Synthesis of Monodisperse α-Hydroxypoly(styrene) in Hydrocarbon Media Using a Functional Organolithium

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Introduction

Functional initiators for living anionic polymerization of diene and styrenic monomers provide access to end-functionalized polymers and block copolymers that find widespread applications in coatings, adhesives, sealants, and asphalt modifiers.[1] In 1991, ω-(*tert*-butyldimethylsilyloxy)-1-alkyllithiums were introduced as "protected" anionic polymerization initiators and enabled the synthesis of α-functionalized semi-telechelic polymers.[2] Compounds of this type, particularly 3-*tert*-butyldimethysilyloxy-1-propyllithium (*t*BDMSOPrLi), have been widely used to prepare functionalized polymers, as the silyl protecting group is readily removed by postpolymerization treatment with hydrochloric acid or fluoride sources (e.g., tetra(*n*-butyl)ammonium fluoride (TBAF)) to unmask the latent hydroxyl group.[3−10] Nearly monodisperse hydroxy-functionalized 1,4-polybutadiene and 1,4-polyisoprene homopolymers have been synthesized with *t*BDMSOPrLi.[3,5] Functionalized polystyrene (PS) with a narrow molecular weight distribution is readily produced at low temperatures in tetrahydrofuran,[9] but the use of cyclohexane as a reaction medium yields PS samples with relatively broad molecular weight distributions ($M_w/M_n > 1.3$).[3] The inability to produce nearly monodisperse PS in nonpolar media limits access to well-defined telechelic styrenic block copolymers containing 1,4-polydiene blocks. Quirk and coworkers attributed these broad molecular weight distributions to slow initiation kinetics that result from intermolecular association of the *t*BDMSOPrLi with the propagating organolithium through coordination of the silyl ether oxygen to the electrophilic lithium cations.[8]

In this Note, we report the synthesis of 3-triisopropylsilyloxy-1-propyllithium (TIPSOPrLi) and characterize its activity in anionic styrene polymerizations at 40 °C in cyclohexane. Our approach is predicated on the notion that the increased steric bulk of the triisopropylsilyl protecting group[11] will reduce the possibility of intermolecular aggregation and increase the rate of styrene initiation. The TIPSOPrLi initiator is used to prepare α-hydroxypoly(styrene) in cyclohexane with significantly narrower polydispersities than are possible with *t*BDMSOPrLi under comparable conditions. Since polar modifiers are not required to obtain nearly monodisperse polymers, the TIPSOPrLi initiator enables facile synthesis of well-defined styrene/diene block copolymers with predominantly 1,4-diene regiochemistry.

Experimental Section

Materials. Standard Schlenk techniques were used to manipulate all moisture- and air-sensitive compounds under a high-purity argon atmosphere. Imidazole, anhydrous *N*,*N*-dimethylformamide, tetrahydrofuran (THF), tetra(*n*-butyl)ammonium fluoride (TBAF), *tert*-butyldimethylchlorosilane, and lithium (3.2 mm diameter wire with 0.5−1.% Na in mineral oil) were purchased from Aldrich and used as received. Triisopropylchlorosilane (Gelest) was used as received without further purification. Styrene (Aldrich) and 1,5-cyclooctadiene (Aldrich) were vacuum transferred from di-*n*-butylmagnesium at 40 °C to remove inhibitors and trace water. Cyclohexane was purified by sequential passage through activated alumina followed by Q-5 (Englehard) to remove protic impurities and trace oxygen.[12] Triisopropylsilyloxy-1-chloropropane (TIPSOPrCl; bp 75 °C/185 mTorr) and *tert*-butyldimethylsilyloxy-1-chloropropane (*t*BDMSOPrCl; bp 68 °C/1100 mTorr) were prepared by a modification of a previously reported procedure;[13] both compounds were purified by fractional vacuum distillation instead of silica gel chromatography to facilitate scalable synthesis.

