Chapter V Facile, Efficient Routes to Diverse Protected Thiols and to Their Deprotection and Addition to Create Functional Polymers by Thiol-Ene Coupling

5.1 Introduction

Well-defined homopolymers and block copolymers containing covalently or noncovalently attached functionalities are of much interest as materials with tailored properties (refer, for instance, to work by Antonietti[1-4] and Weck,[5-9] among others). To synthesize these functional macromolecules, the chemical modification of well-defined prepolymer chains (i.e., polymer analogous synthesis) is a valuable alternative to the traditional route of direct polymerization or copolymerization of functional monomers by living ionic, group-transfer, radical, or ring-opening methods. Living polymerization methods commonly require intense purification of reagents and solvents, protection of functional groups in monomers, and inert reaction conditions. Further, polymerization by any one of the living mechanisms cited above places restriction on the nature of monomers and comonomers that can be used. Polymer analogous synthesis extends the accessible range of functional polymers and copolymers, with important advantages. Control of the polymer architecture and length is afforded by the choice of prepolymer material, while functionality control is achieved by the modification reaction conditions; therefore, control of polymer structure and of polymer functionality are decoupled. In addition, rapid adjustments in the nature of the side-group and/or the extent of functionalization allow fast and effective optimization of molecular properties for a given application.

Chemical functionalization of unsaturated polymers has received particular attention[10] because of the availability of the parent materials and of the reactivity of the featured double bonds. In particular, polybutadiene (PB) has been successfully functionalized with a diversity of side-groups by hydroboration/oxidation,[11-13] epoxidation followed by oxirane ring-opening using nucleophiles or acid chlorides,[1] hydrosilylation,[13, 14] and radical additions of thiols[15-21] and alkyl iodides.[22]

Polymer analogous synthesis becomes attractive when the coupling reaction is efficient and robust, and free of degradation or cross-linking side reactions. We have come to appreciate several advantages of thiol-ene coupling from our experience functionalizing 1,2-PB. First, the method can be used for grafting various functionalities in a one-step polymer reaction (as opposed to hydroboration or epoxidation). Thiol-ene coupling proceeds under mild reaction conditions and is tolerant of a large number of functional groups. In particular, the chemistry is water insensitive, which renders it considerably simpler than hydrosilylation, for instance. Of paramount importance to our work, thiol addition also proceeds with minimal cross-linking or chain scission in comparison to other modification reactions such as hydroboration/oxidation[13] and hydrosilylation.[23, 24] Finally, desired side-groups are incorporated via unobtrusive thioether linkages, without the introduction of additional functionalities (in contrast to functionalization by epoxidation or radical addition of alkyl iodides, which add one molar equivalent of hydroxyl, chloro, or iodo functionalities per grafted side-group).

Thiol-ene addition to PB offers tremendous versatility for molecular design. The excellent tolerance of thiol-ene coupling to numerous functional groups combines with the good availability of PB-containing prepolymers of well-defined microstructures (e.g., content of 1,2-adducts), macromolecular structure (such as chain topology and incorporation of other polymer blocks), and size (from $< 10^4$ to $> 10^6$ g/mol). The method is well suited to produce homologous series of model materials (i.e., having precisely matched degree of polymerization, but varying in functionality and/or in extents of functionalization) that elucidate macromolecular physical phenomena. Examples from our own activities include studies of (i) association behavior of donor-acceptor chains in dilute solutions, (ii) sticky reptation, and (iii) solution properties of liquid-crystalline polymers bearing mesogenic side-groups.[23, 24]

The functional groups required for our research extend beyond the range of commercially available mercaptans (essentially limited to carboxylic acid, alcohol, 1,2-diol, amine, alkyl, and fluoroalkyl functionalities). Therefore, rapid, high-yield synthetic methods to prepare desired functional thiols are needed to make thiol-ene functionalization widely useful. Furthermore, technological application requires that these synthetic methods be amenable to scale up. We found that indirect preparation of thiols through thioester intermediates presents significant advantages with regard to safety, yield, and product stability. We

developed facile procedures to deprotect the thiols and—without isolation—proceed to functionalize 1,2-PB (Scheme 5.1). Thus, this contribution demonstrates how to conveniently extend the number of candidate side-groups for functionalization of polymers by thiol-ene coupling.

The present work documents highly efficient synthetic routes to an array of protected thiols which were chosen both (i) because the featured side-groups are important functionalities in their own right, and (ii) because each is representative of a general pathway for incorporation of the thiol moiety (Scheme 5.2). Specifically, phenol and pyridine functionalities are described because of their relevance as hydrogen-bond donor and acceptor; carbazole and dinitrobenzoate are of interest as electron donor and acceptor, and relevant to materials with novel electronic properties; and 4-cyano-4'-hydroxybiphenyl is of interest for its liquid-crystalline properties. Of paramount practical significance, the featured chemistry involves: (i) inexpensive, readily available reagents of moderate toxicity and reactivity, (ii) no elaborate equipment or procedures, (iii) rapid, quantitative conversions of limiting reagents in all steps without measurable formation of side-products, and (iv) simple purification (enabled by the clean synthetic routes) using scalable separation processes (principally liquid-liquid extraction and washes and occasionally recrystallization but no column separations).

5.2 Experimental

5.2.1 Materials and Instrumentation

Except for thiobenzoic acid (Alfa Aesar, 94%), carbazole (Aldrich, 95%), 4'-hydroxy-4-carbonitrile (TCI, 95%), thioacetic acid (Aldrich, 96%), allyl bromide (Aldrich, 97%), hydrazine monohydrochloride (Acros Organics, 98%), *p*-toluenesulfonyl chloride (Alfa Aesar, 98%), and *p*-toluenesulfonic acid monohydrate (Aldrich, 98.5%), all reagents were obtained at 99% purity from Aldrich, Alfa Aesar, or Mallinckrodt Chemicals. 2,2′-Azobis(2-methylpropionitrile) (AIBN) was recrystallized biweekly in methanol (10 mL solvent per g AIBN) and stored at 4 ºC; all other reagents were used as received without further purification. Polybutadiene polymer chains (98% 1,2-content) of size 92×10^3 and 820×10^3 g/mol and narrow molecular weight distribution (of polydispersity index 1.07 and 1.26, respectively) were kindly donated by Dr. Steven Smith of Procter and Gamble Company. ^{1}H and ^{13}C NMR spectra were obtained using a Varian Mercury 300 spectrometer (300 MHz for

^{1}H and 74.5 MHz for ^{13}C); all spectra were recorded in $CDCl_3$ and referenced to tetramethylsilane. Polymer molecular weight measurements were obtained by gel permeation chromatography using one of two systems. Measurements were either carried out (i) in tetrahydrofuran (THF) at 25 ºC eluting at 0.9 mL/min through four PLgel 10-μm analytical columns (Polymer Labs, 10^6 to 10^3 A in pore size) connected to a Waters 410 differential refractometer detector (λ = 930 nm) or (ii) in THF on two PLgel 5-μm mixed-C columns (Polymer Labs) connected in series to a DAWN EOS multi-angle laser light scattering (MALLS) detector (Wyatt Technology, Ar laser, λ = 690 nm) and an Optilab DSP differential refractometer (Wyatt Technology, λ = 690 nm). In the former case, molecular weight measurements were analyzed based on calibration using polystyrene standards; in the latter case no calibration standards were used, and d*n*/d*c* values were obtained for each injection by assuming 100% mass elution from the columns.

5.2.2 Synthesis of Benzoyl- or Acetyl-Protected Thiols (Scheme 5.2)

All reactions were monitored by ^{1}H NMR spectroscopy. Analysis of reaction mixtures was generally performed by washing a ~ 1-mL aliquot with water and extracting organic reactants and products into an appropriate solvent, followed by solvent evaporation, and redissolving in $CDCl_3$ for NMR analysis. ^{13}C NMR resonances of compounds **1, 3, 6, 8, 10, 12,** and **13** are documented in Appendix B.

2-Chloroethyl-*p*-toluenesulfonate (1). *p*-Toluenesulfonyl chloride (172 g, 0.884 mol) and pyridine (59 g, 0.75 mol) were added to 180 mL of dichloromethane (DCM) in a 1-L round-bottom flask (RBF) which was placed in an ice bath for ~ 5 min. 1-Chloroethanol (40.3 g, 0.496 mol) was added slowly, and the RBF was taken out of the ice bath and left to stir at room temperature for 15 h. The reaction mixture was poured into a 1-L separatory funnel, washed twice with 300 mL water + 50 mL pyridine, and again with 300 mL water + 75 mL 36 wt % aqueous HCl (discarding the aqueous phase after each wash). Removal of the solvent at reduced pressure yielded analytically pure **1** as a faint yellow, thick syrup (116 g, 0.494 mol, 100% yield). ^{1}H NMR: δ = 7.81 (d, 2 aromatic H meta to CH_3, J = 8.3 Hz), 7.37 (d, 2 aromatic H ortho to CH_3, J = 8.3 Hz), 4.23 (t, OCH_2, J = 5.9 Hz), 3.66 (t, CH_2Cl, J = 5.9 Hz), 2.46 (s, CH_3).

4'-(2-(Benzoylthio)ethoxy)[1,1'-biphenyl]-4-carbonitrile (3). 4'-Hydroxy[1,1'-biphenyl]-4-carbonitrile (5.1 g, 0.025 mol), 2-chloroethyl-*p*-toluenesulfonate (**1**, 9.2 g, 0.039

mol), and potassium carbonate (5.3 g, 0.038 mol) were stirred at 57 ºC in 100 mL of dimethyl sulfoxide (DMSO) for 22 h, resulting in quantitative conversion to **2** (verified by NMR analysis). Potassium chloride (2.1 g, 0.028 mol) was added to the reaction mixture, which was stirred 3 h at 85 ºC to convert the excess **1** into dichloroethane. The reaction mixture was poured into a 1-L separatory funnel containing 300 mL water and extracted with 200 mL of 2-butanone (MEK). The aqueous phase was extracted with another 300 mL MEK, and the organic extracts were combined and washed 3 times with 300 mL water. Finally, solvent and dichloroethane were evaporated under reduced pressure at 80 ºC to give **2** (6.4 g, 0.025 mol, 100% yield) as a brown-orange syrup which solidifies upon cooling. To the previous product in 100 mL of *N*,*N*-dimethylformamide (DMF) in a 250 mL RBF were added thiobenzoic acid (7.3 g, 0.050 mol) and potassium bicarbonate (6.8 g, 0.068 mol), and the mixture was stirred at room temperature until CO_2 effervescence ceased and then at 45 ºC for 4 h. The reaction mixture was transferred to a 1-L separatory funnel containing 250 mL of water, extracted with 400 mL of ethyl acetate, and the organic phase was washed twice with 250 mL of water before solvent removal under reduced pressure. The crude product was purified by dissolving in 300 mL of ethanol at 90 ºC (under slight pressure), and allowing to recrystallize by slowly cooling to room temperature, then by letting stand overnight at 4^{o} C. Filtration of the crystals and removal of solvent under reduced pressure gave analytically pure **3** as ultra-fine, pale brown needles (7.9 g, 0.022 mol, 88% overall yield in 2 steps). ^{1}H NMR: δ = 8.02-7.96 (m, 2 aromatic H ortho to COS), 7.72-7.43 (m, 3 aromatic H meta and para to COS, 4 aromatic H ortho and meta to CN, and 2 aromatic H meta to OCH_2), 7.05 (d, 2 aromatic H ortho to OCH_2, J = 8.7 Hz), 4.25 (t, OCH_2, J = 6.6 Hz), 3.50 (t, SCH_2, J = 6.6 Hz).

