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Baylis–Hillman Reaction as a Versatile Platform for the Synthesis of Diverse Functionalized Polymers by Chain and Step Polymerization

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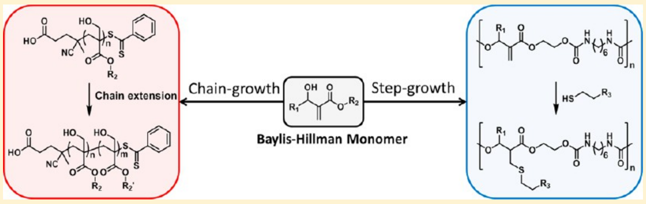
Supporting Information

ABSTRACT: The Baylis–Hillman reaction, which is a carbon–carbon bond forming reaction between an aldehyde and an activated alkene, was utilized to prepare densely functionalized monomers suitable for chain and step polymerization. By reacting formaldehyde with various alkyl acrylates, a series of alkyl α-hydroxymethyl acrylate monomers were synthesized. These monomers efficiently underwent RAFT polymerization to provide α-hydroxymethyl-substituted polyacrylates with well controlled molecular weight and low polydispersity. The resulting homopolymers were also efficient macro-chain transfer agents for further RAFT polymerization. The Baylis–Hillman reaction was also utilized to synthesize alkene functionalized diols which underwent step-growth polymerization to provide polyesters and poly(ester urethane)s. Furthermore, it was demonstrated that the alkene group can be quantitatively functionalized by thiol–ene click chemistry to provide a series of polymers with diverse physical properties.



INTRODUCTION

Polymer properties are modulated by the presence of various functional groups and the design and synthesis of functionalized polymers is an area of research that is witnessing rapid advances.[1−4] Currently, the assimilation of synthetic organic methodologies into the design of polymers has provided remarkable examples of precisely engineered polymers such as polyacrylates and polynorbornenes,[2,5,6] polyesters,[7−11] and polyurethanes[12] with various functional groups. Different designs of functionalized polymers have been reported including pendant,[13,14] chain end functionalized,[15−18] graft,[19−21] and hyperbranched[22−24] polymers. Functionalized polymers have demonstrated several advantages over their nonfunctionalized counterparts, such as tailored physical, mechanical, and biological properties. For example, the antifouling nature of polyacrylonitrile membranes is improved by functionalization with hydroxyl or carboxyl functionalities.[25] Cell attachment and proliferation onto polymeric substrates are improved by functionalization with the RGD tripeptide.[26,27]

Conventional and controlled radical polymerizations have been the most widely studied methods for synthesis of functionalized polymers.[3,28,29] Several examples have been reported and a representative example is a functionalized polymethacrylate reported by Maynard et al. containing a reactive ketone side chain, which can be used to prepare polymer–drug conjugates.[30] Furthermore, interesting examples exist wherein each monomer is designed to have multiple functional groups. Thayumanavan et al. reported a class of styrene-based amphiphilic homopolymers in which the phenyl group is substituted with both hydrophilic carboxyl and hydrophobic benzyl groups, which enables their self-assembly into spherical micelles in aqueous solution.[31] Similarly, Du et al. designed an amphiphilic homopolymer, poly(2-hydroxy-3-phenoxypropyl acrylate) (PHPPA), which can self-assemble into a wide range of nanostructures.[32,33] Additionally, there has been a concerted effort in designing biodegradable polyesters and poly(ester amide)s bearing various functional groups in our lab and elsewhere.[7−9,34,35]

A novel method for the generation of functionalized polymers that has largely been under-explored is the use of monomers derived from the Baylis–Hillman reaction. The Baylis–Hillman reaction is a carbon–carbon bond forming reaction between an aldehyde and an activated alkene in presence of a tertiary amine such as DABCO (1,4-diazabicyclo[2.2.2]octane), and provides densely functionalized molecules in a one-pot process (Figure 1).[36−40] Several activated alkenes such as acrylates,[41−43] acrylamides,[44] acrylonitriles,[45] vinyl ketones[46] or vinyl phosphonates[47] are substrates for the Baylis–Hillman reaction.

Although the wide substrate diversity of the Baylis–Hillman reaction provides a route to several classes of functionalized polymers, the number of studies describing their synthesis from Baylis–Hillman substrates remains rather limited. Klok has shown the synthesis of polyesters by the Baylis–Hillman reaction of diacrylates with dialdehydes. However, the reported degree of polymerization was rather low (DP_n = 4–25; M_n = 630–4200 g/mol).[48] Mathias has reported proof of principle experiments demonstrating the feasibility of Baylis–Hillman monomers as substrates for radical polymerization. His group showed that methyl acrylate reacts with formaldehyde to

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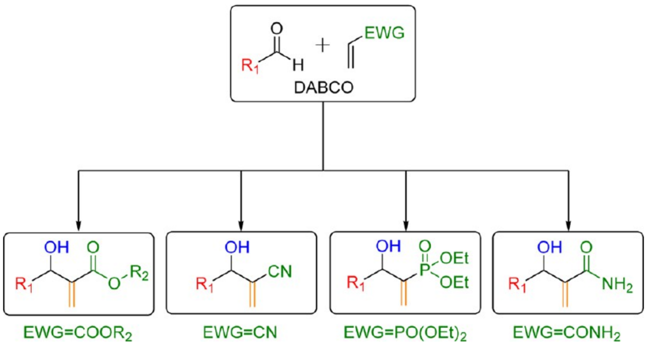
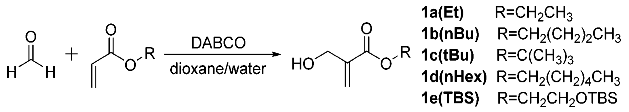


Figure 1. Baylis−Hillman reaction and its utility for the synthesis of densely functionalized molecules. EWG = electron withdrawing group.

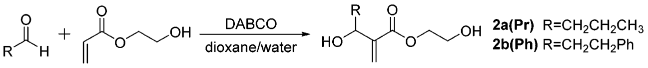
provide methyl α-hydroxymethyl acrylate, which underwent homo or copolymerization with styrene or methyl methacrylate.[49,50] Huang has utilized the Baylis−Hillman reaction to synthesize a novel acrylate monomer containing an ATRP initiating group. This monomer was subsequently polymerized by sequential RAFT and ATRP methods to provide poly(*tert*-butyl acrylate)-*g*-poly(methyl acrylate) graft copolymers.[51]

As outlined in Scheme 1, the work reported here describes the synthesis of Baylis−Hillman based monomers and their polymerization by chain or step polymerization routes. In the first part of this article, we present the synthesis of a series of alkyl α-hydroxymethyl acrylate monomers by the Baylis−Hillman reaction of formaldehyde with alkyl acrylates (Scheme 2). The corresponding alkyl α-hydroxymethyl acrylates efficiently undergo reversible addition−fragmentation chain transfer (RAFT) polymerization to provide functionalized homopolymers or block copolymers. We also demonstrate that such functionalized polyacrylates can readily form nanostructures in aqueous solution due to their amphiphilic nature. In the second part, we show the reaction of 3-phenylpropionaldehyde or butyraldehyde with 2-hydroxyethyl acrylate to provide alkene-functionalized diols (Scheme 3) which can undergo step growth polymerization to provide poly(ester urethane)s or polyesters. The alkene group can be functionalized either pre or postpolymerization using the thiol−ene reaction. The current work demonstrates the utility of the Baylis−Hillman reaction as a versatile platform for the synthesis of multiple classes of functionalized polymers.

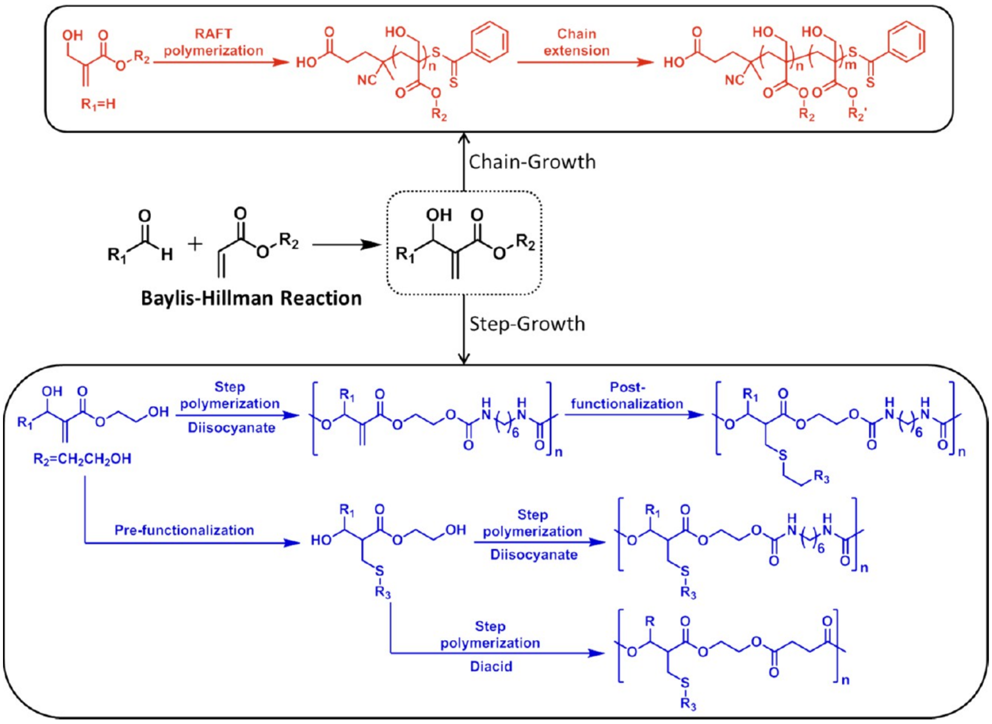
Scheme 2. Synthesis of Alkyl α-Hydroxymethyl Acrylate Monomers



