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Synthesis of multiarm star block copolymer based on host-guest inclusion complexation

Neşe Çakır Yiğit[a,b,*], Gürkan Hızal[a] and Ümit Tunca[a]

[a]*Department of Chemistry, Faculty of Science and Letters, Istanbul Technical University, Istanbul, 34469, Turkey.*
[b]*Department of Polymer Materials Engineering, Faculty of Engineering, Yalova University, Yalova, 77200, Turkey.*

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ABSTRACT

Supramolecular multiarm star block copolymer ((CD-PEG)$_p$-(Ada-PS)$_n$-polyDVB) was prepared by host-guest interaction of β-cyclodextrin (β-CD) end functionalized polyethylene glycol (β-CD-PEG) and adamantane peripherally functionalized multiarm star polymer ((Ada-PS)$_n$-polyDVB). The β-CD-PEG was synthesized by copper-catalyzed azide/alkyne cycloaddition reaction (CuAAC) of alkyne functional PEG with mono azide functional β-CD (β-CD-N$_3$). Adamantane functional polystyrene (Ada-PS) was prepared by atom transfer radical polymerization (ATRP) of styrene (St) and was allowed to react with divinyl benzene (DVB) as a linking agent giving (Ada-PS)$_n$-polyDVB multiarm star polymer. The structures of β-CD-PEG and (Ada-PS)$_n$-polyDVB multiarm star formation were determined by ^{1}H NMR and GPC. 2D ROESY NMR and DLS analysis of (CD-PEG)$_p$-(Ada-PS)$_n$-polyDVB were carried out to validate the formation of the inclusion complex. The evidence of increased molecular weights and size distributions supported the supramolecular multiarm star block copolymer formation.

I. INTRODUCTION

Star polymers represent a broad class of branched macromolecules with a precisely controlled architecture containing multiple linear polymer chains radiating from a central core. These macromolecules have been the subject of immense interest for researchers because of the synthetic challenges associated with preparing them and different properties and behaviors from those of corresponding linear analogs. Star polymers have compact structure (small hydrodynamic volume and radius of gyration, and therefore low viscosity), multiple functionalities, and high solubility characteristics that are unattainable for linear polymers [1–4].

Atom transfer radical polymerization (ATRP) is a special class of controlled/“living” radical polymerization (C/LRP) technique, which has revolutionized the synthesis of multiarm star polymers with wide range of monomers under less strict reaction conditions with improved control over chemical composition [5, 6]. Two general synthetic methods have been widely applied for the synthesis of well-defined star polymers: the arm-first approach and the core-first approach. The ‘‘arm first’’ approach involves the reaction of previously synthesized living polymer chains as a macroinitiator for the polymerization of a divinyl cross-linker. The resulting star polymers have a unique three-dimensional globular structure surrounding the large number of arms consisting of a densely cross-linked core. In the “core-first” approach, a multifunctional initiator is a core that initiates the polymerization of vinylic monomers, thus forming the star polymers with the desired number of arms [7, 8].

*Corresponding author. Tel.: +90-000-000-0000; e-mail: author@university.edu.tr

Supramolecular polymer chemistry focuses on providing new complex polymeric materials through the incorporation of noncovalent interactions, such as hydrogen bonding interaction, electrostatic interaction, ionic interactions, and host–guest inclusion complexation [9-11]. β-cyclodextin (β-CD) has been widely used as host molecule of supramolecular in the research and application of polymer chemistry [12]. β-CD is characteristic of an external hydrophilic shell and inner hydrophobic cavity, which can accommodate of appropriate size of hydrophobic molecules as the guest into its cavity to generate host–guest inclusion complexes by noncovalent bond [13]. Adamantane (Ada) is one of the most important guests for β-CD due to its effective inclusion entrapment and high binding affinity. Previous studies have shown that the inclusion complexation between Ada and β-CD has shown powerful capacity in water with high association constant [14-16]. In recent years, the studies of the polymeric systems based on β-CD and Ada have appeared in some papers. Stenzel et al. used this feature as a driving force to generate reversible comb-shaped polymers [17]. Li et al. synthesized four-arm poly(N-isopropylacrylamide) PNIPAAm star polymer with a β-CD core which forms supramolecular self-assembly with Ada functionalized poly(ethylene glycol) PEGs by host-guest inclusion complexation [18]. Davis et al. published β-CD functionalized biodegradable star polymers via CD/cholesterol inclusion complexation [19]. Recently, Barner-Kowollik et al. synthesized a wide range of novel macromolecular architectures including X- and H-shaped star block copolymers, ABA triblock copolymers, three-armed star polymers and miktoarm star polymers through CD/Ada host–guest inclusion complexation [20-23]. A similar approach was explored by Zhu et al. who reported the supramolecular ABC miktoarm star terpolymers based on host−guest interaction [24].

Herein, we executed the synthesis of adamantane terminated multiarm star polymer and β-CD functionalized PEG precursor in order to prepare the supramolecular multiarm star block copolymer by host-guest interaction. The formation of the inclusion complex was confirmed by the ^{1}H NMR, 2D ROESY NMR, and DLS analysis techniques. The absolute molecular weights of multiarm star polymer and multiarm star block copolymer were also investigated in this paper.

II. EXPERIMENTAL METHOD

2.1 Materials

Styrene (St, 99% Aldrich) and divinylbenzene (DVB, 80%, Aldrich) were passed through a column filled with basic alumina to remove the inhibitor immediately before use. *N,N,N′,N″,N″*-Pentamethyldiethylenetriamine (PMDETA, Aldrich) was distilled over NaOH prior to use. α-bromoisobutryl bromide (98%, Aldrich), triethylamine (Et_3N, 99.5%, Aldrich), *N,N'*-dicyclohexylcarbodiimide (DCC, 99%, Aldrich), 4-dimethylaminopyridine (DMAP, 99%, Aldrich), 4-pentynoic acid (98%, Aldrich), 1-adamantanemethanol (99%, Aldrich), β-cyclodextrin (≥97%, Aldrich), and CuBr (99.9%, Aldrich) were used as received. Poly(ethylene glycol) monomethylether (mPEG, M_n = 5000, Fluka) were dried by azeotropic distillation with anhydrous toluene. Dichloromethane (CH_2Cl_2, ≥99.8%, Aldrich) was used after distillation over P_2O_5. Tetrahydrofuran (THF; 99.8%, J.T. Baker) was distilled over benzophenone-Na. *N,N*-Dimethylformamide (DMF, 99.8%, Aldrich) was dried and distilled under vacuum over CaH_2. Diethyl ether (99.7%, Aldrich), 1,4-dioxane (99.8%, Aldrich), methanol (99.8%, Aldrich) were used without further purification. Ethyl acetate (EtOAc), acetone and hexane were in technical grade and distilled prior to use. The mono-6-deoxy-6-azido-β-cyclodextrin (β-CD-N_3) was synthesized according to our published procedure [25]. Alkyne end-functionalized PEG (Alkyne-PEG) was prepared according to a published procedure and adopted to molecular weight of PEG (M_n = 5000) [26].

