Cyclopropenone-Masked Dibenzocyclooctyne End-Functionalized Polymers from Reversible Addition-Fragmentation Chain Transfer Polymerization

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Abstract

Functional reversible addition-fragmentation chain transfer polymerization (RAFT) agent was developed to have a cyclopropenone-masked dibenzocyclooctyne end group. RAFT polymerization was then explored on three typical types of vinyl monomers in free radical polymerization such as styrene, methyl methacrylate, and *tert*-butyl acrylate. The living polymerization behaviors were demonstrated for all three cases, which guaranteed the production of well-defined polystyrene, poly(methyl methacrylate), and poly(*tert*-butyl acrylate) end-functionalized with cyclopropenone-masked dibenzocyclooctyne groups from the convenient RAFT polymerization technique. Under UV irradiation, the cyclopropenone-masked dibenzocyclooctyne end group could be quantitatively changed to dibenzocyclooctyne clickable group, which was widely used in the metal-free strain-promoted azide-alkyne cycloaddition (SPAAC) click reaction. Subsequently, using

the dibenzocyclooctyne end-functionalized polymers as building blocks, a practical and efficient metal-free method was developed for the formation of topological polymers including block and bottlebrush polymers based on the SPAAC click reaction.

Keywords: Reversible addition-fragmentation chain transfer polymerization; Topological polymer; Strain-promoted azide-alkyne cycloaddition

1. Introduction

Since the concept was coined by Sharpless in 2001 [1], the click chemistry has become a powerful and excellent tool for fabricating molecules and materials in varied fields such as organic synthesis [1], polymer chemistry [2-4], biomedicine [5-7], interfacial and surface science [8-10], etc. Although a series of reactions have been developed and recognized as click chemistry to date including copper(I)-catalyzed azide-alkyne cycloaddition (CuAAC) [11], Diels-Alder reactions [12], and thiol-ene coupling reactions [13], the traditional CuAAC from Sharpless and co-workers is still the most popular and widely used reaction in the click chemistry family. The click characteristics of CuAAC is derived from the usage of copper(I) catalyst to catalyze the coupling reaction between azide and alkyne groups. The employment of copper(I) catalyst, however, restricts its application in certain situations such as biological research fields due to the cytotoxicity of copper catalyst [14,15]. To overcome this, the strain-promoted azide-alkyne cycloaddition (SPAAC) click reaction between cyclooctyne derivatives and azide has been developed and gained systematically investigation in recent years [16-24]. Especially in biological research fields, SPAAC has been viewed as one of the most successful bioorthogonal reaction candidates for preparing the bio-synthetic polymer conjugates in both in-vivo and in-vitro situations. For the formation of bio-synthetic polymer conjugates by covalently connecting synthetic polymer segments and biological entities, it is vital

for the preparation of well-defined polymers end-functionalized with bioorthogonally clickable groups [25-29].

As a matter of fact, end-functionalized polymers play a critical role in fabricating polymer related materials, especially after the emergence of combination between click chemistry and living polymerization techniques [30-34]. Based on the specifically designed initiators with clickable end groups, the living polymerization techniques could produce variously well-defined polymers end-functionalized with clickable groups. By virtue of the modular synthesis concept introduced by click chemistry, these end-clickable polymers have demonstrated their magnificent power not only in the formation of varied polymer conjugates, but also in the preparation of topological polymers with a library of macromolecular topologies including cyclic, star-like, and bottlebrush polymers. Similar to the formation of bio-synthetic polymer conjugates, the metal-free method is strongly preferred for preparing these topological polymers considering their time-consuming synthesis and purification process and unique applications usually in the biology fields. To perform this, the preparation method for end-functionalized polymers with cyclooctyne derivatives was urgently required to build on the metal-free living polymerization techniques.

