Communications to the Editor

Multifunctional Initiators Containing Orthogonal Sites. One-Pot, One-Step Block Copolymerization by Simultaneous Free Radical and Either Cationic Ring-Opening or Anionic Ring-Opening Polymerization

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The preparation of block copolymers from monomers that polymerize by different mechanisms has been a challenge facing polymer chemists for many years.[1] Often, either the mechanisms are inherently incompatible or the reaction conditions are significantly different. Currently, block copolymers are prepared by coupling preformed polymers, by sequential addition of monomers to a living initiator or by using a mixture of monomers having substantially different rates of polymerization.[1a,2] Where two different polymerization mechanisms are involved the living end of the first block has to be transformed into an appropriate reactive group capable of initiating polymerization of the second monomer.[2] In many cases, the block copolymer is contaminated by homopolymers due to inefficient initiation of the second stage polymerization, chain transfer, or termination. Our objective in this study is to develop a general one-pot, one-step method for the synthesis of block copolymers by simultaneous initiation of two or
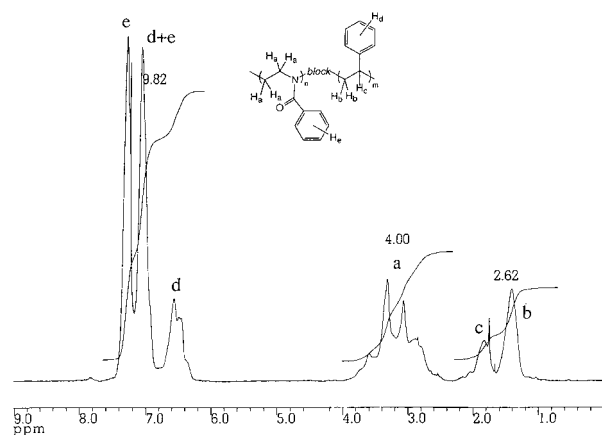

Figure 1. ^{1}H NMR (300 MHz) spectrum in $CDCl_3$ of the polymer from run no. 2, Table 1, showing the presence of both polystyrene (PS) and poly(2-phenyl-2-oxazoline) (PPhOXA). Integration of the appropriate peaks gave PhOXA:S = 1.14

more polymerization mechanisms and, by so doing, eliminate the need for intermediate steps. This requires, among other things, that the different monomers polymerize under similar reaction conditions and by mechanisms that neither cross over nor interfere with each other.

