal group, while the B-blocks are terminated with azides. The two blocks are clicked via a copper-catalyzed azide-alkyne click reaction. The blocks can be further derivatized via a hydrosilylation reaction.

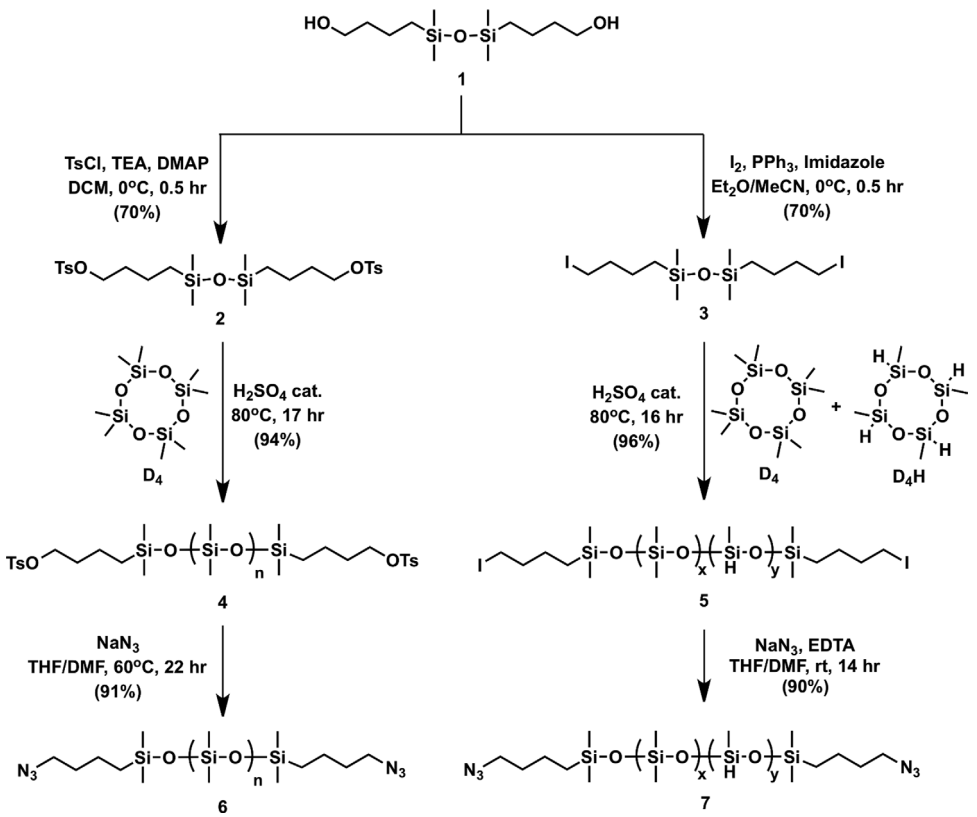
methodology for the synthesis of poly(oxazoline)–poly(siloxane)–poly(oxazoline)-based block copolymers (Scheme 1).

RESULTS AND DISCUSSION

Although our main objective was to demonstrate the synthesis of amphiphilic ABA triblock copolymers that contain a poly(siloxane) B-block and poly(oxazoline) A-blocks (Scheme 2), we used a cohesive approach that optimized every step. We began with the synthesis of two telechelic bis-azide poly(siloxane) B-blocks; one consists of poly(dimethylsiloxane) (PDMS), the other is a copolymer of dimethylsiloxane and methylhydrosiloxane [P(DMS-*co*-MHS)], with free Si—H groups available for further derivatization. Synthesis of the poly(methyloxazoline) (PMOXA) A-block with alkyne functionality was accomplished in high yield using a propargyl tosylate initiator. We envisioned the alkyne end-group would allow for facile and modular attachment of a PMOXA block to each end of the bis-azide poly(siloxane)s block via CuAAC. The bis-azide PDMS was used as a model for CuAAC reactions with PMOXA, with that methodology later applied to the more functionally complex P(DMS-*co*-MHS) copolymer. The polymer–polymer conjugation of these blocks was thoroughly investigated using an array of CuAAC click conditions.



SCHEME 2 Synthesis of ABA triblock copolymer from alkyne-functionalized poly(oxazoline) A-block and bis-azide poly(siloxane) B-block homopolymers via copper-catalyzed alkyne-azide cycloaddition (CuAAC) click reaction.



SCHEME 3 Synthesis of bis-azide poly(siloxane) B-blocks **6** and **7** via cationic ring-opening polymerization of cyclic siloxane monomers using the end-blocker method.

Synthesis of Bifunctional Disiloxane End-Blockers

The synthesis of bifunctional poly(siloxane)s was achieved via cationic ring-opening polymerization (CROP) of cyclic siloxane monomers, terminated by a short-chain disiloxane (Scheme 3). This short-chain disiloxane is commonly referred to as the end-blocker, because it serves as the end-groups of poly(siloxane) and also terminates the polymerization. The reactivity of short-chain disiloxanes is higher than the corresponding cyclic in a CROP, allowing the disiloxane to serve as an initiator.[15] Acid-labile Si—O bonds are constantly broken and reformed during the cationic polymerization; thus, the acid-stable Si—C bonds of the end-blocker terminate the growing chain and serve as end-groups.[15] Bis-tosylate end-blocker (**2**) was synthesized from commercially available 1,3-bis(4-hydroxybutyl)tetramethyldisiloxane (**1**). Previously, we reported the synthesis of tosylate end-blockers that suffered from poor yields.[14] This was primarily due to acidic cleavage of the highly acid-labile disiloxane bond, probably due to the hydrochloric acid by-product produced during the course of the reaction and/or acidic cleavage by silica chromatography used for purification. The addition of 10 equiv of triethylamine (rather than the 4 equiv of triethylamine used previously) ensured neutralization of the hydrochloric acid by-product during the course of the reaction. Siloxane cleavage during purification was circumvented by passing the crude product through a silica gel plug that had been deactivated by spinning in a triethylamine solution. These additional steps reduced the acidic cleavage of disiloxane, providing the bis-tosylate end-blocker in an improved yield of 70%. Bis-iodide end-blocker (**3**) was synthesized in 70% yield, by conversion of the hydroxyl groups of **1** using a known iodination procedure.[16]

Synthesis of Bifunctional Poly(siloxane)s

Bifunctional poly(siloxane)s were synthesized rapidly and in excellent yields via CROP of cyclic siloxane monomers (Scheme 3). Molecular weight control was achieved using the end-blocker method. When octamethylcyclotetrasiloxane (D_4) was used as the siloxane monomer and bis-tosylate disiloxane (**2**) as the end-blocker, TsO-PDMS-OTs (**4**) was synthesized in high yield. Using bis-iodide disiloxane end-blocker (**3**) with a combination of D_4 and 1,3,5,7-tetramethylcyclotetrasiloxane (D_4H) afforded the copolymer of dimethylsiloxane and methylhydrosiloxane, I-P(DMS-*co*-MHS)-I (**5**). Bis-iodide disiloxane (**3**) was used as the end-blocker for the siloxane copolymer synthesis as opposed to bis-tosylate disiloxane (**2**), which allows for room-temperature conversion of the poly(siloxane) end-groups to azides. This prevents undesired heat-activated reaction pathways that give rise to side products as discussed in the next section. Our group previously reported the synthesis of a TsO-P(DMS-*co*-MHS)-OTs polymer that used a bis-tosylate end-blocker and used *p*-toluenesulfonic acid as the catalyst.[14] However, this method suffered from moderate yields and long reaction times, with

