Synthesis and Characterization of Amphiphilic Poly(urethaneurea)-*comb*-polyisobutylene Copolymers

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ABSTRACT: In this paper we describe the synthesis and characterization of modified polyurethaneurea−polyether (PEUU) multiblock copolymers, designed to elicit lower permeability to water vapor and gases. The approach was to create polyisobutylene (PIB) segments, which were linked to the PEUU copolymer as combs. Macromonomers of PIB were synthesized, containing two hydroxyl sites on the initiating ends of the molecules for subsequent condensation polymerization. By using a polymerization scheme that offered no termination and no chain transfer, the PIB macromonomer would be assured of having two (and only two) hydroxyl groups. Characterization of the macromonomers and their precursors was performed by GPC, ^{1}H NMR, and FTIR. Using these products, amphiphilic copolymers, with a polyurethaneurea−polyether multiblock backbone and polyisobutylene combs, were synthesized by a condensation reaction. PIB incorporation varied between about 2 and 30%, with comb lengths ranging from ∼3000 to 29 000 g/mol. Characterization of this new multiblock multicomb copolymer was performed by GPC, FTIR, solid state ^{13}C NMR, and Soxhlet extraction techniques.

Introduction

Poly(ether urethaneurea) segmented block copolymers (PEUU) are used in a variety of biomedical applications, most prominently as blood sacs in ventricular assist devices and total artificial hearts.[1] These materials are solution-processable elastomers that exhibit good mechanical properties, while simultaneously exhibiting good in vivo biocompatibility. One undesirable characteristic however is the relatively rapid permeation of air and water vapor through PEUU membranes, e.g., ref 2.

One approach to resolving this problem, the focus of this research, consists of synthesizing a polymer that has a backbone essentially identical to the PEUU copolymer, but which also possesses polymeric combs of a material with superior barrier properties. The PEUU backbone should render the new copolymer "compatible" with existing PEUU multiblock copolymers, while the combs, which are anticipated to microphase separate, should reduce the transport of air and water vapor. The combs could also be designed to increase compatibility with an external barrier layer; i.e., the comb polymer could act as an effective tie layer between biocompatible PEUU and a barrier film. Polyisobutylene (PIB) was chosen as the comb material in our work due to the combination of its good barrier properties with respect to air and water, its controllable (living cationic) polymerization, and its mechanical properties.

There are a number of possible routes for attaching PIB chains to PEUUs. One approach is to perform a post-polymerization grafting reaction, reacting a site on the PIB chains to an active site on the polymer backbone.[3] Another option is to perform a post-fabrication grafting reaction, which leads to the selective attachment of PIB chains to the surface of a film or form.[4] [For additional background on telechelic PIBs and incorporation of PIB soft segments into polyurethane copolymers see, for example, refs 5−9.] In this paper we describe an alternative approach: the attachment of PIB chains as combs during the formation of the multiblock PEUU backbone. To this end, a polyisobutylene macromonomer with dual functionality at one end of the molecule (for subsequent condensation polymerization) was synthesized. It is possible for the functional groups to be incorporated onto either the initiating or terminating end of the molecule. An initiator was designed so that the difunctionality was placed on the initiating end, in order for it to be well characterized and present throughout the reaction. This unique initiator possessed one site for initiating the polyisobutylene polymerization and two protected sites for subsequent polymerization. If any chain transfer occurred, PIB chains would either have two functional groups or none. To decrease the possibility of chain transfer or termination occurring, the reaction conditions were deliberately chosen to be as similar as possible to those of known living cationic systems. Once the polymerization took place, the two protected sites were converted to form an α,α′-dihydroxy-polyisobutylene, the desired macromonomer.

Having synthesized the functionalized PIB macromonomer in varying molecular weights, the next step was to copolymerize the macromonomers with the PEUU monomers. This results in the formation of a multiblock backbone with PIB combs. The synthetic method mimics, as closely as was possible/practical, the reaction conditions for conventional biomedical PEUUs. As such, the relative ratio of reactants was kept at 1:2:

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1, diol:diisocyanate:diamine. A one-pot, two-step synthesis scheme was adapted. A mixture of 25/75 v/v dimethylacetamide/*m*-xylene was used to solubilize the reactants (and products) as much as possible. At elevated temperatures, the telechelic polyether diol macromonomer and the diisocyanate were allowed to react to form a "prepolymer", which was subsequently chain extended at room temperature with the diamine.

In this paper, we describe the synthesis and initial characterization of these amphiphilic PEUU−PIB comb polymers. The permeability characteristics as well as insight into their solid-state structure will be presented in future publications.

Experimental Section

Materials. Argon (99.9%) was obtained from MG Industries and used as received. Anhydrous hydrochloric acid (HCl gas, 99.995+%) was purchased through Aldrich Chemical and was used as received. Isobutylene (2-methylpropene) was also obtained from Aldrich and was distilled through a Drierite column before each use.

Two different grades of tetrahydrofuran were used: HPLC grade (Thomas Scientific) and anhydrous (99.995+%, Aldrich). The anhydrous THF was stored under argon. Lithium bromide (99.9995%) and HPLC grade *N*,*N*-dimethylformamide were obtained from Acros Organics. All of the following chemicals were purchased from Aldrich Chemical and were used as received: deuterated chloroform (99.8 at. % deuterated), diethyl ether, *n*-butyllithium solution (2.5 M in hexanes), methylene chloride (99.995+% anhydrous), hexanes (99.995+% anhydrous), methanol (99.995+% anhydrous), *N*,*N*-dimethylacetamide (99.995+% anhydrous), *m*-xylene (99.995+% anhydrous), Terathane 2000 polyether glycol, butyl acetate, ethylenediamine (redistilled, 99.5+%), hydrochloric acid (37 wt % in water, 99.999%), tetrabutylammonium fluoride (1 M in THF), silica gel (50−250 Å, 70−130 mesh), 3,4-dihydroxybenzaldehyde (97%), sodium hydride (60% dispersion in mineral oil), *tert*-butyldimethylsilyl chloride (97%), ammonium chloride (99.5+%), magnesium sulfate (98%), methyltriphenylphosphonium bromide (98%), 4-*tert*-butylcatechol (97%), pyridine (anhydrous, 99+%), 2,6-di-*tert*-butylpyridine (97%), titanium tetrachloride (99.995+%), and sodium bicarbonate (99%).

Equipment. Air- and water-sensitive experiments were conducted in a double size Vacuum Atmospheres Corp. model HE−43 Dri-Lab glovebox, under an argon atmosphere. The inert gas was recycled and kept air- and water-free by the Vacuum Atmospheres Corp. model MO-40−1H Dri-Train unit.

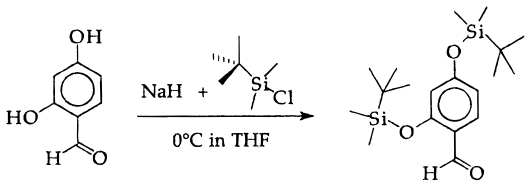
Gel permeation chromatograph experiments were conducted using a Waters model 510 pump and model 410 refractive index detector. Two separate eluents were used, correspondingly, with two different column sets. When tetrahydrofuran (35 °C) was used, the system was equipped with one 5 μm A8530N-LMB linear mixed bed column (obtained from Polymer Standards Service). For dimethylformamide (80 °C) with lithium bromide salt (0.05 M), two PLgel 5 μm Mixed-C columns (Polymer Laboratories) were used. Data analysis was performed using Waters Millennium Chromatography Manager software. Standard calibrations in THF were performed using narrow poly(isobutylene) standards (Dr. R. F. Storey, University of Southern Mississippi), ranging from 3400 to 128 100 g/mol. In the more polar DMF/salt solution, narrow poly(ethylene oxide) standards (Polymer Laboratories), ranging from 10 000 to 963 000 g/mol, were used.