Living radical polymerization methods such as atom transfer radical polymerization (ATRP) [35] and reversible addition-fragmentation chain transfer (RAFT) polymerization [36] have been demonstrated as the most powerful methods for preparing well-defined polymers from vinyl monomers with varied clickable end groups. Recently, by virtue of dibenzocyclooctyne functionalized and cyclopropenone-masked dibenzocyclooctyne functionalized ATRP initiators, we have developed the well-defined polymethacrylates, polystyrenics, and polyacrylates with dibenzocyclooctyne end groups from a standard ATRP protocol [37,38]. Although the metal-free SPAAC reaction has been successfully applied to prepare topological polymers including star and bottlebrush polymers, these end-functionalized polymer building blocks were unfortunately

As far as we know, RAFT polymerization has not been applied to prepare the well-defined polymers end-functionalized with cyclooctyne derivatives. Resultantly, the functional RAFT agent **1** was synthesized for the first time to have a cyclopropenone-masked dibenzocyclooctyne end group. By virtue of the standard RAFT polymerization process, variously well-defined polymers with cyclopropenone-masked dibenzocyclooctyne end groups were produced including polymethacrylates, polystyrenics, and polyacrylates. In addition, the UV-induced SPAAC clickable property of these end-functionalized polymers was demonstrated to successfully prepare the corresponding block and bottlebrush polymers.

Figure 1. (A) Preparation of cyclopropanone-masked dibenzocyclooctyne end-functionalized and the corresponding dibenzocyclooctyne end-functionalized polymers. (B) Preparation of the PS₂₆-*b*-PEO₂₃ diblock copolymer based on SPAAC click reaction. (C) Preparation of the PGA₁₀₀-*g*-PS₂₆ bottlebrush polymer based on SPAAC click reaction.

2. Experimental

2.1. Materials

Bromobenzene, 4,4'-azobis(4-cyanovaleric acid), 4-dimethylaminopyridine (DMAP), 2-hydroxybenzaldehyde, 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (EDC), magnesium powder, iodine, potassium carbonate (K₂CO₃), 3-bromopropanol, 3-methoxybenzylchloride, triphenylphosphine, Pd on charcoal (10%), aluminum chloride (AlCl₃), tetrachlorocyclopropanone, sodium hydroxide, carbon disulfide, triethylamine (TEA), methyl methacrylate (MMA), styrene (St), *tert*-butyl acrylate (*t*BA), glycidyl methacrylate (GMA), 2,2'-azoisobutyronitrile (AIBN), sodium azide (NaN₃), poly(ethylene glycol) monomethylether (*M_n*=1000, corresponding to DP=23) (PEG₂₃), methanesulfonyl chloride (MsCl), ammonium chloride (NH₄Cl), hexane, methanol, toluene, petroleum ether, ethyl acetate, diethyl ether, dichloromethane (DCM), tetrahydrofuran (THF) and *N,N*-dimethylformamide (DMF) were purchased as reagent grade from Alfa Aesar, Aldrich, Acros, J&K Chemical, or Beijing Chemical Reagent Co. and used as received unless otherwise noted. MMA and St were dried over calcium hydride overnight and distilled under the reduced pressure. GMA and *t*BA were filtered by the alkaline alumina column to remove the inhibitor. TEA was dried over KOH. AIBN was recrystallized from methanol and stored at 4 °C. For making dry solvents: DCM was refluxed over calcium hydride; THF was distilled from sodium/benzophenone. A compact fluorescent lamp (Actinic BL PL-L, Philips) emitting at 370 nm (± 50 nm, 36 W) was used as the UV light source.

2.2. Characterization

^1H -NMR spectra were recorded on a Bruker Avance 400 spectrometer at room temperature.

Ultraviolet Spectra were recorded using a TU-1901 Ultraviolet Spectrophotometer.

Fourier transform infrared spectroscopy (FT-IR) was performed on a Thermo Nicolet Avatar-330 Spectrometer at room temperature.

Gel permeation chromatography (GPC) in THF was performed using three Agilent PL gel columns (Mixed C, Mixed C, and Mixed D), a Waters 1515 isocratic HPLC pump, and a Waters 2414 RI detector. THF was used as the eluent at a flow rate of 1.00 mL/min. Polystyrene standards were used for the calibration.

