Polyisobutylene Chain End Transformations: Block Copolymer Synthesis and Click Chemistry Functionalizations

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POLYISOBUTYLENE CHAIN END TRANSFORMATIONS:

BLOCK COPOLYMER SYNTHESIS AND CLICK CHEMISTRY

FUNCTIONALIZATIONS

by

Andrew Jackson David Magenau

Abstract of a Dissertation
Submitted to the Graduate School
of The University of Southern Mississippi
in Partial Fulfillment of the Requirements
for the Degree of Doctor of Philosophy

May 2010
ABSTRACT

POLYISOBUTYLENE CHAIN END TRANSFORMATIONS: BLOCK COPOLYMER SYNTHESIS AND CLICK CHEMISTRY FUNCTIONALIZATIONS

by Andrew Jackson David Magenau

May 2010

The primary objectives of this research were twofold: (1) development of synthetic procedures for combining quasiliving carbocationic polymerization (QLCCP) of isobutylene (IB) and reversible addition fragmentation chain transfer (RAFT) polymerization for block copolymer synthesis; (2) utilization of efficient, robust, and modular chemistries for facile functionalization of polyisobutylene (PIB). Two site transformation strategies were employed to create block copolymers effectively linking PIB with either poly(methylmethacrylate) (PMMA), polystyrene (PS), and poly(N-isopropylacrylamide) (PNIPAM) block segments. Functionalization of PIB was accomplished by utilizing two click chemistries, the azide-alkyne 1,3-dipolar cycloaddition and the thiol-ene hydrothiolation reaction, and by efficient transformation of the thiol functional group.

In the first study block copolymers consisting of PIB, and either PMMA or PS block segments, were synthesized by a site transformation approach combining living cationic and reversible addition-fragmentation chain transfer (RAFT) polymerizations. The initial PIB block was synthesized via quasiliving cationic polymerization using the TMPCl/TiCl4 initiation system and was subsequently converted into a hydroxyl-terminated PIB. Site transformation of the hydroxyl-terminated PIB into a macro chain
transfer agent (PIB-CTA) was accomplished by N,N'-dicyclohexylcarbodiimide/dimethylaminopyridine-catalyzed esterification with 4-cyano-4-(dodecylsulfanylthiocarbonylsulfanyl)pentanoic acid. Structure of the PIB-CTA was confirmed by both $^1$H and $^{13}$C NMR spectroscopy. The PIB-CTA was then employed in a RAFT polymerization of either methyl methacrylate or styrene resulting in PIB block copolymers with narrow polydispersity indexes and predetermined molecular weights, confirmed by both $^1$H NMR and GPC.

In the second study another site transformation approach was developed to synthesize a novel block copolymer, composed of PIB and PNIPAM segments. The PIB block was prepared via quasiliving cationic polymerization and end functionalized by in-situ quenching to yield telechelic halogen-terminated PIB. Azido functionality was obtained by displacement of the terminal halogen through nucleophilic substitution, which was confirmed by both $^1$H and $^{13}$C NMR. Coupling of an alkyne-functional chain transfer agent (CTA) to azido PIB was successfully accomplished through a copper catalyzed click reaction. Structure of the resulting PIB-based macro-CTA was verified with $^1$H NMR, FTIR, and GPC; whereas coupling reaction kinetics were monitored by real time variable temperature (VT) $^1$H NMR. Subsequently, the function of this macro-CTA was demonstrated by RAFT polymerization of NIPAM for synthesis of the second block. RAFT kinetics was investigated under a variety of reaction conditions using VT NMR, and the resulting block copolymers were characterized by $^1$H NMR and GPC. Aqueous solution properties were probed by dynamic light scattering confirming the presence of self assembled aggregates with reversible temperature sensitive responsiveness.
In a third study, a click chemistry functionalization procedure was developed based upon the azide-alkyne 1,3-dipolar cycloaddition reaction. 1-(ω-Azidoalkyl)pyrrolyl-terminated PIB was successfully synthesized both by substitution of the terminal halide of 1-(ω-haloalkyl)pyrrolyl-terminated PIB with sodium azide and by \textit{in situ} quenching of quasiliving PIB with a 1-(ω-azidoalkyl)pyrrole. Azide substitution of the terminal halide was carried out in 50/50 heptane/DMF at 90°C for 24 h using excess azide. The 1-(ω-haloalkyl)pyrrolyl-PIB precursors included 1-(2-chloroethyl)pyrrolyl-PIB, 1-(2-bromoethyl)pyrrolyl-PIB, and 1-(3-bromopropyl)pyrrolyl-PIB. \textit{In-situ} quenching involved direct addition of 1-(2-azidoethyl)pyrrole to quasiliving PIB initiated from 5-\textit{tert}-butyl-1,3-di(1-chloro-1-methylethyl)benzene (\textit{t}-Bu-\textit{m}-DCC)/TiCl$_4$ at -70°C in hexane/CH$_2$Cl$_2$ (60/40, v/v). $^1$H NMR analysis of the quenched product revealed mixed isomeric end groups in which PIB was attached at either C$_2$ or C$_3$ of the pyrrole ring (C$_2$/C$_3$ = 0.40/0.60). GPC indicated the absence of coupled PIB under optimized conditions, confirming exclusive mono-substitution on each pyrrole ring. 1-(3-Azidopropyl)pyrrolyl-PIB was reacted in modular fashion with various functional alkynes, propargyl alcohol, propargyl acrylate, glycidyl propargyl ether, and 3-dimethylamino-1-propyne, \textit{via} the Huisgen 1,3-dipolar cycloaddition “Click” reaction, using Cu(I)Br/N,N,N′,N″,N‴-pentamethyldiethylnetriamine or bromtris(triphenylphosphine)Cu(I) as catalyst. The reactions were quantitative and produced PIBs bearing terminal hydroxyl, acrylate, glycidyl, or dimethylaminomethyl groups attached \textit{via} exclusively 4-substituted triazole linkages.

In a fourth study, radical thiol-ene hydrothiolation “Click” chemistry was explored and adapted to easily and rapidly modify \textit{exo}-olefin PIB with an array of thiol
compounds bearing useful functionalities, including primary halogen, primary amine, primary hydroxyl, and carboxylic acid. The thiol-ene “click” procedure was shown to be applicable to both mono and difunctional *exo*-olefin polyisobutylene. Telechelic mono- and difunctional *exo*-olefin PIBs were synthesized *via* quasiliiving cationic polymerization followed by quenching with the hindered amine, 1,2,2,6,6-pentamethylpiperidine. Lower reaction temperatures were found to increase *exo*-olefin conversion to near quantitative amounts. Thiol-ene reactions with cysteamine and cysteamine hydrochloride resulted in no thioether formation. Primary amine-terminated PIB was successfully obtained via a two–step, one-pot procedure, by using a tert-butoxycarbonyl (BOC) protected amine during the hydrothiolation step and subsequent deblocking with trifluoroacetic acid (TFA). A sunlight-activated hydrothiolation reaction was also demonstrated; although detectable byproducts resulted.

In the fifth study, thiol-terminated polyisobutylene (PIB-SH) was synthesized by reaction of thiourea with α,ω-bromine-terminated PIB in a three step one-pot procedure. First the alkylisothiouronium salt was produced using a 1:1 (v:v) DMF:heptane cosolvent mixture at 90°C. Hydrolysis of the salt by aqueous base produced thiolate chain ends, which were then acidified to form the desired thiol functional group. Structural evidence of the thiol functionality was provided by $^1$H and $^{13}$C NMR, indicating complete conversion of the terminal halogen. Competing sulfide formation was effectively suppressed during the base-hydrolysis step, as verified by GPC, by increased reaction temperature. Utility of PIB-SH was demonstrated through a series of thiol-based “click” reactions. Alkyne-terminated PIB was synthesized by a phosphine-catalyzed thiol-ene Michael addition reaction with propargyl acrylate. An extension of this reaction was
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DEDICATION

This dissertation is dedicated to my family for their love and support.

To my grandfather and grandmother, John Martin Jr. and Carol Magenau, for encouragement of an open mind, creativity, and temperance.

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CHAPTER I
BACKGROUN

Polyisobutylene (PIB) is a fully saturated hydrocarbon elastomer possessing superior gas barrier and mechanical damping characteristics, oxidative and chemical stability, and biocompatibility.\textsuperscript{1-3} PIB is synthesized from isobutylene exclusively through carbocationic polymerization. When combined with other materials, the inherent properties of PIB help produce commercially viable materials such as butyl rubbers, thermoplastic elastomers, and biomaterials. PIB-based materials have found applications ranging from inner liners, tubeless tires, electrical insulators, adhesives, motor oil dispersants, sealants, to coronary stents. Over the last 25 years, methods for controlled or quasiliiving carbocationic polymerization (QLCCP) have been developed. These advancements have enabled new synthetic strategies to produce precisely tailored block copolymers from PIB and to efficiently functionalize PIB with a variety of useful functional groups.

The work presented in this dissertation focuses on transformation of PIB chain ends. Depending on the transformation used, chain ends can be converted into macro-initiators for block copolymer synthesis, or a multitude of other useful functional end groups through the use of robust, efficient, and modular chemistries. Novel approaches were developed to combine QLCCP and reversible addition fragmentation chain transfer (RAFT) polymerizations for block copolymers synthesis. In addition, two click chemistry approaches and efficient thiol group modifications were utilized as versatile functionalization tools for PIB. This introduction will give a brief background of controlled polymerizations, focusing on QLCCP and RAFT polymerization, and two
click chemistries, namely, 1) the 1,3-dipolar Huisgen cycloaddition reaction of azides with terminal alkynes, and 2) the thiol-ene family of reactions including radical hydrothiolation and nucleophilic Michael addition to electrophile enes.

Quasiliving Carbocationic Polymerization

Since discovery of the first living polymerizations, by Szwarc in 1956, preparation of precise polymers and complex architectures has been possible. Living polymerizations, unlike conventional chain polymerizations, proceed in the absence of termination and chain transfer events. Szwarc’s original definition stated, that “propagation proceeds with the exclusion of termination and chain transfer, and yields polymers retaining, virtually indefinitely, their ability to add further monomer whenever supplied to the system.” Suppression of unwanted termination and chain transfer has allowed for the synthesis of well-defined polymers and block copolymers of predetermined molecular weight and narrow molecular weight distributions, and other advanced architectures. A few examples of the architectures obtainable through controlled/living polymerizations include statistical (a), alternating (b), AB diblock (c), and ABA triblock (d) copolymers, ABC block terpolymers (e), tapered block (f) and graft copolymers(g), and star (h) structures, as shown in Figure 1.1.

Living anionic polymerization was the first technique to enable production of polymers and block copolymers with controlled molecular weights and narrow PDIs in the absence of any detectable chain transfer or termination. Extending this idea of “ideal” living polymerizations to carbocationic systems was initially thought to be impossible. Because carbenium ions are highly unstable (i.e. possess high reactivity), in comparison to carbanions, they readily participate in undesired side reactions. These
reactions typically consist of β-proton elimination, chain transfer to monomer, or unimolecular carbenium ion rearrangement (Figure 1.2). Highly reactive β-protons are extremely susceptible to abstraction by basic species within polymerization systems (e.g. monomers, anionic counterions, and other basic additives). Therefore, carbocation lifetimes are typically short, on the order of a few milliseconds, resulting in uncontrolled polymerizations plagued with termination/transfer events.

In order to realize prolonged lifetime of the growing chain ends (i.e., QLCCP), and create controlled high molecular weight polymers, three main factors had to be recognized and implemented: (1) control of initiation, (2) realization of reversible termination, (3) suppression of chain transfer. Chain transfer and termination were circumvented by employing cryogenic reaction conditions, introducing common ions to suppress ion-pair dissociation, depicted in Figure 1.3 as the equilibrium between species (b) and (c), and implementation of reaction conditions whereby termination becomes reversible, i.e., establishment of a dynamic equilibrium between “dormant” and “active” chain ends, depicted in Figure 1.3 as the equilibrium between species (a) and (b). In the latter equilibrium, the “dormant” polymer chains (a) cannot participate in chain transfer or irreversible termination; whereas, further polymerizations can occur by ionization to the paired ion or “active” state (b). Free ions (c) generally possess higher rates of decomposition compared to paired ions and are thus suppressed using the common ion effect.

Early developments toward living cationic polymerization began with the recognition that certain known systems partially resembled those of a living system. For example, polymerization of p-methoxystyrene initiated by I₂ (i.e. nucleophilic
counterion) was observed to yield fairly low PDIs, increased molecular weight upon sequential monomer addition, and a linear correlation between $M_n$ and monomer conversion; however, chain end concentrations were observed to increase with monomer conversion indicating slow initiation.$^{11,12}$ Another important early cationic polymerization system was the so-called inifer method, useful for the synthesis of telechelic PIB, which utilized a molecule functioning as both initiator and chain transfer agent.$^{13,14}$ The inifer system was recognized to provide controlled initiation and chain-end functionality, but it was thought to be non-living. The authors believed that collapse of ion pairs in these cationic polymerizations was an irreversible termination event. Later, however, Faust et al. demonstrated that in monomer starved environments, with a cumyl chloride/BCl$_3$/α-methylstyrene system, a rapid and reversible chain end equilibrium existed which exhibited “quasiliving” characteristics.$^{15}$ The basic premise of quasiliving polymerization is that if termination or chain transfer reactions are present, but reversible, the system will yield a polymerization that kinetically behaves as a living system.

The first QLCCP was reported in 1984 by Higashimura et al.$^{16}$ This system involved a binary initiating system of HI/I$_2$, in equimolar amounts, for the “living” cationic polymerization of isobutyl vinyl ether (IBVE). Solvent effects were substantial due to their profound influence on the dormant-active equilibrium ($K_{eq}$). It was found that $n$-hexane at -15 °C provided the best results by reducing the amount of ionized species within the system. As previously mentioned, I$_2$ produces the nucleophilic counteranion, I$_3^-$, which provides control by stabilization of the carbocation, *i.e.* diminishing chain transfer and spontaneous termination.$^{17}$ Selection of a “suitably
nucleophilic counterion” was of paramount importance; the correct nucleophilicity is required to create a reversible ionization equilibrium that causes the majority of chain ends to exist in their dormant state. It was proposed that both initiation and propagation occurred through a monomer insertion mechanism. “Living” behavior in this system was attributed to fast initiation, a result of rapid addition of HI to monomer, thereby producing an initiating species in situ, and the simultaneous absence of chain transfer reactions due to carbocation stabilization. These systems achieved predetermined (Xn = [IBVE]/[HI]) and narrow (M_w/M_n ≈ 1.1) molecular weights, proportional increases in M_n with monomer conversion, constant chain end concentrations, and continued polymerizations with addition of further monomer. Expansion of this dual initiator system to other reactive monomers, including p-methoxystyrene and N-vinylcarbazole, was also demonstrated. Further variations were explored using other dual initiator systems (e.g. HI/ZnI_2) which allowed controlled polymerizations over larger temperature ranges (-40 °C to 40 °C) and with higher polymerization rates. Near the same time, Faust and Kennedy were using a similar “suitably nucleophilic counterion” approach with IB in alkyl and aromatic ester or ether/BCl_3 initiation systems. When targeting low molecular weight PIB, fairly monodisperse (PDI ≈ 1.2-1.3) polymers were successfully synthesized.

The next significant advancement to further suppress chain transfer and termination, and improve PDIs in cationic polymerization was the addition of external electron donors (EDs) to create the common ion effect. Higashimura and coworkers demonstrated that IBVE polymerizations with strong lewis acids (e.g. SnCl_2, TiCl_4) resulted in an uncontrolled system, but could be easily transformed to have quasiliving
behavior by charging the reactor with chloride salts. Improved control was also observed with less reactive styrene and IB monomers by including salts within the polymerization. Styrene polymerizations were conducted with 1-phenylethyl chloride/SnCl$_4$ coinitiation system in CH$_2$Cl$_2$ at -15 °C. To achieve controlled behavior it was necessary to add $n$Bu$_4$N$^+$Cl$^-$, which resulted in narrow PDI's and targeted molecular weights. Analogous results were found for IB/TiCl$_4$ polymerizations conducted in the presence of EDs, including DMSO and DMA. Kaszas et al. demonstrated the profound effect of EDs and their ability to impart control by monitoring molecular weights (Figure 1.4). Interestingly, IB polymerizations conducted using TiCl$_4$ or BCl$_3$ were found to proceed optimally under conditions of excess of lewis acid relative to ED; whereas IBVE systems appeared to require excess ED relative to lewis acid.

The exact function of externally added EDs in quasiliving carbocationic polymerization has been a subject of much debate. Initial theories proposed that EDs provide “carbocation stabilization.” Later, Faust and coworkers declared their function was solely to serve as protic scavenger. The latter work demonstrated that IB polymerization rates, using a TiCl$_4$/cumyl-type coinitiation system, were independent of ED concentration. If indeed the ED served to provide carbocation stability the polymerization rate should have slowed with higher ED concentrations. The authors believed that protic initiation was extremely fast, and if not suppressed would pre-empt the much slower controlled QLCCP. Storey and coworkers supported the proposal by Faust et al. that the ED served as a protic scavenger, but they also postulated that protic scavenging produced common ion salts, as shown in Figure 1.5, which reduced the rate of polymerization and conferred livingness by eliminating propagation by unpaired...
The ED function was therefore two-fold: prevention of protic initiation and in situ creation of common ions. The latter suppress ion pair dissociation via the “common ion effect.” In terms of the Winstein spectrum of ionicities shown in Figure 1, due to mass action, addition of the common ion $X^-$ shifts the population of chains dramatically away from dissociated ions (c) in the direction of paired ions (b).

Living carbocationic processes are referred to as “quasiliving” to indicate the existence of the dormant-active equilibrium, i.e., all of the chains are not active all of the time. QLCCPs display characteristics of living behavior (i.e. targeted molecular weights, narrow PDIs, ability to form block copolymers); however, they all exhibit termination. Since these termination reactions are completely reversible, as illustrated by the dormant-active chain equilibrium, the polymerizations appear to be truly living.

Reversible Addition-Fragmentation Chain Transfer (RAFT) Polymerization

Although ionic polymerizations give precise control of polymeric architecture, these techniques require stringent reaction conditions and have a limited selection of monomers. Radical polymerizations, however, offer many advantages including a large selection of monomers, tolerance to a broad scope of functionalities and reaction conditions, and are fairly simple and inexpensive in comparison to other methods. In spite of these advantages, free radicals terminate at nearly diffusion controlled rates leading to limited control of molecular weights, PDIs, and polymer composition and architecture. Controlled/living polymerizations (CRP) were developed in an effort to maintain the versatile monomer selection and robust reaction conditions of conventional free radical polymerization and advanced architectures achievable with living polymerizations.
CRP relies on the same principles characteristic of living polymerizations by reducing termination through an equilibrium strongly favoring dormant chains over propagating chains. This equilibrium effectively lowers radical concentrations, which reduces the overall rate of polymerization, but in a greater magnitude suppresses the rate of termination due to its second order dependence on radical concentration. The most commonly used CRP techniques can be categorized by the mechanism with which activated/deactivated chains are created. The majority of CRPs rely on a reversible termination mechanism (Figure 1.6 (a,b)) to impart control; these include iniferters,\textsuperscript{35,36} stable free radical polymerization,\textsuperscript{37,38} and atom transfer radical polymerization.\textsuperscript{39,40} The second mechanism used to impart control in radical polymerizations is a degenerative chain transfer process involving a rapid exchange between polymer species (Figure 1.6 (c)) and can be illustrated by RAFT.

RAFT polymerization was first reported in literature by Rizzardo and Moad in 1988.\textsuperscript{41,42} It is considered to be one of the most versatile controlled/free radical polymerizations, because of its wide range of applicable monomers and reaction conditions.\textsuperscript{43} Controlled/living RAFT polymerizations have been reported with acrylates and methacrylates, acrylamides and methacrylamides, acrylonitrile, styrene and styrenic derivatives, butadiene, vinyl acetate, and N-vinylpyrrolidone. In addition, RAFT is tolerant to a vast range of solvent systems (\textit{e.g.} organic, heterogeneous, and aqueous), initiators (\textit{e.g.} azo, peroxide, photo, $\gamma$ – radiation, and redox initiating systems), and functionalities (\textit{e.g.} OH, NR$_2$, CO$_2$H, SO$_3$H, CONR$_2$). RAFT polymerizations are similar to conventional radical polymerizations (\textit{i.e.} same solvents, temperatures, monomers, and initiator) with the exception of one additional component, a chain transfer agent (CTA).
In common with living polymerizations, RAFT polymerizations operate with constant concentration of growing chain ends, linear increases in molecular weight with conversion, and preservation of active chains at the end of polymerization.

A series of reversible chain transfer reactions (i.e. addition fragmentation equilibrium) is responsible for imparting control in RAFT polymerization; the accepted mechanism is shown in Figure 1.7.\textsuperscript{44,45} Initiation and termination occur in the same manner as conventional radical polymerization. Commonly, azo initiators (Figure 1.8) are used to generate radials (I\textbullet) by thermal decomposition in the initiation stage (Figure 1.7 (a)). It is generally believed that these initiator-derived radicals first add to monomer to produce an oligomeric propagating radical species (P\textsubscript{n}\textbullet) (Figure 1.7 (b)), due to large relative ratio of monomer to initiator.\textsuperscript{46} In the early stages of polymerization, P\textsubscript{n}\textbullet adds to the thiocarbonyl compound (Z-(C=S)-SR) to produce an intermediate carbon centered radical, followed by fragmentation into an oligomeric CTA (P\textsubscript{n}-(C=S)-SR) species and a new CTA derived radical (R\textbullet) (Figure 1.7 (c)).\textsuperscript{44} The pre-equilibrium is defined as the time required for all R\textbullet fragments to form propagating chains P\textsubscript{m}\textbullet, and is governed by the four rate constants k\textsubscript{add}, k\textsubscript{-add}, k\textsubscript{b} and k\textsubscript{-b}. This new CTA derived radical (R\textbullet) then proceeds through re-initiation, forming another oligomeric propagating radical species (P\textsubscript{m}\textbullet). Eventually a rapid equilibrium is reached between the actively propagating radicals (P\textsubscript{n}\textbullet and P\textsubscript{m}\textbullet) and the dormant polymeric thiocarbonylthio compounds (Figure 1.7 (d)). The main reversible degenerative chain transfer equilibrium provides an equal probability for all propagating chains to grow resulting in narrow polydispersity polymers. Most monomer consumption occurs during the main equilibrium and the frequency of monomer additions can vary depending on reaction conditions; however, it
has been shown that in most RAFT polymerizations, less than one monomer unit adds to a propagating chain per transfer step. RAFT polymerizations are properly formulated so that the CTA concentration relative to initiator concentration is high, therefore ensuring that most chains are initiated by CTA derived radical ($R\cdot$) instead of initiator radicals ($I\cdot$). Initiator-derived chains are thought to have a negative effect on the control of the molecular weight. With free radical processes, termination inevitably occurs through radical coupling and disproportionation, and the rate of termination is inherently related to the radical concentration. When termination is a result of bimolecular combination, the number of dead chains is equal to half the number of initiator derived chains; whereas when disproportionation is dominant the number of dead chains is equal to the total number of initiator derived chains. The RAFT process effectively suppresses termination events by limiting the instantaneous concentration of radicals and typically preventing the number of terminated chains from exceeding 5%. The key component of RAFT polymerization is the CTA, which consists of a thiocarbonylthio moiety of the general structure $Z-(C=S)-S-R$. CTAs can be categorized into four main classes depending on their $Z$ group, including dithioesters, xanthates, dithiocarbamates, and trithiocarbonates (Figure 1.9). To design a successful RAFT polymerization the appropriate CTA must be selected in order to establish the appropriate balance between reversible addition and fragmentation reactions (Figure 1.7); otherwise loss of control, retardation, and long induction periods can occur. RAFT agents are chosen based on their $Z$ and $R$ groups. Generally, the $Z$ group controls the level of activation/deactivation of the thio carbonyl double bond. Activating $Z$ groups
efficiently promote rapid radical addition thereby inhibiting prolonged propagation by initiator and CTA derived radicals.\textsuperscript{48} If the Z group is not chosen correctly it can lead to an overly stable intermediate radical, increasing the probably of polymerization retardation\textsuperscript{50} and intermediate radical termination.\textsuperscript{51,52} The R group is directly related to the pre equilibrium and must have the necessary stability to function as an efficient leaving group with the ability to reinitiate polymerization of monomer.\textsuperscript{49}

According to the RAFT mechanism, two potential sources of polymer chains are possible, either initiator-derived or CTA-derived (\textit{i.e.} R group). Therefore the theoretical number-average molecular weight ($M_n$) is defined by equation 1,

\[ M_{n,th} = \frac{[M]_0 M_{MW} \rho}{[CTA]_0 + 2f[I]_0 (1-e^{-k_d t})} + CTA_{MW} \]  \textit{(1)}

where $[M]_0$ is the initial monomer concentration, $M_{MW}$ is the molecular weight of the monomer, $\rho$ is the monomer conversion, $[CTA]_0$ is the initial CTA concentration, $f$ is the initiator efficiency, $[I]_0$ is the starting initiator concentration, $k_d$ is the initiator decomposition rate constant, and $CTA_{MW}$ is the molecular weight of the CTA.\textsuperscript{43,45} In RAFT polymerizations with high CTA to initiator ratios, the effective amount of initiator-derived chains should be less than 5\% allowing these terms to be neglected.\textsuperscript{45} Thus Equation 1 can be approximated as the following Equation 2.

\[ M_{n,th} = \frac{[M]_0 M_{MW} \rho}{[CTA]_0} + CTA_{MW} \]  \textit{(2)}

\textbf{Azide-alkyne Click Chemistry}

With the advent of living polymerizations and click chemistry, complex and precise polymeric architectures are now possible.\textsuperscript{53} Sharpless originally defined click chemistry as a reaction that, “\textit{must be modular, wide in scope, give very high yields,}
generate only inoffensive byproducts that can be removed by nonchromatographic methods, and be stereospecific (but not necessarily enantioselective). The required process characteristics include simple reaction conditions (ideally, the process should be insensitive to oxygen and water), readily available starting materials and reagents, the use of no solvent or a solvent that is benign (such as water) or easily removed, and simple product isolation. Purification – if required – must be by nonchromatographic methods, such as recrystallization or distillation, and the product must be stable under physiological conditions."\textsuperscript{54}

The most popular click chemistry reaction is the copper (I)-catalyzed azide-alkyne 1-3 dipolar cycloaddition.\textsuperscript{53} Until recently, this reaction was unable to meet the stringent click chemistry criteria, failing to satisfy the requirements of simple reaction conditions and stereospecificity. Initially, the azide-alkyne (Huisgen) cycloaddition was performed at high temperature resulting in two regioisomers (\textit{i.e.} 1,4- and 1,5-substituted-1,2,3-triazoles) as shown in Figure 1.10. Later, research groups directed by Sharpless\textsuperscript{55} and Meldal\textsuperscript{56} reported the synthesis of strictly 1,4-substituted-1,2,3-triazoles at room temperature (\textit{i.e.} accelerated reaction rates) through copper (I) catalysis. The proposed mechanism offered by Sharpless (Figure 1.11)\textsuperscript{55} briefly states that first a copper(I) acetylide complex is generated. Then through a “stepwise, ligation process” a six member intermediate is formed, and lastly the triazole is formed releasing the copper(I) catalyst. In 2005, Jia \textit{et al.} also discovered that ruthenium (II) catalysts, instead of copper (I), would reverse the stereospecificity producing only the 1,5-substituted-1,2,3 triazole.\textsuperscript{57}

Because of the many advantages of click type reactions, a profound impact and wide scale usage of these chemistries has been seen in many areas of research. Various
literature examples have been reported in biochemistry,\textsuperscript{58,59} surface functionalization,\textsuperscript{60,61} organic synthesis,\textsuperscript{62} drug discovery,\textsuperscript{63} and in polymer chemistry.\textsuperscript{53,64-66} The first reported usage of click chemistry in the field of polymer science was by Hawker, Sharpless, and coworkers,\textsuperscript{67} and since that time, click chemistry has been demonstrated to have a broad range of utility in the field. A few examples include step growth polymerizations of dialkyne and diazide monomers/polymers,\textsuperscript{68,69} end and side chain functionalizations,\textsuperscript{70-74} block copolymers,\textsuperscript{75,76} cyclic polymers,\textsuperscript{77} hyperbranched/dendritic structures, stars, and cross-linked networks.

