One-Pot Synthesis of ABC Type Triblock Copolymers via in situ Click [3 + 2] and Diels−Alder [4 + 2] Reactions

Hakan Durmaz, Aydan Dag, Ozcan Altintas, Tuba Erdogan, Gurkan Hizal,* and Umit Tunca*

Department of Chemistry, Istanbul Technical University, Maslak 34469 Istanbul, Turkey

Received August 10, 2006; Revised Manuscript Received November 6, 2006

ABSTRACT: We report a one-pot synthesis of ABC triblock copolymers of poly(ethylene glycol)− (PEG−) polystyrene− (PS−) poly(methyl methacrylate) (PMMA), and poly(ϵ-caprolactone)− (PCL−) PS−PMMA by combining in situ click [3 + 2] and Diels−Alder [4 + 2] reactions. For this purpose, furan-protected maleimide end-functionalized PMMA, PS with α-anthracene and ω-azide end-functionality, and PEG or PCL with an alkyne end-functional group were reacted in *N*,*N*-dimehtylformamide (DMF) for 36 h at 120 °C in order to give the corresponding triblock copolymers. All polymeric precursors with narrow molecular weight distribution and well-defined chain-end functionalities were achieved from living polymerization methods, except PEG. The obtained polymers were characterized by ^{1}H NMR (250 MHz), gel permeation chromatography (GPC), and differential scanning calorimetry (DSC) measurements.

Introduction

In recent years, the use of the controlled/living radical polymerization (CRP) techniques for the synthesis of well-defined narrow polydispersity polymers has rapidly increased because of the variety of applicable monomers and more tolerant experimental conditions than the living ionic polymerization routes require. The reversible addition fragmentation chain transfer (RAFT) polymerization,[1] the nitroxide-mediated free radical polymerization[2] (NMP), and the metal mediated controlled/living radical polymerization, often called atom transfer radical polymerization[3−5] (ATRP), are versatile methods for the controlled/living radical polymerizations. However, the latter two cases turned out to be more extensive. One of the advantages of CRP methods compared to conventional free radical polymerization is the control of the molecular weight and chain end-functionality. A wide range of functionality may be introduced into a polymer chain using a hetero-functional initiator if one of the functional groups remains intact during the polymerization. This provided the synthesis of well-defined block copolymers by a sequential two-step or one-pot polymerization method without any chemical transformation or protection of initiating sites. Using this strategy, a number of block copolymers have been prepared by combination of different polymerization mechanisms, such as ATRP−NMP,[6,7] ATRP−living ring-opening polymerization (ROP),[8−11] NMP−ROP,[8,9,12,13] and ATRP−living cationic polymerization.[14]

There are alternative routes for the preparation of block copolymers. Recently, Sharpless and co-workers used Cu(I) as a catalyst in conjunction with a base in Huisgen's 1,3-dipolar cycloadditions,[15] [3 + 2] system, between azides and alkynes or nitriles, and termed them click reactions.[16,17] Later, click chemistry strategy was successfully applied to macromolecular chemistry, offering polymeric materials varying from the block copolymers[18] to the complex macromolecular[19−32] structures. Click reactions permit C−C bond (or C−N) formation in a quantitative yield without side reactions and a requirement for an additional purification step.

* Corresponding authors. E-mail: (U.T.) tuncau@itu.edu.tr; (G.H.) hizal@itu.edu.tr.

The second strategy involves the fact that the Diels−Alder reaction, a [4 + 2] system, is a cycloaddition between a conjugated diene (a 4π-electron system) and a dienophile (a 2π-electron system).[33] Recently, Diels−Alder reaction has attracted much attention based on the macromolecular chemistry, particularly in providing new materials.[34−42]

We report here an efficient way for the preparation of ABC type triblock copolymers in one-pot via a combination of Diels−Alder and click reactions. Polystyrene (PS) (A), poly(methyl methacrylate) (PMMA) (B), and poly(ethylene glycol) (PEG) or poly(ϵ-caprolactone) (PCL) (C segment) with low molecular weight distributions and proper end-functional groups for Diels−Alder and click reactions were prepared using living polymerization systems, except PEG that was commercially available.

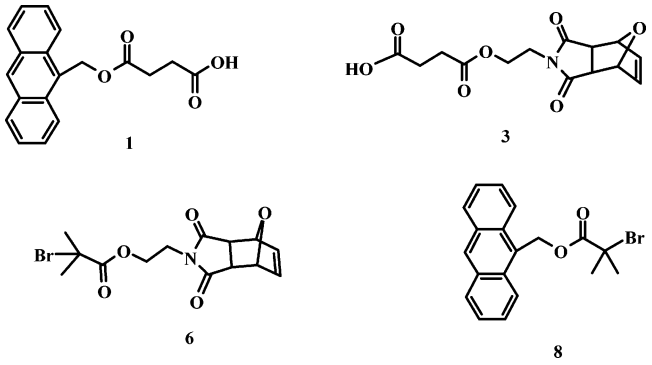
Experimental Section

Materials. Styrene (St, 99%, Merck), methyl methacrylate (MMA, 99%, Aldrich) were passed through basic alumina column to remove inhibitor and then distilled from CaH_2 in vacuum prior to use. Propargyl alcohol (99%, Aldrich), *N*,*N*′-dicyclohexylcarbodiimide (DCC, 99%, Aldrich), 4-dimethylaminopyridine (DMAP, 99%, Aldrich), 4-pentynoic acid (98%, Alfa Aesar), tin(II) 2-ethylhexanoate (Aldrich), tributyltinhydride (97%, Aldrich), CuBr (99.9%, Aldrich), and CuCl (99.9%, Aldrich) were used as received. *N*,*N*,*N*′,*N*″,*N*″-Pentamethyldiethylenetriamine (PMDETA, 99%, Aldrich) was distilled over NaOH prior to use. ϵ-Caprolactone (ϵ-CL, 99%, Aldrich) was distilled from CaH_2 in vacuum. Poly(ethylene glycol) monomethyl ether (Me-PEG, M_n = 2000, Fluka) was dried by azeotropic distillation with anhydrous toluene. Tetrahydrofuran (THF, 99.8%, J.T. Baker) was dried and distilled from benzophenone−Na. *N*,*N*-Dimethylformamide (DMF, 99.8%, Aldrich) was dried and distilled under vacuum over CaH_2. Dichloromethane (CH_2Cl_2, 99%, J. T. Baker) was dried and distilled over and P_2O_5. Other solvents were purchased from J. T. Baker and used without further purification.

Instrumentation. The ^{1}H NMR (250 MHz) and ^{13}C NMR (62.89 MHz) spectra were recorded on a Bruker NMR spectrometer in $CDCl_3$. Gel permeation chromatography (GPC) measurements were obtained from an Agilent instrument (model 1100) consisting of a pump, a refractive index detector, and four Waters Styragel high-resolution HR columns (HR 5E, HR 4E, HR 3, and HR 2) (4.8 mm internal diameter, 300 mm length, packed with 5 μm particles).