Gel permeation chromatography (GPC) in DMF was conducted on a system comprised of a Waters 515 HPLC pump, and a Waters 2414 RI detector equipped with three Agilent mixed columns (Mixed A, Mixed A and Mixed B). DMF with 0.01 M LiBr was used as the eluent at a flow rate of 1.00 mL/min. Polystyrene standards were used for the calibration.

Matrix-Assisted Laser Desorption/Ionization Time of Flight (MALDI-TOF) mass spectrum was recorded on a Autoflex III MALDI-TOF mass spectrometer equipped with a 355 nm YAG laser. It was operated at an accelerating potential of 20 kV in linear modes. The MALDI mass spectrum represents averages over 256 consecutive laser shots (3 Hz repetition rate). The polystyrene was dissolved in THF with a concentration of 2 g/L. Dithranol (DI; 20 g/L in THF) was used as the matrix and silver trifluoroacetate (saturated in THF) was used as the cation source. The sample was prepared by mixing 10 μL of the polymer solution with 10 μL of the matrix solution and 2 μL of the trifluoroacetate solution. A 1 μL portion of the final solution was deposited onto the sample target and allowed to dry in air at 25°C. Internal standards (peptides or porphyrine derivatives) were used to calibrate the mass scale using the two-point calibration software 3.07.1 from Autoflex III systems.

2.3. Preparation of RAFT agent 1

Compound **a** [39] and **b** [40] were synthesized according to our previous publications. Compound **a** (1.25 g, 4.46 mmol) and **b** (1.00 g, 2.97 mmol) were dissolved in the mixture of DCM (100 mL) and THF (100 mL), into which EDC (1.14 g, 5.95 mmol) and DMAP (72.60 mg, 0.60 mmol) were sequentially added at 0 °C. The reaction was then performed at room temperature for 48 h. After that, the crude product was purified by a silica gel column with DCM/MeOH = 100:1 (v/v) as the eluent to afford the red solid product of RAFT agent **1** (0.32 g, 18% yield). ¹H-NMR (CDCl₃), δ (ppm): 7.96-7.88 (m, 4H), 7.59-7.54 (t, 1H), 7.41-7.36 (t, 2H), 6.92-6.87 (m, 4H), 4.36-4.32 (t, 2H), 4.16-4.11 (m, 2H), 3.89 (s, 3H), 3.36-3.33 (d, 2H), 2.74-2.58 (m, 6H), 2.22-2.14 (m, 2H), 1.93 (s, 1H).

2.4. RAFT polymerization protocol

The PS, PMMA, and *Pt*BA were prepared by a similar RAFT polymerization protocol. The preparation of PS was used as an example to demonstrate the detailed polymerization procedure. A mixed solution of St (5.00 g, 48 mmol), RAFT agent **1** (95.80 mg, 0.16 mmol), and AIBN (2.63 mg, 0.016 mmol) was degassed via three freeze-thaw-pump cycles. After stirring at 60 °C for 12 h, the reaction was terminated by exposing system to air. The polymer was precipitated from an excess of methanol three times. The light red product was obtained with a monomer conversion of 8.7% from ¹H NMR. GPC characterization: $M_n = 3590$, $M_w/M_n = 1.05$.

2.5. Preparation of PS₂₆-*b*-PEO₂₃ diblock copolymer

PEO₂₃-N₃ was synthesized from PEO₂₃-OH according to literature [37]. PS₂₆ (17.80 mg, 5.00 μmol) in 10 mL THF was stirred upon the UV irradiation for 5 minutes at room temperature. After concentrating the solution to 1 mL, PEO₂₃-N₃ (7.80 mg, 7.50 μmol) was then added in-situ. The

reaction mixture was stirred at room temperature in air for another 12 h to produce the diblock copolymer of PS₂₆-*b*-PEO₂₃. GPC characterization: $M_n = 5220$, $M_w/M_n = 1.04$.