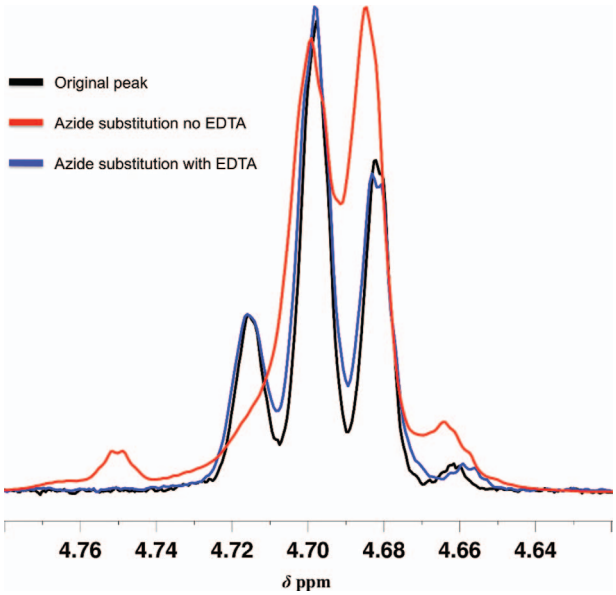


FIGURE 1 ^{1}H NMR spectra of the Si—H peak of I-P(DMS-*co*-HMS)-I (**5**) and N_3-P(DMS-*co*-HMS)-N_3 (**7**) when EDTA was not added to the substitution reaction and when EDTA was included. The peak was perturbed when EDTA was not present, but remained unaffected with EDTA in the reaction.

subsequent experiments revealing incomplete monomer consumption and precipitation of the acid catalyst, indicating the need for a different acid catalyst. When bulk polymerizations of siloxanes were conducted using sulfuric acid as the ring-opening catalyst at 80 °C, the reactions proceeded overnight in excellent yields with high-monomer consumption, probably due to the better solubility of the acid catalyst. ^{1}H NMR was used to monitor reaction progress. After the removal of unreacted cyclics *in vacuo*, followed by aqueous workup, the poly(siloxane)s were provided. TsO-PDMS-OTs (**4**) was synthesized in 94% yield with $M_n \sim 5300$, while I-P(DMS-*co*-MHS)-I (**5**) was synthesized in 96% yield with $M_n \sim 5300$. Molecular weights of the poly(siloxane)s were determined by ^{1}H NMR using end-group analysis.

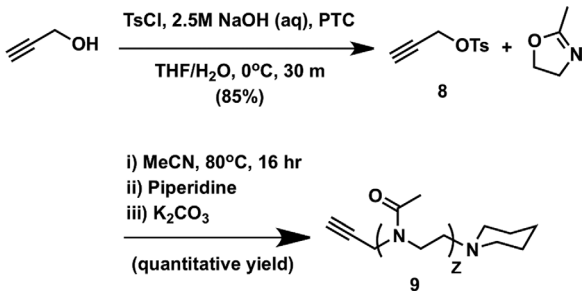
Synthesis of Bis-azide Poly(siloxane)s

Poly(siloxane)s were converted into clickable partners for the alkyne-functionalized poly(oxazoline) A-blocks by conversion of the iodide or tosylate end-groups into azides, using sodium azide (Scheme 3). Although we experienced no safety issues when handling azides, we chose to convert the poly(siloxane)s end-groups to azides postpolymerization, because azides can be explosive—especially under acidic conditions.[17] The tosylate end-groups of TsO-PDMS-OTs (**4**) were easily converted to azides via nucleophilic substitution using sodium azide at 60 °C to give N_3-PDMS-N_3 (**6**) in high yield. DMF is the classic solvent used for this reaction,[17] although the insolubility of siloxanes in DMF required a binary solvent system of THF:DMF v/v 2:1 to ensure complete solubility of the siloxanes. However, when azide substitution was conducted on I-P(DMS-*co*-MHS)-I (**5**) using the same procedure, ^{1}H NMR revealed that the Si—H peak at 4.7 ppm was perturbed (Fig. 1). Poly(methylhydrosiloxane) is a known reducing agent[18] and thus interacted with radicals produced during the reaction. We therefore hypothesized an antioxidant radical scavenger such as ethylenediaminetetraacetic acid (EDTA) would preserve the Si—H groups. Indeed, when the reaction was repeated with the addition of EDTA, ^{1}H NMR revealed that the Si—H peaks were unaffected while the desired substitution at the end-groups occurred quantitatively to give N_3-P(DMS-*co*-MHS)-N_3 (**7**). In addition, we attempted an azide substitution reaction on a TsO-P(DMS-*co*-MHS)-OTs polymer using the conditions used to synthesize **7**, but found that conversion to the azide was incomplete at room temperature. Upon heating to 60°C conversion to the azide proceeded to completion, however, the Si—H peaks were perturbed in a similar manner to Figure 1. Hence, as mentioned earlier, we chose to use iodo-functionalized end-blockers when reactive Si—H groups were present. Azide conversion of **6** and **7** was further supported by FTIR spectroscopy with the appearance of an azide peak at 2096 cm^{-1} (see Supporting Information).

Synthesis of Alkyne-Functionalized Poly(methyloxazoline)

The hydrophilic poly(methyloxazoline) (PMOXA) A-block was synthesized via CROP using a propargyl tosylate initiator, which ensured terminal alkyne functionality on one end of the polymer (Scheme 4). Tosylation of propargyl alcohol proceeded rapidly and in good yield at 0 °C when a biphasic solvent system of NaOH (aq) and THF was used. Tosylation of alcohols is generally carried out with an excess of tosyl chloride; however, chromatography is usually required to remove unreacted tosyl chloride. Using a slight excess of propargyl alcohol ensured complete tosyl chloride consumption while allowing for easy removal of excess propargyl alcohol by aqueous workup to provide propargyl tosylate (**8**) in 85% yield.

Preparation of PMOXA with an acetylene end-group using a microwave irradiation approach has been previously published.[19] In contrast, our synthesis used conventional methods and is described next. Propargyl tosylate (**8**) was kept under reduced pressure overnight to remove trace water, freshly distilled 2-methyl-2-oxazoline was then added to a solution of the tosylate initiator in acetonitrile, and heated to 80 °C. After 16 h, ^{1}H NMR revealed quantitative initiation



SCHEME 4 Synthesis of alkyne-functionalized poly(methyloxazoline) (**9**) was achieved via cationic ring-opening polymerization of 2-methyl-2-oxazoline using propargyl tosylate (**8**) initiator.