Scheme 3. Synthesis of Alkene-Functionalized Diols



Scheme 1. Utility of Baylis−Hillman-Based Monomers for Chain and Step-Growth Polymerizations



EXPERIMENTAL SECTION

Materials. Tin(II)2-ethylhexanoate ($Sn(Oct)_2$), and 2-hydroxy-4′-(2-hydroxyethoxy)-2-methylpropiophenone (Irgacure 2959) were purchased from Sigma-Aldrich. 2-Mercaptoethanol was purchased from TCI. All other reagents were purchased from Alfa Aesar. Unless otherwise stated, all reagents were used as received. 2,2′-Azobis-(isobutyronitrile) (AIBN) was recrystallized multiple times from methanol before use. 4-(4-Cyanopentanoic acid) dithiobenzoate (CPDB) and 4-(dimethylamino)pyridinium *p*-toluenesulfonate (DPTS) were synthesized according to reported procedures.[7,52,53]

Analytical Methods. NMR spectra were recorded on a Varian NMRS 300 or 500 MHz instrument. ^{1}H NMR chemical shifts are reported in ppm relative to the solvent's residual ^{1}H signal. ^{13}C NMR spectra were recorded at 125 MHz. Size exclusion chromatography (SEC) analysis in DMF was performed on a HLC-8320 GPC from

Table 1. Synthesis of α-Hydroxymethyl-Substituted Polyacrylates via RAFT Polymerization[a]

entry	polymer	$[M]_0/[CTA]_0/[I]_0$	$[M]_0$ (mol L^{-1})	time (h)	$M_{n,SEC}$ (kg/mol)[b]	PDI[b]	convn (%)[d]	$M_{n,theory}$ (kg/mol)[e]
1	**P1a(Et)**	180/3/1	2	24	7.6	1.15	92	7.6
2	**P1b(nBu)**	180/3/1	2	24	8.0	1.16	80	8.0
3	**P1c(tBu)**	180/3/1	2	24	5.4	1.21	48	5.0
4	**P1d(nHex)**	180/3/1	2	24	9.6	1.16	73	8.5
5	**P1a(Et)**	200/1/0.2	2	24	19.8	1.18	62	15.8
6	**P1b(nBu)**	220/1/0.2	2	24	25.4	1.19	58	20.5
7	**P1c(tBu)**	200/1/0.2	2	24	11.7	1.28	41	13.2
8	**P1d(nHex)**	220/1/0.2	2	24	29.6	1.17	63	26.1
9	**P1b(nBu)**	180/3/1	2	24	10.3[c]	1.07[c]	80	8.0
10	**P1b(nBu)-*b*-P1e(TBS)**	180/3/1	1.5	24	24.1[c]	1.25[c]	73	19.4

[a] All the experiments (entry 1−10) used AIBN as initiator and 1,4-dioxane as solvent. The reaction temperature was kept at 70 °C. [b] Determined by SEC using DMF as the eluent and PMMA as the standard. [c] Determined by SEC using THF as the eluent and PS as the standard. [d] Monomer conversion determined by ^{1}H NMR. [e] Calculated based on the monomer conversion.

TOSOH equipped with RI and UV detectors using PMMA or PS as the standards. ESI MS was performed on Bruker HTC ultra QIT. Size exclusion chromatography (SEC) in THF was performed on a Waters 150-C Plus instrument equipped with RI and LS detectors and PS was used as the standard. The decomposition temperature (T_d) of the polymers was determined by thermal gravimetric analysis (TGA) using TA Q500 thermal gravimetric analysis instrument. The glass transition temperature (T_g) of the polymers was determined by differential scanning calorimetry (DSC) using TA Q2000 differential scanning calorimetry instrument. The morphology of the nanoparticles was characterized by scanning electron microscope (SEM) using JEOL-JSM-7401F with operating voltage as 4 kV. The size and distribution of the nanoparticles were determined by dynamic light scattering (DLS) using a Malvern Instruments Zetasizer Nano ZS.

Synthesis of Alkyl α-Hydroxymethyl Acrylate Monomers. As an example, the synthesis of **1b(nBu)** is as follows: *n*-butyl acrylate (14.0 g, 0.109 mol), formaldehyde aqueous solution (2.7 mL, 0.036 mol), and 1,4-diazabicyclo[2.2.2]octane (DABCO) (4.1 g, 0.036 mol) were added to a round-bottom flask equipped with a magnetic stir bar. Then 1,4-dioxane (10.0 mL) and distilled water (7.3 mL) were added, and the mixture was stirred at room temperature for 12 h. The compound was extracted by ethyl acetate followed by washing with brine and subsequent drying over anhydrous Na_2SO_4. The filtrate was then concentrated under reduced pressure and purified by column chromatography (30% ethyl acetate and 70% hexane, $R_f = 0.5$) to give a colorless liquid. (2.9 g, 51%)

1a(Et). ^{1}H NMR (300 MHz, $CDCl_3$), δ (ppm): 1.33 (t, *J* = 7.50 Hz, 3H), 2.23 (t, *J* = 6.00 Hz, 1H), 4.26 (q, *J* = 7.00 Hz, 2H), 4.35 (d, *J* = 3.00 Hz, 2H), 5.83 (s, 1H), 6.27 (s, 1H). ^{13}C NMR (125 MHz, $CDCl_3$), δ (ppm): 14.09 (s), 60.80 (s), 62.36 (s), 125.37 (s), 139.59 (s), 166.29 (s). MS(ESI): 152.8 ($[M + Na]^+$).

1b(nBu). ^{1}H NMR (300 MHz, $CDCl_3$), δ (ppm): 0.96 (t, *J* = 7.50 Hz, 3H), 1.36−1.49 (m, 2H), 1.64−1.73 (m, 2H), 2.25 (t, *J* = 6.00 Hz, 1H), 4.20 (t, *J* = 7.50 Hz, 2H), 4.35 (d, *J* = 3.00 Hz, 2H), 5.84 (s, 1H), 6.27 (s, 1H). ^{13}C NMR (125 MHz, $CDCl_3$), δ (ppm): 13.62 (s), 19.13 (s), 30.56 (s), 62.41 (s), 64.69 (s), 125.34 (s), 139.61 (s), 166.36 (s). MS(ESI): 180.9 ($[M + Na]^+$).

1c(tBu). ^{1}H NMR (300 MHz, $CDCl_3$), δ (ppm): 1.52 (s, 9H), 2.32 (t, *J* = 6.00 Hz, 1H), 4.30 (d, *J* = 6.00 Hz, 2H), 5.75 (s, 1H), 6.16 (s, 1H). ^{13}C NMR (125 MHz, $CDCl_3$), δ (ppm): 28.03 (s), 62.61 (s), 81.31 (s), 124.62 (s), 140.88 (s), 165.65 (s). MS(ESI): 180.9 ($[M + Na]^+$).

1d(nHex). ^{1}H NMR (300 MHz, $CDCl_3$), δ (ppm): 0.90 (t, *J* = 7.50 Hz, 3H), 1.32−1.43 (m, 6H), 1.65−1.74 (m, 2H), 2.26 (s, 1H), 4.19 (t, *J* = 6.00 Hz, 2H), 4.34 (s, 2H), 5.84 (s, 1H), 6.27 (s, 1H). ^{13}C NMR (125 MHz, $CDCl_3$), δ (ppm): 13.90 (s), 22.46 (s), 25.57 (s), 28.48 (s), 31.35 (s), 62.46 (s), 65.01 (s), 125.37 (s), 139.61 (s), 166.34 (s). MS(ESI): 208.9 ($[M + Na]^+$).

1e(TBS). ^{1}H NMR (300 MHz, $CDCl_3$), δ (ppm): 0.08 (s, 6H), 0.90 (s, 9H), 2.39 (t, *J* = 3.00 Hz, 1H), 3.86 (t, *J* = 3.00 Hz, 2H), 4.27 (t, *J* = 3.00 Hz, 2H), 4.34 (d, *J* = 6.00 Hz, 2H), 5.84 (s, 1H), 6.28 (s, 1H). ^{13}C NMR (125 MHz, $CDCl_3$), δ (ppm): 5.38 (s), 18.25 (s), 25.79 (s), 61.09 (s), 62.63 (s), 66.00 (s), 125.89 (s), 139.47 (s), 166.19 (s). MS(ESI): 283.0 ($[M + Na]^+$).

Synthesis of Poly(alkyl α-hydroxymethyl acrylate) by RAFT Polymerization. In a typical experiment (entry 2 in Table 1), **1b(nBu)** (316.4 mg, 2.0 mmol), the RAFT agent CPDB (9.3 mg, 0.033 mmol), AIBN (1.8 mg, 0.011 mmol) and anhydrous 1,4-dioxane (1.0 mL) were added to a Schlenk flask equipped with a magnetic stir bar. The Schlenk flask was subjected to three freeze−pump−thaw cycles. Then the flask was sealed and placed in a heated oil bath at 70 °C for 24 h under magnetic stirring. The polymer was precipitated in hexane, centrifuged and dried in vacuum oven to give a pink solid. (M_n = 8.0 kg/mol, PDI = 1.16)

P1a(Et). ^{1}H NMR (500 MHz, acetone-d_6), δ (ppm): 1.30 (m, 3H), 1.95 (m, 2H), 3.74−4.13 (m, 4H), 7.48 (m, end group), 7.62 (m, end group), 7.92 (m, end group).

P1b(nBu). ^{1}H NMR (500 MHz, $CDCl_3$), δ (ppm): 0.97 (m, 3H), 1.42 (m, 2H), 1.64 (m, 2H), 1.92 (m, 2H), 3.59−4.07 (m, 4H), 7.36 (m, end group), 7.52 (m, end group), 7.88 (m, end group).