Standard ^{1}H NMR spectra in $CDCl_3$ acquired on a Varian UI-300 spectrometer were referenced to the residual protiated solvent peak. "No-D" ^{1}H NMR spectra[14,15] were acquired on a Varian UI-500 spectrometer in cyclohexane using 1,5-cyclooctadiene as both a chemical shift reference (δ 5.58 ppm) and an internal standard to determine analyte concentrations. The latter experiments employed an acquisition time of 25 s and a pulse repetition delay of 35 s.

Room temperature size-exclusion chromatography (SEC) analyses employing THF as the mobile phase (flow rate 1.0 mL/min) were performed on a Waters 717 GPC equipped with three Polymer Labs Mixed-C columns and a Waters 410 differential refractometer. A calibration curve constructed using 10 polystyrene standard samples with M_n ranging from 580 to 377 400 g/mol (Polymer Labs) was used to determine the molecular weights and polydispersities of all polymers.

Triisopropylsilyloxy-1-propyllithium. Lithium (2.55 g, 0.37 mol) was placed in a 500 mL three-neck round-bottom flask equipped with a Telfon-coated stirbar (1 $^1/_2$ in. × $^3/_8$ in.), a condenser, and a pressure equalizing addition funnel. The surface of the lithium metal was prepared by the following two-step procedure to ensure reliable reactivity: (i) the wire was stirred vigorously for 1 h with cyclohexane (50 mL) to remove the mineral oil, before decanting the solution; (ii) the wire was treated with fresh cyclohexane (50 mL) and stirred vigorously overnight at 22 °C to activate the surface by mechanical abrasion. The second cyclohexane wash was decanted, and fresh cyclohexane (50 mL) was added to the lithium as the reaction solvent. The pressure equalizing addition funnel was then charged with triisopropylsilyloxy-1-chloropropane (6.45 g, 0.026 mol), which was added dropwise to the lithium in cyclohexane at 40 °C over 0.5 h. [NOTE: *Beware of unpredictable initiation period.* The reaction may initiate slowly, and the rapid addition of the triisopropylsilyloxy-1-chloropropane can lead to uncontrollable exotherms.] Occasionally, a slight exotherm (1−2 °C) in the temperature bath was observed; in such cases, the addition was slowed to maintain a constant reaction temperature. Upon complete addition, the reaction was heated to 60 °C until "No-D" ^{1}H NMR of reaction aliquots indicated complete consumption of the starting material (up to 31 h). The reaction was cooled to 22 °C and Schlenk filtered through a pad of Celite to yield a transparent, faint yellow or orange solution of the organolithium reagent.

^{1}H NMR (500 MHz, C_6H_{12}, 22 °C): δ (ppm) 3.85 (br *m*, 2H, $Si{-}O{-}CH_2$), 2.20 (br *m*, 2H, $O{-}CH_2CH_2CH_2Li$), −0.73 (br *m*, 2H, $-CH_2Li$). Final concentration: 0.55 M based on the COD internal reference.

3-*tert*-Butyldimethylsilyloxy-1-propyllithium. The *t*BDMSOPrLi initiator was synthesized using the TIPSOPrLi procedure, except *t*BDMSOPrCl was used instead of TIPSOPrCl.

^{1}H NMR (500 MHz, C_6H_{12}, 22 °C): δ (ppm) 3.83 (br *m*, 2H, $Si{-}O{-}CH_2$), 2.18 (br *m*, 2H, $O{-}CH_2CH_2CH_2Li$), −0.80 (br *m*,

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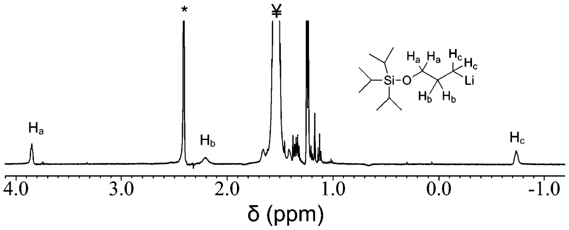

Figure 1. Truncated ^{1}H NMR spectrum of the TIPSOPrLi initiator in cyclohexane, with the peaks corresponding to the propyl protons on the initiator labeled H_a, H_b, and H_c. The cyclohexane resonance is marked with a ¥, and the sharp peak labeled * corresponds to protons on the 1,5-cyclooctadiene used to reference the spectrum and determine the concentration of the initiator solution.

