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Reversible Light-Triggered Transition of Amphiphilic Random Copolymers

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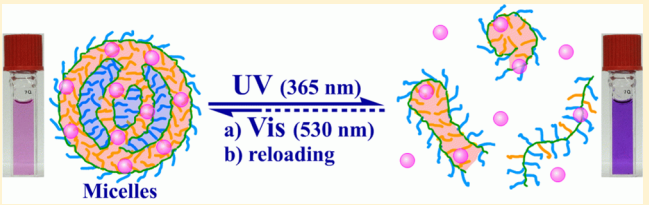
Supporting Information

ABSTRACT: A new set of amphiphilic random copolymers has been constructed directly by hydrophilic, hydrophobic, and functional spiropyran monomers in one-pot ROMP. The resulting copolymers are able to self-assemble in water to polymeric micelles, which exhibit reversible disruption and regeneration characteristics upon ultraviolet (UV) and visible-light irradiation. When hydrophobic dyes Nile red, which served as a model for drug delivery, are encapsulated within the core of polymeric micelle, their releasing and reloading have been realized by exposure to UV and visible light, respectively, in the aqueous solution.



INTRODUCTION

Amphiphilic polymers, namely those that carry both hydrophilic and hydrophobic segments in a determined proportion, can self-assemble in solutions or at interfaces to generate a variety of well-defined nano- or microscopic architectures.[1] Of particular significance is the formation of polymeric micelles or vesicles in aqueous media for use in drug delivery systems, where guest molecules can be encapsulated into their either hydrophobic or hydrophilic domains. Up to date, such kinds of polymers are generally from amphiphilic block copolymers,[2] apart from few exceptions.[3] When stimuli-responsive functional groups are incorporated into these building blocks to engineer "smart" systems, however, the synthetic processes are always tedious and time-consuming, involving multistep copolymerization, different polymerization methods, and postpolymerization treatment (grafting, substitution, hydrolysis, etc.). Unlike amphiphilic block copolymers, random copolymers, on the other hand, can be achieved from diverse components in a single polymerization step, but the fact of modification of functional monomers, tolerance of initiators, control of polymeric molecular weights, and polydispersity indices (PDIs) makes the preparation of amphiphilic random copolymers rather challenging.

Ring-opening metathesis polymerization (ROMP) is a powerful method for the preparation of random, block, and alternating functionalized copolymers.[4−11] Using ruthenium *N*-heterocyclic carbene complexes as initiators, controlled polymer backbones such as polynorbornenes have been obtained from varied monomers containing hydrogen-bond interfaces, oligopeptides, ionic and/or metallic compounds.[6−11] In the present work, we wish to report a water-soluble amphiphile random polynorbornene, PNB-SP$_x$-*co*-P3$_y$-*co*-A1$_z$, bearing a hydrophobic moiety NB-A1, a hydrophilic tail NB-P3, and functional group NB-SP. As shown in Scheme 1, the amphiphilic random copolymer PNB-SP$_x$-*co*-P3$_y$-*co*-A1$_z$ can be easily made in one-pot ROMP using a Grubbs' third-generation initiator. Spiropyran (SP) is here selected as a functional group because it undergoes reversible photochromic behaviors between colorless SP and colored merocyanine (MC) upon irradiation by UV and visible light.[12] More interestingly, SP isomer, a ring-closed structure, is hydrophobic, while MC isomer, a ring-opened zwitterionic structure, is hydrophilic.[12−23] It is anticipated that when SP is incorporated into its backbone, a light-triggered stimuli is able to tune the morphology of the amphiphilic random copolymer reversibly in aqueous solution, similar to those observed in block copolymers.[2f,g,15,22,23] This expectation was found to be the case. The amphiphilic random copolymer PNB-SP$_x$-*co*-P3$_y$-*co*-A1$_z$ can self-assemble to form polymeric micelles in water, which responds to the applied light stimuli reversibly. When hydrophobic dyes Nile red (NR), which served as a model for drug delivery, are encapsulated within the core of a polymeric micelle, the releasing and reloading have been realized by exposure to UV and visible light, respectively, in the aqueous solution.

EXPERIMENTAL SECTION

General. All experiments with air- and moisture-sensitive intermediates and compounds were carried out under an inert atmosphere using standard Schlenk techniques. NMR spectra were recorded on a Bruker Advance DPX 400 MHz spectrometer and referenced using the residual proton signal of the solvent. Mass spectra were obtained on either a Bruker APEX II or a Bruker BIFLEX III

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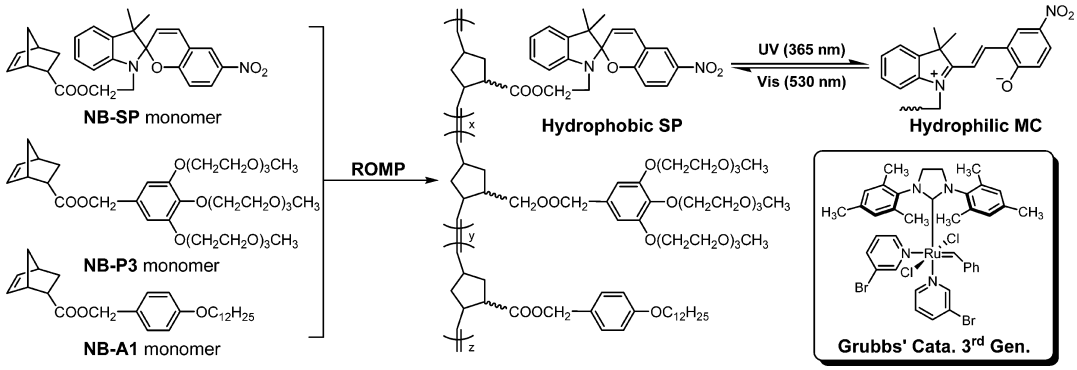
Scheme 1. Syntheses of PNB-SP$_x$-*co*-P3$_y$-*co*-A1$_z$ Amphiphilic Random Copolymers



spectrometer. Elemental analyses were performed on a Carlo Erba 1106 elemental analyzer. UV−vis spectra were obtained using a Shimadzu 1601PC spectrophotometer. Fluorescence spectra were recorded on a Hitachi 4500 fluorescence spectrophotometer. Dynamic light scattering (DLS) measurements were performed on a DynaPro NanoStar system (Wyatt) with Dynamics 7.0 software package. Gel-permeation chromatography (GPC) analyses were carried out on a multiangle, digital signal processing light scattering system (Wyatt) using a Shimadzu LC-10A pump coupled to a Dawn Heleos II light scattering detector (equipped with a 100 mW GaAs laser) and a Optilab rEX interferometeric refractometer with THF as an eluent on a 10 μm linear MZ-Gel SDplus column; the flow rate used for all measurements was 0.5 mL/min. No calibration standards were used, and dn/dc values were obtained for each injection by assuming 100% mass elution from the columns. M_w, M_n, and PDIs were treated using an Astra 5 software package. Scanning electron microscopy (SEM) images were obtained on a Hitachi S-4300 system. Transmission electron microscopy (TEM) and cryo-TEM measurements were carried out on a JEOL JEM-2100 or JEM-2200FS instrument. The commercially available LEDs were employed as UV (365 nm, input 350 mA, 3.7 V, output ~125 mW/cm^2) and visible (530 nm, input 350 mA, 3.4 V, output ~120 mW/cm^2) light sources, and the intensities were determined by a Newport (Irvine, CA) Optical Power/Energy Meter (Model 842-PE).