Of particular interest in this dissertation is end and pendent functionalization of well defined polymers. Lutz \textit{et al.} performed a unique combination of ATRP and click chemistry to prepare functional polymers (Figure 1.12).\textsuperscript{70} Narrow molecular weight telechelic polystyrene was synthesized, and the terminal bromide was substituted with azide. Afterward, a 1,3-dipolar cycloaddition was conducted with copper bromide/4,4'-di-(5-nonyl)-2,2'-bipyridine (dNbipy) to achieve quantitative conversion of bromide chain ends into $\omega$-hydroxyl, $\omega$-carboxyl, and $\omega$-methyl vinylidene end groups. In another example involving ATRP, Opsteen and van Hest synthesized PMMA, PS, and PEG polymers with terminal alkynes and azides.\textsuperscript{75} Subsequently, using click chemistry, the authors successfully coupled these polymers to create tri and diblock copolymers. Alkyne-terminal polymers were quantitatively synthesized using two approaches: use of a unique blocked-alkyne ATRP initiator (Figure 1.13 (a)), which was deprotected after polymerization, and use of carbodiimide coupling chemistry (Figure 1.13 (b)). Azide terminal polymers were synthesized with a variety of substitution chemistries (Figure
1.14) to produce both mono and difunctional polymers. The resulting block copolymers were easily purified and had monomodal, narrow PDIs.

Functionalization of polymer pendent groups has been demonstrated in combination with numerous controlled polymerization techniques including ring opening metathesis polymerization (ROMP), ATRP, and nitroxide mediated polymerization (NMP). Binder and Kluger prepared functionalized poly(oxynorbornene)s by two synthetic methods: (a) incorporation of functionality through 1,3-dipolar cycloaddition to azide and alkyne functional 7-oxynorborene monomers prior to ROMP; (b) performing ROMP and subsequent attachment of the functional groups to the prefabricated polymer. Both synthetic strategies proved successful in attaching several functional moieties both before and after ROMP polymerization while maintaining a well defined poly(oxynorborne). Matyjaszewski and coworkers attempted direct ATRP polymerization of functionalized monomers containing both azido and acetylene pendent groups. Although limited success was achieved with propargyl methacrylate (i.e. $M_n/M_w > 3$), theorized to be a result of catalyst interaction, radical addition to the acetylene, and/or chain transfer, well controlled polymers were synthesized with 3-azidopropyl methacrylate. Later these polymers were utilized as highly functional scaffolds for click reactions; producing alcohol, acid, halogen, and triphenylphosphine functionalized macromolecules.

Thiol-ene Click Chemistry

The thiol and hydroxyl groups share some common features, but fundamentally they are different, owing to their disparate chemical and physical properties. To begin, sulfur has less electronegative character and a larger atomic radius, attributing to its
longer and weaker covalent bonds.\textsuperscript{78} Geometrically, when comparing thiol and alcohol functional groups, the bonds angles in alcohols are larger. For example, methanethiol has a bond angle of $100.3^\circ$, whereas methanol has a larger bond angle of $109.5^\circ$. Other characteristic differences include the inability of thiols to participate in hydrogen bonding, unlike their alcohol counterpart, resulting in typically lower boiling points. A few examples of this can be viewed in Table 1.1. One crucial attribute of the thiol group is the labile nature of the hydrogen sulfur bond in comparison to a hydrogen oxygen bond. Thiols are readily deprotonated (heterolytic bond cleavage), which is exemplified by their more acidic nature in contrast to alcohols ($\text{CH}_3\text{S-H } pK_a = 10.3; \text{CH}_3\text{O-H } pK_a = 15.5$).\textsuperscript{78,79} As a result, thiols easily converted by bases into highly nucleophilic thiolate anions. Thiols also readily undergo homolytic cleavage of the S-H bond to produce thyl radicals when exposed to photo or thermal initiating processes. Various types of thiol chemistries exist and have been studied extensively;\textsuperscript{78} although more recently, a series of thiol-based reactions including thiol-ene,\textsuperscript{80-83,100} thiol-yne,\textsuperscript{84,93} and thio-isocyanate\textsuperscript{85,86} have been recognized for their “click” characteristics.\textsuperscript{87}

Hydrothiolation, more commonly known as the “thiol-ene” reaction, is the addition of a thiol across any unsaturated carbon-carbon double bond regardless of the reaction mechanism (Figure 1.15).\textsuperscript{87} In the past, much work was conducted by Hoyle \textit{et al.}\textsuperscript{88} and Bowman \textit{et al.}\textsuperscript{89,90,91} in the materials/polymer fields by utilizing the thiol-ene reaction as a means to prepare near-perfect networks. Recently though, the thiol-ene reaction has been recognized as a powerful synthetic tool for preparation of complex functional architectures because of its many attractive features and “click” characteristics.\textsuperscript{92,81} This process has proven to be versatile and can proceed through a
broad range of reaction conditions including a radical-mediated pathway (i.e. homolytic S-H lysis),\textsuperscript{88} base/nucleophile-mediated addition with activated enes (i.e. heterolytic S-H lysis),\textsuperscript{93,94} through solvent-mediated conditions,\textsuperscript{95} and by supramolecular catalysis.\textsuperscript{96} This being the case, an extensive assortment of tools are available to the synthetic chemist, including a broad range of mono and multivalent ene substrates with varying reactivities, and a vast array of functional thiols of variable S-H bond strength. Numerous click characteristics are exemplified by the thiol ene reaction, including its extremely rapid reaction rate, tolerance to oxygen and water, and (near) quantitative conversions to a regioselective thioether product.

Of the many thiol-ene reactions, the photochemically induced radical-mediated addition process is most often used.\textsuperscript{87,88,97,98} Extensive work has been conducted with this technique for network formation,\textsuperscript{88,89} polymer modification,\textsuperscript{99,83} and synthesis of complex polymeric architectures.\textsuperscript{93,100} In general, the radical-mediated process proceeds through a chain mechanism consisting of initiation, propagation, chain transfer, and termination steps (Figure 1.16). Initiation begins by irradiation of thiol groups in the presence of photoinitiator, which rapidly produces thyl radicals and other photoinitiator fragments. Radical generation can also be accomplished thermally.\textsuperscript{101} After thyl radical generation, propagation begins by radical addition across a double bond to produce a carbon-centered radical species. Through homolysis of another sulfur hydrogen bond, chain transfer occurs by hydrogen abstraction from the thiol to the carbon centered radical and simultaneous regeneration of a new thyl radical. Lastly, termination processes involve typical radical-radical coupling reactions.
Reactivities of the thiol-ene radical mediated process can vary considerably based upon the thiol and double bond structures. Double bond reactivity is typically a function of electron density; where electron rich species have increased reactivity in comparison to their electron deficient counterparts. In general, double bond reactivity is observed in the following order: norbornene > vinyl ether > propenyl > alkene ≈ vinyl ester > N-vinylamide > allyl ether ≈ allyl triazine ≈ alkyl isocyanurate > acrylate > N-substituted maleimide > acrylonitrile ≈ methacrylate > styrene > conjugated diene. With the exception of norbornene and the last three species, reactivity decreases with diminished electron density. The exceptionally high reactivity of norbornene can be explained by relief of ring strain after thyl radical addition; whereas, the stability of the carbon centered radicals, in the last three molecules, may impede facile hydrogen abstraction, retarding their reactivity. While considerable analysis of double bond reactivity has been conducted, limited literature is available on thiol reactivity. Some general trends exist, showing that mercaptopropionates and thiolglycolates have significantly higher reactivities relative to alkyl thiols. Some authors explain this as a hydrogen bonding phenomenon, while other researchers claim this may be a result of polar effects.

In addition to the radical-mediated thiol-ene reaction, hydrothiolation can be performed with activated double bonds with mildly basic or nucleophilic catalysts (Figure 1.17). Activated double bonds are electron deficient; containing carbonyl, cyano, or similar electron withdrawing groups adjacent to the α-carbon. This type of thiol-ene reaction, commonly referred to as the thiol-Michael addition reaction, can be performed with a vast array of available substrates. A few examples of activated double bond
substrates are shown in Figure 1.18. In comparison to typical Michael additions, only mildly basic catalysts are required for the thiol-Michael reaction.\textsuperscript{87} Because of the slightly more acidic nature of thiols, in comparison to their corresponding alcohols, thiolate anions are readily formed.\textsuperscript{78}

During the base-catalyzed thiolation mechanism (Figure 1.19), first deprotonation by a basic species (\textit{e.g.} triethylamine) occurs to form the thiolate anion and triethylammonium cation. The thiolate anion, a strong nucleophile, then attacks the electron deficient double at the $\beta$-carbon producing an even stronger intermediate carbon centered anion (\textit{i.e.} enolate). Rapid proton transfer, from either the ammonium cation or another thiol, to the enolate species results in the desired regioselective anti-Markovnikov thioether product and concomitant regeneration of another thiolate anion.

In contrast to the base-catalyzed mechanism, recently an alternative nucleophile-based mechanism was proposed for thiol-ene Michael reaction with phosphine catalysis (Figure 1.20).\textsuperscript{93} With a similar reaction, but for the hydration and hydroxylation of activated double bonds, Steward \textit{et al.} declared that the catalyst served as a nucleophile instead of as a base.\textsuperscript{103} Evidence to support this nucleophilic mechanism was provided by another study involving a series of thiol-Michael reaction kinetics mediated with amine catalysis.\textsuperscript{87} In one study, three catalysts were examined, all of which had similar basicities (\textit{i.e.} all $pK_a$ values between 10.56 and 11.0) but varying degrees of nucleophilicity. It was found that reaction rates increased with more powerful nucleophiles, \textit{e.g.} hexylamine, di-$n$-propylamine, and triethylamine achieved approximately 90, 60, and $> 1\%$ conversion in 500 s, respectively. However, when catalyst nucleophilicity was kept fairly constant and instead basicity was varied, little
variation in reaction rates were observed for pyridine (pK$_a$ = 5.15), aniline (pK$_a$ = 9.34), and 1,8-bis(dimethylamino)naphthalene (pK$_a$ = 12.1). These results imply that the mechanism is not governed purely by catalyst basicity but instead by nucleophilicity. For the phosphine-mediated thiol-Michael addition, the mechanism dictates that initial attack on the activated carbon occurs at the β-carbon and a subsequent zwitteronic enolate species is then formed. This intermediate species is a powerful base therefore promoting rapid proton abstraction from another thiol to begin the extremely rapid thiol-ene chain process. Thiol-Michael additions have been reported to proceed very rapidly to 100% conversion without sensitivity to moisture.
References


2. Kennedy, J. P. *TRIP* 1993, 12, 381.


42. Le, T. P.; Moad, G.; Rizzardo, E.; Thang, S. H. Int. Pat. 9801478.


55. Rostovtsev, V. V.; Green, L. G.; Fokin, V. V.; Sharpless, K. B. *Angew. Chem. Int. Ed.* **2002**, *41*, 2595.


Table 1.1. Boiling points of alcohols and thiols.

<table>
<thead>
<tr>
<th>Thiols</th>
<th>Alcohol</th>
<th>Temperature</th>
</tr>
</thead>
<tbody>
<tr>
<td>Methanethiol</td>
<td>Methanol</td>
<td>6 °C</td>
</tr>
<tr>
<td>Ethanethiol</td>
<td>Ethanol</td>
<td>35 °C</td>
</tr>
<tr>
<td>1-Butanethiol</td>
<td>1-Butanethiol</td>
<td>98 °C</td>
</tr>
</tbody>
</table>
Figure 1.1. Polymeric architectures via controlled living polymerization.
1. Bimolecular Chain Transfer

\[
\text{biomolecular\ chain\ transfer} = \text{biomolecular\ chain\ transfer}\n\]

2. Spontaneous $\beta$-Proton Elimination (Unimolecular Chain Transfer)

\[
\text{spontaneous $\beta$-proton\ elimination} = \text{spontaneous $\beta$-proton\ elimination}\n\]

2. Carbenium Ion Rearrangement (Unimolecular Chain Termination)

\[
\text{carbenium\ ion\ rearrangement} = \text{carbenium\ ion\ rearrangement}\n\]

**Figure 1.2.** Chain breaking events in the cationic polymerization of IB.
Figure 1.3. Chain equilibrium between (a) dormant, (b) ion pair, (c) free-ion pair chains.

P is the propagating chain end, X is the counterion, $K_{eq}$ is the ionization equilibrium constant, and $K_{dis}$ is the ion pair dissociation equilibrium constant.
Figure 1.4. GPC (RI) traces of PIB prepared by the TMPCl/TiCl₄ system in the absence and the presence of ED.
Figure 1.5. Proposed mechanism for the formation of common ions through the scavenging of protic impurities by 2,4-dimethylpyridine.
Figure 1.6. CRP equilibrium between active and dormant chains with (a) SFRP, (b) ATRP, and (c) RAFT.
**initiation**

(a) Initiator $\xrightarrow{k_d} I^* \rightarrow_M P_n^*$

**reversible chain transfer/propagation**

(b) $P_n^* \xrightarrow{k_{add}} \frac{k_{add}}{k_{-add}} Z^* C - S - R \xrightarrow{k_b} P_m^* S - C - S - R \xrightarrow{k_{-add}} \frac{k_{-add}}{k_{add}} Z^* C - S - P_n + R^*$

**reinitiation**

(c) $R^* +$ Monomer $\rightarrow P_m^*$

**reversible (degenerate) chain transfer/propagation**

(d) $P_m^* \xrightarrow{k_{add}} \frac{k_{add}}{k_{-add}} Z^* C - S - P_n \xrightarrow{k_{-add}} \frac{k_{-add}}{k_{add}} P_m^* S - C - S - P_n \xrightarrow{k_b} \frac{k_b}{k_{-b}} Z^* C - S - P_n + P_n^*$

**termination**

(e) $I^*, R^*, P_n^*, P_m^* \xrightarrow{k_t} $ Dead Polymer

**Figure 1.7.** The RAFT polymerization mechanism.
Figure 1.8. Thermal initiators employed in RAFT polymerizations.
Figure 1.9. Generic structures of RAFT chain transfer agents.
Figure 1.10. Dipolar cycloadditions between alkynes and azides.
Figure 1.11. Proposed catalytic cycle for the Cu(I)-catalyzed azide alkyne reaction.
Figure 1.12. Preparation of chain-end functionalized PS via a combination of ATRP and click chemistry.
Figure 1.13. Incorporation of azide end groups in polystyrene via an end group modification procedure.
Figure 1.14. Introduction of terminal alkyne functionality in polymers utilizing functionalized ATRP initiator.
Figure 1.15. Anti-markovnikov hydrothiolation of C=C bond.
Initiation
R-SH + PI $\xrightarrow{hv}$ R-S•

Propagation
R-S• + \( \rightarrow \) R-S•

Chain Transfer
R-S• + R-SH $\rightarrow$ R-S•

**Figure 1.16.** Radical mediated thiol-ene photoinitiated reaction.
Figure 1.17. Base/Nucleophile catalyzed hydrothiolation.
Figure 1.18. Activated double bonds applicable to the base/nucleophile-mediated hydrothiolation.
Figure 1.19. Base catalyzed hydrothiolation mechanism.
Figure 1.20. Nucleophilic phosphine catalyzed hydrothiolation mechanism.
As stated earlier, the primary objectives of this research were twofold: (1) development of synthetic procedures for combining quasiliving carbocationic polymerization (QLCCP) of isobutylene (IB) and reversible addition fragmentation transfer chain (RAFT) polymerization for block copolymer synthesis; (2) utilization of efficient, robust, and modular chemistries for facile functionalization of polyisobutylene (PIB). Two site transformation strategies were employed to create block copolymers effectively linking PIB with either poly(methylmethacrylate) (PMMA), polystyrene (PS), and poly(N-isopropylacrylamide) (PNIPAM) block segments. Functionalization of PIB was accomplished by utilizing two click chemistries, the azide-alkyne 1,3-dipolar cyclo addition and thiol-ene hydrothiolation reactions, and by efficient transformation of the thiol functional group. Specifically, the objectives of this work are briefly stated below:

1. Development of a synthetic strategy to combine quasiliving carbocationic IB polymerization and RAFT polymerization.

2. Development of a synthetic strategy which combines quasiliving carbocationic IB polymerization and RAFT polymerization to synthesize amphiphilic block copolymers.

3. Investigate the utility of the azide-alkyne 1,3-dipolar cyclo addition to create functional polyisobutylenes from a common azide functional precursor.

4. Investigate the utility of the radical mediated thiol-ene click reaction to create functional polyisobutylenes from a common exo-olefin precursor.
5. Synthesis and transformation of $\alpha,\omega$-thiol-functional isobutylene into multi-functional telechelics, macro-CTAs, and PIB based thiourethanes.
CHAPTER III
SITE TRANSFORMATION OF POLYISOBUTYLENE CHAIN ENDS INTO FUNCTIONAL RAFT AGENTS FOR BLOCK COPOLYMER SYNTHESIS

Introduction

Polyisobutylene (PIB) is a fully saturated hydrocarbon elastomer with outstanding oxidative and chemical resistance, superior gas-barrier and mechanical damping characteristics, and excellent biocompatibility. Due to these characteristics, block copolymers based on PIB elastomeric segments are currently of great interest as self assembling materials with unique properties. For example, PIB-based triblock copolymers have become an attractive candidate as a biomaterial and have found a niche market in this field. Poly(styrene-b-isobutylene-b-styrene) (SIBS) is currently being used as a drug-eluting coating for coronary stents because of its effectiveness as a drug delivery matrix, vascular biocompatibility, and advantageous mechanical properties. Faust et al. have studied drug release characteristics of similar materials possessing outer blocks derived from methyl methacrylate (MMA), 2-hydroxyethyl methacrylate (HEMA), and hydroxyl and acetylated styrene (S) derivatives. Recently, much progress has been made in the synthesis of self assembling PIB-based polymersomes and micelles to create new delivery/encapsulation systems and interpolyelectrolyte complexes for biotechnology and medicine. In other application areas, Binder and Machl have synthesized poly(ether ketone-b-PIB–b-ether ketone) triblock copolymers with potential uses as high-temperature thermoplastic elastomers (TPEs) with outer block Tg’s above 150°C. ABA rod-coil-rod triblock copolymers containing a PIB center block and
mesogen-jacketed liquid crystalline polymer outer blocks exhibit liquid crystalline properties and have been suggested to have potential electrochemical applications.\(^9\)

The examples above demonstrate that a number of methods have been devised for the creation of novel block copolymers, in addition to traditional sequential monomer addition. Specifically, the technique of site transformation can be used to greatly expand the library of polymer segments that can be mated to PIB to form new and interesting block copolymers. In this method, PIB block segments derived through cationic polymerization are converted into functional macroinitiators for a chain polymerization process other than cationic. For PIB-based systems this has typically involved combinations of living cationic polymerization with atom transfer radical polymerization (ATRP),\(^{10,11,12,13}\) condensation polymerization,\(^{14}\) or anionic polymerization.\(^{15,16}\)

The relatively new controlled/living radical polymerization technique, reversible addition-fragmentation chain transfer (RAFT) polymerization, has proven to be very versatile regarding monomers, solvents, and reaction conditions to yield macromolecules with predetermined molecular weights and narrow polydispersities.\(^{17}\) In addition, chain transfer agents (CTAs) used in the RAFT process can be synthesized to carry many useful reactive end-groups. These end groups can later be used for coupling reactions to various macromolecules allowing for subsequent block copolymer synthesis.\(^{18}\) This type of approach has been demonstrated with poly(ethylene glycol) (PEO),\(^{19}\) commercially available Kraton polymers,\(^{20}\) and solid polymer supports derived from cotton,\(^{21}\) and was successfully used to convert these macromolecules into functional macro–CTA’s for block and graft copolymer synthesis. Because of the versatility of RAFT polymerizations and its capability to polymerize many monomers which are inherently troublesome for
other polymerization techniques, RAFT is potentially an ideal polymerization technique to combine with cationic polymerization by site transformation. This unique combination would allow the synthesis of a variety of PIB based block copolymers with potentially new or greatly improved properties compared to what is now currently available. Herein, we report an initial example of combining living cationic polymerization of isobutylene with the subsequent RAFT polymerization of methyl methacrylate (MMA) and styrene (S) through site transformation of PIB chain ends into functional macro-CTAs. With these model monomers as a template, further expansion of this technique can be used for the synthesis of PIB based copolymers with monomers traditionally inaccessible to PIB and cationic polymerization.

Experimental

Materials

Hexane (anhydrous, 95 %), TiCl₄ (99.9 %, packaged under N₂ in sure-seal bottles), 2,6-lutidine (redistilled, 99.5%), chloroform-d (99.8 atom% D), N,N′-dicyclohexyl carbodiimide (99%) (DCC), 4-(dimethylamino)pyridine (99%) (DMAP), anhydrous dichloromethane (99.8%) (DCM), 1,2,2,6,6-pentamethylpiperidine (97%) (PMP), and 1,3,5-trioxane (≥ 99%) were purchased from Sigma-Aldrich and used as received. Methyl methacrylate (MMA) (99%), benzene (≥ 99.0%), and styrene (S) (99.5%) were distilled from calcium hydride under a N₂ atmosphere. 2,2′-Azobis(2-methylpropionitrile) (98%) (AIBN) was recrystallized from ethanol. Isobutylene (IB) (BOC, 99.5 %) and CH₃Cl (Alexander Chemical Corp.) were dried through columns packed with CaSO₄ and CaSO₄/4 Å molecular sieves, respectively.
Synthesis of Exo-olefin and Hydroxyl Terminated PIB

Two monofunctional exo-olefin-terminated PIB precursors were synthesized using quasiliving polymerization of isobutylene followed by in-situ quenching with 1,2,2,6,6-pentamethylpiperidine according to a previously reported method. A representative procedure is as follows: quasiliving polymerization of IB with TMPCl as an initiator was carried out within a N₂ atmosphere glovebox, equipped with an integral cryostated hexane/heptanes bath. Into a round bottom flask with a mechanical stirrer, infrared probe, and thermocouple were added 572 mL CH₃Cl, 860 mL hexane, 2.50 mL (2.19 g, 0.0147 mol) TMPCl, and 0.86 mL (0.79 g, 0.0074 mol) of 2,6-lutidine. The mixture was allowed to equilibrate to -60 °C, and then 29.0 mL (19.9 g, 0.354 mol) of IB was added to the reactor and allowed to reach thermal equilibrium. To begin the polymerization, 4.8 mL (8.3 g, 0.044 mol) of TiCl₄ was charged to the reactor. Full monomer conversion (≥ 98 %) was achieved in 90 min, after which time 8.0 mL (6.9 g, 0.044 mol) PMP and an additional 4.8 mL TiCl₄ (8.3 g, 0.044 mol) were added to the polymerization. PMP was allowed to react with the living chain ends for 90 min. Finally, the reaction was terminated by addition of excess prechilled methanol. The contents of the reaction flask were allowed to warm to room temperature, and the polymer in hexane was immediately washed with methanol and then precipitated into methanol from hexane. The precipitate was collected by dissolution in hexane; the solvent was washed with water, dried over MgSO₄, and concentrated on a rotary evaporator. Residual solvent was removed under vacuum at 40 °C. A representative ¹H and ¹³C NMR spectra of exo-olefin PIB is shown in Figure 3.1 and 3.2 respectively, whereas GPC traces before and after quenching is shown in Figure 3.3. Their
characterization result is summarized in Table 3.1. The \textit{exo}-olefin PIB precursors were converted into hydroxyl PIBs through hydroboration-oxidation as reported by Ivan \textit{et al.}\textsuperscript{23} Representative \textsuperscript{1}H NMR, \textsuperscript{13}C NMR, and GPC are in Figures 3.4, 3.5, and 3.6 respectively.

\textit{Synthesis of 4-Cyano-4-(dodecylsulfanylthiocarbonylsulfanyl)-pentanoic Acid (CTA)}

The chain transfer agent (CTA) was synthesized according to previously reported literature methods.\textsuperscript{18} \textit{n}-Dodecylthiol (15.4 g, 76 mmol) was added over 10 min to a stirred suspension of sodium hydride (60\% in oil) (3.15 g, 79 mmol) in diethyl ether (150 mL) at a temperature between 5 and 10 °C. A vigorous evolution of hydrogen was observed and the greyish sodium hydride was transformed to a thick white slurry of sodium thiododecylate. The reaction mixture was cooled to 0 °C and carbondisulfide (6.0 g, 79 mmol) added to provide a thick yellow precipitate of sodium S-dodecyl trithiocarbonate which was collected by filtration and used in the next step without purification.

A suspension of sodium S-dodecyl trithiocarbonate (14.6 g, 0.049 mol) in diethyl ether (100 mL) was treated by portion-wise addition of solid iodine (6.3 g, 0.025 mol). The reaction mixture was then stirred at room temperature for 1 h when the white sodium iodide which settled was removed by filtration. The yellow–brown filtrate was washed with an aqueous solution of sodium thiosulfate to remove excess iodine and water and dried over sodium sulfate and evaporated to leave a residue of bis-(dodecylsulfanylthiocarbonyl)disulfide. A solution of 4,4’-azobis(4-cyanopentanoic acid) (2.10 g, 0.0075 mol) and the above bis-(dodecylsulfanylthiocarbonyl) disulfide (2.77 g, 0.005 mol) in ethylacetate (50 mL) was heated at reflux for 18 h. After removal of the
volatiles in vacuum, the crude product was extracted with water (5 X 100 mL) to afford 4-cyano-4-(dodecylsulfanylthiocarbonyl) sulfanyl pentanoic acid as a pale yellow solid after recrystallization from hexane.

*Synthesis of 4-Cyano-4-(dodecylsulfanylthiocarbonylsulfanyl)pentanoic Acid-Functionalized PIB (PIB-CTA)*

To a 25 mL one-neck round-bottom flask equipped with a magnetic stir bar were added DCC (0.32 g, 1.54 mmol), DMAP (38 mg, 0.31 mmol), and CTA (0.39 g, 0.96 mmol) under a dry nitrogen atmosphere. In a separate vessel, hydroxyl-functional PIB-1 (1.25 g, 0.77 mmol) was dissolved in 13.5 mL DCM and the resulting solution was charged to the reaction flask. After 12 h, the reaction was filtered, and the solvent was removed under reduced pressure. The resulting product was dissolved in hexane, washed with methanol, and then precipitated into methanol from hexane. The precipitate was dissolved in hexane and washed first with a saturated NaCl solution and then with deionized water. The solution was then dried over magnesium sulfate and filtered, and the hexane was stripped under reduced pressure until a constant weight was reached.

*Polymerization of MMA and S from PIB-CTA*

A representative RAFT polymerization was conducted as follows. To a 25 mL Schlenk-style, long-neck round-bottom flask were charged PIB-1-CTA (0.069 g, 0.031 mmol), 1,3,5-trioxane (0.048 g, 0.533 mmol), MMA (0.394 g, 3.94 mmol), and AIBN (0.0025 g, 0.015 mmol) in 0.18 mL of benzene. After dissolution of the reagents an initial aliquot was taken to establish the initial monomer concentration relative to the internal standard 1,3,5-trioxane, via $^1$H NMR spectroscopy. The solution was then subjected to three freeze-pump-thaw cycles to remove oxygen, sealed under N₂, and
submerged in an oil bath at 60°C. After approximately 16 h the reaction was exposed to oxygen and quenched in liquid nitrogen. A final aliquot was taken for $^1$H NMR analysis, and then the crude reaction product was precipitated into hexane and placed under vacuum until a constant mass was reached. Conversion was calculated from the initial and final monomer concentrations relative to 1,3,5-trioxane.

