Revisiting Thiol-yne Chemistry: Selective and Efficient Monoaddition for Block and Graft Copolymer Formation

This manuscript is for the special edition celebrating Prof. Frechet's 70th birthday and is dedicated to his extraordinary contributions to field of polymer science.

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ABSTRACT: The untapped potential of radical thiol-yne monoaddition chemistry is exploited to overcome the known limitations of thiol-ene chemistry in polymer coupling and block copolymer formation. By careful choice of alkyne, the reaction can selectively lead to the mono-addition product with efficiencies surpassing those achieved by traditional thiol-ene chemistry. This improvement is illustrated by the nearly quantitative synthesis of a variety of diblock and graft copolymers. © 2014 Wiley Periodicals, Inc. J. Polym. Sci., Part A: Polym. Chem. **2014**, *00*, 000–000

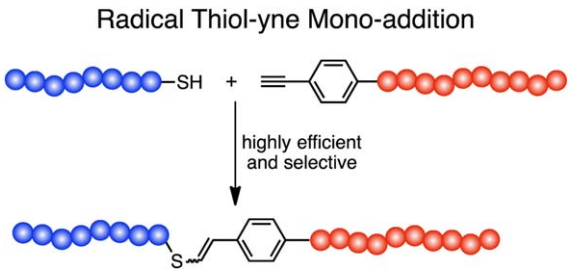
KEYWORDS: block copolymers; click chemistry; functionalization of polymers; synthesis; thiol-yne

INTRODUCTION Block copolymers and related advanced macromolecular architectures have played a pivotal role in the development of nanostructured materials, enabling transformative technologies ranging from thermoplastic elastomers to drug delivery vehicles.[1] Polymer–polymer coupling provides an efficient synthetic route to a wide variety of block copolymers, particularly when it is challenging to find sequential polymerization conditions compatible with various monomer families. An additional benefit from a polymer-coupling strategy is the ability to start from stable, well-defined starting polymers leading to the reproducible synthesis of block copolymers with predetermined molecular weights (Scheme 1).[2] Synthetically, polymer coupling reactions are among the most challenging chemical transformations and are limited by low end group concentration, steric effects and decreased reactivity.

In recent years, the potential of polymer–polymer coupling reactions for the preparation of block copolymers have been illustrated by "click" strategies, a set of highly efficient and orthogonal chemistries that have been widely used in the synthesis of small molecules and the functionalization of polymers.[3] The additional challenges inherent in the coupling of two polymer chain ends have been highlighted by Barner-Kowollik et al.[4] who proposed further requirements, including equimolar stoichiometries, simplified purification, high yields and fast timescales. One of the most widely used reactions in the context of click chemistry is the radical hydrothiolation of alkenes, referred to as thiol-ene chemistry, which has been used in the synthesis of polymer networks,[5] functional surfaces,[6] and dendrimers.[7,8] Advantages of this reaction over other methodologies include facile synthetic access to both alkenes and thiols as well as spatiotemporal control that can be achieved by using a radical photoinitiator. Efficient polymer–polymer coupling, which can be regarded as a litmus test for any "click" reaction, has, despite significant efforts, thus far been elusive by means of thiol-ene chemistry with reported coupling efficiencies reaching only 25%.[9]

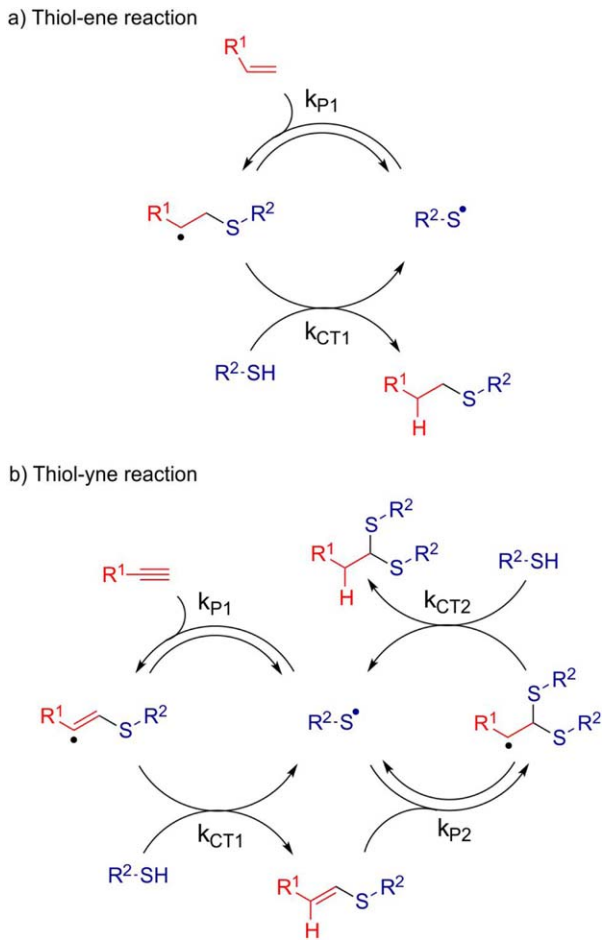
Johannes K. Sprafke and Jason M. Spruell contributed equally to this work.

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



SCHEME 1 Graphical representation of thiol-yne monoaddition as a "Click" reaction for block copolymer formation.