4'-(2-(2-(Benzoylthio)ethoxy)ethoxy) [1,1'-biphenyl]-4-carbonitrile (6). 4'-Hydroxy[1,1'-biphenyl]-4-carbonitrile (4.9 g, 0.024 mol), 2-(2-chloroethoxy)ethanol (12.7 g, 0.101 mol) and potassium phosphate tribasic ($K_3PO_4.xH_2O$, 22 g at ~ 25 wt % water, 0.078 mol) were stirred at 110 ºC in 150 mL of DMSO for 12 h, resulting in quantitative conversion to **4** (verified by NMR analysis). The reaction mixture was poured into a 1-L separatory funnel containing 200 mL of chloroform and washed 5 times with 400 mL of water to remove all of the chloroalcohol. The resultant organic phase was dried with $MgSO_4$ and filtered, and the solvent was removed under reduced pressure at 60 ºC to afford analytically pure **4** (6.5 g, 0.023 mol, 96% yield) as a pale yellow-orange syrup which solidifies upon

cooling. To this product in 100 mL of DCM at 0 ºC were added *p*-toluenesulfonyl chloride (22.2 g, 0.115 mol) and pyridine (7.2 g, 0.091 mol), after which the reaction vessel was allowed to warm up to room temperature and left to stir at room temperature for 24 h. The reaction mixture was transferred to a 500-mL separatory funnel, washed twice with 150 mL of water + 25 mL of pyridine, and again with 150 mL of water and 40 mL of 36 wt % aqueous HCl (discarding the aqueous phase after each wash). The organic phase was again dried with $MgSO_4$, filtered, and the solvent was removed under reduced pressure at 40 ºC to yield analytically pure **5** (9.5 g, 0.022 mol, 95% yield), which was finally reacted to generate **6** as follows. To 1.96 g (4.5 mmol) of the said product in 40 mL of DMF were added thiobenzoic acid (0.69 g, 4.7 mmol, 1.05 equiv) and potassium bicarbonate (1.0 g, 10 mmol), and the mixture was stirred at room temperature until CO_2 effervescence ceased, then at 40 ºC for 12 h. The reaction mixture was transferred to a 500-mL separatory funnel containing 200 mL of water, extracted with 100 mL of ethyl acetate, and the organic phase was washed three additional times with 200 mL of water, dried with $MgSO_4$, and gravity filtered before solvent removal at 80 ºC under reduced pressure to give analytically pure **6** as an orange syrup which crystallizes upon cooling (1.80 g, 4.5 mmol, 91% overall yield in 3 steps). ^{1}H NMR: δ = 8.00-7.93 (m, 2 aromatic H ortho to COS), 7.72-7.39 (m, 3 aromatic H meta and para to COS, 4 aromatic H ortho and meta to CN, and 2 aromatic H meta to OCH_2), 7.02 (d, 2 aromatic H ortho to OCH_2, J = 8.7 Hz), 4.19 (t, $ArOCH_2$, J = 4.8 Hz), 3.90 (t, $ArOCH_2CH_2$, J = 4.8 Hz), 3.79 (t, SCH_2CH_2, J = 6.5 Hz), 3.33 (t, SCH_2CH_2 , J = 6.5 Hz).

Thiobenzoic Acid *S*-[2-(9-carbazolyl)ethyl] Ester (8). Carbazole (15.2 g, 0.086 mol), 2-chloroethyl-*p*-toluenesulfonate (**1**, 60.2 g, 0.256 mol), and potassium hydroxide (88 wt % pellets, 13.7 g, 0.215 mol) were stirred at room temperature in 300 mL of DMSO for 18 h, resulting in quantitative conversion to **7** (verified by NMR analysis). Trichloroacetic acid (TCA, 22 g, 0.135 mol) and potassium chloride (20 g, 0.268 mol) were added to the reaction mixture, which was stirred 4 h at 100 ºC to convert the excess **1** to dichloroethane. After titration of the excess TCA by potassium bicarbonate (15.5 g, 0.155 mol), the reaction mixture was poured into a 1-L separatory funnel containing 180 mL of water and extracted with 300 mL of chloroform. The organic phase was washed twice with 400 mL of water; the solvent was evaporated under reduced pressure; and the crude product was purified by dissolving in 475 mL of boiling ethanol and allowing it to recrystallize at room temperature overnight, yielding analytically pure **7** (16.5 g, 0.072 mol, 83% yield) after filtration and

solvent removal. To 6.8 g (0.030 mol) of this product in 110 mL of DMF were added thiobenzoic acid (8.9 g, 0.061 mol) and potassium bicarbonate (8.0 g, 0.080 mol); the mixture was swirled with gentle heating until CO_2 effervescence ceased and then was allowed to react for 4 h at 50 ºC. The reaction mixture was poured into a 500-mL separatory funnel containing 100 mL of water, extracted with 100 mL of chloroform, and the organic phase was washed twice with 150 mL of water before solvent removal under reduced pressure. The crude product was purified by first dissolving in 35 mL of hot chloroform, adding 200 mL of boiling ethanol, and allowing it to recrystallize overnight at room temperature. Filtration of the crystals and removal of solvent under reduced pressure gave analytically pure **8** as very fine, orange-pink needles (8.3 g, 0.025 mol, 70% overall yield in 2 steps). ^{1}H NMR: δ = 8.10 (d, 2 carbazole H, J = 7.5 Hz), 8.03-7.96 (m, 2 aromatic H ortho to COS), 7.64-7.57 (m, 3 aromatic H meta and para to COS), 7.54-7.43 (m, 4 carbazole H), 7.30-7.21 (m, 2 carbazole H), 4.55 (t, NCH_2, J = 7.8 Hz), 3.44 (t, SCH_2, J = 7.8 Hz).

3,5-Dinitrobenzoic Acid 3-(acetylthio)propyl Ester (10). Potassium bicarbonate (7.2 g, 0.072 mol) was added to 3,5-dinitrobenzoic acid (10.0 g, 0.047 mol) in 150 mL of DMSO in a 500-mL RBF, and the slurry was swirled with gentle heating until CO_2 effervescence ceased. Allyl bromide (11.8 g, 0.095 mol) was added next, and the RBF was placed in an oil bath to stir at 70 ºC for 2.5 h. The reaction mixture was poured into a 1-L separatory funnel containing 250 mL of chloroform and washed twice with 400 mL of water (discarding the aqueous phase after each wash), yielding **9** (10.7 g, 0.042 mol, 91% yield) in > 99% purity after removal of allyl bromide and solvent at 80 ºC under reduced pressure. To this product in 100 mL of toluene was added thioacetic acid (9.8 g, 0.124 mol), and the reaction was carried out at 85 ºC with argon purge via radical mechanism using AIBN as the initiator (0.70 g, 4.3 mmol, in 0.175-g increments at 1-hr intervals). After 6 h the reaction mixture was poured into a 1-L separatory funnel containing 16 g sodium bicarbonate ($NaHCO_3$, 0.19 mol) in 300 mL of water, extracted with 100 mL of chloroform, and the organic phase was washed twice with 300 mL of water before solvent removal under reduced pressure. The crude product was purified by washing four times in 50 mL of hexane at 60 ºC, yielding **10** in > 99% purity as a viscous, dark brown syrup (9.1 g, 0.028 mol, 59% overall yield in 2 steps). ^{1}H NMR: δ = 9.24 (t, 1 aromatic H para to CO_2, J = 2.1 Hz), 9.19 (d, 2 aromatic H ortho to CO_2, J = 2.1 Hz), 4.52 (t, OCH_2, J = 6.3 Hz), 3.07 (t, SCH_2, J = 6.9 Hz), 2.37 (s, CH_3), 2.15 (tt, $OCH_2CH_2CH_2S$, J = 6.9, 6.3 Hz).

4-Hydroxybenzoic acid 2-(benzoylthio)ethyl Ester (12). 4-Hydroxybenzoic acid (10 g, 0.072 mol) and 1-chloroethanol (60 g, 0.73 mol) were reacted in the bulk at 110 ºC for 16 h with *p*-toluenesulfonic acid monohydrate (2.7 g, 0.014 mol) as catalyst. The reaction mixture was transferred to a 500-mL separatory funnel containing 5 g of sodium bicarbonate in 125 mL of water, extracted with 150 mL of ethyl acetate, and the organic phase was washed 4 times with 125 mL of water before solvent removal under reduced pressure, yielding **11** in ~ 97% purity (13 g, 0.063 mol, 88% yield). To this product in 100 mL of DMF were added thiobenzoic acid (18 g, 0.12 mol) and potassium bicarbonate (16 g, 0.16 mol), and the mixture was stirred at room temperature until CO_2 effervescence ceased and then at 50 ºC for 4 h. The reaction mixture was poured into a 500-mL separatory funnel containing 100 mL of water and extracted with 100 mL of chloroform, and the organic phase was washed 3 times with 150 mL of water before solvent removal at reduced pressure. The crude product was finally purified by first dissolving it in 50 mL of hot chloroform, then adding 25 mL of boiling hexane and allowing it to recrystallize overnight in the freezer. Filtration of the crystals and removal of the solvent under reduced pressure gave analytically pure **12** as a pink powder (14.5 g, 0.048 mol, 67% overall yield in 2 steps). ^{1}H NMR: δ = 8.02-7.93 (m, 2 aromatic H ortho to CO_2 and 2 aromatic H ortho to COS), 7.59 (tt, 1 aromatic H para to COS, J = 7.5, 1.2 Hz), 7.51-7.42 (m, 2 aromatic H meta to COS), 6.87 (d, 2 aromatic H meta to CO_2, J = 8.7 Hz), 5.8 (br, ArO*H*), 4.50 (t, OCH_2, J = 6.5 Hz), 3.47 (t, SCH_2, J = 6.5 Hz).