All ^{1}H NMR analyses were performed on a 200 MHz Brüker WP-200 FT-NMR spectrometer in deuterated chloroform. Solid state ^{13}C NMR analyses were performed on a Chemagnetics CMX 300 spectrometer. For solid-state NMR samples, cross polarization and magic angle spinning (CPMAS) and CPMAS with total suppression of spinning sidebands (TOSS) experiments were used. For the physical polymer mixture samples, high-speed CPMAS with spin rates above 10 kHz were used to suppress the spinning sidebands. All solid-state NMR samples were prepared by drying the bulk copolymer samples or polymer mixtures from solution at ≥80 °C under vacuum for at least 24 h to remove the solvents.

Fourier transform infrared (FTIR) spectroscopic studies were performed on a Bio-Rad FTS-45 spectrometer. Samples were in the form of thin films, cast from a concentrated solution of each copolymer in 25/75 v/v DMF/*m*-xylene onto KBr windows. Cast samples were heated to ≥80 °C under vacuum for 16 h to remove residual solvent. Neat PIB samples were cast from THF and dried at room-temperature overnight. Analyzed in transmission, the spectral absorbances for all the materials were kept within the Beer's law region (≤0.6 absorbance units).

Soxhlet extractions were performed on the amphiphilic PEUU−PIB copolymers by extracting a small sample in THF for 48 h. Extracts were dried and analyzed by ^{1}H NMR.

Initiator Synthesis. The first step, the protection of the diphenolic compound, is shown in reaction 1. First, in a drybox,

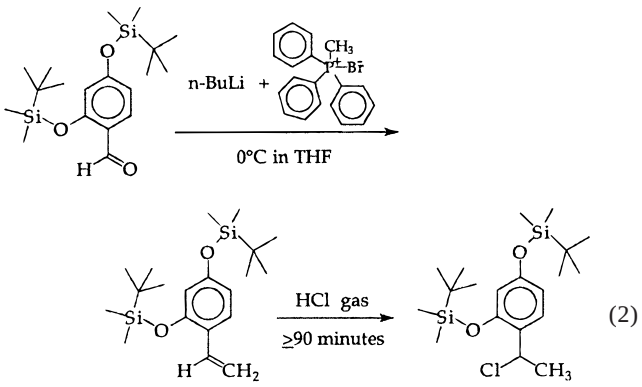


(1)

3.57 g (0.0259 mol) of 3,4-dihydroxybenzaldehyde (DHBA), was dissolved in anhydrous THF. Then, 2.275 g (1.40 g pure, or 0.057 mol) of sodium hydride, in dispersion, was added slowly to the reaction flask. After approximately 30 min, 9.35 g (0.062 mol) of *tert*-butyldimethylsilyl chloride was added, also slowly, and the resulting solution was allowed to stir for at least 4 h. The reaction flask now contained primarily 3,4-di(*tert*-butyldimethylsiloxy)benzaldehyde. The diprotected benzaldehyde (DPBA) was washed using ether and ammonium chloride solution. The ether/THF solution was dried with magnesium sulfate and filtered and the DPBA isolated by rotary evaporation.

The DPBA was converted to a styryl moiety, utilizing a Wittig reaction, as shown in reaction 2. In a 250 mL round-bottom flask, 11.08 g (0.031 mol) of methyltriphenylphosphonium bromide and ∼100 mL of anhydrous THF were stirred under an inert atmosphere. Then, approximately 11.4 mL *n*-butyllithium solution (about 0.03 mol of *n*-BuLi) was added to the slurry to form the Wittig reagent, to which the DPBA was added. The mixture was allowed to stir at ambient temperature for at least 4 h. The product was subsequently washed three times with water and dried. A trace amount of *tert*-butylcatechol was added to the solution after filtration, to inhibit the polymerization of the 3,4-di(*tert*-butyldimethylsiloxy)styrene. The diprotected styrene (DPS) was isolated by rotary evaporation and then dissolved in cyclohexane. The DPS−cyclohexane solution was filtered to remove the insoluble impurities. Finally, silica gel was added to trap the remaining polar impurities, which were then filtered from the cyclohexane solution. The approximate yield of DPS was about 93% (9.47 g of DPS was expected, and 8.82 g was observed).

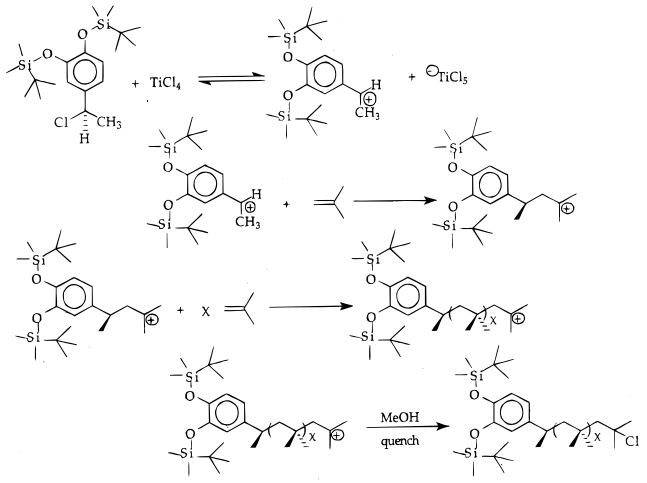
The DPS was hydrochlorinated (see reaction 2), while still



(2)

in solution in cyclohexane (with trace inhibitor), by bubbling

HCl gas through it for at least 90 min. The pure 1-chloro-1-[3,4-di(*tert*-butyldimethylsiloxy)phenyl]ethane, CDPPE (for chloro-diprotected phenylethane), was isolated by rotary evaporation. The CDPPE was used as the initiator for the polymerization of isobutylene, as shown in reaction 3.



(3)

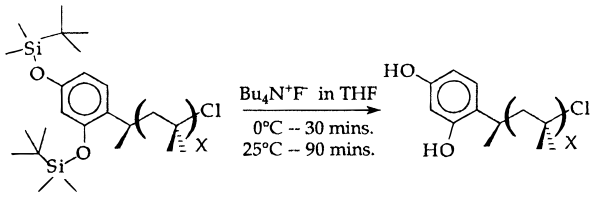
Macromonomer Synthesis. As an example of the macromonomer synthesis, the details of the 17 800 (number-average) molecular weight polyisobutylene material are given below. In a completely inert argon atmosphere (glovebox), 24 mL each of anhydrous hexanes and anhydrous methylene chloride were placed in a three-necked 100 mL round-bottom flask. Also in the flask were placed, each by a clean syringe, 385 mg (0.00096 mol) of CDPPE initiator, 388 μL (0.0048 mol) of pyridine, and 312 μL (0.0019 mol) of 2,6-di-*tert*-butylpyridine. In an addition funnel, 12 mL of the anhydrous hexanes was placed, along with 1.055 mL (0.0096 mol) titanium tetrachloride. The funnel was sealed and attached to one neck of the reaction flask. In another graduated vacuum addition funnel, 15−20 mL of methanol was added, and the funnel was sealed and attached to another neck of the three-neck flask. The third neck of the reaction flask was fitted with a 180° valve, so that the inert atmosphere could be maintained during removal from the drybox and attachment to the vacuum line.

The assembly was fitted to a vacuum line and degassed with three freeze/thaw cycles. At −78 °C, in a liquid nitrogen/butyl acetate bath, the reaction flask was under the partial pressure of its contents. Then, ∼9.1 mL of liquid isobutylene (0.096 mol) was condensed from the gas on the vacuum line into a graduated tube and subsequently vacuum transferred into the reaction flask. The contents of the flask were then stirred at −78 °C until they were well mixed. Then, the $TiCl_4$ solution in the addition funnel was added, and the time was noted as the beginning of the reaction. At this point a deep yellow tinge in the reaction flask was observed, indicating the formation of the active carbenium ion species. The reaction was allowed to proceed, while stirring, for 90 min and was then quenched with anhydrous methanol.