2.2 Instrumentation

^{1}H NMR (500 MHz), ^{13}C NMR (125 MHz) and ROESY NMR (500 MHz) measurements were performed on an Agilent VNMRS 500 instrument at room temperature. Gel permeation chromatography (GPC) was carried out at 30 °C on an Agilent instrument (Model 1100) connected to refractive index (RI), and ultraviolet (UV) detectors and four Waters Styragel columns using THF as eluent (flow rate: 0.3 mL/min). The apparent molecular weights of polymers were calculated relative to linear PS standards using PL Caliber Software from Polymer Laboratories. Molecular weights of the samples which insoluble in THF were determined with DMF GPC, Agilent 1100 series, consisting of a pump, two Styragel columns, a differential refractive index (RI) detector with a DMF flow rate of 1.0 mL min^{-1} at 35°C and toluene as an internal standard. The other GPC set-up (TD-GPC) with an Agilent 1200 model isocratic pump, four Waters Styragel columns, and a Viscotek TDA 302 triple detector including RI, dual laser light scattering (DLLS) (λ = 670 nm, 90° and 7°) and a differential pressure viscometer was conducted to measure the absolute molecular weights ($M_{w,TDGPC}$) in THF with a flow rate of 0.5 mL/min at 35 ºC. Three detectors were calibrated with a PS standard having narrow molecular weight distribution (M_n = 115,000 g/mol, M_w/M_n = 1.02, $[\eta]$ = 0.519 dL/g at 35°C in THF, dn/dc = 0.185 mL/g) provided by Viscotek company. Data were analyzed with OmniSec 4.5 software from Viscotek Company. DVB conversion was determined using the Agilent 6890N gas chromatograph, equipped with an FID detector using a wide-bore capillary column (HP5, 30 m x 0.32 mm x 0.25µm, J&W Scientific). Injector and detector were kept constant at 280 and 285 ºC, respectively. The chromatographic conditions: Injector and detector were kept constant at 280 °C and 285 ºC, respectively. For the samples, the temperature range was from 40 to 120 ºC. The heating was 10 ºC/min. FT-IR spectra were recorded on an Agilent Technologies Cary 630 FTIR instrument over the range 4000–500 cm^{-1}. Electrospray ionization-mass spectra (ESI-MS) were recorded on a Thermo Finnigan LCQ Decaquadrupole ion trap mass spectrometer (Thermo Finnigan, San Jose, CA), equipped with an atmospheric pressure ionization source operating in the nebulizer assisted electrospray mode and was used in positive ion mode. Dynamic light scattering (DLS) measurements were carried out in a Malvern Instrument Nano ZS using a He-Ne laser with a 633 nm wavelength, at an angle of 173 ºC.

2.3 Synthesis Methods

2.3.1 CuAAC click reaction of Alkyne-PEG with β-CD-N$_3$ (β-CD-PEG)

Alkyne-PEG (1.00 g, 0.19 mmol, $M_{n,\,NMR}$ =5180 g/mol) and β-CD-N$_3$ (0.456 g, 0.38 mmol) were dissolved in DMF (10 mL). CuBr (0.0277 g,0.4 mmol) and PMDETA (40.0 µL, 0.19 mmol) were also dissolved in DMF (2 mL) and purged with N$_2$. The reaction tube was degassed by three FPT cycles, and heated in an oil bath at 60 °C for 2 days. Thereafter, the reaction mixture was concentrated, and the viscous liquid was dissolved in CHCl$_3$ and precipitated in chilled diethyl ether. The precipitated polymer was redissolved in CHCl$_3$, passed through a neutral alumina column to remove copper, then concentrated, dissolved in 10 mL water, extracted with CHCl$_3$ to remove unreacted β-CD-N$_3$, and dried over anhydrous Na$_2$SO$_4$. After evaporated to 5 mL, the crude product was precipitated in chilled diethyl ether, and dried in a vacuum oven at 40 ºC for 24 h. Yield = 1.0 g (82 %). ^{1}H NMR ($CDCl_3$, δ) 7.78 (br, C*H* of triazole), 5.69 (br, 14H, OH-2,3), 5.02 (s, H, H-1), 4.82 (d, 6H, H-1), 4.56-4.43 (br, 6H, OH-6), 3.77-3.60 (br, 28H, H-3,5,6,6'), 3.58-3.25 (m, 4H, -OCH_2CH_2, repeating unit of PEG, br, 14H, H-2,4 overlap with H2O), 3.23 (s, 3H, PEG-OCH_3).

2.3.2 Synthesis of 1-adamantane methyl-2-bromo isobutyrate (ada-initiator)

1-Adamantane methanol (2.00 g, 0.012 mol), DMAP (0.73 g, 6.00 mmol), and Et_3N (3.35 mL, 0.024 mol) were dissolved in CH_2Cl_2 (120 mL). After stirring for 0.5 h, α-bromoisobutyryl bromide (2.22 mL, 0.018 mol) in CH_2Cl_2 (30 mL) was added dropwise over 1 h at 0 ºC. The reaction mixture was stirred at 0°C for another 1 h and then at room temperature for 16 h. After removing the insoluble salts by suction filtration, the filtrate was concentrated and then the crude product was dissolved in CH_2Cl_2. The organic phase was washed successively with HCl (3 M, 3 × 30 mL), NaOH (3 M, 3×30 mL), and then deionized water (3×30 mL). The extracts were dried over anhydrous Na_2SO_4. The product was purified by passing through a silica column hexane/EtOAc (9/1; v/v) as eluent and isolated as a white solid (Yield= 3.22 g, 85%). ^{1}H NMR ($CDCl_3$, δ) 3.77 (s, 2H, CH_2-adamantyl), 2.01 (s, 3H, C*H*), 1.96 (s, 6H, C(CH_3)$_2$-Br), 1.71 (dd, J = 27.8 Hz, 6H, CH_2), 1.59 (s, 6H, CH_2).

2.3.3 Synthesis of adamantyl end-functionalized PS (ada-PS)

Adamantane end-functional PS (Ada-PS) was prepared by ATRP of St at 110 ºC. St (10.0 mL, 87.0 mmol), PMDETA (0.091mL, 0.435 mmol), CuBr (0.062 g, 0.435 mmol), and ada-initiator (0.138 g, 0.435 mmol) were charged into a Schlenk flask and degassed by three freeze-pump-thaw (FPT) cycles and left in vacuum. The polymerization was conducted at 110 °C for 40 min. The polymerization mixture was diluted with THF, filtered through a column of neutral alumina and precipitated in methanol. The polymer was dried under vacuum. ^{1}H NMR ($CDCl_3$, δ) 7.20-6.25 (br, Ar*H* of PS), 4.66-4.35 (br, 1H, C*H*(Ph)-Br), 3.35-3.00 (br, 2H, CH_2-adamantane), 2.32-0.82 (br, aliphatic protons of PS and adamantane).

2.3.4 Preparation of (ada-PS)$_n$-polyDVB multiarm star polymer

In a typical procedure, ada-PS macroinitiator (1.50 g, 0.417 mmol), anisole (19.82 mL), PMDETA (87.0 µL, 0.417 mmol), DVB (0.890 mL, 6.25 mmol), and CuBr (0.060 g, 0.417 mmol) in anisol (19 mL) were added to a Schlenk flask and degassed by three FPT cycles (before degassing the reaction mixture, the first sample was quickly taken for GC measurement). The flask was then immersed in an oil bath at 110 °C. At time intervals, samples were taken from the reaction mixture. The samples were diluted with THF and purified by passing through a short neutral alumina column to remove the copper salt and analyzed directly by GPC. After 18 h at 85 % conversion, the reaction was stopped by opening the flask to air and diluting with THF. The copper catalyst was removed by passing the solution through a neutral alumina column. The star polymer was precipitated in methanol, redissolved in THF, and then reprecipitated in methanol–diethyl ether mixture (1/3 v/v). Finally, the polymer was dried under vacuum at 40 °C for 24 h. ^{1}H NMR ($CDCl_3$, δ) 7.24-6.24 (br, Ar*H* of PS), 3.42-3.02 (br, 2H, CH_2-adamantane), 2.26-0.78 (br, aliphatic protons of PS and adamantane).