**Instrumentation**

NMR spectra were acquired using a Varian Mercury$^{\text{plus}}$ 300 MHz NMR spectrometer. Samples were dissolved in chloroform-$d$ (3-7 %, w/v) and analyzed using 5 mm NMR tubes. $^{13}$C and $^1$H resonances were correlated with gradient enhanced heteronuclear single-quantum coherence (gHSQC) spectroscopy, using the average of 16 transients for each of 2 x 512 increments and phase sensitive detection in the F1 dimension.

Variable-temperature NMR (VT NMR) data were acquired using a Varian Mercury$^{\text{plus}}$ 300 MHz NMR spectrometer fitted with a Bruker Eurotherm VT controller. RAFT polymerizations were performed in benzene-$d$ at 333 K, with a 250 s pre-acquisition delay between each spectrum. The probe was allowed to equilibrate for 10 min prior to data acquisition. Temperatures reported in this study are within plus/minus 2 degrees, based on ethylene glycol calibration.$^{24,25}$ RAFT polymerizations for VT NMR were prepared by first charging a Schlenk-style round bottom flask with the crude reaction mixture and performing three freeze-thaw-pump cycles. After degassing, and just prior to analysis, the contents were transferred into an air-tight NMR tube within a dry nitrogen atmosphere glovebox. Conversion was calculated by comparison of the vinyl proton areas of the monomer to the internal standard, 1,3,5-trioxane.
Number average molecular weight ($M_n$) and polydispersity index (PDI) of the polymeric materials were measured using a Gel Permeation Chromatography (GPC) system consisting of a Waters Alliance 2695 separation module, an on-line multiangle laser light scattering (MALLS) detector fitted with a gallium arsenide laser (power: 20 mW) operating at 690 nm (MiniDAWN, Wyatt Technology Inc.), an interferometric refractometer (Optilab DSP, Wyatt Technology Inc.), and two Polymer Laboratories mixed E columns (pore size range 50-10³ Å, 3 µm bead size) connected in series. Freshly distilled THF served as the mobile phase and was delivered at a flow rate of 1.0 ml/min. Sample concentrations were ca. 6-7 mg of polymer/mL of THF, and the injection volume was 100 µL. The detector signals were simultaneously recorded using ASTRA software (Wyatt Technology Inc.), and absolute molecular weights were determined by MALLS. The $dn/dc$ values for PIB homopolymer, PIB-CTA, PIB-$b$-poly(methyl methacrylate) (PIB-$b$-PMMA), and PIB-$b$-polystyrene (PIB-$b$-PS) were calculated from the response of the Optilab DSP and assuming 100% mass recovery from the columns.

*Diblock Copolymer Molecular Weight and Blocking Efficiency by $^1H$ NMR*

The number average molecular weights of the diblock copolymers were calculated using $^1H$ NMR and equation 1 for PIB-$b$-PMMA and equation 2 for PIB-$b$-PS. $A_{\text{methoxy}}$ and $A_{\text{aromatic}}$ represent the area of the methoxy protons of PMMA and the aromatic protons of PS; $M_{\text{MMA}}$ and $M_S$ are the molecular weights of the corresponding monomer units, and $M_n,\text{PIB-CTA}$ equals 2,200 g/mol for PIB-1 and 3,100 g/mol for PIB-2. The methylene protons on carbon two of the CTA were used to normalize $A_{\text{methoxy}}$ and $A_{\text{aromatic}}$.

$$M_{n,\text{NMR}} = \frac{A_{\text{methoxy}}}{3} \times M_{\text{MMA}} + M_{n,\text{PIB-CTA}}$$ (1)
\[ M_{n,NMR} = \frac{A_{aromatic}}{5} \times M_s + M_{n,PIB-CTA} \]  

(2)

Blocking efficiency (B_{eff} \%) was calculated using GPC (equation 3) and \(^1\)H NMR (equation 4).

\[ B_{eff} % = \frac{M_{n,\text{theo}} - M_{n,PIB-CTA}}{M_{n,GPC} - M_{n,PIB-CTA}} \]  

(3)

\[ B_{eff} % = \frac{M_{n,\text{theo}} - M_{n,PIB-CTA}}{M_{n,NMR} - M_{n,PIB-CTA}} \]  

(4)

M_{n,GPC} is the number average molecular weight of the diblock copolymer determined using GPC-MALLS. M_{n,\text{theo}} is the theoretical number average molecular weight of the diblock copolymer calculated according to equation 5 for PIB-\(b\)-PMMA (the calculation is analogous for PIB-\(b\)-PS), where \(p\) is monomer conversion for the RAFT polymerization and \([\text{MMA}]_o\) and \([\text{PIB-CTA}]_o\) refer to the initial MMA and PIB-CTA concentrations, respectively.

\[ \frac{p[MMA]_o}{[\text{PIB-CTA}]_o} M_{\text{MMA}} + M_{n,\text{PIB-CTA}} \]  

(5)

Results and Discussion

The method employed for site transformation from living carbocationic polymerization to RAFT polymerization is shown in Figure 3.7. The initial PIB block was synthesized by quasiliving cationic polymerization using the 2-chloro-2,4,4-trimethylpentane/TiCl\(_4\) initiation system. After reaching full conversion of the IB monomer, \textit{in-situ} quenching with the hindered nucleophile, PMP, was used to convert the quasiliving cationic chain ends into \textit{exo}-olefin functionality.\(^{22}\) After quenching, \(^1\)H NMR integration was used to characterize the end group composition of the product by
assuming that tert-chloride, endo-olefin, exo-olefin, and coupled PIB chain ends represent 100% of the chain ends. The results indicated that the PIB precursors were functionalized to near quantitative amounts (Table 3.1) showing only trace quantities of tert-chloride, endo-olefin, and coupled products. Terminal exo-olefin PIB functionality was selected because of the convenience of in-situ quenching and the facile transformation of this end group into a variety of other functional groups. Low molecular weight PIB was targeted in this work to facilitate accurate NMR analysis. For discussion purposes all NMR and GPC characterization results will correspond to PIB-1, Table 3.1, unless otherwise stated. $^1$H and $^{13}$C NMR spectra of exo-olefin PIB are shown in Figures 3.1 and 3.2, respectively. GPC traces of both the pre-quench tert-chloride PIB and quenched exo-olefin PIB are also shown in Figure 3.3.

Exo-olefin PIB was converted into hydroxyl PIB by hydroboration oxidation. Complete characterization of hydroxyl PIB using $^1$H/$^{13}$C NMR along with the GPC traces before and after functionalization demonstrated its successful synthesis (Figures 3.4-6). From $^1$H NMR the disappearance of the methylene (2.00 ppm), methyl (1.78 ppm), and olefinic protons (4.85 and 4.64 ppm) and formation of the new methylene protons (3.53-3.41 ppm and 3.36-3.26 ppm) adjacent to the hydroxyl group indicated near quantitative conversion from the exo-olefin PIB. $^{13}$C NMR revealed that the exo-olefin carbons at 144.53 and 114.03 ppm were absent in the hydroxyl PIB, and new shifts for these carbons appeared at 31.99 and 69.86 ppm, respectively. Carbons immediately adjacent to the exo-olefin functionality also shifted from 53.87 to 49.58 ppm and from 25.91 to 20.04 ppm. The GPC traces in Figure 3.6 did not show significant changes in $M_n$ and indicated the absence of any coupling.
The CTA, 4-cyano-4-(dodecylsulfanylthiocarbonylsulfanyl)pentanoic acid, was synthesized according to previously reported literature methods and characterized using $^1$H and $^{13}$C NMR, as shown in Figure 3.8 and 3.9. This particular CTA was chosen due to its solubility in low-polarity media, facile synthesis, reduced odor, and established ability to polymerize MMA. $^{18}$ $^1$H NMR peak assignments were obtained from the literature. $^{18}$

$^{13}$C NMR peak assignments were made using two dimensional gHSQC (Figures 3.10) and further bolstered by an attached proton test, which can be found in Figure 3.11. In Figure 3.9, the carbon assignments were made by correlation with their respective proton peaks; although some ambiguity exists in identification of carbon 12 (associated with protons b' in Figure 3.8) due to overlap of its signal with the numerous carbon peaks of the dodecyl group. Carbons 11, 14, 16, and 17 had no correlations during the HSQC experiment, confirming that they were indeed quaternary carbons.

Synthesis of a PIB-based macro-CTA was accomplished by esterification of the CTA with hydroxyl PIB. The esterification reaction utilized DMAP as a catalyst and DCC as a water scavenger. This reaction successfully yielded CTA-functionalized PIB to near quantitative conversion. Structural evidence of the resulting PIB-CTA can be seen in the $^1$H and $^{13}$C NMR spectra shown in Figures 3.12 and 3.13, respectively. In Figure 3.12, the methylene protons (a') adjacent to the hydroxyl group on the PIB shifted from their original location at approximately 3.53-3.26 to 4.00-3.74 ppm. In addition, no residual methylene protons of the hydroxyl-terminated PIB were visible, indicating complete conversion was achieved. Also, the methylene protons (b') adjacent to the acid
functionality on the CTA shifted slightly upfield from their original location after coupling with the hydroxyl PIB.

In the $^{13}$C NMR spectrum of the PIB-CTA (Figure 3.13) peaks from both the CTA and hydroxyl PIB are visible, indicating that both structures are present and coupled together after purification. If the CTA were not covalently attached to the PIB, it would have been removed during washing and precipitation of the polymer. Due to the number of peaks present in Figure 3.13, direct comparisons of expanded, partial spectra of the CTA, hydroxyl PIB, and PIB-CTA were performed for accurate identification of each peak. These expanded spectral comparisons can be found in Figures 3.14-16. Strong shifts were observed for the methylene carbon (C-10) adjacent to oxygen in the PIB precursor and the carbonyl carbon of the CTA (C-11), as displayed in Figure 3.17. After esterification, the methylene carbon shifted from 69.86 to 71.33 ppm; whereas the carbonyl carbon shifted from 177.39 to 171.69 ppm. No residual carbonyl carbon or methylene carbon peaks from the precursors were visible in the resulting product. Carbon atoms two and three bonds away also shifted slightly including C-9 (20.04 to 20.37 ppm) and C-8 (31.99 to 29.97 ppm) of hydroxyl PIB and C-12 (29.64 to 28.70 ppm) and C-13 (33.38 to 34.11 ppm) of the CTA.

Upon addition of the CTA to hydroxyl PIB a molecular weight increase should have been observed. GPC results confirmed that the PIB-CTA molecular weights were 2,200 and 3,100 g/mol for PIB-1 and PIB-2, respectively. These values are close to the predicted molecular weights after the coupling reaction.

Once the CTA-functionalized PIB was obtained, RAFT polymerizations were conducted for the synthesis of both PIB-\textit{b}-PMMA and PIB-\textit{b}-PS. Initial RAFT
polymerizations were conducted with MMA using a variety of reaction conditions to optimize polymerization rate and blocking efficiency of the macro CTA. This preliminary experimentation revealed that monomer concentrations below 3 M and [CTA]:[AIBN] ratio above five resulted in unreasonably long reaction times, and that lower temperatures (e.g. 60 – 70 °C) afforded increased blocking efficiency at the expense of longer reaction times. Figures 3.17 and 3.18 show the $^1$H NMR spectrum and GPC traces, respectively, of a representative PIB-$b$-PMMA copolymer polymerized at optimal conditions, after purification. Due to the relatively long PMMA block, fractional precipitation of the crude reaction product into hexanes was effective at removing unreacted PIB-CTA. The $^1$H NMR spectrum shows characteristic peaks from both PIB and PMMA. The CTA methylene proton peak (b) was used to normalize the methoxy peak of the PMMA for NMR molecular weight calculations. In addition, the GPC traces illustrate a substantial decrease in elution volume from the macro PIB-CTA starting material to the PIB-$b$-PMMA indicating an increase in molecular weight.

Next, a series of RAFT polymerizations was performed in which monomer concentration ([M]), [M]:[CTA]:[AIBN], and type of monomer were varied in order to probe their influence on blocking efficiency. Table 3.2 summarizes the conditions of each polymerization and its respective conversion, PDI, molecular weight, and blocking efficiency. Blocking efficiency was determined using both GPC and $^1$H NMR as described in the Experimental section.

Experiments R – 1, 2, 3, 4 were all conducted with near identical [M]:[CTA]:[I] concentration ratios but differ in overall system concentration, which was dictated by the selected monomer concentration [M]. No clear trends can be observed concerning the
blocking efficiency of the macro CTA regarding the system concentration. It is possible
that an optimal system concentration may exist at or around [M] of 4.5 M (R-3) indicated
by blocking efficiency values greater than 95%. Additionally, less concentrated
systems (R – 2, 3, 4) resulted in slightly improved blocking efficiencies compared to that
of the more concentrated system (R-1). The various polymerizations detailed in Table
3.2 demonstrate the capability of this system to yield targeted molecular weights over a
fairly broad range (12,000 to 18,000 g/mol) and low PDIs, even when the
polymerizations are taken to high monomer conversion.

Experiments R-3 and R-4 were divided into two portions prior to initiation. One
portion was transferred into a round bottom flask for a traditional RAFT polymerization
and the other into an NMR tube for VT NMR. These VT NMR experiments were
utilized to obtain real time conversion and polymerization rate verses time data, as a
function of system concentration, as shown in Figure 3.20. Except for an initial induction
period, the RAFT polymerizations exhibited linear first-order plots, indicating an
approximately constant number of growing species. Such an induction period is
commonly observed in RAFT polymerizations, and is generally attributed to the
establishment of the main RAFT equilibrium. As expected, the more concentrated
system, curve A, achieved larger conversion values in the same duration of time, without
causing any increase in PDI or decrease in the degree of molecular weight control (see
data in Table 3.2). This shows that shorter reactions times can be achieved with higher
system concentrations without deleterious effects to the resulting block copolymer.

In addition to monitoring the conversion of the system with 1H NMR, aliquots
were taken during the polymerization for GPC analysis. Figure 3.21 shows the GPC
traces of reaction aliquots removed from reaction R-3 at various conversions, along with the final purified block copolymer. A gradual increase in molecular weight with conversion can be seen. At full conversion a small fraction of residual PIB-CTA remained in the crude reaction product. This residual fraction was isolated by fractional precipitation and found to contain some PMMA in its structure. This suggests that the failure of this fraction to form the desired second block may result from a combination of poor initiation efficiency, \textit{i.e.}, all MMA is consumed before all PIB-CTA’s react, and early termination, resulting in a very short PMMA block.

To test whether the less-than-quantitative initiation efficiency might be due specifically to the selection of MMA, styrene was selected as a second monomer to conduct RAFT polymerization from the PIB macroinitiator. Styrene polymerization was conducted in the bulk thereby simplifying the system greatly by elimination of solvent and initiator, and styrene polymerization has been shown to proceed in a controlled fashion in the RAFT process.\textsuperscript{28} In Figure 3.22 the same PIB-CTA was used to polymerize MMA (R-1) and S (R-8). It is apparent that styrene yielded substantially improved blocking efficiency as evidenced by the significantly reduced amount of residual PIB-CTA. The molecular weight data in Table 3.2 show that styrene also yielded diblock copolymers with low PDI. However, the polymerization of styrene yielded experimental $M_n$ values (both GPC and NMR) slightly lower than that of the theoretical value giving apparent blocking efficiency values exceeding 100%.

Conclusion

Site transformation of PIB chain ends into functional macro-CTAs was successfully accomplished. The macro CTA synthesized in this work represents the first
report of combining cationic IB polymerization and subsequent RAFT polymerization for block copolymer synthesis. Structural of the macro CTA was confirmed by both $^1$H and $^{13}$C NMR after coupling the CTA to PIB. RAFT polymerizations using the PIB-CTA were demonstrated with both MMA and S to yield block copolymers with predetermined molecular weights and narrow PDIs, as characterized by GPC and $^1$H NMR. VT NMR experiments verified that MMA polymerizations progressed in a controlled fashion and that the rate was concentration dependant. Blocking efficiency values were found to be slightly improved with S compared MMA.
References


Table 3.1. Characterization of *exo*-Olefin PIB Precursors

<table>
<thead>
<tr>
<th>Sample</th>
<th>$M_n^a$ (g/mol)</th>
<th>PDI ($M_n/M_w$)</th>
<th><em>exo</em>-olefin$^b$ (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>PIB – 1</td>
<td>1,600</td>
<td>1.04</td>
<td>98</td>
</tr>
<tr>
<td>PIB – 2</td>
<td>2,500</td>
<td>1.03</td>
<td>97</td>
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</tbody>
</table>

$^a$ determined by GPC
$^b$ determined by $^1$H NMR
Table 3.2. RAFT Polymerizations of PMMA and PS

<table>
<thead>
<tr>
<th>Exp.</th>
<th>PIB-CTA</th>
<th>Monomer</th>
<th>[M] (mol/L)</th>
<th>[M]:[CTA]:[I]</th>
<th>Time (h)</th>
<th>Conv.</th>
<th>PDI</th>
<th>GPC</th>
<th>NMR</th>
<th>Theo</th>
<th>GPC</th>
<th>NMR</th>
</tr>
</thead>
<tbody>
<tr>
<td>R-1</td>
<td>PIB-2</td>
<td>MMA</td>
<td>6.50</td>
<td>130:1:0.52</td>
<td>10.8</td>
<td>94.6</td>
<td>1.04</td>
<td>17,000</td>
<td>17,840</td>
<td>15,410</td>
<td>88.6</td>
<td>83.5</td>
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<tr>
<td>R-2</td>
<td>PIB-2</td>
<td>MMA</td>
<td>5.52</td>
<td>142:1:0.53</td>
<td>11.8</td>
<td>93.0</td>
<td>1.04</td>
<td>17,100</td>
<td>16,810</td>
<td>16,300</td>
<td>94.3</td>
<td>96.3</td>
</tr>
<tr>
<td>R-3</td>
<td>PIB-2</td>
<td>MMA</td>
<td>4.48</td>
<td>146:1:0.53</td>
<td>19</td>
<td>100</td>
<td>1.04</td>
<td>18,200</td>
<td>17,820</td>
<td>17,480</td>
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<td>97.7</td>
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<tr>
<td>R-4</td>
<td>PIB-2</td>
<td>MMA</td>
<td>3.51</td>
<td>143:1:0.51</td>
<td>14.8</td>
<td>80.9</td>
<td>1.06</td>
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<td>14,200</td>
<td>14,670</td>
<td>90.4</td>
<td>104.2</td>
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<td>12,500</td>
<td>11,020</td>
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<td>MMA</td>
<td>6.48</td>
<td>85:1:0.51</td>
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<td>100</td>
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<td>14,000</td>
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<td>10,720</td>
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<td>MMA</td>
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<td>100</td>
<td>1.04</td>
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<tr>
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<td>S</td>
<td>301:1:0.0</td>
<td>20</td>
<td>82.2</td>
<td>1.02</td>
<td>26,700</td>
<td>26,160</td>
<td>28,910</td>
<td>109.4</td>
<td>111.9</td>
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</tr>
<tr>
<td>R-9†</td>
<td>PIB-2</td>
<td>S</td>
<td>200:1:0.0</td>
<td>20.8</td>
<td>52.8</td>
<td>1.04</td>
<td>13,000</td>
<td>14,100</td>
<td>14,080</td>
<td>110.9</td>
<td>99.8</td>
<td></td>
</tr>
</tbody>
</table>

1 Bulk polymerization of styrene with thermal initiation at 100°C
2 Elapsed time between initiation and quenching of RAFT polymerization
Figure 3.1. $^1$H NMR spectrum of exo-olefin PIB.
Figure 3.2. $^{13}$C NMR spectrum of exo-olefin PIB.
Figure 3.3. GPC traces of pre-quenched and quenched *exo*-olefin PIB.
Figure 3.4. $^1$H NMR spectrum of hydroxyl PIB.
Figure 3.5. \(^{13}\text{C}\) NMR spectrum of hydroxy PIB.
Figure 3.6. GPC traces of hydroxy PIB and exo-olefin PIB.
Figure 3.7 Site transformation from living carbocationic polymerization to RAFT polymerization.
Figure 3.8. $^1$H NMR spectrum of CTA.
Figure 3.9. $^{13}$C NMR spectrum of CTA
Figure 3.10. gHSQC of CTA
Figure 3.11. $^{13}$C NMR spectrum of CTA: attached proton test.
Figure 3.12. $^1$H NMR spectrum of PIB-CTA
Figure 3.13. $^{13}$C NMR spectrum of PIB-CTA
Figure 3.14. $^{13}$C NMR spectra of CTA (top), PIB-OH (middle), and PIB-CTA (bottom).
Figure 3.15. Partial $^{13}$C NMR spectra of CTA (top), PIB-OH (middle), and PIB-CTA (bottom).
Figure 3.16. Expanded $^{13}$C NMR of CTA (top), PIB-OH (middle), and PIB-CTA (bottom).
Figure 3.17. Partial $^{13}$C NMR spectra comparing PIB-CTA to CTA and PIB-OH precursors
Figure 3.18. $^1$H NMR spectrum of PIB-b-PMMA
Figure 3.19. GPC traces of PIB-CTA and PIB-\textit{b}PMMA after purification.
Figure 3.20. Effect of system concentration on rate of RAFT polymerization.
Figure 3.21. GPC traces of reaction aliquots removed from reaction R-3 at various conversions, along with the final purified block copolymer.
Figure 3.22. Dependency of blocking efficiency on monomer selection: MMA vs. S.
CHAPTER IV

POLYISOBUTYLENE RAFT CTA BY A CLICK CHEMISTRY SITE TRANSFORMATION APPROACH: SYNTHESIS OF POLY(ISOBUTYLENE-\(b\)-N-ISOPROPYLACRYLAMIDE)

Introduction

Development of controlled/living polymerizations has enabled synthetic polymer chemists to design complex polymeric architectures with great precision.\(^1\) Block copolymers in particular have gained significant attention because of their unique material properties resulting from compositionally different block segments, and ability to self assemble into highly organized structures.\(^2\) Self assembling materials have many potential applications, both as dispersions and in the solid state, due to their ability to form versatile and functional morphologies.\(^1\) Thus, block copolymer systems are being developed for and have found numerous applications in the areas of biomedical devices,\(^3,4,5,6\) biomaterials,\(^4,7,8\) thermoplastic elastomers (TPEs),\(^9\) fuel cells,\(^10,11\) and electronics.\(^12,13\)

Polyisobutylene (PIB) is a completely saturated hydrocarbon rubber that can only be produced through cationic polymerization. Inherent attractive properties of this synthetic elastomer are its exceptional oxidative and chemical resistance, superior gas barrier and mechanical damping characteristics, and excellent biocompatibility. Because of these properties PIB-based block copolymers have continued to be a topic of great interest. Poly(styrene-\(b\)-isobutylene-\(b\)-styrene) (SIBS) block copolymer has found a niche market as a biomaterial and is used as the matrix polymer for the drug-containing coating on a commercial drug-eluting coronary stent.\(^14,15,16\) Recently, prospective
materials for biotechnology and medicine were created from self-assembling PIB-based polymersomes and micelles creating novel delivery/encapsulation systems and interpolyelectrolyte complexes. In addition, Kennedy et al. have recently developed PIB-based segmented thermoplastic polyurethane/ureas (TPUs) exhibiting unprecedented resistance to oxidative/hydrolytic degradation for long term medical applications. In other areas, novel PIB-based TPEs were synthesized, with poly(ether ketone) outer blocks for increased thermal stability and dendritic PIB-core TPEs with carbon black and silica fillers for increased mechanical properties.

PIB-based block copolymers have been synthesized by four different strategies: sequential monomer addition, macromolecular coupling, dual-site initiators, and site transformation. Sequential monomer addition offers unparalleled simplicity, but in the case of PIB-based block copolymers, allows combinations of cationically polymerizable monomers only. This selection of monomers is confined essentially to isobutylene, isoprene, vinyl ethers, styrenics, and N-vinylcarbazole, and the process is no longer simple when the monomer pair exhibit large reactivity differences. Macromolecular coupling of previously fabricated functional polymers requires quantitative functionalization of the chain ends of both polymers, a high-conversion coupling reaction, and a common solvent system; otherwise the yield of the desired block copolymer is low and a tedious separation of homopolymers is often involved. Dual-site initiators contain initiating sites for two mechanistically different polymerizations and require no intermediate transformation steps to affect the second polymerization after the first. Site transformation involves conversion of the head or tail group of the PIB block segment into an initiator for a mechanistically different chain polymerization process.
This technique effectively expands the library of polymers segments that can be mated to PIB. Block copolymer synthesis using site transformation has been successfully demonstrated with atom transfer radical polymerization (ATRP), condensation polymerization,\textsuperscript{30} anionic polymerization,\textsuperscript{31,32} and most recently by reversible addition fragmentation transfer (RAFT) polymerization.\textsuperscript{33}

RAFT has proven to be very versatile regarding monomers, solvents, and reaction conditions, and yields macromolecules with predetermined molecular weights and narrow polydispersities.\textsuperscript{34,35} Because of its versatility and capability to polymerize many monomers that are inherently troublesome for other polymerization techniques, RAFT is potentially an ideal polymerization technique to combine with cationic polymerization by site transformation. In addition, chain transfer agents (CTAs) used in the RAFT process can be synthesized to carry many useful reactive end groups including azide\textsuperscript{36} and alkyne\textsuperscript{37} for copper(I)-catalyzed Huisgen [3 + 2] dipolar cycloadditions. This reaction, categorized by Sharpless et al. as a “click” reaction, is known to be quantitative, devoid of side reactions and byproducts, tolerant to a wide range of functional groups, and requiring only mild reaction conditions.\textsuperscript{38,39} Due to these attributes, the azide/alkyne reaction has received significant attention in macromolecular chemistry and has found use in specific systems for postpolymerization functionalization, novel polymers synthesis, and chain extension for block copolymer synthesis.\textsuperscript{40}

Stimuli-responsive block copolymers are of immense importance and have attracted significant attention as “smart” materials.\textsuperscript{41} Poly(N-isopropylacrylamide) (PNIPAM) is known to display a sharp, thermally-reversible phase transition in aqueous solution at approximately 32 °C.\textsuperscript{42} Investigation of this phase transition has revealed that
PNIPAM macromolecules experience dehydration and collapse from a hydrated, extended coil to a hydrophobic globule, upon raising the temperature through the cloud point, ultimately resulting in intermolecular aggregation. Various hydrophobically-modified PNIPAM-based polymers have been reported in literature and are being studied for many potential applications. Functional PNIPAM’s have been synthesized to be joined with various hydrophobic polymer blocks including, for example, polystyrene and tetrahydrofuran-protected 2-hydroxyethyl methacrylate, as well as alkyl groups, alkyl chain transfer agents, and chromophores. Herein, we report the synthesis of a novel amphiphilic diblock copolymer, composed of PIB and PNIPAM segments, through the combination of quasiliving cationic polymerization and RAFT by a click chemistry site transformation procedure.