The factors that determine the efficiency of the radical thiol-ene reaction are well understood, as is the reaction mechanism [Scheme 2(a)].[8(b),10] In short, a radical initiator activated by either heat or light converts a thiol into a thiyl radical that then adds to the alkene, generating a sp^3 carbon-centered radical (propagation step). This radical then abstracts a hydrogen atom from another thiol to form the thioether product and regenerates a thiyl radical that propagates a further cycle (chain transfer step). Electron-rich alkenes have the highest radical addition rates, while the rate of hydrogen abstraction is limited by the stability of the carbon centered radical. Indeed, thiol-ene reactions of styrene or methacrylates involving highly stabilized radicals have much lower hydrogen abstraction rates, resulting in a variety of side reactions, particularly homopolymerization, that lower the efficiency of the coupling reaction.[8(b)]



SCHEME 2 Mechanism of (a) the thiol-ene reaction and (b) the thiol-yne reaction.

In order to improve the efficiency of reactions involving readily available thiol chain ends for block copolymer synthesis, we turned our attention to radical intermediates that are less stable than the sp^3-centered radicals formed from the commonly used alkenes in thiol-ene chemistry. Vinyl radicals are intermediates in the thiol-yne reaction and are known to be significantly less stable than alkyl radicals. This suggests that thiol-yne monoaddition may be a more efficient alternative to the classic thiol-ene reaction.

While the thiol-yne reaction has recently gained popularity for its ability to cleanly form bis-adducts without significant monoadduct accumulation,[11] initial studies nearly a century ago demonstrated that for select substrates, such as phenylacetylene derivatives, quantitative monoaddition could be achieved.[12] This selectivity can be explained by the generally accepted mechanism for the thiol-yne reaction that follows the identical propagation and chain transfer steps as the thiol-ene reaction [Scheme 2(b)].[11(a)] The first addition of the thiol to the alkyne forms a vinyl sulfide intermediate that can then react with another thiol to form the bis-adduct. In both reactions, the addition of the thiyl radical is reversible, whereas the hydrogen abstraction is irreversible. Therefore, the selectivity for mono- or bis-addition is solely determined by the ratio of the two hydrogen abstraction steps, k_{CT1} and k_{CT2}, which in turn depends on the relative stability of the carbon-centered radical intermediates. In the case of the thiol-yne reaction with phenylacetylene, the stabilized benzyl radical formed in the second addition step results in a significantly lower k_{CT2} when compared to k_{CT1}, and the initial vinyl radical. A direct consequence of this is the high selectivity for monoaddition when 1 equiv of thiol is used in conjugation with phenylacetylene derivatives, which as noted above is in direct contrast to the bis-additions typically observed for thiol-yne reactions.

EXPERIMENTAL

Additional examples can be found in the Supporting Information.

General Information

Unless otherwise noted, all commercially obtained solvents and reagents were used without further purification. Poly(dimethylsiloxane-*co*-[(mercaptopropyl)methylsiloxane]) (PDMS-*co*-$PMMS_{8k}$) **9** was purchased from Gelest. Methyl 4-ethynylbenzoate was purchased from Sigma-Aldrich. Polyethylene oxide (PEO) samples PEO_{1k} **3**, PEO_{2k} **4**, and PEO_{5k} **5** were synthesized according to a published procedure.[13] NMR spectra were collected on a Varian VNMRS 600 MHz SB, Bruker Avance DMX 500 MHz SB, or a Varian Unity Inova 400-MHz spectrometer. All diffusion measurements were

carried out on a Bruker 300-MHz super-wide bore NMR spectrometer. Chemical shifts are reported in parts per million (ppm) and referenced to the residual solvent signal. Matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (MALDI-TOF MS) data were collected on a Bruker Microflex LRT, with a 60-Hz nitrogen laser (337 nm). Micromass QTOF2 Quadrupole/time-of-flight tandem mass spectrometer was used for high-resolution mass analysis using electrospray ionization (ESI). Photoluminescence spectra were recorded on a Cary Eclipse fluorescence spectrophotometer and UV–vis absorption spectra on a Shimadzu UV3600 UV-NIR spectrometer. Gel permeation chromatography (GPC) analysis was performed on a Waters Alliance HPLC system equipped with two 300 × 7.5 mm Agilent PLGEL 5 mm MIXED-D columns, a Waters 2410 differential refractometer (refractive index, RI), and a Waters 2998 photodiode array detector. Thiol-yne reactions were irradiated using a UVP Black Ray UV bench lamp XX-15L, which emits 365-nm light at 15 W. Reactions under microwave irradiation were carried out in a Biotage microwave reactor.

Representative Synthesis of Hydroxyl-Terminated Polystyrene: Preparation of PS-OH$_{6k}$

Styrene polymerization with *s*-BuLi as initiator was performed in dry cyclohexane under a purified argon atmosphere. About 1.4 M *s*-BuLi (6.4 mL, 9.0 mol) was added to 500 mL cyclohexane at room temperature followed by the addition of purified styrene (50 mL, 0.43 mol). After stirring for 10 min, the reaction mixture was heated to 45 °C and stirred overnight (ca. 12 h). Before the termination of the reaction, an excess amount of ethylene oxide (3.0 g) was added to the resulting reaction solution in order to end-cap the polystyrene (PS). After stirring for 10 min, the polymerization was quenched by the addition of an excess amount of MeOH (10 mL). The resultant PS was purified by precipitation into MeOH from CH_2Cl_2.

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.31–6.32 (br, 277H, CH_{Ar}), 3.31 (s, 2H, CH_2OH), 2.53–0.87 (br, 210H, CH_2, CHAr), 0.78–0.60 (br, 6H, CH_3); M_n (^{1}H NMR) = 5770 g·mol^{-1}; GPC ($CHCl_3$, PS standard): M_n = 5900 g·mol^{-1}, polydispersity index (PDI) (M_w/M_n) = 1.05; MALDI-TOF MS: M_n = 5930 g·mol^{-1}.