We have recently reported the synthesis of multifunctional initiators **1−4** (Chart 1) all of which possess initiating sites for more than one type of polymerization.[3] For example, **1** possesses initiating sites that can be independently and selectively utilized for free radical, anionic, anionic ring-opening, and cationic ring-opening
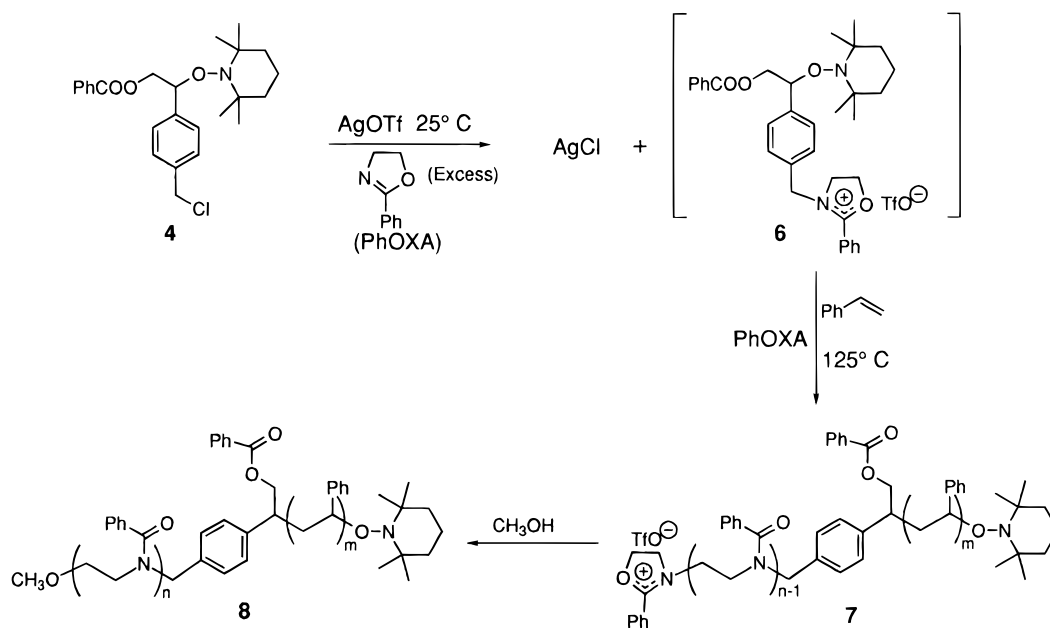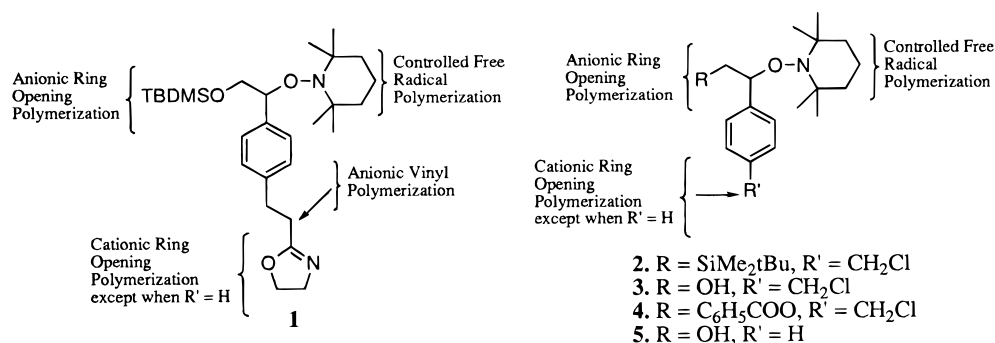
Scheme 1

Chart 1

2. R = SiMe$_2$tBu, R' = CH$_2$Cl
3. R = OH, R' = CH$_2$Cl
4. R = C$_6$H$_5$COO, R' = CH$_2$Cl
5. R = OH, R' = H

Table 1. Polymerization Conditions and Results[a]

run no.	initiator (mmol)	PhOXA[b] (mmol)	S[c] (mmol)	yield (%)	S/PhOXA (NMR)[d]	M_n(calc)[e] $\times 10^{-3}$	M_n(GPC)[f] $\times 10^{-3}$	PDI	S:PhOXA (DP)[g]
1	0.12	11.4	0	>99	0	14.0	26.8	1.32	0:182
2	0.13	11.4	13.1	80	0.87	18.7	28.0	1.36	102:118
3	0.11	3.8	21.8	45	7.50	11.6	24.3	1.27	198:25
4	0.13	19.0	4.4	99	0.14	25.0	33.5	1.40	29:207

[a] Polymerization was performed neat at 125 °C for 18 h. [b] 2-Phenyl-2-oxazoline. [c] Styrene. [d] Molar ratio obtained by integrating the aliphatic region of PS (1–2.3 ppm) relative to that of PPhOXA (2.4–4 ppm). [e] Molecular weight calculated based on the percent yield and the relative amounts of the monomers obtained from NMR. [f] Gel permeation chromatography was performed in *N*,*N*-dimethylacetamide with respect to PS standards. [g] Degree of polymerization of each segment based on M_n from GPC and molar ratios from NMR.