2.6. Preparation of poly(3-azido-2-hydroxypropyl methacrylate) (PGA) grafted PS (PGA₁₀₀-*g*-PS₂₆) bottlebrush polymer

PGA₁₀₀ polymer main chain was synthesized according to literature [37]. PS₂₆ (30.70 mg, 8.50 μ mol) in 17 mL THF was stirred upon the UV irradiation for 5 minutes at room temperature. After evaporating THF solvent, the resultant PS was redissolved in 0.5 mL DMF containing 25 μ L toluene. Toluene was used as an internal standard for calculating the percentage of reacted side chains via GPC characterization. After adding PGA₁₀₀-N₃ (1.00 mg, 5.50 μ mol of azide group) into above solution, the reaction was performed at room temperature for another 24 h to produce the corresponding PGA₁₀₀-*g*-PS₂₆ bottlebrush polymer. GPC characterization: $M_n = 97160$, $M_w/M_n = 1.16$.

3. Results and Discussion

3.1. Synthesis of cyclopropanone-masked dibenzocyclooctyne functionalized RAFT agent **1**

The cyclopropanone-masked dibenzocyclooctyne functionalized RAFT agent **1** (Scheme 1) was prepared by an esterification between compounds **a** and **b**, which was detailed in Experimental section. Figure 2A shows the corresponding ¹H NMR spectrum and the related peak assignments, which clearly indicated the successful preparation of RAFT agent **1**. Subsequently, the RAFT agent **1** was employed to explore the RAFT polymerization of three typical types of vinyl monomers in free radical polymerization such as styrene, methyl methacrylate, and *tert*-butyl acrylate.

Figure 2. ^1H -NMR spectra of functional RAFT agent **1** (A), the resultant cyclopropenone-masked dibenzocyclooctyne end-functionalized PS_{26} (B), and the raw reaction mixture for the formation of PS_{26} -*b*-PEO $_{23}$ diblock copolymer (C), in which CDCl_3 was used as deuterated solvent.

3.2. RAFT polymerization of varied types of monomers

3.2.1. RAFT polymerization of styrene

Styrene was chosen as a model to demonstrate the RAFT polymerization of styrenic monomers using cyclopropanone-masked dibenzocyclooctyne functionalized RAFT agent **1**. Figure 3 shows the characterization of polymerization kinetics, where the RAFT polymerization was carried out at 60 °C in bulk with a ratio of 300/1/0.1 of [St]₀/[RAFT agent **1**]₀/[AIBN]₀. This polymerization produced a St conversion of 26% in 32 h. Ln[M]₀/[M] are plotted in Figure 3A as function of reaction time, and linear relationship was observed, indicating St consumption by first-order kinetics and a constant concentration of active centers during the polymerization. From Figure 3B, the GPC peaks shifted to high molecular weight direction with increasing the polymerization time. The monomodal and symmetrical peak shapes were obtained in 12 h corresponding to a St conversion below 10%. After that, a slight shoulder peak was observed at higher molecular weight direction, which was caused by the notorious propagating radical combination side reaction during the St radical polymerization. Moreover, as shown in Figure 3C, $M_{n,GPC}$ increased linearly with St conversion and the M_w/M_n remained lower than 1.10 throughout the polymerization. Accordingly, these kinetic data confirmed the living nature of RAFT polymerization for St in the presence of cyclopropanone-masked dibenzocyclooctyne functionalized RAFT agent **1**.

Figure 3. RAFT kinetics for polymerization of St with cyclopropenone-masked dibenzocyclooctyne functionalized RAFT agent **1**. Polymerization conditions: $[St]_0/[RAFT \text{ agent } 1]_0/[AIBN]_0 = 300/1/0.1$, 60 °C, in bulk.

3.2.2. RAFT polymerization of methyl methacrylate

MMA was selected as a typical model to illustrate the RAFT polymerization of methacrylate monomers with RAFT agent **1**. The kinetics of MMA polymerization was shown in Figure 4, in which the RAFT polymerization was performed at 60 °C in bulk with a ratio of 110/1/0.2 of $[MMA]_0/[RAFT \text{ agent } 1]_0/[AIBN]_0$. A MMA conversion of 59% was achieved in 7 h by virtue of this polymerization condition. From Figure 4A, the semilogarithmic plot of $\ln[M]_0/[M]$ versus

reaction time was linear, which indicated that MMA was consumed by a first-order kinetics during the polymerization. Furthermore, as can be seen from Figure 4B, all GPC curves of the resultant PMMA showed mono-modal and symmetric peak shapes. From Figure 4C, the $M_{n,GPC}$ increased linearly with MMA conversion and M_w/M_n was kept lower than 1.10 for all cases. Above results strongly demonstrated the living characteristics of RAFT polymerization of MMA using compound **1** as RAFT agent.