Materials. 2-(3′,3′-Dimethyl-6-nitro-3′*H*-spiro[chromene-2,2′-indo]-1′-yl)ethanol,[24] 3,4,5-tris(1,4,7,10-tetraoxaundecyl)benzyl alcohol,[25] 4-dodecyloxybenzyl alcohol,[26] and *exo*-bicyclo[2.2.1]hept-5-ene-2-carboxylic acid[27] were synthesized according to published procedures. Other reagents and solvents were used as received without further purification.

2-(3′,3′-Dimethyl-6-nitro-3′H-spiro[chromene-2,2′-indo]-1′-yl)-ethanol. Purple solids. ^{1}H NMR (400 MHz, CDCl$_3$, ppm) δ: 8.00 (m, 2H), 7.19 (dt, 1H, J = 7.6 and 1.2 Hz), 7.09 (d, 1H, J = 6.8 Hz), 6.90 (m, 2H), 6.75 (d, 1H, J = 8.8 Hz), 6.66 (d, 1H, J = 7.6 Hz), 5.88 (d, 1H, J = 6.4 Hz), 3.75 (m, 2H), 3.46 (m, 1H), 3.33 (m, 1H), 1.78 (br, 1H), 1.30 (s, 3H), 1.20 (s, 3H).

2-(3′,3′-Dimethyl-6-nitro-3′H-spiro[chromene-2,2′-indo]-1′-yl)-ethyl-exo-bicyclo[2.2.1]hept-5-ene-2-carboxylate (NB-SP Monomer). A mixture of 2-(3′,3′-dimethyl-6-nitro-3′*H*-spiro[chromene-2,2′-indo]-1′-yl)ethanol (1.60 g, 4.54 mmol), *exo*-bicyclo[2.2.1]hept-5-ene-2-carboxylic acid (0.70 g, 5.07 mmol), DCC (*N*,*N*-dicyclohexylcarbodiimide, 1.60 g, 7.75 mmol), and DMAP (4-(dimethylamino)pyridine, 80 mg, 0.65 mmol) was stirred in dry methylene chloride (30 mL) under inert atmosphere for 24 h. After removal of the solvent, the crude product was purified by silica gel column chromatography to give NB-SP monomer as yellow powders (1.80 g, 3.81 mmol, yield 84%). TLC, R_f = 0.30 (petroleum ether:ethyl acetate = 10:1). EI-MS: m/z = 472 (M$^+$). ^{1}H NMR (400 MHz, CDCl$_3$, ppm) δ: 8.01 (m, 2H), 7.21 (t, 1H, J = 10.6 Hz), 7.09 (d, 1H, J = 7.2 Hz), 6.91 (m, 2H), 6.72 (m, 2H), 6.13 (m, 1H), 6.07 (m, 1H), 5.89 (d, 1H, J = 10.4 Hz), 4.29 (m, 1H), 4.21 (m, 1H), 3.53 (m, 1H), 3.43 (m, 1H), 2.92 (m, 1H), 2.90 (s, 1H), 2.14 (m, 1H), 1.86 (m, 1H), 1.46 (m, 1H), 1.34 (m, 2H), 1.29 (m, 3H), 1.18 (m, 3H). ^{13}C {^{1}H} NMR (100 MHz, CDCl$_3$, ppm) δ: 176.06, 159.36, 146.64, 141.01, 138.06, 138.01, 135.59, 135.54, 128.24, 127.77, 125.89, 122.70, 121.75, 119.84, 118.39, 115.49, 106.74, 106.45, 62.36, 52.79, 46.49 and 46.41 (*isomers*), 46.28, 42.99 and 42.96 (*isomers*), 42.40, 41.53, 30.38 and 30.34 (*isomers*), 25.80, 19.80. Anal. Calcd for $C_{28}H_{28}N_2O_5$: C, 71.17; H, 5.97; N, 5.93. Found: C, 70.82; H, 5.95; N, 5.87.

3,4,5-Tris(1,4,7,10-tetraoxaundecyl)benzyl Alcohol. Transparent oil. TLC, R_f = 0.15 (ethyl acetate:methylene chloride = 1:1). ^{1}H NMR (400 MHz, CDCl$_3$, ppm) δ: 6.53 (s, 2H), 4.48 (s, 2H), 4.07 (m, 6H), 3.77 (m, 4H), 3.72 (m, 2H), 3.65 (m, 6H), 3.59 (m, 12H), 3.48 (m, 6H), 3.29 (s, 9H), 2.84 (br, 1H).

3,4,5-Tris(1,4,7,10-tetraoxaundecyl)benzyl-exo-bicyclo[2.2.1]-hept-5-ene-2-carboxylate (NB-P3 Monomer). Prepared as NB-SP monomer, transparent oil (yield 87%). TLC, R_f = 0.15 (ethyl acetate:methanol = 50:1). EI-MS: m/z = 714 (M$^+$). ^{1}H NMR (400 MHz, CDCl$_3$, ppm) δ: 6.57 (s, 2H), 6.10 (m, 2H), 4.99 (s, 2H), 4.14 (t, 6H, J = 4.6 Hz), 3.83 (m, 4H), 3.77 (m, 2H), 3.70 (m, 6H), 3.63 (m, 12H), 3.52 (m, 6H), 3.35 (s, 9H), 3.04 (m, 1H), 2.91 (m, 1H), 2.25 (m, 1H), 1.91 (m, 1H), 1.50 (m, 1H), 1.36 (m, 2H). ^{13}C {^{1}H} NMR (100 MHz, CDCl$_3$, ppm) δ: 175.49, 152.30, 137.99, 137.69, 135.31, 131.24, 107.49, 71.91, 71.55, 70.43, 70.30, 70.14, 69.33, 68.53, 65.83, 58.58, 46.24, 45.95, 42.74, 41.25, 30.02. Anal. Calcd for $C_{36}H_{58}O_{14}$: C, 60.49; H, 8.18. Found: C, 60.65; H, 8.13.

4-Dodecyloxybenzyl Alcohol. White solids. TLC, R_f = 0.30 (petroleum ether:ethyl acetate = 5:1). ^{1}H NMR (400 MHz, CDCl$_3$, ppm) δ: 7.25 (d, 2H, J = 8.8 Hz), 6.87 (d, 2H, J = 8.8 Hz), 4.59 (s, 2H), 3.95 (t, 2H, J = 6.6 Hz), 1.84 (s, 1H), 1.78 (m, 2H), 1.46 (m, 2H), 1.28 (s, 16H), 0.90 (t, 3H, J = 6.8 Hz).