Representative Synthesis of Phenylacetylene End-Functionalized PS from Hydroxyl-Terminated Precursor: Preparation of PS$_{6k}$ (1)

PS-OH$_{6k}$ (2.7 g, 0.45 mmol), 4-ethylbenzoic acid (0.55 g, 3.8 mmol), 4-dimethylaminopyridine (99 mg, 0.81 mmol), and 4-(dimethylamino)pyridinium *p*-toluenesulfonate (0.24 g, 0.81 mmol) were placed in a dry flask under argon atmosphere and dissolved in dry CH_2Cl_2 (30 mL). Dicyclohexylcarbodiimide (0.78 g, 3.8 mmol) was added and the reaction stirred under argon at room temperature for 24 h. The reaction mixture was then filtered and the solvent removed. The crude product was passed through a short plug of silica (CH_2Cl_2) to obtain the pure PS$_{6k}$ **1** (2.5 g, 0.42 mmol, 93%) as a colorless solid.

^{1}H NMR (600 MHz, $CDCl_3$): δ 7.74–7.72 (br, 2H, CH_{Ar}), 7.52–7.49 (br, 2H, CH_{Ar}), 7.33–6.31 (br, 282H, CH_{Ar}), 4.15–3.87 (br, 2H, CH_2O_2C), 3.23 (s, 1H, CCH), 2.57–0.84 (br, 182H, CH_2, CHAr), 0.80–0.57 (br, 6H, CH_3); M_n (^{1}H NMR) = 6070 g·mol^{-1}; GPC ($CHCl_3$, PS standard): M_n = 6000 g·mol^{-1}, PDI (M_w/M_n) = 1.08; MALDI-TOF MS: M_n = 6060 g·mol^{-1}.

Preparation of Hydroxyl-Terminated Polycaprolactone (PCL): PCL-OH$_{11k}$

In a flame-dried sealed tube, dry ε-caprolactone (4.0 g, 35 mmol, 3.7 mL) (distilled from CaH_2) and benzyl alcohol (14 mg, 0.13 mmol, 13 mL) were dissolved in dry toluene (9 mL) under argon and the mixture was heated to 110 °C. Freshly distilled $Sn(Oct)_2$ (100 mg, 0.25 mmol, 63 mL) was added and the reaction mixture stirred for 2 h at 110 °C. The product PCL-OH$_{11k}$ (2.7 g) was obtained as a colorless solid from precipitation into hexanes.

^{1}H NMR (600 MHz, $CDCl_3$): δ 7.36–7.31 (br, 5H, CH_{Ar}), 5.11 (s, 2H, ArCH_2OR), 4.05 (t, J = 6.7 Hz, 182 H, CH_2OCO), 3.64 (t, J = 6.5 Hz, 2H, CH_2OH), 2.30 (t, J = 7.5 Hz, 185H, O_2CCH_2), 1.67–1.61 (m, 397H, CH_2), 1.41–1.35 (m, 185H, CH_2); M_n (^{1}H NMR) = 10,700 g·mol^{-1}; GPC ($CHCl_3$, PS standard): M_n = 20,200 g·mol^{-1}, PDI (M_w/M_n) = 1.15.

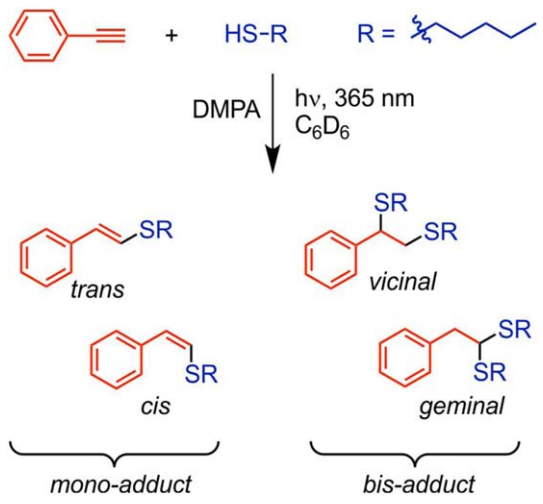
Synthesis of Phenylacetylene End-Functionalized PCL from Hydroxyl-Terminated Precursor: Preparation of PCL$_{11k}$ (2)

PCL-OH$_{11k}$ (0.75 g, 70 mmol), 4-ethylbenzoic acid (52 mg, 0.35 mmol), and 4-(dimethylamino)pyridinium *p*-toluenesulfonate (21 mg, 70 mmol) were placed in a dry flask under argon atmosphere and dissolved in dry CH_2Cl_2 (8 mL). Dicyclohexylcarbodiimide (73 mg, 0.35 mmol) was added and the reaction stirred under argon at room temperature for 24 h. Then, the reaction mixture was filtered and the solvent removed. The crude product was passed through a short plug of silica (CH_2Cl_2) and then purified using a short gravimetric SEC column (toluene). The product PCL$_{11k}$ **2** was obtained by precipitation from CH_2Cl_2 into hexanes as a colorless powder (690 mg, 64 mmol, 92%).

^{1}H NMR (600 MHz, $CDCl_3$): δ 7.98 (d, J = 8.2 Hz, 2H, CH_{Ar}), 7.54 (d, J = 7.9 Hz, 2H, CH_{Ar}), 7.38–7.31 (br, 5H, CH_{Ar}), 5.11 (s, 2H, ArCH_2OR), 4.32 (t, J = 6.5 Hz, 2H, CH_2OCOAr), 4.06 (t, J = 6.7 Hz, 187 H, CH_2OCO), 3.23 (s, 1H, CCH), 2.30 (t, J = 7.5 Hz, 189H, O_2CCH_2), 1.68–1.62 (m, 410H, CH_2), 1.41–1.36 (m, 190H, CH_2); M_n (^{1}H NMR) = 11,400 g·mol^{-1}; GPC ($CHCl_3$, PS standard): M_n = 21,800 g·mol^{-1}, PDI (M_w/M_n) = 1.12.