Thiobenzoic Acid *S*-[3-pyridinylmethyl] Ester (13). Potassium bicarbonate (12.3 g, 0.123 mol) was added to thiobenzoic acid (14.2 g, 0.097) in 200 mL of ethanol in a 500-mL RBF, and the slurry was swirled with gentle heating until CO_2 effervescence ceased. 3-(Chloromethyl)pyridine hydrochloride (10.2 g, 0.060 mol) was added next, and the RBF was placed in an oil bath to stir at 50 ºC for 2.5 h. The reaction mixture was poured into a 1-L separatory funnel containing 10 g of potassium carbonate (K_2CO_3, 0.072 mol) in 250 mL of water and extracted with 150 mL of DCM, and the organic phase was washed twice with 250 mL of water, gravity filtered, and evaporated to dryness under reduced pressure. The crude product was purified further by washing in 50 mL of hot hexane to give, after removal of leftover solvent under reduced pressure, **13** as a brown solid in ~ 96% purity (11.4 g, 0.050 mol, 80% yield). ^{1}H NMR: δ = 8.64 (d, 1 aromatic H ortho to CH_2 at the second C of the pyridine ring, J = 1.8 Hz), 8.50 (dd, 1 aromatic H para to CH_2 at the sixth C of the pyridine ring, J = 4.8, 1.5 Hz), 7.99-7.90 (m, 2 aromatic H ortho to COS), 7.71 (ddd, 1 aromatic H

ortho to CH_2 at the fourth C of the pyridine ring, J = 7.8, 1.8, 1.5 Hz), 7.58 (tt, 1 aromatic H para to COS, J = 7.5, 1.2 Hz), 7.49-7.39 (m, 2 aromatic H meta to COS), 7.24 (dd, 1 aromatic H meta to CH_2 at the fifth C of the pyridine ring, J = 7.8, 4.8 Hz), 4.29 (s, CH_2).

5.2.3 Polymer Functionalization

General Procedure for 1,2-PB Functionalization Using a Protected Thiol PhCOSR (Scheme 5.1). To the thioester PhCOSR (1–4 mmol) dissolved in 25–75 mL of DMF in a 250-mL RBF were added hydrazine monohydrochloride (~ 4 equiv, 4–16 mmol) and sodium acetate (~ 8 equiv, 8–32 mmol). The RBF was purged with argon for ~ 10 min and left to stir at room temperature for 2–4 h, resulting in 95–100% cleavage of the thioester (verified by NMR analysis). The thiol product was extracted into 30–40 mL of chloroform after addition of 100 mL of water; the organic phase was washed 4 times with 150 mL of water, and transferred into a 100-mL Schlenk tube containing 1,2-PB (0.1–0.2 g, 2–4 mmol, dissolved in 10 mL of chloroform) and AIBN (50–250 mg, 0.3–1.5 mmol). The contents of the Schlenk tube were degassed in three freeze-pump-thaw cycles, and then allowed to react at 55 ºC for 2–6 h. Following reaction, the polymer solution was transferred to a 100-mL jar containing a small amount of 2,6-di-*tert*-butyl-4-methylphenol (BHT), concentrated by evaporation of all but the last 10 mL solvent under an argon stream, and precipitated with cold methanol. Final purification of the polymer was achieved by reprecipitation from a DCM or THF solution (containing ca. 1 wt % BHT) with cold methanol (repeated 2–4 times), followed by drying to constant weight under vacuum at room temperature.

General Procedure for 1,2-PB Functionalization Using an Acyl Chloride RCOCl (Scheme 5.3). To 1,2-PB (0.1–0.5 g, 2–9 mmol) dissolved in 15–30 mL THF in a 100-mL Schlenk tube was added a 10 mL THF solution of 2-mercaptoethanol (BME, 0.5–2 equiv, 1–20 mmol) and AIBN (15–50 mg, 0.1–0.3 mmol). The contents of the Schlenk tube were degassed in three freeze-pump-thaw cycles, and then allowed to react at 55 ºC for 2–3 h. Following reaction, the polymer solution was transferred to a 100-mL jar containing a small amount of BHT and precipitated in cold methanol. The polymer was purified by reprecipitation from a THF solution (containing ~ 1 wt % BHT) with cold methanol (repeated 1–2 times), followed by drying to constant weight under vacuum at room temperature. To the 2-hydroxyethylthio-functionalized 1,2-PB polymer (0.1–0.5 g) dissolved in 10–25 mL of DCM in a 100-mL RBF were added triethylamine (Et_3N, 3–5 mol equiv of functionalized

monomer units) and the acyl chloride RCOCl (2.5–3 mol equiv of functionalized monomer units), and the reaction mixture was stirred 3–4 h at room temperature. Following reaction, the polymer solution was transferred to a 100- or 250-mL jar containing a small amount of BHT, washed with 50–100 mL of water and again with 50–100 mL of aqueous sodium bicarbonate (discarding the wash each time), concentrated by evaporation of all but the last 10 mL of DCM under an argon stream, and finally precipitated with cold methanol. Final purification of the polymer was achieved by reprecipitation from a DCM solution (containing ~ 1 wt % BHT) with cold methanol (repeated 2–3 times), followed by drying to constant weight under vacuum at room temperature.

5.3 Results

5.3.1 Synthesis of Protected Thiols

The set of protected thiols was chosen to illustrate clean, high-yield synthetic routes to introduce the thiol moiety onto functional molecules. Molecules were selected for the importance of their functionalities and for their reactive groups available for derivatization (Scheme 5.2). Thus, we exemplify the synthesis of protected mercaptans using an accessible phenol or alcohol group (compounds **3** and **6**), a heterocyclic nitrogen atom (compound **8**), an accessible carboxylic acid group (compounds **10** and **12**), a terminal olefin group (compound **10**), or an available halide atom (compounds **3**, **8**, **12**, and **13**). Compounds **3** and **6** illustrate convenient methods to control the distance between the grafted side-group and the polymer backbone after thiol-ene coupling. Note that an 8-atom spacer can be incorporated by replacing $H(OCH_2CH_2)_2Cl$ with commercially available $H(OCH_2CH_2)_3Cl$ in the described procedure for the synthesis of **4**. We will return to address synthetic crossroads for introduction of the thioester functionality in Section 5.4.3.

Reaction conditions for the synthesis of compounds **2–13** demonstrate highly efficient and *scalable* methods of significant synthetic utility. ^1H NMR analysis of crude reaction mixtures showed that all reaction steps resulted in quantitative conversion to desired product (except synthesis of **9** and **11**, for which conversion was ~ 90%). The clean synthetic steps made it possible to isolate products in 95–100% purity and 90–100% yield by mere use of liquid-liquid extraction/washes, and evaporation of low-boiling compounds. In some cases, further purification was achieved by recrystallization to yield analytically pure product (compounds **3**, **7**, **8**, and **12**).

5.3.2 Alkylation of Nucleophiles to Introduce Primary Halide or Alcohol Moieties

To generate ω-chloroalkyl or ω-bromoalkyl derivatives, alkylation of nucleophiles is usually done using α,ω dibromo- or dichloroalkanes, e.g., reaction of 4'-hydroxy-biphenyl-4-carbonitrile with 1,6-dibromohexane[25] or carbazole with 1,2-dichloroethane.[26] Unfortunately, when using these reagents bisubstitution is always an issue. In addition, in the case of very basic nucleophiles (e.g., deprotonated carbazole), elimination competes effectively; hence, yields tend to be low and product purification usually requires column chromatography. We were not, for instance, able to achieve yields > 50% for the synthesis of **7** according to published methods[26] using KOH/K_2CO_3 as base in 1,2 dichloroethane with tetrabutylammonium bromide as phase-transfer catalyst. We found, however, that chloroethylation of nucleophiles with 2-chloroethyl-*p*-toluenesulfonate (**1**) in DMSO at low to moderate temperatures overcame both problems stated above. First, the use of *p*-toluenesulfonate (tosylate) as the leaving group and of a polar aprotic solvent both favor substitution over elimination;[27] second, because tosylate is a significantly better leaving group than chlorine, quantitative conversion of both carbazole and 4'-hydroxy-biphenyl-4-carbonitrile to the chloroethyl derivatives (compounds **7**, **2**) was achieved without measurable formation of side-products. Excess **1** could be reacted quantitatively to 1,2-dichloroethane with KCl in a few hours, so that product in quantitative yields and > 95% purity could be obtained by mere liquid-liquid extraction and removal of solvent and dichloroethane at reduced pressure.

Alkylation of nucleophiles to generate ω-hydroxyalkyl derivatives is usually done using ω-bromo-1-alkanols or ω-chloro-1-alkanols with K_2CO_3 or NaH as base in DMF, acetone, or ethanol as solvent (for instance, alkylation of 4'-hydroxy-biphenyl-4-carbonitrile with bromodecanol[28] or chlorohexanol[29]). Published yields for such reactions are usually < 85 %, and column chromatography is typically necessary for isolation of the product. We found, however, that alkylation of 4'-hydroxy-biphenyl-4-carbonitrile with commercially available $H(OCH_2CH_2)_nCl$ (n = 1–3, inexpensively available from Wako Chemicals) in DMSO with K_3PO_4 as base gave quantitative conversion, and that product (compound **4** or analog) in > 99% purity could be obtained by mere washes due to the good water solubility of the chloride reagent.