4-Dodecyloxybenzyl-exo-bicyclo[2.2.1]hept-5-ene-2-carboxylate (NB-A1 Monomer). Prepared as NB-SP monomer, transparent oil (yield 87%). TLC, R_f = 0.50 (petroleum ether:ethyl acetate = 25:1). EI-MS: m/z = 412 (M$^+$). ^{1}H NMR (400 MHz, CDCl$_3$, ppm) δ: 7.28 (d, 2H, J = 8.4 Hz), 6.87 (d, 2H, J = 8.8 Hz), 6.10 (m, 2H), 5.07 (s, 2H), 3.96 (t, 2H, J = 6.4 Hz), 3.05 (m, 1H), 2.92 (m, 1H), 2.25 (m, 1H), 1.94 (m, 1H), 1.78 (m, 2H), 1.53 (m, 1H), 1.46 (m, 2H), 1.28 (s, 18H), 0.90 (t, 3H, J = 6.8 Hz). ^{13}C {^{1}H} NMR (100 MHz, CDCl$_3$, ppm) δ: 176.04, 159.11, 138.00, 135.70, 129.85, 128.11, 114.45, 67.98, 66.07, 46.59, 46.31, 43.16, 41.62 31.89, 30.32, 29.60 (2C), 29.56 (2C), 29.36, 29.32, 29.22, 26.01, 22.66, 14.09. Anal. Calcd for $C_{27}H_{40}O_3$: C, 78.60; H, 9.77. Found: C, 78.61; H, 9.72.

General Polymerization Procedure. A solution of Grubbs' third-generation initiator[4e] (~0.01 M) was added to a methylene chloride solution (~0.05 M) containing spiropyran monomer NB-SP, hydrophilic monomer NB-P3, and hydrophobic monomer NB-A1 in varied ratios. The reaction mixture was stirred for 15 min at ambient temperature. After complete monomer conversion (>99%, monitored by ^{1}H NMR), the polymerization was quenched by the addition of ethyl vinyl ether and stirred for an additional 15 min. The polymer was isolated and purified by precipitation from ice-cold petroleum ether or methanol and followed by prolonged drying at room temperature under high vacuum.

Polymer PNB-SP. ^{1}H NMR (400 MHz, CDCl$_3$, ppm) δ: 7.96 (br, 2H), 7.14 (br, 1H), 7.05 (br, 1H), 6.86 (br, 2H), 6.66 (br, 2H), 5.83

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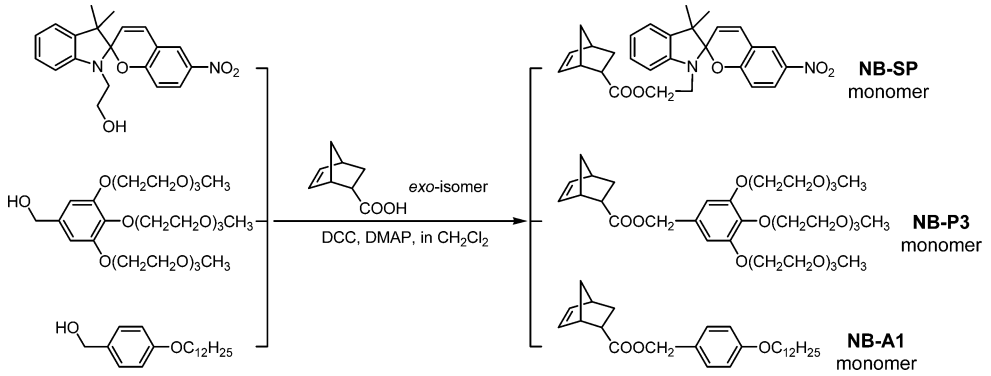
Scheme 2. Syntheses of NB-SP, NB-P3, and NB-A1 Monomers



(br, 1H), 5.27 (br, 2H), 4.16 (br, 2H), 3.37 (br, 2H), 2.92 (br, 1H), 2.57 (br, 1H), 1.92 (br, 2H), 1.60 (br, 1H), 1.26 (br, 5H), 1.12 (br, 3H).

Polymer PNB-P3. ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ: 6.53 (br, 2H), 5.35 (m, 2H), 4.88 (br, 2H), 4.10 (br, 6H), 3.81 (m, 4H), 3.76 (m, 2H), 3.69 (m, 6H), 3.63 (m, 12H), 3.52 (m, 6H), 3.34 (br, 9H), 3.10 (m, 1H), 2.75 (m, 1H), 2.53 (br, 1H), 2.03 (br, 2H), 1.66 (br, 1H), 1.13 (br, 1H).

Polymer PNB-A1. ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ: 7.22 (br, 2H), 6.83 (br, 2H), 5.31 (m, 2H), 5.01 (br, 2H), 3.90 (br, 2H), 3.11 (m, 1H), 2.67 (m, 1H), 2.53 (br, 1H), 2.05 (br, 2H), 1.75 (br, 2H), 1.62 (br, 1H), 1.42 (br, 2H), 1.26 (br, 16H), 1.10 (br, 1H), 0.88 (t, 3H, J = 6.6 Hz).

Copolymer PNB-P3$_{50}$-co-A1$_{50}$. ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ: 7.20 (br, 1H), 6.80 (br, 1H), 6.52 (br, 1H), 5.33 (m, 2H), 4.98 (br, 2H), 4.09 (br, 3H), 3.88 (br, 1H), 3.80 (m, 2H), 3.75 (m, 1H), 3.68 (m, 3H), 3.61 (m, 6H), 3.51 (m, 3H), 3.33 (br, 4.5H), 3.09 (m, 1H), 2.71 (m, 1H), 2.51 (br, 1H), 2.03 (br, 2H), 1.72 (br, 1H), 1.62 (br, 1H), 1.40 (br, 1H), 1.23 (br, 8H), 1.10 (br, 1H), 0.85 (t, 1.5H, J = 6.6 Hz).

Copolymer PNB-SP$_{30}$-co-P3$_{40}$-co-A1$_{30}$. ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ: 7.97 (br, 0.6H), 7.21 (br, 0.9H), 7.04 (br, 0.3H), 6.82 (br, 1.2H), 6.67 (br, 0.6H), 6.54 (br, 0.8H), 5.83 (br, 0.3H), 5.29 (m, 2H), 5.00 (br, 1.4H), 4.11 (br, 2.4H), 3.90 (br, 0.6H), 3.82 (br, 1.6H), 3.77 (m, 0.8H), 3.70 (m, 2.4H), 3.63 (m, 4.8H), 3.53 (m, 2.4H), 3.35 (m, 4.2H), 3.09 (br, 0.7H), 2.96 (br, 0.3H), 2.54 (m, 1.7H), 2.03 (br, 2H), 1.74 (br, 0.6H), 1.62 (br, 1H), 1.41 (br, 0.6H), 1.25 (br, 6.3H), 1.12 (br, 1.3H), 0.87 (t, 0.9H, J = 6.6 Hz).

RESULTS AND DISCUSSION

The ROMP of norbornenyl monomers, readily synthesized via the condensation reactions between *exo*-norbornenyl carboxylic acid[27] and alcohols, such as 2-(3′,3′-dimethyl-6-nitro-3′*H*-spiro[chromene-2,2′-indo]-1′-yl)ethanol,[24] 3,4,5-tris(1,4,7,10-tetraoxaundecyl)benzyl alcohol,[25] and 4-dodecyloxybenzyl alcohol,[26] in the presence of DCC and DMAP in methylene chloride with reasonable yields of ~85% (Scheme 2). For the preparation of our designed copolymers, the living character of the polymerization for hydrophilic monomer NB-P3 and hydrophobic monomer NB-A1 was first investigated. Each monomer was subject to ROMP using Grubbs' third-generation initiator at room temperature in degassed methylene chloride. Figure 1 shows the molecular weights (M_n) of these homopolymers versus the monomer-to-initiator ratios (Table S1 and Figures S1 and S2, see Supporting Information). Four different polymerizations were carried out with monomer-to-initiator ratios of 25:1, 50:1, 75:1, and 100:1. A linear plot suggested a high degree of control over the polymerization. Moreover, ^{1}H NMR spectra (Figure 2) showed complete disappearance of the carbene signal of the initiator at 19.1 ppm

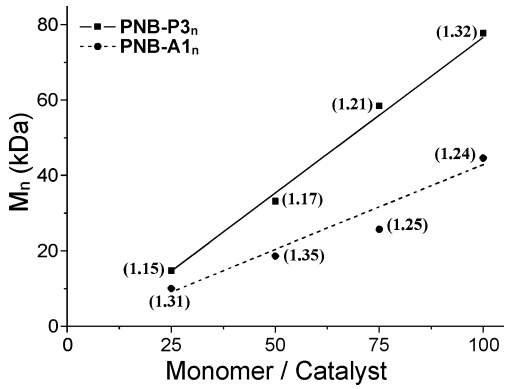


Figure 1. Plot of M_n vs the monomer to initiator ratios for the ROMP of hydrophilic NB-P3 and hydrophobic NB-A1 monomers. Numbers in parentheses are PDIs of the polymers.