Figure 4. RAFT kinetics for polymerization of MMA with cyclopropanone-masked dibenzocyclooctyne functionalized RAFT agent **1**. Polymerization conditions: $[MMA]_0/[RAFT \text{ agent } \mathbf{1}]_0/[AIBN]_0 = 110/1/0.2$, 60 °C, in bulk.

3.3.3. RAFT polymerization of *tert*-butyl acrylate

Based on the successful RAFT polymerization of St and MMA, *t*BA was selected as a model to explore the RAFT polymerization behavior of acrylate monomers. Figure 5 shows the corresponding kinetics of *t*BA RAFT polymerization with the functional RAFT agent **1**, where the polymerization was carried out in bulk at 60 °C with a ratio of 200/1/0.25 of $[tBA]_0/[RAFT\ agent]_0/[AIBN]_0$. Finally, a *t*BA conversion of 55% was achieved in 8 h. The semilogarithmic plot of $\ln[M]_0/[M]$ versus reaction time exhibited a linear relation as shown in Figure 5A, implying *t*BA consumption by a first-order kinetics during the polymerization. Moreover, the monomodal and symmetrical peak shapes were obtained for all GPC curves of the resultant *Pt*BA (Figure 5B). Figure 5C illustrates that $M_{n, GPC}$ increased linearly with *t*BA conversion and the M_w/M_n remained below 1.10 throughout the polymerization. These results supported the living characteristic of the RAFT polymerization of *t*BA.

Figure 5. RAFT kinetics for polymerization of *t*BA with cyclopropenone-masked dibenzocyclooctyne functionalized RAFT agent **1**. Polymerization conditions: $[t\text{BA}]_0/[\text{RAFT agent } \mathbf{1}]_0/[\text{AIBN}]_0 = 200/1/0.25$, 60 °C, in bulk.

3.4. UV-induced SPAAC click reaction

The UV-induced SPAAC clickable property of the cyclopropenone-masked dibenzocyclooctyne end-functionalized polymers was demonstrated to successfully prepare the block and bottlebrush polymers by virtue of PS₂₆ with cyclopropenone-masked dibenzocyclooctyne end group as building blocks. Figure 2B shows the ¹H-NMR spectrum of the resultant PS₂₆ end-functionalized with cyclopropenone-masked dibenzocyclooctyne group. Comparing to that (Figure 2A) of RAFT agent

1, the characteristic proton signals of a, c, d, f, h, and l were preserved in the resultant PS₂₆ at the same position with the same area ratio. In addition, the area ratio of 2 between peak a and o confirmed the existence of cyclopropanone-masked dibenzocyclooctyne end group in every PS chain. This was again demonstrated by the MALDI-TOF MS characterization. As shown in Figure 6, a single peak distribution was observed for the MALDE-TOF MS spectrum of the resultant PS₂₆, which was accurately assigned to the cyclopropanone-masked dibenzocyclooctyne end-functionalized PS. Figure 7A (red curve) shows the UV-VIS spectrum of PS₂₆, which was nearly overlapped with that (black curve) of RAFT agent **1**. The strong adsorption peaks at 323 nm and 345 nm were ascribed to the cyclopropanone-masked dibenzocyclooctyne end group [40], again suggesting the inheritance of cyclopropanone masked dibenzocyclooctyne end group from RAFT agent **1** to the resultant end-functionalized PS₂₆. The corresponding GPC curve of the resultant PS₂₆ was shown in Figure 8 (black curve), where a monomodal and symmetrical peak shape was obtained corresponding to $M_n = 3590$, $M_w/M_n = 1.05$.