5.3.3 Functionalization of 1,2-PB

Reaction conditions for 1,2-PB functionalization given in Table 5.1 incorporate functional side-groups while preserving the narrow molar mass distribution of the precursor polymer material (Table 5.1, Figures 5.1–5.4). Depending on the application, degrees of functionalization from ≤ 1% to ≥ 50% are of interest; here, we demonstrate systematic control of functionalization (X_{funct}) from a few % to 40% (Table 5.1). PB chains with very high 1,2-content tend to form cyclic adducts, which limit functionalization to ≤ 50% unless very high thiol concentrations are used.[18, 19] Accounting for the formation of ring structures by random cyclization of adjacent repeat units during the addition reaction, the general structure of the functionalized polymer is as shown in Figure 5.1. That structure is solved by considering that either five- or six-member rings can be formed, and that polycyclic structures are possible. Note that any cyclic or polycyclic structure involves at most one five-member ring (on either side of which can be fused any number of six-member rings), and that there are exactly as many methyl groups in the functionalized polymer as there are five-member rings. Let X_{funct} be the fraction of reacted 1,2-PB repeat units bearing functional groups, $X_{unreact}$ be the fraction of unreacted 1,2-PB repeat units, and X_{cycl} be the fraction of reacted 1,2-PB repeat units that are unfunctionalized. Thankfully, analysis of the general structure (Figure 5.1) provides an unambiguous relationship between X_{funct}, $X_{unreact}$, X_{cycl} and three quantities that are readily determined from the ^{1}H NMR spectra: the relative values of the integrals of RC**H$_2$**S- methylene protons (S_1), **H$_2$**C=CH- alkenic protons (S_2), and aliphatic protons of chemical shifts below 2.2 ppm (S_3). In terms of the indices defined in Figure 5.1, $S_1 \sim 2(n + m + m')$ and $S_2 \sim 2u$. Furthermore, since none of the side-groups R in the present study display protons with $\delta < 2.2$ ppm, $S_3 \sim [5\,n + 4\,(m + m') + 6\,(p + p' + t) + 7\,(q + v) + 3\,u]$. Because there are as many beginnings as ends in both *y* and *z* structures (Figure 5.1, top), $m = q$, and $m' = v$; therefore, $(p + p' + t + q + v) = (2S_3 - 3S_2 - 5S_1)/12$. Thus, X_{funct}, $X_{unreact}$, and X_{cycl} can be calculated by the expressions below without any knowledge of the relative amounts of the repeat units *m*, *m*', *p*, *p*', *q*, *t*, or *v* in the functionalized polymer:

$$X_{funct} = \frac{n+m+m'}{n+m+m'+p+p'+t+q+v+u} = \frac{6S_1}{S_1+3S_2+2S_3}$$

$$X_{unreact} = \frac{u}{n+m+m'+p+p'+t+q+v+u} = \frac{6S_2}{S_1+3S_2+2S_3}$$

$$X_{cycl} = 1 - X_{funct} - X_{unreact} \quad .$$

Functional polymer could also be obtained in a two-step polymer modification procedure, by thiol-ene addition of β-mercaptoethanol (BME), followed by esterification of the incorporated hydroxyl groups with a suitable acyl halide (Scheme 5.3, Table 5.2). We found that the narrow polydispersity of well-defined precursor polymer material could also be preserved throughout this process (Table 5.2), so that the procedure offers a useful alternative to direct coupling of a thiol derivative when an acyl chloride compound featuring the desired functionality is readily accessible.

5.3.4 Molecular Structure of Functionalized 1,2-PB Polymer

Let us first see why there are indisputably cyclic structures. To begin, the potential to form cyclic structures follows from the reaction mechanism. The addition reaction is initiated by abstraction of a thiol hydrogen by a cyanopropyl free radical. The resultant thiyl radical (RS·) adds to a double bond of 1,2-PB in anti-Markovnikov fashion,[16-18] generating a polymeric alkyl radical (e.g., structure **I** in Figure 5.5). As shown in the figure, transfer of hydrogen from another thiol molecule completes the addition reaction (structure **II**) and regenerates a new RS$^{\bullet}$ participant; alternatively, intramolecular reactions of **I** compete with hydrogen transfer to form structures **III** and **IV**. As evidence for the formation of ring structures by intramolecular cyclization, Schlaad[18, 19] pointed to incomplete functionalization at full conversion of double bonds using 1,2-PB-*block*-poly(ethylene oxide) as starting material, i.e., typically only 60–80 functional side-groups were found for every 100 reacted 1,2-PB repeat units. Direct evidence of cyclization is seen in the ^{1}H NMR spectra in the present study (bottom trace in Figure 5.2 and spectra in Appendix B): the broad peaks below 2.2 ppm are not consistent with the structures of repeat units *w* and *x* in Figure 5.1, but consistent with cyclohexyl or cyclopentyl proton signals. Further, the observed multiple peaks assignable to the $RCH_2SC\mathbf{H_2}$- protons of the functionalized polymer (protons 4, 5, 6; Figure 5.2) cannot be explained in the absence of cyclization, but are consistent with a combination of the repeat units *n*, *m*, and *m*' in Figure 5.1.

The question now arises whether radical **I** in Figure 5.5 predominantly forms **III** or **IV** during cyclization. On the basis of the relative thermodynamic stability of secondary vs. primary radical intermediates, Schlaad and coworkers[18] have suggested that six-member rings (**III**) should be preferred over their five-member counterparts (**IV**); however, experimental results discussed in the next few paragraphs give instead evidence to the contrary. First, our

data reveals a high content of five-member rings in reacted polymer. NMR analysis of our product for highly functionalized chains shows (i) a strong peak around 17 ppm in the solid state ^{13}C spectra (Figure 5.3), and (ii) a strong signal at 1–0.9 ppm in the ^{1}H NMR spectra (Figure 5.2, bottom). Both these signals are consistent with the methyl group of structure *v* in Figure 5.1. Since there are exactly as many five-member rings as methyl groups in the functionalized polymer, we deduce that a large number of unfunctionalized, reacted monomers cyclized into five-member rings.

Next, literature results[22, 30] on the radical addition of primary alkyl iodides to 1,2-PB and α,ω-alkadienes provides further evidence. Although the initiation, addition, and transfer steps for RI vs. RSH radical addition involve molecules of substantially different reactivity, the intermediate radicals involved in *intra*molecular cyclization have essentially the same structure (i.e., replace RS by R in structures **I**, **III**, and **IV** of Figure 5.5). Thus, the relative rates of formation of five- vs. six-member ring structures should be comparable. According to reports on the radical addition of perfluoroalkyl iodides to 1,2-PB[22] and 1,6 heptadiene,[30] intramolecular reaction of polymer radical **I** is expected to form primarily five-, instead of six-, member cyclic intermediates (structure **IV** rather than **III**).

In order to make further progress, let us now consider the competition between H-abstraction by **I** (forming **II**) vs. cyclization of **I** (to form **III** or **IV**). This competition depends on both thiol concentration and steric hindrance as chain modification proceeds. Let r_1, r_2, r_3 and p_1, p_2, p_3 denote the reaction rates and transition probabilities for the pathways **I→ II**, **III,** or **IV**, respectively (Figure 5.5). Consider a thiol-ene coupling event that yields a radical with a neighboring vinyl group, such as **I**. The fraction of events that proceed to form simple pendant groups **II** vs. cycles (**III** or **IV**) is $p_1/(p_2+p_3)$. Furthermore, $p_1/(p_2+p_3) = r_1/(r_2+r_3)$, which is proportional to [RSH], since r_1 is first-order and r_2 and r_3 are zero-order in thiol concentration. Let the coefficient of proportionality be k, i.e., $p_1/(p_2+p_3) = k$[RSH], where k may vary with the extent of conversion due to steric hindrance. Given that $p_1/(p_2+p_3) = p_1/(1-p_1)$, we see that $p_1 = k$[RSH]/(1+k[RSH]); hence, p_1 increases linearly with [RSH] at low thiol concentration ([RSH]<<1/k) and saturates to 1 at [RSH]>>1/k (Figure 5.6). Schlaad[18] reported saturation of the extent of functionalization for [RSH] >10M. With decreasing [RSH], he further observed that cyclization began to compete significantly at [RSH] ≤ 5M. Using k[RSH] ~ O(10) at the onset of competition (Figure 5.6), we deduce k ~ O(1 M^{-1}).

The above result has important implications for the relative formation of five- vs. six-member rings. First, the finding that $k \sim O(1\ M^{-1})$ leads immediately to the realization that under the functionalization conditions used in the present study ([RSH] ~ $O(10^{-1}$ M or less), radical **I** (Figure 5.5) primarily undergoes intramolecular reaction, i.e., $p_1 \approx p_1/(p_2+p_3) \sim O(10^{-1}$ or less). Second, the fact that very little of radical **I** proceeds to abstract H from RSH under these conditions suggests that likewise very little of radical **III** would abstract H under the same conditions (judging reactivity based on structure similarity). Therefore, if, as Schlaad suggests, intramolecular cyclization of **I** led primarily to the six-member rings **III**, the similarity of **I** and **III** would cause **III** to propagate a ladder of many six-member cycles prior to concluding with H-abstraction from RSH. In that case, our functionalized polymer would then display (i) very high ratios of cyclization to functionalization, $X_{cycl}/X_{funct} >> 1$, and (ii) very few five-member rings. Both these results are contrary to our observations.

We conclude by suggesting that the data is consistent with the following predominant pathway: **I** → **IV** → **V** (Figure 5.5) for thiol concentrations on the order of 10^{-2}–10^{-1} M. That is, **I** cyclizes predominantly (and preferably to form five-member rings), but **IV** abstracts hydrogen predominantly. Note that such different relative reactivity for radicals **I** and **IV** are reasonable based on their structures. Further, this reaction pathway successfully explains the observed ratios of X_{funct}/X_{cycl} in the relatively narrow range of 0.65–1 (Tables 5.1 and 5.2) over the > 1 order of magnitude range of thiol concentration spanned by our experiments. If the reaction proceeded exclusively from **I** to **IV** to **V** ($p_1 = p_2 = p_5 = 0$), then $X_{funct}/X_{cycl} = 1$ and the polymer structure would consist exclusively of unreacted 1,2 units and functionalized five-member rings. In reality, deviations from $p_2 = 0$ or $p_5 = 0$ account for values of X_{funct}/X_{cycl} smaller than 1, and deviation from $p_1 = 0$ account for values of X_{funct}/X_{cycl} larger than 1. Increasing [RSH] increases p_1, leading to a greater number of acyclic functionalized units. The general predominant polymer structure is therefore the one given in Scheme 5.1.

5.4 Discussion

5.4.1 Direct or Indirect Functionalization?

The utility of indirect functionalization by esterification of 2-hydroxyethylthio-modified PB (Scheme 5.3) is somewhat limited by the high reactivity of acyl halides, which renders them incompatible with a number of important functional groups and working conditions. Furthermore, our experience with polymers that are susceptible to cross-linking (such as high

MW 1,2-PB) indicates that best results are typically achieved by minimizing the number of synthetic steps involving macromolecules. Finally, we found that the time invested in the synthesis of protected thiols is easily regained in subsequent tailoring of polymer properties by quicker adjustments in the number density of grafted side-groups. Thus, we find that direct polymer functionalization according to Scheme 5.1 is preferable in most cases. However, indirect functionalization according to Scheme 5.3 becomes useful when (i) a suitable acyl halide is commercially available, and (ii) Scheme 5.1 fails for one reason or another; e.g., due to unsatisfactory deprotection of a suitable thiol. For instance, deprotection of compound **10** to give the corresponding mercaptan did not give acceptable results due to apparent partial reduction of the nitro groups.