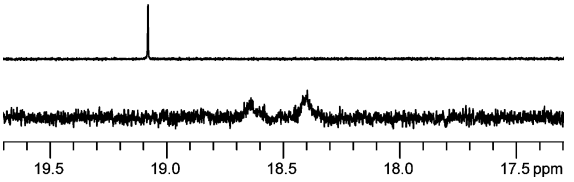


Figure 2. Carbene ^{1}H NMR signals for Grubbs' third-generation initiator (top) and during the polymerizations of NB-P3 monomer (bottom) in $CDCl_3$.

and at the same time the formation of two new broad carbene signals at 18.7 and 18.4 ppm. These observations clearly demonstrated a living fashion of ROMP for hydrophilic NB-P3 and hydrophobic NB-A1 monomers.[9]

To make amphiphilic random copolymers, two-component copolymers PNB-P3$_m$-*co*-A1$_n$ were prepared directly from NB-P3 and NB-A1 monomers with a degree of polymerization (DP) at 100; i.e., the molar ratio of total feeding amounts of monomers to Grubbs' third-generation initiator was 100:1. The PDIs of the resulting copolymers were relatively narrow ranging from 1.15 to 1.34 (Table 1), and the GPC measurement provided a relationship between M_n and total feeding amounts of the monomers. The critical proportion of hydrophilic to hydrophobic units was evaluated as 33:67, which means that a greater ratio of *m*:*n* would lead to water-soluble PNB-P3$_m$-*co*-A1$_n$ copolymers.

Furthermore, the self-assembling behavior of PNB-P3$_m$-*co*-A1$_n$ copolymers was noted to be dependent on the ratio of *m*:*n* very much. When the hydrophobic unit is small (n < 25), the

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Table 1. DLS and GPC Data for PNB-P3$_m$-*co*-A1$_n$ Copolymers

copolymer	diam[a] (nm)	M_n[c] (kDa)	M_w[c] (kDa)	PDI[c]
PNB-P3$_{100}$	8.5	77.8	103	1.32
PNB-P3$_{75}$-*co*-A1$_{25}$	8.6	60.4	72.1	1.19
PNB-P3$_{60}$-*co*-A1$_{40}$	11.0	55.9	73.2	1.31
PNB-P3$_{50}$-*co*-A1$_{50}$	16.7	53.2	62.5	1.17
PNB-P3$_{40}$-*co*-A1$_{60}$	42.7	54.1	72.4	1.34
PNB-P3$_{35}$-*co*-A1$_{65}$	178.6, 40.1	52.4	60.2	1.15
PNB-P3$_{33}$-*co*-A1$_{67}$	240.4, 38.8	54.7	65.5	1.20
PNB-P3$_{30}$-*co*-A1$_{70}$	–[b]	55.2	68.1	1.23

[a]Measured by DLS with the copolymer concentration at 0.125 mg/mL in aqueous solution at 298 K. [b]The copolymer is insoluble in water. [c]Determined by GPC using a LS detector in THF at 298 K.

size of PNB-P3$_{100}$ and PNB-P3$_{75}$-*co*-A1$_{25}$ determined by dynamic light scattering (DLS) technique is 8.5 and 8.6 nm, respectively. It seems likely that the polymers stay as single-chain coils in aqueous solution. With changing proportion of hydrophobic units (n > 25) in PNB-P3$_{40}$-*co*-A1$_{60}$, the particle size rapidly increases to 42.7 nm. When the proportion approaches to critical condition (33:67), the copolymers aggregate to form larger micelles in addition to the smaller ones. SEM images revealed corresponding spherical particles with diameters around 200 nm (Figure S3, see Supporting Information), which closely matched the values for PNB-P3$_{35}$-*co*-A1$_{65}$ (178.6 nm) and PNB-P3$_{33}$-*co*-A1$_{67}$ (240.4 nm) micelles measured by DLS (Table 1).

Considering slightly larger molecular weight of NB-SP monomer than that of hydrophobic NB-A1, we chose the proportion of hydrophilic NB-P3 monomer, y = 40, to synthesize a series of three-component PNB-SP$_x$-*co*-P3$_y$-*co*-A1$_z$ copolymers. After ROMP with Grubb's third-generation initiator, the M_n of copolymers was found in the range of 48–60 kDa with the PDI around 1.2 (Table 2). As expected, all

Table 2. DLS and GPC Data for PNB-SP$_x$-*co*-P3$_y$-*co*-A1$_z$ Amphiphilic Random Copolymers

copolymer	M_n[a] (kDa)	M_w[a] (kDa)	PDI[a]	diam[b] (nm)	diam$_{UV}$[b,c] (nm)
PNB-P3$_{40}$-*co*-A1$_{60}$	54.1	72.4	1.34	42.7	
PNB-SP$_5$-*co*-P3$_{40}$-*co*-A1$_{55}$	56.1	65.3	1.16	43.5	37.1
PNB-SP$_{10}$-*co*-P3$_{40}$-*co*-A1$_{50}$	52.3	61.8	1.18	40.2	38.0
PNB-SP$_{15}$-*co*-P3$_{40}$-*co*-A1$_{45}$	56.9	70.1	1.23	41.2	36.0
PNB-SP$_{20}$-*co*-P3$_{40}$-*co*-A1$_{40}$	48.7	63.7	1.31	34.3	30.3
PNB-SP$_{25}$-*co*-P3$_{40}$-*co*-A1$_{35}$	58.3	66.9	1.15	39.6	28.7
PNB-SP$_{30}$-*co*-P3$_{40}$-*co*-A1$_{30}$	60.1	70.5	1.17	39.4	24.3

[a]Determined by GPC using a LS detector in THF at 298 K. [b]Measured by DLS with polymer concentration of 0.125 mg/mL in aqueous solution at 298 K. [c]Measured after UV irradiation at 365 nm.

the amphiphilic random copolymers exhibit good solubility in water. More interestingly, they can self-assemble to polymeric micelles with the average diameter around 40 nm in aqueous solution.