TABLE 1 Results for the Formation of PMOXA-PDMS-PMOXA (**10**) and PMOXA-P(DMS-*co*-HMS)-PMOXA (**11**) Triblock Copolymers Using Various CuAAC Methods

No.	Poly(siloxane) B-block	Copper source	Solvent	Time (h)	Result	Product
1	N_3-PDMS-N_3	Cu/Asc	H_2O/THF	12	<60% conversion	**10**
2	N_3-PDMS-N_3	Cu/Asc	EtOH	2	Quantitative conversion	**10**
3	N_3-PDMS-N_3	$CuSO_4$	EtOH	15	Quantitative conversion	**10**
4	N_3-PDMS-N_3	CuBr/PMDETA	PhMe/DMF	1	Quantitative conversion	**10**
5	N_3-PDMS-N_3	CuNPs	EtOH	2	Quantitative conversion	**10**
6	N_3-P(DMS-*co*-PHS)-N_3	Cu/Asc	H_2O/THF	2	Insoluble gel produced	**11**
7	N_3-P(DMS-*co*-PHS)-N_3	CuNPs no EDTA	EtOH	2	Si—H peak perturbed	**11**
8	N_3-P(DMS-*co*-PHS)-N_3	CuNPs with EDTA	EtOH	2	Quantitative conversion	**11**

along with complete monomer consumption. Choosing the correct termination procedure is of the utmost importance as side reactions with the acetylene end-group occur with certain popular oxazoline-terminating methods. For example, termination with methanolic potassium hydroxide[20] resulted in a side reaction at the acetylene group—as evidenced by the absence of acetylene peaks in ^{1}H NMR. Termination with water is another popular method[19]; however, this does not lead to well-defined end-groups.[21] Secondary amines are an ideal choice for termination due to their good nucleophilicity; thus, the living chain ends of PMOXA were terminated with piperidine. The resulting piperidine salt can be deprotonated with potassium carbonate,[22] but doing so *in situ* resulted in a side reaction at the acetylene group. Therefore, excess piperidine must be removed before adding potassium carbonate to ensure no side reactions occur. ^{1}H NMR was used to follow the termination progress as a shift in peaks was seen with each termination step (see Supporting Information). After workup, PMOXA (**9**) was obtained in quantitative yield. End-group analysis using ^{1}H NMR revealed $M_n \sim 1350$, close to the expected M_n of 1500, and GPC indicated a PDI of 1.17 using a poly(styrene) standard.

Synthesis of PMOXA–PDMS–PMOXA Triblock Copolymer Via CuBr/PMDETA Method

Polymer–polymer conjugation of amphiphilic blocks is especially challenging due to the inherent incompatibility of the blocks. We explored several popular CuAAC methods including Copper(I) salt with an amine ligand, Copper(II) salt in conjunction with a reducing agent, and a heterogeneous coupling catalyst, namely copper nanoparticles. ^{1}H NMR was used to monitor reaction progress for all click reactions using the appearance of the triazole-CH_2-PMOXA peak at 4.58 ppm as a standard for percent conversion to triazole from azide. The results of all methods studied are shown in Table 1.

Click reactions with polymer applications frequently use CuBr/PMDETA as the catalyst[23]; thus, we attempted to conjugate homopolymers PMOXA (**9**) and N_3-PDMS-N_3 (**6**) using this catalytic method. Although tetrahydrofuran and dimethylformamide are frequently used solvents, we found that the toulene:dimethylformamide v/v 1:1 solvent system was most effective, because toluene is a theta solvent for siloxanes.[24] Many CuAAC reactions are known to proceed at room temperature; however, full conjugation did not occur at room temperature-even after 2 days. Thus, heat was required to drive the reaction to completion. Quantitative conversion occurred after 1 h using 1 equiv of N_3-PDMS-N_3 (**6**) and 2 equiv of PMOXA (**9**), circumventing the need for an excess of either block. These results were confirmed by ^{1}H NMR with the disappearance of the PDMS-CH_2-azide peak at 3.3 ppm and PMOXA-CH_2-alkyne peak at ~4.0–4.3 ppm, coupled with the appearance of triazole peaks at ~4.2–4.6 and 7.6 ppm (Fig. 2). Further evidence was provided by FTIR spectroscopy with the disappearance of the azide peak at 2096 cm^{-1} (see Supporting Information). Although

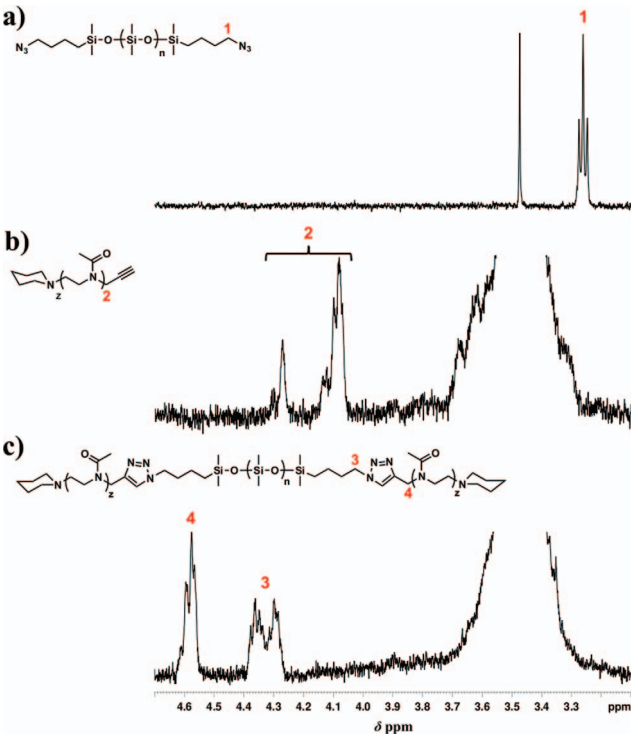
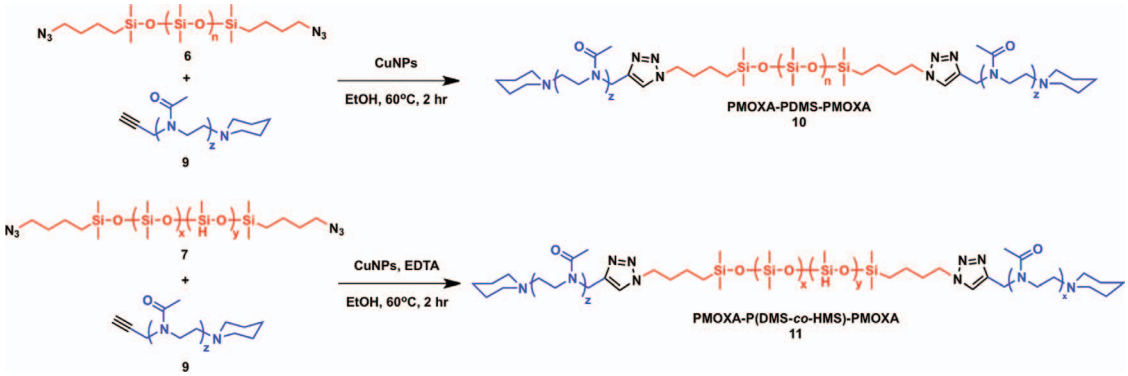


FIGURE 2 ^{1}H NMR spectra of N_3-PDMS-N_3, **6** (a), PMOXA, **9** (b), and CuAAC product PMOXA-PDMS-PMOXA, **10** (c). The disappearance of azide and alkyne peaks along with the appearance of triazole peaks indicated quantitative conversion to the triazole click product (see Supporting Information for full ^{1}H NMR).



SCHEME 5 Synthesis of PMOXA-PDMS-PMOXA (**10**) and PMOXA-P(DMS-*co*-PHS)-PMOXA (**11**) was achieved via a copper-catalyzed azide-alkyne (CuAAC) click reaction using copper nanoparticles (CuNPs) as the catalyst.

conversion was quantitative and rapid, the reaction yielded a dark-green product due to the presence of copper, which was rather difficult to purify.

Removal of copper contaminate from PMOXA–PDMS–PMOXA (**10**) was challenging for two reasons. First, the polyamide functionality of PMOXA can chelate copper, making its disassociation from the polyamide difficult. Second, any attempt to remove copper in a solvent that does not solubilize both blocks can cause polymer aggregation, allowing the copper to be "hidden" in the polymer aggregate. Efficient copper removal from CuBr/PMDETA click reactions proved unsuccessful-even after purification steps such as EDTA (aq) wash, solvent precipitation, soxhlet extraction, silica chromatography, alumina chromatography, or the use of Dowex M4195-chelating resin.[25] Sodium sulfide has been used for the removal of copper from amine groups,[26] owing to the insoluble copper sulfide salt that is formed. When 1 equiv (to copper) of 1 M Na_2S (aq) was added to a solution of copper-contaminated triblock in dichloromethane, a brown solution immediately formed along with the insoluble copper sulfide, which was removed by filtration. Although copper was successfully removed using this method, the product was pale orange, indicating the presence of trace amounts of sulfur.