2.3.5 Preparation of supramolecular (CD-PEG)$_p$-(ada-PS)$_n$-polyDVB multiarm star block copolymer via CD/adamantane host-guest interaction

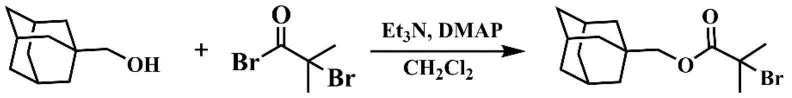
Adamantane end-functionalized multiarm star polymer ((ada-PS)$_n$-polyDVB; $M_{n,\text{TD-GPC}}$ = 74320 g mol^{-1}; 40.0 mg, 0.538 µmol, 1.0 eq.) was dissolved in DMF (3.0 mL) and added dropwise to a solution of β-CD end-functionalized

PEG (β-CD-PEG; $M_{n,NMR}$ = 6130 g mol^{-1}; 42.9 mg, 6.994 mmol, 1.0 eq. per arm) in DMF (3.0 mL) under vigorous stirring. The resulting solution was dialysed (MW cut-off, 3.5 kDa) against a deionized water–DMF mixture. The water content was gradually increased from 30 % to 100 % over 3 day and the dialysis was continued with deionized water at room temperature. Finally, a white solid was produced by freeze-drying to yield the supramolecular (CD-PEG)$_p$-(ada-PS)$_n$-polyDVB multiarm star block copolymer in quantitative yield. Yield = 77.0 mg (93 %).

III. RESULTS AND DISCUSSIONS

In order to study host-guest interactions from multiarm star block copolymers, the preparation of host and guest molecules is required. For this purpose, β-cyclodextrin compound and adamantane were chosen as host and guest molecules, respectively. Then, multiarm star homopolymer with adamantane functionality as reactive periphery groups was created by ATRP of by adamantane end-functionalized PS (ada-PS) macromonomer in the presence of DVB as a bifunctional crosslinker. Furthermore, obtained (ada-PS)$_n$-polyDVB multiarm star polymer was reacted with β-cyclodextrin end-functionalized PEG (β-CD-PEG) resulting in the (CD-PEG)$_p$-(ada-PS)$_n$-polyDVB multiarm star block copolymer via host-guest inclusion complexation.

To begin with, linear adamantane functional initiator (ada-ini) was obtained through an esterification reaction of 1-adamantanemethanol via α-bromoisobutryl bromide as described in Scheme 1.



Scheme 1. Synthetic route for the synthesis of adamantane functional initiator (ada-ini)

Figure 1 shows the ^{1}H NMR spectrum of ada-ini in $CDCl_3$ that could be clearly confirmed via signal assignments. After esterification reaction methylene protons next to ester unit was shifted to 3.77 ppm, methyl protons next to Br was assigned at 1.96 ppm and characteristic adamantane signals (b-d) appear unchanged at 2.1-1.5 ppm.

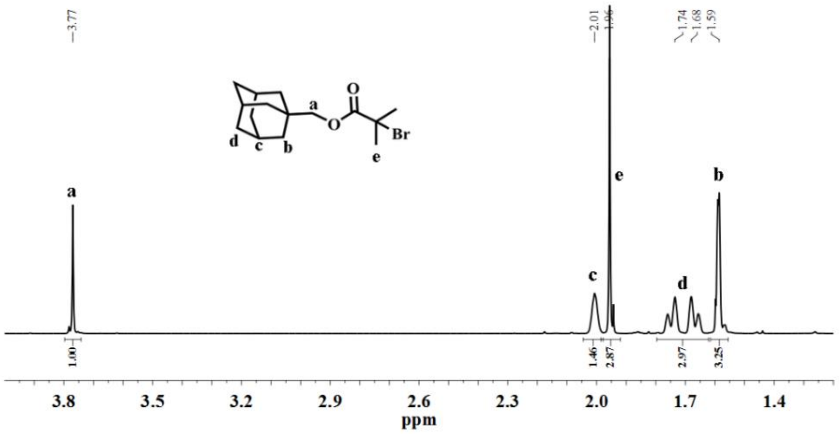
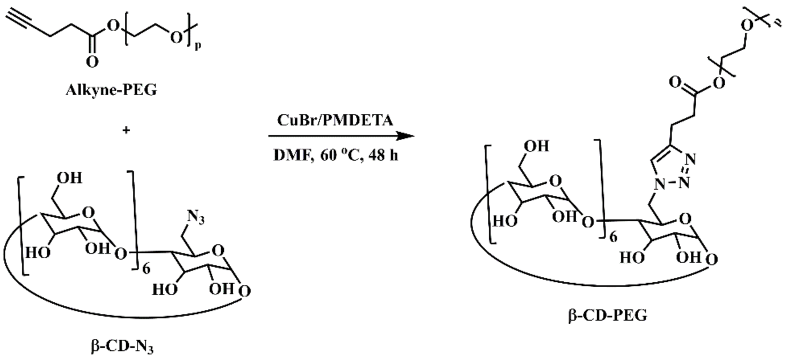


Figure 1. ^{1}H NMR spectrum of 1-adamantane methyl-2-bromo isobutyrate (ada-ini) in $CDCl_3$

Recently, monotosylation and monoazidation of β-CD was prepared by our group [25]. The ESI-MS and ^{1}H-NMR spectroscopies were utilized to enlighten the structure of the β-CD-N_3 while showing dominant ions at m/z 1182.3 signals (1160+Na^+) in ESI-MS m/z spectrum, and the ratio of peaks corresponding to 1-positioned hydroxyl group and CH_2 protons next to the N_3 group of the β-CD ring in ^{1}H-NMR spectrum verifies the monoazidation process. On the other hand, the alkyne-PEG was successfully prepared by esterification reaction of mPEG with 4-pentynoic acid according to the literature [26]. The appearance of characteristic peaks such as a triplet ($C\mathit{H}{\equiv}C$-) at 1.9 ppm and a multiplet ($CH{\equiv}CC\mathit{H}_2C\mathit{H}_2C{=}O$) at 2.5 ppm confirmed the successful transformation of hydroxyl groups of PEG to alkyne functionalities.

The interaction (click reaction) of alkyne-PEG with excess of β-CD-N_3 permits synthesis of β-CD-PEG (Scheme 2). Since β-CD-N_3 is insoluble in $CHCl_3$, it can be purified by repeating extraction with $CHCl_3$ at the end of the reaction.



Scheme 2. CuAAC click reaction of alkyne-PEG with β-CD-N_3 (β-CD-PEG)

Figure 2 gives the ^{1}H NMR spectrum of β-CD-PEG. The integrated ratios of the resonances of the 1,2,3-triazole ring protons at about 8.0 ppm and the 2,3-positioned hydroxyl groups of β-CD at 5.69 ppm were found to be 1:12.2, suggesting the formation of β-CD-PEG with high (87 %) click efficiency.

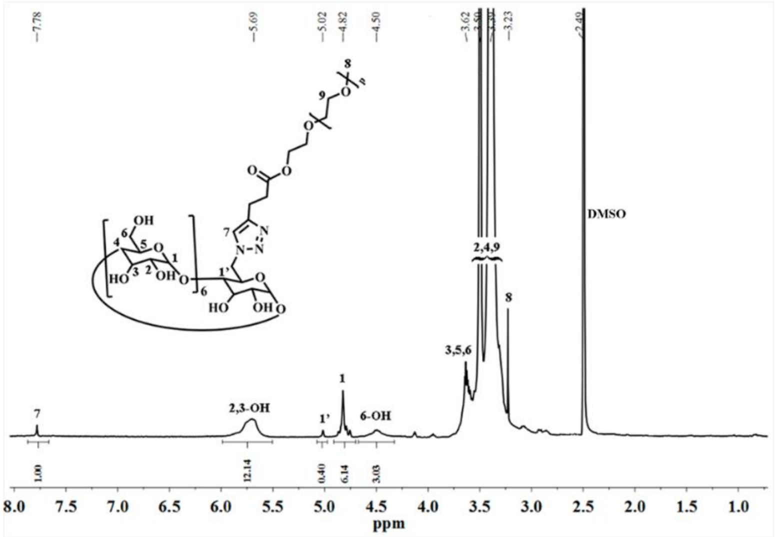


Figure 2. ^{1}H NMR spectrum of β-CD-PEG in DMSO-d_6 at room temperature

Completion of click reaction as well as the coplete removal of of the excess β-CD-N_3 was confirmed by disappearance of azide signal at 2107 cm^{-1} in FTIR spectra, as illustrated in Figure 3. Moreover, the appearance of the intense band centered at 1030 cm^{-1} that is assigned to the C-O-C stretching vibration in the CD observed in all CD species.