Irradiation of the random polymeric micelles of PNB-SP$_x$-*co*-P3$_y$-*co*-A1$_z$ with UV light in water resulted in isomerization of the hydrophobic SP to hydrophilic MC and subsequently disrupting the polymeric micelles. An aqueous micellar solution was prepared by simply dissolving into water and then irradiated with either UV light (365 nm LED, input 350 mA, 3.7 V, output ~125 mW/cm^2) or visible light (530 nm LED, input 350 mA, 3.4 V, output ~120 mW/cm^2). Reversible photoisomerization of SP units was clearly evidenced by UV–vis absorption spectra. When irradiated the aqueous micellar solution of PNB-SP$_{30}$-*co*-P3$_{40}$-*co*-A1$_{30}$ by 365 nm light for 6 s, the photostationary states were reached. A strong absorption band at 564 nm, characteristic of MC isomer, appeared (Figure 3a), and the colorless solution became deep blue. Then irradiated the blue solution with 530 nm visible light, the MC unit isomerized back to SP isomer in 5 min, and the absorption

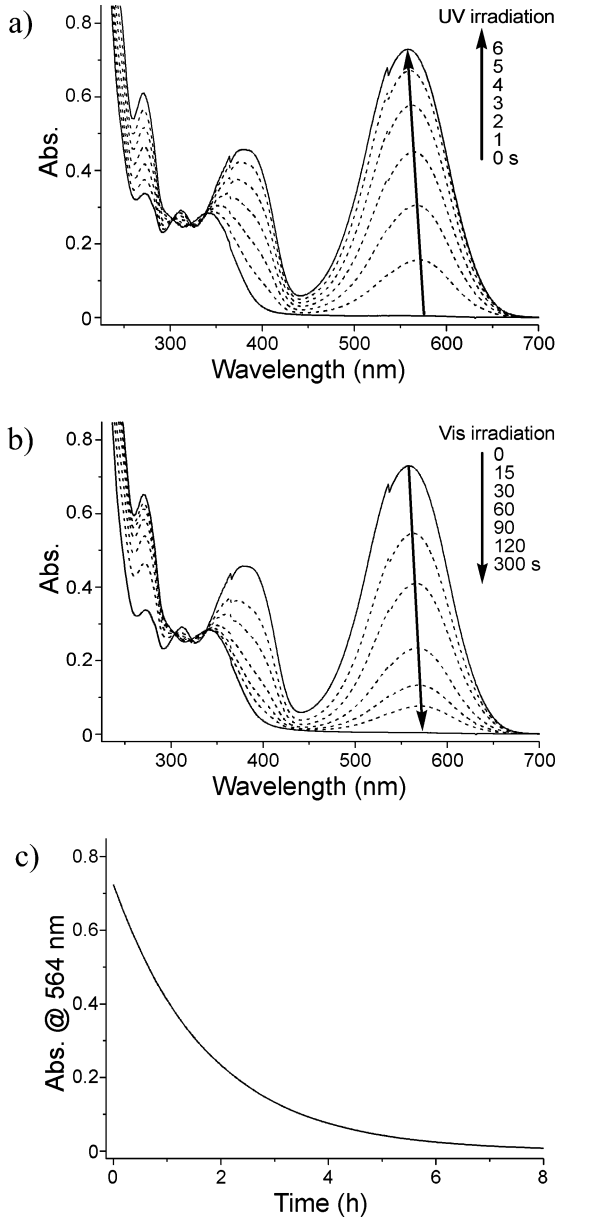

Figure 3. UV–vis absorption spectra for the PNB-SP$_{30}$-*co*-P3$_{40}$-*co*-A1$_{30}$ micelles upon (a) UV at 365 nm and (b) visible light at 530 nm irradiation with polymer concentration of 0.085 mg/mL in aqueous solution. (c) Decay profile of absorption at 564 nm for MC; it gives a lifetime of 1.77 h.

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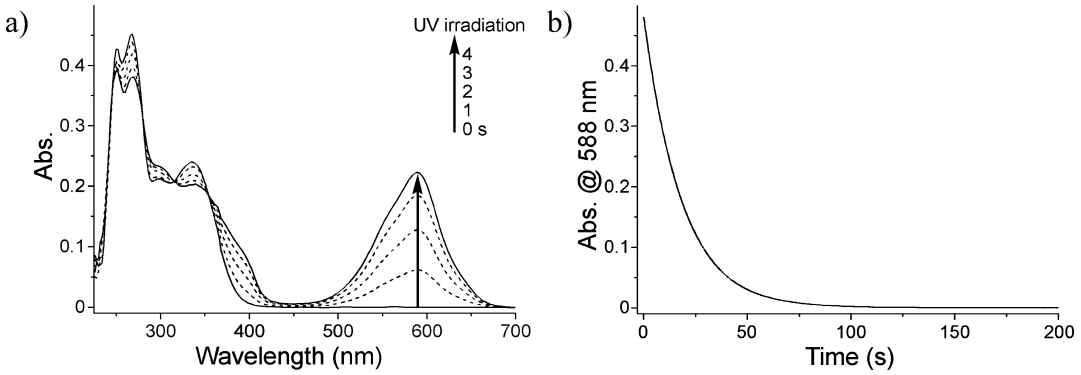

Figure 4. (a) UV−vis absorption spectra for NB-SP monomer upon UV at 365 nm irradiation in THF. (b) Decay profile of absorption at 588 nm for MC; it gives a lifetime of 18.1 s.

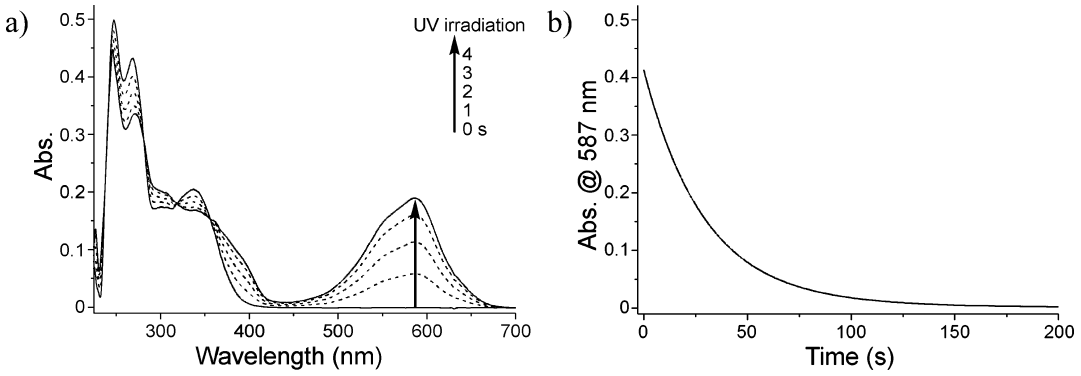

Figure 5. (a) UV−vis absorption spectra for PNB-SP_{30}-*co*-$P3_{40}$-*co*-$A1_{30}$ copolymer upon UV at 365 nm irradiation in THF. (b) Decay profile of absorption at 587 nm for MC; it gives a lifetime of 30.0 s.