P1c(tBu). ^{1}H NMR (500 MHz, $CDCl_3$), δ (ppm): 1.53 (m, 9H), 1.95 (m, 2H), 3.67 (m, 2H), 7.36 (m, end group), 7.51 (m, end group), 7.90 (m, end group).

P1d(nHex). ^{1}H NMR (500 MHz, $CDCl_3$), δ (ppm): 1.53 (m, 9H), 1.95 (m, 2H), 3.67 (m, 2H), 7.36 (m, end group), 7.51 (m, end group), 7.90 (m, end group).

Synthesis of Block Copolymer, P1b(nBu)-*b*-P1e(TBS), by RAFT Polymerization (entry 10 in Table 1). **P1b(nBu)** (192.2 mg, 2.4×10^{-5} mol), AIBN (1.3 mg, 8.0×10^{-6} mol), **1e(TBS)** (374.5 mg, 1.438×10^{-3} mol), and anhydrous 1,4-dioxane (1.0 mL) were added to a Schlenk flask equipped with a magnetic stir bar. The Schlenk flask was subjected to three freeze−pump−thaw cycles. The flask was then sealed and placed in a heated oil bath at 70 °C for 24 h under magnetic stirring. The polymer was precipitated in cold hexane, centrifuged and dried in vacuum oven to give a pink solid. (M_n = 24.1 kg/mol, PDI = 1.25)

P1b(nBu)-b-P1e(TBS). ^{1}H NMR (500 MHz, $CDCl_3$), δ (ppm): 0.10 (m, 6H), 0.92 (m, 9H), 0.97 (m, 3H), 1.42 (m, 2H), 1.64 (m, 2H), 1.92 (m, 4H), 3.59−4.07 (m, 8H)

Preparation of Nanoparticles by Dialysis Method. **P1b(nBu)** (entry 2 in Table 1, M_n = 8.0 kg/mol, PDI = 1.16) was dissolved in DMF at a concentration of 1.0 mg/mL and dialyzed against distilled water for 24 h. The water was refreshed every 6 h. Morphology and size of the nanoparticles were investigated by SEM and DLS.

Preparation of Nanoparticles by the Dropping Method. **P1b(nBu)** (entry 2 in Table 1, M_n = 8.0 kg/mol, PDI = 1.16) was dissolved in acetone at a concentration of 1.0 mg/mL, and distilled water was added dropwise to the polymer solution under vigorous stirring until the solution became faint blue (~15 wt% water). The morphology of the nanoparticles was characterized by SEM.

Synthesis of Alkene-Functionalized Diol. As an example, the synthesis of **2b(Ph)** is as follows: 2-hydroxyethyl acrylate (6.0 g, 0.052

mol), 3-phenylpropionaldehyde (2.3 g, 0.017 mol), and 1,4-diazabicyclo[2.2.2]octane (5.8 g, 0.052 mol) were added to a round-bottom flask equipped with a magnetic stir bar. Then 1,4-dioxane (8.0 mL) and distilled water (8.0 mL) were added to the flask and the mixture was stirred at room temperature for 24 h. The compound was extracted by ethyl acetate followed by washing with brine and subsequent drying over anhydrous Na_2SO_4. The filtrate was then concentrated under reduced pressure and purified by column chromatography (30% ethyl acetate and 70% hexane, R_f = 0.3) to give a colorless liquid. (1.8 g, 43%)

2a(Pr). ^{1}H NMR (300 MHz, $CDCl_3$), δ (ppm): 0.96 (t, J = 7.50 Hz, 3H), 1.32–1.54 (m, 2H), 1.62–1.70 (m, 2H), 2.00 (s, 1H), 2.51 (s, 1H), 3.90 (t, J = 4.50 Hz, 2H), 4.34 (t, J = 4.50 Hz, 2H), 4.44 (t, J = 6.00 Hz, 1H), 5.84 (s, 1H), 6.28 (s, 1H). ^{13}C NMR (125 MHz, $CDCl_3$), δ (ppm): 13.79 (s), 18.97 (s), 38.15 (s), 60.80 (s), 66.27 (s), 71.11 (s), 125.26 (s), 142.60 (s), 166.77 (s). MS(ESI): 210.9 ([M + Na]$^+$).

2b(Ph). ^{1}H NMR (300 MHz, $CDCl_3$), δ (ppm): 1.96–2.05 (m, 2H), 2.67–2.89 (m, 2H), 3.87 (t, J = 6.00 Hz, 2H), 4.32 (t, J = 4.50 Hz, 2H), 4.66 (t, J = 7.50 Hz, 1H), 5.86 (s, 1H), 6.30 (s, 1H), 7.18–7.32 (m, 5H); ^{13}C NMR (125 MHz, $CDCl_3$), δ (ppm): 31.95 (s), 37.47 (s), 60.69 (s), 66.25 (s), 70.50 (s), 125.58 (s), 128.83 (s), 128.32 (s), 128.38 (s), 141.53 (s), 142.39 (s), 166.64 (s). MS(ESI): 273.0 ([M + Na]$^+$).

General Procedure of the Thiol–Ene "Click" Reaction of the Alkene-Functionalized Diols. As an example, the synthesis of **2b(Ph)-Dodecyl** is as follows: **2b(Ph)** (1.0 g, 4 mmol), 1-dodecanethiol (8.1 g, 40 mmol), Irgacure 2959 (448.6 mg, 2 mmol), and anhydrous DMF (3.6 mL) were added to a quartz glass test tube. The solution was irradiated at 350 nm for 30 min. The product was purified by column chromatography (50% ethyl acetate and 50% hexane, R_f = 0.3) to give a colorless liquid. (1.5 g, 83%)

2a(Pr)-nBu. ^{1}H NMR (300 MHz, MeOD), δ (ppm): 0.93 (t, J = 7.5 Hz, 6H), 1.31–1.61 (m, 8H), 2.54 (t, J = 7.5 Hz, 2H), 2.66–2.95 (m, 3H), 3.71–3.80 (m, 3H), 4.18 (m, 2H). ^{13}C NMR (125 MHz, Acetone-d_6), δ (ppm): 13.99 (s), 14.32 (s), 19.69 (s), 22.57 (s), 31.12 (s), 32.51 (s), 37.85 (s), 38.15 (s), 54.59 (s), 60.85 (s), 66.71 (s), 72.33 (s), 173.86 (s). MS(ESI): 301.0 ([M + Na]$^+$).

2b(Ph)-Dodecyl. ^{1}H NMR (300 MHz, MeOD), δ (ppm): 0.90 (t, J = 7.5 Hz, 3H), 1.29–1.37 (m, 18H), 1.55 (m, 2H), 1.70–1.90 (m, 2H), 2.51 (t, J = 7.5 Hz, 2H), 2.63–2.90 (m, 5H), 3.71–3.81 (m, 3H), 4.18 (m, 2H), 7.21 (m, 5H). ^{13}C NMR (125 MHz, $CDCl_3$), δ (ppm): 22.68 (s), 28.84 (s), 29.20 (s), 29.34 (s), 29.46 (s), 29.51 (s), 29.59 (s), 29.64 (s), 31.61 (s), 31.91 (s), 32.03 (s), 32.12 (s), 32.65 (s), 36.08 (s), 37.38 (s), 51.28 (s), 60.84 (s), 66.27 (s), 71.50 (s), 126.03 (s), 128.44 (s), 128.49 (s), 143.89 (s), 173.81 (s). MS(ESI): 475.2 ([M + Na]$^+$).

Synthesis of Poly(ester urethane)s. In a typical reaction (entry 2 in Table 3), **2b(Ph)** (0.6554 g, 2.62 mmol) and hexamethylene diisocyanate (0.4407 g, 2.62 mmol) were added to a Schlenk flask. The flask was evacuated and backfilled with nitrogen three times. Then anhydrous dichloromethane (3.0 mL) was added. After that, one drop of $Sn(Oct)_2$ was added under N_2 and the solution was stirred at room temperature for 48 h. The product was precipitated in diethyl ether, centrifuged and dried in vacuum oven. (M_n = 9.4 kg/mol, PDI = 1.47)

PEU2a(Pr). ^{1}H NMR (300 MHz, $CDCl_3$), δ (ppm): 0.92 (t, J = 7.5 Hz, 3H), 1.35–1.65 (m, 12H), 3.17 (m, 5H), 4.30 (m, 4H), 4.93 (br, 2H), 5.51 (s, 1H), 5.78 (s, 1H), 6.29 (s, 1H).

PEU2b(Ph). ^{1}H NMR (300 MHz, $CDCl_3$), δ (ppm): 1.33–1.64 (m, 8H), 1.98–2.10 (m, 2H), 2.67 (m, 2H), 3.14 (m, 4H), 4.28 (m, 4H), 4.84 (br, 2H), 5.56 (s, 1H), 5.81 (s, 1H), 6.32 (s, 1H), 7.18 (m, 3H), 7.25 (m, 2H).

PEU2a(Pr)-nBu. ^{1}H NMR (300 MHz, $CDCl_3$), δ (ppm): 0.91 (m, 6H), 1.28–1.65 (m, 16H), 2.51 (m, 2H), 2.69 (m, 1H), 2.85 (m, 2H), 3.16 (s, 4H), 4.23–4.32 (m, 4H), 5.02 (s, 1H).

PEU2b(Ph)-Dodecyl. ^{1}H NMR (300 MHz, $CDCl_3$), δ (ppm): 0.89 (m, 3H), 1.26–1.63 (m, 28H), 1.92 (m, 2H), 2.48 (m, 2H), 2.67 (m, 3H), 2.86 (m, 2H), 3.14 (m, 4H), 4.22–4.31 (m, 4H), 5.08 (m, 1H), 7.19–7.30 (m, 5H).