Representative Synthesis of Chlorine-Terminated Polysiloxane: Preparation of PDMS-Cl$_{1k}$

About 20 g of hexamethylcyclotrisiloxane (D3) was dried with 500 mg of NaH in a Schlenk tube over night at 80 °C. The pure D3 monomer was distilled bulb to bulb to a three-neck round bottom flask cooled in liquid nitrogen bath. The net weight of pure D3 monomer was 13.8 g. About 200 mL of



SCHEME 3 Product distribution of the thiol-yne reaction between phenylacetylene and 1-hexanethiol.

tetrahydrofuran (THF) was added into the flask. 10 mL of 1.4 M *s*-BuLi was added into the solution at room temperature. After 2 h, 4.5 mL of chloro(3-chloropropyl)dimethylsilane was added to quench the reaction. About 10 h later, the mixture was precipitated in 500 mL of MeOH/H_2O twice. ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.51 (t, $J = 7.0$ Hz, 2H, CH_2CH_2Cl), 1.84–1.76 (m, 2H, CH_2CH_2Cl), 1.61–1.51 (m, 1H, CH_2CH_3), 1.19–1.09 (m, 1H, CH_2CH_3), 0.96–0.90 (2 x t, 6H, CH_3), 0.68–0.61 (m, 2H, $SiCH_2$), 0.58–0.49 (m, 1H, CH_3CH), 0.16–0.03 (m, 78H, $Si(O)(CH_3)(CH_3)$); M_n (^{1}H NMR) = 1160 g·mol^{-1}; GPC ($CHCl_3$, PS standard): M_n = 1100 g·mol^{-1}, PDI (M_w/M_n) = 1.27.

Synthesis of Thiol-Terminated Polysiloxane from Chlorine-Terminated Precursor: Preparation of $PDMS_{1k}$ (6)

Polydimethylsiloxane (PDMS)-Cl_{1k} (1.00 g, 862 mmol) and potassium thioacetate (520 mg, 4.55 mmol) were dissolved in a mixture of *N*,*N*-dimethylformamide (2.5 mL) and dimethoxyethane (2.5 mL) and heated at 110 °C for 2 h in a microwave reactor. To the reaction, mixture were added CH_2Cl_2 and water. The phases were separated and the organic phase washed twice with water and once with brine. The crude product was dried under high vacuum and directly used for the following deprotection. The crude product (700 mg) was dissolved in THF (3 mL) under argon atmosphere and cooled to 0 °C. To the solution was added hydrazine (35% in H_2O, 0.29 mL, 8.18 mmol) and then stirred at room temperature for 30 min, followed by stirring at 35 °C for 2 h. After the addition of glacial acetic acid (1 mL) and water (10 mL), the organic phase was washed twice with water and then dried over sodium sulfate. After removal of the solvent, the pure product (600 mg) was obtained as a colorless oil.

^{1}H NMR (600 MHz, $CDCl_3$): δ 2.53 (dt, $J = 7.5$ Hz, 2H, CH_2CH_2SH), 1.67–1.62 (m, 2H, CH_2CH_2SH), 1.60–1.53 (m, 1H, CH_2CH_3), 1.32 (t, $J = 7.9$ Hz, 1H, CH_2SH), 1.18–1.11 (m, 1H, CH_2CH_3), 0.95–0.91 (2 x t, 6H, CH_3), 0.66–0.62 (m, 2H, $SiCH_2$), 0.57–0.51 (m, 1H, CH_3CH), 0.13–0.01 (m, 85H, $Si(O)(CH_3)(CH_3)$); M_n (^{1}H NMR) = 1240 g·mol^{-1}; GPC ($CHCl_3$, PS standard): M_n = 1300 g·mol^{-1}, PDI (M_w/M_n) = 1.30.

TABLE 1 Product Distribution of the Thiol-yne Reaction Between Phenylacetylene and 1-Hexanethiol

Alkyne Conc. (mM)	Alkyne:Thiol (Feed)	Mono-Adduct (%)	*Cis/trans* Ratio	Bis-Adduct (%)
5	1:1	100	72/28	0
50	1:1	100	40/60	0
500	1:1	100	19/81	0
500	1:1.25	97	16/84	3
500	1:1.5	94	15/85	6
500	1:2	86	16/84	14
500	1:5	36	14/86	64
500	1:10	5	20/80	95

Synthesis of Poly[styrene-co-(4-ethynyl styrene)] ($PS\text{-}co\text{-}PES_{20k}$ 8)

Styrene (1.10 mL, 8.91 mmol), 4-(3′-trimethylsilylpropargyloxy)styrene[14] (0.309 g, 1.54 mmol), and azobisisobutyronitrile (0.012 g, 0.071 mmol) were diluted in benzene (8 mL) in a Schlenk tube. The solution was deoxygenated by freezing in liquid nitrogen, evacuating the flask, and then thawing at room temperature. This process was repeated four times, upon which the vessel was placed in an oil bath heated to 70 °C for 14 h. The reaction was terminated by exposing to air, concentrating the solution *in vacuo*, then precipitating twice into MeOH (100 mL) affording a white powder (0.325 g, conversion = 25%). This solid was dissolved in THF (3 mL) at room temperature, after which a solution of tetra-*n*-butylammonium fluoride (TBAF, 3.0 mL of 1.0 M in THF) was added dropwise. The reaction mixture was stirred for 12 h, concentrated *in vacuo*, and precipitated twice into MeOH (100 mL) affording **8** as a white powder (0.301 g): M_n = 20,400 g·mol^{-1}, PDI (M_w/M_n) = 1.65.