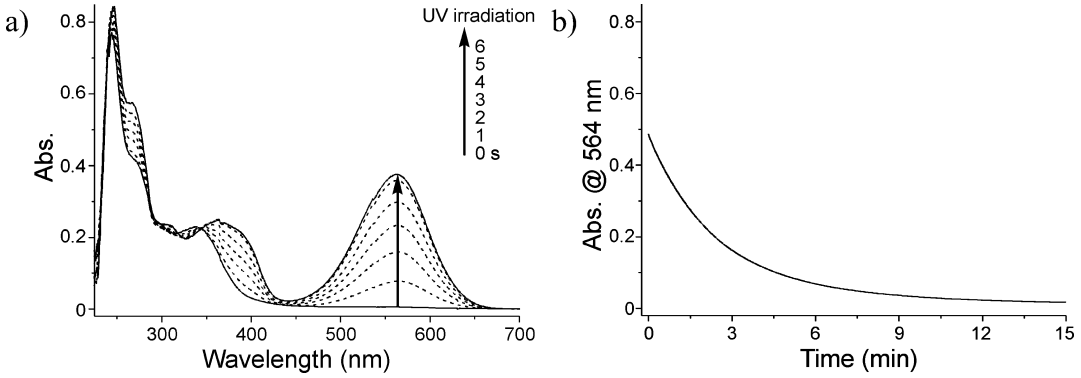

Figure 6. (a) UV−vis absorption spectra for PNB-SP_{30}-*co*-$P3_{40}$-*co*-$A1_{30}$ copolymer upon UV at 365 nm irradiation in 5% THF aqueous solution. (b) Decay profile of absorption at 564 nm for MC; it gives a lifetime of 157.5 s.

spectra almost reverted to the original one (Figure 3b). Reversible stokes shifts between 559 and 573 nm imply an environmental change in aqueous solution for MC isomers during photoisomerization. The conversion from MC to SP isomers also took place in the dark. The lifetime (1.77 h, Figure 3c) of MC isomer could be fitted by a clean monoexponential decay profile of the absorbance at 564 nm. A comparison of those for NB-SP monomer (18.1 s in THF at 588 nm, Figure 4) and PNB-SP_{30}-*co*-$P3_{40}$-*co*-$A1_{30}$ copolymer (30.0 s in THF at 587 nm, Figure 5; ∼150 s in the mixture of THF and H_2O at 564 nm, Figure 6 and Figure S4) showed prolonged lifetime in the aqueous solution, which might be attributed to the solvents and morphology transition nature from the hydrophilic MC to hydrophobic SP isomers.

Cryogenic transmission electron microscopy (cryo-TEM) was performed to gain a direct visualization of the formation, disruption, and regeneration of the polymeric micelles in aqueous solution. As shown in Figure 7a,b, individual spherical micelles were clearly observed with the diameter in the range of 36−40 nm, consistent with those obtained by SEM (Figure 7d,e), conventional TEM (Figure 7f), and DLS (39.4 nm, Figure 7g). Once the aqueous solution was exposed to UV light for 6 s, the spherical aggregates of PNB-SP_{30}-*co*-$P3_{40}$-*co*-$A1_{30}$ disassembled (Figure 7c). Such a disassembling fact was also confirmed by the DLS, providing the average diameter (24.3 nm, Figure 7h) smaller than that before UV irradiation, and then the resultant solution was further irradiated under visible light for ∼5 min. The regeneration of the well-defined

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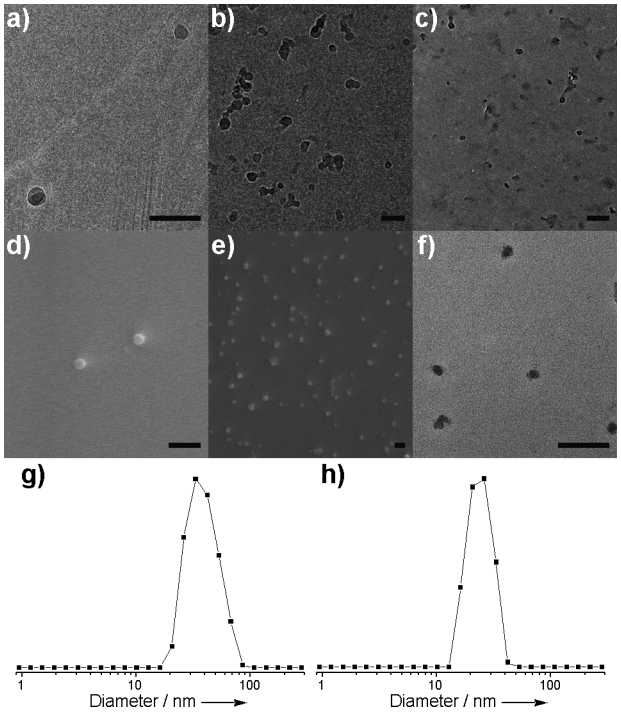

Figure 7. PNB-SP_{30}-*co*-$P3_{40}$-*co*-$A1_{30}$ polymeric micelles: Cryo-TEM (a, b) before and (c) after UV irradiation at 365 nm; (d, e) SEM with no irradiation; (f) TEM with no irradiation; the scale bar is 100 nm. Size distribution profiles by DLS measurements (g) before and (h) after UV irradiation at 365 nm with polymer concentration of 0.125 mg/mL in aqueous solution at 298 K.

polymeric micelles with the average particle size of 41.0 nm was clearly detected by the DLS measurement (Figure S11c, see Supporting Information).

On the basis of the above results, a new set of reversible light-triggered transition of amphiphilic random copolymers, PNB-SP_x-*co*-$P3_y$-*co*-$A1_z$, has been established. To examine its potential use in drug delivery, we attempted to utilize the system for reversible encapsulation and release of a hydrophobic dye Nile red (NR). Typically, 20 μL of NR solution in THF was slowly injected into 4 mL of stirred aqueous solution of PNB-SP_{30}-*co*-$P3_{40}$-*co*-$A1_{30}$ micelles through a microsyringe; a violet-red solution formed immediately, indicating that the dyes of NR have been incorporated into the polymeric micelles (Figure 8a). In this case, the loading wt % of NR is 1.31% with PNB-SP_{30}-*co*-$P3_{40}$-*co*-$A1_{30}$ concentration of 0.085 mg/mL in the aqueous solution. On irradiation with 365 nm light, the pink micellar solution changed to deep blue, accompanied by the disruption of the micelles and subsequent release of NR (Figure 8b). After 530 nm visible-light irradiation, the color of the deep blue solution faded out and finally reached a pink solution (Figure 8c). The entire processes could be followed by the absorption spectra. It was about 40% recovery of NR absorption intensity at 547 nm on regeneration of the micelles (Figure 9). Incomplete re-encapsulation of NR might be interpreted by the fact that the dye NR is not soluble in water, and the relatively high rate of micelle regeneration would prevent all of the released NR molecules from incorporating into the hydrophobic core. The speculation was also consistent with the observation that, after standing for several hours, a purple insoluble NR suspension appeared in the solution. Nevertheless, the micelles could be reloaded via the injection of

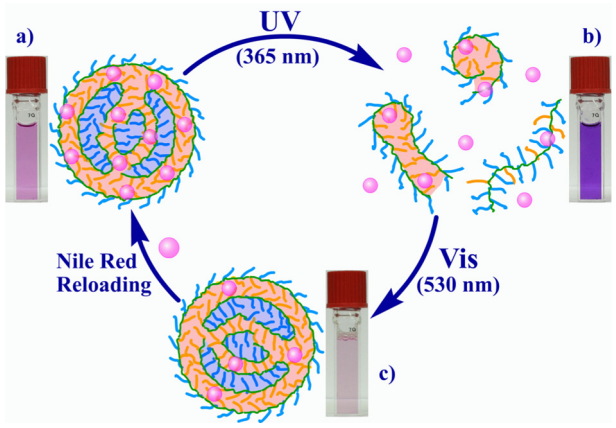

Figure 8. Scheme and photographs for the NR encapsulated PNB-SP_{30}-*co*-$P3_{40}$-*co*-$A1_{30}$ micelles (a) upon UV irradiation at 365 nm, (b) then visible-light irradiation at 530 nm, and (c) reloading of NR.