5.4.2 Choice of Protecting Group

The motivation for using protected thiols arises from issues of safety, yield, efficiency, and product stability. Direct preparation of thiols can be achieved by addition of hydrogen sulfide (H_2S) to alkenes or by substitution of alkyl halides with hydrogen sulfide or hydrosulfide (HS^-). These methods have the following disadvantages: first, both hydrogen sulfide and hydrosulfide present considerable health hazards, and second, sulfide byproducts are usually formed in significant amounts.[27, 31] Alternatively, the thiol functionality can be incorporated indirectly using other sulfur-containing compounds such as thiolcarboxylic acids, thiourea, or the thiolsulphate ion, followed by bond cleavage via, e.g., hydrolysis of the intermediates to generate the desired mercaptan.[31] The extra step required by any indirect method is balanced by the advantages of cleaner, less-wasteful reactions, and the use of less-toxic reagents. Because thiols are prone to oxidation (e.g., in air on standing), storage of protected thiols is also often considered a wiser choice.

On the basis of adverse side reactions that occur with the triphenylmethyl (trityl) group, we found it necessary to turn to other protecting groups. The widespread use of the trityl group[32] reflects the ease by which it is first incorporated by substitution of halides using triphenylmethyl mercaptan, and the ease with which it is quantitatively removed (< 2 hours in DCM at room temperature in the presence of TFA and triethyl- or triisopropylsilane[33-36]). Our interest in the trityl sulfide group was generated by the hope that both deprotection of the sulfide and addition of the resultant thiol to PB could be successfully carried out in one pot by using chloroform as the solvent (procedure described in Appendix B). Unfortunately,

experiments with 9-[2-(triphenylmethyl)thio]ethyl]carbazole (**14**, Scheme 5.4, Appendix B) showed that although both deprotection and addition reactions proceeded as desired, unacceptable degradation of the polymer also occurred under such conditions (Figure 5.7, right; Appendix B). It is also worth noting that triphenylmethyl mercaptan is a comparatively expensive reagent for the introduction of the thiol functionality.

Thioesters have been used extensively in the past as protecting groups of the thiol functionality, with more or less success towards selective deprotection based on the reagents and method used[37]. Recent literature reports[38-40] described selective, quantitative hydrolysis of thioesters to thiols under mild conditions, i.e., in < 2 hours at room temperature with hydrazine acetate in DMF. Oxygen esters were found to be resistant to hydrolysis under these conditions. These reports motivated us to use thioacetic acid or thiobenzoic acid as reagents for the indirect synthesis of mercaptans, with good success toward preparation of functionalized polybutadienes as documented in the present report. We found that thioacetic acid and thiobenzoic acid were essentially equivalent in reactivity, but that thiobenzoic acid offers the advantage of simpler purification of the thioester product due to differences in both solubility and melting point between products and impurities. For instance, the higher molecular weight products obtained with PhCOSH were usually solid compounds amenable to recrystallization.

5.4.3 Synthetic Crossroads for the Introduction of the Thioester Functionality

Thioesters can be generated using thioacetic acid or thiobenzoic acid either from nucleophilic displacement of a leaving group or from radical addition to a terminal alkene (Scheme 5.2). Reaction of a halide or tosylate is considerably more convenient than reaction of an alkene, since the nucleophilic displacement (i) does not require oxygen-free conditions and (ii) essentially does not generate any impurities. Indeed, quantitative radical reaction of alkenes (e.g., synthesis of **10**) is accompanied by the formation of radical termination products (0.05 to 0.3 molar equiv) which can greatly complicate the purification process.

In some cases a leaving group (e.g., synthesis of **13**) or alkene may be directly available, otherwise they can be introduced in one of the following ways: (i) alcohols can be converted into good leaving groups by tosylation (e.g., synthesis of **5**), (ii) carboxylic acids can be reacted by Fisher esterification with, e.g., 2-chloroethanol (e.g., synthesis of **11**), and (iii) nucleophiles can be alkylated with, for instance, allyl bromide (e.g., synthesis of **9**) or 2-

chloroethyl-*p*-toluenesulfonate (compound **1**, e.g., synthesis of **2** or **7**). The following considerations affect decision making regarding alkylation of nucleophiles. On the one hand, allyl bromide is considerably more reactive and available than **1**, and its reaction with nucleophiles proceeds cleanly (in contrast, care must be taken in choosing reaction conditions with compound **1** to prevent bisubstitution and minimize elimination). On the other hand, the use of allyl bromide suffers in the conversion of the resulting alkene to the desired protected thiol (e.g., **9** to **10**). As noted earlier, that reaction is air sensitive, and the side-products are often difficult to separate from the desired one. As a result, the ease of conversion and purification of thioesters from halides (e.g., **3** from **2**) often justifies the additional care required in the coupling of **1** to the molecule of interest (e.g., **1** to **2**).

Functional precursors bearing nucleophilic atoms also afford a convenient method to control the spacer length between the functional group of interest and the polymer backbone. For instance, 3-, 5- and 8-atom spacers can be accessed by alkylation of a nucleophile with inexpensively available $H(OCH_2CH_2)_nCl$ (n = 1,2,3; Wako Chemicals), followed by conversion to a protected thiol as in the synthesis of **6**.

5.4.4 Deprotection of Acetyl- or Benzoyl-Thioesters

In all cases (with the exception of compound **10**), cleavage of thioesters was achieved in > 95% yields (verified by ^{1}H NMR analysis) in 2–4 h with hydrazine acetate in DMF at room temperature (Scheme 5.1, step 1.1). Significantly, we found that hydrazine acetate could be generated in situ by ion exchange in DMF from considerably less expensive hydrazine hydrochloride and sodium acetate, with equally successful results.

A most compelling advantage of Scheme 5.1 for functionalization of PB using acetyl or benzoyl thioesters consists in the direct addition of the deprotected mercaptan to PB without its isolation as a purified intermediate. Extraction of the DMF reaction mixture with chloroform or DCM and subsequent washing of the organic phase (Scheme 5.1, step 1.2) yields in ~ 30 min a remarkably pure solution of the thiol in which the only impurities are *small amounts* of disulfide (due to exposure to air), unreacted thioester (< 5% of initial amount), DMF, and moisture. Radical addition of the thiol to PB is highly tolerant of these impurities and proceeds unaffected by their presence (Table 5.1).

5.4.5 Effect of Impurities

The radical addition of mercaptans to alkenes is known to be highly tolerant of a vast array of functional groups.[27] Indeed, we found that most impurities (such as disulfides, thioesters, solvents, water, etc.) were inconsequential during thiol-ene functionalization of PB, with the following notable exceptions. First, in one-pot reaction procedures after detritylation of triphenylmethyl sulfides, some unidentified compound(s) caused chain scission of 1,2-PB (as mentioned earlier, Figure 5.7, right). Second, we found that the presence of benzoyl disulfide (PhCOSSOCPh) resulted in significant cross-linking. For example, use of a sample of thiobenzoic acid *S*-[3-(9-carbazolyl)propyl] ester (**16**, Appendix B) containing ~ 0.2 molar equiv of benzoyl disulfide caused polydispersity to increase from PDI = 1.07 to 1.34 at 19% functionalization (Figure 5.7, left; Appendix B).

5.4.6 Implications of Extents of Cyclization for 1,2-PB

Depending on the reason for modifying the polymer, degrees of functionalization from a few % up to ~100% are of interest. Our experiments show cyclization to functionalization ratios X_{cycl}/X_{funct} of 1–1.5, meaning that during the course of the addition reaction, approximately as many reacted monomers were functionalized as were consumed without functionalization by intramolecular cyclization. We found this to be the case for reaction conditions spanning more than 1 order of magnitude in thiol concentration in the range $10^{-2} < [\text{RSH}] < 3 \times 10^{-1}$ M. That is, 1,2-PB functionalization at moderately low to very low thiol concentrations proceeds without excessive amounts of cyclization (which would be expected if radical **I** in Figure 5.5 led primarily to six-member rings, as explained earlier). The implications of this result are 2-fold. First, low target levels of functionalization can be readily achieved at low or very low [RSH], with minimal changes in the physical properties of the polymer product resulting from cyclic/polycyclic structures. This enables good control of the extent of reaction and minimizes waste of potentially highly valuable thiol reagent. Second, the result suggests an alternative synthetic strategy to using extremely high thiol concentration (on the order of 10 M!) in order to achieve high degrees of functionalization (e.g., > 70%). Taking advantage of the fact that cyclization to functionalization ratios remain in the narrow range of 1–1.5 at thiol concentrations of 0.01–0.1 M, the strategy involves synthesis of thioester compounds featuring two functional side-groups per molecule. Deprotection and addition to 1,2-PB according to Scheme 5.1 using thiol concentrations on

the order of 0.1 M will result in incorporation of, e.g., 80% side-groups at 40% functionalization. For instance, our lab is now attempting to synthesize compound **17** as shown in Scheme 5.5.

5.5 Conclusion

Functionalization of polymers bearing pendant vinyl groups by thiol-ene coupling is quickly gaining popularity as a powerful and versatile method to prepare well-defined polymeric materials with tailored properties. However, commercially available mercaptans are limited to a select few functional groups. Our research interests have prompted us to develop rapid, high-yield synthetic methods to prepare new functional thiols. In this contribution, we show that the synthesis of acetyl or benzoyl thioesters to introduce the thiol moiety enables clean, nonwasteful, scalable preparation of stable compounds suitable for long-term storage; these can then be painlessly deprotected and added to the polymer in one continuous, straightforward procedure (Scheme 5.1). The deprotection and addition can be completed in a matter of hours, and the addition is devoid of degradation or cross-linking side reactions. Hence, the method enables synthesis of new polymeric materials whose molecular properties can be rapidly tailored by quick adjustments in the nature or quantity of the side-group(s). The facile routes for both synthesis of the protected thiols and their deprotection-addition make thiol-ene functionalization attractive for diverse applications including drug delivery, organic electronics, and polymer compatibilization. Future work might explore surface modification, which could be performed in a spatially resolved manner using photogeneration of radicals in the absence of photoinitiators[41] to perform thiol-ene coupling in the irradiated region.