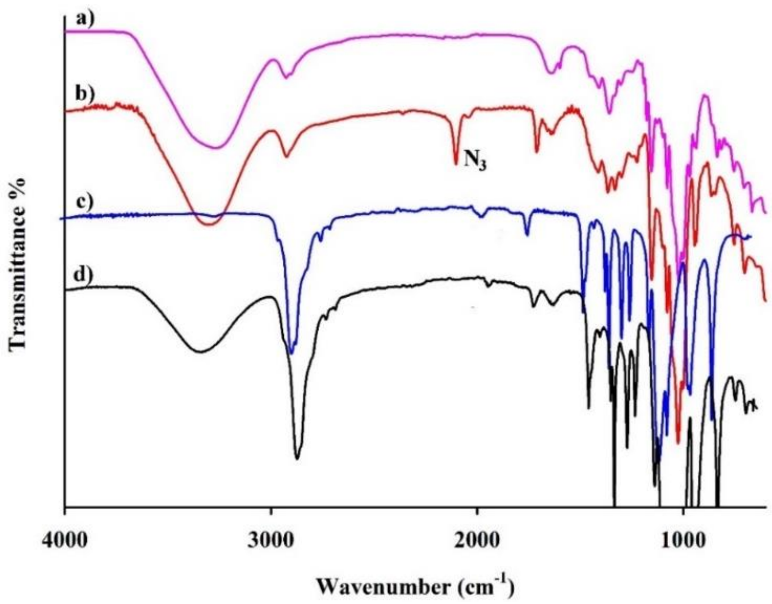


Figure 3. FT-IR spectra of β-CD-OTs (pink) (a), β-CD-N_3 (red) (b), Alkyne-PEG (blue) (c) and obtained compound β-CD-PEG (black) (d).

Figure 4 shows the evolution of GPC traces of β-CD-PEG, Alkyne-PEG and β-CD-N_3 in DMF, due to poor solubility of β-CD-N_3 in THF. A shift for β-CD-PEG is clearly observed with respect to those of precursors.

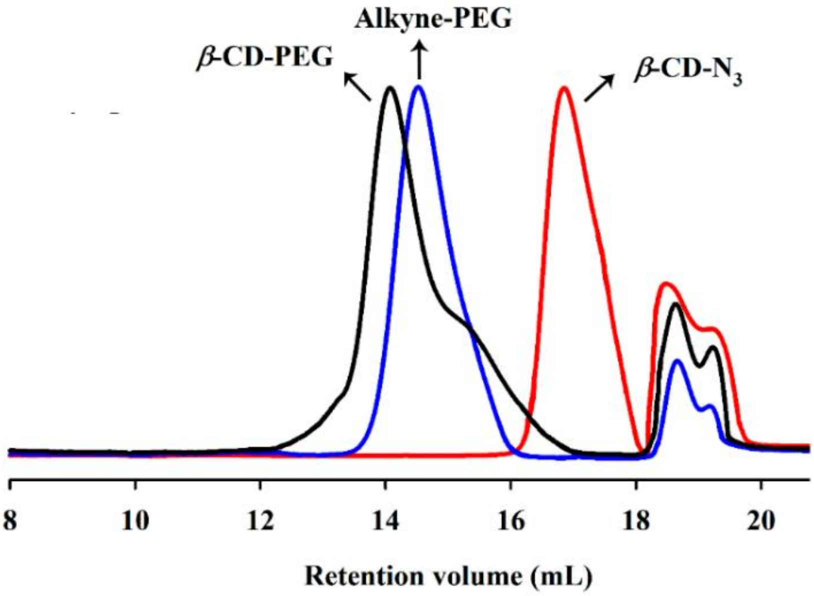
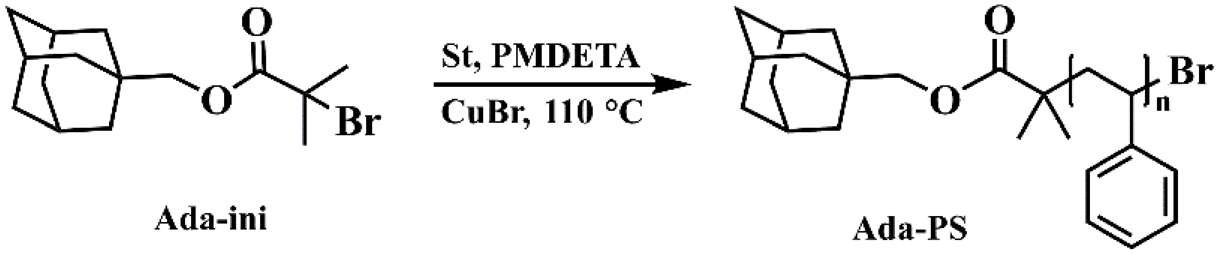


Figure 4. Evolution of GPC traces of β-CD-PEG, Alkyne-PEG and β-CD-N_3 using RI detector in DMF at 60 °C.

For the preparation of (ada-PS)$_n$–polyDVB multiarm star polymer bearing adamantane functionality at the periphery, initially linear ada-PS was obtained via ATRP of St concurrently initiated by using ada-ini in the presence of CuBr/PMDETA at 110 ^{o}C for 40 min (Scheme 3).



Scheme 3. Synthesis of adamantane end-functional PS (ada-PS) by ATRP reaction

The NMR number–average molecular weight ($M_{n,NMR}$ = 4060 g/mol) of ada-PS was determined from a ratio of integrated signals at 7.5–6.3 ppm (aromatic protons of St) and 4.45 ppm (end-group proton of PS), while including the MW of ada-ini (315 g/mol) (Figure 5). $M_{n,NMR}$ = 4060 is consistent with $M_{n,GPC}$ = 3600 (obtained from GPC instrument calibrated with PS standards) and $M_{n,theo}$ =3570 values.

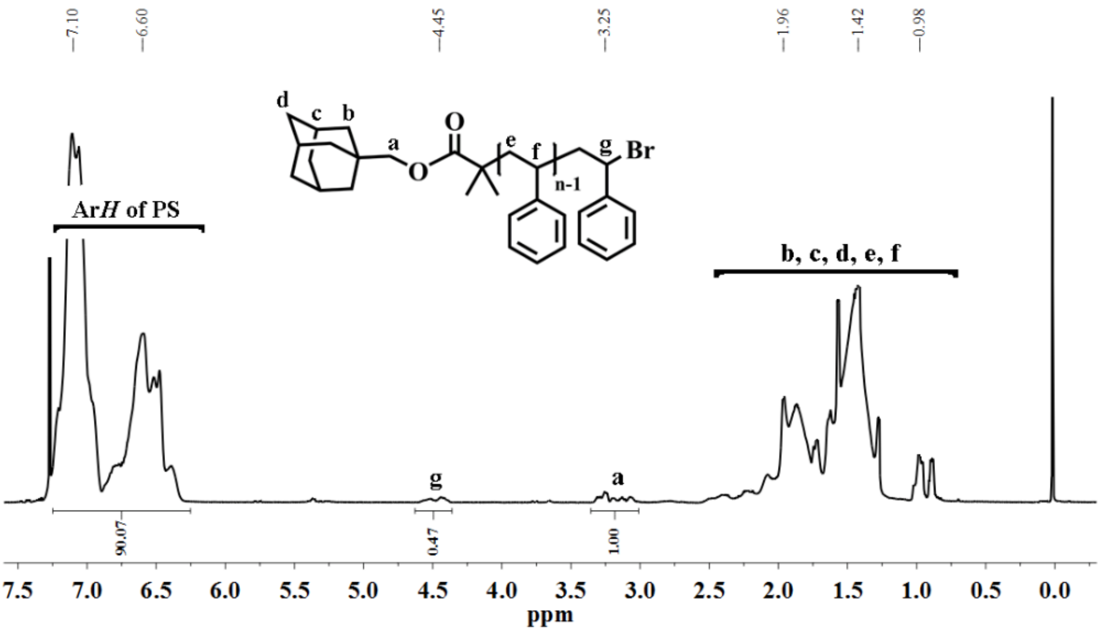


Figure 5. ^{1}H NMR spectrum of adamantane end-functional PS (ada-PS) in $CDCl_3$