^{1}H NMR (600 MHz, $CDCl_3$): δ 7.33–6.18 (br, 21H, CH_{Ar}), 3.04 (s, 1H, CH_{acet}), 2.27–0.86 (br, 15H, CH_2, CHAr). Styrene:alkyne ratio = 77:23.

Synthesis of Silyl-Protected Catechol Derivative CatSH (19)

To a round bottom flask were added ((4-allyl-1,2-phenylene)bis(oxy))bis(triethylsilane)[15] (10.9 g, 28.9 mmol), ethane dithiol (19.4 mL, 231 mmol) and 2,2-dimethoxy-2-phenylacetophenone (148 mg, 0.58 mmol) and sparged with argon for 30 min. The reaction was irradiated with UV light for 1 h and checked by gas chromatograph (GC) to ensure complete consumption of alkene. The excess ethane dithiol was removed by vacuum distillation and the resulting mixture was passed through a column using 25% CH_2Cl_2/hexanes as the eluent to remove residual impurities to afford (CatSH **19**) (11.6 g, 85%) as a colorless oil.

^{1}H NMR (500 MHz, $CDCl_3$): δ 6.72 (d, $J = 8.0$ Hz, 1H), 6.63 (d, $J = 2.0$ Hz, 1H), 6.59 (dd, $J = 8.0$, 2.0 Hz, 1H), 2.79–2.64

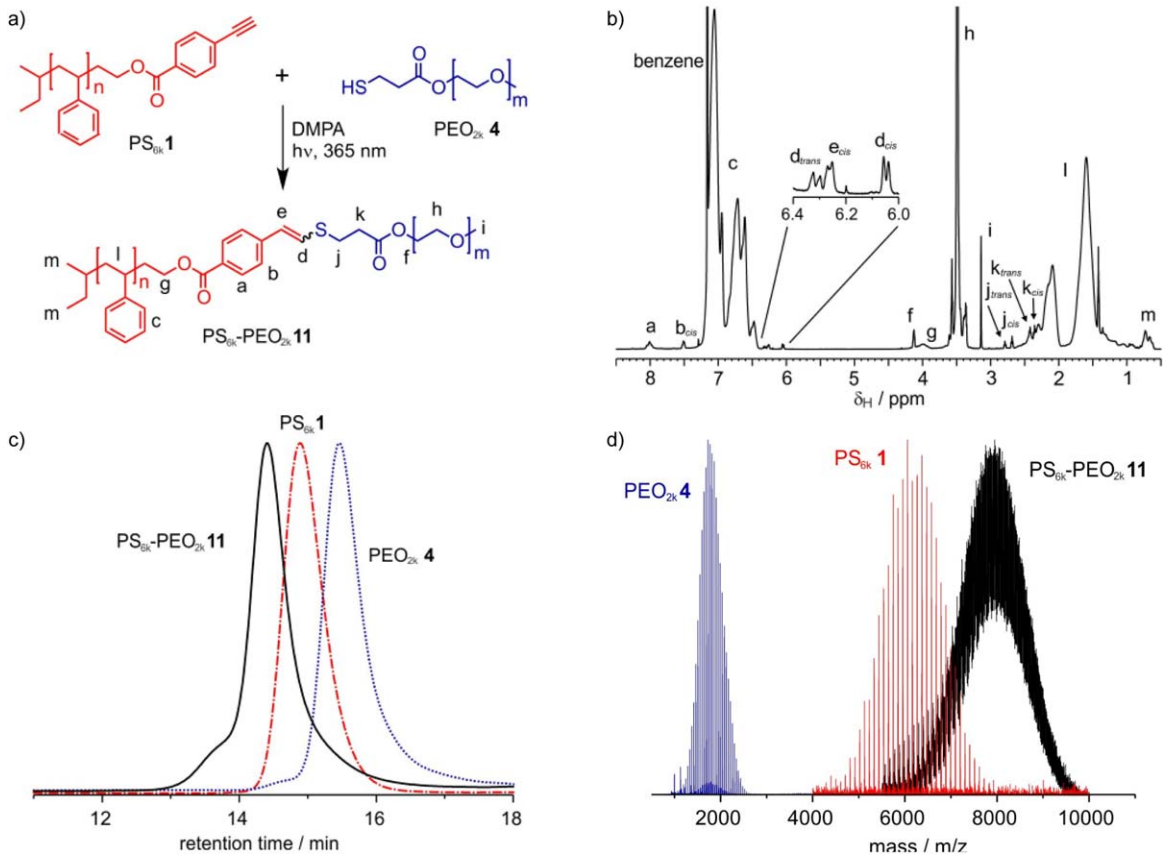


FIGURE 1 Thiol-yne monoaddition of PS_{6k} **1** and PEO_{2k} **4**. (a) Reaction scheme, (b) ^1H NMR spectrum of diblock PS_{6k}-*b*-PEO_{2k} **11** (C_6D_6, 298 K, 600 MHz) (c) GPC traces of PEO_{2k} **4** (blue dotted line), PS_{6k} **1** (red dashed-dotted line), and PS_{6k}-*b*-PEO_{2k} **11** (black line) (d) Overlay of the MALDI-TOF mass spectra of PS_{6k}-*b*-PEO_{2k} **11** (black), PS_{6k} **1** (red), and PEO_{2k} **4** (blue) allowing determination of the exact molecular weights M_n (PEO_{2k} **4**) = 1750 g·mol^{-1}, M_n (PS_{6k} **1**) = 6060 g·mol^{-1} and M_n (PS_{6k}-*b*-PEO_{2k} **11**) = 7810 g·mol^{-1}. The mass of the diblock corresponds to the sum of the two homopolymers.