Synthesis of Polyesters. In a typical reaction (entry 2 in Table 6), **2b(Ph)-Dodecyl** (1.0275 g, 2.27 mmol), succinic acid (0.2681 g, 2.27 mmol), and DPTS (0.2657 g, 0.91 mmol) were added to a Schlenk flask. The flask was evacuated and backfilled with nitrogen three times. Anhydrous dichloromethane (4.3 mL) was added followed by diisopropylcarbodiimide (DIC) (0.8581 g, 6.81 mmol) and the reaction was stirred at room temperature for 24 h. The polymer was precipitated in methanol three times to give a viscous liquid. (M_n = 8.3 kg/mol, PDI = 1.34)

PE2a(Pr)-nBu. ^{1}H NMR (300 MHz, $CDCl_3$), δ (ppm): 0.92 (t, J = 7.5 Hz, 6H), 1.29–1.64 (m, 8H), 2.52 (m, 2H), 2.62–2.91 (m, 7H), 4.33 (m, 4H), 5.19 (m, 1H).

PE2b(Ph)-Dodecyl. ^{1}H NMR (300 MHz, $CDCl_3$), δ (ppm): 0.89 (t, J = 6.0 Hz, 3H), 1.20–1.33 (m, 18H), 1.55 (m, 2H), 1.95 (m, 2H), 2.45–2.83 (m, 8H), 2.92 (m, 1H), 4.29 (m, 4H), 5.24 (m, 1H), 7.15–7.33 (m, 5H).

General Procedure for the Thiol–Ene "Click" Reaction of the Alkene-Functionalized Polymers. In a typical experiment (entry 4 in Table 4), **PEU2b(Ph)** (0.1 g) and 3-mercaptopropionic acid (0.25 g, 2.4 mmol), Irgacure 2959 (26.9 mg, 0.12 mmol) and anhydrous chloroform (1.0 mL) were added to a quartz glass test tube. The solution was irradiated at 350 nm for 30 min. The product was precipitated in diethyl ether, centrifuged and dried in a vacuum oven.

PEU2a(Pr)-OH. ^{1}H NMR (300 MHz, MeOD), δ (ppm): 0.93 (t, J = 7.5 Hz, 3H), 1.35–1.61 (m, 12H), 2.66 (m, 2H), 2.78–2.90 (m, 3H), 3.10 (m, 4H), 3.68 (t, J = 7.5 Hz, 2H), 4.26–4.31 (m, 4H), 5.01 (m, 1H).

PEU2a(Pr)-COOH. ^{1}H NMR (300 MHz, DMSO-d_6), δ (ppm): 0.85 (t, J = 6.0 Hz, 3H), 1.22–1.50 (m, 12 H), 2.63–2.84 (m, 7H), 2.95 (m, 4H), 4.13–4.21 (m, 4H), 4.89 (m, 1H), 6.99–7.11 (m, 2H), 12.24 (s, 1H).

PEU2b(Ph)-OH. ^{1}H NMR (300 MHz, MeOD), δ (ppm): 1.34–1.50 (m, 8H), 1.93 (m, 2H), 2.65 (m, 4H), 2.76–2.96 (m, 3H), 3.09 (m, 4H), 3.65 (t, J = 7.5 Hz, 2H), 4.23–4.28 (m, 4H), 5.02 (m, 1H), 7.16–7.28 (m, 5H).

PEU2b(Ph)-COOH. ^{1}H NMR (300 MHz, DMSO-d_6), δ (ppm): 1.23–1.38 (m, 8H), 1.83 (m, 2H), 2.44–2.67 (m, 9H), 2.94 (m, 4H), 4.12–4.19 (m, 4H), 4.89 (m, 1H), 7.08 (m, 2H), 7.17–7.26 (m, 5H), 12.23 (s, 1H).

■ RESULTS AND DISCUSSION

Monomer Synthesis. The two types of monomers used for the polymerizations were synthesized using a one-step Baylis–Hillman reaction as outlined in Schemes 2 and Scheme 3. The Baylis–Hillman reaction of formaldehyde with alkyl acrylate in

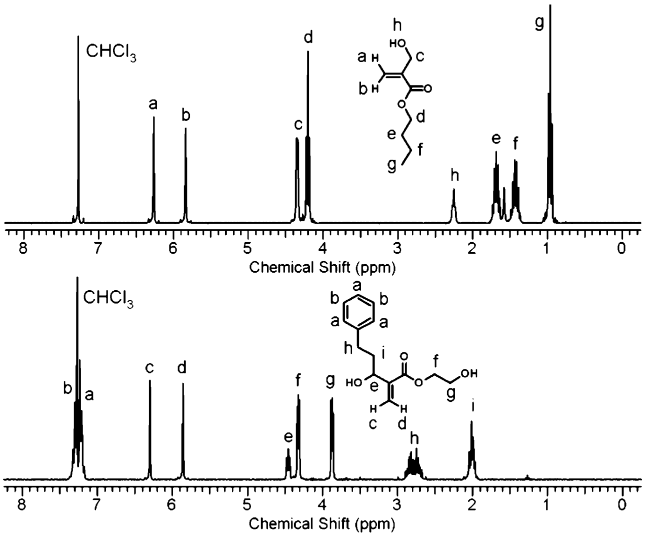
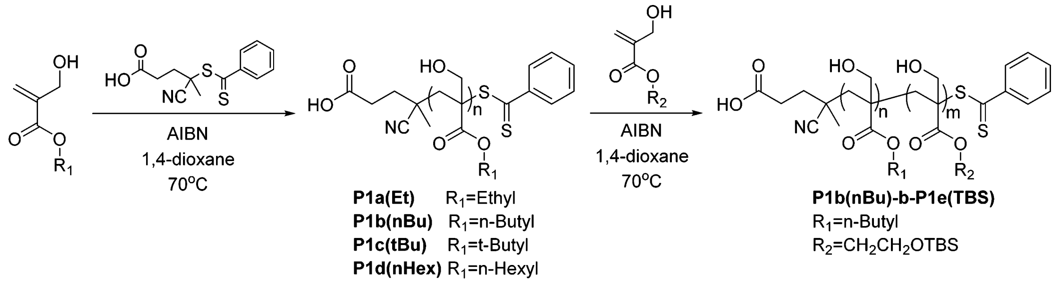


Figure 2. ^{1}H NMR spectra of **1b(nBu)** (top) and **2b(Ph)** (bottom).

Scheme 4. Synthesis of Poly(alkyl α-hydroxymethyl acrylate) via RAFT Polymerization



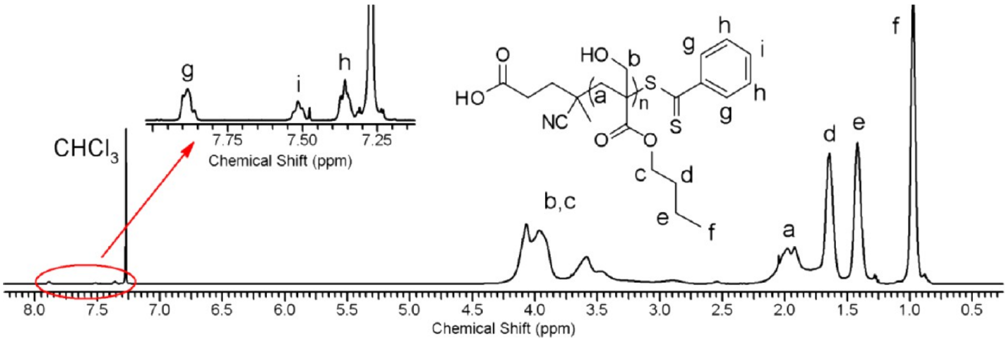


Figure 3. ^{1}H NMR spectra of **P1b(nBu)** synthesized via RAFT polymerization.

Table 2. Thermal Properties of the Polymers

polymer	comment	$T_{5\%}$ (°C)^a	T_{d1} (°C)^a	T_{d2} (°C)^a	T_g (°C)^b
P1a(Et)	entry 5 in Table 1	165	153	284	86
P1b(nBu)	entry 6 in Table 1	170	166	292	56
P1c(tBu)	entry 7 in Table 1	162	164	283	88
P1d(nHex)	entry 8 in Table 1	168	165	293	28

[a] Temperature of 5% mass loss ($T_{5\%}$) and decomposition temperature (T_d) were determined by thermal gravimetric analysis (TGA). [b] Glass transition temperature (T_g) was determined by differential scanning calorimetry (DSC).

the presence of DABCO generated alkyl α-hydroxymethyl acrylate (**1a**−**1e**) and the reaction of aldehyde with 2-hydroxyethyl acrylate in the presence of DABCO provided the unsaturated diol (**2a(Pr)** and **2b(Ph)**) in approximately 50% yield for both reactions.

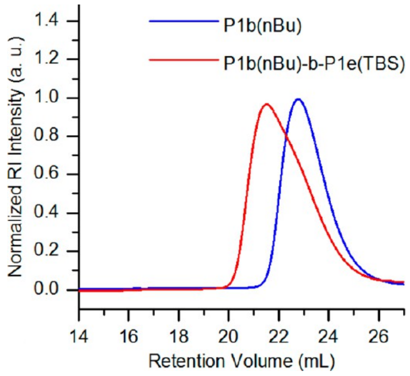


Figure 5. SEC traces of **P1b(nBu)** (entry 9 in Table 1) and **P1b(nBu)-*b*-P1e(TBS)** (entry 10 in Table 1).

The Baylis−Hillman reaction to give **1(a−e)** and **2(a,b)** was carried out in a 1,4-dioxane/water (1/1, v/v) medium as it has been reported to accelerate the progress of the reaction.[54] As representative examples, the 300 MHz ^{1}H NMR spectrum of **1b(nBu)** and **2b(Ph)** is shown in Figure 2.