2H, $-CH_2Li$). Final concentration: 0.18 M based on the COD internal reference.

α-Hydroxypoly(styrene) Synthesis. Anionic polymerization of styrene at 40 °C in cyclohexane was initiated by *t*BDMSOPrLi or TIPSOPrLi. In a typical "unseeded" polymerization, TIPSOPrLi (3.5 mL) was added to cyclohexane (500 mL) thermostated at 40 °C. After 15 min, styrene monomer (12.8 g) was added and allowed to react for 8 h at 40 °C. Reactions were terminated by the addition of degassed MeOH (10 mL), and the polymer was isolated by precipitation in MeOH (1.5 L), followed by freeze-drying from C_6H_6. In the freeze-drying process, the polystyrene was dissolved in 200 mL of C_6H_6 and placed in a stainless steel beaker (500 mL). The beaker was partially submerged in liquid nitrogen to freeze the solution, and the polymer was freeze-dried overnight in a vacuum oven until the pressure reached the baseline oven pressure (500 mTorr). In "seeded" reactions, three aliquots of styrene monomer (0.5 g) initially were added at 20 min intervals before the balance of the monomer was added to the reaction.

The resultant trialkylsilyloxypoly(styrene) (10 g) was dissolved in THF (100 mL) and treated with excess TBAF (10 equiv per Si) for 48 h at 22 °C. The THF was removed using a rotary evaporator. The polymer was redissolved in CH_2Cl_2 (200 mL), and aqueous extractions (3 × 200 mL) of the solution were used to remove any residual salts. The washed polymer was recovered by precipitation in MeOH from the CH_2Cl_2 solution, dissolved in C_6H_6, and freeze-dried.

Results and Discussion

The reaction between a silyloxy-protected alkyl chloride and elemental lithium is very sensitive to the condition of the lithium surface. We found that lithiation of TIPSOPrCl or *t*BDMSOPrCl does not proceed without first preparing the lithium wire by vigorously stirring it in cyclohexane overnight to mechanically abrade the surface and expose fresh metal. Bromobutane, in contrast, lithiates without any special surface preparation. Tong et al. previously noted a similar sensitivity in the synthesis of *t*BDMSOPrLi using a mineral oil dispersion of lithium and reported washing the lithium repeatedly to obtain "a silvery metal surface".[6]

The use of "No-D" ^{1}H NMR enabled real-time monitoring of the progress of the lithiation reaction and final determination of the concentration of the initiator solution.[14,15] Previous syntheses of *t*BDMSOPrLi employed a reaction time of 2 h at 60 °C with Gilman double-titration assays to confirm the presence of an active organolithium; however, the initiator solution was not analyzed with any other techniques.[1,6] The full ^{1}H NMR spectrum of the TIPSOPrLi solution is presented in Figure 1, in which the upfield peak at −0.73 ppm associated with protons bound to the carbanionic center indicates lithiation has occurred.[15] A portion of the ^{1}H NMR spectrum of the TIPSOPrLi solution at five different reaction times is presented in Figure 2. The broad initiator multiplet (δ 3.85 ppm, H_a in Figure 2) increases in intensity, while the sharp TIPSOPrCl triplets (δ 3.93 ppm, δ 3.68 ppm, H_d and H_e, respectively, in Figure 2) concurrently diminish in intensity as the reaction progresses. It is crucial that all of the TIPSOPrCl is consumed during lithiation since the alkyl halide starting material can serve as a chain termination agent in anionic polymerizations. The reaction time necessary to achieve complete lithiation varied for every batch of initiator prepared. Although the source of this variation was not identified, we speculate that variability in the condition of the lithium surface results in different reaction rates. "No-D" ^{1}H NMR serves as a convenient means of monitoring the extent of reaction and confirming complete consumption of TIPSOPrCl.