Figure 6. MALDI-TOF MS of cyclopropanone-masked dibenzocyclooctyne end-functionalized PS₂₆.

Figure 7. (A) UV-VIS spectra of functional RAFT agent 1 (black), the cyclopropanone-masked dibenzocyclooctyne end-functionalized PS₂₆ without UV irradiation (red) and with 5 min UV irradiation (blue), and the resultant PS₂₆-b-PEO₂₃ diblock copolymer (dark cyan), in which THF was used as solvent. (B) FT-IR spectra of the PGA₁₀₀ polymer main chain (black) and the resultant bottlebrush polymer of PGA₁₀₀-g-PS₂₆ (red).

3.4.1. Preparation of block copolymer

The dibenzocyclooctyne clickable group could be quantitatively released from the cyclopropanone-masked dibenzocyclooctyne group under UV irradiation. To perform this, a compact fluorescent lamp (Actinic BL PL-L, Philips) emitting at 370 nm (± 50 nm, 36 W) was used as the UV light source. As shown in Figure 7A (blue curve), after applying 5 min UV irradiation on a THF solution (10 mL) of PS₂₆ with cyclopropanone-masked dibenzocyclooctyne end group (17.80 mg), the characteristic adsorption peak of cyclopropanone-masked dibenzocyclooctyne disappeared at 345 nm (red curve) and two new adsorption peaks appeared at 303 nm and 320 nm ascribed to

newly released dibenzocyclooctyne end group [41]. Subsequently, the solution was concentration to 1 mL and 1.5 times molar excess of PEO₂₃-N₃ was added in-situ to produce the corresponding PS₂₆-*b*-PEO₂₃ diblock copolymer in 12 h. Dark cyan curve in Figure 7A shows the UV-VIS spectrum of the corresponding reaction solution, in which the adsorption peaks of dibenzocyclooctyne group disappeared at 303 nm and 320 nm after the reaction. Additionally, as compared with the ¹H-NMR spectrum of PS₂₆ precursor end-functionalized with cyclopropenone-masked dibenzocyclooctyne group (Figure 2B), the characteristic Ha proton signal of cyclopropenone-masked dibenzocyclooctyne at 7.95 ppm disappeared after the UV-induced SPAAC coupling reaction (Figure 2C). Figure 8A (red curve) shows the GPC characterization of the resultant PS₂₆-*b*-PEO₂₃ diblock copolymer, in which the minor peak distribution with lower molecular weight was contributed by the excessively unreacted PEO₂₃-N₃ building block. Comparing to that (black curve) of the building block of PS₂₆ end-functionalized with cyclopropenone-masked dibenzocyclooctyne group, the major peak position shifted completely to the higher molecular weight direction and the well-defined monomodal and symmetric peak shape was preserved. This strongly indicated the successful formation of the PS₂₆-*b*-PEO₂₃ diblock copolymer by the UV-induced SPAAC click reaction.

Figure 8. (A) GPC characterization of cyclopropenone-masked dibenzocyclooctyne end-functionalized PS₂₆ (black, $M_n = 3590$ and $M_w/M_n = 1.05$), azide end-functionalized PEO₂₃ (blue, $M_n = 1790$ and $M_w/M_n = 1.02$), and the resultant PS₂₆-*b*-PEO₂₃ diblock copolymer (red, $M_n = 5220$ and $M_w/M_n = 1.04$), in which THF was used as elute and polystyrene standards were used for the calibration. (B) GPC characterization of dibenzocyclooctyne end-functionalized PS₂₆ side chain (black), azide functionalized PGA₁₀₀ main chain (blue, $M_n = 49160$ and $M_w/M_n = 1.20$), and the resultant PGA₁₀₀-*g*-PS₂₆ bottlebrush polymer (red, $M_n = 97160$ and $M_w/M_n = 1.16$), in which DMF with 0.01 M LiBr was used as elute and polystyrene standards were used for the calibration.