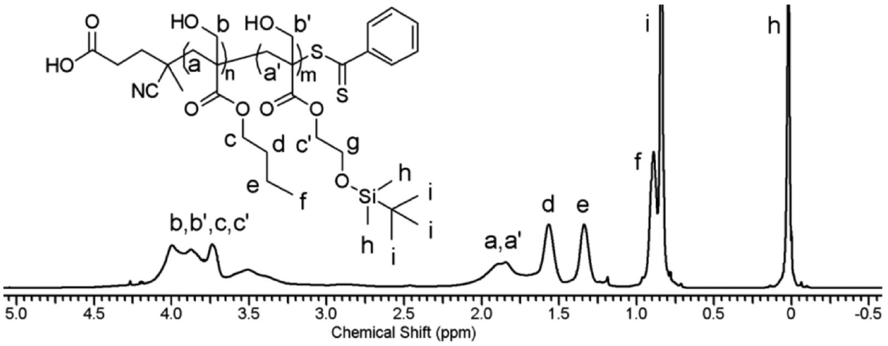


Figure 4. ^{1}H NMR spectra of **P1b(nBu)-*b*-P1e(TBS)** synthesized via RAFT polymerization.

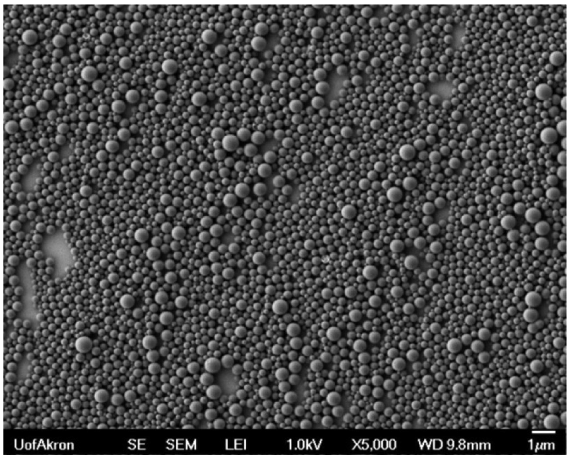


Figure 6. SEM image (without sputtering) of **P1b(nBu)** nanoparticles prepared by dialysis method. scale bar = 1 μm.

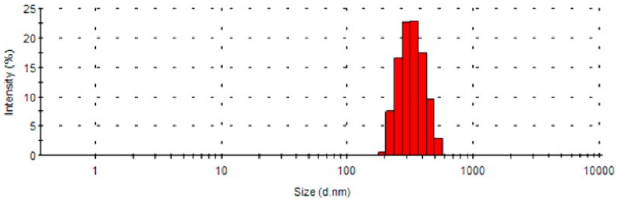


Figure 7. Size distribution of **P1b(nBu)** nanoparticles prepared by dialysis method.

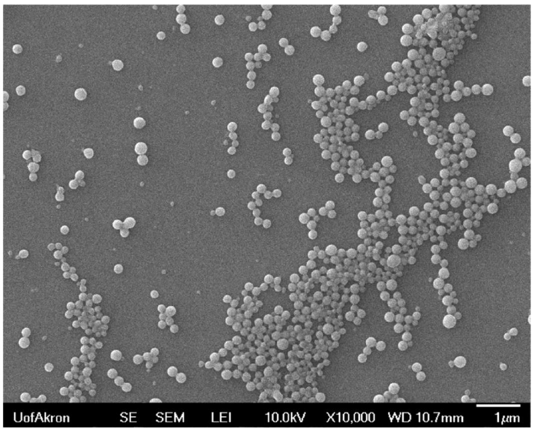


Figure 8. SEM image (with sputtering) of **P1b(nBu)** nanoparticles prepared by the dropping method. Scale bar = 1 μm.

Synthesis of the α-Hydroxymethyl-Substituted Polyacrylate Library by RAFT Polymerization. A library of α-hydroxymethyl substituted polyacrylates was synthesized using RAFT polymerization (Scheme 4). Within this series, the pendant groups of the polymers were varied, such as ethyl, *n*-butyl, *tert*-butyl, or *n*-hexyl. The homopolymers were synthesized by RAFT polymerization at 70 °C using AIBN as initiator. 4-(4-Cyanopentanoic acid) dithiobenzoate, CPDB, was selected as the chain transfer agent to control the polymerization as it was found to be compatible with the α-hydroxymethyl substituted acrylate monomers. The structures of the polymers were confirmed by ^{1}H NMR spectroscopy. A typical example is shown in Figure 3 (entry 2 in Table 1) with the proton assignments corresponding to the repeating unit. As shown in the expanded region of the spectrum between 7.2 and 8.0 ppm, the signals of the RAFT end group were detected around 7.38, 7.54, and 7.98 ppm, which confirmed the retained RAFT end group. In order to calculate the monomer conversion, aliquots of the reaction mixture were withdrawn by syringe at the end of the reaction and analyzed by ^{1}H NMR spectroscopy. The conversion was determined by integration of the backbone methylene proton resonances $I(-CH_2)^p$ relative to the monomer olefinic proton resonances $I(=CH_2)^m$ by eq 1. Theoretical number-average molecular weights were calculated based on eq 2, where $\mathrm{MW_{CTA}}$ and $\mathrm{MW_m}$ are the molecular weights of RAFT agent and monomer, respectively. $[\mathrm{M}]_0$ and $[\mathrm{CTA}]_0$ are the initial concentrations of monomer and RAFT agent, respectively. The theoretical molecular weight shows good agreement with the experimental molecular weight.

$$\text{conversion (\%)} = \frac{I(-\mathrm{CH_2})^p}{I(-\mathrm{CH_2})^p + I(=\mathrm{CH_2})^m} \times 100\% \tag{1}$$

$$M_\mathrm{n}^{calc} = \frac{[M]_0 \times \mathrm{MW}_m \times \text{conversion}}{[\mathrm{CTA}]_0} + \mathrm{MW_{CTA}} \tag{2}$$

Table 1 summarizes the results for the polymers prepared by RAFT polymerization as obtained from the SEC and ^{1}H NMR data. It is shown that high $[\mathrm{M}]_0/[\mathrm{CTA}]_0$ molar ratio such as 200:1 or 220:1 afforded a molecular weight between 11.7 and 29.6 kg/mol. With a low $[\mathrm{M}]_0/[\mathrm{CTA}]_0$ molar ratio 60:1, relatively low molecular weight between 5.4 and 9.6 kg/mol was obtained. SEC analysis indicated unimodal molecular weight distributions and the $M_\mathrm{w}/M_\mathrm{n}$ was around 1.2. It is worth noting that slightly broader polydispersity was observed for the polymer with a *tert*-butyl pendant group, which may be due to the steric hindrance of the monomer or potential side reactions that may occur with *tert*-butyl moieties via thermal pathways.

The thermal properties (decomposition temperature ($\mathrm{T_d}$) and glass transition temperature (T_g)) of the homopolymers were determined by TGA and DSC. The polymers from entry 5–8 (Table 1) were selected for thermal analysis and the results are summarized in Table 2. TGA experiments revealed that the polymers began decomposition at around 152–165 °C and they showed two stages of weight loss (Supporting Information). On the basis of DSC experiments, the T_g decreases with increasing length of the alkyl side chain. **P1b(nBu)** (M_n = 25.4 kg/mol, T_g = 56 °C) and **P1d(nHex)** (M_n = 29.6 kg/mol, T_g = 28 °C) showed lower glass transition temperatures (T_g) than **P1a(Et)** (M_n = 19.8 kg/mol, T_g = 85 °C), which was consistent with the higher flexibility of *n*-butyl and *n*-hexyl side groups in **P1b(nBu)** and **P1d(nHex)**. The polymers with t-butyl and ethyl groups provided similar T_g values; T_g of **P1a(Et)** (M_n = 19.8 kg/mol) and **P1c(tBu)** (M_n = 11.7 kg/mol) are 86 and 88 °C, respectively.

Copolymerization Studies. In the previous section, we demonstrated successful RAFT polymerization of the alkyl α-hydroxymethyl acrylate monomers and confirmed the retained end-group functionality by 500 MHz ^{1}H NMR spectroscopy. The homopolymer was subsequently tested as a macro-CTA to prepare block copolymers. To investigate this, we selected **P1b(nBu)** (entry 9 in Table 1, M_n = 10.3 kg/mol, PDI = 1.07) as the macro-CTA. In order to minimize the signal overlap of the two blocks in the ^{1}H NMR spectra, the TBS (*tert*-butyldimethylsilyl) protected hydroxyl monomer, **1e(TBS)**, was selected for block copolymer synthesis as the difference in chemical shifts of the pendant groups corresponding to each

Scheme 5. Synthesis of Functionalized Poly(ester urethane)s

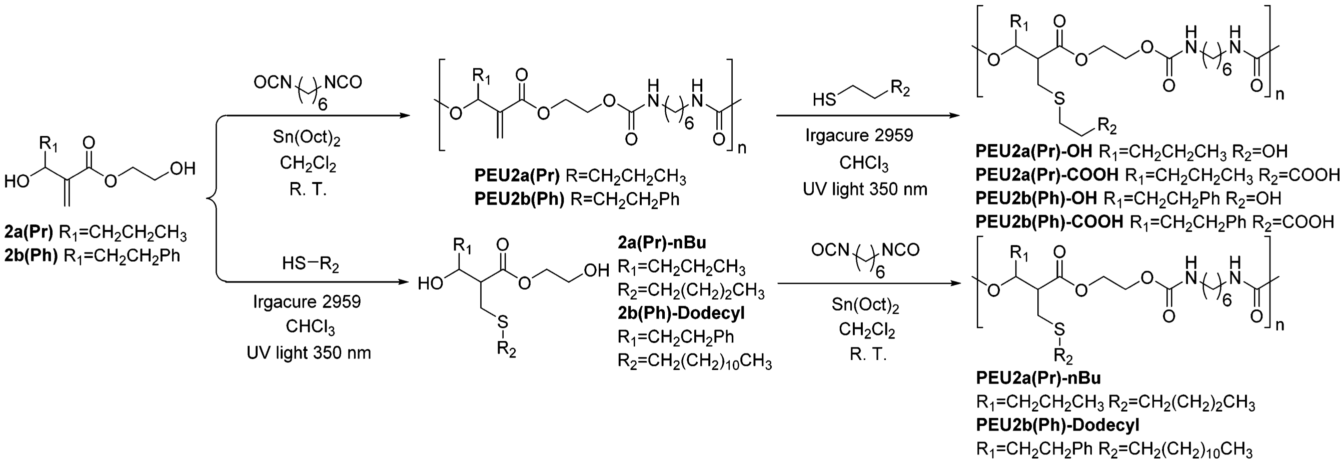


Table 3. Synthesis of Alkene-Functionalized Poly(ester urethane)s

entry	polymer	time (h)	$M_{n,SEC}$ (kg/mol)[a]	PDI[a]	DP_n[b]
1	**PEU2a(Pr)**	24	6.2	1.46	35
2	**PEU2b(Ph)**	24	9.4	1.47	45

[a] Determined by SEC using DMF as the eluent and PS as the standard. [b] Number-average degree of polymerization.