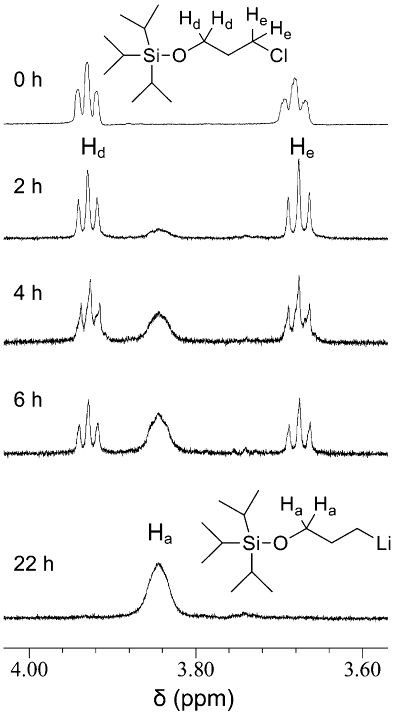

Figure 2. ^{1}H NMR spectra of the TIPSOPrLi at five different reaction times. The TIPSOPrCl peaks diminish in intensity as the starting material is consumed, while the TIPSOPrLi peak grows in intensity as the initiator is produced.

Table 1. Styrene Polymerizations Using Two Functionalized Initiators

initiator	initiation strategy[a]	M_n (kg/mol)[a]	expected M_n (kg/mol)[b]	M_w/M_n[c]	F_n[d]
*t*BDMSOPrLi	unseeded	4.8	5.0	1.40	0.96
*t*BDMSOPrLi	seeded	6.0	5.0	1.30	1.03
*t*BDMSOPrLi	seeded	7.1	6.8	1.32	0.99
TIPSOPrLi	unseeded	7.1	6.9	1.33	0.95
TIPSOPrLi	seeded	4.0	4.9	1.22	0.87
TIPSOPrLi	seeded	6.8	6.9	1.11	1.01
TIPSOPrLi	seeded	8.7	8.5	1.10	1.10
TIPSOPrLi	seeded	10.2	9.7	1.08	0.98
TIPSOPrLi	seeded	16.5	unknown[e]	1.07	0.95

[a] See Experimental Section. [b] Calculated using the initiator concentration and the amount of styrene added. [c] Measured using size exclusion chromatography against polystyrene standards at 22 °C in a tetrahydrofuran mobile phase. [d] Calculated using the M_n values measured using (1) size exclusion chromatography against polystyrene standards and (2) ^{1}H NMR end-group analysis. [e] The syringe containing the TIPSOPrLi leaked as the initiator was injected into the reactor, making the added TIPSOPrLi volume unknown.

The polydispersities and molecular weights of the end-functionalized PS initiated using *t*BDMSOPrLi and TIPSOPrLi in cyclohexane are reported in Table 1. Some researchers have suggested that "seeding" the initiator by mixing a small fraction of monomer with all of the initiator can prevent the broadening

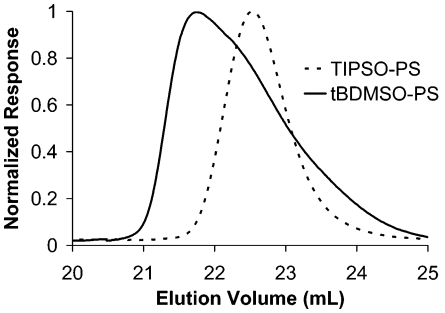

Figure 3. SEC traces of the TIPSO-PS ($M_n = 6.8$ kg/mol) and *t*BDMSO-PS ($M_n = 7.1$ kg/mol) synthesized using the "seeding" technique.