Scheme 2
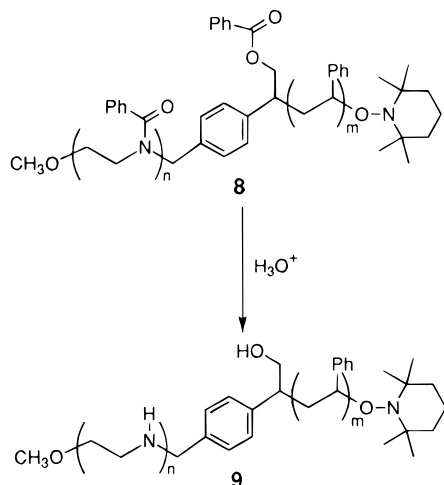
polymerizations. The reactive sites survived several different polymerization conditions enabling successful preparation of block and graft copolymers of vinyl pyridine, styrene, and 2-oxazolines.[3] Even though the use of **1** eliminated the need for intermediate steps and chain end transformations and a preliminary one-pot simultaneous polymerization of oxazoline and styrene monomers was reported for initiator **2**,[3a] conclusive data are available for only the sequential process.[3,4] We now report that a one-step, one-pot simultaneous block copolymerization involving different polymerization mechanisms is, indeed, feasible and is generally applicable to several mechanisms. The concept is illustrated herein for simultaneous nitroxide-mediated free radical polymerization[5] and either cationic ring-opening[6] or anionic ring-opening polymerization to produce poly-(styrene-*b*-2-phenyl-2-oxazoline) and poly(styrene-*b*-ε-caprolactone). Since the appearance of our report in print[3] and since the completion of the work described herein, Hawker, Jérôme, and co-workers reported a complementary method involving simultaneous dual anionic ring-opening and living/controlled free radical

polymerizations using **5** to prepare block copolymers of caprolactone (CL) and styrene (S).[7]

The simultaneous cationic ring-opening and controlled free radical polymerizations were accomplished in the following manner:[8] First, **4** was treated with silver triflate (AgOTf) followed by addition of excess PhOXA at 25 °C. This led to the formation of the corresponding triflate salt **6** (not isolated) in a pool of PhOXA (Scheme 1). Second, styrene was added to the mixture of **6** and PhOXA at 25 °C followed by heating the mixture at 125 °C overnight. Simultaneous polymerization of both monomers occurred to give **7**. Finally, **7** was quenched with methanol to give **8** in moderate to excellent isolated yield. The ^{1}H NMR spectrum of **8** in CDCl$_3$ (Figure 1) showed the presence of both segments in approximately 1:1 ratio. In absence of AgOTf the reaction was too slow to be practical probably due to the benzyl chloride operating by the so-called covalent mechanism.[6,9,10]

Table 1 summarizes the polymerization conditions and results. The molecular weights determined by size exclusion chromatography (SEC) in DMAC with respect to PS were moderate with the degree of polymerization (DP) for each block varying over a broad range: S$_m$(PhOXA)$_n$ with $m = 29$–198 and $n = 25$–207. In all cases, the polydispersity indices (PDI) were relatively low (1.27–1.40). The M_n(SEC) values were, however, slightly higher than M_n(calc) (based on percent conversion and the actual styrene/PhOXA incorporated (from NMR)). This is probably because either PS standards are not exactly appropriate for these block copolymers or there were chain termination reactions taking place to some extent which are known for the above polymerization processes).[5,6] The SEC traces of the samples especially polymers containing vastly different relative block lengths (S:PhOXA = 198:25 to 29:207, runs 3 and 4, Table 1) were unimodal. Furthermore, Soxhlet extraction of PS$_{198}$-*b*-P(PhOXA)$_{25}$ with methanol and PS$_{29}$-*b*-P(PhOXA)$_{207}$ with cyclohexane left their compositions and molecular weights unchanged as evidenced by their ^{1}H NMR spectra which showed both segments and SEC traces which remained unimodal.[11] This is

Table 2. Thermal Analyses Data from DSC and TGA

sample no.	polymer[a]	T_g (°C)	T_m (°C)
1	P(PhOXA)$_{182}$	109	237
2	PS$_{102}$-b-P(PhOXA)$_{118}$	104	237
3	PS$_{198}$-b-P(PhOXA)$_{25}$	103	237
4	PS$_{29}$-b-P(PhOXA)$_{207}$	109	235
5	PS$_{198}$-b-PEI$_{25}$	82	None
6	PS$_{29}$-b-PEI$_{207}$	−2	None