Experimental

Materials

Hexanes (anhydrous, 95%), 2,6–lutidine (redistilled, 99.5%), TiCl₄ (99.9%, packaged under N₂ in sure-seal bottles), chloroform-d (99.8 atom% D), DMF (anhydrous, 99.8%), bromotris(triphenylphosphine)copper(I) (Ph₃PCuBr) (98%), and 1,3,5-trioxane (≥99%) were purchased from Sigma-Aldrich and used as received. 1-(3-Bromopropyl)pyrrole (PyBr) (>95%, TCI America), THF, heptanes, and dioxane were distilled from calcium hydride under a N₂ atmosphere. N-Isopropylacrylamide (NIPAM) was recrystallized twice from a hexane/benzene mixture (3/2, v/v). 2,2′-Azobis(2-methylpropionitrile) (98%) (AIBN) was recrystallized twice from ethanol. Isobutylene (IB) (BOC, 99.5%) and CH₃Cl (Alexander Chemical Corp.) were dried by passing the gaseous reagent through columns packed with CaSO₄ and CaSO₄/4 Å molecular sieves,
respectively, and condensed within a N$_2$-atmosphere glove box immediately prior to use. 2-Chloro-2,4,4-trimethylpentane (TMPCl) was prepared by bubbling HCl gas through neat 2,4,4-trimethyl-1-pentene (Sigma-Aldrich) at 0°C. The HCl-saturated TMPCl was stored at 0°C, and was neutralized with NaHCO$_3$, dried over anhydrous MgSO$_4$, and filtered immediately prior to use. Alkyne-functional CTA, propargyl 2-(1-dodecylsulfanylthiocarbonylsulfanyl)-2-methylpropionate, was synthesized as previously reported.$^{37}$

*Synthesis of 1-(3-Azidopropyl)pyrrole-terminated PIB (PIB-$N_3$)*

Three 1-(3-bromopropyl)pyrrole-terminated PIB precursors (Table 4.1) were synthesized by quenching TMPCl-initiated quasiliving IB polymerizations with 1-(3-bromopropyl)pyrrole.$^{51}$ A representative procedure to produce PIB$_{44}$-Br was as follows. Quasiliving polymerization of IB with TMPCl as an initiator was carried out within a N$_2$ atmosphere glovebox, equipped with an integral, cryostated hexane/heptanes bath. Into a round-bottom flask equipped with a mechanical stirrer, infrared probe, and thermocouple were added 144 mL CH$_3$Cl, 216 mL hexanes, and 0.15 mL (0.14 g, 1.3 mmol) of 2,6-lutidine. The mixture was allowed to equilibrate to –70 °C, and then 20.4 mL (14.2 g, 0.253 mol) of IB was charged to the reactor. After thermal equilibration, 1.113 mL (0.9730 g, 6.545 mmol) of TMPCl was added to the reactor. To begin the polymerization, 2.16 mL (3.74 g, 0.0197 mol) of TiCl$_4$ was charged to the reactor. Full monomer conversion (>98 %) was achieved in 40 min, after which time a prechilled solution of PyBr, prepared by dissolving 1.81 mL of PyBr (2.46 g, 13.1 mmol) into 25 mL of hexane/CH$_3$Cl (60/40, v/v, –70 °C), was added to the polymerization. PyBr was allowed to react with the living chain ends for 40 min. Finally, the reaction was
quenched by addition of excess prechilled methanol. The contents of the reaction flask were allowed to warm to room temperature, and the polymer in hexane was immediately washed with methanol and then precipitated into methanol from hexane. The precipitate was collected by dissolution in hexane; the solution was washed with water, dried over MgSO$_4$, and concentrated on a rotary evaporator. Residual solvent was removed under vacuum at room temperature.

Each of three 1-(3-azidopropyl)pyrrole-terminated PIB’s was prepared by reaction of the corresponding 1-(3-bromopropyl)pyrrole-terminated PIB with NaN$_3$ in a mixture of heptanes/DMF. A representative procedure to produce PIB$_{44}$-N$_3$ was as follows. To a 200 mL round bottom flask, under a dry nitrogen atmosphere, were added 1-(3-azidopropyl)pyrrole-terminated PIB$_{44}$ (11.56 g, 4.4 mmol) and 25.5 mL of dry heptanes. The reaction vessel was agitated until complete dissolution of the PIB-N$_3$ occurred resulting in a clear solution. To the resulting solution was then added a separate solution of sodium azide (0.853 g, 13.1 mmol) in 25.5 mL of DMF. After stirring for approximately 20 min, the resulting biphasic mixture was submerged in an oil bath at 90 °C and soon became monophasic as the reaction reached equilibrium temperature. The reaction was allowed to proceed with agitation for 17 h. Afterward, the monophasic reaction mixture was removed from the oil bath and allowed to cool to room temperature whereupon a biphasic mixture again formed. At this point, hexanes and DI water were added and the DMF/water layer was separated. The organic phase was immediately washed with DI water and then precipitated into methanol from hexane. The precipitate was collected by dissolution in hexane; the solution was washed with water, dried over
MgSO₄, filtered, and concentrated on a rotatary evaporator. Residual solvent was removed under vacuum at room temperature.

**Synthesis of PIB-CTA by Click Chemistry**

To a 25 mL one-neck round-bottom flask equipped with a magnetic stir bar were added PIB₄₄-N₃ (2.032 g, 0.79 mmol) and 2.5 mL THF. The reaction vessel was agitated until complete dissolution of the PIB-N₃ occurred resulting in a clear solution. In a separate vessel, CTA (0.622 g, 1.55 mmol) and (Ph₃P)₃CuBr (0.0515 g, 0.0554 mmol) were dissolved in 2.5 mL of THF, and the resulting solution was charged to the one-neck round-bottom flask. After 38 h, the solvent was removed under reduced pressure, and the crude product was redissolved in hexane. The resulting solution was washed with methanol three times, filtered, and precipitated twice into methanol from hexanes. The precipitate was collected by dissolution in hexanes and then stripped of solvent under reduced pressure until a constant weight was reached. A clear, yellow, viscous material was obtained.

**RAFT polymerization of NIPAM with PIB-CTA**

A representative RAFT polymerization was conducted as follows. To a 25 mL Schlenk-style, long-neck round-bottom flask were added three solutions: first a solution of PIB₄₄−CTA (0.0493 g, 0.0165 mmol) in 0.69 mL of heptanes, a second solution of 1,3,5-trioxane (0.0458 g, 0.509 mmol) and NIPAM (0.5467 g, 5.0961 mmol) in 2.82 mL dioxane, and a finally 0.5 mL of a 0.0099 M AIBN stock solution in dioxane. After mixing the three solutions an initial aliquot was taken to establish the initial monomer concentration relative to the internal standard 1,3,5-trioxane, via ¹H NMR spectroscopy. The solution was then subjected to three freeze–pump–thaw cycles to remove oxygen,
sealed under N₂, and submerged in an oil bath thermostatted at 85 °C. After ~4 h the reaction was exposed to oxygen and quenched in liquid nitrogen. A final aliquot was taken for ¹H NMR analysis, and then the crude reaction product was precipitated into hexanes twice, dialyzed against water, and lyophilized. Conversion was calculated from the initial and final monomer concentrations relative to 1,3,5-trioxane.

**Instrumentation**

NMR spectra were acquired using a Varian Mercury™plus 300 MHz NMR spectrometer. Samples were dissolved in chloroform-d (3−7%, w/v) and analyzed using 5 mm NMR tubes.

Variable-temperature NMR (VT NMR) data were acquired using a UNITY™Inova 500 MHz NMR spectrometer equipped with a Highland VT controller. RAFT polymerizations were performed in dioxane-d between 355.5 and 363 K, with a 45 s pre-acquisition delay between each spectrum. The probe was allowed to equilibrate for 15 min prior to data acquisition. Temperatures reported in this study are within ±2 °C based on ethylene glycol calibration.⁵²,⁵³ RAFT polymerizations for VT NMR were prepared by charging a J Young NMR tube equipped with a Teflon seal with the crude reaction mixture and performing three freeze−pump−thaw cycles. After degassing, the NMR tube was backfilled with N₂. Conversion was calculated by comparison of the vinyl proton areas of the monomer to the internal standard, 1,3,5-trioxane.

Number-average molecular weight (Mₙ) and polydispersity index (PDI) of the polymeric materials were measured using gel permeation chromatography (GPC). The GPC system, operating at 35 °C for PIB-Br, PIB-N₃, and PIB-CTA, and 25 °C for PIB-b-PNIPAM, consisted of a Waters Alliance 2695 Separations Module, an on-line
multiangle laser light scattering (MALLS) detector (MiniDAWN™, Wyatt Technology Inc.), an interferometric refractometer (Optilab rEX™, Wyatt Technology Inc.), an online differential viscometer (ViscoStar™, Wyatt Technology, Inc.), and either two mixed E (3 µm bead size) or two mixed D (5 µm bead size) PL gel (Polymer Laboratories Inc.) GPC columns connected in series. Freshly distilled THF for PIB-homopolymer (PIB-Br, PIB-N₃, and PIB-CTA) and 0.25 wt% tetrabutylammonium bromide in THF (25 °C) for PIB-b-PNIPAM served as the mobile phase at a flow rate of 1.0 mL/min. Sample concentrations were 10-12 mg/mL, with an injection volume of 100 µL. The detector signals were recorded using ASTRA™ software (Wyatt Technology Inc.) and molecular weights were determined using $dn/dc$ values calculated from a known $dn/dc$ equation reported elsewhere or by the response of the Optilab DSP assuming 100% mass recovery from the columns.

Dynamic light scattering (DLS) was used to determine the hydrodynamic size of particles in aqueous solution, as well as their distribution of sizes. Solutions of PIB-b-PNIPAM block copolymers were prepared by dissolving the polymer into purified water (Millipore) to a concentration of 0.01 wt%. Samples were agitated overnight to ensure complete dissolution and then filtered through a 0.22 µm PVDF syringe-driven filter (Millipore) directly into the scattering cell. Samples were then sonicated and allowed to equilibrate to temperature for 20 min prior to analysis. Scattering was performed using incident light at 633 nm from a Spectra Physics HeNe laser operating at 40 mW. For DLS, the angular dependence of the autocorrelation functions was measured using a Brookhaven BI-200SM goniometer with a TurboCorr correlator. Correlation functions were analyzed according to the method of cumulants using the companion software, from
which a hydrodynamic diameter is extracted via the Stokes-Einstein relation. All data reported correspond to the average decay rate and normalized variance (polydispersity) obtained from the second-order cumulant fit.

Results and Discussion

Synthesis of PIB-CTA

Site transformation of PIB into a macro-CTA for RAFT polymerization was accomplished using a click chemistry site transformation approach. This synthetic strategy, shown in Figure 4.1, offers a number of advantages over our previously published method, which involved quenching of quasiliving PIB with a hindered base to form \textit{exo}-olefin PIB, followed by hydroboration/oxidation to form hydroxyl-terminated PIB, followed finally by esterification with a carboxylic acid-functional trithiocarbonate CTA.\textsuperscript{55} Most notably, \textit{in situ} quenching of quasiliving PIB with an N-substituted pyrrole provides higher chain-end functionality compared to the \textit{exo}-olefin route, and the expensive and difficult hydroboration/oxidation reaction is eliminated.

As shown in Figure 4.1, PIB-N\textsubscript{3} was synthesized in two steps. The first involved \textit{in situ} quenching of a TiCl\textsubscript{4}-activated quasiliving cationic polymerization of IB with 1-(3-bromopropyl)pyrrole to obtain the primary bromide-terminated PIB.\textsuperscript{51} This reaction was quantitative and yielded a mixture of two isomers, corresponding to attachment of the PIB chain at either the C2 or C3 position of the pyrrole ring. The C3 isomer was the major isomer and constituted about 60% of the chain ends. Table 4.1 lists molecular weights ($M_n$) and PDIs ($M_w/M_n$) of three bromide-functional PIBs synthesized by this method. This series of functional polymers was designed to probe the influence of PIB-CTA molecular weight on the RAFT polymerization of NIPAM and the properties of the
resulting block copolymers. The results obtained from GPC and $^1$H NMR agree very well, differing by about 6% in the worst case. In addition, the PDI’s were uniformly low. The second step involved displacement of the terminal bromide by azide ion via nucleophilic substitution. The reaction was biphasic at room temperature, with the hydrophobic PIB located in the top heptanes layer, and the polar sodium azide located in the bottom DMF layer. Upon heating, the reaction became homogeneous, and after approximately 12 h at 90 °C, complete substitution of the halogen to the terminal azide was accomplished without any noticeable coupling or loss of terminal functionality. Upon cooling, the layers separated once again, and this greatly facilitated removal of excess sodium azide and the byproduct sodium bromide.

The final step to create the PIB-CTA was the copper-catalyzed Huisgen cycloaddition reaction between PIB-N$_3$ and the alkyne-functionalized CTA (Figure 4.1). The latter was synthesized by DCC/DMAP coupling as previously reported in literature.$^{37}$ The azide-alkyne click reaction is attractive for the final coupling step since it can be carried out quantitatively at room temperature and in the presence of both oxygen and water. Conversion of PIB-N$_3$ into PIB-CTA (Figure 4.2) was monitored using real-time $^1$H NMR analysis by observing the decrease in area of the propargyl methylene proton signal of the CTA. From this graph nearly 80 % of the product was obtained after 8 h; whereas the remaining 20 % required an additional 27 h to reach full conversion. Since both the CTA and PIB-N$_3$ had to be synthesized, it was impractical to use the former in large excess and thereby reduce the overall order of the reaction. Thus, the initial molar ratio (M) of alkyne to azide ([CTA]:[PIB-N$_3$]) was set only to 2. As expected under these conditions, the click reaction displayed second order kinetics, as shown in the inset to
Figure 4.2. Initial scouting experiments did reveal that the reaction rate can be dramatically increased by small increases in temperature (30 – 35 °C), higher catalyst concentrations, or by using a more reactive copper catalyst. Although full conversion takes approximately 35 h under these conditions, the simplicity and forgiving nature of the reaction makes it very appealing. The product was purified by vacuum-stripping of THF, dissolution in hexanes, and washing the resulting solution with methanol. The solution was then filtered to remove the copper catalyst, which has limited solubility in hexane, and finally, the polymer was isolated by precipitation into methanol, which also served to remove any residual catalyst and unreacted alkyne CTA. After removal of methanol, the purified PIB-CTA was a transparent yellow color instead of its originally colorless appearance, as shown in Figure 4.2.

The structure of PIB-CTA was confirmed by $^1$H NMR, FTIR, and GPC. Figure 4.3 shows $^1$H NMR spectra of the PIB-N$_3$ precursor (top), the alkyne CTA (middle), and the final PIB-CTA (bottom). A clear downfield shift of the PIB-N$_3$ tether protons (a′,b′,c′) and disappearance of the alkyne (d′) and methylene (e′) protons of CTA were observed upon triazole formation. No residual resonances from either PIB-N$_3$ or alkyne CTA were detectable in the resulting product indicating quantitative functionalization. Formation of the triazole ring brings the alkyne proton into the general aromatic/heteroaromatic proton region. This proton (d) was observed as two separate peaks reflecting the mixture of 2-PIB and 3-PIB pyrrole isomers.

FTIR spectroscopy, Figure 4.4, clearly showed the disappearance of the azide at 2100 cm$^{-1}$ and presence of three CTA frequencies representing the carbonyl, ester, and thiocarbonyl at approximately 1735, 1150 and 1124, and 1067 cm$^{-1}$ respectively. Further
characterization with GPC, Figure 4.5, confirmed a small increase in molecular weight after coupling, due to addition of the 403 g/mol CTA, and absence of any chain extension or other side reactions as evidenced by a uni-modal trace. Additionally, no detectable residual lower molecular weight PIB-N$_3$ was visible in the PIB-CTA trace.

**RAFT Polymerization of NIPAM**

After successful synthesis of PIB-CTA, it was employed in the RAFT polymerization of NIPAM, as depicted in Scheme 4.6. A mixed solvent system of dioxane/heptane was used to achieve a homogeneous reaction medium. For some formulations, the reaction was slightly heterogeneous upon initial mixing at room temperature, but the system became homogenous after submerging the reaction in an oil bath during polymerization. It should also be noted that dissolution of the PIB-CTA in heptanes prior to its addition to the other reagents added in its facile solvation substantially.

Table 4.2 summarizes the results of RAFT polymerizations formulated using various combinations of PIB-CTA molecular weight ($M_n$,PIB-CTA), [NIPAM]:[CTA] ratio, and NIPAM fractional conversion ($p_{NIPAM}$), conducted to demonstrate control of both the PIB and PNIPAM block lengths. Theoretical degree of polymerization of the PNIPAM block ($\bar{X}_{n,\text{theo}}$) was targeted as $p_{NIPAM} \times [\text{NIPAM}] / [\text{CTA}]$. Reactions R1–R3 employed the same PIB-CTA and targeted different $\bar{X}_{n,\text{theo}}$ ranging from approximately 190 to 370. Experiments R-3 through R-5 utilized three different PIB-CTA molecular weights ranging from approximately 3,000 to 6,000 g/mol. In all cases, good to excellent agreement was observed between theoretical and experimental degree of polymerization.
of the PNIPAM block ($\bar{X}_{n,GPC}$), and the resulting diblock copolymers all possessed narrow PDI.

The resulting block copolymer was characterized using $^1$H NMR and GPC. $^1$H NMR (Figure 4.7) shows clear, strong resonances from both segments of the block copolymer. PIB backbone resonances are identified “a” and “b” while the PNIPAM resonances are labeled “c” through “g.” Purification of the block copolymer was accomplished by precipitation into hexanes, for removal of residual PIB-CTA, and dialysis against water for removal of unreacted NIPAM. A representative GPC trace, Figure 4.8, shows lower elution time of the block copolymer in comparison to the PIB-CTA homopolymer, indicative of increased molecular weight of the former. Moreover, the crude GPC trace shows a small amount of residual PIB-CTA and its effective removal by the hexanes precipitation.

**RAFT Polymerization Kinetics**

Kinetics of RAFT polymerizations from various PIB-CTA was monitored using variable temperature real time $^1$H NMR. Figure 4.9 shows the temperature dependence of the RAFT polymerization with a NIPAM concentration of 1.2 M and $[\text{NIPAM}]:[\text{CTA}]:[\text{I}] = 250:1:0.25$. After a characteristic induction period, the polymerizations were first-order up to $p_{\text{NIPAM}} \approx 0.7$, indicating a constant concentration of actively propagating radicals; whereas at higher conversions the plots displayed a slight downward curvature implying a decreasing concentration of active species. Eventually a maximum conversion was reached beyond which no further polymerization occurred; for the higher polymerization temperatures this was at $p_{\text{NIPAM}} \approx 0.9$. The apparent first-order rate constants, $k_{\text{app}}$, extracted from the linear portion of the plots, were fitted to the
Arrhenius equation (Figure 4.10) to yield activation energy of 31.0 kcal/mol and prefactor of $2.71 \times 10^{17}$ min$^{-1}$. This is very close to the reported activation energy for AIBN dissociation and confirms the strong effects of reaction temperature on polymerization rate. In addition, the duration of the induction period decreased with increasing temperature and was practically eliminated at 90 °C.

The kinetics and energetics information obtained in the VT NMR experiments were consistent with RAFT polymerization kinetics observed in the batch reactions of Table 4.2. For the latter, the external bath temperature was 85°C; however, the internal reactor temperature was typically only 78-79°C, after a thermal equilibration period of about 15-20 min. A replicate of experiment R-2 was performed in which aliquots were removed for conversion analysis using $^1$H NMR. The data revealed first-order kinetics ($k_{\text{app}} = 0.0127$ s$^{-1}$) and an induction period of 50 min (taken as the x-intercept from the first-order plot). This $k_{\text{app}}$ value agrees very well with that predicted from the Arrhenius relationship ($k_{\text{app}} = 0.0139$ s$^{-1}$) above for a reaction temperature of 78°C. The previously mentioned Arrhenius relationship and experimentation help to verify the slower reaction rate observed for the batch reaction, specifically R-2, which accounts for it achieving a lower than expected conversion value ($p_{\text{NIPAM}} = 0.376$). Using either of the above rate constants and the empirically determined induction period, theoretical conversion values between 0.32 and 0.34 can be calculated which fall in close proximity to the experimental conversion value of R-2.

Figure 4.11 shows the dependence of RAFT polymerization kinetics on the concentration of the thermal initiator, AIBN. The maximum conversion achieved in the polymerization decreased with lower concentrations of initiator, from just over 0.9 at
[CTA]:[I] = 0.25 to approximately 0.73 at [CTA]:[I] = 0.125. In addition, increasing initiator concentration reduced the duration of the induction period and increased the apparent rate constant of the polymerization, as expected.

Conversion and rate of RAFT polymerizations were observed to be independent of both PIB-CTA molecular weight and concentration (Figures 4.12 and 4.13).

**Aqueous Self-assembly of PIB-b-PNIPAM**

Below the critical point of PNIPAM (ca. 32 °C), amphiphilic PIB-PNIPAM block copolymers are expected to self-assemble into higher-ordered structures. In addition, these structures are expected to show temperature-dependent dimensions near the critical point for PNIPAM. The self-assembly and temperature responsiveness for PIB₄₄-PNIPAM₄₅₀ (R-6 from Table 4.2) was studied using DLS. Based on the large weight fraction of hydrophilic PNIPAM, it is expected that spherical micelles will form. At room temperature, direct solvation of PIB₄₄-PNIPAM₄₅₀ resulted in a clear solution (Figure 4.14). The correlation functions fit well to a second-order cumulant relation, indicative of a relatively monodisperse, unimodal distribution of scattering species. A plot of the average decay rate of the correlation function (Γ) vs. the square of the scattering vector (q²) yields a linear relation (Figure 4.14 inset), indicating that the scattering comes solely from Brownian motion of spherical aggregates.

The hydrodynamic diameter (Dₜ) was determined as a function of temperature at a 90° scattering angle. At 15 °C, the Dₜ was 107 nm. As the temperature increases, the hydrodynamic size remains relatively constant until 26 °C where it begins to decrease. When the temperature is further increased towards the nominal critical point of PNIPAM, the aggregate diameter continues decreasing to 76 nm. The decrease in size with
increased temperature is explained by the PNIPAM chains transforming from a coil to a globular conformation.\textsuperscript{57} This conformational change results in the expulsion of water due to the increased hydrophobicity of the PNIPAM corona chains. It is important to note that the overall structure of the aggregates does not change over the temperature range studied, \textit{i.e.}: the $\Gamma$ vs. $q^2$ plot retains linearity over the temperature range, suggesting that spherical aggregates are still present at 32 °C (Figure 4.14 inset). In addition, the polydispersity (normalized variance) in the size distribution systematically decreased from 0.187 to 0.133 as temperature increased from 15 to 33 °C. Finally, a fairly broad transition ranging from 26 to 33 °C occurs with PIB\textsubscript{44-b-PNIPAM\textsubscript{450}} block copolymer, in contrast to sharp transitions which occur in PNIPAM homopolymer systems.\textsuperscript{42} Broadened PNIPAM transitions are theoretically expected with hydrophobically modified PNIPAM\textsuperscript{58} and have been observed with PS-\textit{b}-PNIPAM systems.\textsuperscript{59} Once the temperature of the system exceeded 33 °C intermolecular aggregation occurred between assemblies, which was accompanied by a visual change in the aqueous solution from transparent to turbid (Figure 4.14).

\textbf{Conclusion}

A novel block copolymer composed of PIB and PNIPAM block segments was synthesized by a unique site transformation process combining quasiliving cationic and RAFT polymerizations. PIB with a terminal halogen was functionalized by \textit{in situ} quenching and successfully convert into a “clickable” PIB by substitution with an azide ion. Afterward, the azido functionalized PIB was transformed into a macro-CTA by copper catalyzed click chemistry utilizing an alkyne functionalized CTA. The utility of the macro-CTA was demonstrated by polymerization of NIPAM to produce a novel block copolymer.
copolymer with predetermined molecular weights and low PDIs. The kinetic behavior of this RAFT polymerization was studied and found to be strongly dependant on temperature and initiator concentration. Conversely, the PIB-CTA molecular weight and concentration had little effect on the kinetic behavior. Light scattering experiments confirmed the presence of polymeric aggregates with stimuli responsive behavior display a broad temperature induced transition.
References


<table>
<thead>
<tr>
<th>Sample</th>
<th>Mn, GPC&lt;sup&gt;a&lt;/sup&gt; (g/mol)</th>
<th>Mn, GPC&lt;sup&gt;b&lt;/sup&gt; (g/mol)</th>
<th>Mn, NMR (g/mol)</th>
<th>Mw/Mn</th>
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<sup>a</sup> M<sub>n</sub>, GPC determined using 100% mass recovery \(dn/dc\)

<sup>b</sup> M<sub>n</sub>, GPC determined using known \(dn/dc\)
<table>
<thead>
<tr>
<th>Sample</th>
<th>RAFT Polymerization Conditions</th>
<th>PNIPAM Block</th>
<th>PIB-b-PNIPAM</th>
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<tr>
<td></td>
<td>$\overline{M}_{n,\text{PIB-CTA}}$ (\text{g/mol})</td>
<td>$[\text{NIPAM}]:[\text{CTA}]:[\text{I}]$</td>
<td>Time (\text{h})</td>
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<td>485:1:0.5</td>
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$^a$ Stirred glass reactors; temperature (external bath) = 85°C, internal reactor temperature = 78-79°C; [NIPAM] = 1.2 M

$^b$ $\overline{M}_{n,\text{PIB-CTA}} = \overline{M}_{n,\text{PIB-Br}}$ (100 % mass recovery $dn/dc$) + (MW$_{N3}$ - MW$_{Br}$) + MW$_{CTA}$

$^c$ $\overline{X}_{n,\text{theo}} = p_{\text{NIPAM}} \times [\text{NIPAM}]/[\text{CTA}]$

$^d$ $\overline{X}_{n,\text{GPC}} = (\overline{M}_{n,\text{GPC}} - \overline{M}_{n,\text{PIB-CTA}})/\text{MW}_{\text{NIPAM}}$

$^e$ $\overline{M}_{n,\text{Theo}} = \overline{M}_{n,\text{PIB-CTA}} + \overline{X}_{n,\text{theo}} \times \text{MW}_{\text{NIPAM}}$

$^f$ $\overline{M}_{n,\text{GPC}}$ determined using 100 % mass recovery $dn/dc$
Figure 4.1. Synthesis of PIB-CTA for RAFT polymerization.
Figure 4.2. Real-time $^1$H NMR analysis of click reaction between CTA and PIB$_{44}$-N$_3$. 
Figure 4.3. $^1$H NMR spectra of (top) PIB-N$_3$, (middle) CTA, and (bottom) PIB-CTA.
Figure 4.4. FTIR spectra of (top) PIB-N$_3$ and (bottom) PIB-CTA.
Figure 4.5 GPC trace before and after click reaction.
PIB-CTA

PIB-b-PNIPAM

[Figure 4.6. RAFT polymerization of NIPAM with PIB-CTA.]
Figure 4.7. $^1$H NMR spectrum of PIB-$b$-PNIPAM.
Figure 4.8. GPC traces before and after RAFT polymerization of PNIPAM.
Figure 4.9. Conversion vs. time and first-order kinetic plot (inset) for RAFT polymerization from PIB$_{44}$-CTA as a function of temperature. [NIPAM] = 1.2 M; [NIPAM]:[CTA]:[I] = 250:1:0.25.
**Figure 4.10.** \( \ln k_{\text{app}} \) for RAFT polymerization vs. reciprocal temperature to determine activation energy and prefactor (min\(^{-1}\)).
Figure 4.11. Conversion vs. time and first-order kinetic plot (inset) for RAFT polymerization from PIB$_{44}$-CTA as a function of thermal initiator concentration. [NIPAM] = 1.2 M; [NIPAM]:[CTA] = 250:1; T = 90 °C
Figure 4.12. Conversion vs. time and first-order kinetic plot (inset) for RAFT polymerization as a function of PIB-CTA molecular weight. [NIPAM] = 1.2 M; [NIPAM]:[CTA]:[I] = 250:1:0.25; T = 85 °C.
Figure 4.13. Conversion vs. time and first-order kinetic plot (inset) for RAFT polymerization as a function of PIB-CTA concentration. \([\text{NIPAM}] = 1.2 \text{ M}; \text{[NIPAM]}:\text{[I]}=1:0.001; T = 85 \, ^\circ\text{C}.\)
Figure 4.14. Diameter of Micelles with Temperature ($\Theta = 90^\circ$)
CHAPTER V

FUNCTIONAL POLYISOBUTYLENES VIA A CLICK CHEMISTRY APPROACH

Introduction

Polyisobutylene (PIB) is recognized for its environmental stability, gas-barrier and mechanical damping characteristics, and excellent biocompatibility, and thus PIB chain segments carrying functional end groups are useful intermediates toward a variety of products including fuel and lubricating oil additives,\(^1\) soluble catalyst supports,\(^2\) polyurethane/urea thermoplastic elastomers,\(^3,4,5\) and biomedical devices.\(^6,7\) Often though, placement of the desired functionality onto the PIB chain end has required cumbersome and expensive post-polymerization chemistries, ultimately making it a less feasible option in some research and commercial applications.

