

A Simple Method to Generate Side-Chain Derivatives of Regioregular Polythiophene via the GRIM Metathesis and Post-polymerization Functionalization

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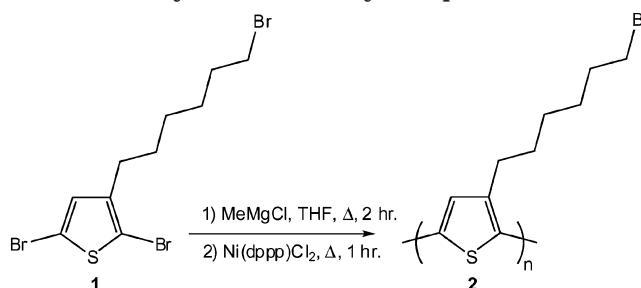
ABSTRACT: Regioregular poly(3-bromohexylthiophenes) have been synthesized via the GRIM method in high yield. Functionalization of these polymers with various groups afforded poly(3-alkylthiophenes) bearing 6-carboxylic acid, 6-amine, or 6-thiol functionalities. Analytical data for all polymers are consistent with quantitative functional group substitution.

Regioregular polythiophenes are important building blocks for new electrical applications such as field effect transistors and nanoscale materials. We discovered that regioregular polythiophene could self-assemble into polycrystalline structures that contribute to the high conductivity of the sample. One method that can add complexity to the family of polythiophene is side chain elaboration. The electronic and photonic properties of polyalkylthiophenes with functionalized side chains are remarkably sensitive to chemical and electrochemical perturbations, chemical structure, and ordering in solution.¹ These properties have made polythiophenes with functionalized side chains interesting materials for chemosensors.²

Generally, regioregular polythiophenes are made by incorporating the desired side chain in the reactive monomer, which is then polymerized by one of several methods. This strategy can be useful, however, due to functional group incompatibility may not afford high molecular weight polymers or may completely quench polymerization. As an example, our group has reported the synthesis of regioregular poly(thiophene-3-propionic acid) using a modified Stille method. However, CuO has to be used as cocatalyst, and we believe the low molecular weight of the polymer was around 8 kDa can be attributed to some degree of functional group incompatibility.^{2d} Another example of the limits of direct polymerization using the Rieke or McCullough methods is found in the preparation of regioregular poly(3-alkylthiophenes). The resultant polymer was found to be insoluble in chloroform, THF, and xylene, and the molecular weight was less than 5 kDa.³ Therefore, a synthetic strategy that allows for the functionalization of the thiophene after polymerization could be important and allow for a simple generation of plethora of polythiophenes.

Progress toward this goal has been made by several groups. Initially, Bäuerle and co-workers synthesized a thiophene monomer that incorporated an *N*-hydroxy-succinimide ester side chain.⁴ These side chains could withstand electrochemical polymerization, and was then easily substituted with other amine-containing functionalities. In the studies of redox states of well-defined para-conjugated oligothiophenes functionalized with poly(benzyl ether) dendrons performed in Fréchet's

Scheme 1. GRIM Method to Synthesize Regioregular Poly(3-(6-bromohexyl)thiophene)