[a] Polymer samples with degrees of polymerization (DP) for each block given as subscripts. PEI refers to poly(ethylenimine) obtained by hydrolysis of poly(-2-phenyl-2-oxazoline) block.
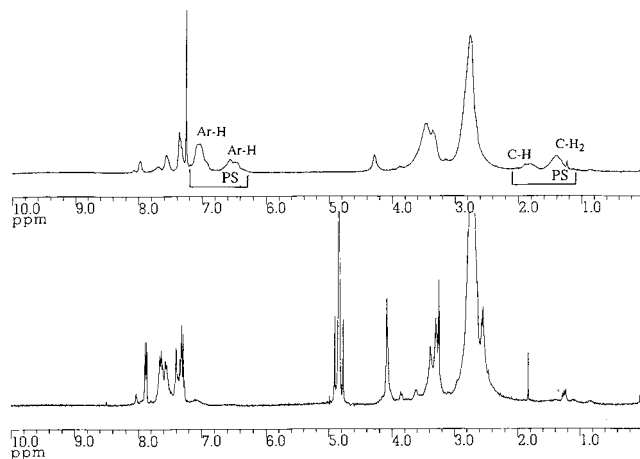

Figure 2. Comparison of the ^{1}H NMR (300 MHz) spectrum of the hydrolyzed polymer (sample no. 6, Table 2) in CDCl$_3$ (a) and CD$_3$OD (b). The peaks due to PS at 1.2−2 and 6.3−7.2 ppm in part a are absent in part b.

taken as evidence for the absence of homopolymers.

To provide further evidence for the formation of block copolymers, the oxazoline segment was hydrolyzed (Scheme 2) in either aqueous hydrochloric acid (PS$_{29}$-b-P(PhOXA)$_{207}$) or dioxane (PS$_{198}$-b-P(PhOXA)$_{25}$) to give the corresponding PS$_{29}$-b-poly(ethylene imine)$_{207}$ (PS$_{29}$-b-PEI$_{207}$, sample no. 6, Table 2) and PS$_{198}$-b-PEI$_{25}$ (sample no. 5, Table 2; M_n (SEC) = 17 800, PDI = 1.25), respectively.[12] The dissimilar polarities of the blocks allowed for purification of the hydrolyzed polymer by dialysis against water. Remarkably, the SEC traces from both UV and RI detectors were found to be superimposable on each other and showed no evidence of low MW peak. The non-UV-active PEI would have given a peak in a different region if it were not attached to PS especially since the molecular weights of the blocks differed by an order of magnitude. The results thus far obtained strongly indicate that the two segments are attached to each other.

The hydrolyzed polymers (**9**) will be amphiphilic and expected to exhibit micellar behavior only if they are block copolymers. Such micellar behavior has been demonstrated for other polymers by examining their behavior in different solvents using ^{1}H NMR spectroscopy.[13] For our studies, the polymer with the shortest PS segment (PS$_{29}$-b-PEI$_{207}$) was used since it dissolved completely in methanol to give a homogeneous solution. Figure 2 shows the ^{1}H NMR spectra in CDCl$_3$ (part a) and CD$_3$OD (part b). Clearly, no signal due to PS was observed in the polar CD$_3$OD while in CDCl$_3$ signals due to both segments were detected. Even when the CD$_3$OD solution was evaporated to dryness and the residue redissolved in CDCl$_3$ the NMR spectrum of the recovered sample was identical to that in Figure 2a. The results suggest that the hydrophobic PS block is sur-

rounded by the hydrophilic PEI and, thus, protected from the polar methanol molecules. This confirms the micellar behavior of the hydrolyzed polymers and provides conclusive evidence that these are, indeed, block copolymers. The solution behavior is reminiscent of protein behavior in water where hydrophobic groups are kept in the interior of the protein and away from water molecules.[14] Our results are consistent with those reported by Meijer and co-workers for the micellar behavior of their amphiphilic PS−PEI dendrimer.[13a]

Table 2 shows the thermal data for the various samples. All of the unhydrolyzed polymers showed two transitions: T_g = 103−109 °C and T_m = 235−237 °C. The independently prepared P(PhOXA) (run 1, Table 1) gave T_g = 109° and T_m = 237 °C (Lit.[15a] T_g = 107 °C; T_m = 210 °C). The reason for the discrepancy in the T_m is not clear to us but the values for all our samples are approximately the same and internally consistent. The T_g's of PS (100 °C[15b]) and PPhOXA are too close to be resolved in the DSC. In the case of the hydrolyzed polymers, the block lengths were apparently too short to give separate T_g's. Thus, sample no. 5 which is mostly PS gave T_g = 82 while sample no. 6 (mostly PEI) gave T_g = −2 °C (Lit.[16] T_g (PEI) = −23.5 °C). For comparison, the T_g's of the hydrolyzed copolymers were estimated from the T_g's of the homopolymers to be approximately 90° and −7 °C, respectively.