(m, 4H), 2.59 (t, J = 7.4 Hz, 2H), 2.50 (t, J = 7.4 Hz, 2H), 1.85 (p, J = 7.4 Hz, 2H), 1.71 (t, J = 7.8 Hz, 1H), 0.98 (td, J = 7.9, 2.6 Hz, 18 H), 0.79 (qd, J = 7.9, 2.7 Hz, 12H); ^{13}C NMR (500 MHz, $CDCl_3$): δ 146.7, 145.1, 134.5, 121.4, 120.9, 120.4, 36.3, 34.1, 31.4, 24.9, 6.8, 5.3; high-resolution mass spectrometry (ESI-/TOF) calculated $(M + Na)^+$ 495.2219, observed $(M + Na)^+$ 495.2204.

General Procedure for Thiol-yne Coupling Reactions

The phenylacetylene-functionalized polymer (25 mM), thiol (27.5 mM), and photoinitiator 2,2-dimethoxy-2-phenylacetophenone (DMPA) (0.2 equiv per thiol) were dissolved in benzene. The reaction mixture was purged with argon and irradiated with UV light (365 nm, 15 W) until the reaction was complete, as indicated by ^1H NMR, and the product could be isolated.

RESULTS AND DISCUSSION

Small Molecule Model Studies

To demonstrate the potential of this modified thiol-yne reaction for polymer–polymer coupling and functionalization, a series of model reactions between phenylacetylene and 1-hexanethiol with 5 mol % DMPA as the photoinitiator were investigated.[12(f)] The reactions were carried out in d_6-benzene and followed by ^1H NMR spectroscopy, which allowed complete identification and quantification of the products (Scheme 3 and Table 1). After 1 h of irradiation, complete and selective conversion to the vinyl sulfide monoadduct (mixture of *cis* and *trans* products) was observed under various starting concentrations (5–500 mM). It should be noted that no evidence of the 1,1-disubstituted vinyl sulfide monoadduct was observed under any conditions.[16]

This high efficiency, particularly at low concentrations, demonstrates the potential of this reaction for polymer coupling given the molecular weight dilution of the chain ends even for low molecular weight polymers. The strong preference for monoaddition is further emphasized by the formation of only 14% bis-adduct when 2 equiv of thiol are used under the highest concentration conditions. Surprisingly, to push the bis-addition reaction to near completion, 10 equiv of thiol were required. Encouraged by the selectivity and efficiency of the model reactions, we then applied the reaction to polymer–polymer coupling.

TABLE 2 GPC Data of Starting Homopolymers and Coupling Products

No.	Homopolymer	M_n (kDa)[a]	PDI[a]
1	PS_{6k} (alkyne)	6.0	1.08
2	PCL_{11k} (alkyne)	21.8	1.12
3	PEO_{1k} (thiol)	1.9	1.10
4	PEO_{2k} (thiol)	4.0	1.10
5	PEO_{5k} (thiol)	11.0	1.06
6	$PDMS_{1k}$ (thiol)	1.3	1.30
7	$PDMS_{3k}$ (thiol)	3.3	1.16
8	PS-*co*-PES_{20k} (alkyne)	20.4	1.65
9	PDMS-*co*-$PMMS_{8k}$ (thiol)	8.1[b]	1.81
No.	Coupling Product	Mn (kDa)[a]	PDI[a]
10	PS_{6k}-*b*-PEO_{1k}	9.1	1.10
11	PS_{6k}-*b*-PEO_{2k}	10.1	1.11
12	PS_{6k}-*b*-PEO_{5k}	16.4	1.14
13	PS_{6k}-*b*-$PDMS_{1k}$	8.7	1.10
14	PS_{6k}-*b*-$PDMS_{3k}$	10.4	1.08
15	PCL_{11k}-*b*-PEO_{5k}	30.4	1.22
16	PS_{20k}-*g*-Catechol	83.9	2.12
17	PS_{20k}-*g*-Octyl	28.1	2.20
18	$PDMS_{8k}$-*g*-PS_{6k}	82.0[c]	1.57

All values determined by GPC ($CHCl_3$) using:
[a] PS standards.
[b] PDMS standards.
[c] MALS detector.

Structural Evidence for Diblock Formation

To demonstrate the applicability of this modified thiol-yne reaction for block copolymer formation, coupling of phenylacetylene end-functionalized PS PS_{6k} **1** and thiol-terminated PEO_{2k} **4** to form the PS_{6k}-*b*-PEO_{2k} diblock copolymer **11** was investigated (Fig. 1). The starting polymers were synthesized by postpolymerization modification of hydroxyl-terminated precursors that were either commercially available (PEO_{2k} **4**) or synthesized by anionic polymerization (PS_{6k} **1**). After optimizing the reaction conditions for polymer coupling (25 mM reactant concentration, 2 h irradiation, 20 mol % DMPA), a range of analytical techniques were used to confirm the high efficiency of diblock copolymer formation. For example, GPC analysis revealed a reduction in retention time for the product obtained from the coupling reaction when compared to both starting polymers with a low PDI being maintained [Fig. 1(c)]. In a similar fashion, the ^{1}H NMR spectrum of **11** shows the expected disappearance of the resonance for the terminal alkyne group of the starting PS_{6k} **1** with peaks corresponding to the linker group derived from the end functionalities of **1** and **4** (peaks a, b, j, k) being shifted compared to the starting polymers (Supporting Information Fig. S2). Direct evidence for formation of the vinyl sulfide group comes from the appearance of doublets "***e***" and "***d***," for both the *cis* and the *trans* vinylic protons, between 6.0 and 6.5 ppm [Fig. 1(b)]. These and all other peaks were assigned unambiguously using a model compound with the help of correlation spectroscopy and nuclear Overhauser effect spectroscopy two-dimensional NMR techniques (see Supporting Information). Further evidence for formation of diblock PS_{6k}-*b*-PEO_{2k} **11** comes from both matrix-assisted laser desorption/ionization [Fig. 1(d)] and diffusion-ordered spectroscopy (DOSY) which showed an array of peaks corresponding to a single diffusing species (Supporting Information Fig. S3).