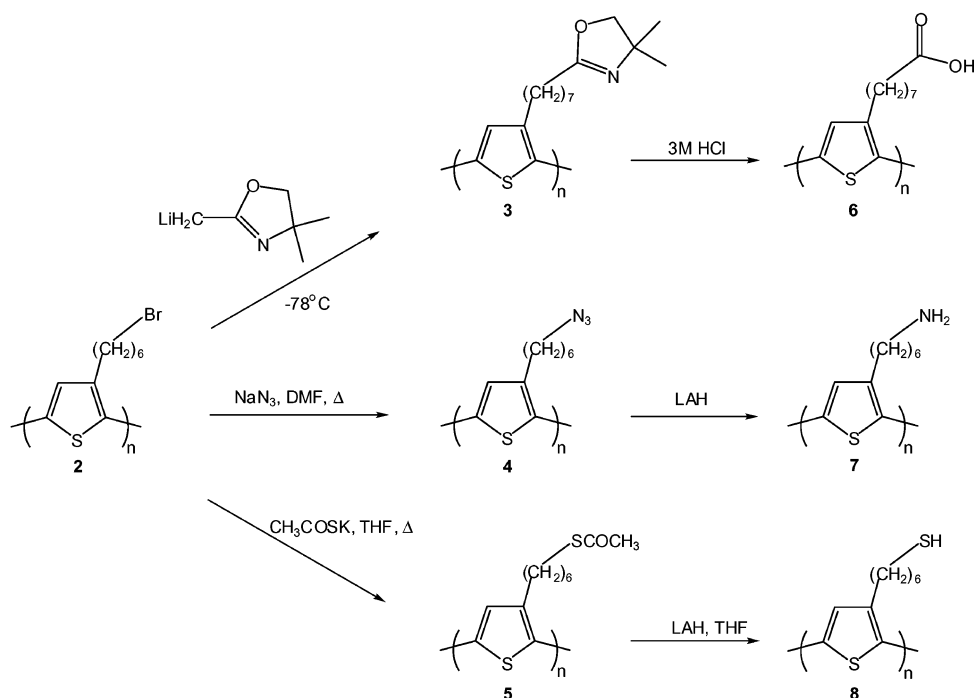


group, poly(benzyl ether) dendrimer grew from the benzyl ether attached onto one thiophene ring in thiophene oligomer.⁵

In 1998, Iraqi and co-workers synthesized a polymer of 3-(6-bromohexyl)thiophene by the McCullough method and functionalized the resulting material with 2-carboxyanthroquinone.⁶ The reaction afforded polymers which were ~87% functionalized. Additionally, other groups have reported the synthesis of regiorandom poly(3-(6-bromoalkyl)thiophenes) by FeCl₃ chemical oxidation.^{7,8}

Recently, we reported a simple method of synthesizing highly regioregular polythiophenes by Grignard metathesis method or GRIM method.⁹ We have been using this method in our lab to produce many different types of polythiophene with great success. Here, we report our attempts to produce poly[3-(6-bromoalkyl)thiophenes] by the Grignard metathesis method. Additionally, we will present typical results of our post-polymerization functionalization.

The GRIM polymerization of **1** to produce regioregular poly(3-(6-bromohexyl)thiophene) is shown in Scheme 1. We have found that the molecular weight and polydispersity of the polymer products can vary between individual polymerizations, depending upon monomer concentration and fractionation scheme. Our typical procedure calls for a monomer concentration of 0.125 M. This concentration yields polymers that have number-average molecular weights of 25 000–30 000 (by GPC in chloroform relative to polystyrene) and polydispersities of 1.5–2.2. If the monomer concentration is increased to 0.25 M, the resulting polymers have mo-

Scheme 2. Post-polymerization Functionalization of Poly(3-(6-bromohexyl)thiophene)

lecular weights of about 15 000–18 000 and polydispersities of 1.5–1.7. This can be attributed to the solubility of high molecular weight polythiophene in THF. As the molecular weight of polythiophene increases, the polymer becomes insoluble and precipitates out of solution, which results in lower M_n and polydispersities.

Fractionation of the polymer directly impacts the polydispersity. In our standard procedure, the crude polymer is first extracted with methanol, then with acetone, followed by hexanes, and last chloroform. This solvent series is quite acceptable and useful to obtain high molecular weight polymers with low polydispersities.¹⁰

The ultimate goal of synthesizing poly[3-(ω -bromoalkyl)thiophenes] is to further functionalize the polymer. We have successfully substituted several functionalities, such as carboxylic acids, amines, and thiols, as shown in Scheme 2. Typically, conversion from the bromoalkyl to the desired functionality is quantitative by ^1H NMR. Polymer **2** is quite stable to all of the reaction conditions we have attempted thus far. This provides a convenient route to polythiophenes with useful functional groups that are not stable to the standard polymerization conditions.

Polymer **6** was synthesized by reacting polymer **2** with excess lithiated 2,4,4-trimethyloxazoline at low temperature to form polymer **3**, followed by hydrolysis in 3M hydrochloric acid. The reaction is clean, with quantitative conversion in each step and an overall yield of 70%. The polymer is soluble in DMF and aqueous basic solvents.