of the molecular weight distribution that results from initiation kinetics that are slow relative to the rate of propagation.[16,17] Although the efficacy of this "seeding" strategy has been questioned,[18] the polydispersities we obtained using both *t*BDMSOPrLi and TIPSOPrLi clearly narrowed with the use of the "seeding" technique. The "seeding" strategy has only a limited effect on reactions initiated with *t*BDMSOPrLi, as the polydispersities remain significantly higher than the values typically obtained for living anionic polymerizations using *sec*-butyllithium ($M_w/M_n < 1.1$).[19] The measured polydispersity index for the 4.0 kg/mol TIPSO-PS ($M_w/M_n = 1.22$) was higher than the measured polydispersity indices for the TIPSO-PS samples with $M_n \geq 6.8$ kg/mol ($M_w/M_n \leq 1.11$). This increase may not reflect a lower molecular weight limit for achieving narrow polydispersity indices using the "seeding" technique given the variations in the concentrations of TIPSOPrLi and styrene for different polymerizations. The relative rates of initiation and propagation of polystyrene in cyclohexane may depend on the concentration of either the initiator or the monomer (or both) when using *t*BDMSOPrLi or TIPSOPrLi.[17]

The SEC traces of functional polystyrene samples synthesized using the "seeding" strategy with *t*BDMSOPrLi ($M_n = 7.1$ kg/mol) and TIPSOPrLi ($M_n = 6.8$ kg/mol) are presented in Figure 3. The TIPSO-PS molecular weight distribution is significantly narrower than that of the *t*BDMSO-PS. We attribute the narrower molecular weight distribution of the TIPSO-PS to an increase in the rate of styrene initiation and suggest that this enhanced initiation rate is due to a reduction in intermolecular association that results from coordination of the silyl ether oxygen to lithium. The use of the more sterically hindered TIPSOPrLi, along with the "seeding" technique to initiate polymerizations, facilitates the synthesis of nearly monodisperse protected polystyrene in cyclohexane.

Functionalized alkyllithium initiators derive their value from the ability to install a protected group that can be readily converted into an α-functionality on every polymer chain. The degree of functionality (F_n) can be assessed by comparing the molecular weight of the polystyrene measured using ^{1}H NMR end-group analysis and that measured by SEC using PS standards. The F_n values for all of the polystyrene samples are presented in Table 1. All of the values are within 13% of $F_n = 1.0$, indicating one TIPS group is present on each polystyrene chain. Treatment with TBAF under mild conditions cleaves the silyl ether to unmask a hydroxyl functionality, a common treatment applicable to TIPS and *t*BDMS functionalities.[11] The absence of the ^{1}H NMR resonance at 0.98 ppm corresponding to the isopropyl protons of the TIPS group after TBAF treatment indicates complete deprotection to produce α-hydroxypoly(styrene) with a narrow molecular weight distribution.

Well-defined telechelic block copolymers containing 1,4-polydiene blocks can be synthesized from the nearly monodisperse living polystyrene; we are currently using the TIPSOPrLi initiator to synthesize a variety of these macromolecules. For example, we prepared an α,*ω*-dihydroxypoly(styrene-*b*-isoprene-*b*-styrene) triblock copolymer ($M_n = 32.5$ kg/mol, $M_w/M_n = 1.09$) that contained 93.7% 1,4-polyisoprene linkages in cyclohexane via sequential addition of styrene, isoprene, and styrene followed by ethylene oxide end-capping using the TIPSOPrLi initiator along with the "seeding" technique. An aliquot from the reactor was taken to analyze the initial polystyrene block ($M_n = 8.7$ kg/mol, $M_w/M_n = 1.10$, both based on calibration with PS standards), and TBAF was used to cleave the silyl ether and unmask the latent α-hydroxyl group.

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