10.1021/ma061819l CCC: $37.00
Published on Web 12/21/2006

Chart 1. Starting Compounds Used in this Work: Succinic Acid Monoanthracen-9-yl Methyl Ester (1), 4-(2-{[(3-Acetyl-7-oxabicyclo[2.2.1]hept-5-en-2-yl)carbonyl] amino}ethoxy)-4-oxobutanoic Acid (3), 2-Bromo-2-methylpropionic Acid 2-(3,5-Dioxo-10-oxa-4-azatricyclo[5.2.1.02,6]dec-8-en-4-yl) Ethyl Ester (6), and 9-Anthyrylmethyl 2-bromo-2-methyl Propanoate (8)

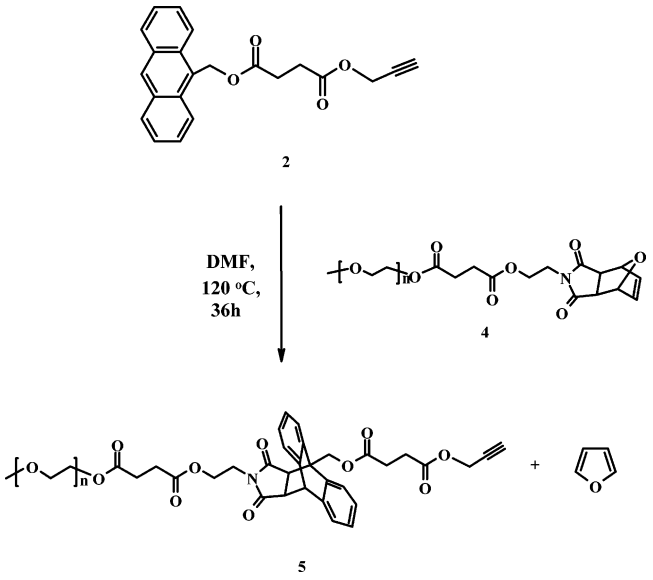


The effective molecular weight ranges were 2000−4000000, 50−100000, 500−30000, and 500−20000, respectively. THF was used as eluent at a flow rate of 0.3 mL/min at 30 °C. Toluene was as an internal standard. Data analyses were performed with Polymer Laboratories Caliber Software Calibration with linear PS standards (Polymer Laboratories) was used to estimate the molecular weights of PS, PCL, PEG, and all triblock copolymers, whereas linear PMMA standards (Polymer Laboratories) were only used for the molecular weight determination of the PMMA homopolymer. The conversions for all polymerizations were determined gravimetrically. Elemental analyses (C, H, and N) were obtained from a FlashEA 1112 (Thermo Electron Corporation). UV spectra were recorded on a Perkin-Elmer Lambda 2 spectrophotometer in CH_2Cl_2. FT−IR spectra were recorded on a Perkin-Elmer FT−IR Spectrum One spectrometer. Differential scanning calorimetry (DSC) measurements were performed on a Diamond DSC (Perkin-Elmer) at a heating rate of 10 °C/min under nitrogen atmosphere. DSC instrument was calibrated using indium for temperature and enthalpy changes. All data were collected from a second heating cycle and the glass transition (T_g) and melting temperatures (T_m) were calculated as a midpoint and a peak apex of thermograms, respectively.

Syntheses and Polymerizations. Succinic acid monoanthracen-9-yl methyl ester,[43] **1**, 4-(2-{[(3-acetyl-7-oxabicyclo[2.2.1]hept-5-en-2-yl)carbonyl]amino}ethoxy)-4-oxobutanoic acid,[44] **3**, 2-bromo-2-methylpropionic acid 2-(3,5-dioxo-10-oxa-4-azatricyclo-[5.2.1.02,6]dec-8-en-4-yl) ethyl ester,[45] **6**, and 9-anthyrylmethyl 2-bromo-2-methyl propanoate,[46] **8**, were synthesized according to previously reported procedures (see Chart 1). All polymerizations were performed under inert atmosphere with Schlenk techniques.

Synthesis of Succinic Acid Anthracen-9-yl Methyl Ester Prop-2-ynyl Ester (2). Propargylalcohol (0.545 g, 9.74 mmol, 1.5 equiv) and DMAP (0.396 g, 3.25 mmol, 0.5 equiv) were dissolved in 30 mL of dry CH_2Cl_2. **1** (2.00 g, 6.49 mmol, 1 equiv) was added to this solution. After the reaction was stirred for 5 min at room temperature, DCC (2.00 g, 9.74 mmol, 1.5 equiv) dissolved in 15 mL of CH_2Cl_2 was added. The reaction mixture was stirred overnight at room temperature. After the urea byproduct was filtered off, the solvent was removed, and the remaining product was extracted with CH_2Cl_2 and water. The aqueous phase was again extracted with CH_2Cl_2 and combined organic phase was dried with Na_2SO_4. The solution was concentrated and the crude product was purified by column chromatography over silica gel eluting with ethylacetate/hexane (1:2) to give the product as a yellow solid (yield = 1.9 g, 85%). Mp = 77−78 °C. ^{1}H NMR ($CDCl_3$, δ): 8.51 (s, 1H, Ar*H* of anthracene), 8.31 (d, J = 8.8 Hz, 2H, Ar*H* of anthracene), 8.03 (d, J = 8.3 Hz, 2H, Ar*H* of anthracene), 7.60−7.45 (m, 4H, Ar*H* of anthracene), 6.16 (s, 2H, CH_2−anthracene), 4.61 (d, J = 2.4 Hz, 2H, CH≡CCH_2O), 2.67 (s, 4H, C═OCH_2CH_2C═O), 2.44 (t, J = 2.4 Hz, 1H, C*H*≡CCH$_2$O). ^{13}C NMR ($CDCl_3$, δ): 172.07 (C═O), 171.24 (C═O), 131.44 (Ar−C), 131.11 (Ar−C), 129.21 (Ar−C), 129.07 (Ar−C), 126.65 (Ar−C), 126.05 (Ar−C), 125.08 (Ar−C), 123.92 (Ar−C), 74.79 (*C*H≡CCH$_2$O), 59.22 (Ar−*C*H$_2$), 52.06 (CH≡C*C*H$_2$O), 29.11 (*C*H$_2$C═OO), 29.01 (*C*H$_2$C═OO). Anal. Calcd for $C_{22}H_{18}O_4$: C, 76.29; H, 5.24. Found: C, 76.25; H, 5.23.

Scheme 1. Model Diels−Alder Reaction between Succinic Acid Anthracen-9-yl Methyl Ester Prop-2-ynyl Ester (2) and Maleimide End-Functionalized PEG (PEG−MI 4) in *N,N*-Dimethylformamide (DMF) for 36 h at 120 °C



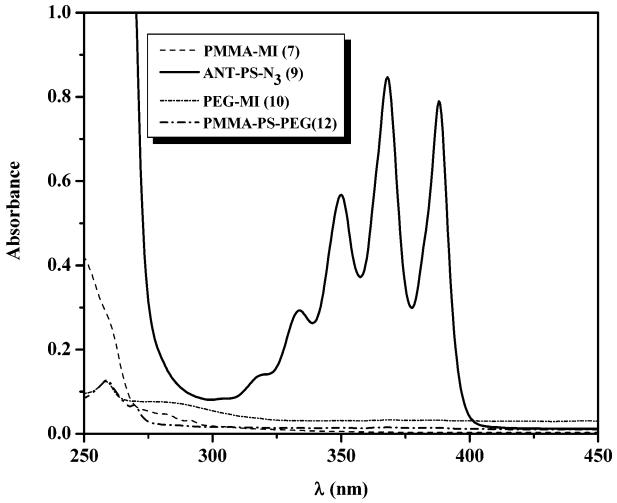
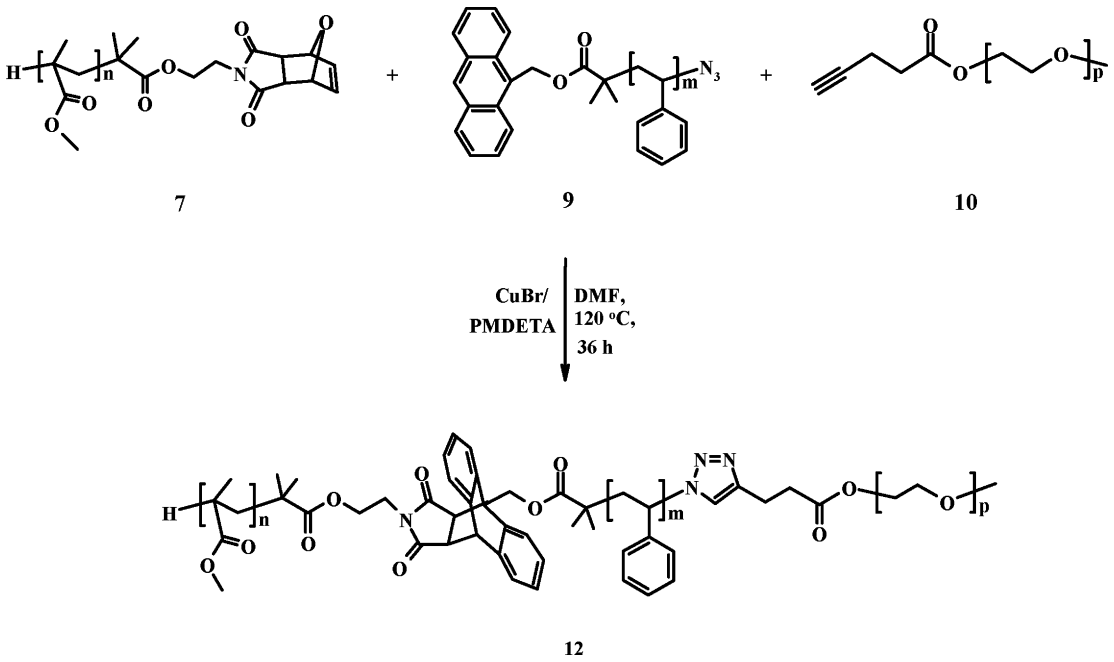