5.6 Figures, Schemes, and Tables

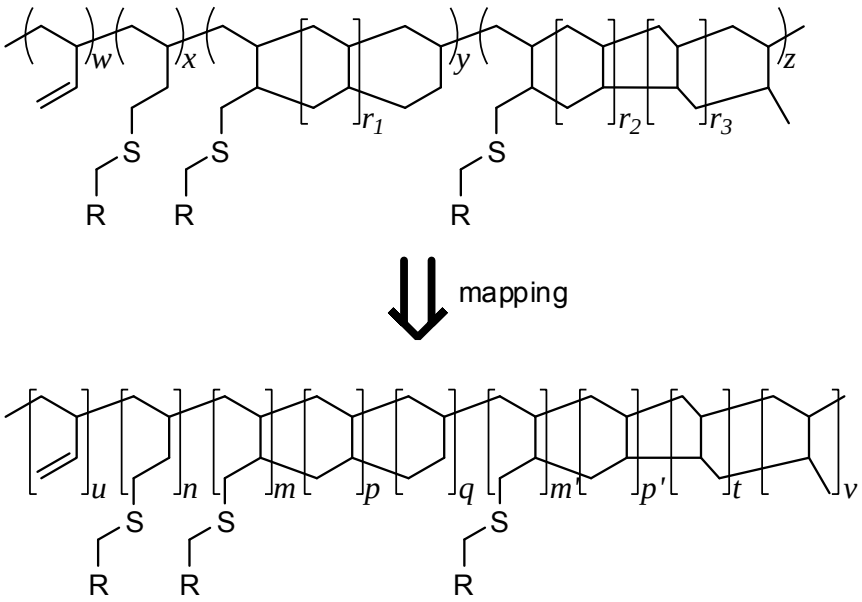


Figure 5.1 General structure of functionalized 1,2-polybutadiene (1,2-PB) and calculation of the fraction of 1,2-PB repeat units that are functionalized, cyclized, and unreacted. For any cyclic or polycyclic structure of type *y* or *z*, the number of repeat units r_1, r_2, and r_3 can be any non-negative integers. The mapping is interpreted as follows: *u* is the total number of unreacted monomers in the polymer chain; *p* is the total number of reacted, unfunctionalized monomers involved in six-member rings "in the middle" of a polycyclic ring structure of type *y*; *p*' and *v* are the total number of reacted, unfunctionalized monomers involved in six member rings "to the left" and "to the right," respectively, of the five-member ring in a polycyclic structure of type *z*; etc. Pairs of indices (*m* and *m*', *p* and *p*') refer to groups that contribute identically to NMR spectra.

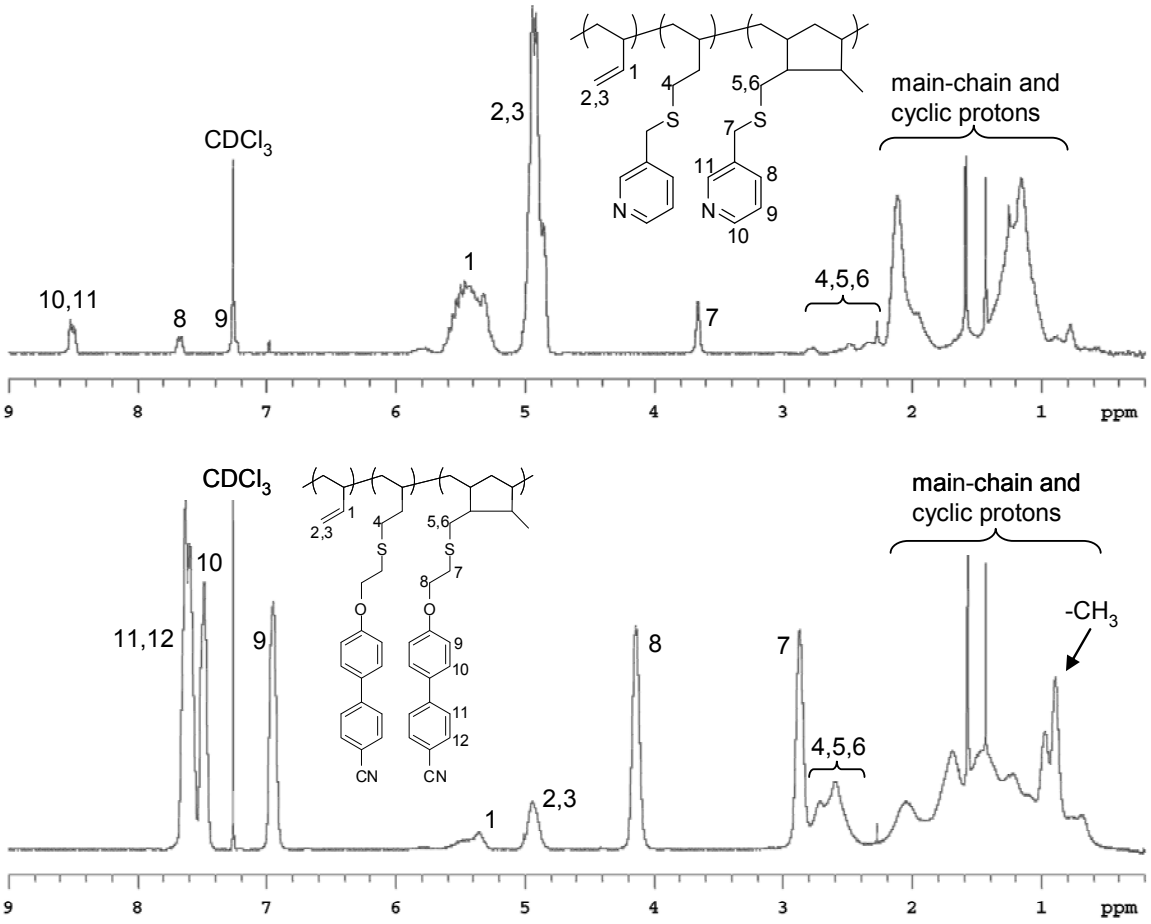


Figure 5.2 Representative ^{1}H NMR spectra of functionalized 1,2-polybutadiene polymers (92kPB13, top trace, and 92kPB3, bottom trace; refer to Table 5.1). Note that the two protons of the $RCH_2SC\mathbf{H_2}$- methylene groups directly attached to ring structures are not equivalent and hence give separate signals. In both spectra, visible peaks at δ = 6.97, 2.27, and 1.43 ppm belong to 2,6-di-*tert*-butyl-4-methylphenol (BHT), and peaks near δ = 1.6 ppm correspond to water.

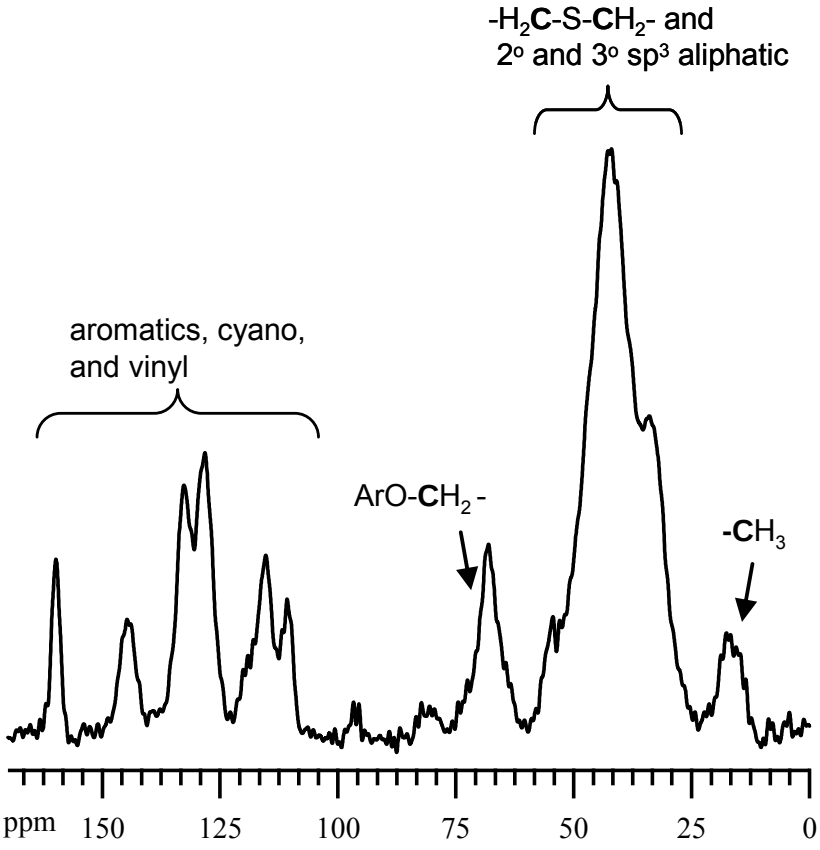


Figure 5.3 Representative solid-state ^{13}C NMR spectrum of functionalized 1,2-polybutadiene polymer (92kPB3; refer to Table 5.1 and to the structure at the bottom of Figure 5.2).

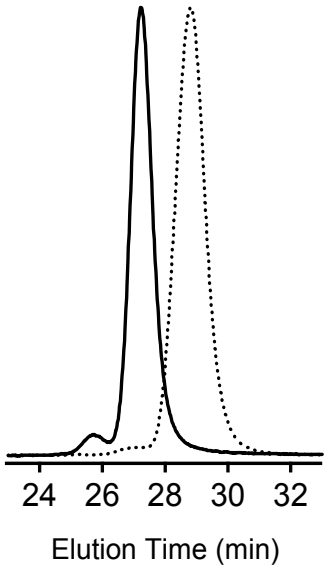


Figure 5.4 Representative gel permeation chromatography trace of functionalized 1,2-polybutadiene (1,2-PB) polymer. The solid line corresponds to 92kPB3 (refer to Table 5.1); the dashed line is 92 kg/mol 1,2-PB prepolymer.