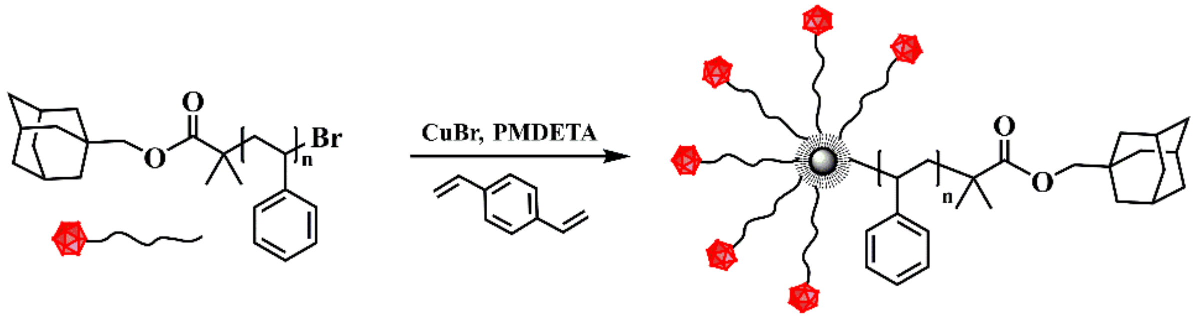
All polymerization conditions and results of the linear precursors used in the synthesis of multiarm star polymer and multiarm star block copolymers were tabulated in Table 1.

Table 1. The conditions and results of linear polymers used in the synthesis of multiarm star and multiarm star block copolymer

Polymer	**Ini.**	**Time (min)**	**Conv.**[b] **(%)**	$M_{\mathrm{n,GPC}}$[c] **(g/mol)**	$M_{\mathrm{w}}/M_{\mathrm{n}}$	$M_{\mathrm{n,theo}}$[d] **(g/mol)**	$M_{\mathrm{n,NMR}}$ **(g/mol)**
Ada-PS[a]	ada-ini	40	15	3600	1.10	3570[d]	4060
Alkyne-PEG[f]	-	-	-	5000	1.06	5100[g]	5180
β-CD-PEG	-	-	-	4750	1.06	6340[h]	6130

[a] $[M]_0$:$[I]_0$:[CuBr]:[PMDETA] = 200:1:1:1; polymerization was carried out at 110 °C.
[b] Determined by gravimetrically.
[c] Determined by conventional GPC calibrated relative to linear PS standards in THF at 30 °C.
[d] $M_{\mathrm{n,theo}} = ([M]_o/[I]_o)$ x conversion % x molecular weight (MW) of monomer + MW of initiator.
[f] Obtained by an esterification reaction between 4-pentynoic acid and Me-PEG (5000).
[g] $M_{\mathrm{n,theo}}$ = Mn of Me-PEG (5000) + MW of 4-pentynoic acid.
[h] $M_{\mathrm{n,theo}}$ = sum of $M_{\mathrm{n,NMR}}$ and ESI-MS values of the precursor polymers.

The (ada-PS)$_n$-polyDVB multiarm star polymer was obtained by ATRP of DVB in the presence of ada-PS as a macroinitiator and CuBr/PMDETA as catalyst at 110 °C (Scheme 4).



Scheme 4. Synthetic route for the synthesis of (ada-PS)$_n$-polyDVB multiarm star polymer with crosslinked core

The progress of star formation was followed by GC and GPC while taking samples at time intervals. During polymerization, the peak originating from macroinitiator was decreased and a new peak gradually shifted toward higher molecular weight region. Reaction was terminated after 18 h at 85 % of DVB conversion. (Ada-PS)$_n$-polyDVB multiarm star polymer was purified by two dissolution-precipitation cycles from THF into methanol/diethyl ether mixture (1/3, v/v) to remove unreacted linear ada-PS. The relevant chromatograms and the purified multiarm star polymer are overlaid in Figure 6.

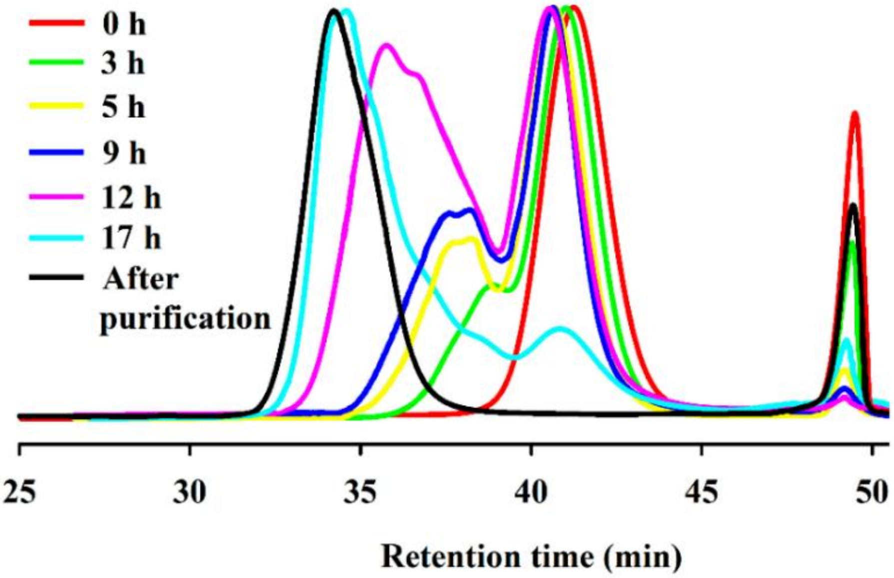


Figure 6. Evolution of GPC traces of (ada-PS)$_n$-polyDVB multiarm star polymer using RI detector in THF at 30 ^{o}C. ([DVB]$_0$/15 = [ada-PS]$_0$ = [CuBr]$_0$ = [PMDETA]$_0$ = 0.020 M in anisole at 110 ^{o}C)

As shown in Table 2, TD-GPC measurement is used to measure the absolute molecular weight ($M_{w,TD\text{-}GPC}$ = 74300) of (ada-PS)$_n$-polyDVB multiarm star polymer with introducing the dn/dc = 0.185 mL/g of linear PS standard. Also, the number of arms (f) per molecule of the multiarm star polymer was calculated to be 13 by using equation (1) and found to be consistent with that obtained from equation (2) [27].

$$f = \frac{WF_{arm}\ x\ M_{w,star}}{M_{w,arm}} = \frac{M_{w,star}}{M_{w,arm} + \ M_{DVB}\ x\ conv_{DVB}\ x\ [DVB]/[ada-PS]} \tag{1}$$

Where WF$_{arm}$, M_{DVB}, conv$_{DVB}$, [DVB]/[ada-PS] are the weight fraction of PS arm, the molecular weight of DVB, conversion of DVB (determined by GC analysis), and the feed molar ratio of the DVB to ada-PS (before polymerization), respectively.

$$g' = [\eta]_{star} / [\eta]_{linear} \quad (M = \text{constant})$$
$$\log g' = 0.36 - 0.8 \log f \tag{2}$$

Where $[\eta]_{star}$, $[\eta]_{linear}$ and g' are the intrinsic viscosity of star polymer, intrinsic viscosity of linear polymer (same molecular weight and the composition with star polymer), and contraction factor, respectively [27].