Table 4. Post-Polymerization Modification of Poly(ester urethane)s

entry	polymer	thiol	time (min)	conversion (%)
1	**PEU2a(Pr)**	$HSCH_2CH_2OH$	30	100
2	**PEU2a(Pr)**	$HSCH_2CH_2COOH$	30	100
3	**PEU2b(Ph)**	$HSCH_2CH_2OH$	30	100
4	**PEU2b(Ph)**	$HSCH_2CH_2COOH$	30	100

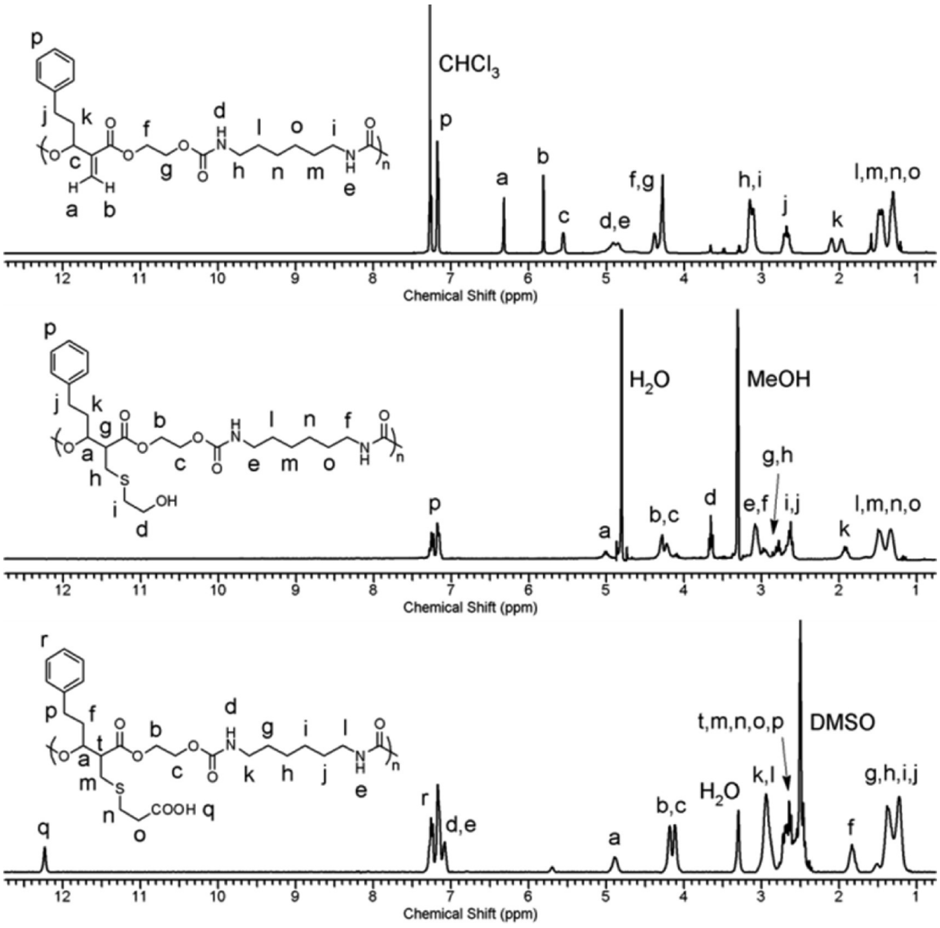


Figure 9. Postpolymerization modification of poly(ester urethane)s as evidenced by ^{1}H NMR; **PEU2b(Ph)** (top), **PEU2b(Ph)-OH** (middle), and **PEU2b(Ph)-COOH** (bottom).

Table 5. Thermal Properties of Post-Functionalized Poly(ester urethane)s

polymer	$T_{5\%}$ (°C)[a]	T_d (°C)[a]	T_g (°C)[b]
PEU2a(Pr)	147	142	5
PEU2a(Pr)-OH	187	186	16
PEU2a(Pr)-COOH	206	207	21
PEU2b(Ph)	190	166	9
PEU2b(Ph)-OH	201	199	21
PEU2b(Ph)-COOH	205	210	22

[a] Temperature of 5% mass loss ($T_{5\%}$) and decomposition temperature (T_d) were determined by thermal gravimetric analysis (TGA). [b] Glass transition temperature (T_g) was determined by differential scanning calorimetry (DSC).

Table 6. Synthesis of Pre-Functionalized Polyesters and Poly(ester urethane)s

entry	polymer	time (h)	$M_{n,SEC}$ (kg/mol)[a]	PDI[a]	DP_n[b]
1	**PE2a(Pr)-nBu**	48	11.8	1.16	60
2	**PE2b(Ph)-Dodecyl**	48	8.3	1.34	29
3	**PEU2a(Pr)-nBu**	24	3.5	1.61	16
4	**PEU2b(Ph)-Dodecyl**	24	5.2	1.66	17

[a] Determined by SEC using DMF as the eluent and PS as the standard. [b] Number-average degree of polymerization.

block are easily distinguished in the ^{1}H NMR spectra. The structure of the block copolymer, **P1b(nBu)-*b*-P1e(TBS)**, was confirmed by ^{1}H NMR spectroscopy (Figure 4) The characteristic peaks of the second block (TBS group at 0.10 and 0.92 ppm) are observed as well as that of the first block (methyl group at 0.97 ppm). SEC analysis showed unimodal distribution for the homopolymer and block copolymer (Figure 5). The first block **P1b(nBu)** (M_n = 10.3 kg/mol, PDI = 1.07) was successfully chain extended, as indicated by the distinct shift in the SEC retention volume. The polydispersity of the **P1b(nBu)-*b*-P1e(TBS)** (M_n = 24.1 kg/mol, PDI = 1.25) block copolymer increased slightly after chain extension but remained low, indicating good living character of the polymerization.

Preparation of Nanoparticles by Dialysis Method. The repeating unit of the described α-hydroxymethyl substituted polyacrylates is amphiphilic due to the presence of a hydrophilic hydroxyl group and a hydrophobic alkyl group. As a result, these amphiphilic polymers self-assemble into nanoparticles when dissolved in DMF and dialyzed against water. The SEM image (Figure 6) of the nanoparticles prepared from **P1b(nBu)** (M_n = 8.0 kg/mol, PDI = 1.16) shows that the homopolymer forms well-defined spherical nanoparticles with an average diameter of 283 nm.

The average hydrodynamic diameter determined by DLS is 323 nm with a PDI of 0.18 (Figure 7). The slight difference in reported size obtained from SEM and DLS analysis is probably due to nanoparticle swelling in the aqueous medium.

Preparation of Nanoparticles by the Dropping Method. Self-assembly properties of **P1b(nBu)** was also investigated by the dropping method. In this experiment, **P1b(nBu)** (M_n = 8.0 kg/mol, PDI = 1.16) was initially dissolved in acetone at a concentration of 1 mg/mL and then an appropriate amount of water was added dropwise into the solution under vigorous stirring. It was observed that the polymer solution became faint blue after adding 15% water (weight fraction), which indicated self-assembly of the polymer. The SEM image (Figure 8) shows the size of the obtained nanoparticles to be about 200 nm.

The above section described the chain polymerization of Baylis–Hillman monomers to provide homo and copolymers. In the next section, the use of Baylis–Hillman based monomers for the synthesis of poly(ester urethane)s and polyesters is described.