Figure 1. UV spectra of maleimide end-functionalized PMMA (PMMA−MI) ([**7**] = 3.8 × 10^{-4}), PS−α-anthracene-ω-azide ([**9**] = 9.8 × 10^{-5}), alkyne end-functionalized PEG (PEG−alkyne) ([**10**] = 1.3 × 10^{-4}), and poly(methyl methacrylate)−polystyrene−poly(ethylene glycol) (PMMA−PS−PEG) triblock copolymer ([**12**] = 3.1 × 10^{-4}) in CH_2Cl_2.

Preparation of Maleimide End-Functionalized PEG (PEG-MI) (4). Me-PEG (M_n = 2000) (1.0 g, 0.50 mmol) was dissolved in 10 mL of CH_2CI_2. **3** (0.46 g, 1.5 mmol) and DMAP (0.060 g, 1.5 mmol) were added to the reaction mixture. DCC (0.92 g, 4.5 mmol) in 5 mL of CH_2Cl_2 was added and the reaction mixture was stirred overnight at room temperature. It was filtered and evaporated, and the remaining product was purified by column chromatography over silica gel eluting first with CH_2Cl_2/ethylacetate (1:1) and then with methanol/CH_2Cl_2 (1:10). The recovered polymer was dissolved in tetrahydrofuran (THF) and precipitated in cold diethyl ether to give **4** as a white solid. The polymer was dried for 24 h in a vacuum

Scheme 2. One-Pot Synthesis of Poly(ethylene glycol)−Polystyrene−Poly(methyl methacrylate) (PEG−PS−PMMA) Triblock Copolymer 12 in the Presence of CuBr/*N*,*N*,*N*′,*N*″,*N*″-Pentamethyldiethylenetriamine (PMDETA) in *N*,*N*-Dimethylformamide (DMF) at 120 °C



7 9 10

12

oven at 25 °C. $M_{n,theo}$ = 2300; $M_{n,NMR}$ = 2600; $M_{n,GPC}$ = 3200 (relative to linear PS); M_w/M_n = 1.03 (yield = 0.95 g, 82%). ^{1}H NMR ($CDCl_3$, δ) 6.50 (s, 2H, C*H*═C*H*), 5.25 (s, 2H, C*H* as bridge-head protons), 4.23 (m, 4H, CH_2OC═O, and NCH$_2$CH_2OC═O), 3.78−3.51 (m, OCH_2CH_2 repeating unit of PEG, C═ONCH_2, and CH_2−PEG repeating unit), 3.36 (s, 3H, PEG-OCH_3), 2.87 (s, C*H*-C*H*, as bridge protons), 2.61−2.56 (m, 4H, C═OCH_2CH_2C═O).

Model Diels—Alder Reaction between 2 and PEG-MI (4). PEG-MI **4** (0.50 g, 0.19 mmol, 1 equiv) was added to 0.200 g of **2** (0.578 mmol, 3 equiv) in 10 mL of DMF. The mixture was bubbled with nitrogen for 30 min and stirred at 120 °C for 36 h. The solvent was removed and the resulting product **5** was precipitated in cold diethylether. This procedure was repeated two times. (Yield = 0.5 g, 90%.) $M_{n,theo}$ = 2600; $M_{n,NMR}$ = 2800; $M_{n,GPC}$ = 3700 (relative to linear PS); M_w/M_n = 1.02. ^{1}H NMR ($CDCl_3$, δ) 7.40−7.14 (m, 8H, Ar*H*), 5.48 (dd, 2H, CH_2OC═O), 4.76 (s, 1H, C*H*, bridge-head proton), 4.59 (d, 2H, CH≡CCH_2O), 4.23 (t, 2H, PEG−OCH$_2$CH_2OC═O), 3.90 (t, 2H, NCH$_2$CH_2OC═O), 3.78−3.46 (m, CH$_2$CH$_2$O of PEG), 3.36 (s, 3H, CH_3-OCH$_2$-CH$_2$), 3.34 (m, 4H, NC═OC*H*−*CH* bridge protons and NCH_2CH$_2$-OC═O), 2.8−2.5 (m, 8H, C═OCH_2CH_2C═O), 2.47 (t, 1H, C*H*≡CCH$_2$O).

Synthesis of Maleimide End-Functionalized PMMA, PMMA—MI (7). PMMA−MI (**7**) was prepared by ATRP of MMA. In a 50 mL Schlenk tube, MMA (5.00 mL, 46.7 mmol), toluene (5 mL), PMDETA (0.196 mL, 0.940 mmol), CuCl (0.093 g, 0.94 mmol), and **6** (0.336 g, 0.940 mmol) were added, and the reaction mixture was degassed by three freeze−pump−thaw cycles and left in argon. The tube was then placed in an oil bath thermostated at 40 °C for 3.5 h. Tributyltinhydride (2.73 g, 9.40 mmol) was added to the reaction mixture and stirred further for 30 min. The polymerization mixture was then diluted with THF, passed through a basic alumina column to remove the catalyst, and precipitated in hexane. The polymer was dried for 24 h in a vacuum oven at 25 °C. $[M]_0/[I]_0$ = 50; $[I]_0$:[CuCI]$_0$:[PMDETA]$_0$ = 1:1:1; conversion = 16%; $M_{n,theo}$ = 1100; $M_{n,NMR}$ = 2700; $M_{n,GPC}$ = 2600 (relative to linear PMMA); M_w/M_n = 1.21. ^{1}H NMR ($CDCl_3$, δ) 6.5 (C*H*═C*H*, oxatricyclo vinyl), 5.3 (CH, bridgehead), 4.1 (NCH$_2$CH_2OC═O), 3.8 (NCH_2CH$_2$OC═O), 3.6−3.5 (OCH_3 of PMMA), 2.9 (C*H*−C*H*, bridge), 0.6−2.0 (aliphatic protons).

Preparation of PS with α-Anthracene and ω-Azide (9). PS-α-anthracene-ω-bromide was prepared by ATRP of St. In a 50 mL of Schlenk tube, St (15.0 mL, 130 mmol), PMDETA (0.136 mL, 0.655 mmol), CuBr (0.0939 g, 0.655 mmol), and **8** (0.234 g, 0.655 mmol) were added, and the reaction mixture was degassed by three freeze−pump−thaw cycles and left in vacuum. The tube was then placed in a thermostated oil bath at 110 °C for 45 min. The dark-green polymerization mixture was diluted with THF, passed through a basic alumina column to remove the catalyst, and precipitated in methanol. The polymer was dried for 24 h in a vacuum oven at 50 °C. $[M]_0/[I]_0$ = 200; $[I]_0$:$[CuBr]_0$:$[PMDETA]_0$ = 1:1:1; conversion = 27%; $M_{n,theo}$ = 5900; $M_{n,NMR}$ = 6600; $M_{n,GPC}$ = 6100 (relative to linear PS); M_w/M_n = 1.09.