Upon quenching with methanol from the other addition funnel, a stringy, translucent precipitate usually formed. The mixed solvent was then decanted off, the product washed with dry methanol, and the solvent was decanted off again. The polyisobutylene was further purified by being redissolved in methylene chloride and washed twice with 5% hydrochloric acid, followed by two washes with a sodium bicarbonate solution and three washes with distilled water. The organic layer was dried with magnesium sulfate and filtered. The solvent was removed by rotary evaporation to isolate the purified polymer product, the protected PIB macromonomer.

Macromonomer Deprotection. Once isolation of the protected macromonomer had been accomplished, the final step was to regenerate the two phenolic moieties on the initiator end of the polymer chain. Deprotection of (and protection with) *tert*-butyldimethylsilyl groups is common practice in the chemistry of both small molecules[10,11] and polymers.[12] The deprotection scheme involves the reaction of the protected groups with tetrabutylammonium fluoride (TBAF) in THF, at 0 °C for 5 min, then at room temperature for 40 min.[11]

A slightly modified version of this method was used for the deprotection of the polyisobutylene macromonomer (reaction 4). 3.95 g (containing about 0.45 mmol of protective groups) of



(4)

the protected polyisobutylene macromonomer was dissolved in approximately 250 mL of anhydrous THF at 0 °C. About 2.2 equiv (∼1.0 mL) of TBAF (∼0.99 mmol) in solution was added to the THF solution. The reaction was allowed to proceed for 30 min at 0 °C, at which point the ice bath was removed. The reaction proceeded for another 90 min at room temperature. Because of the very high equivalent weight and small quantities used, quantitative reaction yield could not be established. However, spectroscopic analysis of the reactants and products indicates qualitatively that there is significant completion of the deprotection reaction.

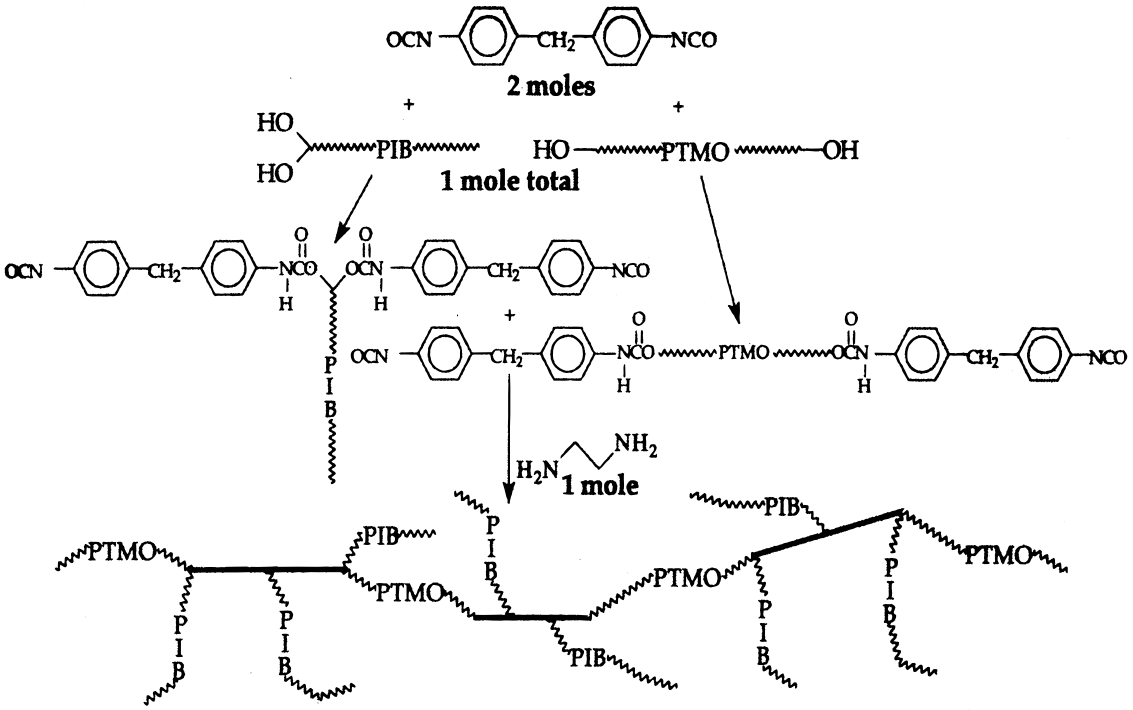
When the reactions were complete, the deprotected PIB macromonomers were purified in the same way as the protected materials, to isolate the α,α′-dihydroxypolyisobutylene.

Amphiphilic Copolymer Synthesis. In an effort to preserve the stoichiometry and to create terpolymers having hard segment contents similar to the PEUUs currently used in biomedical devices, reactant ratios were kept at 1:2:1, total diol:diisocyanate:diamine. As a result, increasing amounts of dihydroxylpolyisobutylene were essentially substituted for the polyether diol in the copolymerizations. The general synthesis scheme is summarized in Scheme 1. As PIB substitution for polyether altered the total weight of the reaction product, sufficient DMAc/*m*-xylene 25/75 v/v solvent mixture was introduced to compensate and keep the pre-reaction concentration at 10% w/v. The weight percent of hard segments decreased modestly with PIB incorporation. For the copolymer with maximum PIB incorporation (the 32% 29K copolymer—see later), the wt % of hard segments was determined to be approximately 15% from solid-state NMR measurements vs ∼21% for the unmodified PEUU.

As an example of the reaction scheme, the specifics of the copolymerization of the 29 100 M_n PIB (to a nominal 15 wt % level) were as follows. In the argon atmosphere of a glovebox, a 750 mL Erlenmeyer flask was heated to ∼85 °C in a silicone oil bath. Then, 29.75 mL of DMAc and 87.00 mL of *m*-xylene were added to the reaction flask (the remaining 2.30 mL of xylene was saved for later use with the diamine). At this point, the mixture was vigorously and continually stirred by an external mechanical stirrer. To the flask was added 7.877 g (0.0039 mol) of Terathane (a 2000 g/mol telechelic poly(tetramethylene oxide) [PTMO] diol). Next, 1.786 g (0.000 062 mol) of the 29 000 M_n dihydroxylpolyisobutylene macromonomer were allowed to dissolve. Then, 2.002 g (0.008 mol) of freshly distilled methylene bis(phenyl isocyanate), MDI, was added to form the "prepolymer". This initial step was essentially complete at the end of 2 h, at which point the reaction flask was allowed to cool to room temperature.

Once cool, 2.30 mL of *m*-xylene was placed into an addition funnel. To the funnel, 267 μL (0.004 mol) of ethylenediamine (EDA) was added, and the contents were well mixed. This solution was added extremely slowly, dropwise, into the "prepolymer" solution. Even before all of the EDA was added, the solution viscosity increased rapidly. The mechanical stir-

Scheme 1. One-Pot, Two-Step Synthesis Reaction for Amphiphilic PEUU−PIB Multiblock Comb Copolymers



ring rate was increased to compensate, over the next 30 min. The reaction was left stirring in this manner for at least four more hours.

Terpolymers were synthesized aiming at 5, 15, and 25% incorporation for the 29.1K, 17.8K, and 7.6K PIB macromonomers (the nominal 15% copolymer for the 7.6K PIB was not synthesized). For the 3.4K PIB macromonomer, 5 and 15% terpolymers were targeted. For comparison, a neat PEUU multiblock copolymer was synthesized using the same reaction pathway and conditions.