The simultaneous anionic ring-opening and controlled free radical polymerizations were demonstrated for ϵ-caprolactone and styrene. In the reported preliminary work of Hawker, Jérôme, and co-workers concerning the dual polymerization of styrene and CL, they used Sn-(oct)$_2$ as catalyst and **5** as initiator.[7] Since Sn(oct)$_2$ can initiate lactone polymerization,[17] we preformed the alkoxide multifunctional initiator by reacting **5** with Et$_3$Al in the absence of CL in order to prevent or minimize homopolymer formation. When this was allowed to react at 125 °C with a mixture of CL and styrene, PS$_{113}$-b-PCL$_{92}$ (M_n(calc) = 24 600, M_n(SEC) = 22 300, PDI = 1.55) was produced in 75% yield. Similarly, PS-b-PCL (S:CL = 2:1) was prepared with M_n(SEC) = 84 760 and PDI = 1.28. The method was used to generate a library of diblock copolymers with number-average molecular weights varying from 12 800 to 90 000 in various monomer ratios. These results confirm the generality of the approach, and their details will be published subsequently.

In conclusion, we have shown that the multifunctional initiator approach to block copolymer synthesis is not limited to sequential polymerization involving different mechanisms but is also applicable to one step, one-pot block copolymer production. Further work is in progress regarding application to other polymerization mechanisms.

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(8) *Typical simultaneous polymerization of styrene and PhOXA*: A round-bottom flask fitted with a condenser and stirring bar was charged with **4** (54.0 mg, 0.13 mmol) and AgOTf (41.3 mg, 0.16 mmol). The vessel was purged for 15 min with argon. Then PhOXA (1.5 mL, 1.67 g, 11.4 mmol) was added via a syringe followed by addition of styrene (1.5 mL 1.36 g, 13.1 mmol). The reaction mixture was placed in a preheated thermostated bath at 125 °C and stirred for 44 h. The solid polymer was cooled, dissolved in 20 mL of CH_2Cl_2, and treated with 1 mL of MeOH. The solution was filtered to remove AgCl and then poured into a 10-fold excess of hexane. The precipitate that formed was collected by vacuum filtration, redissolved in CH_2Cl_2, and precipitated into hexanes/ethyl acetate (9/1, v/v). The polymer was dried under vacuum overnight to yield 2.47 g (80%) of polymer. ^1H NMR (300 MHz, $CDCl_3$): δ 1.2−1.6 ($PS-CH_2$), 1.6−2.2 ($PS-CH$), 2.5−4 (br, $P(PhOXA)-CH_2$), 6.3−6.8 ($PS-ArH$), 6.8−7.2 (ArH's for PS + P(PhOXA)), 7.2−7.5 (P(PhOXA)−ArH); styrene:PhOXA = 0.87. SEC (DMAC, PS std): M_n = 28 000, PDI = 1.36; M_n(calc) = 18 700. DSC: T_g = 104 °C, T_m = 237 °C. SEC was performed on a Viscotek GPC equipment with a model 200 differential refractometer, an on-line viscometer, and two linear mixed-bed columns and one 500 Å column (10 μm). *Hydrolysis of PS_{29}-b-P(PhOXA)$_{207}$*: The polymer (1.523 g) was charged to a round-bottom flask, and 60 mL of water and 15 mL of concentrated HCl were added. The mixture was refluxed for 48 h. After cooling, it was bought to pH 10 (pH paper) using 1 M KOH and then dialyzed in a cellulose acetate membrane with molecular weight cutoff of 2000. The solution after dialysis showed pH = 7. The bulk of the water was removed in vacuo, and then the reaction was lyophilized to dryness.

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