With the recent developments of *in-situ* quenching (a.k.a. end-capping) techniques\(^8,9,10,11\) and highly effective Sharpless-style “Click” chemistries,\(^12\) simpler chain end reactions and new functionalities on PIB are now possible. In particular, the copper(I)-catalyzed Huisgen 1,3-dipolar cycloaddition of azides and terminal alkynes has proven to be a highly reliable, selective, and quantitative reaction.\(^13,14\) It is tolerant of a wide variety of reactions conditions, proceeds at ambient temperature, is insensitive to both H\(_2\)O and O\(_2\), and can easily be performed in the presence of many types of functional groups without side reactions.\(^13\) Click chemistry has shown great utility toward the syntheses of triazole-based monomers,\(^15,16\) stimuli responsive polymers,\(^17,18\) step growth polymers,\(^18\) miktoarm star polymers,\(^19\) block copolymers,\(^20,21\) dendrimers,\(^22\) and polymer-modified substrates.\(^23,24\)
Despite the above-mentioned efforts, limited research has been conducted on the unique combination of PIB and Click chemistry. Binder et al. functionalized trivalent PIB with hydrogen bonding moieties through Click chemistry to generate novel supramolecular gels.\textsuperscript{25,26} Bergbreiter et al. reported the synthesis of PIB-supported Cu(I) catalyst complexes by reacting azide-terminated PIBs with acetylene functionalized ligands;\textsuperscript{27} this system exploited the inherent selective solubility of the PIB support for facile catalyst removal. Storey et al.\textsuperscript{28} reacted azide-terminated PIBs with an alkyne-functional chain transfer agent for reversible addition-fragmentation chain transfer (RAFT) polymerization as a site transformation approach to novel PIB-based block copolymers. With the exception of these reported examples, to our knowledge, no other investigations into this area of research have been conducted.

Preparation of PIB chain ends for the azido/alkyne Click reaction has become facile due to the ready availability of primary halide-terminated PIB via \textit{in situ} quenching techniques.\textsuperscript{8,9,10} In this report we show that 1-(ω-haloalkyl)pyrroles\textsuperscript{9} can be used to place primary bromo- or chloroalkyl functionalities onto quasiliving PIB, followed by displacement of halogen by azide ion, or alternatively, 1-(ω-azidoalkyl)pyrrole may be used as quencher to directly yield the terminal azide (Figure 5.1). This process produces a “Clickable” PIB intermediate that may be reacted with functional alkynes to tether a variety of useful functional groups to the PIB chain ends through a common 1,4-disubstituted-1,2,3-triazole linkage. We have demonstrated this modular process by producing PIBs with quantitative end-group functionalities including hydroxyl, acrylate, glycidyl, and tertiary amine.
Experimental

Materials

Hexane (anhydrous, 95%), TiCl$_4$ (99.9%, packaged under N$_2$ in sure-seal bottles), 2,6-lutidine (26Lut) (redistilled, 99.5%), $N,N$-dimethylformamide (anhydrous, 99.8%), heptane (anhydrous, 99%), tetrahydrofuran (anhydrous, 99.9%), propargyl alcohol (≥99%), sodium azide (≥99.5%), bromotris(triphenylphosphine)copper(I) (98%), propargyl acrylate (99%), glycidyl propargyl ether (≥90%), 3-dimethylamino-1-propyne (97%), $N,N,N',N'',N''$-pentamethyldiethylenetriamine (PMDETA, 99%), copper(I) bromide, CuBr, (99.99%) and chloroform-$d$ (0.01% H$_2$O maximum) were purchased from Sigma-Aldrich Co. and used as received. 1-(2-Bromoethyl)pyrrole (PyBr) and 1-(2-chloroethyl)pyrrole (PyCl) were purchased from TCI and distilled from calcium hydride. Isobutylene (IB) and CH$_3$Cl (both BOC, 99.5%) were dried through columns packed with CaSO$_4$ and CaSO$_4$/4 Å molecular sieves, respectively. 2-Chloro-2,4,4-trimethylpentane (TMPCl)$_2$ and 5-tert-butyl-1,3-di(1-chloro-1-methylethyl)benzene (t-Bu-$m$-DCC) were synthesized according to the literature. 1-(3-Bromopropyl)pyrrole (PyBrP) was synthesized by $N$-alkylation of pyrrolyl sodium salt with 1,3-dibromopropane in DMSO according to the literature and purified by fractional distillation.

Polyisobutylene precursors. 1-(ω-Haloalkyl)pyrrolyl-terminated PIBs were synthesized as previously described. tert-Chloride-terminated masterbatch PIBs, difunctional ($M_n$=2,100 g/mol) and monofunctional ($M_n$=1,970 g/mol), were prepared via the BCl$_3$-catalyzed polymerization of isobutylene from t-Bu-$m$-DCC and TMPCl, respectively, in methyl chloride at -60°C.
1-((ω-Azidoalkyl)pyrrole quenchers. Synthesis of 1-(2-azidoethyl)pyrrole (PyAz) was carried out under a dry nitrogen atmosphere in a round bottom flask according to the following representative procedure. To a solution of 1-(2-bromoethyl)pyrrole (3.57 mL, 5.0 g, 28.7 mmol) in \(N,N\)-dimethylformamide (3 mL) was added sodium azide (3.0 g, 46 mmol). The mixture was reacted for 12 h at 90 °C, with stirring. It was allowed to cool to room temperature and excess sodium azide was removed by filtration. The filtrate was dissolved in CH\(_2\)Cl\(_2\), washed with water, dried over MgSO\(_4\), and concentrated on a rotary evaporator. The crude product was finally purified by vacuum distillation. \(^1\)H NMR (CDCl\(_3\)): \(\delta = 3.59\) (t, 2H, CH\(_2\)N\(_3\)), 4.06 (t, 2H, NCH\(_2\)), 6.24 (d, 2H, 3-H), 6.72 (d, 3H, 2-H) ppm. \(^{13}\)C NMR (CDCl\(_3\)): \(\delta = 48.51\) (NCH\(_2\)), 52.16 (CH\(_2\)N\(_3\)), 108.88 (C3), 120.36 (C2) ppm.

The synthesis of 1-(3-azidopropyl) pyrrole (PyPAz) was analogous to that of 1-(2-azidoethyl)pyrrole. The crude product was purified by distillation. \(^1\)H NMR (CDCl\(_3\)): \(\delta = 2.02\) (m, 2H, CH\(_2\)), 3.28 (t, 2H, CH\(_2\)N\(_3\)), 4.01 (t, 2H, NCH\(_2\)), 6.19 (d, 2H, 3-H), 6.67 (d, 2H, 2-H) ppm. \(^{13}\)C NMR (CDCl\(_3\)): \(\delta = 30.58\) (CH\(_2\)), 46.04 (NCH\(_2\)), 48.09 (CH\(_2\)N\(_3\)), 107.35 (C3), 120.09 (C2) ppm.

Instrumentation

NMR spectra were acquired using a Varian Mercury\(^{\text{plus}}\) 300 MHz NMR spectrometer. Samples were prepared by dissolving the sample in chloroform-\(d\) (5-7%, w/v) and charging this solution to a 5 mm NMR tube.

Molecular weights and polydispersities (PDI) of the polymeric materials were measured using Size Exclusion Chromatography (SEC) (Waters Alliance 2695 separations module and two mixed E Polymer Laboratories Inc. columns) with on-line
multi-angle laser light scattering detection (Wyatt Technology Inc. MiniDAWN), as described previously.⁹

ATR-FTIR spectroscopic monitoring, using a ReactIR 1000 reaction analysis system (ASI Applied Systems, Millersville, MD), previously described,³³,³⁴ was integrated with an inert atmosphere glovebox (MBraun Labmaster 30) to obtain real-time FTIR spectra and temperature profiles of the isobutylene polymerizations. Reaction conversion was determined by monitoring the area, above a two-point baseline, of the absorbance centered at 887 cm⁻¹, associated with the =CH₂ wag of IB.

*Synthesis of 1-(ω-Azidoalkyl)pyrrolyl-PIB by Nucleophilic Substitution*

Functionalizations of monofunctional PIB with sodium azide were carried out under a dry nitrogen atmosphere in a flask according to the following representative procedure (Table 5.1, Entry 5). 1-(2-Bromoethyl)pyrrolyl-PIB (2.0 g, 1.00 mmol) was dissolved in 5 mL of dry heptane in a flask, and then sodium azide (0.196 g, 3.02 mmol) in 5 mL of DMF was added. The resulting biphasic mixture was stirred and heated to 90 °C, upon which it formed a single, homogeneous solution, and the reaction was conducted at 90°C for 24 h. Finally, the monophasic reaction mixture was allowed to cool, whereupon a biphasic mixture re-formed, and the heptane and DMF layers were separated. The heptane phase was washed with methanol, and subsequently, the polymer was precipitated two times into methanol. The precipitate was collected by dissolution in hexane; the solution was concentrated on a rotary evaporator, and the polymer was finally vacuum dried at room temperature.
Synthesis of Difunctional 1-(ω-Azidoalkyl)pyrrolyl-PIB using Masterbatch PIB

Synthesis of difunctional 1-(2-azidoethyl)pyrrolyl-PIB was carried out under a dry nitrogen atmosphere in a glove box according to the following representative procedure (Table 5.2, Entry 1). Large culture tubes equipped with Teflon-lined caps were used as reactors. Into a test tube containing 0.53 g of masterbatch difunctional PIB (Mn= 2,100 g/mol, 0.25 mmol) were added 10 mL of CH$_3$Cl, 15 mL of hexane, and 0.009 mL (0.008 g, 0.07 mmol) of 2,6-lutidine. The polymer was allowed to dissolve, and the solution was equilibrated to -70 °C with agitation. Then, 0.55 mL (0.95 g, 5.0 mmol) of TiCl$_4$ was transferred to the reactor, followed by a pre-chilled solution containing 0.124 g (0.911 mmol) 1-(2-azidoethyl)pyrrole in 25 mL of hexane/CH$_3$Cl (60/40, v/v, -70°C). The color of the reaction mixture changed from slightly yellow to brown. PyAz was allowed to react with the living chain ends for 10 min. Finally, the reaction was quenched by addition of prechilled methanol. The reactor contents were allowed to warm to room temperature, and the polymer in hexane was washed with methanol and then precipitated one time into methanol from hexane. The precipitated polymer was collected by dissolution in hexane; the solution was concentrated on a rotary evaporator, and the polymer was finally vacuum dried at room temperature.

Isobutylene Polymerization and N-(ω-Azidoalkyl)pyrrole Quenching

Quasiliving polymerizations of IB with either TMPCl or t-Bu-\textit{m}-DCC as initiator were carried out within a N$_2$ atmosphere glovebox, equipped with an integral, cryostated hexane/heptane bath according to the following representative procedure (Table 5.3, Entry 3). Into a round-bottom flask equipped with a mechanical stirrer, infrared probe, and thermocouple were added 72 mL of CH$_3$Cl, 108 mL of hexane, 0.07 mL (0.06 g, 0.6
mmol) of 2,6-lutidine, 5.4 mL (3.8 g, 67 mmol) of IB, and 0.323 g (1.12 mmol) of t-Bu-
m-DCC. The mixture was allowed to equilibrate to -70°C, and then, 0.99 mL (1.7 g, 9.0 mmol) of TiCl$_4$ was charged to the reactor. The reaction was allowed to proceed for 37 min, and then a pre-chilled solution of 1-(2-azidoethyl)pyrrole (PyAz) prepared by dissolving 0.551 g PyAz (4.05 mmol) into 25 mL of hexane/CH$_3$Cl (60/40, v/v, -70°C), was added, followed by an additional 1.48 mL (2.56 g, 13.5 mmol) TiCl$_4$. The color of the solution changed from slightly yellow to brown. PyAz was allowed to react with the living chain ends for 60 min. Finally, the reaction was quenched by addition of excess prechilled methanol. The reactor contents were allowed to warm to room temperature, and the polymer in hexane was washed with methanol and then precipitated one time into methanol from hexane. The precipitate was collected by dissolution in hexane; the solution was washed with water, dried over MgSO$_4$, and concentrated on a rotary evaporator. The polymer was finally vacuum dried at room temperature.

*Synthesis of 1-[2-(4-Hydroxymethyl-1H-1,2,3-triazol-1-yl)ethyl]pyrrole*

*(Table 5.4, Entry 2)*

Under a dry nitrogen atmosphere, 1-(2-azidoethyl)pyrrole (1.23 g, 9.03 mmol) and propargyl alcohol (0.76 mL, 0.73 g, 13 mmol) were mixed in a round-bottom flask. In a separate vessel, a solution of copper(I) bromide (0.0057 g, 0.040 mmol) and PMDETA (0.0083 mL, 0.0069 g, 0.040 mmol) in 1 mL THF was prepared. With stirring, the catalyst solution in THF was added to the azide/alkyne mixture. A very exothermic reaction ensued. After 5 min, the mixture was diluted with tetrahydrofuran and passed through a column of aluminum oxide (neutral) using THF as eluent. The resulting solution of 1-[2-(4-hydroxymethyl-1H-1,2,3-triazol-1-yl)ethyl]pyrrole was collected and
concentrated on a rotary evaporator, and the crude product was purified by distillation.

$^1$H NMR (CDCl$_3$): $\delta = 3.19$ (broad, 1H, OH), 4.35 (t, 2H, 1-CH$_2$-triazole), 4.64 (t, 2H, CH$_2$-pyrrole), 4.69 (s, 2H, 4-CH$_2$-triazole), 6.13 (d, 2H, 3-H-pyrrole), 6.45 (d, 2H, 2-H-pyrrole), 6.93 (s, 1H, 5-H-triazole) ppm. $^{13}$C NMR (CDCl$_3$): $\delta = 49.24$ (CH$_2$-pyrrole), 51.47 (1-CH$_2$-triazole), 56.18 (4-CH$_2$-triazole), 109.33 (C3-pyrrole), 120.09 (C2-pyrrole), 123.47 (C5-triazole), 147.64 (C4-triazole) ppm.

Synthesis of 1-[3-(4-Hydroxymethyl-1H-1,2,3-triazol-1-yl)propyl]pyrrole

(Table 5.4, Entry 3)

Synthesis of 1-[3-(4-hydroxymethyl-1H-1,2,3-triazol-1-yl)propyl]pyrrole was analogous to the synthesis of 1-[2-(4-hydroxymethyl-1H-1,2,3-triazol-1-yl)ethyl]pyrrole.

$^1$H NMR (CDCl$_3$): $\delta = 2.37$ (m, 2H, CH$_2$), 3.36 (broad, 1H, OH), 3.92 (t, 2H, 1-CH$_2$-triazole), 4.25 (t, 2H, CH$_2$-pyrrole), 4.77 (s, 2H, 4-CH$_2$-triazole), 6.16 (d, 2H, 3-H-pyrrole), 6.62 (d, 2H, 2-H-pyrrole), 7.47 (s, 1H, 5-H-triazole) ppm. $^{13}$C NMR (CDCl$_3$): $\delta = 31.56$ (CH$_2$), 46.04 (CH$_2$-pyrrole), 47.20 (1-CH$_2$-triazole), 56.27 (4-CH$_2$-triazole), 108.71 (C3-pyrrole), 120.44 (C2-pyrrole), 121.87 (C5-triazole), 147.47 (C4-triazole) ppm.

Synthesis of Monofunctional 1-[3-(4-Hydroxymethyl-1H-1,2,3-triazol-1-yl)propyl]pyrolyl-PIB by Click Chemistry

Synthesis of hydroxyl-PIB by Click chemistry was carried out under a dry nitrogen atmosphere in a flask according to the following procedure (Table 5.5, Entry 1). 1-(3-Azidopropyl)pyrolyl-PIB ($M_n = 1,380$ g/mol, 0.537 g, 0.389 mmol) was dissolved in 5 mL of dry THF in a flask, and then 0.061 mL of propargyl alcohol (0.059 g, 1.0 mmol) and 0.074 g of bromotris(triphenylphosphine)copper (I) (0.080 mmol) were
added. With stirring, the resulting mixture was heated to 55 °C, and the reaction was allowed to proceed for 24 h. Finally, the reaction mixture was allowed to cool, and THF and excess propargyl alcohol were removed at 40 °C using a rotary evaporator. Subsequently, the polymer was dissolved in hexane and washed with methanol and then precipitated one time into methanol from hexane. The precipitate was collected by dissolution in hexane; the solution was concentrated on a rotary evaporator, and the polymer was finally vacuum dried at room temperature.

Synthesis of Monofunctional 1-[3-(4-Vinylcarbonyloxymethyl-1H-1,2,3-triazol-1-yl)propyl]pyrrolyl–PIB by Click Chemistry

Synthesis of acrylate-terminated PIB by Click chemistry was carried out under a dry nitrogen atmosphere in a flask according to the following procedure (Table 5.5, Entry 2). 1-(3-Azidopropyl)pyrrolyl-PIB (\( M_n = 2,950 \) g/mol, 1.4 g, 0.47 mmol) was dissolved in 3 mL of dry THF in a flask, and then 0.105 mL of propargyl acrylate (0.105 g, 0.950 mmol) and 0.074 g of bromotris(triphenylphosphine)copper (I) (0.080 mmol) were added. The resulting mixture was stirred and allowed to react for 24 h at 25 °C. The reaction mixture was then allowed to cool, and THF and excess propargyl acrylate were removed at 40 °C using a rotary evaporator. Subsequently, the polymer was dissolved in hexane, filtrated and then precipitated one time into methanol from hexane. The precipitate was collected by dissolution in hexane; the solution was concentrated on a rotary evaporator, and the polymer was finally vacuum dried at room temperature.
Synthesis of Monofunctional 1-[3-(4-Glycidyloxymethyl-1H-1,2,3-triazol-1-yl)propyl]pyrrolyl-PIB by Click Chemistry

Synthesis of glycidyl-terminated-PIB by Click chemistry was carried out under a dry nitrogen atmosphere in a flask according to the following procedure (Table 5.5, Entry 3). 1-(3-Azidopropyl)pyrrolyl-PIB ($M_n =$ 2,950 g/mol, 1.0 g, 0.34 mmol) was dissolved in 2.5 mL of dry THF in a flask, and then 0.073 mL of glycidyl propargyl ether (0.076 g, 0.68 mmol) and 0.074 g of bromotris(triphenylphosphine)copper (I) (0.080 mmol ) were added. The resulting mixture was stirred and allowed to react for 24 h at 25 °C. The reaction mixture was then allowed to cool, and THF and excess glycidyl propargyl ether were removed at 40 °C using a rotary evaporator. Subsequently, the polymer was dissolved in hexane, filtrated and then precipitated one time into methanol from hexane. The precipitate was collected by dissolution in hexane; the solution was concentrated on a rotary evaporator, and the polymer was finally vacuum dried at room temperature.

Synthesis of Monofunctional 1-[3-(4-Dimethylaminomethyl-1H-1,2,3-triazol-1-yl)propyl]pyrrolyl–PIB by Click Chemistry

Synthesis of dimethylamino-terminated PIB by Click chemistry was carried out under a dry nitrogen atmosphere in a flask according to the following procedure (Table 5.5, Entry 4). 1-(3-Azidopropyl)pyrrole-PIB ($M_n =$ 2,950 g/mol, 1.0 g, 0.34 mmol) was dissolved in 2.5 mL of dry THF in a flask, and then 0.073 mL of 3-dimethylamino-1-propyne (0.056 g, 0.68 mmol) and 0.074 g of bromotris(triphenylphosphine)copper (I) (0.080 mmol ) were added. The resulting mixture was stirred and allowed to react for 24 h at 25 °C. The reaction mixture was then allowed to cool, and THF and excess 3-dimethylamino-1-propyne were removed at 40 °C using a rotary evaporator.
Subsequently, the polymer was dissolved in hexane, filtrated and then precipitated one time into methanol from hexane. The precipitate was collected by dissolution in hexane; the solution was concentrated on a rotary evaporator, and the polymer was finally vacuum dried at room temperature.

**Results and Discussion**

*Synthesis of N-(ω-Azidoalkyl)pyrrolyl-PIB by Nucleophilic Substitution*

We recently reported\(^9\) that quasiliving cationic PIB reacts quantitatively with 1-(ω-haloalkyl)pyrroles to yield an isomeric mixture of 2- and 3-PIB-1-(ω-haloalkyl)pyrroles, with no detectable di-substitution (coupled) products. The resulting primary halide end groups are useful intermediates toward many alternative end groups including azides.

To obtain the desired 1-(ω-azidoalkyl)pyrrolyl-PIB, two synthetic strategies were attempted, as shown in Figure 5.1. The first approach involved substitution of the terminal halogen of 1-(ω-haloalkyl)pyrrolyl-PIB with sodium azide (Figure 5.1, Route A); whereas the second involved *in-situ* functionalization with 1-(2-azidoethyl)pyrrole (Route B). The 1-(ω-haloalkyl)pyrrole-PIBs used for the first approach were synthesized as previously reported.\(^9\)

Direct conversion of the terminal halide to the corresponding azide was achieved using sodium azide,\(^{35}\) which is readily available, inexpensive, and soluble in polar solvents such as *N,N*-dimethylformamide. However, the hydrophobic nature of PIB necessitated a cosolvent system consisting of a 1:1 (v/v) mixture of heptane and *N,N*-dimethylformamide. This cosolvent mixture was optimal for dissolution of both PIB and NaN\(_3\) at elevated temperatures, and it offered the useful process advantage of forming
two immiscible phases at room temperature. Upon cooling the reaction, this allowed facile separation of the PIB-azide product, contained in the upper heptane-rich layer, from excess NaN$_3$ and Na halide byproduct, which resided in the lower DMF-rich layer.

Initial experimentation showed that for chain end concentrations [CE] in the range 0.06 to 0.12 mol/L, and for [azide]/[CE] = 3, reaction temperatures less than 90°C resulted in unreasonably long reaction times (in excess of 24 h) for either chloride or bromide substrates. For example, Table 5.1, Entries 1 and 2 show that for chloride at 70°C, no greater than 40% conversion was reached in 24 h depending upon [CE]. At 90°C, however, complete reaction was observed within 24 h, for either chloride or bromide regardless of tether length (2 or 3 carbons) over a range of chain end concentrations as demonstrated in Table 5.1, Entries 3-9.

Figure 5.2 shows the $^1$H NMR spectrum with peak assignments of 1-(2-azidoethyl)pyrrolyl-PIB from 1-(2-bromoethyl)pyrrolyl-PIB (Table 1, Entry 5, which is representative). Quantitative reaction was indicated by the complete absence of peaks due to the tether unit of the bromide precursor, which would have been visible as triplets centered at 3.53, 3.55, 4.18, and 4.31 ppm (see inset, Figure 5.2). To confirm quantitative reaction, difunctional 1-(3-azidopropyl)pyrrolyl-PIB was synthesized (Table 5.1, Entry 8) and characterized by $^1$H NMR (Figure 5.3). Integration of the resonances due to the terminal 1-(3-azidopropyl)pyrrole moieties in comparison with the aromatic initiator resonance at 7.17 ppm indicated near-quantitative capping and production of difunctional, telechelic primary azide PIB. Difunctional 1-(2-azidoethyl)pyrrolyl-PIB was also synthesized and quantitative functionalization was confirmed by $^1$H NMR analysis (Figure 5.4). Complete $^1$H and $^{13}$C NMR chemical shift assignments for
monofunctional 2- and 3-PIB-1-(2-azidoethyl)pyrrole are listed in Tables 5.6 and 5.7, respectively. The same data for the 2- and 3-PIB-1-(3-azidopropyl)pyrroles are listed in Tables 5.8 and 5.9, respectively.

Examination of the products obtained in low conversion reactions such as Entries 1 and 2 (Table 5.1) indicated that the isomeric 2- and 3-PIB-1-(ω-haloalkyl)pyrroles might possess different reactivities toward the S\textsubscript{N}2 reaction with azide. Thus, the kinetics of azide substitution at 90°C, with [azide]/[CE] = 3, were examined in detail using \textsuperscript{1}H NMR spectroscopy. Figure 5.2 provides a comparison of the methylene tether resonances of the bromide reactant (inset) and azide product, and thus indicates the characteristic chemical shifts that were observed upon substitution. Reaction progress was monitored by observing the resonance due to the methylene unit adjacent to the pyrrole nitrogen. For the C\textsubscript{3} isomer, appearance of the azide product was monitored using the peak at 3.95 ppm; for the C\textsubscript{2} isomer, disappearance of the halogen reactant was observed at 4.27 (Cl) or 4.31 ppm (Br). Figure 5.5 shows a plot of reaction conversion vs. time for 1-(2-bromoethyl)pyrrolyl-PIB (difunctional), with C\textsubscript{3} and C\textsubscript{2} isomer conversions plotted individually. Complete reaction of both isomers was achieved after about 10 h. As suspected, reaction at the C\textsubscript{3} isomer was considerably faster than at the C\textsubscript{2} isomer. This is probably a steric effect; since for S\textsubscript{N}2 reactions, steric effects are generally more important than electronic effects for substituents located at the \(β\) position or more remotely.\textsuperscript{36} Figure 5.6 shows a plot of reaction conversion vs. time for 1-(2-bromopropyl)pyrrolyl-PIB, with C\textsubscript{3} and C\textsubscript{2} isomer conversions plotted individually. Reactivities were observed to be opposite of those found with the two carbon tether, although reactive isomer reactive was more similar.
Rate of the azide substitution reaction can be dramatically increased by using a large excess of the inexpensive NaN$_3$ (pseudo-first-order conditions) and maximizing the temperature to the reflux temperature of the heptane/DMF cosolvents. In recent preparative work, we have reduced reaction times for the bromide substrate to about 45 min using a 20-fold excess of azide at reflux temperature. Further increases in azide concentration produce diminishing returns due to solubility limitations in the cosolvent system.

*Synthesis of 1-(ω-Azidoalkyl)pyrrolyl-PIB by Quenching with 1-(2-Azidoethyl)pyrrole*

To avoid the post-polymerization substitution reaction, we next attempted to quench quasiliving carbocationic PIB directly with a 1-(ω-azidoalkyl)pyrrole (Figure 5.1, Route B). We expected that an aliphatic primary azide would not decompose TiCl$_4$ and therefore would not prevent electrophilic aromatic substitution at the pyrrole ring. For this purpose, 1-(2-azidoethyl)pyrrole was synthesized from the corresponding bromide by nucleophilic substitution with NaN$_3$ in DMP at 90°C for 12 h. Reaction progress was monitored using $^1$H NMR by observing the disappearance of the tether resonances of the bromide reactant at 4.30 ppm (Py-CH$_2$-CH$_2$-Br) and 3.61 ppm (Py-CH$_2$-CH$_2$-Br) and the appearance of the corresponding resonances of the product at 4.06 and 3.59 ppm.