Synthesis of PMOXA–PDMS–PMOXA Triblock Copolymer Via $CuSO_4$/Sodium L-Ascorbate Method

Both PDMS[27] and PMOXA[19] have been used successfully in CuAAC reactions using the $CuSO_4$/sodium L-ascorbate (Cu/Asc) method, leading us to consider it for PMOXA–PDMS–PMOXA triblock synthesis. Most conditions involve a binary solvent system that includes water, which serves to solubilize Cu/Asc. All attempts to synthesize triblock **10** using an aqueous-based binary solvent system were met with moderate conversion $<60\%$. We reasoned that the extreme hydrophobicity of poly(siloxane) causes self-aggregation in the presence of water, thus hiding the azide end-groups and preventing the reaction from proceeding to completion. We therefore attempted the CuAAC reaction in ethanol, which has the ability to solubilize both blocks, minimizing self-aggregation. Despite the heterogeneous nature of Cu/Asc in ethanol, the CuAAC reaction occurred quantitatively in 2 h at 60 °C. Furthermore, the product can be isolated by simple filtration, albeit the triblock polymer was yellow/green—indicating the presence of trace amounts of copper. When $CuSO_4$ was used as the catalyst, in the absence of sodium L-ascorbate reducing agent, the reaction proceeded to 50% completion after 2 h and quantitative completion in 15 h at 60 °C. This reaction was also successful when acetone, 2-propanol, or chloroform was used as the solvent system.

The heterogeneous nature of Cu/Asc in ethanol led us to attempt our conjugation reactions using copper nanoparticles (CuNPs), owing to their use in the synthesis of block copolymers.[28] When the CuAAC reaction was conducted using CuNPs in ethanol with 1 equiv of N_3-PDMS-N_3 (**6**) and 2 equiv of PMOXA (**9**) at 60 °C, ^{1}H NMR revealed quantitative conjugation after 2 h (Scheme 5). Furthermore, after the removal of the CuNPs via filtration, triblock copolymer **10** was obtained as a beige solid, unlike the yellow, green, or blue products of previous methods, indicating negligible copper contamination.

Synthesis of PMOXA-P(DMS-*co*-PHS)-PMOXA Triblock Copolymer

The click methodology used for the synthesis of triblock **10** containing a PDMS B-block was used for the conjugation of N_3-P(DMS-*co*-MHS)-N_3 (**7**) and PMOXA (**9**). Silanes are often used as reducing agents in organometallic chemistry[18]; therefore, complications during the CuAAC reactions due to the presence of copper were anticipated. Furthermore, Copper(I) can also act as a hydrosilylation catalyst.[29] Indeed, when the aqueous Cu/Asc procedure was applied to the synthesis of PMOXA-P(DMS-*co*-MHS)-PMOXA (**11**), an insoluble product was produced indicating significant cross-linking of the Si—H groups of the poly(siloxane) block. When the click reaction was conducted using CuNPs in ethanol at 60 °C, conjugation was quantitative after 2 h (Scheme 5). However, ^{1}H NMR showed the Si—H peak was perturbed in a similar manner that occurred during azide substitution seen previously (Fig. 1). As with the synthesis of N_3-P(DMS-*co*-MHS)-N_3 (**7**), the addition of EDTA to the CuAAC reaction using CuNPs preserved the integrity of the Si—H groups due to EDTA's radical scavenging ability. Using CuNPs as the catalyst with EDTA in ethanol at 60 °C, PMOXA-P(DMS-*co*-MHS)-

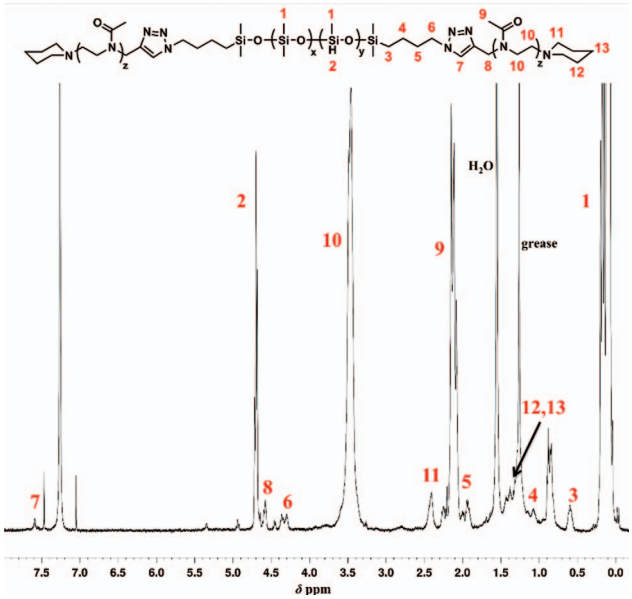


FIGURE 3 ^{1}H NMR spectrum of PMOXA-P(DMS-*co*-HMS)-PMOXA (**11**) triblock copolymer.

PMOXA (**11**) was obtained after 2 h as a beige solid in quantitative yield, as confirmed by ^{1}H NMR (Fig. 3).

In all of our triblock preparations, the proof of triblock rather than diblock formation was gleaned by carefully comparing the integration of the Si—CH_3 protons of the poly(siloxane)s block to the N—CH_2—CH_2 and O=C—CH_3 protons of the poly(oxazoline) block using ^{1}H NMR. The integration of the Si—CH_3 protons in the triblock was set to the value obtained for the poly(siloxane) homopolymer, and the resulting value of the poly(oxazoline) protons in the triblock integrated to twice the value (within experimental error) of that obtained from the poly(oxazoline) homopolymer. The procedure for the NMR-based triblock validation is as follows: the integration of the proton peak closest to the azide end-group (Si—CH_2—CH_2—CH_2—CH_2—N_3) was set to 4; because there are two end-groups, this resulted in an integration of 438 for the Si—CH_3 protons of N_3-P(DMS-*co*-HMS)-N_3 (**7**). Similarly, using the proton peak next to the alkyne initiator (OTs-CH_2-alkyne), the integration of the N—CH_2—CH_2 protons of poly(oxazoline) (**9**) was determined to be 64. When the integration of the Si—CH_3 protons in the triblock was set to 438, the integration of the N—CH_2—CH_2 protons of the triblock resulted in a value of 128, double the integration for the poly(oxazoline) homopolymer, thereby confirming triblock formation. The proton integration values yield a M_n of ~8000 g/mol for the triblock.

This clearly indicates triblock formation and further lends credence to power of the modular approach. Such characterization is not trivial, because in a macrointiation method, it could always be argued that the hydrophilic block is just longer than anticipated. Furthermore, the amphiphilic nature of these polymers does not allow for corroboration using classical characterization techniques such as GPC due to aggregation in the column. The ease of characterization, due to the excellent PDI of the poly(oxazoline) obtained due to the modular synthesis, makes the click-based approach very attractive for synthesizing this family of triblock polymers.