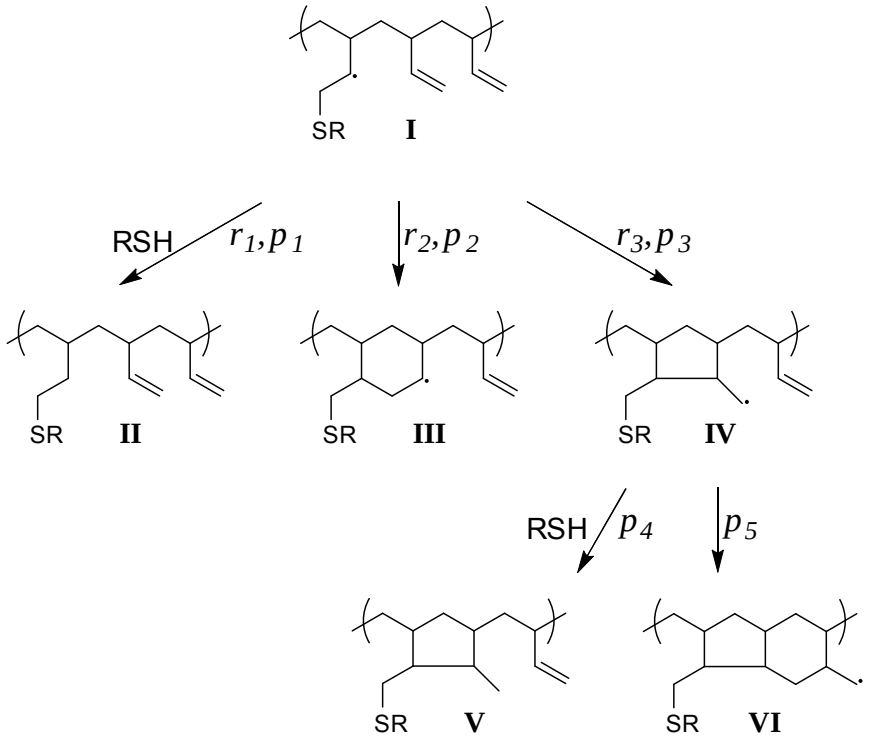


Figure 5.5 Possible reaction pathways for radical thiol addition to 1,2-polybutadiene and competing cyclization reactions.

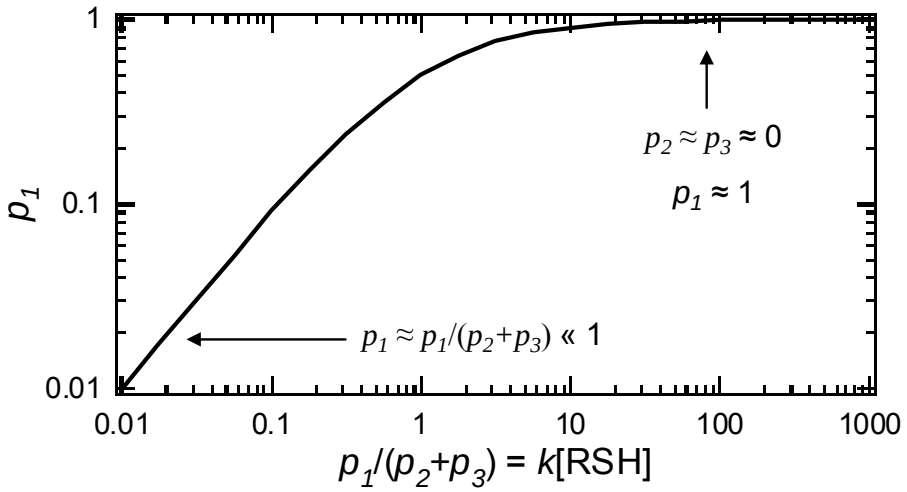


Figure 5.6 Fraction p_1 of species **I** (Figure 5.5) to proceed to abstract hydrogen from RSH as a function of [RSH]. It exhibits a linear increase at low concentration and saturates above a characteristic concentration that corresponds to $p_1/(p_2 + p_3) \approx 10$ (refer to text).

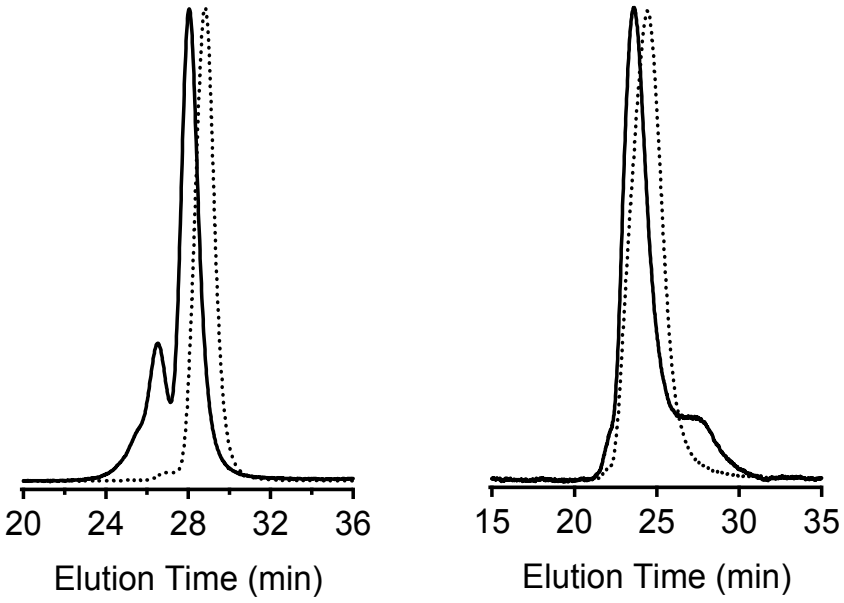
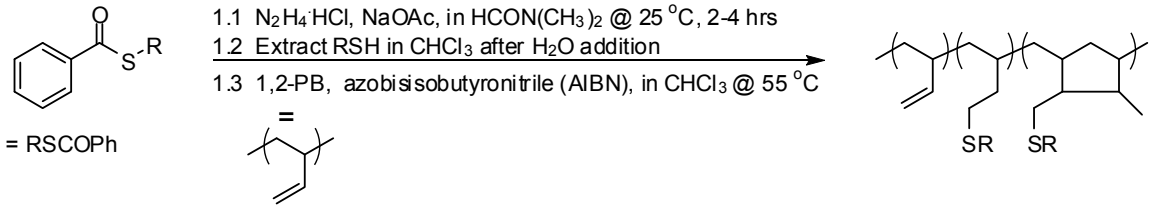
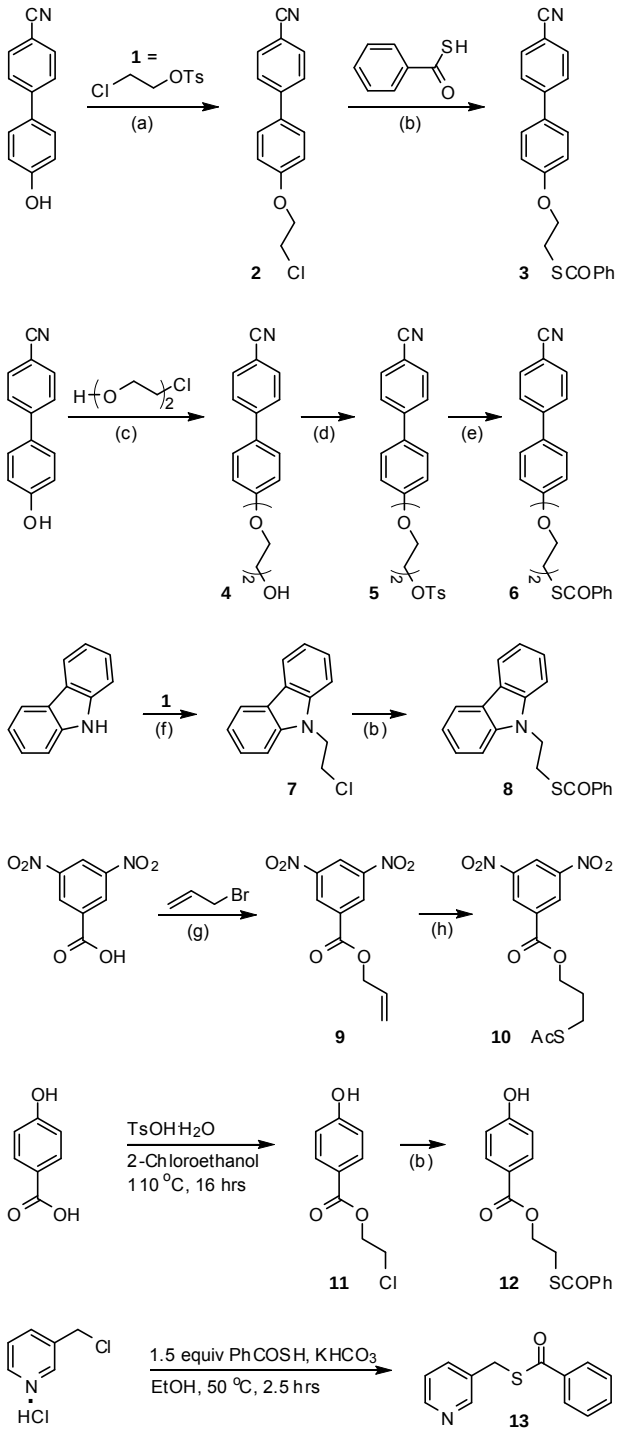


Figure 5.7 Particular reaction conditions (refer to Appendix B, Sections 3 & 4 and Table B.1) to be avoided because of cross-linking (left) or chain scission (right): gel permeation chromatography traces of 1,2-polybutadiene functionalized by reaction in the presence of dibenzoyl disulfide (solid line, left, 92kPB16), and in a one pot synthesis after deprotection of triphenylmethyl sulfide derivatives (solid line, right, 820kPB14). The dashed lines correspond to prepolymer starting materials.