Results and Discussion

A. PIB Macromonomer. Characterization of Initiator and Its Precursors. The protected phenolic aldehyde was characterized by ^{1}H NMR in deuterated chloroform (protonated chloroform can be seen at 7.24 ppm), as shown in Figure 1. The peaks associated with the protecting groups are located at ∼0.16 and ∼0.95 ppm. The peaks at 1.7 and 3.6 ppm are associated with unevaporated THF[13] while those at 1.25 and 0.87 ppm are indicative of the presence of alkane contaminants (from the mineral oil in the NaH dispersion).[14]

As noted above, after isolation of the protected aldehyde, a styrenic compound was formed by reaction with a Wittig reagent. ^{1}H NMR characterization of the DPS product in $CDCl_3$ solution is shown in Figure 2. The appearance of the peaks at ∼5.1 and ∼5.5 ppm, combined with the disappearance of the peak at ∼9.7 ppm, indicate the completion of this reaction. A signal appearing in the range 7.4−7.7 ppm represents the very stable byproduct of the Wittig reaction, triphenylphosphonium oxide. THF, $CHCl_3$, and mineral oil are all present again as contaminants.

Upon removal of the phosphonium oxide from the solution, the isolated DPS was dissolved in cyclohexane and underwent hydrochlorination for at least 90 min. The secondary chloro-initiator, CDPPE, was isolated from cyclohexane by rotary evaporation. The disappearance of the ^{1}H NMR peaks in the 5−6 ppm range provides evidence of the completion of the hydrochlorination reaction (Figure 3). The new peaks at ∼1.8 and ∼5.0 ppm confirm the proposed structure of the product. It is important to emphasize that the silyl protective groups remain intact despite the presence of HCl gas.

Macromonomerization Scheme. The cationic polymerization of isobutylene was undertaken in a manner similar to that Storey and Lee,[15] with several notable differences. The isobutylene is polymerized here using a monofunctional initiator, rather than a difunctional one (used to synthesize telechelic PIB). Second, the chemical structure of the initiator contains a secondary chloride as its active site, not the traditional tertiary chloride site (of a blocked dicumyl chloride). The consequences of a secondary chloride reactive site in this system are that the initiation of the chains will be slower than that of a tertiary chloride reactive site.[16] The effects of this slower initiating species will be discussed in more detail later. Third, the reaction is conducted under partial vacuum (the atmosphere consists of the partial pressures of the contents of the reaction flask at −78 °C), instead of in an argon atmosphere. Methylene chloride is used in the solvent mixture instead of methyl chloride. The effect of this change in solvent is to increase the polarity of the solvent mix. The modest increase in polarity probably results in a slight increase in the reaction rate.[17] Last, 2,6-di-*tert*-butylpyridine was used as a free proton scavenger, in addition to pyridine. The presumption is that the pyridine−titanium tetrachloride (electron donor−Lewis acid) complex acts as the gegenion to stabilize the growing polyisobutylene chain.[18] The consumption of the pyridine in this manner makes it necessary to add an additional proton scavenger. In this case, an extra, sterically hindered electron donor was added to scavenge any protic impurities or any protons released during any termination or side reactions.

Macromonomer Characterization. Characterization of the PIB macromonomers was accomplished by ^{1}H NMR and GPC. A typical ^{1}H NMR spectrum, that of the protected 18K material, is shown in Figure 4. Two peaks dominate the spectrum at ∼1.1 and ∼1.4 ppm,

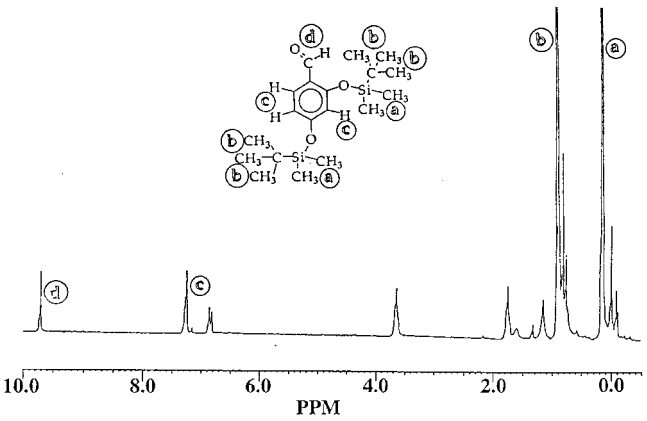


Figure 1. ^{1}H NMR spectrum, in $CDCl_3$, of the product from the protection of dihydroxybenzaldehyde.

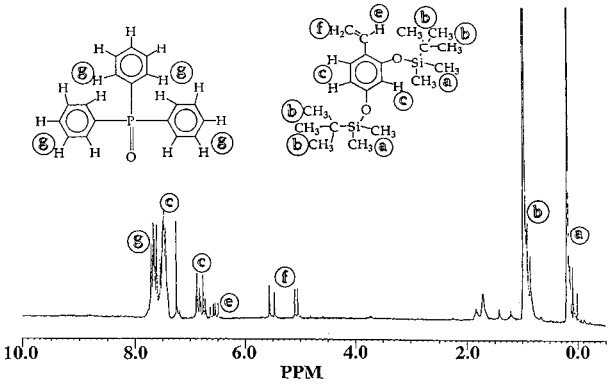


Figure 2. ^{1}H NMR spectrum, in $CDCl_3$, of the product from the Wittig reaction to synthesize diprotected styrene.

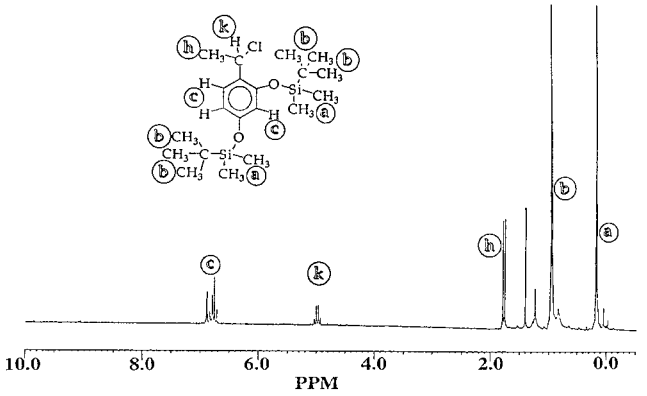


Figure 3. ^{1}H NMR spectrum, in $CDCl_3$, of the product from the hydrochlorination of diprotected styrene to form the cationic initiator.

which are typical of signals from pendant $-CH_3$ protons and backbone methylene protons, respectively.

Number and weight-average molecular weights of all synthesized macromonomers (protected), relative to narrow PIB molecular weight standards, are provided in Table 1. [In the text, the four macromonomers are referred to by the M_n of the protected species, rounded to the nearest 1000.] Given that we were attempting to attain a living polymerization of the PIB, the fact that polydispersities are not all near 1.1 indicates a departure from the expected kinetics. The distributions are monomodal, despite their relative breadth (for living systems), indicating the lack of any appreciable side reactions. Also, the measured molecular weights were notably higher than the expected values. If chain transfer were occurring, a reduction in molecular weight from the target value would have been expected.

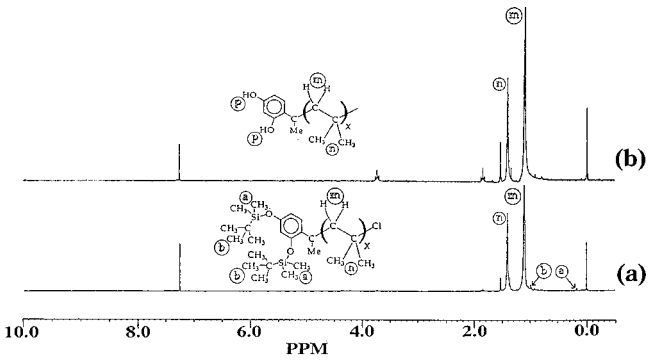


Figure 4. ^{1}H NMR spectra, in $CDCl_3$, of (a) protected and (b) deprotected PIB 18K macromonomers.