Figure 7 shows the ^{1}H NMR spectrum of (ada-PS)$_n$-polyDVB multiarm star polymer recorded in CDCl$_3$. It was detected that end-group proton of PS (4.45 ppm) completely disappeared as a result of star formation. The characteristic signal of methylene proton adjacent to adamantane (3.26 ppm) were identified again in the multiarm star spectrum.

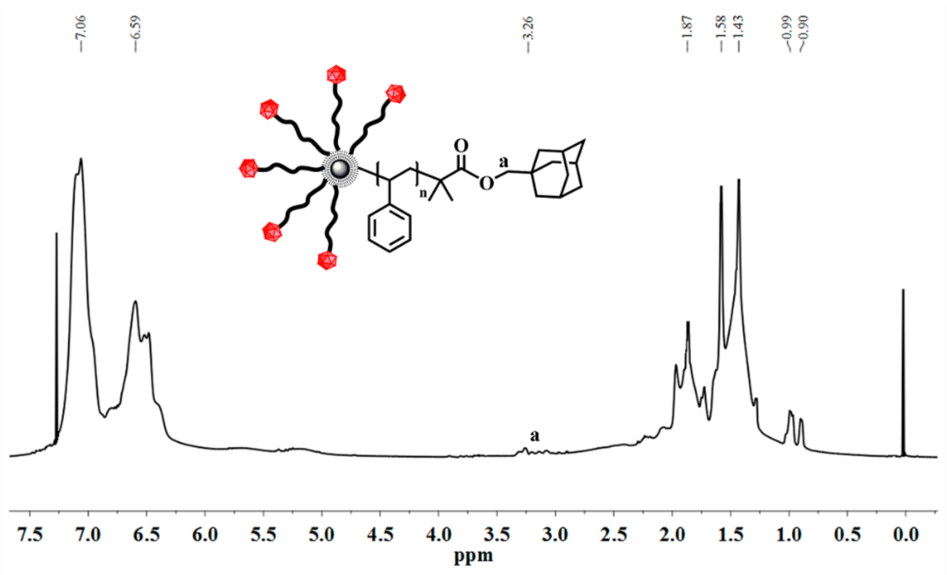
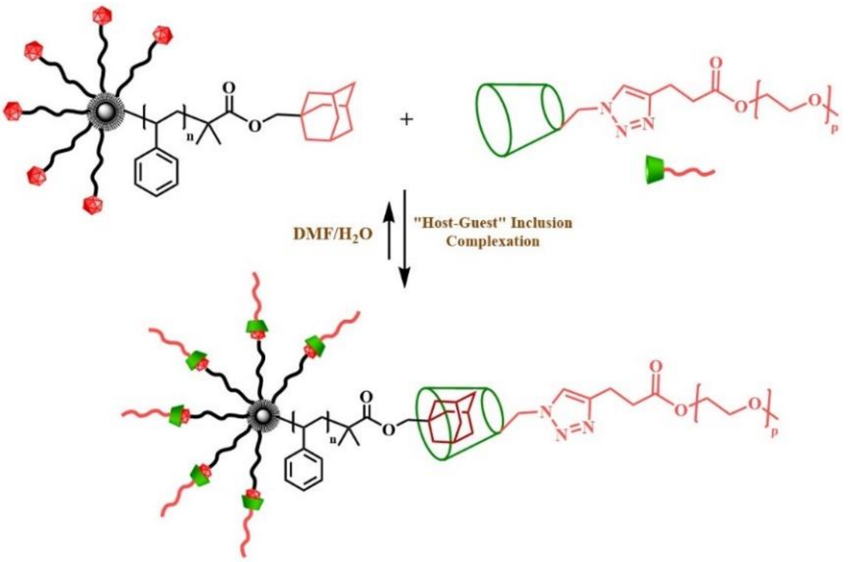


Figure 7. ^{1}H NMR spectrum of (ada-PS)$_n$-polyDVB multiarm star polymer in $CDCl_3$

The supramolecular (CD-PEG)$_p$-(ada-PS)$_n$-polyDVB multiarm star block copolymer was prepared via host−guest interaction between β-CD and ada as presented in Scheme 5.



Scheme 5. Host-guest inclusion complexation of (ada-PS)$_n$-polyDVB multiarm star polymer with β-CD-PEG molecule

In brief, the (ada-PS)$_n$-polyDVB multiarm star polymer and β-CD-PEG (equimolar per arm) were dissolved in DMF and one solution was added to other solution drop by drop. Subsequently, the resulting solution was dialyzed against a deionized DMF:water mixture at room temperature with increasing water content over time (Figure 8). Excess water content resulted the turbid polymer solution and subsequently formed a white precipitate. Finally, the solution was freeze-dried to yield the supramolecular (CD-PEG)$_p$-(ada-PS)$_n$-polyDVB multiarm star block copolymer.

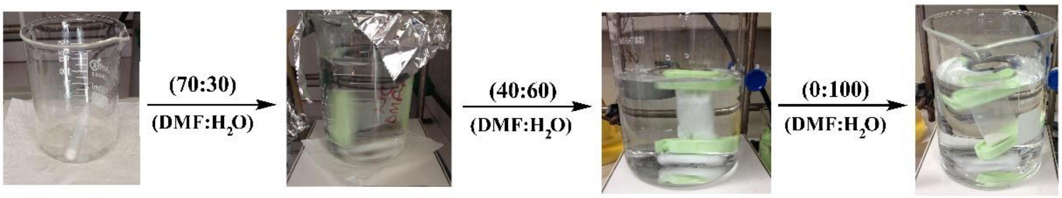


Figure 8. Preparation of supramolecular (CD-PEG)$_p$-(ada-PS)$_n$-polyDVB multiarm star block copolymer with gradually decreased DMF amount in mixture.

Figure 9 presents the ^{1}H NMR spectrum of the supramolecular (CD-PEG)$_p$-(ada-PS)$_n$-polyDVB multiarm star block copolymer, the characteristic peaks of the two polymeric blocks (PEG and PS) can be well observed.

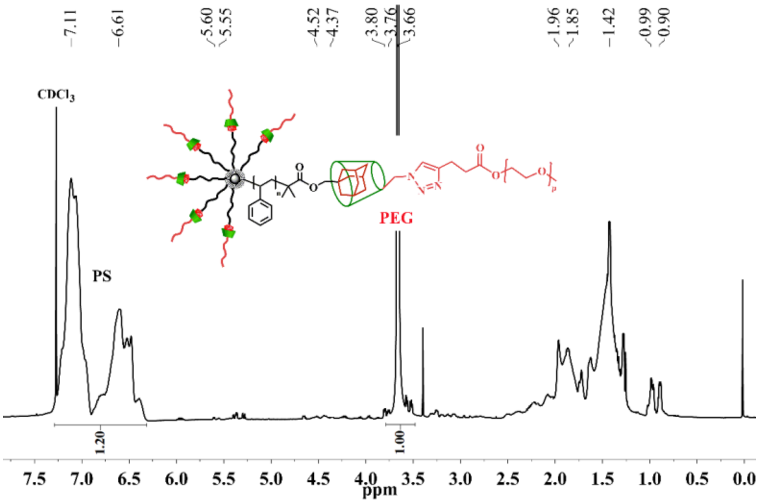


Figure 9. ^{1}H NMR spectrum of supramolecular (CD-PEG)$_p$-(ada-PS)$_n$-polyDVB multiarm star block copolymer in $CDCl_3$

To study the structure of the inclusion complex of β-CD-PEG with (ada-PS)$_n$-polyDVB multiarm star polymer, the ROESY NMR measurement was carried out. Figure 10 shows the ROESY NMR spectrum of the 1:1 mixture of β-CD-PEG and (ada-PS)$_n$-polyDVB multiarm star polymer. The peaks of methylene proton of the ada moiety at 1.0−1.5 ppm were correlating with inner protons of β-CD (the 3-, 5-, and 6-H protons), strongly indicating that adamantyl moiety was included in the cavity of β-CD units.