Synthesis of polymer **7** was accomplished by reacting polymer **2** with sodium azide in DMF at reflux to form the azide derivative, **4**. Subsequently, polymer **4** was reduced with LAH to form the amine, **7**, in 70% overall yield. Once again, the individual reactions were extremely successful, with quantitative conversion in each. The resulting amine-substituted polymer was soluble in aqueous acidic solvents.

The derivatized polymer **8** was formed by the reaction of potassium thioacetate with polymer **2** to form the

thioester, **5**. Conversion to the thiol was accomplished by reduction with LAH. As with the previous polymers, conversion to the thiol was quantitative, with an overall yield of 80%. The resulting polymer was soluble in standard organic solvents.

The complete conversion of post-polymerization functionalization of polymer **2** was confirmed by the comparison of NMR spectrum of polymer **2** with NMR spectra of polymer **3**, **4**, and **5**. As shown in Figure 1a, the triplet at δ 3.4 assigned as the terminal methylene group α to the bromine shifts upfield to δ 2.2 as shown in Figure 1b. It is consistent with 2,4,4-trimethyl-2-oxazoline substitution. The singlet (δ = 3.88) in Figure 1b is assigned as the methylene group α to oxygen atom in 2,4,4-trimethyl-2-oxazoline. The complete substitution of bromide groups with azide groups is proved by the shift of the triplet representing methylene group α to the bromine from δ 3.40 (Figure 1a) to δ 3.25 (Figure 1c). After bromide groups were replaced by thiol acetate groups, the triplet at δ 3.4 assigned as the terminal methylene group α to the bromine shifts upfield to δ 2.9 as shown in Figure 1d, the singlet at δ 2.3 is assigned as the acetate methyl group of polymer **5**. This is consistent with thiolacetate substitution.

In conclusion, the Grignard metathesis or GRIM synthesis of poly[3-(6-bromoalkyl)thiophene], **2**, produces a good polymer with low polydispersity. The reaction is easily performed, and avoids the cryogenic conditions required by other methods for synthesizing regioregular polymers. Additionally, the resulting polymer can be readily transformed into a variety of functionalized polymers with outstanding efficiency.

Experimental Section

Synthesis of 3-Bromohexylthiophene. HPLC grade hexane was dried over CaH_2 , and dried THF were used as solvents. To a 500 mL three-necked round-bottom flask equipped with stirring was added 3-bromothiophene (30 g, 0.18 mol), and 250 mL of hexanes was added via syringe. The flask was chilled down to -40°C and the solution was stirred for 10 min. $n\text{-BuLi}$ (72 mL, 0.18 mol) was added dropwise via