To demonstrate its utility as a quencher, 1-(2-azidoethyl)pyrrole was reacted with difunctional tert-chloride-terminated masterbatch PIB in the presence of TiCl$_4$ under the conditions listed in Table 5.2. Typically, alkylation of a 1-substituted pyrrole by PIB cations is sufficiently rapid that ionization of tert-chloride PIB is rate limiting.$^{9,11}$ However, the rate of ionization is dependent on the effective or free [TiCl$_4$], and the latter is difficult to specify because of uncertainty with regard to the extent of complexation of
TiCl₄ by the quencher and, particularly, the alkylated product. For example, Cheradame et al. reported the synthesis of azide-terminated PIB initiated from 1,4-di(1-azido-1-methylethyl)benzene/TiCl₄ at -70 °C in CH₂Cl₂ (the products actually possessed mixed azide, tert-chloride, and olefin end groups). These authors reported that relatively high [TiCl₄] was necessary for polymerization due to a complexation between TiCl₄ and the azide groups. The data in Table 5.2, obtained using a uniform quencher concentration of 0.018 mol/L, indicate that a nominal [TiCl₄] = 0.10 mol/L was sufficient to achieve quantitative alkylation in under 3 min (Exp. 1, 4, and 5); whereas nominal [TiCl₄] = 0.02 (Exp.2) or 0.03 mol/L (Exp. 4) was insufficient even for a reaction time of 15 min.

The ¹H NMR spectrum of the product of Table 5.2, Entry 1, acquired after a quenching time of 10 min is shown in Figure 5.7. Resonances at 1.68 and 1.96 ppm due to residual tert-chloride end groups were not observed, indicating complete conversion. A new set of peaks at 1.67, 3.52, 3.95, 6.07, 6.40 and 6.57 ppm (C₃-isomer, major) and 1.72, 3.64, 4.13, 5.90, 6.10 and 6.60 ppm (C₂-isomer, minor) appeared due to the presence of N-(2-azidoethyl)pyrrolyl moieties at the chain ends. The integration data indicated that the combined peak areas (C₂ and C₃ isomers) of the CH₂N₃ protons at 3.52 and 3.64, and the NCH₂ protons at 3.95 and 4.13 ppm were 1.31 and 1.32 times that of the aromatic proton resonance at 7.2 ppm, indicating that 98-99% of the chain ends were functionalized with the desired azide groups; a similar analysis applied to the pyrrole ring protons yielded a slightly lower estimate of about 97%. The balance of the chain ends consisted of mixed olefins, visible in the spectrum at 4.64 and 4.85 (exo) and 5.05 ppm (endo). A prequench control aliquot revealed that there were exactly two tert-chloride
end groups per aromatic initiator residue and no detectable olefin; therefore, this small amount of olefin was created during the quenching reaction. Similar quenching reactions with 1-(ω-haloalkyl)pyrroles did not produce olefin,\(^9\) and so we believe that elimination is induced by competitive nucleophilic interaction of azide groups of the quencher with the PIB carbocations.

The integration data in Figure 5.7 revealed a \(C_2/C_3\) isomer ratio of 40/60. This is consistent with our general experience with 1-substituted pyrrole quenching.\(^9,11,39\) Mixed isomers are invariably observed, with the \(C_3\) isomer dominant, but the nature of the 1-substituent attached to the pyrrole ring, and the tether length, effect the ratio. In previous reports, we showed that 1-methylpyrrole yielded a nearly balanced \(C_2/C_3\) isomer ratio of 48/52;\(^39\) 1-(3-bromopropyl)pyrrole showed a greater tendency toward \(C_3\), yielding an average \(C_2/C_3 = 39/61\), and 1-(2-haloethyl)pyrroles showed the greatest tendency toward \(C_3\), averaging \(C_2/C_3 = 28/72\).\(^9\)

Functionalization was also confirmed by \(^{13}\)C NMR spectroscopy, by observing the disappearance of the resonances at 71.9 and 35.2 ppm, representing the quaternary and geminal dimethyl carbons, respectively, adjacent to the terminal \(\text{tert}\)-chloride group, and appearance of new peaks in both the aromatic and the aliphatic regions of the spectrum. The \(^{13}\)C NMR spectrum of 1-(2-azidoethyl)pyrrolyl-PIB, along with peak assignments, is shown in Figure 5.8.

Figure 5.9 compares GPC traces of 1-(2-azidoethyl)pyrrole-quenched PIB with an aliquot removed from the reaction prior to quenching. The GPC traces prior to and after quenching were indistinguishable, indicating the absence of any coupling reactions or polymer degradation.
Entries 1 and 4 (difunctional) and 5 (monofunctional) of Table 5.2 demonstrate the reproducibility of the quenching reaction. In all three cases, quantitative conversion of tert-chloride chain ends was obtained, but the resulting polymers all contained 1 to 2% olefinic chain ends (mixed exo and endo). No difference was observed between difunctional and monofunctional PIBs; particularly, difunctional samples did not show a greater tendency toward coupling via dialkylation of a pyrrole ring compared to the monofunctional sample. Although quenching required less than 3 min under these conditions, the product of Entry 1 was indistinguishable from the product of Entry 3; thus no apparent harm was caused by prolonged reaction time after complete conversion. However, such was not the case for prolonged reaction times at incomplete conversion. For the two experiments run at lower [TiCl$_4$] (Entries 2 and 4), GPC analysis of the PIB after quenching showed that coupling products were present.

The experiments of Table 5.2, which involved pre-formed, tert-chloride-terminated PIB, showed that quenching with a 1-(ω-azidoalkyl)pyrrole requires relatively high [TiCl$_4$]. If used for IB quasiliving polymerization, such high [TiCl$_4$] would produce inconveniently high rates; therefore, for the case of IB polymerization followed immediately by quenching, a lower [TiCl$_4$] was used during polymerization, with an additional charge of TiCl$_4$ added for quenching. Table 5.3 lists several in situ quenching experiments that illustrate this strategy. Entry 1 was a control experiment in which the additional charge of TiCl$_4$ was omitted. With [TiCl$_4$] = 0.053 M, this recipe yielded a convenient polymerization time of about 30 min, but quenching was only 36% complete after a 40 min quenching reaction, with the balance of the chain ends returned as tert-chloride. Entry 2 used a polymerization recipe similar to Entry 1, but in this case an
additional increment of TiCl₄ was added with the quencher to yield a total [TiCl₄] = 0.060 during the quench. In this case the extent was quenching was 87% after a quenching time of 60 min. However, an aliquot removed from the reaction after 2 min indicated that 65% alkylation had already occurred, suggesting that the initial rate of reaction was sufficiently fast but that it soon stalled, presumably due to loss of catalyst. In Entry 3, the additional TiCl₄ increment was increased to yield a total [TiCl₄] = 0.10 during the quench. This resulted in quantitative functionalization within 2 min.

The structure of the polymer obtained from Table 5.3, Entry 3 above was essentially identical in all respects to that of the polymers obtained from the pre-formed PIB of Table 2. About 97-99% of the chains carried the desired 1-(2-azidoethyl)pyrrole functions and the remainder of the chains were mixed olefin. It is noteworthy to mention that Entries 1 and 2, Table 3, produced polymers with visible coupling in the GPC chromatogram. This is consistent with the results for quenching of pre-formed PIB (Table 5.2) and suggests that coupling is generally observed when functionalization is incomplete.

Functionalization of 1-(ω-Azidoalkyl)pyrrolyl-PIB by Click Chemistry

An important advantage of 1-(ω-azidoalkyl)pyrrolyl-PIB is its ability to react with alkynes via Click chemistry, i.e., the copper(I)-catalyzed Huisgen 1,3-dipolar cycloaddition reaction. This reaction is a versatile tool for macromolecular engineering and allows the fabrication of complex structures with various functionalities. In the present context, it provides a modular approach to various telechelic PIBs.

To define appropriate conditions for Click chemistry at the PIB chain end, including the preferred catalyst, 1-(2-azidoethyl)pyrrole and 1-(3-azidopropyl)pyrrole,
were used to mimic the end group of 1-(ω-azidoalkyl)pyrrolyl–PIB in model reactions with a representative alkyne, propargyl alcohol (Table 5.4). Two copper(I)-based catalysts were examined, bromotris(triphenylphosphine)copper(I) and Cu(I)Br/PMDETA. Both catalysts promoted high regioselectivity to yield exclusively the 4-hydroxymethyltriazole products. For example, Figure 5.10 shows the $^1$H NMR spectrum of 1-[2-(4-hydroxymethyl-1H-1,2,3-triazolyl)ethyl]pyrrole obtained from reaction of 1-(2-azidoethyl)pyrrole with propargyl alcohol using copper(I) bromide/PMDETA as catalyst (Table 5.4, Entry 2). Conversion exclusively to the 4-substituted regio isomer was indicated by a single resonance for the C$_5$ triazole proton at 6.93 ppm. The methylene and hydroxyl protons of the propargyl alcohol residue were observed at 4.69 and 3.19 ppm, respectively, and the protons of the ethylene tether were observed at 4.35 and 4.64 ppm. The length of the alkylene tether appeared to make little difference in the reaction; both azide model compounds behaved similarly with regard to reactivity toward the alkyne and structure of the resulting triazole (Table 5.4, Entries 2 and 3).

Copper(I) bromide/PMDETA produced very rapid, highly exothermic Click reactions. Complete conversion was obtained within 5 min for the two model reactions in Table 5.4 (Entries 2 and 3). However, Cu(I)Br/PMDETA is very soluble in organic solvents, including non-polar solvents such as hexane, which are good solvents for PIB. Thus we found it necessary to pass the product through an alumina column to remove the catalyst. Compared to Cu(I)Br/PMDETA, bromotris(triphenylphosphine)copper(I) produced much slower reactions; full conversion of 1-(2-azidoethyl)pyrrole to the triazole required 12 h (Table 5.4, Entry 1). However, although
bromotris(triphenylphosphine)copper(I) is soluble in most organic solvents, its solubility in hexane is limited. This suggested an attractive strategy for Click reactions at the PIB chain end, involving bromotris(triphenylphosphine)copper(I)-catalyzed reaction in THF, followed by dissolution of the product in hexane and removal of the catalyst by simple filtration and precipitation.

After obtaining positive Click chemistry results with the model compounds, we next explored the reaction of propargyl alcohol with azide-terminated PIB. Kinetics were measured using real-time $^1$H NMR analysis by observing the decrease in area of the propargyl methylene protons signal of propargyl alcohol. Figure 5.11 shows plots of reaction conversion vs. time, at 25°C in THF, for an initial molar ratio of alkyne/azide of 2.0. The inset plots show the data fitted to an integrated second-order rate equation. The upper plot (A) shows reaction of 1-(3-azidopropyl)pyrrolyl-PIB (3-carbon tether) using 1/1 CuBr(I)/PMDETA; the lower plot (B) (solid circles) shows reaction of the same polymer in the presence of bromotris(triphenylphosphine)copper(I). In plot (A), as expected, reaction rate for CuBr(I)/PMDETA was very high, requiring less than 20 min for complete reaction, and on the order of 30 times higher than for bromotris(triphenylphosphine)copper(I). Poor temperature control due to exotherm of the CuBr(I)/PMDETA-catalyzed reaction was suggested by the upward curvature in the second-order plot. The second-order rate constant calculated from the initial, linear portion of the curve (first 5 points) was 22 L/mol-s. In plot (B), an induction period was observed for bromotris(triphenylphosphine)copper(I) catalysis, and complete reaction required approximately 16-20 h. The second-order rate constant for the 3-carbon tether
(solid circles), using the entire data set, was 0.68 L/mol-s; the 2-carbon tether (open circles) produced a slightly faster reaction, with a rate constant of 0.91 L/mol-s.

To demonstrate the modularity of the Click chemistry approach toward chain-end functionalization, PIBs with various terminal groups were prepared as listed in Table 5.5. Bromotris(triphenylphosphine)copper(I) was used as catalyst in all cases due to the ease of its separation from the polymer (limited solubility in hexane). Reaction of propargyl alcohol at the PIB chain end was identical to the model experiments in terms of structure (Table 5.5, Entry 1). Figure 5.12 shows the $^1$H NMR spectrum of the resulting polymer with peak assignments. Functionalization was indicated by the disappearance of the peaks at 1.95/2.07 ppm (--PIB-Py-CH$_2$-CH$_2$-N$_3$), 3.22/3.44 ppm (--PIB-Py-CH$_2$-CH$_2$-CH$_2$-N$_3$), and 3.90/4.04 ppm (--PIB-Py-CH$_2$-CH$_2$-CH$_2$-N$_3$), and appearance of new peaks at 2.35, 3.85, 4.24, 6.07, 6.40 and 6.57 ppm (3-isomer, major), 2.43, 4.04, 4.46, 5.90, 6.10 and 6.60 ppm (2-isomer, minor) and 4.81 ppm due to presence of the 1-[3-(4-hydroxymethyl-$^1$H-1,2,3-triazol-1-yl)propyl]pyrrole moieties at the chain ends.

Reaction of azide-terminated PIB with propargyl acrylate lead to the easy isolation of a PIB acrylate macromer (Table 5.5, Entry 2), potentially useful for introducing PIB grafts into acrylic copolymers. The reaction was carried out at room temperature in THF solution. Isolation of the polymer consisted simply of dissolving the product in hexanes, filtering to remove catalyst, and evaporation of the solvent and excess propargyl acrylate. To remove all traces of unreacted propargyl acrylate, optionally the polymer may be precipitated into methanol. The $^1$H NMR spectrum of the resulting 1-[3-(4-vinylcarbonyloxymethyl-$^1$H-1,2,3-triazol-1-yl)propyl]pyrrole-PIB is shown in Figure 5.13. Functionalization was indicated by the disappearance of
resonances associated with azide end groups and appearance of a new set of resonances 2.35, 3.85, 4.24, 6.07, 6.40 and 6.57 ppm (3-isomer, major), 2.43, 4.04, 4.46, 6.10 and 6.60 ppm (2-isomer, minor) and 5.31, 6.09, 6.12, 6.15, 6.18, 6.42, 6.47 ppm due to presence of the 1-[3-(vinylcarbonyloxymethyl-1\textit{H}-1,2,3-triazol-1-yl)propyl]pyrrole moieties at the chain ends.

Propargyl glycidyl ether was “Clicked” onto azide-terminated PIB to obtain epoxy-terminated PIB (Table 5.5, Entry 3). This chemistry would be useful for the introduction of PIB graft segments (monofunctional) or network chain segments (difunctional) into epoxy-based networks for toughening. The reaction was carried out at room temperature in THF solution. Isolation of the polymer consisted of dissolving the product in hexanes, filtering to remove catalyst, and precipitation into methanol. Figure 5.14 shows the $^1\text{H}$ NMR spectrum of the resulting polymer with peak assignments. The spectrum shows the characteristic 1,3-propylene tether peaks for both isomers and resonances at 2.63, 2.81, 3.19, 3.45, 4.72 ppm due to the 1-[3-(4-glycidyloxymethyl-1\textit{H}-1,2,3-triazol-1-yl)propyl]pyrrole moieties at the chain ends.

Click reactions involving amine-functional alkynes are potentially challenging due to complexation of copper by the amino group, which could hinder purification of the functionalized polymer. To address this issue, we reacted 1-(3-azidopropyl)pyrrolyl-PIB with 3-dimethylamino-1-propyne in THF at 25 °C in the presence of bromotris(triphenylphosphine)copper(I) (Table 5.5, Entry 4). The progress of the Click reaction itself did not appear to be effected by complexation. However, purification of the product did prove to be more laborious in comparison to the other functionalizations carried out by Click chemistry. Formation of 1-[3-(4-dimethylaminomethyl-1\textit{H}-1,2,3-
triazol-1-yl)propyl]pyrrolyl-PIB was verified by $^1$H NMR (Figure 5.15) by the appearance of characteristic tether peaks from both isomers and resonances at 2.28 and 3.62 ppm due to the dimethylamionomethyl moieties).

**Conclusion**

Synthesis of 1-(ω-azidoalkyl)pyrrolyl-PIB was successfully accomplished by either reaction of 1-(ω-haloalkyl)pyrrolyl-PIB with sodium azide or by quenching of quasiliving PIB with 1-(2-azidoethyl)pyrrole. The former method was found to yield essentially quantitative azide functionality; however, quenching with 1-(2-azidoethyl)pyrrole produced 1-2% olefin (mixed exo and endo) chain ends in addition to the desired azide. The nucleophilic substitution reaction with azide ion was found to proceed substantially more rapidly with the 3-pyrrole isomer compared to the 2-pyrrole isomer.

Structure of 1-(ω-azidoalkyl)pyrrolyl-PIB was investigated by both $^1$H and $^{13}$C NMR. The product of end-quenching was found to be a mixture of 2- and 3-PIB-1-(2-azido)pyrroles, consistent with our previous report concerning end-quenching with 1-(ω-haloalkyl)pyrroles. However, compared to the haloalkylpyrroles, 1-(2-azidoethyl)pyrrole quenching yielded a more balanced isomer ratio of $C_2/C_3 = 0.40/0.60$, similar to the nearly perfectly balanced ratio (0.48/0.52) obtained with 1-methylpyrrole. To our knowledge, the 1-(2-azidoethyl)pyrrolyl-PIB synthesized in this work represents the first successful quenching of quasiliving PIB with a capping agent containing azide groups.

We have described here an easy way to functionalize PIB and provide fast access to a large variety of interesting and potentially useful functional oligomers of uniform molecular weight and high purity. 1-(ω-Azidoalkyl)pyrrolyl-PIB was shown to provide a
modular approach to various telechelic PIBs via the Huisgen 1,3-dipolar cycloaddition (Click reaction) between azides and terminal alkynes. Click reactions, catalyzed by bromotris(triphenylphosphine)copper(I), were conducted between 1-(ω-azidoalkyl)pyrrolyl-PIB and propargyl alcohol, propargyl acrylate, propargyl glycidyl ether, and 3-dimethylamino-1-propyne. PIBs containing hydroxyl, acrylate, glycidyl, and dimethylamino groups were cleanly synthesized by this process. These materials have potential commercial applications in many areas.

Acknowledgments

The research upon which this material is based was generously supported by Chevron Oronite Co., LLC.
References


Table 5.1. Conversion of \(N-(\omega\text{-Haloalkyl})\text{pyrrole-PIB}\) to \(N-(\omega\text{-Azidoalkyl})\text{pyrrole-PIB}\) via Nucleophilic Displacement of Halide by NaN\(_3\) in \(N,N\text{-Dimethylformamide/heptane (50/50, v/v)}\)^a

<table>
<thead>
<tr>
<th>Entry</th>
<th>[PIB] (mol/L)</th>
<th>(M_n) (g/mol)</th>
<th>PDI</th>
<th>End Group</th>
<th>[NaN(_3)] (mol/L)</th>
<th>Temp. (°C)</th>
<th>Azide Functionality(^e)</th>
</tr>
</thead>
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<tr>
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<td>0.113</td>
<td>1,760</td>
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<td>PyCl(^b)</td>
<td>0.339</td>
<td>70</td>
<td>0.39</td>
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<tr>
<td>2</td>
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<td>1,980</td>
<td>1.04</td>
<td>PyCl</td>
<td>0.201</td>
<td>70</td>
<td>0.19</td>
</tr>
<tr>
<td>3</td>
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<td>1,760</td>
<td>1.05</td>
<td>PyCl</td>
<td>0.255</td>
<td>90</td>
<td>~1.0</td>
</tr>
<tr>
<td>4</td>
<td>0.085</td>
<td>1,980</td>
<td>1.04</td>
<td>PyCl</td>
<td>0.255</td>
<td>90</td>
<td>~1.0</td>
</tr>
<tr>
<td>5</td>
<td>0.100</td>
<td>1,980</td>
<td>1.04</td>
<td>PyBr(^d)</td>
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<td>90</td>
<td>~1.0</td>
</tr>
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<td>1,730</td>
<td>1.04</td>
<td>PyBr</td>
<td>0.255</td>
<td>90</td>
<td>~1.0</td>
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<td>~2.0</td>
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<td>2,780</td>
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<td>PyBr</td>
<td>0.424</td>
<td>90</td>
<td>~2.0</td>
</tr>
</tbody>
</table>

\(^a\) Reaction time 24 h  
\(^b\) 1-(2-chloroethyl)pyrrole  
\(^c\) 1-(2-bromoethyl)pyrrole  
\(^d\) 1-(3-bromopropyl)pyrrole  
\(^e\) Determined by \(^1\)H NMR integration of tether proton signals of reactant and product  
\(^f\) Difunctional PIB
Table 5.2. End-Quenching of Difunctional tert-Chloride-Terminated Masterbatch PIB\(^a\) with \(N\)-(2-Azidoethyl)pyrrole in 60/40 (v/v) Hexane/MeCl at -70°C

<table>
<thead>
<tr>
<th>Entry</th>
<th>[(\text{tert-Cl})] (mol/L)</th>
<th>[Lut] (mol/L)</th>
<th>[(\text{TiCl}_4)] (mol/L)</th>
<th>[PyAz] (mol/L)</th>
<th>Functionality(^b)</th>
<th>time (min)</th>
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<td></td>
<td></td>
<td></td>
<td></td>
<td>3</td>
</tr>
<tr>
<td>1</td>
<td>0.010</td>
<td>0.0015</td>
<td>0.10</td>
<td>0.018</td>
<td>--</td>
<td>0.98-0.99</td>
</tr>
<tr>
<td>2</td>
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<td>0.0015</td>
<td>0.020</td>
<td>0.018</td>
<td>--</td>
<td>0.23</td>
</tr>
<tr>
<td>3</td>
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<td>0.0015</td>
<td>0.10</td>
<td>0.018</td>
<td>0.99</td>
<td>--</td>
</tr>
<tr>
<td>4</td>
<td>0.010</td>
<td>0.0015</td>
<td>0.030</td>
<td>0.018</td>
<td>--</td>
<td>--</td>
</tr>
<tr>
<td>5(^c)</td>
<td>0.010</td>
<td>0.0014</td>
<td>0.10</td>
<td>0.018</td>
<td>0.99</td>
<td>--</td>
</tr>
</tbody>
</table>

\(^a\) \(\overline{M}_n = 2,100\) g/mol

\(^b\) Determined by \(^1\)H NMR integration of tether proton signals relative to aromatic proton signals of bDCC initiator residue

\(^c\) Monofunctional PIB: \(\overline{M}_n = 1,970\) g/mol
Table 5.3. End-Quenching of Quasiliving IB Polymerizations with N-(2-azidoethyl)pyrrole in 60/40 (v/v) Hexane/CH$_3$Cl at -70°C$^a$

<table>
<thead>
<tr>
<th>Entry</th>
<th>[IB] mol/L</th>
<th>[bDCC] mol/L</th>
<th>[TiCl$_4$]$^b$ mol/L</th>
<th>$M_n$ g/mol</th>
<th>PDI</th>
<th>[PyAz] [CE]</th>
<th>[TiCl$_4$]$^c$ mol/L</th>
<th>Functionality$^d$</th>
</tr>
</thead>
<tbody>
<tr>
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<td></td>
<td>2</td>
</tr>
<tr>
<td>1</td>
<td>0.38</td>
<td>0.0059</td>
<td>0.053</td>
<td>3,350</td>
<td>1.01</td>
<td>1.8</td>
<td>--</td>
<td>-</td>
</tr>
<tr>
<td>2</td>
<td>0.36</td>
<td>0.0053</td>
<td>0.048</td>
<td>3,280</td>
<td>1.01</td>
<td>1.8</td>
<td>0.053</td>
<td>-</td>
</tr>
<tr>
<td>3</td>
<td>0.36</td>
<td>0.0053</td>
<td>0.048</td>
<td>3,200</td>
<td>1.01</td>
<td>1.8</td>
<td>0.105</td>
<td>0.99</td>
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</table>

$^a$ [2,6-Lutidine] = 0.0028 mol/L  
$^b$ [TiCl$_4$] during polymerization  
$^c$ [TiCl$_4$] during quenching  
$^d$ Determined by $^1$H NMR integration of tether proton signals relative to aromatic proton signals of bDCC initiator residue
Table 5.4. Synthesis of Model Compounds 1-[2-(4-hydroxymethyl-1H-1,2,3-triazol-1-yl)ethyl]pyrrole and 1-[3-(4-hydroxymethyl-1H-1,2,3-triazol-1-yl)propyl]pyrrole\textsuperscript{a}

<table>
<thead>
<tr>
<th>Entry</th>
<th>[PyAz]\textsuperscript{b} mol/kg</th>
<th>[PyPAz]\textsuperscript{c} mol/kg</th>
<th>[PrgOH]\textsuperscript{d} mol/kg</th>
<th>[(PPh\textsubscript{3})\textsubscript{3}CuBr]\textsuperscript{e} mol/kg</th>
<th>[Cu(I)Br] mol/kg</th>
<th>[PMDETA]\textsuperscript{f} mol/kg</th>
<th>Time h</th>
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<tbody>
<tr>
<td>1</td>
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<td>2.9</td>
<td>0.023</td>
<td></td>
<td></td>
<td></td>
<td>12</td>
</tr>
<tr>
<td>2</td>
<td>3.16</td>
<td>-</td>
<td>4.6</td>
<td>-</td>
<td>0.014</td>
<td>0.014</td>
<td>0.083</td>
</tr>
<tr>
<td>3</td>
<td>-</td>
<td>2.84</td>
<td>3.4</td>
<td>-</td>
<td>0.017</td>
<td>0.017</td>
<td>0.083</td>
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</table>

\textsuperscript{a} Initial reaction temperature = 25°C; Entries 2 and 3 were very exothermic
\textsuperscript{b} 1-(2-Azidoethyl)pyrrole.
\textsuperscript{c} 1-(3-Azidopropyl)pyrrole.
\textsuperscript{d} Propargyl alcohol.
\textsuperscript{e} Bromotris(triphenylphosphine)copper(I)
\textsuperscript{f} \textit{N},\textit{N},\textit{N} ‘,’\textit{N} ‘’-pentamethyldiethylenetriamine
Table 5.5. Experimental conditions and results of functionalization of 1-(3-azidopropyl)pyrrole -PIB by Click chemistry in tetrahydrofuran

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<tr>
<td>2</td>
<td>0.10</td>
<td>2.95</td>
<td>1.03</td>
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<td>0.21</td>
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<tr>
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<td>0.093</td>
<td>2.95</td>
<td>1.03</td>
<td>0.022</td>
<td>---</td>
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<td>0.19</td>
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<tr>
<td>4</td>
<td>0.093</td>
<td>2.95</td>
<td>1.03</td>
<td>0.022</td>
<td>---</td>
<td>---</td>
<td>---</td>
<td>0.19</td>
</tr>
</tbody>
</table>

ᵃPropargyl alcohol
ᵇPropargyl acrylate
ᶜGlycidylpropargyl ether
ᵈ3-Dimethylamino-1-propyne
Table 5.6. Chemical shift assignments for 2-and 3-PIB-1-(2-azidoethyl)pyrrole

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<tr>
<th>Assignment</th>
<th>$^1$H NMR chemical shift (ppm)</th>
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<td>k</td>
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<tr>
<td>h</td>
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<tr>
<td>i</td>
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<tr>
<td>f</td>
<td>1.65, s</td>
</tr>
<tr>
<td>f'</td>
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</tr>
<tr>
<td>a</td>
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</tr>
<tr>
<td>a'</td>
<td>3.64, m</td>
</tr>
<tr>
<td>c</td>
<td>3.95, m</td>
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<td>4.13, m</td>
</tr>
<tr>
<td>3'</td>
<td>5.90, m</td>
</tr>
<tr>
<td>4</td>
<td>6.05, m</td>
</tr>
<tr>
<td>4'</td>
<td>6.07, m</td>
</tr>
<tr>
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<td>5</td>
<td>6.56, m</td>
</tr>
<tr>
<td>5'</td>
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</table>

![Chemical structures](image)
### Table 5.7. Chemical shift assignments for 2-and 3-PIB-1-(2-azidoethyl)pyrrole

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<tr>
<td>e</td>
<td>--</td>
</tr>
<tr>
<td>h</td>
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<td>j</td>
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<tr>
<td>d</td>
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<tr>
<td>d'</td>
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![Chemical structure](image)
Table 5.8. Chemical shift assignments for 2-and 3-PIB-1-(3-azidopropyl)pyrrole