Confirmation of High Coupling Efficiency

While the above studies provide structural evidence for diblock formation, it is critical to quantify the coupling efficiency. Initial evidence for the high efficiency of the reaction comes from integration of the ^{1}H NMR signals of the vinyl sulfide protons in the crude reaction mixture. Based on the PS chain end as calibration, the sum of the integrals of the *cis* and *trans* signals of vinyl proton "***d***" is close to the expected value of 1.0 (Supporting Information Fig. S2). Further support for the efficiency of the coupling process comes from comparison of the analytical data of the crude material with that of the purified product. Precipitation of the crude material into methanol would be expected to remove any unreacted PEO_{2k} **4** and possible disulfide byproduct. Significantly, the GPC trace remained essentially unchanged after purification with integration of the PS versus the PEO backbone signals in the ^{1}H NMR spectrum matching the ratio expected for PS_{6k}-*b*-PEO_{2k} **11** (Supporting Information Fig. S5). This absence of change in the NMR and GPC data strongly suggests the minimal presence of unreacted PEO homopolymer/byproducts and confirms the high efficiency of the coupling reaction under a variety of conditions.

The unique absorption feature of the vinyl sulfide linkage (strong absorption at 320 nm, extending to 370 nm, Supporting Information Fig. S6) also provides a useful means of selectively detecting vinyl sulfide containing species in the presence of potential impurities, such as the starting PEO and PS homopolymers, which do not absorb in this region. When overlaid, the GPC trace obtained at 330 nm is in good agreement with the chromatogram obtained from the RI detector. However, a small shoulder at shorter retention times is present in the RI trace that is absent in the 330 nm absorption. This shoulder indicates the presence of a small amount of higher molecular weight polymers that may arise from bis-adduct formation or be products from radical recombination processes. These impurities can be removed by column chromatography and are minor ($\leq$5%) (Supporting Information Fig. S5).

Utilizing Thiol-yne Monoaddition to Prepare Complex Polymer Architectures

Diverse Diblock Copolymers

The generality and utility of thiol-yne monoaddition for polymer coupling was demonstrated by the successful synthesis of a variety of diblock copolymers from both higher molecular weight starting materials and alternate backbones (Table 2). In addition to thiol-terminated PEO_{1k} **3** and PEO_{5k} **5**, two PDMS derivatives $PDMS_{1k}$ **6** and $PDMS_{3k}$ **7** were synthesized

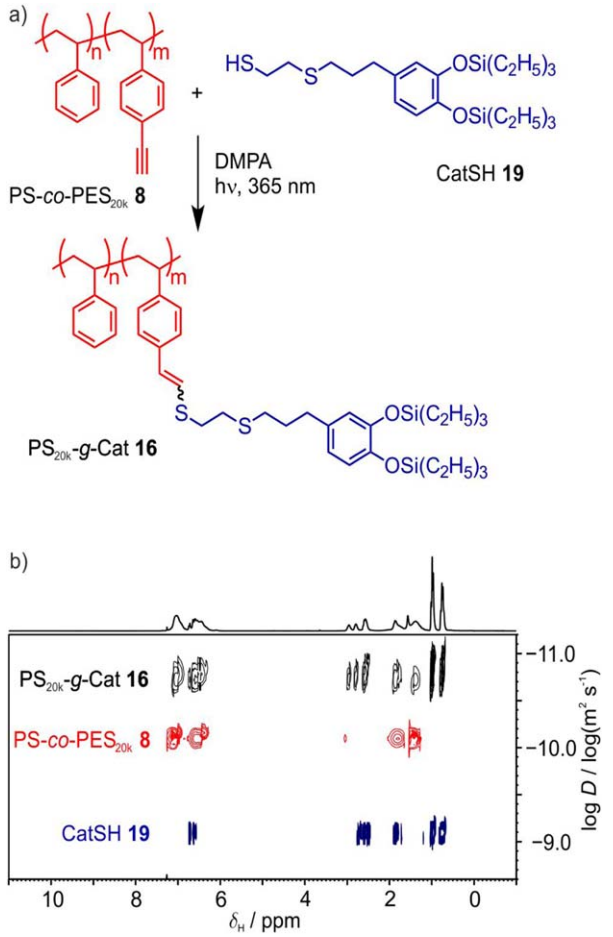


FIGURE 2 Grafting of CatSH **19** onto PS-*co*-PES_{20k} **8**. (a) Reaction scheme, $m = 0.23$, $n = 0.77$, (b) overlaid DOSY plots from independent diffusion measurements of CatSH **19** (blue), PS-*co*-PES_{20k} **8** (red), and PS_{20k}-*g*-Cat **16** (black) in $CDCl_3$ at 298 K.

by anionic polymerization followed by end group conversion into the desired thiol. Significantly, all of these polymers gave excellent coupling efficiencies with PS_{6k} **1** (see Supporting Information). The successful coupling of phenylacetylene-terminated polycaprolactone PCL_{11k} **2** with PEO_{5k} **5** further extends the range of the coupling methodology to alternate diblock copolymers and increased molecular weights with high coupling efficiency.