Table 1. Moleular Weight of Protected Polyisobutylene Macromonomers

	M_n	M_w	PDI
PIB-1	3400	5400	1.58
PIB-2	7600	10 600	1.39
PIB-3	17 800	21 700	1.22
PIB-4	29 100	34 700	1.18

It could be hypothesized that only a certain percentage of the initiator molecules are effective in initiating polymerization, with an initiation complex efficiency of ~30−40%. A more plausible explanation, however, is that the initiator transition reaction (from dormant to active) is slow. Since the rate of initiation is slower than the rate of propagation, then any active cation will propagate comparatively quicker, relative to the formation of another cation site. This effect will make it seem as if only a certain percentage of initiator molecules are "efficient" in initiating the polymerization. This being the case, the CDPPE/$TiCl_4$/mixed electron donor system should not yield a linear molecular weight vs time plot, when studied by a technique such as incremental monomer addition, because there would be some new active sites that were not "efficient" during the last polymerization period.[19]

It has been shown that a secondary benzylic chloride exhibits a much slower transition to a secondary cation than a tertiary benzylic chloride.[20] Due to the fact that secondary cations are much less stable than tertiary cations, the reaction of a secondary chloride requires a larger activation energy to attain its active state than does a tertiary chloride. In the current system, the secondary benzylic chloride was shown to have an S_N1 solvolysis rate constant over 3 orders of magnitude lower than that of the tertiary benzylic chloride.[20] Also, a compound closely resembling the propagating end of a polyisobutylene chain is shown to have a solvolysis rate constant an order of magnitude higher than the secondary benzylic chloride and 2 orders of magnitude lower than the tertiary benzylic chloride. This slow activation of the secondary benzylic chloride results in a synthesis scheme where the initiation step is slower than propagation. Typical results for controlled polymerization systems with slow initiation still indicate a relatively narrow polydispersity (~1.25−1.35) at moderate conversions, while showing a higher molecular weight than expected (from an analogous "living" system).[20] The characterization of our experimental system is directly comparable to the expectations for a controlled polymerization with slow initiation.

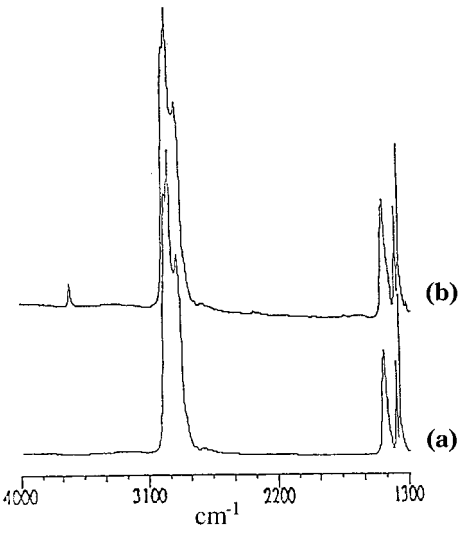


Figure 5. FTIR spectra, cast from tetrahydrofuran, of (a) protected and (b) deprotected PIB 8K macromonomers from 4000 to 1300 cm^{-1}.

Consequently, the PIB polymerization described here should not technically be classified as "living." However, in this study, the livingness of the system is not paramount. The importance of using a "pseudo-living" cationic system lies in the other qualities that living systems offer, namely the absence of chain transfer and the absence of chain termination. The molecular weight is controlled by a simple adjustment, using a linear extrapolation for a constant "initiating efficiency," to obtain a desired molecular weight. However, even without precise control over molecular weight, the functionality of the polymer chain is by far the more important consideration. Since these polymers are macromonomers to be used for subsequent reaction, it is very important that they have exactly two reactive sites (the two protected phenolic sites formerly on the initiator, now at the head of the chain). Only the chains formed by the difunctional initiator will have dual functionality. If any chain transfer occurs, the new chain would not have a difunctional head (it would have a functionality of zero) and would therefore not participate in subsequent polymerizations.

Deprotection Efficiency. Characterization of the deprotected PIB polymers was performed by ^{1}H NMR and FTIR spectroscopy. The ^{1}H NMR spectrum of the 18K deprotected product and the corresponding protected PIB is shown in Figure 4. There are a few subtle differences in the two spectra. The two peaks at ∼0.17 ppm and ∼0.96 ppm in the spectrum of the protected PIB, indicating the methyl and *tert*-butyl moieties attached to the silicon of the protection groups, are small but present. However, these peaks are absent in the deprotected spectrum, indicating that the TBAF reaction effectively deprotected the phenolic groups.

Additional evidence comes from FTIR spectroscopy. Figure 5 shows the spectra of the 8K deprotected and protected PIB products. The spectrum of the protected material contains the bands characteristic of PIB,[21] but those associated with the protecting groups are not evident. This is not surprising due to the very high equivalent weight of these groups and the relatively low absorptivity of the anticipated peaks. However, a distinct peak is seen in the deprotected spectrum at ∼3640 cm^{-1}, indicating the presence of phenolic hydroxyl groups and confirming the deprotection. Secondarily, the appearance of a less intense band around ∼1100 cm^{-1} (not shown) is indicative of the C−O bend of a secondary −OH.

B. PEUU−PIB Copolymers. FTIR and NMR spectroscopy were chosen to characterize PIB content in the copolymers. Solution NMR could not be used since complete solubility of the higher PIB content copolymers could not be achieved in suitable NMR solvents. We therefore used solid state ^{13}C NMR to obtain quantitative information about PIB incorporation.

^{13}C NMR: PIB Content. Peak assignments for the solid-state CPMAS and TOSS−CPMAS ^{13}C NMR spectra of neat PEUU and polyisobutylene were obtained from refs 22 and 23, respectively (see Table 2). It is clear from Figure 6 that the peaks at ∼32 and ∼39 ppm (less so at ∼60 ppm), that arise from PIB in the copolymers, increase significantly in magnitude with the expected increase in PIB content. However, because CPMAS and TOSS−CPMAS spectral intensities depend on NMR relaxation parameters, peak areas from curve fitting cannot yield quantitative PIB concentrations. Quantitative analysis was, however, accomplished by creating a calibration curve derived from physical mixtures of the neat PEUU and neat PIB.

The PIB used in the mixtures was obtained from Polysciences (M_v ∼ 9300 g/mol) and it was physically mixed with neat PEUU in 25/75 v/v DMAc/xylene at known compositions ranging from 5 to 20 wt %. The mixtures were subsequently dried under the same conditions as the copolymers, and curve fitting of the various NMR peaks was accomplished similarly to the copolymers. Only the peaks representing the ether carbons, hard segment methylene carbons, and the PIB carbons from the mixtures were used for calibration. The TOSS correction affected the downfield (highest ppm) part of the spectrum the most. In addition, the individual peaks associated with the carbon bonds from the MDI in the hard segments were difficult to resolve from each other.

The relative ratios of the PIB peak areas (sum of the three peaks) to the total peak area (excluding the hard segment ring carbons and urea/urethane carbons) were plotted against PIB concentration in the mixtures to provide a calibration curve (see Figure 7). The peak area ratios for the copolymers were calculated in the same manner as the mixtures and the PIB concentrations were determined. In a similar manner, a PTMO calibration curve was generated from the mixtures and applied to the terpolymers in order to determine PTMO content. For the purposes of this calculation, it was assumed that the neat PEUU contained the stoichiometric amount of soft segments, i.e., 78 wt %. Hard segment fractions were then determined by difference (see Table 3). The results presented in Table 3 confirm that the hard segment content of the terpolymers varies only modestly, from ∼15 to ∼21 wt %, as expected from the ratio of the different components in the synthesis.