Synthesis of Functionalized Poly(ester urethane)s. Step growth polymerization of the alkene-functionalized diol monomers with diisocyanates provided degradable poly(ester

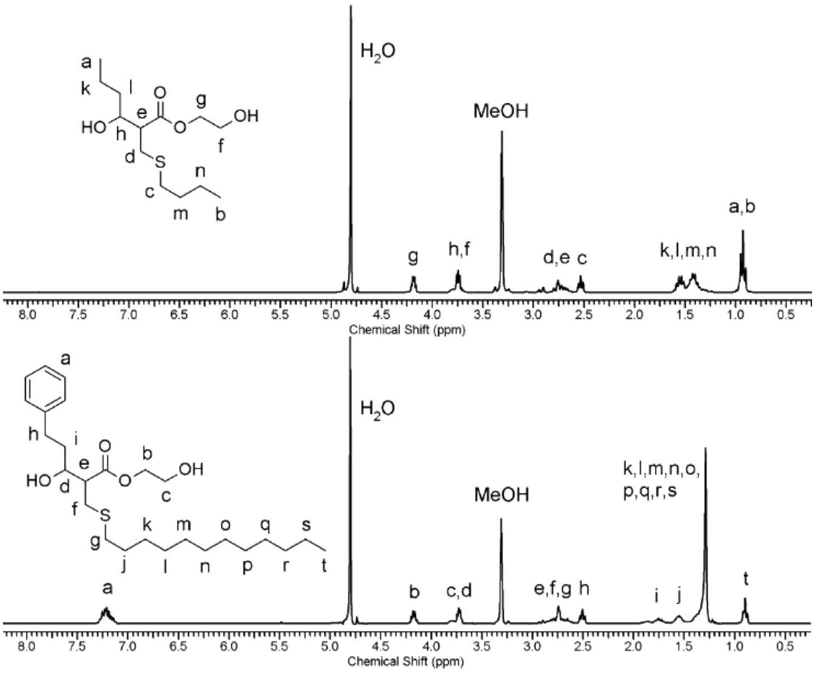


Figure 10. ^{1}H NMR spectra of **2a(Pr)-nBu** (top) and **2b(Ph)-Dodecyl** (bottom).

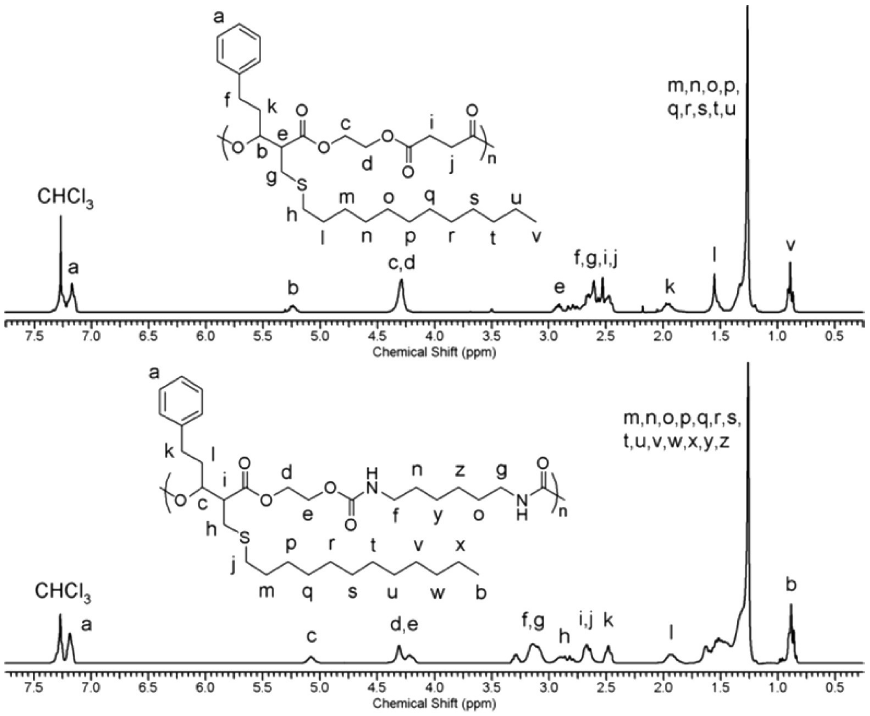
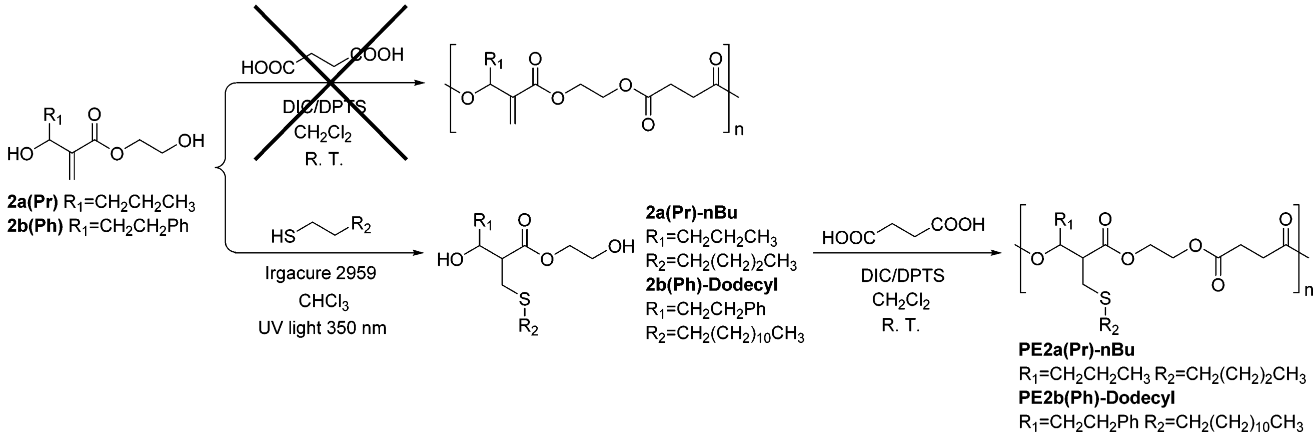


Figure 11. ^{1}H NMR spectra of **PE2a(Ph)-Dodecyl** (top) and **PEU2b(Ph)-Dodecyl** (bottom).

Scheme 6. Synthesis of Functionalized Polyesters



urethane)s. Two synthetic routes were explored for the synthesis of the poly(ester urethane)s (Scheme 5). The first involved the direct polymerization of the unsaturated diol followed by postpolymerization modification. The second involved the conjugate addition of thiols to the unsaturated diol prior to polymerization.

Direct Polymerization with Subsequent Postpolymerization Functionalization. The polymerization of unsaturated diols **2a(Pr)** and **2b(Ph)** with hexamethylene diisocyanate was achieved by solution polymerization in anhydrous CH$_2$Cl$_2$ at room temperature using Sn(Oct)$_2$ as a catalyst. As shown in Table 3, polymerization of **2a(Pr)** and **2b(Ph)** afforded polymers with molecular weights of 6.2 and 9.4 kg/mol, respectively. The low molecular weight is probably a result of differential reactivity of the primary and secondary hydroxyl groups of the monomer. Evidence for the existence of the alkene group in **PEU2b(Ph)** is provided from the ^{1}H NMR peaks at 5.81 and 6.32 ppm (Figure 9). The alkene group can therefore be used for postpolymerization modification via thiol−ene click chemistry.

Postpolymerization Functionalization via Thiol−Ene "Click" Chemistry. The alkene pendant groups in the polymer can be converted to other functional groups via thiol−ene click chemistry.[55] Functional groups which are potentially incompatible with the polymerization conditions such as hydroxyl or carboxyl groups can be incorporated into the polymers in high yields via post polymerization modification using thiol−ene chemistry. In this work, the reaction was carried out with 10 equiv of functionalized thiol and 0.5 equiv of photoinitiator (Irgacure 2959) in anhydrous CHCl$_3$. After irradiation at 350 nm for 30 min, the excess thiol was removed by precipitation in diethyl ether.

As a proof-of-concept, the postpolymerization modification of **PEU2b(Ph)** with 2-mercaptoethanol and 3-mercaptopropionic acid was investigated. The conjugate addition of the thiol to the unsaturated polymers was confirmed by ^{1}H NMR spectroscopy. Figure 9 shows the appearance of new signals consistent with the corresponding functional groups. Additionally, the characteristic peaks of the alkene groups in the ^{1}H NMR spectra have completely disappeared after the thiol−ene reaction, which indicates quantitative conversion of the alkene groups (Table 4). The glass transition temperatures (T_g) of the functionalized polymers were determined by DSC (Table 5). The addition of polar functional groups such as hydroxyl and carboxyl groups leads to an increase in the glass transition temperature. The T_g of **PEU2b(Ph)-OH** is 21 °C as compared to 8 °C for the polymer before functionalization. The T_g of **PEU2b(Ph)-COOH** is 22 °C.

Prefunctionalization and Subsequent Polymerization of Functionalized Monomers. An alternative approach to provide functionalized degradable polymers is the conjugate addition of thiols to the unsaturated diols prior to polymerization. As a proof-of-concept, the thiol−ene reactions of **2a(Pr)** with 1-butanethiol and **2b(Ph)** with 1-dodecanethiol were investigated. The conjugate addition of thiols to the unsaturated diol was carried out by irradiation at 350 nm for 30 min in the presence of Irgacure 2959. The ^{1}H NMR spectra of the prefunctionalized diol monomers are shown in Figure 10.

The prefunctionalized diol monomers can be used to synthesize poly(ester urethane)s by copolymerizing with hexamethylene diisocyanate using $Sn(Oct)_2$ as catalyst. However, for the prefunctionalization method, the degree of polymerization (DP_n) of the poly(ester urethane) was much lower (average of 16) (Table 6) compared to that for the postfunctionalization method (average of 40). This relatively low efficiency is probably the result of increased steric hindrance present in the functionalized diol monomers. The chemical structure of the poly(ester urethane)s was characterized by ^{1}H NMR spectroscopy (Figure 11).

Synthesis of Functionalized Polyesters. The synthesis of unsaturated polyesters was problematic due to the high reactivity of the alkene groups. Our attempts, including $Sn(Oct)_2$-catalyzed melt polycondensation and DIC/DPTS-mediated polycondensation, were unsuccessful, which afforded cross-linked polymers that did not dissolve in common organic solvents such as chloroform, THF, or DMF. Contrary to the unsaturated diol monomers, the prefunctionalized diol monomers can undergo step-growth polymerization with succinic acid under carbodiimide mediated conditions to provide the corresponding polyesters (Scheme 6). The resultant polyester had a moderate molecular weight of 11.8 kg/mol for **PE2a(Pr)-nBu** and 8.3 kg/mol for **PE2b(Ph)-Dodecyl** (Table 6). The chemical structure of the polyester was characterized by ^{1}H NMR spectroscopy (Figure 11).