Previously obtained PS−α-anthracene-ω-bromide (2 g, 0.3 mmol) was dissolved in DMF (20 mL) and NaN_3 (0.39 g, 6.0 mmol) was added. After the reaction mixture was stirred overnight at room temperature, CH_2Cl_2 and water were added and the organic layer was extracted three times with water and dried over Na_2SO_4. The excess of CH_2Cl_2 was evaporated under reduced pressure and the obtained product was precipitated into an excess amount of methanol. PS−α-anthracene-ω-azide **9** was dried for 24 h in a vacuum oven at 25 °C. Yield = 1.9 g, 95%; $M_{n,theo}$ = 5850; $M_{n,NMR}$ = 6600; $M_{n,GPC}$ = 6100 (relative to linear PS); M_w/M_n = 1.09. ^{1}H NMR ($CDCl_3$, δ) 8.4 (Ar*H* of anthracene), 8.3 (Ar*H* of anthracene), 7.9 (Ar*H* of anthracene), 7.5 (Ar*H* of anthracene), 6.5−7.5 (Ar*H* of PS), 5.8 (CH_2−anthracene), 3.9 (C*H*(Ph)−N$_3$), 0.6−2.2 (aliphatic protons).

Preparation of Alkyne End-Functionalized PEG, PEG—Alkyne (10). Me-PEG (M_n = 2000) (2 g, 1 mmol) was dissolved in 25 mL of CH_2Cl_2. 4-Pentynoic acid (0.294 g, 3.00 mmol), DMAP (0.12 g, 1.0 mmol) and DCC (0.62 g, 3.0 mmol) in 5 mL of dichloromethane were added to the solution in that order. The reaction mixture was stirred overnight at room temperature. It was filtered and evaporated, and the remaining product was purified by column chromatography over silica gel eluting first with CH_2Cl_2/ethylacetate (1:1), and then with methanol/ CH_2Cl_2 (1:10). Polymer was dissolved in THF precipitated in cold diethyl ether. The polymer was dried for 24 h in a vacuum oven at 25 °C. $M_{n,theo}$ = 2100; $M_{n,NMR}$ = 2300; $M_{n,GPC}$ = 3000 (relative to linear PS); M_w/M_n = 1.04. ^{1}H NMR ($CDCl_3$, δ) 4.25 (t, 2H, PEG−OCH$_2$CH_2-OC═O), 3.89−3.54 (m, 8H, PEG−OCH_2CH$_2$OC═O, −OCH_2CH_2− of PEG CH$_3$O−, and CH_2CH$_2$−O), 3.36 (s, 3H, CH_3−OCH$_2$CH$_2$). 2.56−2.48 (m, 4H, CH≡CCH_2CH_2C═O), 1.97 (t, 1H, C*H*≡CCH$_2$-CH$_2$C═O).

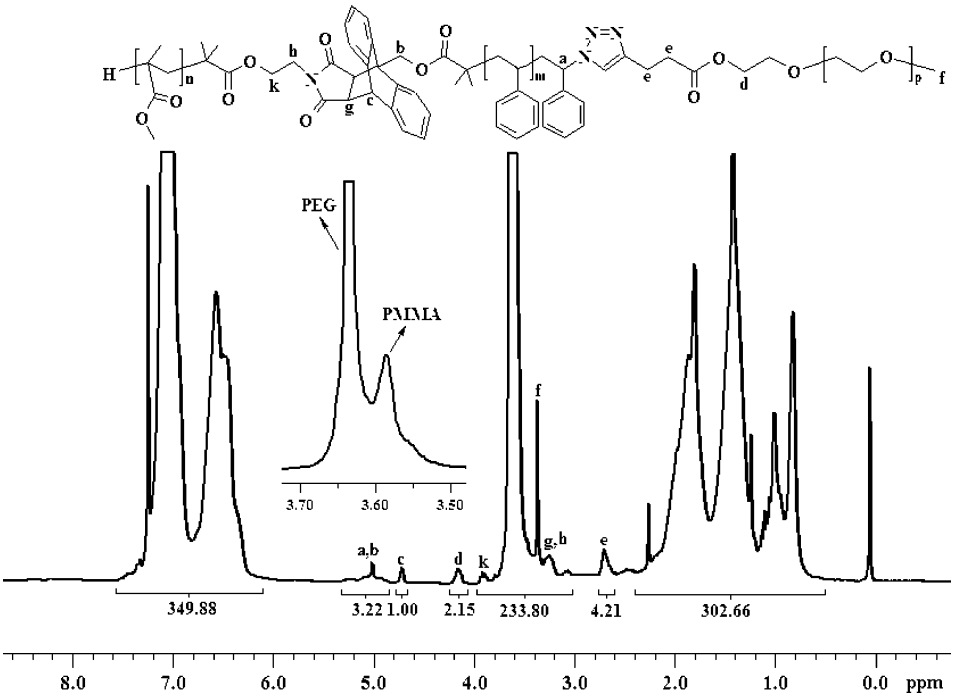


Figure 2. ^{1}H NMR spectrum of poly(methyl methacrylate)−polystyrene−poly(ethylene glycol) (PEG−PS−PMMA) triblock copolymer **12** in $CDCl_3$.

Preparation of Alkyne End-Functionalized PCL, PCL—Alkyne (11). The PCL−alkyne **11** was prepared by ROP of ϵ-CL (5.0 mL, 0.047 mol) in bulk using tin(II) 2-ethylhexanoate as a catalyst and propargyl alcohol (0.056 mL, 0.94 mmol) as an initiator at 110 °C for 28 h., The degassed monomer, catalyst, and initiator were added to a previously flamed Schlenk tube equipped with a magnetic stirring bar in the order mentioned. The tube was degassed with three freeze−pump−thaw cycles, left under argon, and placed in a thermostated oil bath. After the polymerization, the mixture was diluted with THF and precipitated into an excess amount of methanol. It was isolated by filtration and dried at room temperature in a vacuum oven for 24 h $[M]_0/[I]_0 = 50$; conversion = 66%; $M_{n,theo} = 3850$; $M_{n,NMR} = 4200$; $M_{n,GPC} = 8000$ (relative to linear PS); $M_w/M_n = 1.06$. ^{1}H NMR ($CDCl_3$, δ): 4.6 (2H, CH≡C−CH_2O), 4.0 (2H, CH_2OC═O of PCL), 3.6 (2H, CH_2OH, end group of PCL), 2.3 (2H, C═OCH_2 of PCL), 1.2−1.8 (6H, CH_2 of PCL).

One-Pot Synthesis of PEG—PS—PMMA Triblock Copolymer (12). PMMA−MI (**7**) (0.067 g, 0.025 mmol), PS−α-anthracene-ω-azide (**9**) (0.15 g, 0.022 mmol), and PEG−alkyne (**10**) (0.058 g, 0.025 mmol) were dissolved in nitrogen-purged DMF (5 mL) in a Schlenk tube. CuBr (0.004 g, 0.03 mmol) and PMDETA (0.006 mL, 0.03 mmol) were added, and the reaction mixture was degassed by three freeze−pump−thaw cycles and left under argon and stirred at 120 °C for 36 h. Polymer solution was passed through alumina column to remove copper salt, precipitated into methanol and dried in a vacuum oven at 25 °C. Yield = 0.22 g (85%), $M_{n,theo} = 11\,600$; $M_{n,NMR} = 10\,300$; $M_{n,GPC} = 8200$ (relative to linear PS); $M_w/M_n = 1.10$. ^{1}H NMR ($CDCl_3$, δ) 6.3−7.5 (Ar−*H* of PS), 5.2−4.9 (cycloadduct-CH_2OC═O and C*H*(Ph)-triazole), 4.7 (C*H*, bridge-head proton), 4.2 (C═OOCH_2CH$_2$O, end group of PEG), 3.9 (C═OOCH_2CH$_2$N), 3.7−3.6 (OCH_2CH_2O, repeating unit of PEG), 3.6−3.5 (OCH_3 of PMMA), 3.4 (OCH_3 end group of PEG), 3.3 (C*H*-C*H*, bridge protons of cycloadduct and CH_2−N), 2.6 (triazole-CH_2CH_2C═O), 2.2−0.6 (aliphatic protons).