From Table 3 it is evident that the 3K macromonomer was generally incorporated to a lower extent than the other PIB macromonomers. Although the reasons for this are unclear, the relative breadth of the molecular weight distribution might provide some insight. The polydispersity of the 3K macromonomer is a bit larger (∼1.6) than "expected" (∼1.3, see the earlier discussion), which may be indicative of some chain transfer or termination during the polymerization. If some polymer chains did not participate in the reaction due to their

Table 2. ^{13}C NMR Peak Assignments for Amphiphilic PEUU−PIB Copolymers[22,23]

peak location (ppm)	corresponding carbon bond (component)
27	internal (C−**CH_2**−**CH_2**−C) methylenes (PTMO)
31	pendant (>C−(**CH_3**)$_2$) methyls (PIB)
38	quaternary (>**C**<) carbon (PIB)
41	methylene (−Ph−**CH_2**−Ph−) from MDI (hard segment)
41	methylenes (HNCONH−**CH_2**−**CH_2**−NHCONH) from EDA (hard segment)
60	backbone (−**CH_2**−C(CH_3)$_2$−) methylene (PIB)
65	external methylene (HNCOO−**CH_2**−CH_2−) closest to urethane (PTMO)
71	external (**CH_2**−O−**CH_2**) methylenes (PTMO)
119	ring carbons meta to MDI methylenes (hard segment)
129	ring carbons ortho to MDI methylenes (hard segment)
136	ring carbons para to MDI methylenes (hard segment)
136	ring carbons attached to MDI methylenes (hard segment)
154	urethane (−O**C**=**O**NH−) carbonyl (hard segment)
158	urea (−NH−**C**=**O**NH−) carbonyl (hard segment)

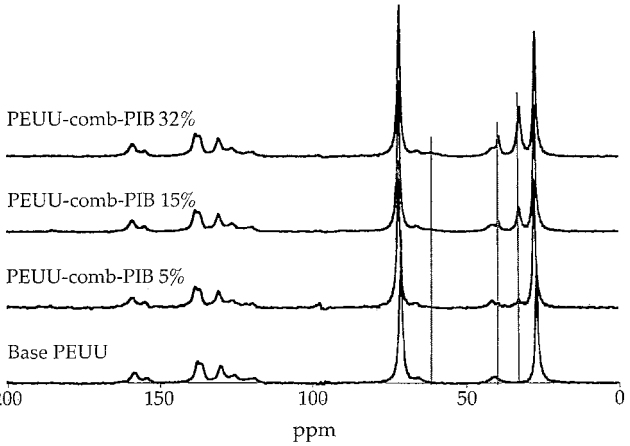


Figure 6. Solid-state CP-MAS, TOSS-corrected ^{13}C NMR spectra of the family of 29K PIB amphiphilic comb copolymers.

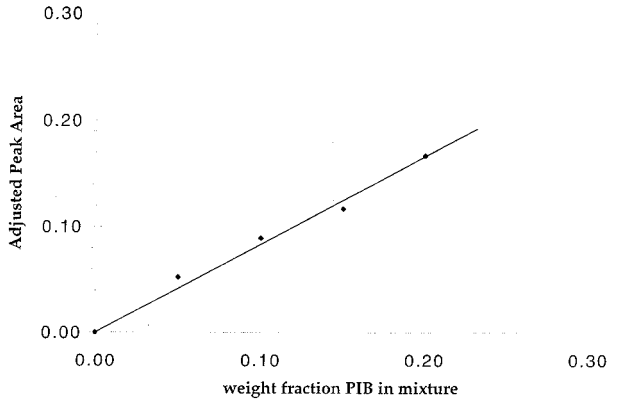


Figure 7. Peak area ratio vs PIB content for PEUU + PIB mixtures analyzed by solid state ^{13}C NMR. The linear fit through the data served as a calibration to determine PIB contents in the amphiphilic terpolymers.

lack of functionality, resulting from chain transfer, then a smaller percentage of PIB would be incorporated in the copolymer.

FTIR. Select regions of the FTIR spectra of the 29K copolymer family are shown in Figure 8. Comparing these spectra to those of the neat PEUU and protected PIB, the qualitative increase in PIB-specific absorptions with increasing PIB content is evident. This is seen most clearly by focusing on the bands at ∼2980 and ∼2870 cm^{-1} (indicative of C−H asymmetric and symmetric stretching, respectively, in −CH_3), as well as the band at ∼1465 cm^{-1} (assigned to asymmetric −CH_3 bending), and two bands at ∼1380 and ∼1360 cm^{-1} (symmetric −CH_3 deformation).[24]

Table 3. Component Concentrations in the Copolymers from ^{13}C NMR

PIB comb M_n	target PIB wt %	actual PIB wt %	PTMO wt %	hard segment wt %
29K	25	33	52	15
29K	15	15	67	19
29K	5	5	75	20
18K	25	27	57	16
18K	15	13	68	19
18K	5	3	77	21
8K	25	22	61	18
8K	5	2	77	21
3K	15	6	74	20
3K	5	3	76	21

FTIR spectroscopy is an excellent probe of the influence of the PIB combs (and comb length) on urea and urethane hydrogen bonding. Since the attachment points for the polyisobutylene combs are mainly within or at the edge of hard segments, it might at first be expected that the PIB would influence hard segment organization and microphase separation. The focus of our analysis was in the carbonyl stretching region of the spectra: between ∼1625 to ∼1750 cm^{-1}.

To facilitate comparison of the FTIR spectra of the various copolymers, the spectra were normalized to an internal thickness band (at 1412 cm^{-1}, associated with the C−C stretch in aromatic rings[24]). There are two components in the PEUU−PIB copolymers that contribute at this frequency: the phenyl rings from the MDI in the hard segments and the relatively small number of rings associated with the difunctional PIB initiator. Since the PIB content is known from the NMR experiments, the "excess" contribution to the 1412 cm^{-1} band from the PIB content of each copolymer could be calculated.

Each 1412 cm^{-1} peak area was evaluated using SpectraFit 1.0.1[25] and the spectra normalized. No quantitative information can be obtained at this point by curve resolving the peaks in the carbonyl region of the spectra, due to a lack of reliable information from oligomers or model compound studies on peak shape, width at half-peak-height and, to a certain extent, peak location for the PEUUs under consideration here.

Nevertheless, it is possible to draw some general conclusions about the state of the hydrogen bonding in these materials. One observation is that the relative area associated with the "free" (non-hydrogen bonded) urethane carbonyl peak (near 1733 cm^{-1}) for the neat PEUU and all terpolymers is significantly larger than observed in model compound studies (see Figure 9 and ref 26). This could arise from the presence of other chemical species in the segmented copolymers that

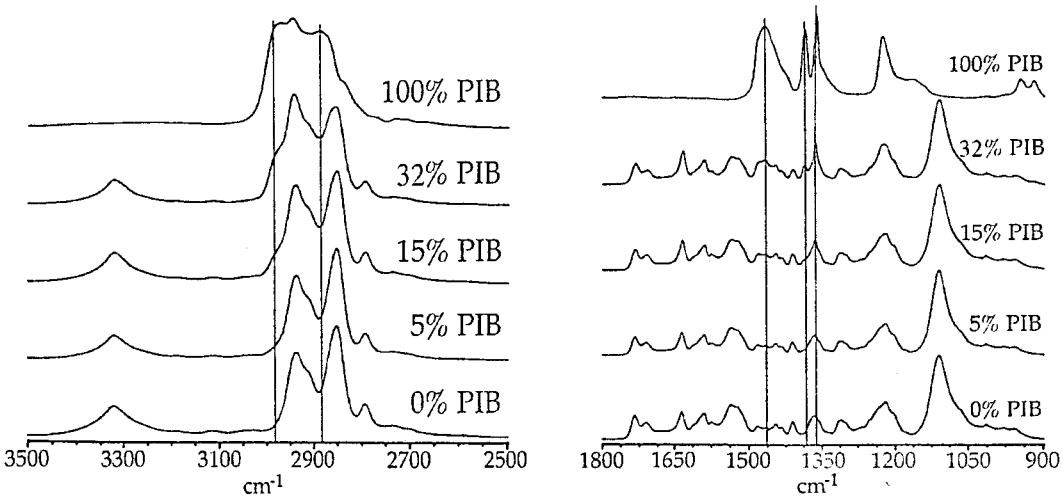


Figure 8. FTIR spectra, cast from 25/75 v/v DMAc/xylene, of the family of 29K PIB amphiphilic comb copolymers in the (a) C−H stretching and (b) fingerprint regions.