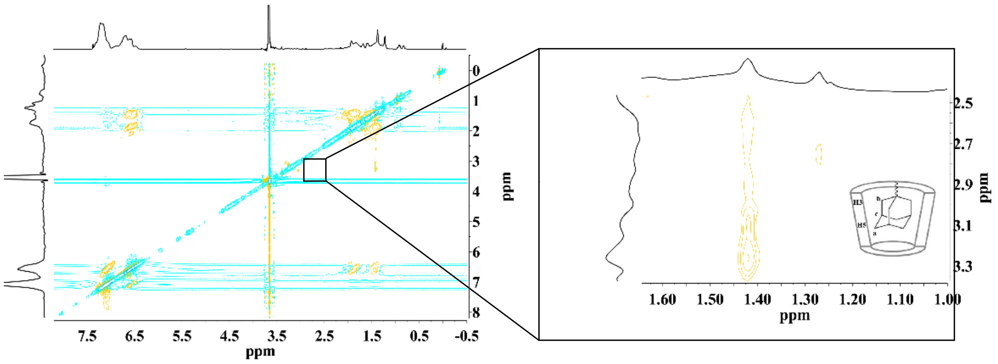


Figure 10. ROESY NMR spectrum of the supramolecular (CD-PEG)$_p$-(ada-PS)$_n$-polyDVB multiarm star block copolymer in $CDCl_3$ at 25°C (magnified in the right side).

The integration ratios of PS and PEG blocks in supramolecular $(CD\text{-}PEG)_p\text{-}(ada\text{-}PS)_n$-polyDVB multiarm star block copolymer were determined by ^1H NMR spectrum and introduced in equation (3), given in literature [28].

$$(dn/dc)_{\text{block copolymer}} = x\,(dn/dc)_{PS} + y\,(dn/dc)_{PEG} \tag{3}$$

Where x and y are the weight fractions (*w)* of PS and PEG blocks from ^1H NMR according to the backbone protons. Using these weight fractions, d*n*/dc value of supramolecular $(CD\text{-}PEG)_p\text{-}(ada\text{-}PS)_n$-polyDVB multiarm star block copolymer was calculated to 0.153 mL/g. In order to determine the absolute molecular weight of the supramolecular $(CD\text{-}PEG)_p\text{-}(ada\text{-}PS)_n$-polyDVB multiarm star block copolymer, the obtained d*n*/dc is then introduced into the Omni-Sec software of TD-GPC. As can be seen in Table 2, after host-guest inclusion complexation, the hydrodynamic radius (R_h) was increased from 4.89 nm to 5.59 nm. DLS is another versatile tool to investigate the complex formation in solution. After host-guest inclusion complexation, the hydrodynamic diameter (D_h) increased from the 7.40 nm to 9.69 nm (Figure 11). All these analysis supported the supramolecular multiarm star block copolymer formation. To the best of our knowledge, it is the first time such multiarm star block copolymer have been obtained using this host-guest interaction.

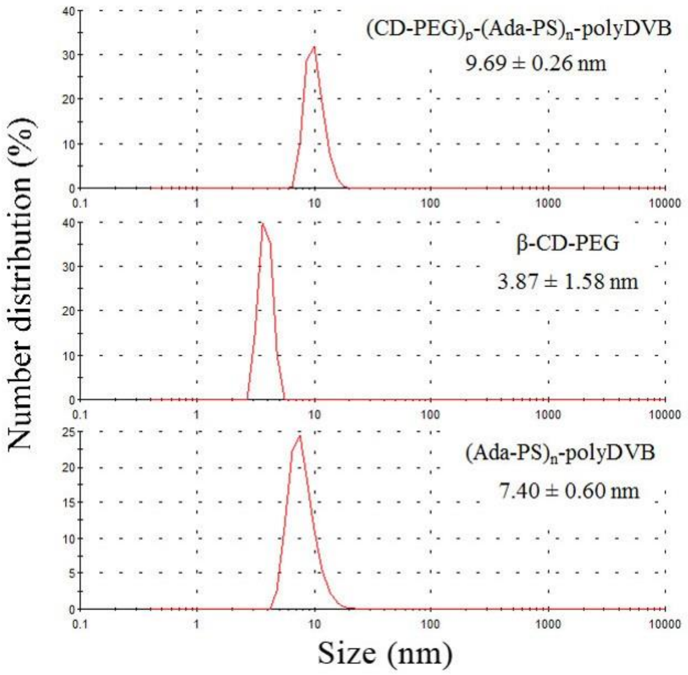


Figure 11. Comparison of the number average particle size determined by DLS for $(ada\text{-}PS)_n$-polyDVB multiarm star polymer, β-CD-PEG and supramolecular $(CD\text{-}PEG)_p\text{-}(ada\text{-}PS)_n$-polyDVB multiarm star block copolymer in DMSO (1 mg/mL) at room temperature.

Table 2. TD-GPC characterization of ada functional homoarm multiarm star polymer and supramolecular multiarm star block copolymer.

Polymers	**TD-GPC**[a]						
	M_n (g/mol)	**M_w (g/mol)**	**M_w/M_n**	**[η] (dL/g)**	**R_h (nm)**	**d*n*/dc (mL/g)**	**f^c**
(Ada-PS)$_n$-polyDVB[b]	68340	74300	1.09	0.105	4.89	0.185	13(15)[d]
(CD-PEG)$_p$-(Ada-PS)$_n$-polyDVB	95400	107300	1.13	0.120	5.59	0.153[e]	-

[a] Calculated from triple detection GPC (TD-GPC) in THF at 35 ºC.
[b] $[DVB]_0/15 = [ada\text{-}PS]_0 = [CuBr]_0 = [PMDETA]_0 = 0.020$ M in anisole at 110 °C;
[c] Calculated according to equation (1).
[d] Calculated according to equations (2).
[e] Calculated according to equation (3).

IV. CONCLUSIONS

We have combined controlled polymerization techniques with supramolecular interactions for multiarm star block copolymer synthesis. The β-cyclodextrin–adamantane (β-CD–ada) host-guest inclusion complexation has been studied as supramolecular interaction on the formation of multiarm star block copolymer. (Ada-PS)$_n$-polyDVB multiarm star polymer was synthesized by a crosslinking reaction of DVB with adamantane functionalized PS (ada-PS) as a macroinitiator. A β-CD end functionalized PEG (β-CD-PEG) was obtained by a two-step procedure: alkyne-functionalized PEG was first generated by esterification reaction of commercially available Me-PEG and subsequently converted in a host system by CuAAC with azide-functionalized β-CD (β-CD-N_3). Subsequent self-assembly of (ada-PS)$_n$-polyDVB multiarm star polymer as a guest molecule and β-CD-PEG as a host molecule in aqueous media afforded the supramolecular (CD-PEG)$_p$-(ada-PS)$_n$-polyDVB multiarm star block copolymer. The occurrence of host–guest inclusion complexation was unambiguously proved by ^{1}H NMR, 2D ROESY NMR, DLS and by TD-GPC measurements.