One-Pot Synthesis of PCL—PS—PMMA Triblock Copolymer (13). PMMA−MI (**7**) (0.067 g, 0.025 mmol), PS-α-anthracene-ω-azide (**9**) (0.15 g, 0.022 mmol), and PCL−alkyne (**11**) (0.092 g, 0.022 mmol) were dissolved in nitrogen-purged DMF (5 mL) in a Schlenk tube. CuBr (0.004 g, 0.03 mmol) and PMDETA (0.006 mL, 0.03 mmol) were added to the reaction mixture. It was degassed by three freeze−pump−thaw cycles and left in argon and stirred at 120 °C for 36 h. Polymer solution was passed through alumina column to remove copper salt, precipitated into methanol and dried in vacuum oven at 25 °C. Yield = 0.27 g (90%), $M_{n,theo} = 13\,500$; $M_{n,NMR} = 12\,300$; $M_{n,GPC} = 10\,450$ (relative to linear PS); $M_w/M_n = 1.11$. ^{1}H NMR ($CDCl_3$, δ) 6.5−7.5 (Ar−*H* of PS), 5.2−4.9 (cycloadduct−CH_2OC═O, C*H*(Ph)−triazole, and triazole−CH_2O), 4.7 (C*H*, bridge-head proton), 4.1−3.9 (CH_2CH$_2$CH$_2$-CH$_2$CH_2OC═O, repeating unit of PCL), 3.6−3.5 (OCH_3 of PMMA), 3.3 (C*H*−C*H*, bridge protons of cycloadduct and CH_2−N), 2.3−2.2 (C═OCH_2CH$_2$CH$_2$CH$_2$CH$_2$O), 0.6−2.2 (aliphatic protons).

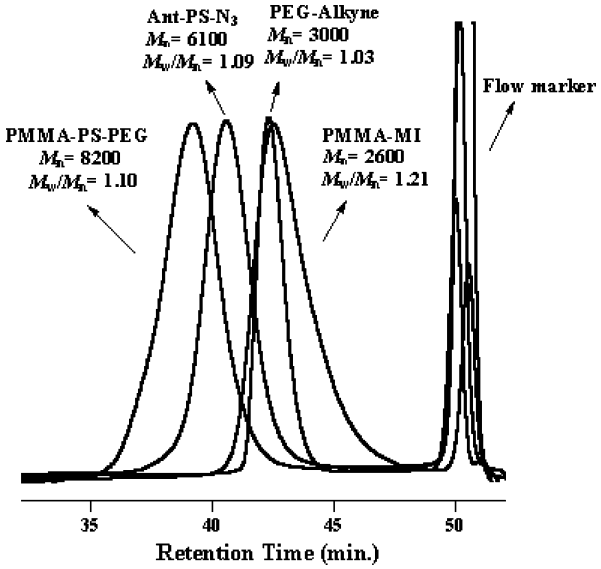


Figure 3. Evolution of the gel permeation chromatography (GPC) traces: maleimide end-functionalized PMMA (PMMA−MI (**7**)), PS with α-anthracene and ω-azide end-functionality (PS−α-anthracene-ω-azide (**9**)), alkyne end-functionalized PEG (PEG−alkyne (**10**)) precursors, and poly(methyl methacrylate)−polystyrene−poly(ethylene glycol) (PMMA−PS−PEG) triblock copolymer **12.**

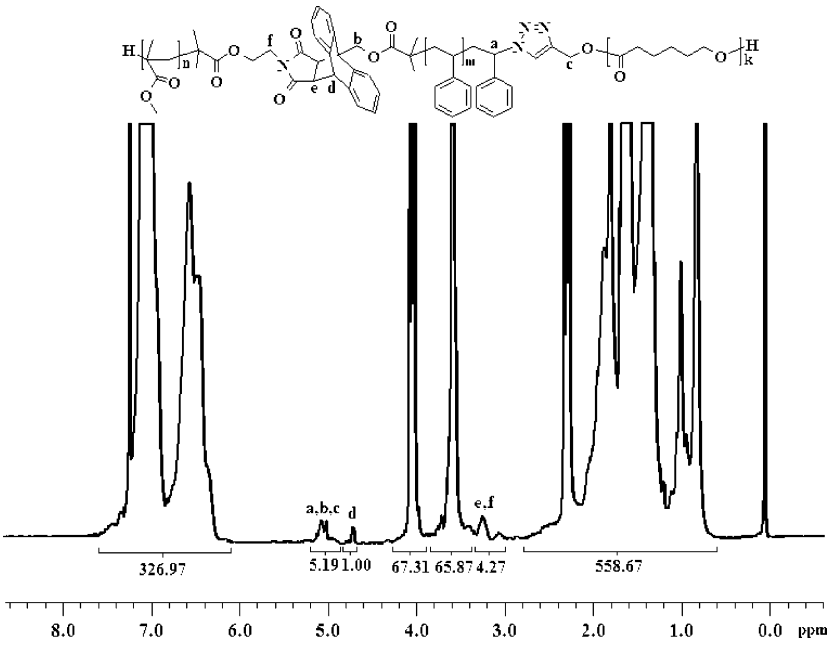


Figure 4. ^{1}H NMR spectrum of poly(methyl methacrylate)−polystyrene−poly(ϵ-caprolactone) (PMMA−PS−PCL) triblock copolymer **13** in $CDCl_3$.

Results and Discussion

It is well-known that both the Diels−Alder [4 + 2] and the click [3 + 2] reactions share a number of important features including high yield and excellent functional group tolerance. One more advantage is that polymer backbone with appropriate end-functional groups for both reactions can be easily prepared via a wide range of living polymerization techniques, such as ATRP and ROP. Therefore, we envisaged the possibility of combining [4 + 2] and [3 + 2] cycloaddition reactions and applying it for the preparation of ABC triblock copolymers. Our synthetic strategy here involved the one-pot reaction of maleimide and alkyne end-functionalized polymers with PS containing both anthracene and azide terminally.

First, it was investigated that whether alkyne would be intact during Diels−Alder reaction between anthracene and maleimide. The compound **2** containing both anthracene and alkyne was allowed to react with PEG-MI, **4** (Scheme 1).

The Diels−Alder cycloaddition reaction occurred in quantitative yield (90%). The reaction was monitored by ^{1}H NMR. From the ^{1}H NMR spectrum of the reaction mixture, three new signals at 5.48 ($CH_2OC{=}O$), 4.76 (one bridge-head proton), and 3.34 ppm (two bridge protons) were detected, confirming the structure of the Diels−Alder adduct, **5**. Moreover, two signals at 4.59 ($CH{\equiv}CC\mathit{H}_2O$) and 2.47 ppm ($C\mathit{H}{\equiv}CCH_2O$) confirmed the presence of an alkyne group.