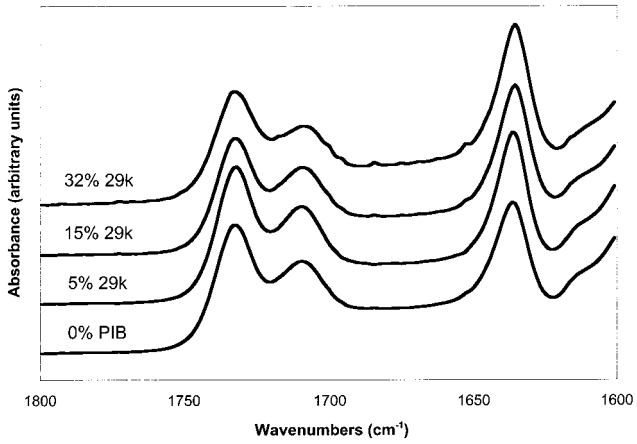


Figure 9. FTIR spectra of neat PEUU and the 29K family of PIB comb copolymers in the region from 1800 to 1600 cm^{-1}.

dilute the population of urethane carbonyls to the point where they are not able to locate hydrogen-bonding partners. This is very unlikely however since the PEUU and terpolymers are populated by a very large number of ether linkages (well-known hydrogen-bonding acceptors) from the soft segment. Alternatively, it is more likely that the population of "non-hydrogen-bonded" urethane carbonyls arises from the association of urethane amides with hydrogen-bonding acceptors, leaving the urethane carbonyl unbonded. This suggests that a significant portion of the urethane moieties reside in interfacial or PTMO-rich regions, for all levels of PIB incorporation.

Figure 9 displays spectra in the carbonyl stretching region for the neat PEUU and the 29K family of terpolymers. It is clear that there are no significant differences between these spectra, indicating no significant change in the hydrogen bonding characteristics upon PIB incorporation. In a few cases (the 6% 3K and the 21% 8K terpolymers) there may be some subtle differences in the urethane carbonyl portion of the spectra but, as noted earlier, the lack of information on peak shape and even the number of peaks in this spectral region, prevents unambiguous analysis.

Finally, while the urethane carbonyls show little ordering in the hydrogen-bonded state (a peak near 1680−1690 cm^{-1} would be expected in that case[26]), the hydrogen-bonded urea carbonyls in all synthesized copolymers are primarily ordered[27,28] (see the prominent peaks at ∼1636 cm^{-1} in Figure 9).

Table 4. Apparent Molecular Weight of Low PIB Content PEUU-*comb*-PIB

	M_n	M_w	PDI
PEUU	69 900	129 000	1.84
PEUU-*comb*-PIB 2.9% 3K	53 400	92 000	1.72
PEUU-*comb*-PIB 1.9% 8K	43 900	79 400	1.81
PEUU-*comb*-PIB 2.5% 18K	60 800	127 100	2.09
PEUU-*comb*-PIB 4.8% 29K	48 400	93 200	1.93
PEUU-*comb*-PIB 6.1% 3K	21 400	44 200	2.06

Molecular Weight Characterization. Because of the strong hydrogen bonding in the regular hard segments, the neat PEUU has limited solubility. It can, however, be dissolved over the course of at least 24 h in DMF/0.05 M LiBr at elevated temperatures. However, as nonpolar PIB concentration in the copolymer rises, there is an increasing dichotomy between the solvating power of the DMF/salt solution toward the hard segments and the immiscibility of the hydrocarbon component in the ionic solvent system. As a result, even copolymers containing a moderate level of PIB are not completely soluble in the GPC eluent. Only the neat PEUU and those copolymers containing the lowest PIB contents were soluble (at low concentration) in DMF/LiBr to permit nominal molecular weight analysis (see Table 4). The apparent molecular weights are all reasonable except for the 6 wt % 3K copolymer, whose apparent molecular weight is only about a third of the neat PEUU. However, in its as-synthesized form, this copolymer is comparable in its gelatinous, semisolid characteristics to the other copolymers and exhibits substantial elastic behavior. It is likely that the apparent reduction in molecular weight arises at least partially from the relatively low hydrodynamic volume of the more nonpolar copolymer, and not necessarily a reduction in chain length.

The high molecular weight nature of all the copolymers was confirmed by solid state ^{13}C NMR. A very rough estimate of absolute molecular weight can be gleaned from comparison of the peaks at ∼71 and ∼65 ppm, corresponding to the external ether carbon and the carbon attached to the urethane, respectively.[22] By this method, the step growth polymerization scheme yielded relatively high and similar molecular weights for the majority of the copolymers.

Confirmation of PIB Attachment. There is always the question in the synthesis of complex copolymers such as those under consideration of the actual attachment of the co-units to the polymer chain. The GPC traces of the lower PIB content copolymers, showed no signs of a multimodal distribution or low molecular weight impurities. Even when copolymer solutions were not filtered, as they generally were before each GPC run, there were no differences in the chromatograms to indicate aggregation or oligomeric products. Since the relative concentrations of attachment points are so low (~0.12 mmol of linkages in ~12 g, for the case of the 15% 29K copolymer), most other conventional analytical techniques were not helpful here.

One piece of evidence supporting attachment is that the PIB macromonomer and PEUU could not be isolated from solution. For example, DMF/0.05 M LiBr, a relatively good solvent for the multiblock copolymer, does not solvate neat PIB, but it solvated the terpolymers. It remained to be seen whether a good solvent for the PIB would be able to induce separation of any unreacted PIB and PEUU.

Using a Soxhlet extraction apparatus, selected samples were subjected to THF extraction for 48 h, and their extract solutions analyzed by ^{1}H NMR. It was found that samples contained small amounts of both PIB and oligomeric polyether, since unreacted PTMO and PIB are soluble in THF but the copolymers are not. It is not uncommon for PEUUs to exhibit ~2−3 wt % extractables (mainly the oligomeric polyether).[29,30] For the vast majority of the extracts performed in our study, the percent extractables were below 7%, with several low PIB content samples, including the neat PEUU and 2% 8K copolymer, exhibiting extract amounts on the order of ~2−3 wt %. As an example, ^{1}H solution NMR showed that the 2% 7K PIB copolymer extract consisted mostly of polyether, with some PIB macromonomer present. PIB contents derived from solid-state NMR were not "corrected" however, due to the relatively small amount of extractables. In combination with the data from other tests, these results validate the feasibility of attaching PIB macromonomers onto a multiblock PEUU backbone.

Summary

A unique protected secondary chloride initiator was synthesized in order to facilitate the polymerization of well-defined polyisobutylene macromonomers. This initiator molecule was isolated using benchtop analytical techniques and characterized in solution by ^{1}H NMR. This new initiator was subsequently combined with a Lewis acid co-initiator, a complexing agent, a proton trap, a certain mixture of solvents and isobutylene monomer, under conditions previously cited to support pseudo-living cationic polymerization.