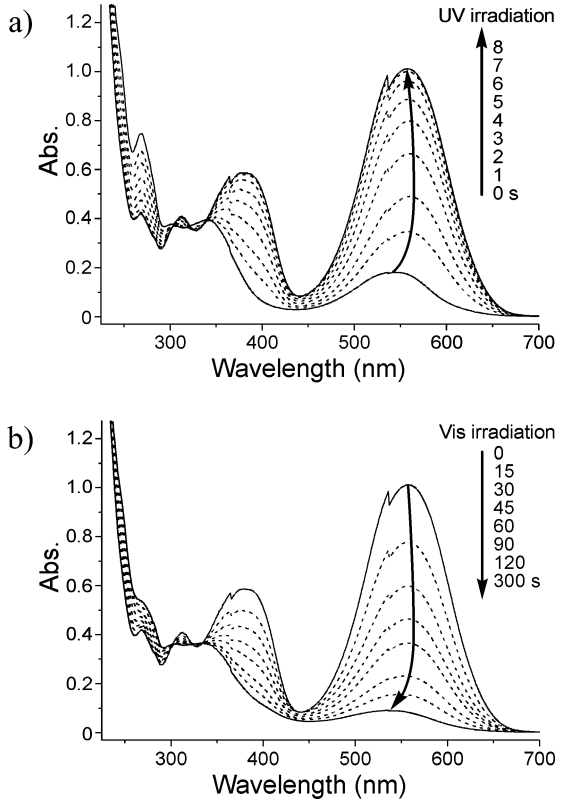

Figure 9. UV–vis absorption spectra for the NR encapsulated PNB-SP_{30}-*co*-$P3_{40}$-*co*-$A1_{30}$ micelles upon (a) UV at 365 nm and (b) visible light at 530 nm irradiation with copolymer concentration of 0.107 mg/mL in aqueous solution.

additional NR in THF, which renders the possibility to reuse the polymeric micelles of PNB-SP_x-*co*-$P3_y$-*co*-$A1_z$ amphiphilic random copolymers.

CONCLUSION

In summary, we have successfully constructed a new set of amphiphilic random copolymers, PNB-$P3_m$-*co*-$A1_n$ and PNB-SP_x-*co*-$P3_y$-*co*-$A1_z$, directly by adjusting the proportion of hydrophilic, hydrophobic, and/or functional monomers in one-pot ROMP. These amphiphilic copolymers are able to self-assemble in water to polymeric micelles spontaneously at room

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temperature. More importantly, on light irradiation at 365 and 530 nm, the copolymer of PNB-SP_{30}-*co*-$P3_{40}$-*co*-$A1_{30}$ undergoes reversible SP/MC photoisomerization, leading to the disrupted and regenerated micellar architectures rapidly. As a result, light-triggered releasing and reloading of hydrophobic dye NR by the polymeric micelles in aqueous solution have been achieved. It is anticipated that this research line would be a promising polymeric drug delivery model with remote control characteristics.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Decay profiles, GPC curves, and DLS, NMR, mass spectra for intermediates, monomers, polymers, and assemblies. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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■ REFERENCES

(1) (a) Uhrich, K. E.; Cannizzaro, S. M.; Langer, R. S.; Shakesheff, K. M. *Chem. Rev.* **1999**, *99*, 3181−3198. (b) Euliss, L. E.; DuPont, J. A.; Gratton, S.; DeSimone, J. *Chem. Soc. Rev.* **2006**, *35*, 1095−1104. (c) Tanner, P.; Baumann, P.; Enea, R.; Onaca, O.; Palivan, C.; Meier, W. *Acc. Chem. Res.* **2011**, *44*, 1039−1049. (d) van Dongen, S. F. M.; de Hoog, H.-P. M.; Peters, R. J. R. W.; Nallani, M.; Nolte, R. J. M.; van Hest, J. C. M. *Chem. Rev.* **2009**, *109*, 6212−6274. (e) Zhao, Y. *Macromolecules* **2012**, *45*, 3647−3657. (f) Mecke, A.; Dittrich, C.; Meier, W. *Soft Matter* **2006**, *2*, 751−759. (g) Lehn, J.-M. *Chem. Soc. Rev.* **2007**, *36*, 151−160. (h) Zhou, Y.; Huang, W.; Liu, J.; Zhu, X.; Yan, D. *Adv. Mater.* **2010**, *22*, 4567−4590.

(2) (a) Nyström, A. M.; Wooley, K. L. *Acc. Chem. Res.* **2011**, *44*, 969−978. (b) Sun, G.; Cui, H.; Lin, L. Y.; Lee, N. S.; Yang, C.; Neumann, W. L.; Freskos, J. N.; Shieh, J. J.; Dorshow, R. B.; Wooley, K. L. *J. Am. Chem. Soc.* **2011**, *133*, 8534−8543. (c) Liu, C.; Hillmyer, M. A.; Lodge, T. P. *Langmuir* **2009**, *25*, 13718−13725. (d) Saito, N.; Liu, C.; Lodge, T. P.; Hillmyer, M. A. *ACS Nano* **2010**, *4*, 1907−1912. (e) Walther, A.; Barner-Kowollik, C.; Müller, A. H. E. *Langmuir* **2010**, *26*, 12237−12246. (f) Lee, H.-i.; Wu, W.; Oh, J. K.; Mueller, L.; Sherwood, G.; Peteanu, L.; Kowalewski, T.; Matyjaszewski, K. *Angew. Chem., Int. Ed.* **2007**, *46*, 2453−2457. (g) Chen, W.; Wei, X.; Balazs, A. C.; Matyjaszewski, K.; Russell, T. P. *Macromolecules* **2011**, *44*, 1125−1131. (h) Im, K.; Park, H.-W.; Kim, Y.; Ahn, S.; Chang, T.; Lee, K.; Lee, H.-J.; Ziebarth, J.; Wang, Y. *Macromolecules* **2008**, *41*, 3375−3383.

(3) (a) Savariar, E. N.; Aathimanikandan, S. V.; Thayumanavan, S. *J. Am. Chem. Soc.* **2006**, *128*, 16224−16230. (b) Hordyjewicz-Baran, Z.; You, L.; Smarsly, B.; Sigel, R.; Schlaad, H. *Macromolecules* **2007**, *40*, 3901−3903. (c) Gao, K.-J.; Li, G.; Lu, X.; Wu, Y. G.; Xu, B.-Q.; Fuhrhop, J.-H. *Chem. Commun.* **2008**, 1449−1451. (d) Dan, K.; Bose, N.; Ghosh, S. *Chem. Commun.* **2011**, *47*, 12491−12493.

(4) (a) Fürstner, A. *Angew. Chem., Int. Ed.* **2000**, *39*, 3013−3043. (b) Trnka, T. M.; Grubbs, R. H. *Acc. Chem. Res.* **2001**, *34*, 18−29. (c) *Olefin Metathesis and Metathesis Polymerization*, 2nd ed.; Ivin, J., Mol, I. C., Eds.; Academic: New York, 1996. (d) *Handbook of Metathesis*; Grubbs, R. H., Ed.; Wiley-VCH: Weinheim, Germany, 2003; Vol. 3. (e) Love, J. A.; Morgan, J. P.; Trnka, T. M.; Grubbs, R. H. *Angew. Chem., Int. Ed.* **2002**, *41*, 4035−4037.