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<th>(^1)H NMR chemical shift (ppm)</th>
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![Chemical structure of 2-and 3-PIB-1-(3-azidopropyl)pyrrole](image)
Table 5.9. Chemical shift assignments for 2-and 3-PIB-1-(3-azidopropyl)pyrrole

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<tr>
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\[ \text{CH}_2\text{CH}_2\text{CH}_2\text{N}_3 \]
Figure 5.1. Clickable polyisobutylene: synthetic approaches and utilization.
Figure 5.2. $^1$H NMR spectrum of 1-(2-azidoethyl)pyrrole-PIB prepared by reaction of 1-(2-bromoethyl)pyrrole-PIB with sodium azide (Table 1, Entry 5). The product is a mixture of isomers with PIB substituted at the 3- (major) and 2- (minor) positions of the pyrrole ring. Inset shows the tether proton resonances of the bromide precursor for comparison.
Figure 5.3. $^1$H NMR spectrum of difunctional 1-(3-azidopropyl)pyrrole-PIB, with peak integrations, prepared by reaction of difunctional 1-(3-bromopropyl)pyrrole-PIB with sodium azide (Table 1, Entry 8). The product is a mixture of isomers with PIB substituted at the 3- (major) and 2- (minor) positions of the pyrrole ring.
Figure 5.4. $^1$H NMR spectrum of difunctional 1-(2-azidoethyl)pyrrole-PIB prepared by post-polymerization reaction of the corresponding difunctional 1-(2-bromoethyl)pyrrole-PIB with sodium azide. The product is a mixture of isomers with PIB substituted at the 3- (major) and 2- (minor) positions of the pyrrole ring (Table 1, Entry 10).
Figure 5.5. Reaction conversion vs. time for reaction of difunctional 1-(2-bromoethyl)pyrrole-PIB with sodium azide: 50/50 (v/v) heptanes/DMF, 90°C, [CE] = 0.10 mol/L, [NaN$_3$] = 0.30 mol/L; C$_3$ isomer (triangles), C$_2$ isomer (squares), overall (circles).
Figure 5.6. Reaction conversion vs. time for reaction of monofunctional 1-(2-bromoethyl)pyrrole-PIB with sodium azide: 50/50 (v/v) heptanes/DMF, 90°C, [CE] = 0.10 mol/L, [NaN$_3$] = 0.30 mol/L; C$_3$ isomer (circles), C$_2$ isomer (squares), overall (triangles).
Figure 5.7. $^1$H NMR spectrum of difunctional 1-(2-azidoethyl)pyrrole-PIB, with peak integrations, prepared by end-quenching of difunctional $\text{tert}$-chloride-terminated PIB with $N$-(2-Azidoethyl)pyrrole in 60/40 (v/v) hexane/MeCl at -70$^\circ$C (Table 5.2, Entry 1).
Figure 5.8. $^{13}$C NMR spectrum of difunctional 1-(2-azidoethyl)pyrrole-PIB prepared by end-quenching of difunctional tert-chloride-terminated PIB with $N$-(2-Azidoethyl)pyrrole in 60/40 (v/v) hexane/MeCl at -70°C (Table 5.2, Entry 1).
Figure 5.9. GPC traces of difunctional tert-chloride-terminated PIB before (dotted line) and after (solid line) end-quenching with 1-(2-azidoethyl)pyrrole (Table 5.4, Entry 1).
Figure 5.10. $^1$H NMR spectrum of 1-[2-(4-hydroxymethyl-1H,1,2,3-triazol-1-yl)ethyl]pyrrole from reaction of 1-(2-azidoethyl)pyrrole with propargyl alcohol catalyzed with Cu(I)Br/PMDETA (Table 5.4, Entry 2).
Figure 5.11. Reaction kinetics of azide-terminated PIB (2- or 3-carbon tether) with propargyl alcohol in THF at 25°C with initial [alkyne]/[azide] = 2.0: A) Cu(I)Br/PMDETA catalyst with 3-carbon tether; B) bromotris(triphenylphosphine)copper(I) with 2-carbon tether (solid circles) or 3-carbon tether (open circles).
Figure 5.12. $^1$H NMR spectrum of 1-[3-(4-hydroxymethyl-1H-1,2,3-triazol-1-yl)propyl] pyrrole-PIB prepared by Click chemistry (Table 5.5, Entry 1).
Figure 5.13. $^1$H NMR spectrum of 1-[3-(4-vinylcarbonyloxymethyl-$1H$-$1,2,3$-triazol-$1$-yl)propyl]pyrrole-PIB prepared by Click chemistry (Table 5.5, Entry 2).
Figure 5.14. $^1$H NMR spectrum of 1-[3-(4-glycidyloxymethyl-$1H$-1,2,3-triazol-1-yl)propyl]pyrrole-PIB prepared by Click chemistry (Table 5.5, Entry 3).
Figure 5.15. $^1$H NMR spectrum of 1-[3-(4-dimethylaminomethyl-1$H$-1,2,3-triazol-1-yl)propyl]pyrrole-PIB prepared by Click chemistry (Table 5.5, Entry 4).
CHAPTER VI

FACILE POLYISOBUTYLENE FUNCTIONALIZATION VIA THIOL-ENE CLICK CHEMISTRY

Introduction

Polyisobutylene (PIB) has commercial utility as a stabilizing fuel and motor oil additive, packaging elastomer, adhesive and sealant, and more recently, as a biomaterial. This completely saturated hydrocarbon elastomer has excellent thermal and oxidative stability, gas-barrier properties, and biocompatibility. Due to these and other unique characteristics, PIB remains the subject of continued research; e.g. as a self-separating homogeneous catalyst support,\(^1\) a matrix for quantum dot-polymer composites for inks with enhanced photoluminescence,\(^2\) and a biostable/biocompatible thermoplastic elastomer (TPU) for the drug-eluting coating on coronary stents.\(^3\)

Efficient methods for the synthesis of PIB carrying functional end groups have long been sought to facilitate the creation of new PIB-based materials. In the past, post-polymerization modification procedures were employed, which were often laborious, time-consuming, and multistep.\(^4\) To circumvent these difficult procedures, \textit{in-situ} quenching has recently been developed to conveniently functionalize PIB through direct reaction of quasiliving PIB with a nucleophilic quenching or capping agent. Various classes of compounds with demonstrated effectiveness include olefins such as alkenylsilanes\(^5\) and butadiene,\(^6\) hindered nucleophiles,\(^7\) and activated aromatic compounds such as 2-alkylfurans, thiophene, \(N\)-substituted pyrroles, and alkoxy benzenes.\(^8\) Although \textit{in-situ} quenching is attractive due to its simplicity, the quenching agents are often expensive or unavailable commercially. Also, \textit{in-situ} quenching is
generally limited to soft nucleophilic ($\pi$) quenching agents, since hard nucleophiles ($\sigma$) inevitably react with the Lewis acid.$^9$

Since adoption of the thiol-ene reaction into the class of Click chemistries,$^{10}$ numerous researchers have utilized this powerful synthetic tool for polymer modification,$^{11}$ polymer-protein conjugate synthesis,$^{12}$ network formation,$^{13}$ and creation of complex polymeric architectures.$^{10a,14}$ Thiol-ene chemistry offers many advantages including mild reaction conditions, tolerance to oxygen and water, simple purification, high reaction rates, modularity, and quantitative conversion in the absence of metal catalyst. Moreover, the vast array of commercially available thiol and alkene functionalities provides an incredibly versatile selection of reagents.

Monofunctional PIB possessing a high proportion (up to 85-90%) of exo-olefin (methyl vinylidene) end groups is available commercially (e.g., Glissopal, BASF; Ultravis, BP Chemicals) and both monofunctional and difunctional PIBs with ~100% exo-olefin termini are readily produced via in-situ quenching of quasiliving PIB.$^7$ Application of thiol-ene chemistry to exo-olefin PIB would thus provide a practical means to a variety of functional PIBs. However, only a few literature reports have appeared on this topic, and reaction conversions were typically low and/or reaction times were long. For example, Blackborow et al.$^{15}$ reported the radical addition of thiols carrying a number of functional groups including hydroxyl, carboxylic acid, and alkoxy silane to Ultravis (52 or 84% exo-olefin end groups), using either photo- or thermal initiation. High conversions were qualitatively claimed but reaction times were long (12-17 h for photoinitiation, 20-50 h for thermal initiation). Gorski et al. reported the radical addition of alkyl and hydroxyl functional thiols to Glissopal; although reaction
kinetics with Glissopal were not reported, a model compound for exo-olefin PIB, 2,4,4-trimethyl-1-pentene, required long reaction times even when reacted neat in the presence of a ten-fold excess of thiol \((p = 85\% \; @ \; 6\; h)\). Later, based partly on their earlier patent, Blackborow et al. reported the radical addition to Ultravis of thiols with various functional groups including hydroxyl, methoxyethoxyethyl, carboxylic acid, and organosilane. Conversions, determined using FTIR, ranged from 35 to 80%, with reaction times of 5 h or more; in the few examples where high conversions were reached \((p \geq 90\%\)), reaction times between 44 and 88 h were necessary.

The PIB modifications described in these previous literature reports do not meet the qualifications of a Click reaction. Herein, we show that the thiol-ene reaction, under appropriate conditions, can be used to simply, rapidly, and quantitatively functionalize exo-olefin PIB with an array of functional thiols (Figure 6.1). These reactions achieve near-quantitative conversion of the exo-olefin in less than 10 min, are applicable to both mono and difunctional PIBs, and require minimal equipment, and the products can be purified by either a simple precipitation or wash.

**Experimental**

**Materials**

All materials were purchased from Aldrich at the highest available purity and used as received unless otherwise stated. Free radical photoinitiator, dimethoxy-2-phenylacetophenone (DMPA), was purchased from CIBA and used as received.

**Instrumentation**

FTIR spectra were recorded using a Bruker Equinox 55 spectrometer. Samples were sandwiched between two sodium chloride plates. Each spectrum was collected as
an average of 64 scans. The data were analyzed using the Bruker OPUS/IR Version 4.0 software.

Real-time FTIR was used to monitor exo-olefin conversion kinetics (1640 cm\(^{-1}\)). Exo-olefin-terminated PIB (0.501 g, 0.40 mmol), DMPA (0.012 g, 1 wt%), and 0.40 mL CH\(_2\)Cl\(_2\) were charged to a 20 mL glass scintillation vial. After dissolution, 2-(tert-butoxycarbonylamino)ethanethiol (100.9 µL, 0.60 mmol) was added, and the contents were shaken for 20 min. The resulting reaction mixture was sandwiched between sodium chloride plates resulting in a sample thickness of approximately 250 microns. The light intensity of the high pressure mercury lamp delivered to the sample via a light pipe was \(\sim 28.3\) mW/cm\(^2\).

NMR spectra were acquired using a Varian Mercury\(^{\text{plus}}\) 500 MHz NMR spectrometer. Samples were dissolved in chloroform-\(d\) (3–7%, w/v) and analyzed within 5 mm NMR tubes.

The number-average molecular weight (\(M_n\)) and polydispersity index (PDI) of the polymeric materials were measured using gel permeation chromatography (GPC). The GPC system, operating at 35 °C, consisted of a Waters Alliance 2695 separations module, an online multiangle laser light scattering (MALLS) detector (MiniDAWN, Wyatt Technology Inc.), an interferometric refractometer (Optilab rEX, Wyatt Technology Inc.), an online differential viscometer (ViscoStar, Wyatt Technology, Inc.), and two mixed E (3 µm bead size) PL gel (Polymer Laboratories Inc.) GPC columns connected in series. Freshly distilled THF served as the mobile phase at a flow rate of 1.0 mL/min. Sample concentrations were 10–12 mg/mL, with an injection volume of 100 µL. The detector signals were recorded using ASTRA software (Wyatt Technology...
Inc.) and molecular weights were determined using $dn/dc$ values calculated from an equation relating $dn/dc$ of PIB in THF as a function of PIB molecular weight.\textsuperscript{18}

\textit{Synthesis of exo-olefin-terminated PIB}

Mono- and difunctional \textit{exo}-olefin-terminated PIBs were prepared and characterized according to literature using 2-chloro-2,4,4-trimethylpentane (TMPCl) or 1,3-di(1-chloro-1-methylethyl)-5-\textit{tert}-butylbenzene, respectively, as initiators and 1,2,2,6,6-pentamethyldapiperidine (PMP) as a hindered-amine quencher.\textsuperscript{19} A representative procedure to prepare monofunctional \textit{exo}-olefin-terminated PIB was as follows: Quasiliving polymerization of isobutylene(IB) with TMPCl as an initiator was carried out within a N\textsubscript{2} atmosphere glovebox, equipped with an integral cryostated hexane/heptanes bath. Into a round bottom flask with a mechanical stirrer, infrared probe, and thermocouple were added 572 mL CH\textsubscript{3}Cl, 860 mL hexane, 2.50 mL (2.19 g, 0.0147 mol) TMPCl, and 0.86 mL (0.79 g, 0.0074 mol) of 2,6-lutidine. The mixture was allowed to equilibrate to -60 °C, and then 29.0 mL (19.9 g, 0.354 mol) of IB was added to the reactor and allowed to reach thermal equilibrium. To begin the polymerization, 4.8 mL (8.3 g, 0.044 mol) of TiCl\textsubscript{4} was charged to the reactor. Full monomer conversion ($\geq$ 98 \%) was achieved in 90 min, after which time 8.0 mL (6.9 g, 0.044 mol) PMP and an additional 4.8 mL TiCl\textsubscript{4} (8.3 g, 0.044 mol) were added to the polymerization. PMP was allowed to react with the living chain ends for 90 min. Finally, the reaction was terminated by addition of excess prechilled methanol. The contents of the reaction flask were allowed to warm to room temperature, and the polymer in hexane was immediately washed with methanol and then precipitated into methanol from hexane. The precipitate was collected by dissolution in hexane; the solvent was washed with water, dried over
MgSO₄, and concentrated on a rotary evaporator. Residual solvent was removed under vacuum at 40 °C.

Synthesis of Mono-functional Primary Chloride-terminated PIB

A representative procedure was as follows: exo-olefin-terminated PIB (0.251 g, 0.20 mmol), DMPA (0.006 g, 1 wt%), and 0.22 mL dichloromethane (CH₂Cl₂) were charged to a 20 mL glass scintillation vial. After dissolution, 3-chloro-1-propanethiol (29.2 µL, 0.30 mmol) was added, and the contents were shaken for 20 min. The sample was then irradiated using a medium pressure Hg lamp (light intensity ~6.68 mW/cm²) for approximately 3.5 min. CH₂Cl₂ was removed under reduced pressure, and the crude reaction mixture was twice precipitated into methanol from hexane. The final precipitate was collected and put under reduced pressure until a constant weight was achieved.

One-pot Synthesis of Mono-functional Primary Amine-terminated PIB

A representative procedure was as follows: exo-olefin-terminated PIB (0.251 g, 0.20 mmol), DMPA (0.006 g, 1 wt. %), and 0.26 mL CH₂Cl₂ were charged to a 20 mL glass scintillation vial. After dissolution, 2-(tert-butoxycarbonylamino)ethanethiol (50.7 µL, 0.30 mmol) was added, and the contents were shaken for 20 min. The sample was then irradiated using a medium pressure Hg lamp (light intensity ~6.68 mW/cm²) for approximately 3.5 min. For deprotection, 4.28 mL of a trifluoroacetic acid and CH₂Cl₂ mixture (50:50 v/v) was injected into the scintillation vial and agitated for 30 min. CH₂Cl₂ was then removed under reduced pressure, and the crude reaction mixture was dissolved in hexane. The resulting solution was washed twice with brine and then twice with deionized water, neutralized with sodium bicarbonate, filtered, and put under reduced pressure until a constant weight was achieved.
Synthesis of Mono-functional Carboxylic Acid-terminated PIB

A representative procedure was as follows: exo-olefin-terminated PIB (0.126 g, 0.10 mmol), DMPA (0.005 g, 1 wt%), and 0.23 mL chloroform (CHCl$_3$) were charged to a 20 mL glass scintillation vial. After dissolution, thiol glycolic acid (20.8 µL, 0.30 mmol) was added, and the contents were shaken for 20 min. The sample was then irradiated using a medium pressure Hg lamp (light intensity $\sim6.68$ mW/cm$^2$) for approximately 8 min. CHCl$_3$ was removed under reduced pressure, and the crude reaction mixture was dissolved in hexane. The resulting solution was washed three times with water and put under reduced pressure until a constant weight was achieved.

Synthesis of Mono-functional Primary Alcohol-terminated PIB

A representative procedure was as follows: exo-olefin-terminated PIB (0.157 g, 1.25 mmol), DMPA (0.061 g, 1 wt%), and 0.26 mL CHCl$_3$ were charged to a 20 mL glass scintillation vial. After dissolution, 1-mercapto-6-hexanol (68.4 µL, 5.00 mmol) was added, and the contents were shaken for 20 min. The sample was then irradiated using a medium pressure Hg lamp (light intensity $\sim6.68$ mW/cm$^2$) for approximately 6 min. CHCl$_3$ was removed under reduced pressure, and the crude reaction mixture was dissolved in hexane. The resulting solution was washed three times with methanol and put under reduced pressure until a constant weight was achieved.

Results and Discussion

Telechelic mono- and difunctional exo-olefin PIBs were synthesized via quasiliving cationic polymerization followed by quenching with the hindered amine, 1,2,2,6,6-pentamethytpiperidine.$^7$ Low molecular weight polymers were targeted to facilitate end group characterization by NMR spectroscopy. Molecular weight,
polydispersity index (PDI), and functionality of the exo-olefin PIBs are summarized in Table 6.1. Both polymers exhibited very low PDIs with unimodal, symmetrical elution peaks in GPC (Figures 6.2 and 6.3) and high chain end functionality (≥ 97 %), calculated as previously reported in literature. Excellent agreement between GPC and $^1$H NMR molecular weights was observed for both PIB precursors.

A variety of photo-initiated thiol-ene reactions were conducted, and the results are summarized in Table 6.2. Particular emphasis was placed on primary halogen and amine functionalities due to their novelty and utility. The clear, transparent nature and inert hydrocarbon backbone of PIB facilitated efficient photochemical reactions. Typical synthetic procedures involved charging a scintillation vial with an appropriate mass of polymer, thiol, and 1 wt% photoinitiator, and then dissolving the mixture in a suitable solvent. Solvent selection (CH$_2$Cl$_2$ or CHCl$_3$) and reagent concentrations were crucial parameters, and were chosen to ensure a homogenous reaction mixture. Reaction conversions were improved by reducing reaction temperature, in agreement with prior literature for thiol-ene functionalization of PIB. In the absence of external cooling, internal reaction temperatures were found to rise as high as 40 °C; whereas by placing the reactor in an ice bath, reaction temperatures were maintained below 15 °C.

Thiol-ene reactions involving 3-chloropropane thiol in 50% excess (Exp. 1-3) achieved high conversions in less than 5 min, with essentially quantitative conversion achieved with cooling. Figure 6.4 depicts $^1$H NMR spectra of the monofunctional exo-olefin PIB precursor and resulting 3-chloropropane thioether functionalized PIB (Exp. 2). Resonances associated with the exo-olefin terminus of the precursor, consisting of methylene (2.00 ppm), methyl (1.78 ppm), and olefinic protons (4.64 and 4.85 ppm),
were all absent in the final product. New resonances in the product associated with the 3-chloropropane thioether moiety were located at 3.66 (triplet), 2.66 (triplet), 2.04 (quintet), and 1.74 ppm. In addition, diastereotopic protons, \( d_1 \) and \( d_2 \), were observed at 2.52 and 2.35 ppm, each appearing as a doublet of doublets due to the adjacent chiral center.

Thiol-ene reactions with cysteamine and cysteamine hydrochloride, Exp. 4 and 5, resulted in no thioether formation. These results were theorized to be a consequence of thiolate formation, due to amine basicity, rendering the thiol group incapable of thyl radical formation. Furthermore, incompatibility of these reagents in a common reaction medium, creating a heterogeneous reaction mixture, impeded their ability to react. Typical solvents for cysteamine, including water, methanol, and DMF, were incompatible with the hydrophobic PIB; THF and THF/H\(_2\)O solvent systems were explored with thermal and photo initiators, respectively, with limited success.

Conversion of the olefin increased dramatically when the amine group of cysteamine was protected with a tert-butoxycarbonyl (Boc) group (Exp. 6). The Boc group produced a completely homogenous reaction mixture and considerably reduced the basicity of the amine, diminishing thiolate formation. Although the Boc-protected cysteamine yielded the desired product, complete conversion was still not achieved in Exp. 6. However, near-quantitative conversion was achieved for both the mono (Exp. 7) and difunctional (Exp. 8) \textit{exo}-olefin polymers by cooling the reaction with an ice-bath. Thiol-ene reaction kinetics by FTIR for cysteamine-Boc are shown in Figure 6.5.

GPC analysis of the PIB-Boc and PIB-Cl products of Table 2 revealed symmetrical traces with no high molecular weight coupled species. Slight decreases in
elution volume were observed, indicative of increased molecular weight, with respect to the \textit{exo}-olefin PIB. Figure 6.6 shows GPC traces of PIB-exo, PIB-Boc, and PIB-Cl.

Sunlight-activated radical generation was also attempted (Exp. 9); however, extended reaction times were required to achieve complete olefin conversion and substantial byproducts were detected. Prolonged exposure to sunlight (3 h) may have caused unwanted photo-oxidization to occur. The susceptibility of thiols and various sulfur derivatives to photo-oxidation is well known in literature.\textsuperscript{20}

In an effort to obtain amine functionality directly from Boc-protected cysteamine, a procedure was developed in which the thiol-ene reaction and subsequent deblocking were carried out in one pot. Deblocing was accomplished by simply charging a 50 vol\% trifloroacetic acid (TFA) solution in CH\textsubscript{2}Cl\textsubscript{2} to the reactor after the thiol-ene reaction was complete (Exp. 10). No by-products were detected while still maintaining near quantitative conversion and simple purification. \textsuperscript{1}H NMR spectra of Boc-protected and deprotected amine functionalized PIB (PIB-Boc and PIB-NH\textsubscript{2}) are shown in Figure 6.7. Peaks due to residual \textit{exo}-olefin were not observed. PIB-Boc resonances appeared at 4.92 (g’), 3.31 (f), 2.62 (e), 1.72 (c), and at 2.51 (d\textsubscript{1}) and 2.37 (d\textsubscript{2}) ppm (diastereotopic protons, doublet of doublets). As expected, after Boc deprotection disappearance of the secondary amine (g’) and \textit{tert} butyl (h’) proton peaks occurred. Furthermore, the ultimate methylene protons adjacent to nitrogen (f) shifted slightly upfield; whereas the penultimate methylene protons (e) shifted downfield. Further confirmation was provided by comparison of FTIR spectra of PIB-exo, PIB-Boc, and PIB-NH\textsubscript{2} as shown in Figure 6.8.
To further demonstrate the versatility and modularity of the thiol-ene approach, two additional functionalities were selected, carboxylic acid (Exp. 11) and hydroxyl (Exp. 12). Both reactions achieved high conversions ($\geq 98$) in minutes ($< 10$ min). Structural evidence by $^1$H NMR, FTIR, and GPC are provided in the supporting information for the carboxylic acid (Figures 9-11) and hydroxyl (Figures 12-14) functional groups.

Conclusion

To conclude, the above described is a simple, rapid synthesis of primary halogen, amine, carboxylic acid, and hydroxyl-functional PIBs (mono- and difunctional) $via$ thiol-ene click chemistry. The methods produce near-quantitative functionalization within 10 min without difficult purification or reaction conditions. Reduced reaction temperature (ice bath) facilitates increased conversion. Functionalization using cysteamine requires Boc protection; however, the Boc protecting group may be easily removed in one pot.
References


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\(a\) – Determined by \(^1\)H NMR.
Table 6.2. Thiol-ene reactions with *exo*-olefin PIB

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<td>8</td>
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<td>HS(CH₂)₅OH</td>
<td>0.38</td>
<td>4.00</td>
<td>6</td>
<td>98</td>
</tr>
</tbody>
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*a* Ice bath.  *b* Difunctional PIB.  *c* Sunlight.  *d* One-pot deprotection.  *e* NMR.
Figure 6.1. Photo-initiated radical addition of functional thiols (halo, NH-Boc, carboxylic acid, hydroxyl) to exo-olefin-terminated PIB and subsequent Boc deprotection.
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CHAPTER VII
TRANSFORMATIONS OF $\alpha,\omega$ - THIOLPOLYISOBUTYLENE: EFFICIENT ROUTES TO A CHAIN TRANSFER AGENT, TELECHELICS, AND PIB BASED THIOURETHANES.

Introduction

Thiol based chemistries are vast and encompass a broad range of reactions.$^1$ Utility of the thiol functional group in materials/polymer synthesis has been extensive, as it provides a practical means for many efficient transformations and complex architectures.$^2$ Chain transfer agents (CTAs) for reversible addition fragmentation transfer (RAFT) are commonly synthesized through sequential treatment of anionic species (e.g. thiolates, alkoxides) with carbon disulfide and an alkylating agent.$^3,4$ Shipp et al. illustrated successful conversion of $\omega$-bromine poly(tert-butyl acrylate) (tBA) into a RAFT macrorinitiator through substitution of the terminal bromide with the a potassium xanthate.$^5$ Subsequent RAFT polymerization of vinyl acetate (Vac) was conducted, demonstrating a convenient method for synthesis poly(tBA-b-Vac) block copolymers, in which the monomers possess large reactivity differences.

Thiol-ene “click” reactions, through either a radical or nucleophile mediated mechanism, provide efficient hydrothiolation routes across virtually any double bond.$^2,6,7$ Numerous examples are available in the literature for polymer end group$^8,9$ and backbone$^{10}$ modification, and many of which are covered in two excellent reviews.$^6,7$ The highly efficient thiol-Michael addition was shown by Finnik and coworkers to be a facile transformation strategy.$^8$ This was accomplished in a consecutive fashion, by reduction of terminal CTAs of RAFT polymers and subsequent addition to an acrylate
Campos et al. prepared ene functional initiators and monomers, for controlled RAFT, ATRP, and ring opening polymerization, and modified the resulting polymer through the photoinitiated thiol-ene reactions. More recently, photoinitiated radical 1,2-diaddition of thiols to alkynes (i.e. thiol-yne) has been recognized as a means for synthesis of highly functional materials. Chan et al. demonstrated the modularity and efficiency of the thiol-yne reaction to produce 16 and 8 arm polyfunctional materials and Hensarling et al. functionalized polymer surface brushes with an array of functionalized thiols. Other research groups have shown utility of this chemistry for third generation dendrimers (i.e. 192 functional groups), highly crosslinked networks, and hyperbranched polymers.

Thiols react quickly and efficiently with isocyanates under basic catalysis, and this reaction was been used for polymer functionalization through thiocarbamate linkages and synthesis of polythiourethane. Lowe and coworkers reacted thiol-terminated poly(N,N-diethylacrylamide), obtained by in-situ reduction of the terminal CTA of RAFT-derived polymers, with functional isocyanates in order to study the effect of various attached functional groups on phase behavior. Segmented polythiourethane elastomers have been synthesized via the thiol-isocyanate reaction, and were reported to exhibit microphase separation between hard and soft segments. Two glass transition temperatures were observed, corresponding to the hard and soft-segment phases respectively. The hard segment Tg was observed at 132 °C, and the soft segment Tg ranged from -57 to -23 °C, depending on the thiourethane composition.