Self-Assembly of Triblock Copolymer

The ability of amphiphilic ABA triblock copolymers to self-assemble into higher architectures is well known[5]; thus, vesicles of PMOXA–PDMS–PMOXA (**10**) were prepared by an ethanol injection method.[7] Briefly, an ethanolic solution of the triblock was dropped into water under vigorous stirring and then filtered through a 200 nm filter. Vesicle size in solution was determined using dynamic light scattering (DLS), which revealed the hydrodynamic diameter of these vesicles to be 80 nm (see Supporting Information). Vesicles were also imaged using transmission electron microscopy (TEM) and shown to posses an average diameter of 150 nm (Fig. 4). The flattening of the vesicles under drying accounts for the larger vesicle size observed with TEM.

EXPERIMENTAL

Materials

Propargyl alcohol (Aldrich, 99%), *p*-toluenesulfonyl chloride (TsCl) (Alfa Aesar, 98%), 4-(dimethylamino)pyridine (DMAP) (Fluka, 99%), benzyltrimethylammonium chloride (Alfa Aesar, 97%), sodium hydroxide (NaOH) (Fisher Chemical), sodium sulfate anhydrous (Na_2SO_4) (Fisher Chemical, 99%), potassium carbonate anhydrous (K_2CO_3) (Fisher Chemical), 1,3-bis(4-hydroxybutyl)tetramethyldisiloxane (Gelest, 95%), sodium azide (NaN_3) (Sigma-Aldrich, 99.8%), sulfuric acid (H_2SO_4) (Fisher Chemical, 98%), Ethanol (EtOH) (Gold Shield, 200 proof), copper(II) sulfate ($CuSO_4$) (Sigma-Aldrich, 99%), (+)-sodium L-ascorbate (Aldrich, 99%), *N,N,N′,N″,N″*-pentamethyldiethylenetriamine (PMDETA) (Aldrich, 99%), triethylamine (TEA) (Fisher Chemical), sodium sulfide nonahydrate ($Na_2S\bullet 9H_2O$) (Sigma-Aldrich, 98%), iodine (I_2) (Sigma-Aldrich, 99%), triphenylphosphine (PPh_3) (Sigma-Aldrich, 99%),

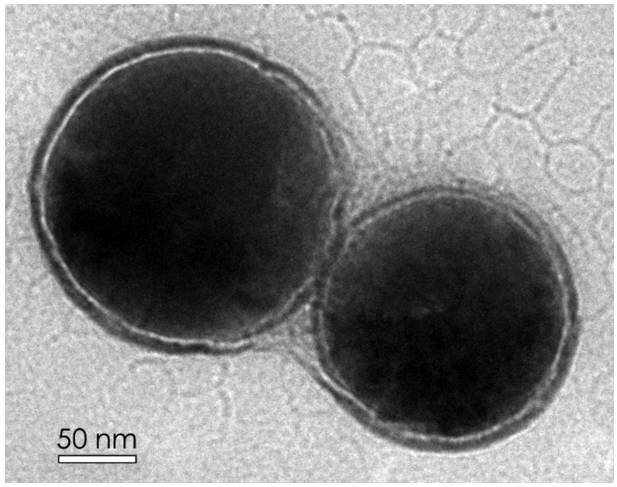


FIGURE 4 Transmission electron micrograph of PMOXA-PDMS-PMOXA (**10**) triblock copolymer vesicles demonstrating the self-assembling nature of these amphiphilic copolymers.

imidazole (Sigma-Aldrich, 99%), EDTA (Sigma-Aldrich, 99–100%), Copper nanopowder (CuNPs) (Aldrich, <50 nm particle size (TEM), 99.5%) were used as received. Copper(I) bromide (CuBr) (Sigma-Aldrich, 98%) was purified by stirring in glacial acetic acid overnight and washing with ethanol then diethyl ether. Silica gel (Silicycle, 230–400 mesh) was deactivated by spinning in an appropriate amount of TEA:hexanes v/v 5:95 solution for 10 minutes followed by filtration and several washes with hexanes. 2-Methyl-2-oxazoline (Aldrich, 98%) was purified by stirring in calcium hydride (CaH_2) overnight then fractionally distilling through a 10 cm vigreux column under argon. Piperidine (Sigma-Aldrich, 99%) was distilled under argon from CaH_2. Octamethylcyclotetrasiloxane (D_4) (Gelest, 95%) and 1,3,5,7-tetramethylcyclotetrasiloxane (D_4H) (Gelest) were distilled from CaH_2 under reduced pressure. Tetrahydrofuran (THF), dichloromethane (DCM), toluene (PhMe), acetonitrile (MeCN) and *N*-*N*-dimethylformamide (DMF) were obtained from a PureSolv solvent purification system.

Instrumentation

^{1}H NMR spectra were recorded on a Bruker Avance DMX500MHz SB NMR Spectrometer or Varian VNMRS 600MHz SB NMR Spectrometer using solutions of samples in deuterated chloroform. Fourier transform infrared spectra (FTIR) were recorded using a Nicolet Magna 850 FTIR Spectrometer. Gel permeation chromatography (GPC) studies were performed using a Waters 2695 Separation Module equipped with a 2414 Refractive Index Detector and 2996 Photodiode Array Detector. DLS experiments were obtained on a DynaPro NanoStar from Wyatt Technology. HRMS data were obtained using A Waters GCT Premier high-resolution time-of-flight mass spectrometer. TEM images were obtained using a FEI Tecnai G2 Sphera Microscope.

Synthesis of Bis-tosylate Disiloxane End-blocker (2)

1,3-Bis(4-hydroxybutyl)tetramethyldisiloxane (**1**) (8.36 g, 30 mmol, 1 equiv) was dissolved in DCM (150 mL) and cooled to 0 °C. TsCl (14.30 g, 75 mmol, 2.5 equiv) and DMAP (0.73 g, 6.0 mmol, 0.2 equiv) were added, followed by TEA (42 mL, 300 mmol, 10 equiv) dropwise, at which time a pale yellow precipitate developed. The reaction was kept at 0 °C, and, after 2 h, thin layer chromatography (TLC) showed complete disappearance of the starting material in addition to the appearance of bis-tosylate. The slurry was filtered, and the DCM layer washed with H_2O, brine, dried over Na_2SO_4, and concentrated to yield a crude yellow oil. This oil was purified by passing through a short plug of deactivated silica gel to give a pale yellow oil. Yield: 11.77 g (70%).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.78 (d, 4H; arom. H), 7.33 (d, 4H; arom. H), 4.03 (t, 4H; —$Si(CH_3)_2$—CH_2—CH_2—CH_2—CH_2—OTs), 2.45 (s, 6H; —Ph—CH_3), 1.65 (m, 4H; —$Si(CH_3)_2$—CH_2—CH_2—CH_2—CH_2—OTs), 1.31 (m, 4H; —$Si(CH_3)_2$—CH_2—CH_2—CH_2—CH_2—OTs), 0.42 (t, 4H; —$Si(CH_3)_2$—CH_2—CH_2—CH_2—CH_2—OTs), −0.01 (s, 12H; —$Si(CH_3)_2$—CH_2—CH_2—CH_2—CH_2—OTs). ^{13}C NMR (600 MHz, $CDCl_3$): δ = 144.8 (arom. C), 133.5 (arom. C), 130.0 (arom. C), 128.0 (arom. C), 70.5 (—Ph—CH_3), 32.4 (—$Si(CH_3)_2$—CH_2—CH_2—CH_2—CH_2—OTs), 21.8 (—$Si(CH_3)_2$—CH_2—CH_2—CH_2—CH_2—OTs), 19.4 (—$Si(CH_3)_2$—CH_2—CH_2—CH_2—CH_2—OTs), 17.8 (—$Si(CH_3)_2$—CH_2—CH_2—CH_2—CH_2—OTs), 0.41 (—$Si(CH_3)_2$—CH_2—CH_2—CH_2—CH_2—OTs). HRMS (*m/z*): calcd for $C_{26}H_{42}O_7S_2Si_2$, 586.19; found, 609.18 $[M + Na]^+$.