(5) (a) Vehlow, K.; Wang, D.; Buchmeiser, M. R.; Blechert, S. *Angew. Chem., Int. Ed.* **2008**, *47*, 2615−2618. (b) Lichtenheldt, M.; Wang, D.; Vehlow, K.; Reinhardt, I.; Kühnel, C.; Decker, U.; Blechert, S.; Buchmeiser, M. R. *Chem.—Eur. J.* **2009**, *15*, 9451−9457.

(6) Drechsler, U.; Thibault, R. J.; Rotello, V. M. *Macromolecules* **2002**, *35*, 9621−9623.

(7) (a) Foster, E. J.; Berda, E. B.; Meijer, E. W. *J. Am. Chem. Soc.* **2009**, *131*, 6964−6966. (b) Berda, E. B.; Foster, E. J.; Meijer, E. W. *Macromolecules* **2010**, *43*, 1430−1437.

(8) (a) Xia, Y.; Olsen, B. D.; Kornfield, J. A.; Grubbs, R. H. *J. Am. Chem. Soc.* **2009**, *131*, 18525−18532. (b) Xia, Y.; Kornfield, J. A.; Grubbs, R. H. *Macromolecules* **2009**, *42*, 3761−3766.

(9) (a) Lienkamp, K.; Madkour, A. E.; Musante, A.; Nelson, C. F.; Nüsslein, K.; Tew, G. N. *J. Am. Chem. Soc.* **2008**, *130*, 9836−9843. (b) Gabriel, G. J.; Madkour, A. E.; Dabkowski, J. M.; Nelson, C. F.; Nüsslein, K.; Tew, G. N. *Biomacromolecules* **2008**, *9*, 2980−2983.

(10) (a) Pollino, J. M.; Stubbs, L. P.; Weck, M. *Macromolecules* **2003**, *36*, 2230−2234. (b) South, C. R.; Burd, C.; Weck, M. *Acc. Chem. Res.* **2006**, *40*, 63−74. (c) Yang, S. K.; Ambade, A. V.; Weck, M. *Chem. Soc. Rev.* **2011**, *40*, 129−137.

(11) (a) Roberts, K. S.; Sampson, N. S. *J. Org. Chem.* **2003**, *68*, 2020−2023. (b) Le, D.; Montembault, V.; Soutif, J. C.; Rutnakornpituk, M.; Fontaine, L. *Macromolecules* **2010**, *43*, 5611−5617. (c) Sutthasupa, S.; Shiotsuki, M.; Matsuoka, H.; Masuda, T.; Sanda, F. *Macromolecules* **2010**, *43*, 1815−1822. (d) Sankaran, N. B.; Rys, A. Z.; Nassif, R.; Nayak, M. K.; Metera, K.; Chen, B.; Bazzi, H. S.; Sleiman, H. F. *Macromolecules* **2010**, *43*, 5530−5537. (e) Biagini, S. C. G.; Parry, A. L. *J. Polym. Sci., Part A: Polym. Chem.* **2007**, *45*, 3178−3190. (f) Miki, K.; Kuramochi, Y.; Oride, K.; Inoue, S.; Harada, H.; Hiraoka, M.; Ohe, K. *Bioconjugate Chem.* **2009**, *20*, 511−517.

(12) Berkovic, G.; Krongauz, V.; Weiss, V. *Chem. Rev.* **2000**, *100*, 1741−1754.

(13) Chen, Q.; Feng, Y.; Zhang, D.; Zhang, G.; Fan, Q.; Sun, S.; Zhu, D. *Adv. Funct. Mater.* **2010**, *20*, 36−42.

(14) Yuan, W.; Sun, L.; Tang, H.; Wen, Y.; Jiang, G.; Huang, W.; Jiang, L.; Song, Y.; Tian, H.; Zhu, D. *Adv. Mater.* **2005**, *17*, 156−160.

(15) (a) Han, D.; Tong, X.; Zhao, Y. *Macromolecules* **2011**, *44*, 437. (c) Zhao, Y. *J. Mater. Chem.* **2009**, *19*, 4887−4895. (b) Jiang, J.; Tong, X.; Morris, D.; Zhao, Y. *Macromolecules* **2006**, *39*, 4633−4640. (c) Babin, J.; Pelletier, M.; Lepage, M.; Allard, J.-F.; Morris, D.; Zhao, Y. *Angew. Chem.* **2009**, *121*, 3379−3382. (d) Li, Y.; Deng, Y.; Tong, X.; Wang, X. *Macromolecules* **2006**, *39*, 1108−1115.

(16) Adelmann, R.; Mela, P.; Gallyamov, M. O.; Keul, H.; Möller, M. *J. Polym. Sci., Polym. Chem.* **2009**, *47*, 1274−1283.

(17) (a) Yagai, S.; Kitamura, A. *Chem. Soc. Rev.* **2008**, *37*, 1520−1529. (b) Yagai, S.; Karatsu, T.; Kitamura, A. *Chem.—Eur. J.* **2005**, *11*, 4054−4063.

(18) Liao, X.; Chen, G.; Liu, X.; Chen, W.; Chen, F.; Jiang, M. *Angew. Chem., Int. Ed.* **2010**, *49*, 4409−4413.

(19) Wang, C.; Chen, Q.; Wang, Z.; Zhang, X. *Angew. Chem., Int. Ed.* **2010**, *49*, 8612−8615.

(20) Fomina, N.; McFearin, C.; Sermsakdi, M.; Edigin, O.; Almutairi, A. *J. Am. Chem. Soc.* **2010**, *132*, 9540−9542.

(21) Orihara, Y.; Matsumura, A.; Saito, Y.; Ogawa, N.; Saji, T.; Yamaguchi, A.; Sakai, H.; Abe, M. *Langmuir* **2001**, *17*, 6072−6076.

(22) Such, G. K.; Evans, R. A.; Davis, T. P. *Macromolecules* **2004**, *37*, 9664−9666.

(23) (a) Li, C.; Zhang, Y.; Hu, J.; Cheng, J.; Liu, S. *Angew. Chem., Int. Ed.* **2010**, *49*, 5120−5124. (b) Hu, J.; Liu, S. *Macromolecules* **2010**, *43*, 8315−8330.

(24) Raymo, F. M.; Giordani, S. *J. Am. Chem. Soc.* **2001**, *123*, 4651−4652.
(25) Jung, S. H.; Kim, H.-J. *J. Porphyrins Phthalocyanines* **2008**, *12*, 109−115.
(26) Percec, V.; Heck, J. *J. Polym. Sci., Part A: Polym. Chem.* **1991**, *29*, 591−597.
(27) (a) Manning, D. D.; Strong, L. E.; Hu, X.; Beck, P. J.; Kiessling, L. L. *Tetrahedron* **1997**, *53*, 11937−11952. (b) Roberts, J. D.; Trumbull, E. R.; Bennett, W.; Armstrong, R. *J. Am. Chem. Soc.* **1950**, *72*, 3116−3124. (c) Ver Nooy, C. D.; Rondestvedt, C. S. *J. Am. Chem. Soc.* **1955**, *77*, 3583−3586.