Preparation of Well-Defined Polymers with Proper Functional Groups. A number of well-defined polymers are prepared using living polymerization techniques, except PEG, which is commercially available. Maleimide end-functionalized PMMA, PMMA−MI (**7**) was prepared via ATRP of MMA in the presence of **6** as an initiator, CuCl/PMDETA as a catalyst system at 40 °C. The maleimide functional group of the initiator **6** was protected with furan due to the copolymerization of maleimide with MMA. The presence of the protected maleimide end-functionality was supported by the observation of a signal at 6.5 ppm (CH=CH) in the ^{1}H NMR spectrum of PMMA−MI (**7**). The theoretical molecular weight of polymers were calculated by using following equation: $M_{n,theo} = ([M]_0/[I]_0) \times$ conversion % × molecular weight (MW) of monomer + MW of initiator. The NMR number-average molecular weight

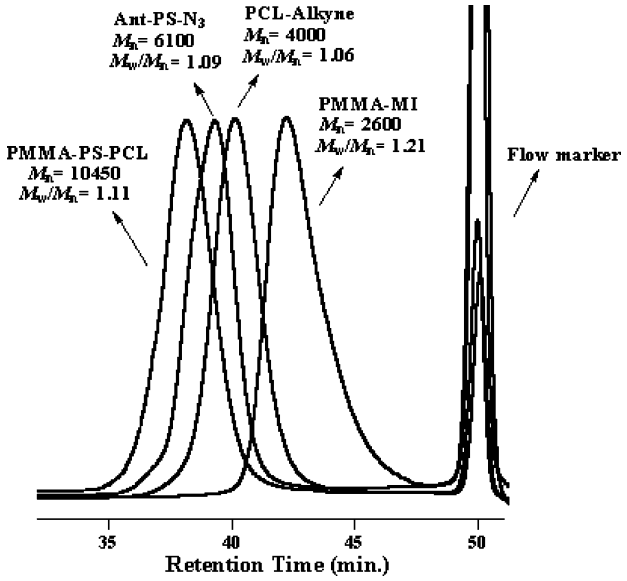


Figure 5. Evolution of the GPC curves: maleimide end-functionalized PMMA (PMMA−MI (**7**)), PS with α-anthracene and ω-azide end-functionality (PS−α-anthracene-ω-azide (**9**)), alkyne end-functionalized PCL (PCL−alkyne (**11**)) precursors, and poly(methyl methacrylate)−polystyrene−poly(ϵ-caprolactone) (PMMA−PS−PCL) triblock copolymer **13**.

($M_{n,NMR}$) of PMMA−MI (**7**) was determined from a ratio of integrated signals at 3.58 ppm (OCH_3 protons of MMA) to 6.5 ppm (oxatricyclo vinyl end protons). $M_{n,NMR} = 2700$ is consistent with that obtained from GPC ($M_{n,GPC} = 2600$) and, however, higher than that from the theoretical molecular weight ($M_{n,theo} = 1100$). It is due to low initiation efficiency of **6** under this polymerization condition. At the end of the polymerization, chloride end-functionality of PMMA−MI was removed by reacting with tributyltinhydride, due to the probability of the radical formation caused by CuBr/PMDETA in the one-pot preparation of the triblock copolymer.

PS−α-anthracene-ω-bromide was prepared by ATRP of St using **8** as an initiator and CuBr/PMDETA as a catalyst at 110 °C. $M_{n,NMR}$ value of PS−α-anthracene was calculated by comparing of the integrals of the aromatic protons of PS at 6.5−

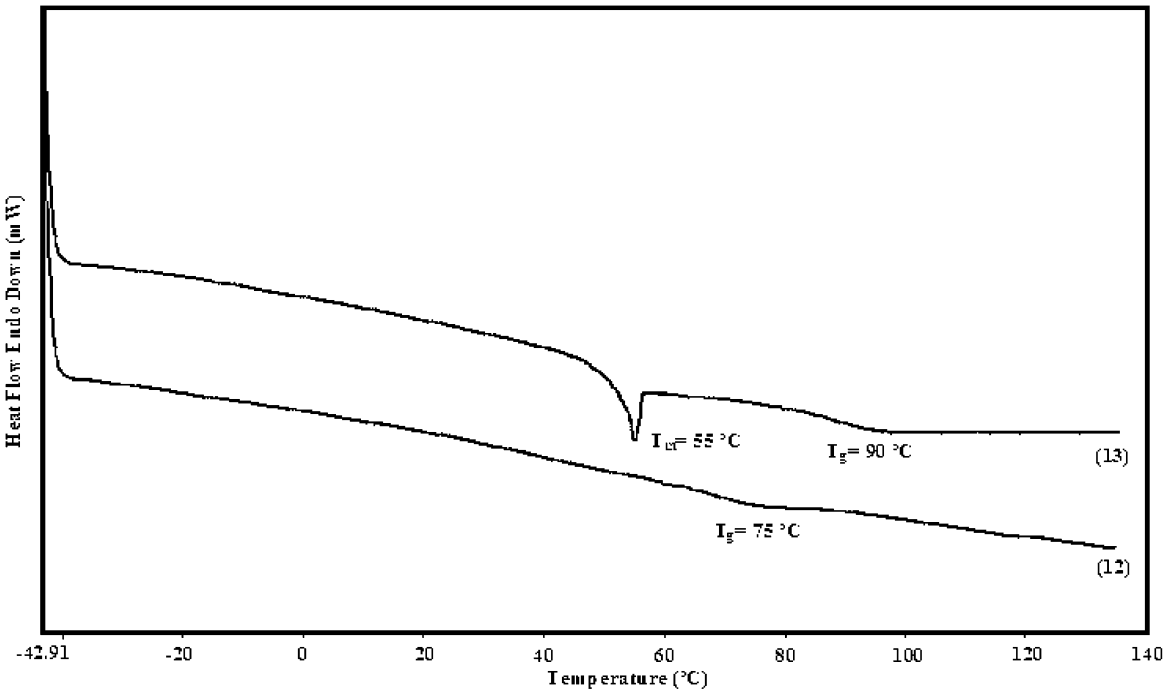


Figure 6. DSC thermograms of poly(methyl methacrylate)−polystyrene−poly(ethylene glycol) (PMMA−PS−PEG **12)**, and poly(methyl methacrylate)−polystyrene−poly(ϵ-caprolactone) (PMMA−PS−PCL **13)** triblock copolymers at a heating rate of 10 °C/ min under nitrogen. The glass transition (T_g) and the melting temperatures (T_m) were calculated as a midpoint and a peak apex of thermograms, respectively.

7.5 ppm and that of two protons of anthracene end group at 7.9 ppm. It was observed that $M_{n,theo}$, $M_{n,NMR}$, and $M_{n,GPC}$ were in good agreement. PS−α-anthracene-ω-bromide was quantitatively converted into PS−α-anthracene-ω-azide (**9**) in the presence of NaN_3/DMF at room temperature. From ^{1}H NMR spectrum of **9,** it was observed that a signal at 4.4 corresponding to C*H*(Ph)−Br disappeared and a new signal (C*H*−Ph linked to an azide end-group) was detected at 3.9 ppm. The structure of **9** was further supported by the observation of the azide stretching band at 2094 cm^{-1} from IR spectrum.

PEG−alkyne (**10**) was obtained from a reaction of Me-PEG with 4-pentynoic acid at room temperature. ^{1}H NMR revealed the structure of PEG−alkyne (**10**), displaying characteristic peaks such as a triplet (C*H*≡C−) at 1.9 ppm and a multiplet (CH≡CCH_2CH_2C═O) at 2.5 ppm. The NMR number-average molecular weight ($M_{n,NMR}$) of **10** was calculated from a ratio of peak areas of PEG repeating unit at 3.60 ppm and CH≡CCH_2CH_2C═O end group at 2.5 ppm. $M_{n,NMR}$ of **10** was consistent with those of $M_{n,theo}$ and $M_{n,GPC}$.