Synthesis of Bis-Iodide Disiloxane End-Blocker (3)

PPh_3 (31.5 g, 120 mmol, 4 equiv) and imidazole (10.8 g, 159 mmol, 5.3 equiv) were dissolved in Et_2O:MeCN v/v 3:1 (151 mL). The solution was cooled to 0 °C, iodine (30.5 g, 120 mmol, 4 equiv) was added, and the solution was allowed to stir for 20 min. 1,3-Bis(4-hydroxybutyl)tetramethyldisiloxane (**1**) (8.37 g, 30 mmol, 1 equiv) was added dropwise at 0 °C, after which the solution was allowed to warm to room temperature. After 1 h, TLC showed complete consumption of the starting material. The precipitate was filtered off and the filtrate concentrated. The resulting solid was washed with hexanes, then filtered, and the solvent was concentrated to give a clear oil. This oil was dissolved in hexanes and washed with $Na_2S_2O_3$ (aq), H_2O, brine, dried over Na_2SO_4, and concentrated to yield a clear oil. Yield: 10.4 g (70%).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 3.21 (t, 4H; —$Si(CH_3)_2$—CH_2—CH_2—CH_2—CH_2—I), 1.84 (m, 4H; —$Si(CH_3)_2$—CH_2—CH_2—CH_2—CH_2—I), 1.44 (m, 4H; —$Si(CH_3)_2$—CH_2—CH_2—CH_2—CH_2—I), 0.52 (t, 4H; —$Si(CH_3)_2$—CH_2—CH_2—CH_2—CH_2—I), and 0.07 (s, 12H; —$Si(CH_3)_2$—CH_2—CH_2—CH_2—CH_2—I). ^{13}C NMR (600 MHz, $CDCl_3$): δ = 36.9 (—$Si(CH_3)_2$—CH_2—CH_2—CH_2—CH_2—I), 24.4 (—$Si(CH_3)_2$—CH_2—CH_2—CH_2—CH_2—I), 17.3 (—$Si(CH_3)_2$—CH_2—CH_2—CH_2—CH_2—I), 7.17 (—$Si(CH_3)_2$—CH_2—CH_2—CH_2—CH_2—I), and 0.53 (—$Si(CH_3)_2$—CH_2—CH_2—CH_2—CH_2—I). HRMS (*m/z*): calcd for $C_{12}H_{28}I_2OSi_2$, 497.98; found, 482.96 $[M\text{-}CH_3]^+$.

Synthesis of TsO–PDMS–OTs (4)

Bis-tosylate end-blocker (**2**) (1.96 g, 3.34 mmol, 1 equiv) was added to an oven-dried round-bottomed flask with a stir bar and stirred at 60 °C under reduced pressure for 2.5 h to remove trace water. The flask was cooled to room temperature, freshly distilled D_4 (19.65 mL, 63.3 mmol, 19 equiv) was added, and the mixture was stirred at room temperature for 15 min. H_2SO_4 (0.15 mL, 2.8 mmol, 0.84 equiv) was then added dropwise, at which time the solution became viscous. The reaction was subsequently heated to 80 °C. After 17 h, an aliquot was taken for ^{1}H NMR, which indicated complete monomer consumption. Unreacted D_4 was removed *in vacuo*, and the polymer was isolated by dissolving in hexanes and washing with H_2O, MeOH, brine, dried over Na_2SO_4, and concentrated to give a clear viscous oil. Yield: 18.86 g (94%), $M_{n,^1HNMR} \sim 5300$.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.78 (d, 4H; arom. H), 7.33 (d, 4H; arom. H), 4.03 (t, 4H; —$Si(CH_3)_2$—CH_2—CH_2—CH_2—CH_2—OTs), 2.45 (s, 6H, —Ph—CH_3), 1.66 (m, 4H; —$Si(CH_3)_2$—CH_2—CH_2—CH_2—CH_2—OTs), 1.34 (m, 4H; —$Si(CH_3)_2$—CH_2—CH_2—CH_2—CH_2—OTs), 0.46 (t, 4H; —$Si(CH_3)_2$—CH_2—CH_2—CH_2—CH_2—OTs), 0.071 (br. s, 432H; —$Si(CH_3)_2$—O—); FTIR (KBr, cm^{-1}): 2963 (aliphatic C—H), 1446 (aromatic C=C), 1413 (CH_2), 1372 (sulfonyl), 1261 ($Si(CH_3)_2$—O), 1098 ($Si(CH_3)_2$—O in poly(siloxane)s, and 809 ($Si(CH_3)_2$).

Synthesis of I-P(DMS-*co*-MHS)-I (5)

Bis-iodide end-blocker (**3**) (2.49 g, 5.00 mmol, 1 equiv) was added to an oven-dried round-bottomed flask with a stir bar and stirred at 60 °C under reduced pressure for 2.5 h to remove trace water. The flask was cooled to room temperature, freshly distilled D_4 (20.17 mL, 65.0 mmol, 13 equiv) was added, followed by freshly distilled D_4H (9.76 mL, 40.0 mmol, 8 equiv), and the mixture was stirred at room temperature for 15 min. H_2SO_4 (0.15 mL, 2.8 mmol, 0.84 equiv) was added dropwise at which time the solution became viscous. The reaction was heated to 80 °C, and, after 16 h, an aliquot was taken for ^{1}H NMR that indicated complete monomer consumption. Unreacted D_4 and D_4H were removed *in vacuo*, and the polymer was isolated by dissolving in hexanes and washing with H_2O, MeOH, brine, dried over Na_2SO_4, and concentrated to give a clear viscous oil. Yield: 28.84 g (96%), $M_{n,^1HNMR} \sim 5300$.

^{1}H NMR (600 MHz, $CDCl_3$): $\delta = 4.70$ (t, 24H; —Si—*H*), 3.19 (t, 4H; —Si$(CH_3)_2$—CH_2—CH_2—CH_2—C*H*$_2$—I), 1.84 (m, 4H; —Si$(CH_3)_2$—CH_2—CH_2—C*H*$_2$—CH_2—I), 1.45 (m, 4H; —Si$(CH_3)_2$—CH_2—C*H*$_2$—CH_2—CH_2—I), 0.55 (t, 4H; —Si$(CH_3)_2$—C*H*$_2$—CH_2—CH_2—CH_2—I), 0.076 (m, 392H; —Si(C*H*$_3$)$_2$—O—); FTIR (KBr, cm^{-1}): 2964 (aliphatic C—H), 2160 (silane), 1348 (CH_2), 1261 (Si$(CH_3)_2$—O), 1096 (Si$(CH_3)_2$—O in poly(siloxane), and 800 (Si$(CH_3)_2$).

Synthesis of N_3-PDMS-N_3 (6)

TsO-PDMS-OTs **(4)** was dissolved in THF (20 mL), and then DMF (10 mL) was added, followed by NaN_3 (0.18 g, 2.83 mmol, 3 equiv) at room temperature. The mixture was heated to 60 °C and after 22 h, ^{1}H NMR showed complete conversion to the bis-azide. The white precipitate that developed during the reaction was filtered off, and THF was removed under reduced pressure. The mixture was diluted with hexanes, then placed in a separatory funnel, and the DMF was removed. The hexanes layer was washed with H_2O × 3, brine, dried over Na_2SO_4, and concentrated to give a clear oil. Yield: 4.56 g (91%).