3.4.2. Preparation of bottlebrush polymer

Inspired by the successful formation of block copolymers, the preparation of bottlebrush polymer was explored to further demonstrate the UV-induced SPAAC click reactivity of the cyclopropenone-masked dibenzocyclooctyne end-functionalized polymers by virtue of the “grafting onto” strategy. The poly(3-azido-2-hydroxypropyl methacrylate) polymer main chain with a degree

of polymerization of 100 (PGA₁₀₀) was prepared from RAFT polymerization according to our previous publication[37], which contained an azide side group at each repeat unit. The corresponding GPC characterization was shown in Figure 8B (blue curve), in which the monomodal and symmetric peak shape was observed having M_n and M_w/M_n of 49160 and 1.20. Similarly, after UV irradiation for 5 min on the THF solution (17 mL) of PS₂₆ with cyclopropenone-masked dibenzocyclooctyne end group (30.70 mg), the THF solvent was completely removed and the resultant dibenzocyclooctyne end-functionalized PS₂₆ polymer side chains were redissolved in 0.5 mL DMF containing 25 μ L toluene. Toluene was used as an internal standard for calculating the percentage of reacted side chains via GPC characterization. Figure 8B (black) shows the GPC curve of the resultant dibenzocyclooctyne end-functionalized PS₂₆ side chains. After adding PGA₁₀₀-N₃ main chain into the above PS₂₆ side chain DMF solution with an initial molar ratio of 1/1.55 between azide and dibenzocyclooctyne groups, the well-defined bottlebrush polymer of PGA₁₀₀-g-PS₂₆ was successfully produced in 24 h. The corresponding GPC curve was shown in Figure 8B (red). Compared to that (blue) of PGA₁₀₀ main chain, the peak position of the resultant PGA₁₀₀-g-PS₂₆ shifted to higher molecular weight direction and the peak shape preserved the well-defined monomodal and symmetric distribution. In addition, by virtue of the preadded internal standard of toluene, the percentage of 62.3% for grafted PS₂₆ side chains could be calculated by comparing the peak intensities of the dibenzocyclooctyne terminated PS₂₆ and toluene in the GPC curves. This finally produced the grafting density of 96.6% for the resultant PGA₁₀₀-g-PS₂₆ by multiplying the initial molar ratio of 1.55 between dibenzocyclooctyne and azide groups. This high grafting density of side chains was further demonstrated by the FT-IR characterization. As shown in Figure 7B, the characteristic azide peak at 2100 cm⁻¹ was clearly observed in the FT-IR spectrum (black curve) of PGA₁₀₀ main chain, which completely disappeared from that (red curve) of the resultant PGA₁₀₀-g-PS₂₆ bottlebrush polymers. As a resultant, based on the combination of RAFT

polymerization technique and UV-induced SPAAC click reaction, a novel, practical, and efficient metal-free method was developed for the formation of bottlebrush polymers.

4. Conclusions

A novel RAFT agent **1** was developed to have a cyclopropenone-masked dibenzocyclooctyne end group, whose RAFT polymerization ability was further testified by polymerizing three typical types of monomers for free radical polymerization such as styrene, methyl methacrylate, and *tert*-butyl acrylate. The living polymerization behaviors were achieved for all three cases, which initiated a direct and metal-free method for the formation of end-functionalized polymers with cyclopropenone-masked dibenzocyclooctyne end groups. By virtue of the mild UV irradiation, cyclopropenone-masked dibenzocyclooctyne end group quantitatively release the clickable dibenzocyclooctyne end group, which is one of the strained alkyne groups widely used in the metal-free SPAAC click reaction. Subsequently, by SPAAC coupling dibenzocyclooctyne end-functionalized and azide functionalized polymer building blocks, a universal, practical, and efficient metal-free technique was developed for the formation of topological polymers including block copolymers and bottlebrush polymers. Derived from the RAFT polymerization and UV-induced SPAAC click reaction, the formation of end-functionalized polymers and the resultant topological polymers completely eliminated the requirement of metal catalysts. This makes the preparation method and the resultant materials from this paper play a vital role in the research fields requiring strictly “clean” materials, such as in biology and life science.

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