Scheme 5.1 Use of a Thioester RSCOPh in the Functionalization of 1,2-Polybutadiene (1,2-PB) by Thiol-Ene Coupling of Unavailable Mercaptans

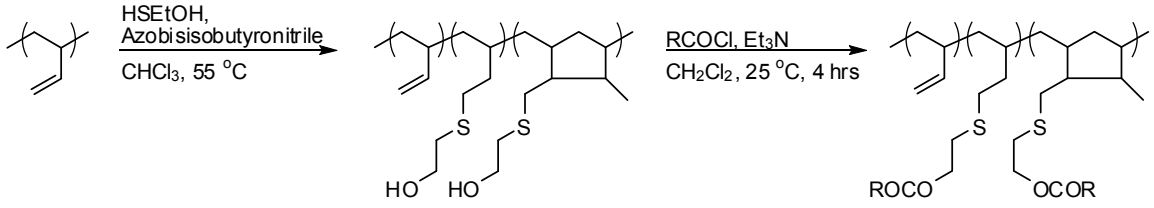


Scheme 5.2 Synthesis of Benzoyl- or Acetyl-Protected Thiols[a]

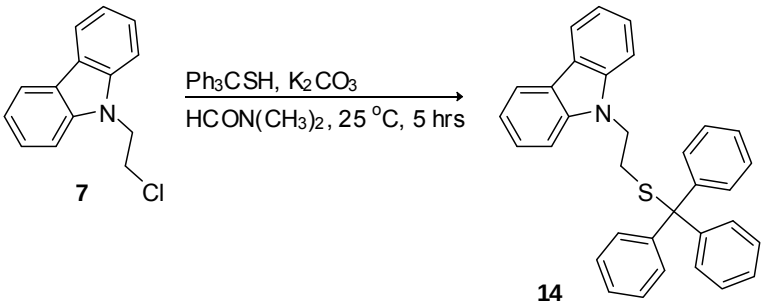


[a] Key: (a) 1.5 equiv of **1**, K_2CO_3, dimethyl sulfoxide (DMSO), 57 ºC, 22 h; (b) 2 equiv of PhCOSH, $KHCO_3$, *N*,*N*-dimethylformamide (DMF), 45–50 ºC, 4 h; (c) 4 equiv of 2-(2-chloroethoxy)ethanol, K_3PO_4, DMSO, 110 °C, 12 h; (d) 5 equiv of tosyl chloride, 4 equiv of pyridine, CH_2Cl_2, 25 ºC, 24 h; (e) 1.05 equiv of PhCOSH, $KHCO_3$, DMF, 40 ºC, 12 h; (f) 3 equiv of **1**, 2.5 equiv of KOH, DMSO, 25 ºC, 18 h; (g) 2 equiv of allyl bromide, $KHCO_3$, DMSO, 70 ºC, 2.5 h; (h) 3 equiv of AcSH, 2,2′-azobis(2-methylpropionitrile), toluene, 85 ºC, 6 h.

Scheme 5.3 Alternative Route to New Functional Derivatives of 1,2-Polybutadiene by Thiol-Ene Coupling Using an Acyl Chloride RCOCl



Scheme 5.4 Synthesis of Trityl-Protected 9-(2-Mercaptoethyl)carbazole



Scheme 5.5 Synthesis of a Protected Thiol Bearing Two Mesogenic Side-Groups

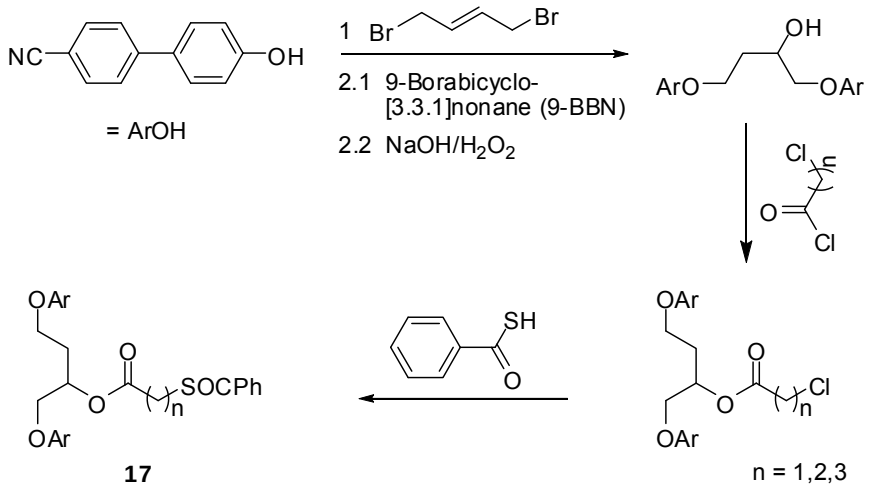


Table 5.1 Reaction Conditions and Results for 1,2-Polybutadiene Functionalization Using a Protected Thiol PhCOSR

entry[a]	[PB] (g/mL	[Thiol][b]	[AIBN] (g/mL)	rxn time (h)	X_{funct}[c] %	X_{cycl}[c] %	M_W[d] (kg/mol)	PDI[d]	new ^{1}H NMR peaks above 2.2 ppm for modified PB (all peaks are broad)
92kPB3[e,g]	0.004	1.6	0.005	6.2	40 ± 2	48 ± 3	199	1.07	7.71-7.43 (6H), 7.01-6.88 (2H), 4.22-4.08 (2H), 2.95-2.43 (4H)
92kPB6[f]	0.003	0.5	0.002	3.7	22 ± 2	34 ± 3	194	1.07	7.71-7.58 (4H), 7.54-7.46 (2H), 7.05-6.95 (2H), 4.19-4.12 (2H), 3.90-3.82 (2H), 3.77-3.67 (2H), 2.77-2.39 (4H)
92kPB8	0.004	1.2	0.001	4.4	36 ± 2	41 ± 3	146	1.06	8.12-7.95 (2H), 7.53-7.12 (6H), 4.53-4.26 (2H), 2.95-2.72 (2H), 2.65-2.2 (2H)
92kPB12	0.009	1.5	0.001	3.6	16 ± 1	18 ± 2	98	1.02	7.93-7.83 (2H), 7.88-7.80 (2H), 4.43-4.34 (2H), 2.87-2.44 (4H)
92kPB13[e]	0.003	1.9	0.001	2.0	4 ± 1	6 ± 2	122	1.07	8.55-8.46 (2H), 7.70-7.63 (1H), 7.28-7.22 (1H), 3.70-3.62 (2H), 2.82-2.43 (2H)
820kPB3	0.003	0.3	0.001	1.5	4 ± 1	4 ± 2	1420	1.45[h]	7.69-7.56 (4H), 7.56-7.45 (2H), 7.00-6.91 (2H), 4.19-4.10 (2H), 2.92-2.80 (2H), 2.74-2.49 (2H)
820kPB8[f]	0.004	1.3	0.002	3.0	27 ± 2	36 ± 3	1200	1.25	8.11-7.95 (2H), 7.49-7.12 (6H), 4.52-4.28 (2H), 2.94-2.71 (2H), 2.61-2.2 (2H)
820kPB12[f]	0.007	0.2	0.002	3.0	7 ± 1	11 ± 2	579	1.48[h]	7.94-7.87 (2H), 6.87-6.79 (2H), 4.45-4.33 (2H), 2.88-2.41 (4H)
820kPB13	0.007	0.2	0.002	2.5	2 ± 1	3 ± 2	1310	1.26	8.55-8.46 (2H), 7.70-7.64 (1H), 7.28-7.22 (1H), 3.68-3.62 (2H), 2.82-2.43 (2H)

[a]Modified PB polymers were named so that the prefix corresponds to the molecular weight of the starting 1,2-PB chain (98% 1,2 content), and the suffix represents the thioester reagent (Scheme 5.2) used. [b]In molar equivalents of 1,2-PB monomer units, estimated from the mass ratio of the protected thiol PhCOSR and 1,2-PB. [c]The fraction of reacted 1,2-PB units that bear functional groups (X_{funct}) and that are not functionalized (X_{cycl}); refer to text. The reported uncertainties were calculated based on the following uncertainties for the integrals S_1, S_2, and S_3: the measurement of S_3 is ~ 3% accurate, and the uncertainties in S_1 and S_2 are both < 1% of (S_1+S_2). [d]Measured as described in Section 5.2.1 using the Waters setup, except for polymer 92kPB12 (measurements obtained by MALLS). The 1,2-PB prepolymers had PDI of 1.07 and 1.26 for the 92 kg/mol and 820 kg/mol 1,2-PB chains, respectively. [e] ^{1}H NMR spectra are given in Figure 5.2. [f] ^{1}H NMR spectra are given in Appendix B. [g] ^{13}C NMR spectrum and GPC trace are given in Figures 5.3 and 5.4, respectively. [h]A small amount of cross-linking is believed to have occurred during workup and handling of the polymer product.

Table 5.2 Reaction Conditions and Results for 1,2-Polybutadiene Functionalization Using 3,5-Dinitrobenzoyl Chloride (DNBC)

entry[a]	[PB] (g/mL)	[BME][b]	[AIBN] (g/mL)	rxn time (h)	X_{funct}[d] %	X_{cycl}[d] %	M_W[e] (kg/mol	PDI[e]	new ^{1}H NMR peaks above 2.2 ppm for modified PB (all peaks are broad)
92kPB-OH[f]	0.03	0.6	0.002	1.9	20 ± 1	28 ± 2	151	1.07	3.77-3.65 (2H), 2.76-2.2 (4H)
820kPB-OH	0.02	0.4	0.001	3.0	15 ± 1	24 ± 2	1170	1.24	3.77-3.66 (2H), 2.76-2.3 (4H)

entry[a]	[PB-OH] (g/mL)	[DNBC][c]	[Et_3N][c]	rxn time (h)	X_{funct}[d] %	X_{cycl}[d] %	M_W[e] (kg/mol)	PDI[e]	new H NMR peaks above 2.2 ppm for modified PB (all peaks are broad)
92kPB-DNB[f]	0.02	3.3	5.0	4.0	20 ± 1	28 ± 2	158	1.08	9.24-9.20 (1H), 9.20-9.12 (2H), 4.64-4.51 (2H), 2.97-2.81 (2H), 2.81-2.41 (2H)
820kPB-DNB	0.02	2.5	3.5	3.3	15 ± 1	24 ± 2	1410	1.28	9.24-9.20 (1H), 9.20-9.12 (2H), 4.65-4.51 (2H), 2.97-2.83 (2H), 2.80-2.42 (2H)

[a]Modified PB polymers were named so that the prefix corresponds to the molecular weight of the starting 1,2-PB chain (98% 1,2 content), and the suffix represents the functional group added. [b]In molar equivalents of 1,2-PB monomer units. [c]In molar equivalents of 2-hydroxyethylthio- functionalized monomer units. [d]The fraction of reacted 1,2-PB units that bear functional groups (X_{funct}) and that are not functionalized (X_{cycl}); refer to text. The reported uncertainties were calculated based on the following uncertainties for the integrals S_1, S_2, and S_3: the measurement of S_3 is ~ 3% accurate, and the uncertainties in S_1 and S_2 are both < 1% of (S_1+S_2). [e]Measured as described in Section 5.2.1 using the Waters setup. The 1,2-PB prepolymers had PDI of 1.07 and 1.26 for the 92 kg/mol and 820 kg/mol 1,2-PB chains, respectively. [f] ^{1}H NMR spectra are given in Appendix B.

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