^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 3.26$ (t, 4H; —Si$(CH_3)_2$—CH_2—CH_2—CH_2—C*H*$_2$—N_3), 1.63 (m, 4H; —Si$(CH_3)_2$—CH_2—CH_2—CH_2—C*H*$_2$—CH_2—N_3), 1.42 (m, 4H; —Si$(CH_3)_2$—CH_2—C*H*$_2$—CH_2—CH_2—N_3), 0.56 (t, 4H; —Si$(CH_3)_2$—C*H*$_2$—CH_2—CH_2—CH_2—N_3), 0.071 (br. s, 432H —Si(C*H*$_3$)$_2$—O—); FTIR (KBr, cm^{-1}): 2963 (aliphatic C—H), 2097 (azide N_3), 1413 (CH_2), 1261 (Si$(CH_3)_2$—O), 1019 (Si$(CH_3)_2$—O in poly(siloxane)s, and 800 (Si$(CH_3)_2$).

Synthesis of N_3-P(DMS-*co*-MHS)-N_3 (7)

I-P(DMS-*co*-MHS)-I (**5**) was dissolved in THF (20 mL), then DMF (10 mL) was added, followed by EDTA (83 mg, 0.28 mmol, 0.3 equiv). The mixture was degassed by bubbling argon through it for 15 min. NaN_3 (0.18 g, 2.83 mmol, 3 equiv) was added, and the mixture was spun at room temperature. After 14 h, ^{1}H NMR showed complete conversion to the bis-azide. The white precipitate that developed during the reaction was filtered off, and THF was removed under reduced pressure. The mixture was diluted with hexanes and then placed in a separatory funnel, and the DMF was removed. The hexane layer was washed with H_2O × 3, brine, dried over Na_2SO_4, and concentrated to give a clear oil. Yield: 4.50 g (90%).

^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 4.70$ (t, 24H, Si—*H*), 3.26 (t, 4H; —Si$(CH_3)_2$—CH_2—CH_2—CH_2—C*H*$_2$—N_3), 1.63 (m, 4H; —Si$(CH_3)_2$—CH_2—CH_2—C*H*$_2$—CH_2—N_3), 1.42 (m, 4H; —Si$(CH_3)_2$—CH_2—C*H*$_2$—CH_2—CH_2—N_3), 0.56 (t, 4H; —Si$(CH_3)_2$—C*H*$_2$—CH_2—CH_2—CH_2—N_3), 0.070 (m, 392H —Si(C*H*$_3$)$_2$—O—); FTIR (KBr, cm^{-1}): 2964 (aliphatic C—H), 2160 (silane), 2097 (azide N_3), 1412 (CH_2), 1261 (Si$(CH_3)_2$—O), 1094 (Si$(CH_3)_2$—O in poly(siloxane)s, and 800 (Si$(CH_3)_2$).

Synthesis of Propargyl Tosylate (8)

To a 2.5 M NaOH (aq) solution (50 mL) cooled to 0 °C, THF (50 mL) was added, followed by propargyl alcohol (5.19 mL, 89.2 mmol, 1.1 equiv) and benzyltrimethylammonium chloride (1.66 g, 8.92 mmol, 0.11 equiv). A solution of TsCl (15.30 g, 80.3 mmol, 1 equiv) in THF (50 mL) was added dropwise over 30 min, and the reaction was kept at 0 °C. After 30 min, TLC showed complete consumption of TsCl. The reaction was then placed in a separatory funnel, and the NaOH (aq) layer was removed. The organic layer was diluted with EtOAc and washed with H_2O × 3, brine, dried over Na_2SO_4, and concentrated to give a clear oil. Yield: 15.95 g (85%).

^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 7.81$ (d, 2H; arom. H), 7.35 (d, 2H; arom. H), 4.70 (d, 2H; alkyne-C*H*$_2$-OTs), 2.47 (t, 1H, alkyne-H), 2.46 (s, 3H; —Ph—C*H*$_3$). ^{13}C NMR (600 MHz, $CDCl_3$): $\delta = 145.4$ (arom. C), 133.1 (arom. C), 130.0 (arom. C), 128.3 (arom. C), 77.5 (CH_3), 75.5 (C), 57.5 (CH), and 21.8 (CH_2).

Synthesis of PMOXA (9)

Propargyl tosylate (**8**) (1.65 g, 7.83 mmol, 1 equiv) was added to an oven-dried round-bottomed flask with a stir bar and stirred at room temperature under reduced pressure overnight to remove trace water. MeCN (10 mL) was added followed by freshly distilled 2-methyl-2-oxazoline (10 mL, 118 mmol, 15 equiv), and the solution was heated to 80 °C. After 17 h, ^{1}H NMR showed complete monomer consumption. After cooling to room temperature, freshly distilled piperidine (2.32 mL, 23.5 mmol, 3 equiv) was added dropwise, and the solution was allowed to stir for 3 h. The solution was then concentrated, and the solid was washed with Et_2O to remove excess piperidine. The solid was dissolved in MeCN, K_2CO_3 (10.8 g, 78.3 mmol, 10 equiv) was added, and the mixture was stirred at room temperature overnight. The solution was then concentrated, dissolved in DCM, filtered, and the filtrate was concentrated to yield PMOXA as a white solid in quantitative yield. $M_{n,^1HNMR} \sim 1350$, PDI 1.17 (PS standards, Eluent: $CHCl_3$ + 0.25% triethylamine).

^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 4.27$–4.08 (br. m, 2H; alkyne—C*H*$_2$—N(=O)), 3.47 (br. m, 64H; —N(=O)—C*H*$_2$—C*H*$_2$—N(=O)), 2.79 (br. m, 2H; —N(=O)—CH_2—C*H*$_2$—pip), 2.41 (br. m, 4H; pip—C*H*$_2$—CH_2—CH_2—), 2.15 (br. m, 48H; N(C*H*$_3$=O), 1.56 (br. m, 4H; pip—CH_2—C*H*$_2$—CH_2—), 13.43 (br. m, 2H; pip—CH_2—CH_2—C*H*$_2$—); FTIR (KBr, cm^{-1}): 2963

(aliphatic C—H), 2117 (alkyne), 1635 (amide C=O), and 1421 (CH_3—N).

General CuBr/PMDETA Click Procedure

N_3-PDMS-N_3 (**6**) (1.0 g, 0.19 mmol, 1 equiv) and PMOXA (**9**) (0.51 g, 0.38 mmol, 2 equiv) were added to an oven-dried round-bottomed flask with a stir bar, and then DMF (5.0 mL) was added followed by PhMe (5.0 mL). PMDETA (40 μL, 0.19 mmol, 1 equiv) was added dropwise, and the solution was degassed by bubbling argon through it for 15 min. CuBr (28 mg, 0.19 mmol, 1 equiv) was added, and the flask was flushed with argon and allowed to stir at 60 °C for 1 h, at which time ^{1}H NMR showed complete conversion of the azide and alkyne to triazole. The solvent was removed *in vacuo* to give a green solid. This solid was dissolved in a minimal amount of DCM and to this solution was added 1 M Na_2S (aq) (0.19 mL, 0.19 mmol, 1 equiv). Upon 1 M Na_2S (aq) addition, the solution turned brown, was filtered, and then concentrated to yield a brown solid. The solid was dissolved in *i*-PrOH, 3 g of $MgSO_4$ was added, and the mixture was stirred overnight at room temperature, filtered, and the filtrate concentrated to yield a pale orange solid in quantitative yield.