Preparation of thiol functional polymers has been accomplished by a variety of synthetic pathways. A popular approach has been the attachment to a polymer or
initiator, for example via an ester linkage, of a molecule such as mercaptoacetic acid or 2-mercaptoethanol, in which the thiol group has been protected with a 2,4-dinitrophenyl moiety. Protection is typically carried out by prior reaction of the thiol with Sangers reagent, i.e. 2,4-dinitrofluorobenzene, in the presence of a base catalyst. In this way, protected thiol initiators for ATRP\textsuperscript{19} and ring opening polymerization of $\varepsilon$-caprolactone,\textsuperscript{20} were developed, and the presence of the protected thiol was reported to have no observable deleterious effects to polymerization. Using a similar approach, poly($\varepsilon$-caprolactone) and poly(ethyleneoxide) were fitted with thiol end groups via reaction of the terminal hydroxyl group on the polymer with 2,4-dinitrophenylmercaptoacetic acid, following by deblocking.\textsuperscript{21} Tsarevsky and Matyjaszewski developed a thio-functional ATRP initiator based on 2-mercaptoethyl 2-bromopropionate, in which the thiol group was blocked by simple disulfide formation (dimerization). After polymerization, polymers containing a thiol head group were obtained by reduction.\textsuperscript{22} Terminal thiol functionality is inherent to RAFT-prepared polymers. CTAs in the presence of primary amines readily reduce into the corresponding thiol.\textsuperscript{8,9,23} Disulfide formation has been observed in these systems, but can be overcome by incorporation of phosphorus oxidizing agents.\textsuperscript{23} Successful substitution of ATRP prepared $\omega$-bromo polystyrene ($p \approx 95\%$),\textsuperscript{24} and a pendent chlorine functional polystyrene derivative with thiol functionality through thiourea has also been demonstrated.\textsuperscript{25} However, thiols have yet to be attached to PIB chain ends and preparation of this telechelic polymer has essentially been overlooked. Owing to the high nucleophilicity of the sulfur atom, thiols can be produced by the nucleophilic substitution of a halogen, using NaSH\textsuperscript{26}, dimethylthioformamide,\textsuperscript{27} and thiourea\textsuperscript{28}. Herein, we report the use of thiourea to produce near quantitative
difunctional thiol-terminated PIB from a bromine-terminated precursor. Subsequent utility of this telechelic polymer is demonstrated with a variety of chemistries for synthesis of a novel RAFT macroinitiator, alkyne terminated and tetrahydroxyl terminated PIB, and PIB based thiourethane polymers.

Experimental

Materials

Hexane (anhydrous, 95%), 2,6-lutidine (redistilled, 99.5%), TiCl₄ (99.9%, packaged under N₂ in sure-seal bottles), 3-phenoxypropyl bromide (96%), chloroform-d (99.8% atom % D), dimethylformamide (DMF) (99%), thiourea (≥ 99%), propargyl acrylate (98%), dimethylphenylphosphine (DMPP) (97%), 6-mercapto-1-hexanol (97%), carbon disulfide (≥ 99.9 %), 2-bromopropionic acid (≥ 99 %), triethylamine (≥ 99%) (TEA), 1,6-hexanediol (Kosher grade, ≥ 97%), tetrahydrofuran-d₈ (99.5 atom % D), and 4,4′-methylenebis(phenyl isocyanate) (MDI) were purchased from Sigma-Aldrich and used as received. Methanol (ACS-grade, 99.9%), hexanes (ACS-grade, 99.9%), and heptane (HPLC-grade, 99.5%) were purchased from Fisher Scientific and used as received. THF (HPLC-grade, 99.9%) was purchased from Fisher Scientific and distilled over CaH₂ prior to use. Free radical photoinitiator, 2.2-dimethoxy-2-phenylacetophenone (DMPA), was purchased from CIBA and used as received. Isobutylene (IB) (BOC, Gases, 99.5%) and CH₃Cl (Alexander Chemical Corp., 99.95%) were dried by passing the gaseous reagent through columns packed with CaSO₄ and CaSO₄/4 Å molecular sieves, respectively, and condensed within a N₂-atmosphere glove box immediately prior to use. Cationic polymerization initiator 1,3-bis-(2-chloro-2-propyl)-5-tert-butylbenzene
(bDCC) and α,ω-bis[4-(3-bromopropoxy)phenyl]polyisobutylene (α,ω PIB-Br) were synthesized as previously described\textsuperscript{9,14}.

**Synthesis of α,ω-Bis[4-(3Thiopropoxy)phenyl]polyisobutylene (α,ω PIB-SH)**

To a dry one-neck 100 mL round-bottom flask equipped with a magnetic stir-bar were added 0.7929 g (10.42 mmol) thiourea, 21 mL DMF, and 10 mL heptane. The flask was placed under a slow N\textsubscript{2} purge and immersed in an oil bath heated to 90°C. In a scintillation vial, α,ω PIB-Br (M\textsubscript{n} = 2,900 g/mol, 1.250 g, 0.43 mmol) was dissolved in 11 mL heptane and added to the reaction flask. The solution was turbid, yet remained monophasic throughout the reaction. After 6 h, the oil bath temperature was raised to 110 °C, and the reaction became a clear homogenous solution. After equilibrating at the higher temperature for 15 min, a solution of 0.324 g (8.1 mmol) NaOH and 2 mL deionized water was injected into vessel, at which time vigorous gas evolution occurred and a white precipitate formed. Approximately 4 h later, the vessel was removed from the oil bath and allowed to cool with stirring for 20 min. Then, 0.8 mL neat H\textsubscript{2}SO\textsubscript{4} was charged to the reaction vessel. After 30 min, the biphasic reaction mixture was placed in a separation funnel and the DMF/H\textsubscript{2}O layer was immediately drained. The remaining organic layer was diluted with hexanes, washed three times with MeOH, and precipitated into MeOH. The precipitate was collected in hexanes, and the solvent was stripped under vacuum to yield the final, α,ω PIB-SH.

**Synthesis of α,ω-bis[4-{3-(Carboxyethylidenesulfanylthiocarbonylsulfanyl)propoxy} - phenyl]polyisobutylene (α,ω PIB-CTA)**

To a scintillation vial, under an N\textsubscript{2} atmosphere, were added 0.1972 g (M\textsubscript{n} = 2900 g/mol, 0.068 mmol) α,ω PIB-SH and 0.19 mL carbon disulfide (3.2 mmol). After a
homogenous solution was obtained, 0.22 mL of TEA (1.6 mmol) was added resulting in a clear yellow solution. The contents were allowed to stir for 7 h, at which time 71.0 µL (0.79 mmol) of 2-bromopropionic acid followed by 0.42 mL chloroform were charged to the vial. Upon addition, the solution briefly turned red and later returned to its original yellow color. This solution was allowed to stir for 12 h, and afterward, the solvent was removed under reduced pressure. The remaining contents were extracted with hexanes (3X) and filtered, and the resulting organic solution was washed with 1 N HCl (3X) and then deionized water (3X). Hexanes were removed under reduced pressure to obtain a viscous yellow polymer.

**Synthesis of α,ω-bis[4-[3-(Propargyloxycarbonylethlenesulfanyl)propoxy]phenyl]-polyisobutylene (α,ω PIB-alkyne)**

To a scintillation vial were added 0.2031 g (Mₙ = 2900 g/mol, 0.070 mmol) α,ω PIB-SH and 1.0 mL THF (or chloroform). After a homogenous solution was obtained, 15.9 µL of propargyl acrylate (0.144 mmol) and then 1.0 µL DMPP (7.0 µmol) were charged to the vial. The contents were allowed to stir for 30 min, at which time the solvent was removed under reduced pressure. The remaining contents were taken up into hexanes and precipitated twice into methanol. The polymer was then redissolved in hexanes, and the solvent stripped under vacuum to yield the final, α,ω PIB-alkyne.

**Sequential Nucleophilic Thiol-ene/Radical Thiol-yne Reactions to Produce Tetrahydroxy-functional PIB (αω PIB-(OH)₂)**

To a scintillation vial were added 0.190 g (Mₙ = 2900 g/mol, 0.065 mmol) α,ω PIB-SH and 1.0 mL d-chloroform. After a homogenous solution was obtained, 15.4 µL of propargyl acrylate (0.140 mmol) and then 0.9 µL DMPP (6 µmol) were charged to the
vial. The contents were allowed to stir for 30 min and then transferred into another scintillation vial containing 0.029 g DMPA (~ 1.6 wt%) and 91.0 µL 6-mercaptophexanol (0.665 mmol). Afterward, the vial was irradiated using a medium pressure Hg lamp (light intensity ~6.00 mW/cm²) for 6 min. Chloroform was removed under reduced pressure, and the crude reaction mixture was twice precipitated into chilled methanol from hexanes, using centrifugation to aid settling. The final precipitate was then collected in hexanes, and the solvent was stripped under vacuum to yield the final, α,ω PIB-(OH)₂.

*Synthesis of α,ω-bis{4-[3-(Phenyliminocarbonylsulfanyl)propoxy]phenyl}polyisobutylene (α,ω PIB-phenyl thiourethane)*

Two drops of neat phenyl isocyanate were added to a solution, consisting of 0.091 g (Mₙ = 2900 g/mol, 0.031 mmol) α,ω PIB-SH, 1 µL TEA (7 µmol), and 0.3 mL d-THF, within a 5 mm NMR tube, and the reaction was allowed to mix for 10 min. After ¹H NMR analysis, to ensure complete conversion of the thiol group, the solvent was removed under reduced pressure. The remaining contents were taken up in hexanes, and the resulting solution was filtered, washed with 1 N HCl (2X), and then precipitated into methanol. The final precipitate was then collected in hexanes, and the solvent was stripped under vacuum to yield the final, α,ω PIB-phenyl thiourethane.

*Synthesis of Polyisobutylene-based Polythiourethane Without Chain-extending Dithiol*

Under a dry nitrogen atmosphere, a solution of 0.297 g (Mₙ = 2,900 g/mol, 0.102 mmol) α,ω PIB-SH, 5 µL TEA (0.036 mmol), and 0.7 mL dry THF was prepared in a scintillation vial equipped with a magnetic stir bar. In a separate scintillation vial, 0.026 g MDI (0.10 mmol) was dissolved in 0.3 mL dry THF, and after dissolution, the contents
were transferred into the first scintillation vial. The sealed vial was then submerged into an oil bath at 50 °C with stirring. After two hours, the vial was removed from the oil bath. The contents were precipitated twice into methanol from a THF, and the final precipitate was collected and dried under vacuum.

*Synthesis of Polyisobutylene-based Polythiourethane with Chain-extending Dithiol (PIB-20-thiourethane)*

Chain-extended PIB-based polythiourethanes were prepared by a two-step, one-prepolymer method. A solution of 0.083 g MDI (0.332 mmol) in 0.8 mL dry THF was prepared in a 25 mL round bottom flask equipped with a magnetic stir-bar. A second solution consisting of 0.5005 g (M_n = 2,900 g/mol, 0.17 mmol) α,ω PIB-SH and 10 µL TEA (0.072 mmol) in 2.5 mL THF was then added dropwise to the flask over a period of 30 min at room temperature. A third solution consisting of 0.025 mL (0.163 mmol) 1,6-hexanedithiol in 2.4 mL THF was then added dropwise over a period of 15 min. This rate of addition was sufficiently slow to maintain the reaction temperature below 23 °C. After addition of the dithiol solution, the reaction was allowed to stir for 1 h at room temperature. Afterward, solvent was removed under reduced pressure. The contents were taken up in THF, precipitated into hexanes, and centrifuged. A clear solid polymer resulted.

**Results and Discussion**

*Synthesis of α,ω PIB-SH*

The initial objective of this research was to development a practical and inexpensive method for synthesis of α,ω PIB-SH. Thiol functionality is commonly obtained through alkyl halide substrates, thus difunctional primary bromide PIB was first
prepared. 3-Bromopropoxyphenyl-terminated PIB was synthesized as previously reported; characterization of the resulting difunctional polymer revealed quantitative conversion of tert-chloride end groups into primary bromide functionality. $^1$H NMR spectrum (Figure 7.1) of the purified $\alpha,\omega$ PIB-Br was devoid of resonances associated with the gem-dimethyl and methylene protons adjacent to the tert-chloride moieties, located at 1.68 and 1.96 ppm, respectively. New resonances characteristic of the trimethylene tether of the 3-bromopropoxyphenyl end group were visible at 4.09 (c), 3.61 (a), and 2.32 (b) ppm. Integration of the latter resonances relative to those of the aromatic initiator revealed essentially quantitative functionality ($f = 1.00-0.99$). In addition, elimination products (i.e. exo and endo olefin) were absent. $^{13}$C NMR analysis (Figure 7.2) bolstered the $^1$H NMR results, indicating quantitative capping of the polymer chain ends. Molecular weight values for the 3-bromopropoxyphenyl-terminated PIB determined by GPC and NMR were in excellent agreement: 2,900 g/mol (GPC-MALLS, known $dn/dc$), 2,800 g/mol (GPC-MALLS, 100% mass recovery $dn/dc$), and 2,990 g/mol (H NMR integration). For all subsequent experimentation a molecular weight value of 2,900 g/mol was used. GPC traces (Figure 7.3) of the pre-quench and post-quench polymer display no detectable coupling and narrow, symmetrical molecular weight distributions (PDI = 1.08).

Conversion of the terminal halogen into thiol functionality was first attempted using NaSH in a heptane/DMF cosolvent system at 90 °C. Substitution with NaSH would allow a direct one-step reaction and low material costs. Results of these preliminary experiments indicated complete displacement of terminal bromine; however, a significant fraction of the product was coupled through formation of disubstituted
Reducing the reaction temperature to room temperature significantly reduced sulfide formation ($f_{\text{mole}} \leq 0.08$) but required unreasonably long reaction times (e.g. > 63 h) for full halide displacement.

The use of thiocarbonyl-based nucleophiles, particularly thiourea, has been reported to effectively reduce or eliminate sulfide formation.$^1$ Reaction of thiourea and subsequent deblocking are shown in Scheme 7.1. First the alkylisothiouronium salt was produced using a 1:1 (v:v) DMF:heptane cosolvent mixture at 90°C. Hydrolysis of the salt by aqueous base produced thiolate chain ends, which were then acidified to form the desired thiol functional group. Upon completion of the thiourea reaction, all three methylene tether resonances of the $\alpha,\omega$ PIB-Br shifted upfield (Figure 7.4, inset). A strong shift from 3.61 to 2.74 ppm was observed for the methylene protons adjacent to the halogen, due to the replacement of the inductively withdrawing bromine with the less electronegative sulfur (i.e. increased shielding). In addition, the splitting pattern changed from a triplet to a quartet. Inspection of the methylene protons two and three units away from the substitution showed less pronounced upfield shifts of 2.32 to 2.08 ppm (b) and 4.09 to 4.06 ppm (c), respectively. $^{13}$C NMR analysis (Figure 7.5) showed a dramatic shift of the methylene carbon adjacent to bromine from 30.2 ppm to 21.5 ppm (1); whereas lesser shifts were observed for methylene carbons further away, from 32.7 to 33.7 ppm (2) and 65.4 to 65.7 ppm (3). Assignments for the precursor $\alpha,\omega$ PIB-Br and product $\alpha,\omega$ PIB-SH were made using two dimensional gHSQC NMR experiments (Figures 7.6 and 7.7).

Initial attempts using the thiourea approach were not successful. It was found that reaction temperature had a significant influence on sulfide formation during the base
hydrolysis step. Preliminary experimentation involved cooling the reaction vessel, by removal from the oil bath, prior to base addition. GPC analysis (Figure 7.8) showed a significant fraction of high molecular weight species and multimodal molecular weight distribution (solid line) when hydrolysis was carried out at low temperature. Maintaining the reaction temperature at 90°C, or preferably raising it to 110°C, dramatically suppressed sulfide formation, as evident by the resulting monomodal elution peak (dotted line). Sulfide formation could also be detected by $^1$H NMR (Figure 7.8 inset), by the appearance of a triplet due to the methylene protons adjacent to the sulfide linkage, which appear slightly upfield from the quartet characteristic of the methylene protons adjacent to the desired thiol group. $^1$H NMR integration revealed that a bath temperature of 110°C (internal reaction temperature $\approx 99°C$) reduced sulfide formation to approximately 1 mole fraction ($f_{\text{mole}} \approx 0.01$).

**Kinetics of Isothiouronium Salt Formation**

Isothiouronium salt formation was probed to optimize reactions condition. In this study, a reaction vessel was charged using the same reactant concentrations listed in the experimental with aliquots drawn at regular intervals. Solvent was removed from the aliquots in a vacuum oven at 40°C over several days. Disappearance of the $\alpha,\omega$ PIB-Br triplet at 3.61 ppm and the appearance of a new peak attributed to the isothiouronium salt at 3.44 ppm was monitored by $^1$H NMR. Conversion of the bromine-terminated PIB to isothiouronium salt PIB vs. time is shown in Figure 7.9. The data indicate that complete conversion of the bromine chain ends occurred within $\sim 200$ min. The reaction contained a large excess of thiourea (*i.e.* 12.7 X bromine chain ends), and thus pseudo first-order kinetics was expected. As shown in Figure 7.9 inset, a semi-logarithmic first-order plot
was indeed linear, with an observed rate constant of $k = 0.025 \text{ s}^{-1}$, confirming pseudo first-order behavior.

*Site Transformations of $\alpha,\omega$ PIB-SH*

The thiol group is a versatile functional group for various chain end transformations. In this section, synthesis of a RAFT macro-CTA, alkyne terminal PIB, tetrafunctional telechelic PIB, and PIB-based segmented thermoplastic polythiourethanes (TPTUs) will be demonstrated. Telechelic PIBs and PIB-based block copolymers, particularly segmented TPUs and TPTUs have many potential applications in material and polymer science.

Earlier chapters in this document have focused on novel strategies to combine quasiliving cationic polymerization of isobutylene and reversible addition fragmentation (RAFT) polymerization. In an effort to directly functionalize PIB with a chain transfer agent without using coupling chemistry, *e.g.*, catalyzed esterification\textsuperscript{30} or click chemistry,\textsuperscript{31} thiol-terminated PIB was of interest. Thiol substrates are commonly used in synthesis of primary and secondary trithiocarbonates.\textsuperscript{3,4,32} Typically, trithiocarbonate salts are formed *in situ* from a thiol and carbon disulfide in the presence of triethylamine, and later reacted with an alkyating agent. Many examples of this are available in the literature for synthesis of asymmetrical trithiocarbonates with different alkyating agents, a few of which are bromopropionyloxy derivatives,\textsuperscript{33} 1-(bromoethyl)benzene,\textsuperscript{34} and N-(bromomethyl)phthalimide.\textsuperscript{35}

$\alpha,\omega$ PIB-SH was thus employed in a pseudo-bulk reaction with carbondisulfide in the presence of triethylamine with 2-bromopropionic acid, using a modification of a procedure given by Evans *et al.*\textsuperscript{33}. Carbon disulfide served both as electrophile for the
thiolate chain ends and as reaction solvent. PIB was observed to have complete solubility in TEA and carbondisulfide. Therefore, bulk conditions were selected to promote rapid formation of the trithiocarbonate salt prior to addition of the 2-bromopropionic acid; when more diluted conditions were used in chloroform, low chain end conversions resulted. Upon dissolution of the α,ω PIB-SH in TEA and carbondisulfide the resulting solution turned a clear yellow color, and during the alkylation step, the reaction briefly turned a red color although eventually returning to its original yellow color. After purification, $^1$$H$ NMR showed a strong shift in the methylene protons adjacent to the thiol group, 2.74 ppm (quartet) to 3.58 (triplet), and two additional resonances associated with the S-propionic acid chain end (Figure 7.10). These two additional resonances, a quartet at 4.88 ppm and a doublet at 1.64 ppm, corresponded with proton assignments for similar molecular.

Further utility of α,ω PIB-SH was shown by converting the thiol telechilic PIB into α,ω PIB-alkyne with propargyl acrylate. Azide and alkyne functional groups are desirable because they can be used in robust and efficient click chemistry reactions; however, a practical means of PIB functionalization with the latter has yet to be demonstrated. Synthesis of α,ω PIB-alkyne was accomplished by using the recently published phosphine catalyzed thiol-ene Michael addition reaction. Mild reaction conditions were used, i.e. without exclusion of oxygen and moisture, 3 % excess propargyl acrylate, and catalytic concentration of DMPP, to produce 100 % alkyne terminated PIB. Reaction rates were fast, with complete conversion in less than 5 minutes. $^1$$H$ NMR was used to verify the structure of the reaction product, as shown in Figure 7.11. Similar to the α,ω PIB-CTA spectrum, the signal of the methylene protons
adjacent to thiol (a) changed from a quartet to a triplet; however its chemical shift changed very little. Four additional resonances located at 4.71 (singlet, -OCH₂CCH₂, 2H), 2.83 (triplet, -SCH₂CH₂COO-, 2H), 2.68 (triplet, -SCH₂CH₂COO-, 2H), and 2.48 (singlet, -OCH₂CCH₂, 1H) ppm were present. ¹³C NMR spectroscopy supplied further structural evidence of the thiol-ene Michael addition, as shown in Figure 7.12. The original α,ω PIB-SH resonances at 65.70 (3), 33.67 (2), and 21.50 (1) were absent, and new resonances for the corresponding nuclei in the product were observed at 66.19 (3), 29.47 (2), and 28.90 (1) ppm. Peak assignments were made using a combination of small-molecule analogy, NMR predictive software, and qHSQC NMR spectroscopy (Figure 7.13).

An inherent advantage of the nucleophilic thiol-ene reaction (Michael addition) is the ability to perform a one-pot, sequential thiol-ene/thiol-yne reaction to fabricate highly functional materials. As demonstrated above, the Michael reaction is tolerant to the presence of an alkyne, and subsequent irradiation of the alkyne and two equivalents of a thiol, in the presence a photoinitiator, has been reported to yield exclusively and quantitatively the 1,2-diaddition product. To demonstrate this procedure in the present case, a formulation was prepared which closely mimicked that which was used for the earlier-described alkyne-functionalization, excepting the solvent. d-Chloroform was used here to facilitate simple ¹H NMR characterization and provide a homogenous reaction mixture. Once the thiol-Michael reaction was completed, 6-mercaptohexanol and DMPA (i.e. photoinitiator) were charged to the reactor. The contents were then exposed to irradiation for 6 min and purified. Figure 7.14 is a ¹H NMR spectrum of the purified polymer with insets providing an expansion and comparison of the α,ω PIB-alkyne
precursor (Figure 7.14 (a)) to the tetrahydroxyl functional PIB product (Figure 7.14 (b)). Protons directly associated with the alkyne moiety (q and o) were absent in the final product, whereas, a series of new protons associated with the 1,2-thiolether addition product appeared. The assignments given in Figure 7.14 were based on those reported in literature for an analogous polyol made from 6-mercaptopohexanol, via the sequential thiol-ene/thiol-yne reaction. Diastereotopic protons (q) were visible at 4.27 and 4.24 ppm, due to the newly formed chiral center (*).

Arguably the most interesting and potentially useful application for a PIB-based polythiol is as a soft segment in polythiolurethanes. PIB-based polyurethanes/polyureas have received significant attention as an emerging biomaterial; with PIB as a key component of these materials offering biocompatibility, and hydrolytic and oxidative stability. The reaction of thiols with isocyanates, as explored by Hoyle and coworkers, has been found to be efficient and rapid, while the resulting materials possessed many unique mechanical and physical properties. Therefore, segmented PIB-based thiourethanes may serve as a potential new class of TPU biomaterials.

Model reactions were first explored between α,ω PIB-SH and phenyl isocyanate. Triethylamine, at approximately 0.2 wt%, was used as a catalyst in the presence of excess phenyl isocyanate. Quantitative conversion of the thiol functional group was observed in less than 10 min as determined by $^1$H NMR. A spectrum of the purified product (bottom) and the α,ω PIB-SH (top) precursor is shown in Figure 7.15. Signals for each of the tether protons (a, b, c) were visible, as well as characteristic peaks of the phenyl thioester carbamate species (f, g, h, i).
After establishing the efficiency of the thiol-isocyanate reaction, PIB-based thiourethane polymers were synthesized, with and without a small-molecule dithiol chain extender. In the former case, stoichiometric amounts of \( \alpha,\omega \) PIB-SH and MDI, and triethylamine (0.3 wt%), were reacted under an dry nitrogen atmosphere at 50°C for 2 h. After the step growth polymerization was complete a substantially more viscous reaction medium resulted. GPC was used to characterize the polythiourethane relative to the \( \alpha,\omega \) PIB-SH precursor (Figure 7.16). The resulting chromatogram (b) indicated that fairly monodisperse polymer was produced (PDI = 1.39) and a large increase in molecular weight (Mn = 63,200 g/mol) relative to the precursor (a) was apparent from the decreased elution time. Next, the reaction was conducted in the presence of a small-molecule dithiol chain extender, in order to create a polythiourethane with phase-separated hard-segment/soft-segment morphology. A typical two–step, one-prepolymer procedure was employed. First, \( \alpha,\omega \) PIB-SH was reacted with excess MDI, followed by addition of 1,6-hexanediethiol chain extender. The stoichiometry between isocyanate and total thiol was 1:1, and the recipe was designed to yield 20 wt% hard segment. The resulting segmented polythiolurethane was insoluble in typical solvents suitable for PIB and was therefore purified by precipitation from THF into hexanes. The purified polymer had a significant increase in molecular weight, to 77,600 g/mole, and a fairly low PDI of 1.45 (Figure 7.16 (a)).
Conclusions

Synthesis of thiol-terminated PIB was accomplished through a three step, one-pot process. Quantitative conversion of primary bromide to thiol was shown using $^1$H NMR and $^{13}$C NMR spectroscopy. The utility of this telechelic polymer as an efficient precursor to a RAFT CTA, various multifunctional telechelics, and PIB-based segmented polythiolurethane was demonstrated. The RAFT CTA was synthesized by a base-catalyzed alkylation reaction. Alkyne- and tetrahydroxy-functional PIB were synthesized through the highly efficient thiol-ene and sequential thiol-ene/thiol-yne click reactions. Polythiourethanes were synthesized through the base catalyzed thiol-urethane reaction.
References


Figure 7.1. $^1$H NMR Spectrum of $\alpha,\omega$-bis[4-(3-bromopropoxy)phenyl] PIB.
Figure 7.2. $^{13}$C NMR Spectrum of $\alpha,\omega$-bis[4-(3-bromopropoxy)phenyl] PIB.
Figure 7.3. GPC traces of prequenched (dotted line) and quenched (solid line) PIB
Figure 7.4. $^1$H NMR spectra of $\alpha,\omega$-bis[4-(3-thiopropoxy)phenyl] PIB with comparison of the endgroup regions to the precursor bromine-terminated PIB.
Figure 7.5. $^{13}$C NMR of $\alpha,\omega$-bis[4-(3-thiopropoxy)phenyl]polyisobutylene with comparison of the endgroup chemical shifts to those of the bromine-terminated PIB.
Figure 7.6. gHSQC of $\alpha,\omega$-bis[4-(3-bromopropoxy)phenyl] PIB.
Figure 7.7. gHSQC of α,ω-bis[4-(3-thiopropoxy)phenyl] PIB.
Figure 7.8. Temperature effects on sulfide formation during base hydrolysis step.
Figure 7.9. Conversion of bromine terminated PIB to isothiouronium salt terminated PIB versus time.
Figure 7.10. $^1$H NMR of $\alpha,\omega$ PIB-CTA.
Figure 7.11. $^1$H NMR of thiol terminated PIB (top) and alkyne terminated PIB (bottom).
Figure 7.12. $^{13}$C NMR of alkyne terminated PIB with expansion of alkyne PIB (bottom) and expansion of thiol terminated PIB (top).
Figure 7.13. gHSQC of alkyne terminated PIB.
Figure 7.14. $^1$H NMR of tetra hydroxyl functional PIB.
Figure 7.15. $^1$H NMR of phenyl thiourethane terminated PIB.
Figure 7.16. GPC traces of (a) chain extended thiourethane with hexane dithiol (b) chain extended thiourethane without hexane dithiol (c) thiol terminated PIB.