Since the "all monomer in" technique[19] was employed in this study, the linearity of the molecular weight vs reaction time plot was not explored. The experiments generally support an absence of chain transfer and chain termination, but it is likely that the reaction conditions do not elicit a linear response with time of the molecular weight. Therefore, this is a controlled cationic polymerization system, though not a living one, even though polydispersities of the resultant polymers are as low as 1.18. Nevertheless, it is paramount that the system provided almost no evidence of chain transfer or termination.

The molecular weights of the protected macromonomers were measured directly by GPC and calibrated using PIB standards, to obtain "absolute" molecular weights. The molecular weights of the macromonomeric products were significantly higher than the targeted values. This was likely caused by the initiation step in the polymerization being somewhat slower than the propagation steps. This did not translate into a lack of control over molecular weight or a deviation from a well-defined, relatively narrow molecular weight distribution.

The combination of FTIR and ^{1}H NMR spectroscopy shows that the deprotection scheme is effective. The siloxyl protecting groups disappeared, while the hydroxyls were formed. The ^{1}H NMR and FTIR spectra of the deprotected product demonstrated the ability to accurately synthesize α,α′-dihydroxypolyisobutylene, a macromonomer which was utilized for further condensation reaction.

The one-pot, two-step synthesis scheme for creating the amphiphilic PEUU−PIB comb copolymers was successful. A solids concentration of 10% w/v in a solution of 25/75 dimethylacetamide/*m*-xylene kept the polymerization homogeneous, up to the point where the viscosity of the copolymer solution became the limiting factor in reaction conversion. The molecular weights of the low PIB content materials (≤5 wt %) were comparable to those of PEUUs used in biomedical applications. However, since the higher PIB content copolymers were insoluble, their molecular weights could not be measured by GPC. For the higher PIB content copolymers, solid state ^{13}C NMR was used to estimate molecular weights, and the entire set of copolymers exhibits reasonably high molecular weights.

The PIB content in the comb copolymers was qualitatively probed by FTIR, but it was solid state ^{13}C NMR that allowed quantitative determination of PIB incorporation. By analyzing physical mixtures of neat PEUU and PIB at known concentrations, a calibration curve was created for determining the PIB concentration in each terpolymer. In addition to confirming the presence of PIB in the copolymer, chemical attachment of PIB to the copolymer in comb form was evidenced through a combination of Soxhlet extraction in THF, molecular weight distribution from GPC, and solution studies.

FTIR was useful in determining that there was no detectable change in the hydrogen-bonding characteristics of the hard segments, either with increasing wt % of PIB or with increasing mol % of PIB combs in the amphiphilic copolymers.

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References and Notes

(1) Lamba, N. M. K.; Woodhouse, K. A.; Cooper, S. L. *Polyurethanes in Biomedical Applications*; CRC Press: Boca Raton, FL, 1998.

(2) Yang, M.; Zhang, Z.; Hahn, C.; Laroche, G.; King, M. W.; Guidoin, R. *J. Biomed. Mater. Res. (Appl. Biomater.)* **1999**, *48*, 13.

(3) Jiang, Y.; Frechet, J. M. J. *Polym. Prepr. (Div. Polym. Chem., Am. Chem. Soc.)* **1989**, *30*, 127.
(4) McGee, M. G.; Szycher, M.; Turner, S. A.; Clay, W.; Trono, R.; Davis, G. L.; Norman, J. C. *Trans. Am. Soc. Artif. Intern. Organs* **1980**, *26*, 299.
(5) Speckhard, T. A.; Gibson, P. E.; Cooper, S. L.; Chang, V. S. C.; Kennedy, J. P. *Polymer* **1985**, *26*, 55.
(6) Speckhard, T. A.; Cooper, S. L. *Rubber Chem. Technol.* **1986**, *59*, 405.
(7) Kennedy, J. P.; Iván, B. *Designed Polymers by Carbocationic Macromolecular Engineering: Theory and Practice*; Hanser Publishers: Munich, Germany, 1991.
(8) Kennedy, J. P. *J. Macromol. Sci.* **1994**, *A31*, 1771.
(9) Yoon, S. C.; Ratner, B. D.; Iván, B.; Kennedy, J. P. *Macromolecules* **1994**, *27*, 1548.
(10) Kendall, P. M.; Johnson, J. V.; Cook, C. E. *J. Org. Chem.* **1979**, *44*, 1421.
(11) Corey, E. J.; Venkateswarlu, A. *J. Am. Chem. Soc.* **1972**, *94*, 6190.
(12) Xu, Y.; Painter, P. C.; Coleman, M. M. *Polymer* **1993**, *34*, 3010.
(13) Silverstein, R. M.; Bassler, G. C.; Morrill, T. C. *Spectrometric Identification of Organic Compounds*; John Wiley & Sons: New York 1991.
(14) Bhacca, N. S., Johnson, L. F., Shoolery, J. N., Eds. *High-Resolution NMR Spectra Catalog*; Varian Books: Palo Alto, CA, 1963; Vol. 2.
(15) Storey, R. F.; Lee, Y. *J. Macromol. Sci.—Pure Appl. Chem.* **1992**, *A29*, 1017.
(16) Matyjaszewski, K. *Polym. Prepr. (Div. Polym. Chem., Am. Chem. Soc.)* **1995**, *36*, 541.
(17) Wang, L.; Svirkin, J.; Faust, R. *Polym. Prepr .(Div. Polym. Sci. Eng., Am. Chem. Soc.*) **1995**, *72*, 173.
(18) Gyor, M.; Wang, H.-C.; Faust, R. *J. Macromol. Sci.—Pure Appl. Chem.* **1992**, *A29*, 639.
(19) Faust, R.; Kennedy, J. P. *J. Polym. Sci., Polym. Chem. Ed.* **1987**, *25*, 1847.
(20) Matyjaszewski, K., Ed. *Cationic Polymerizations: Mechanisms, Synthesis, & Applications*; Marcel Dekker: New York 1996.
(21) Sprouse, J. F. *Sprouse Collection of Infrared Spectra, Book I: Polymers*; Sprouse Scientific Systems, Inc.: Paoli, PA, 1987.
(22) Okamoto, D. T.; Cooper, S. L.; Root, T. W. *Macromolecules* **1992**, *25*, 1068.
(23) Tonelli, A. E. *NMR Spectroscopy and Polymer Microstructure*; VCH Publishers: New York, 1989.
(24) Socrates, G. *Infrared Characteristic Group Frequencies, 2nd ed.;* John Wiley & Sons: New York, 1994.
(25) Coleman, M. M.; Graf, J. F.; Painter, P. C. *Specific Interactions and the Miscibility of Polymer Blends*, Technomic Publishing Co., Inc.: Lancaster, PA, 1991.
(26) Coleman, M. M.; Lee, K. H.; Skrovanek, D. J.; Painter, P. C. *Macromolecules* **1986**, *19*, 2149.
(27) Coleman, M. M.; Sobkowiak, M.; Pehlert, G. J.; Painter, P. C. *Macromol. Chem. Phys.* **1997**, *198*, 117.
(28) Ning, L.; De-Ning, W.; Sheng-Kang, Y. *Macromolecules* **1997**, *30*, 4405.
(29) Grobe, G. L., III.; Gardella, J. A., Jr.; Chin, R. L.; Salvati, L., Jr. *Appl. Spectrosc.* **1988**, *42*, 989.
(30) Renier, M.; Wu, Y. K.; Anderson, J. M.; Hiltner, A.; Lodoen, G. A.; Payet, C. R. *J. Biomater. Sci. Polym. Ed.* **1994**, *5*, 511.

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