^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.56 (br. m, 2H; triazole-H), 4.58 (br. m, 4H; triazole—CH_2—N(=O)), 4.38–4.29 (br. m, 4H; —Si$(CH_3)_2$—CH_2—CH_2—CH_2—CH_2—triazole), 3.48 (br. m, 128H; —N(=O)—CH_2—CH_2—N(=O)), 2.79 (br. m, 4H; —N(=O) —CH_2—CH_2—pip), 2.41 (br. m, 8H; pip —CH_2—CH_2—CH_2—), 2.15 (br. m, 96H; N(CH_3=O), 1.94 (br. m, 4H; —Si$(CH_3)_2$—CH_2—CH_2—CH_2—CH_2—triazole), 1.56 (br. m, 8H; pip—CH_2—CH_2—CH_2—), 1.43 (br. m, 4H; pip—CH_2—CH_2—CH_2—), 1.38 (br. m, 4H; —Si$(CH_3)_2$ —CH_2—CH_2—CH_2—CH_2—triazole), 0.59 (br. m, 4H; —Si$(CH_3)_2$ —CH_2—CH_2—CH_2—CH_2—triazole), 0.071 (br. s, 432H —Si(CH_3)$_2$—O—); FTIR (KBr, cm^{-1}): 2962 (aliphatic C—H), 1636 (amide C=O), 1420 (CH_3—N), 1261 (Si$(CH_3)_2$—O), 1019 (Si$(CH_3)_2$—O in poly(siloxane)s, and 801 (Si$(CH_3)_2$).

General $CuSO_4$/Sodium Ascorbate Click Procedure

N_3-PDMS-N_3 (**6**) (0.33 g, 0.062 mmol, 1 equiv) and PMOXA (**9**) (0.17 g, 0.12 mmol, 2 equiv) were added to an oven-dried round-bottomed flask with a stir bar and dissolved in EtOH (3.3 mL). Sodium L-ascorbate (5 mg, 0.025 mmol, 0.4 equiv) was added, and the mixture was degassed by bubbling argon through it for 15 min. $CuSO_4$ (1 mg, 0.0062 mmol, 0.1 equiv) was added, the flask was flushed with argon, and then allowed to stir at 60 °C for 2 h, at which time ^{1}H NMR showed complete conversion of the azide and alkyne to triazole. The mixture was cooled, concentrated, dissolved in DCM, and filtered to remove sodium L-ascorbate and $CuSO_4$, and then the filtrate was concentrated to yield a yellow/green solid. Yield: (0.47 g, 94 %).

^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.56 (br. m, 2H; triazole-H), 4.58 (br. m, 4H; triazole—CH_2—N(=O)), 4.38–4.29 (br. m, 4H; —Si$(CH_3)_2$—CH_2—CH_2—CH_2—CH_2—triazole), 3.48 (br. m, 128H; —N(=O)—CH_2—CH_2—N(=O)), 2.79 (br. m, 4H; —N(=O) —CH_2—CH_2—pip), 2.41 (br. m, 8H; pip—CH_2—CH_2—CH_2—), 2.15 (br. m, 96H; N(CH_3=O), 1.94 (br. m, 4H; —Si$(CH_3)_2$—CH_2—CH_2—CH_2—CH_2—CH_2—triazole), 1.56 (br. m, 8H; pip—CH_2—CH_2—CH_2—), 1.43 (br. m, 4H; pip—CH_2—CH_2—CH_2—), 1.38 (br. m, 4H; —Si$(CH_3)_2$—CH_2—CH_2—CH_2—CH_2—CH_2—triazole), 0.59 (br. m, 4H; —Si$(CH_3)_2$—CH_2—CH_2—CH_2—CH_2—CH_2—triazole), 0.071 (br. s, 432H —Si(CH_3)$_2$—O—); FTIR (KBr, cm^{-1}): 2962 (aliphatic C—H), 1636 (amide C=O), 1420 (CH_3—N), 1261 (Si$(CH_3)_2$—O), 1019 (Si$(CH_3)_2$—O in poly(siloxane)s, and 801 (Si$(CH_3)_2$).

General Copper Nanoparticles Click Procedure

N_3-P(DMS-*co*-MHS)-N_3 (**7**) (2.50 g, 0.47 mmol, 1 equiv) and PMOXA (**9**) (1.27 g, 0.12 mmol, 2 equiv) were added to an oven-dried round-bottomed flask with a stir bar and dissolved in EtOH (25 mL). EDTA (0.10 g, 0.34 mmol, 0.7 equiv) was added, and the mixture was degassed by bubbling argon through it for 15 min. CuNPs (50 mg) were added, and the flask was flushed with argon and then allowed to stir at 60 °C for 2 h at which time ^{1}H NMR showed complete conversion of the azide and alkyne to triazole. The mixture was cooled, filtered through celite, and concentrated to yield a beige solid. Yield: (3.13 g, 83 %).

^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.56 (br. m, 2H; triazole-H), 4.70 (t, 24H, Si—*H*), 4.58 (br. m, 4H; triazole—CH_2—N(=O)), 4.38–4.29 (br. m, 4H; —Si$(CH_3)_2$—CH_2—CH_2—CH_2—CH_2—triazole), 3.48 (br. m, 128H; —N(=O)—CH_2—CH_2—N(=O)), 2.79 (br. m, 4H; —N(=O) —CH_2—CH_2—pip), 2.41 (br. m, 8H; pip—CH_2—CH_2—CH_2—), 2.15 (br. m, 96H; N(CH_3=O), 1.94 (br. m, 4H; —Si$(CH_3)_2$—CH_2—CH_2—CH_2—CH_2—triazole), 1.56 (br. m, 8H; pip—CH_2—CH_2—CH_2—), 1.43 (br. m, 4H; pip—CH_2—CH_2—CH_2—), 1.38 (br. m, 4H; —Si$(CH_3)_2$—CH_2—CH_2—CH_2—CH_2—triazole), 0.59 (br. m, 4H; —Si$(CH_3)_2$—CH_2—CH_2—CH_2—CH_2—triazole), 0.071 (br. s, 392H; —Si(CH_3)$_2$—O—); FTIR (KBr, cm^{-1}): 2962 (aliphatic C—H), 2160 (silane), 1636 (amide C=O), 1420 (CH_3—N), 1261 (Si$(CH_3)_2$—O), 1019 (Si$(CH_3)_2$—O in poly(siloxane)s, and 801 (Si$(CH_3)_2$).

Vesicle Preparation Procedure

PMOXA–PDMS–PMOXA (**10**) triblock copolymer (10 mg) was dissolved in ethanol (1 mL, 10 wt % polymer). The polymer solution was then added dropwise to water (1 mL, 5 wt % polymer) under vigorous stirring to yield an opaque solution, which cleared after ~1 h of stirring. The vesicles were then filtered twice through 0.2 μL filters (PTFE).

CONCLUSIONS

We have successfully demonstrated a versatile yet facile method for synthesizing amphiphilic triblock copolymers using click chemistry. We have presented a matrix of conditions under which such polymers can be synthesized, the optimal method being that which uses copper nanoparticles. We believe that the modular synthesis of these polymers will allow for systematic investigation of their structure–function relationships. The poly(oxazoline)–poly(siloxane)–poly(oxazoline) ABA blocks can self-assemble into vesicles under appropriate conditions. These polymers are ideal systems for biomedical applications such as drug delivery and synthetic lipid bilayers for ion-channel studies. Furthermore,

we have shown that polymers with the Si—H functionality in the middle block allows for further functionality via a hydrosilylation reaction. We are currently exploring the functionalization of these polymers and their use in bioengineering and medicine.

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