Functionalization of Polyfunctional Backbones

The utility of selective radical thiol-yne monoaddition for the preparation of complex macromolecular architectures was further examined by grafting small molecules or polymer chains to a polyfunctional backbone. It should be noted that grafting reactions can be even more challenging than diblock formation due to steric crowding along the backbone and the likelihood of radical-radical coupling between the multifunctional backbones.[17]

As a further demonstration of the efficiency of thiol-yne monoaddition for the preparation of complex macromolecular architectures, a variety of graft copolymers were prepared. Copolymerization of styrene with silyl-protected 4-ethynyl styrene followed by TBAF deprotection, afforded the random copolymer poly[styrene-*co*-(4-ethynyl styrene)] PS-*co*-PES_{20k} **8** with 23% backbone incorporation of phenylacetylene groups. This polymer was successfully functionalized with both 1-octanethiol **20** and the more complex catechol derivative CatSH **19** (Fig. 2) that has been shown to provide polymers with strong adhesion under a variety of environments.[18]

Formation of Grafted Copolymers

The grafting process maintains its high degree of fidelity if the backbone functionalities are thiols rather than phenylacetylene groups and even tolerates the grafting of polymer chains. This is exemplified by the grafting of PS_{6k} **1** onto the commercially available, PDMS-based copolymer, PDMS-*co*-$PMMS_{8k}$ **9**, where 13% of the repeat units bear a mercaptopropyl side chain (Fig. 3). GPC of the crude product shows a dramatic increase in molecular weight after 2 h of irradiation [Fig. 3(b) and Supporting Information Fig. S32]. The M_n of the graft polymer was found to be 82 kg·mol^{-1}, which correlates with efficient grafting and the near-quantitative nature of this process is supported by the complete conversion of end-functional group resonances as determined by ^{1}H NMR spectroscopy (Supporting Information Fig. S31).

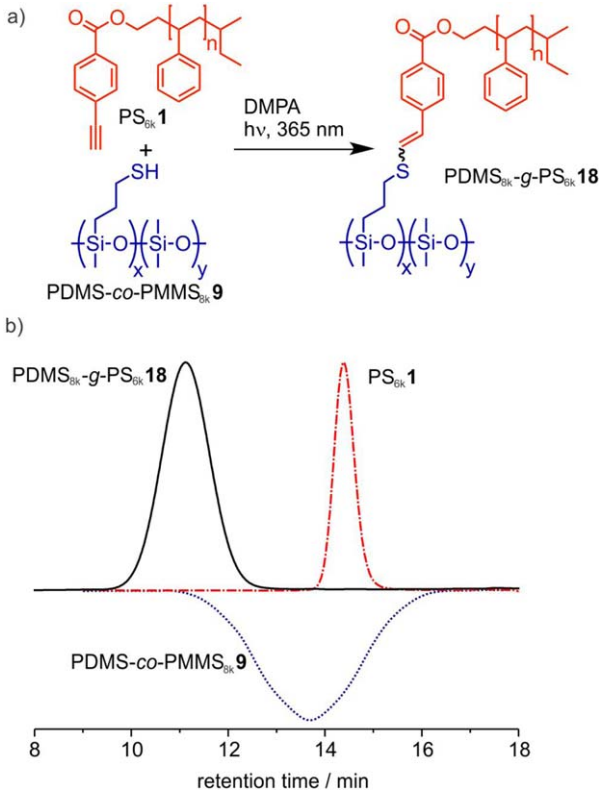


FIGURE 3 Grafting of PS_{6k} **1** onto PDMS-*co*-$PMMS_{8k}$ **19**. (a) Reaction scheme, (b) GPC ($CHCl_3$) traces of PDMS-*co*-$PMMS_{8k}$ **9** (blue dotted line), PS_{6k} **1** (red dashed-dotted line), and $PDMS_{8k}$-*g*-PS_{6k} **18** after purification by precipitation (black line).

CONCLUSIONS

In summary, we have identified selective thiol-yne monoaddition to phenylacetylene derivatives as a powerful synthetic tool for the construction of macromolecular architectures, as demonstrated by the efficient synthesis of both diblock and graft copolymers. Advantages of this new approach include facile synthesis of starting materials, equimolar stoichiometries of building blocks, high overall yields and efficient coupling. The high functional group tolerance of thiol-yne chemistry makes this methodology applicable to the synthesis of a wide range of functionalized polymers. In a wider context, the use of phenylacetylene derivatives also represents a critical improvement over vinyl substrates traditionally used in the radical thiol-ene reaction and offers wide application in many areas of materials chemistry.

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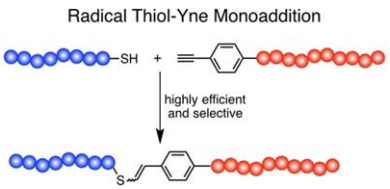

Polymer coupling reactions are some of the most challenging chemical transformations due to low end-group concentration, steric hindrance, and decreased reactivity. Thiol-yne chemistry is shown to be a near-quantitative and selective strategy for the coupling of pre-formed polymers to give block and graft copolymers. With aromatic alkynes under a wide range of conditions, specific mono-addition is achieved with efficiencies surpassing those of traditional thiol-ene chemistry.