■ CONCLUSIONS

The Baylis−Hillman reaction provides an efficient platform for the synthesis of densely functionalized monomers, from which polymers with multiple functional groups can be readily synthesized. Although several classes of functionalized polymers can in principle be synthesized from Baylis−Hillman substrates, the current literature has only a few examples of polymers obtained from such substrates. In the above-described work, we showed that Baylis−Hillman substrates are versatile monomers for both controlled radical and step-growth polymerizations. We described the synthesis of various alkyl α-hydroxymethyl acrylates which underwent efficient RAFT polymerization to provide homo and copolymers with controlled molecular weight and low polydispersity. In addition we demonstrated that alkene functionalized diols synthesized from the Baylis−Hillman reaction underwent step-growth polymerization to provide polyesters and poly(ester urethane)s. The alkene group can be further functionalized (pre- or postpolymerization) to provide an additional functionality to the polymer.

The current work demonstrates the versatility of the Baylis−Hillman based monomers for the synthesis of functionalized polyacrylates, polyesters and poly(ester urethane)s. In addition to the polymers demonstrated here, several other polymers can also be synthesized by this strategy, including poly(α-hydroxymethyl vinylphosphonic acid), poly(α-hydroxymethyl acrylamide), and poly(α-hydroxymethyl acrylonitrile). Studies directed toward the synthesis and use of such polymers are currently underway in our laboratory.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

NMR, TGA, and DSC data. 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) Hawker, C. J.; Wooley, K. L. *Science* **2005**, *309*, 1200.

(2) Iha, R. K.; Wooley, K. L.; Nystrom, A. M.; Burke, D. J.; Kade, M. J.; Hawker, C. J. *Chem Rev* **2009**, *109*, 5620.

(3) Gao, H. F.; Matyjaszewski, K. *Prog. Polym. Sci.* **2009**, *34*, 317.

(4) Gauthier, M. A.; Gibson, M. I.; Klok, H. A. *Angew. Chem., Int. Ed.* **2009**, *48*, 48.

(5) Boyer, C.; Stenzel, M. H.; Davis, T. P. *J. Polym. Sci., Polym. Chem.* **2011**, *49*, 551.

(6) Tasdelen, M. A.; Kahveci, M. U.; Yagci, Y. *Prog. Polym. Sci.* **2011**, *36*, 455.

(7) Gokhale, S.; Xu, Y.; Joy, A. *Biomacromolecules* **2013**, *14*, 2489.

(8) Seyednejad, H.; Ghassemi, A. H.; van Nostrum, C. F.; Vermonden, T.; Hennink, W. E. *J. Controlled Release* **2011**, *152*, 168.

(9) Pounder, R. J.; Dove, A. P. *Polym. Chem.-U.K.* **2010**, *1*, 260.

(10) Dwan'Isa, J. P. L.; Lecomte, P.; Dubois, P.; Jerome, R. *Macromolecules* **2003**, *36*, 2609.

(11) Kim, H.; Olsson, J. V.; Hedrick, J. L.; Waymouth, R. M. *ACS Macro Lett.* **2012**, *1*, 845.

(12) Hahn, C.; Keul, H.; Moller, M. *Polym. Int.* **2012**, *61*, 1048.

(13) Sumerlin, B. S.; Tsarevsky, N. V.; Louche, G.; Lee, R. Y.; Matyjaszewski, K. *Macromolecules* **2005**, *38*, 7540.

(14) Beers, K. L.; Boo, S.; Gaynor, S. G.; Matyjaszewski, K. *Macromolecules* **1999**, *32*, 5772.

(15) Quirk, R. P.; Ma, J. J. *J. Polym. Sci., Polym. Chem.* **1988**, *26*, 2031.

(16) Willcock, H.; O'Reilly, R. K. *Polym. Chem.-U.K.* **2010**, *1*, 149.

(17) O'Bryan, G.; Ningnuek, N.; Braslau, R. *Polymer* **2008**, *49*, 5241.

(18) Matyjaszewski, K.; Nakagawa, Y.; Gaynor, S. G. *Macromol. Rapid Commun.* **1997**, *18*, 1057.

(19) Yuan, W. Z.; Yuan, J. Y.; Zhang, F. B.; Xie, X. M. *Biomacromolecules* **2007**, *8*, 1101.

(20) Hahn, C.; Keul, H.; Moller, M. *Macromol. Chem. Phys.* **2010**, *211*, 752.

(21) Feng, C.; Li, Y. J.; Yang, D.; Hu, J. H.; Zhang, X. H.; Huang, X. Y. *Chem Soc Rev* **2011**, *40*, 1282.

(22) Gao, C.; Yan, D. *Prog. Polym. Sci.* **2004**, *29*, 183.
(23) Voit, B. I.; Lederer, A. *Chem. Rev.* **2009**, *109*, 5924.
(24) Pugh, C.; Singh, A.; Samuel, R.; Ramos, K. M. B. *Macromolecules* **2010**, *43*, 5222.
(25) Rana, D.; Matsuura, T. *Chem. Rev.* **2010**, *110*, 2448.
(26) Koo, L. Y.; Irvine, D. J.; Mayes, A. M.; Lauffenburger, D. A.; Griffith, L. G. *J. Cell Sci.* **2002**, *115*, 1423.
(27) Joy, A.; Cohen, D. M.; Luk, A.; Anim-Danso, E.; Chen, C.; Kohn, J. *Langmuir* **2011**, *27*, 1891.
(28) Johnson, J. A.; Lu, Y. Y.; Burts, A. O.; Lim, Y. H.; Finn, M. G.; Koberstein, J. T.; Turro, N. J.; Tirrell, D. A.; Grubbs, R. H. *J. Am. Chem. Soc.* **2011**, *133*, 559.
(29) Tang, T.; Castelletto, V.; Parras, P.; Hamley, I. W.; King, S. M.; Roy, D.; Perrier, S.; Hoogenboom, R.; Schubert, U. S. *Macromol. Chem. Phys.* **2006**, *207*, 1718.
(30) Liu, J. Q.; Li, R. C.; Sand, G. J.; Bulmus, V.; Davis, T. P.; Maynard, H. D. *Macromolecules* **2013**, *46*, 8.
(31) Kale, T. S.; Klaikherd, A.; Popere, B.; Thayumanavan, S. *Langmuir* **2009**, *25*, 9660.
(32) Zhu, Y. Q.; Liu, L.; Du, J. Z. *Macromolecules* **2013**, *46*, 194.
(33) Fan, L.; Lu, H.; Zou, K.; Chen, J.; Du, J. *Chem. Commun.* **2013**, *49*, 11521−11523.
(34) You, Z.; Wang, Y. *Adv. Funct. Mater.* **2012**, *22*, 2812.
(35) Deng, M. X.; Wu, J.; Reinhart-King, C. A.; Chu, C. C. *Biomacromolecules* **2009**, *10*, 3037.
(36) Basavaiah, D.; Rao, P. D.; Hyma, R. S. *Tetrahedron* **1996**, *52*, 8001.
(37) Basavaiah, D.; Rao, A. J.; Satyanarayana, T. *Chem. Rev.* **2003**, *103*, 811.
(38) Basavaiah, D.; Veeraraghavaiah, G. *Chem. Soc. Rev.* **2012**, *41*, 68.
(39) de Souza, R. O. M. A.; Pereira, V. L. P.; Esteves, P. M.; Vasconcellos, M. L. A. A. *Tetrahedron Lett.* **2008**, *49*, 5902.
(40) Price, K. E.; Broadwater, S. J.; Jung, H. M.; McQuade, D. T. *Org. Lett.* **2005**, *7*, 147.
(41) Fort, Y.; Berthe, M. C.; Caubere, P. *Tetrahedron* **1992**, *48*, 6371.
(42) Drewes, S. E.; Emslie, N. D. *J. Chem. Soc., Perkins Trans. 1* **1982**, 2079.
(43) Hoffmann, H. M. R.; Rabe, J. *Angew. Chem., Int. Ed. Engl.* **1983**, *22*, 795.
(44) Kundu, M. K.; Mukherjee, S. B.; Balu, N.; Padmakumar, R.; Bhat, S. V. *Synlett* **1994**, 444.
(45) Amri, H.; Villieras, J. *Tetrahedron Lett.* **1986**, *27*, 4307−4308.
(46) Basavaiah, D.; Gowriswari, V. V. L. *Tetrahedron Lett.* **1986**, *27*, 2031.
(47) Amri, H.; Elgaied, M. M.; Villieras, J. *Synth. Commun.* **1990**, *20*, 659.
(48) Ji, S. H.; Bruchmann, B.; Klok, H. A. *Macromolecules* **2011**, *44*, 5218.
(49) Mathias, L. J.; Kusefoglu, S. H.; Kress, A. O. *Macromolecules* **1987**, *20*, 2326.
(50) Kress, A. O.; Mathias, L. J.; Cei, G. *Macromolecules* **1989**, *22*, 537.
(51) Zhang, Y. Q.; Shen, Z.; Yang, D.; Feng, C.; Hu, J. H.; Lu, G. L.; Huang, X. Y. *Macromolecules* **2010**, *43*, 117.
(52) Thang, S. H.; Chong, Y. K.; Mayadunne, R. T. A.; Moad, G.; Rizzardo, E. *Tetrahedron Lett.* **1999**, *40*, 2435.
(53) Stayshich, R. M.; Meyer, T. Y. *J. Polym. Sci., Polym. Chem.* **2008**, *46*, 4704.
(54) Yu, C. Z.; Liu, B.; Hu, L. Q. *J. Org. Chem.* **2001**, *66*, 5413.
(55) Lowe, A. B. *Polym. Chem.-U.K.* **2010**, *1*, 17.