PCL−alkyne (**11**) was prepared by ROP of ϵ-CL in bulk using Sn(Oct)$_2$ as a catalyst and propargyl alcohol as an initiator at 110 °C. Alkyne end-functionality was confirmed by the observation of a signal at 4.65 (CH≡CCH_2OC═O) in the ^{1}H NMR spectrum of **11**. $M_{n,NMR}$ of **11** was determined accordingly from the integration of the signals at 4.03 and 4.65 ppm related to PCL repeating unit and CH≡CCH_2OC═O end group protons, respectively. $M_{n,GPC}$ of **11** was calculated to be 8000, based on linear PS standards (RI detector), however, determining more precise the molecular weight for PCL, a correction formula is used: $M_{n,PCL} = 0.259 \times M_{n,GPC}^{1.073}$ ($M_{n,PCL} = 4000$), where $M_{n,GPC}$ is the molecular weight determined from GPC using PS standards.[47] $M_{n,NMR}$, $M_{n,theo}$, and $M_{n,PCL}$ values are in good agreement.

Preparation of PEG—PS—PMMA Triblock Copolymer (12) via a Combination of Diels−Alder [4 + 2] and Click [3 + 2] Reactions. PMMA−MI (**7**), PS−α-anthracene-ω-azide (**9**), and PEG−alkyne (**10**) were reacted in one-pot in order to give the corresponding triblock copolymer **12** using a combination of Diels−Alder and click reaction strategy (Scheme 2).

A click [3 + 2] reaction was accomplished between the ω-azide of **9** and the alkyne end-functional group of **10** catalyzed by CuBr/PMDETA in DMF at 120 °C. Simultaneously, a retro-Diels−Alder reaction of **7** occurred to give PMMA with a deprotected maleimide end group evolving furan, followed by a Diels−Alder [4 + 2] reaction to α-anthracene of **9**. In the preparation of PEG−PS−PMMA triblock copolymer **12**, slightly excess amounts of PMMA−MI (**7**) (0.025 mol) and PEG−alkyne (**10**) (0.025 mol) are used compared to PS−α-anthracene-ω-azide (0.022 mol). PEG and PMMA blocks are completely soluble in MeOH in the range of the molecular weights studied in this work and, therefore, are easily removed from the reaction mixture using only precipitation.

An evidence for the formation of Diels−Alder cycloadduct and triazole ring (click) of the resulting triblock copolymer **12** was obtained from ^{1}H NMR spectroscopy. The, characteristic peaks for aromatic protons of anthracene (7.4−8.5 ppm) completely disappeared as a result of Diels−Alder cycloaddition, and a new signal corresponding to a bridgehead proton (C*H*) of the cycloadduct appeared at 4.7 ppm. The broad signals in the range of 5.2−4.9 ppm were assigned as methylene protons linked to the cycloadduct and C*H* proton of styrene end group linked to triazole ring. Moreover, a new signal corresponding to CH_2 protons linked to the triazole ring was also observed at 2.7 ppm, confirming the structure of triblock copolymer, **12**. Diels−Alder cycloadduct formation is also monitored by UV spectrophotometer (Figure 1).

Although PS−α-anthracene-ω-azide (**9**) displayed characteristic five-finger absorbance in the range of 300−400 nm, PEG−PS−PMMA triblock copolymer **12** showed no absorbance in this region indicating that Diels−Alder reaction occurred quantitatively.

$M_{n,theo}$ of PEG−PS−PMMA triblock copolymer (11600) is calculated by an equation: $M_{n,theo} = M_{n,NMR}$ of PEG + $M_{n,NMR}$ of PS + $M_{n,NMR}$ of PMMA. $M_{n,NMR}$ of the triblock copolymer

(10300) is calculated from the ^{1}H NMR spectrum, taking into account a ratio of the integrated values of the PS ($DP_n = 60$) to the PEG and the PMMA segments. The triblock formation efficiency is found to be 89% from a ratio of $M_{n,NMR}$ to $M_{n,theo}$ of the triblock copolymer. GPC curves of the PEG−PS−PMMA triblock copolymer and the corresponding precursors displayed unimodal and narrow molecular weight distribution, and a tail was not observed in the molecular weight region of the precursors (Figure 2).

Preparation of PCL—PS—PMMA Triblock Copolymer (13) via a Combination of Diels−Alder [4 + 2] and Click [3 + 2] Reactions. PMMA−MI (**7**), PS−α-anthracene-ω-azide (**9**), and PCL−alkyne (**11**) were reacted in one-pot in order to obtain the corresponding triblock copolymer **13** using a combination of Diels−Alder and click reaction strategy. The details were given in the Experimental Section. For the preparation of PCL−PS−PMMA triblock copolymer **13**, only PMMA−MI (**7**) block is used as a slight excess relative to the PS−α-anthracene-ω-azide (**9**) and PCL−alkyne (**11**). The solubility of PMMA can be stressed for this case. The structure of PCL−PS−PMMA **13** triblock copolymer was confirmed by ^{1}H NMR spectroscopy (Figure 3).

Disappearance of the peaks for the characteristic aromatic protons of anthracene at 7.4−8.5 ppm was clearly observed, indicating successful Diels−Alder cycloaddition. The broad signals in the range of 5.2−4.9 ppm were assigned as C*H*$_2$O− linked to the triazole ring, CH$_2$− linked to the Diels−Alder cycloadduct, and the C*H* proton of the styrene end group linked to a triazole ring. Moreover, new signals corresponding to the bridgehead proton (C*H*) of the cycloadduct, C*H* of the fused maleimide ring, and C*H*$_2$ protons adjacent to the fused maleimide ring appeared at 4.7, and 3.3−3.0 ppm, respectively. An efficiency of Diels−Alder and click reaction for the formation of the PCL−PS−PMMA triblock copolymer was calculated as 91% from a ratio of $M_{n,NMR}$ (12300) to $M_{n,theo}$ (13500). $M_{n,NMR}$ calculation is based on a ratio of the PS ($DP_n = 60$) to the PCL and the PMMA segments. GPC trace of the triblock copolymer clearly shifted to the higher molecular weight region compared to the corresponding polymeric precursors (Figure 4). Notably, a unimodal shape for the GPC curve without a tail was obtained, confirming an efficient triblock formation.

The glass transition temperatures (T_g) of triblock copolymers were determined by DSC at a heating rate of 10 °C/min under a nitrogen atmosphere. As demonstrated in Figure 5, any T_g for PEG segment of triblock copolymer **12** was not observed because of relatively shorter PEG segment compared to those of PS and PMMA. Only one T_g is evident at 75 °C, corresponding to the PS/PMMA segments. This value is lower than the expected T_g for the PS/PMMA precursor (95−105 °C) and might cause us to consider that PEG segment is miscible with PS/PMMA segment.

In the case of PCL−PS−PMMA triblock copolymer **13**, two transitions such as a melting temperature (T_m) for PCL and a T_g for PS/PMMA precursor are observed at 55 and 90 °C, respectively. Moreover, a T_g of PCL segment is not determined.