REFERENCES

[1] Gao H, Matyjaszewski K (2007) Low-polydispersity star polymers with core functionality by crosslinking macromonomers using functional ATRP initiators. Macromolecules 40(3):399–401. https://doi.org/10.1021/ma062640d

[2] Gao H, Matyjaszewski K (2008) Synthesis of star polymers by a new, ‘‘Core-First’’ method: sequential polymerization of cross-linker and monomer. Macromolecules 41(4):1118–1125. https://doi.org/10.1021/ma702560f

[3] Hadjichristidis N (1999) Synthesis of miktoarm star (μ-star) polymers. J Polym Sci, Part A: Polym Chem 37(7):857–871. https://doi.org/10.1002/(SICI)1099-0518(19990401)37:7<857::AID-POLA1>3.0.CO;2-P

[4] Hadjichristidis N, Pitsikalis M, Pispas S, Iatrou H (2001) Polymers with complex architecture by living anionic polymerization. Chem Rev 101(12):3747–3792. https://doi.org/10.1021/cr9901337

[5] Blencowe A, Tan JF, Goh TK, Qiao GG (2009) Core cross-linked star polymers via controlled radical polymerisation. Polymer 50(1):5–32. https://doi.org/10.1016/j.polymer.2008.09.049

[6] Ren JM, McKenzie TG, Fu Q, Wong EHH, Xu J, An Z, Shanmugam S, Davis TP, Boyer C, Qiao GG (2016) Star polymers. Chem Rev 116(12):6743–6836. https://doi.org/10.1021/acs.chemrev.6b00008

[7] Kuckling D, Wycisk A (2013) Stimuli-responsive star polymers. J Polym Sci, Part A: Polym Chem 51(14):2980–2994. https://doi.org/10.1002/pola.26696

[8] Altintas O, Vogt AP, Barner-Kowollik C, Tunca U (2012) Constructing star polymers via modular ligation strategies. Polym Chem UK 3(1):34. https://doi.org/10.1039/c1py00249j

[9] Altintas, O, Schulze-Suenninghausen, D, Luy, B, Barner-Kowollik, C (2013). Facile Preparation of Supramolecular H-Shaped (Ter)polymers via Multiple Hydrogen Bonding. Acs Macro Lett 2(3):211-216. https://doi.org/10.1021/mz400066r

[10] Fustin, C. A, Guillet, P, Schubert, U. S, Gohy, J. F (2007). Metallo-Supramolecular Block Copolymers. Advanced Materials 19(13):1665-1673. https://doi.org/10.1002/adma.200602170

[11] Chen, G, Jiang, M (2011). Cyclodextrin-based inclusion complexation bridging supramolecular chemistry and macromolecular self-assembly. Chemical Society reviews 40(5):2254-2266. https://doi.org/10.1039/C0CS00153H

[12] Zou, C, Zhao, P, Ge, J, Lei, Y, Luo, P (2012). β-Cyclodextrin modified anionic and cationic acrylamide polymers for enhancing oil recovery. Carbohydr. Polym 87(1):607–613. https://doi.org/10.1016/j.carbpol.2011.08.031

[13] Xiao, H, Cezar, N (2005). Cationic-modified cyclodextrin nanosphere/anionic polymer as flocculation/sorption systems. Colloid Interface Sci 283(2):406–413. https://doi.org/10.1016/j.jcis.2004.09.008

[14] Stadermann, J, Komber, H, Erber, M, Däbritz, F, Ritter, H, Voit, B (2011). Diblock Copolymer Formation via Self-Assembly of Cyclodextrin and Adamantyl End-Functionalized Polymers. Macromolecules 44(9):3250-3259. https://doi.org/10.1021/ma200048a

[15] Zeng, J, Shi, K, Zhang, Y, Sun, X, Zhang, B (2008). Construction and micellization of a noncovalent double hydrophilic block copolymer. Chem Commun 32:3753-3755. https://doi.org/10.1039/B806858E

[16] Liu, H, Zhang, Y, Hu, J, Li, C, Liu, S (2009). Multi-Responsive Supramolecular Double Hydrophilic Diblock Copolymer Driven by Host-Guest Inclusion Complexation between β-Cyclodextrin and Adamantyl Moieties. Macromol Chem Phys 210: 2125-2137. https://doi.org/10.1002/macp.200900279

[17] Bertrand, A, Stenzel, M, Fleury, E, Bernard, J (2012). Host–guest driven supramolecular assembly of reversible comb-shaped polymers in aqueous solution. Polym Chem 3(2):377-383. https://doi.org/10.1039/C1PY00478F

[18] Zhang, Z.-X, Liu, X, Xu, F. J, Loh, X. J, Kang, E.-T, Neoh, K.-G, Li, J (2008). Pseudo-Block Copolymer Based on Star-Shaped Poly(N-isopropylacrylamide) with a β-Cyclodextrin Core and Guest-Bearing PEG:

Controlling Thermoresponsivity through Supramolecular Self-Assembly. Macromolecules 41(16):5967-5970. https://doi.org/10.1021/ma8009646

[19] Setijadi, E, Tao, L, Liu, J, Jia, Z, Boyer, C, Davis, T. P (2009). Biodegradable star polymers functionalized with beta-cyclodextrin inclusion complexes. Biomacromolecules 10(9):2699-2707. https://doi.org/10.1021/bm900646g

[20] Schmidt, B. V. K. J, Hetzer, M, Ritter, H, Barner-Kowollik, C (2013). UV Light and Temperature Responsive Supramolecular ABA Triblock Copolymers via Reversible Cyclodextrin Complexation. Macromolecules 46(3):1054-1065. https://doi.org/10.1021/ma302386w

[21] Schmidt, B. V. K. J, Hetzer, M, Ritter, H, Barner-Kowollik, C (2012). Miktoarm star polymers via cyclodextrin-driven supramolecular self-assembly. Polym Chem-Uk 3(11):3064-3067. https://doi.org/10.1039/C2PY20214J

[22] Schmidt, B. V. K. J, Rudolph, T, Hetzer, M, Ritter, H, Schacher, F. H, Barner-Kowollik, C (2012). Supramolecular three-armed star polymers via cyclodextrin host–guest self-assembly. Polym Chem-Uk 3(11):3139-3145. https://doi.org/10.1039/C2PY20293J

[23] Schmidt, B. V. K. J, Barner-Kowollik, C (2014). Supramolecular X- and H-shaped star block copolymers via cyclodextrin-driven supramolecular self-assembly. Polym Chem-Uk 5(7):2461-2472. https://doi.org/10.1039/C3PY01580G

[24] Huan, X, Wang, D, Dong, R, Tu, C, Zhu, B, Yan, D, Zhu, X (2012). Supramolecular ABC Miktoarm Star Terpolymer Based on Host–Guest Inclusion Complexation. Macromolecules 45(15):5941-5947. https://doi.org/10.1021/ma300693h

[25] Cakir, N, Hizal, G, Becer C. R (2015). Supramolecular glycopolymers with thermo-responsive self-assembly and lectin binding. Polym Chem-Uk 6 (37):6623-6631. https://doi.org/10.1039/C5PY00939A

[26] Durmaz, H, Dag, A, Altintas, O, Erdogan, T, Hizal, G, Tunca, U (2007). One-Pot Synthesis of ABC Type Triblock Copolymers via in situ Click [3 + 2] and Diels−Alder [4 + 2] Reactions. Macromolecules 40 (2): 191-198. https://doi.org/10.1021/ma061819l

[27] Cakir, N, Tunca, U, Hizal, G, Durmaz, H (2016). Heterofunctionalized multiarm star polymers via sequential thiol-para-fluoro and thiol-ene double “click” reactions. Macromol Chem Phys 217: 636-645. https://doi.org/10.1002/macp.201500300

[28] Cakir Yigit, N, Hizal, G, Tunca, U (2018). A powerful tool for preparing peripherally post-functionalized multiarm star block copolymer. Polym Bull 75:3523–3538. https://doi.org/10.1007/s00289-017-2218-5