Conclusions

We combined efficiently Diels−Alder [4 + 2] and click [3 + 2] reaction strategy (modular approach) for the synthesis of ABC type block copolymers in one-pot technique, e.g., PEG−PS−PMMA (M_n = 8200, M_w/M_n = 1.10) and PCL−PS−PMMA (M_n = 10 450, M_w/M_n = 1.11). Well-defined polymeric precursors, except PEG are obtained using living polymerization techniques, ATRP and ROP. This modular approach can furthermore afford production of the polymers with different compositions and topologies

References and Notes

(1) Chiefari, J.; Chong, Y. K.; Ercole, F.; Krstina, J.; Jeffery, J.; Le, T. P. T.; Mayadunne, R. T. A.; Meijs, G. F.; Moad, C. L.; Moad, G.; Rizzardo, E.; Thang, S. H. *Macromolecules* **1998**, *31*, 5559−5562.
(2) Georges, M. K.; Veregin, R. P. N.; Kazmaier, P. M.; Hamer, G. K. *Macromolecules* **1993**, *26*, 2987−2988.
(3) Kato, M.; Kamigaito, M.; Sawamoto, M.; Higashimura, T. *Macromolecules* **1995**, *28*, 1721−1723.
(4) Wang, J. S.; Matyjaszewski, K. *Macromolecules* **1995**, *28*, 7901−7910.
(5) Percec, V.; Barboiu, B. *Macromolecules* **1995**, *28*, 7970−7972.
(6) Tunca, U.; Karliga, D.; Ertekin, S.; Ugur, A. L.; Sirkecioglu, O.; Hizal, G. *Polymer* **2001**, *42*, 8489−8493.
(7) Tunca, U.; Erdogan, T.; Hizal, G. *J. Polym. Sci., Part A: Polym. Chem.* **2002**, *40*, 2025−2032.
(8) Hawker, C. J.; Hedrick, J. L.; Malmstrom, E. E.; Trollsas, M.; Mecerreyes, D.; Moineau, G.; Dubois, Ph.; Jerome, R. *Macromolecules* **1998**, *13*, 213−219.
(9) Mecerreyes, D.; Moineau, G.; Dubois, Ph.; Jerome, R.; Hedrick, J. L.; Hawker, C.J.; Malmstrom, E. E.; Trollsas, M. *Angew. Chem., Int. Ed. Engl.* **1998**, 37, 1274−1278.
(10) Xu, Y.; Pan, C.; Tao, L. *J. Polym. Sci., Part A: Polym. Chem.* **2000**, *38*, 436−443.
(11) Bernaerts, K. V.; Schacht, E. H.; Goethals, E. J.; Du Prez, F. E. *J. Polym. Sci., Part A: Polym. Chem.* **2003**, *41*, 3206−3217.
(12) Puts, R. D.; Sogah, D. Y. *Macromolecules* **1997**, *30*, 7050−7055.
(13) Weimer, M. W.; Scherman, O. A.; Sogah, D. Y. *Macromolecules* **1998**, *31*, 8425−8428.
(14) Bernaerts, K. V.; Du Prez, F. E. *Polymer* **2005**, *46*, 8469−8482.
(15) Huisgen, R. In *1,3-Dipolar Cycloaddition Chemistry*; Padwa, A., Ed.; Wiley: New York, 1984; pp 1−176.
(16) Kolb, H. C.; Finn, M. G.; Sharpless, K. B. *Angew. Chem., Int. Ed.* **2001**, *40*, 2004−2021.
(17) Rostovtsev, V. V.; Green, G.; Fokin, V. V.; Sharpless, K. B. *Angew. Chem., Int. Ed.* **2002**, *41*, 2596−2599.
(18) Opsteen, J. A.; Van Hest, J. C. M. *Chem. Commun.* **2005**, 57−59.
(19) Diaz, D. D.; Punna, S.; Holzer, P.; Mcpherson, A. K.; Sharpless, K. B.; Fokin, V. V.; Finn, M. G. *J. Polym. Sci., Part A: Polym. Chem.* **2004**, *42*, 4392−4403.
(20) Wu, P.; Feldman, A. K.; Nugent, A. K.; Hawker, C. J.; Scheel, A.; Voit, B.; Pyun, J.; Frechet, J. M. J.; Sharpless, K. B.; Fokin, V. V. *Angew. Chem., Int. Ed.* **2004**, *43*, 3928−3932.
(21) Helms, B.; Mynar, J. L.; Hawker, C. J.; Frechet, J. M. J. *J. Am. Chem. Soc.* **2004**, *126*, 15020−15021.
(22) Binder, W. H.; Kluger, C. *Macromolecules* **2004**, *37*, 9321−9330.
(23) Sumerlin, B. S.; Tsarevsky, N. V.; Louche, G.; Lee, R. Y.; Matyjaszewski, K. *Macromolecules* **2005**, *38*, 7540−7545.
(24) Li, H.; Cheng, F.; Duft, A. M.; Adronov, A. *J. Am. Chem. Soc.* **2005**, *127*, 14518−14524.
(25) Joralemon, M. J.; O'Reilly, R. K.; Matson, J. B.; Nugent, A. K.; Hawker, C. J.; Wooley, K. L. *Macromolecules* **2005**, *38*, 5436−5443.
(26) Parrish, B.; Breitenkamp, R. B.; Emrick, T. *J. Am. Chem. Soc.* **2005**, *127*, 7404−7410.
(27) Riva, R.; Schmeits, S.; Stoffelbach, F.; Jerome, R.; Lecomte, P. *Chem. Commun.* **2005**, 5334−5336.
(28) Luxenhofer, R.; Jordan, R. *Macromolecules* **2006**, *39*, 3509−3516.
(29) Ladmiral, V.; Mantovani, G.; Clarkson, G. J.; Cauet, S.; Irwin, J. L.; Haddleton, D. M. *J. Am. Chem. Soc.* **2006**, *128*, 4823−4830.
(30) Laurent, B. A.; Grayson, S. M. *J. Am. Chem. Soc.* **2006**, *128*, 4238−4239.
(31) Sun, X.-L.; Stabler, C. L.; Cazalis, C. S.; Chaikof, E. L. *Bioconjugate Chem.* **2006**, *17*, 52−57.
(32) Altintas, O.; Hizal, G.; Tunca, U. *J. Polym. Sci., Part A: Polym. Chem.* **2006**, *44*, 5689−5707.
(33) Kwart, H.; King, K. *Chem. Rev.* **1968**, *68*, 415−447.
(34) Jones, J. R.; Liotta, C. L.; Collard, D. M.; Schiraldi, D. A. *Macromolecules* **1999**, *32*, 5786−5792.
(35) Imai, Y.; Itoh, H.; Naka, K.; Chujo, Y. *Macromolecules* **2000**, *33*, 4343−4346.
(36) McElhanon, J. R.; Wheeler, D. R. *Org. Lett.* **2001**, *3*, 2681−2683.
(37) Gheneim, R.; Berumen, C. P-.; Gandini, A. *Macromolecules* **2002**, *35*, 7246−7253.
(38) Vargas, M.; Kriegel, R. M.; Collard, D. M.; Schiraldi, D. A. *J. Polym. Sci., Part A: Polym. Chem.* **2002**, *40*, 3256−3263.
(39) Kim, C.; Kim, H.; Park, K. *J. Organomet. Chem.* **2003**, *667*, 96−102.

(40) Kriegel, R. M.; Saliba, K. L.; Jones, G.; Schiraldi, D. A.; Collard, D. M. *Macromol. Chem. Phys.* **2005**, *206*, 1479−1489.
(41) Durmaz, H.; Colakoglu, B.; Tunca, U.; Hizal, G. *J. Polym. Sci., Part A: Polym. Chem.* **2006**, *44*, 1667−1675.
(42) Gacal, B.; Durmaz, H.; Tasdelen, M. A.; Hizal, G.; Tunca, U.; Yagci, Y.; Demirel, A. L. *Macromolecules* **2006**, *39*, 5330−5336.
(43) Lei, X.; Porco, J. A. *Org. Lett.* **2004**, 6, 795−798.
(44) Durmaz, H.; Karatas, F.; Tunca, U.; Hizal, G. *J. Polym. Sci., Part A: Polym. Chem.* **2006**, *44*, 3947−3957.
(45) Mantovani, G.; Lecolley, F.; Tao, L.; Haddleton, D. M.; Clerx, J.; Cornellisen, J. J. L. M.; Velonia, K. *J. Am. Chem. Soc.* **2005**, *127*, 2966−2973.
(46) Erdogan, M.; Hizal, G.; Tunca, U.; Hayrabetyan, D.; Pekcan, O. *Polymer* **2002**, *43*,1925−1931.
(47) Dubois, Ph.; Barakat, I.; Jerome, R.; Teyssie, Ph. *Macromolecules* **1993**, 26, 4407−4412.

MA061819L