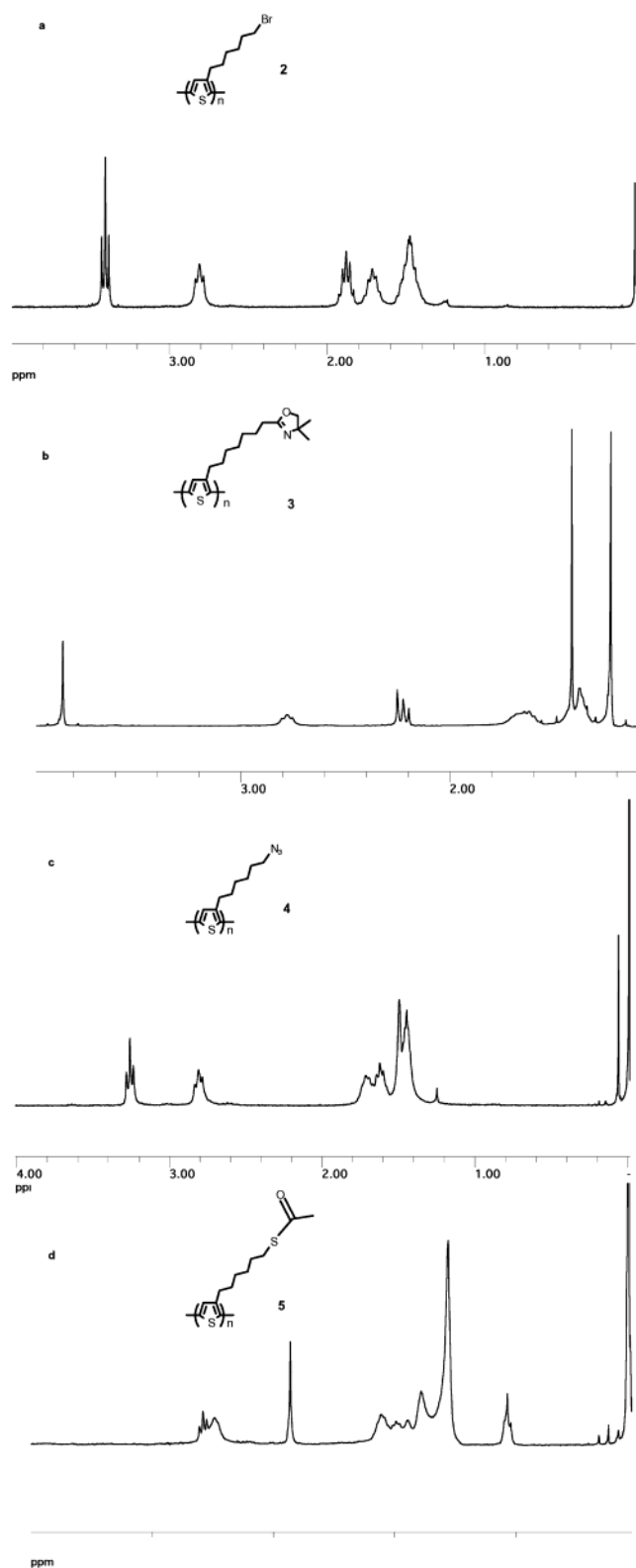


Figure 1. NMR comparison of polymers from post-polymerization functionalization of poly(3-bromohexylthiophene).

syringe at this temperature. After the mixture was stirred for 10 min, 15 mL of THF was added dropwise via syringe. The solution was stirred for 1 h, the cooling bath was removed, and the solution was allowed to warm to -10°C . Dibromohexane (110 mL, 0.72 mol) was added in one portion and the solution was warmed to room temperature. The solution was stirred for 2 h at room temperature, and then extracted with Et_2O (3×20 mL) and organic extracts were washed with water

(3×20 mL). The organic layer was dried over anhydrous MgSO_4 and the removal of solvent gave a crude product. The product was further purified by vacuum distillation. ^1H NMR (δ , CDCl_3): 7.24 (d, 1H), 6.92 (d, 1H), 3.40 (t, 2H), 2.64 (t, 2H), 1.86 (m, 2H), 1.65 (m, 2H), 1.5 (m, 2H), 1.2 (m, 2H). Anal. Calcd for $\text{C}_{10}\text{SH}_{15}\text{Br}$: C, 48.59; H, 6.12; Br, 32.32. Found: C, 48.38; H, 6.04; Br, 32.32.

Synthesis of 2,5-Dibromo-3-bromohexylthiophene, 1. 3-bromohexylthiophene (27.39 g, 0.11 mol) was dissolved in THF and acetic acid (135 mL:135 mL/v:v) in a 500 mL one-necked flask equipped for stirring. *n*-Bromosuccinimide (39.16 g, 0.22 mol) was added to the solution in one portion, and the solution was stirred for 1 h. Then the solution was extracted with Et_2O (3×50 mL); the organic extracts were washed with water (3×50 mL) and $\text{NaHCO}_3(\text{aq})$ (2×50 mL). The organic layer was dried over anhydrous MgSO_4 and the removal of solvent gave a crude product. Distillation at 134°C under 0.05 Torr gave 30.77 g of colorless 2,5-dibromo-3-bromohexylthiophene. ^1H NMR (δ , CDCl_3): 6.78 (s, 1H), 3.40 (t, 2H), 2.58 (t, 2H), 1.87 (m, 2H), 1.51 (m, 6H). Anal. Calcd for $\text{C}_{10}\text{SH}_{13}\text{Br}_3$: C, 29.63; H, 3.2; Br, 59.25. Found: C, 29.63; H, 3.18; Br, 59.21.

Synthesis of HT-Poly(3-bromohexylthiophene), 2. To a three-necked 100 mL round-bottom flask equipped for stirring was added 2,5-dibromo-3-hexylbromothiophene (4.05 g, 10 mmol) and 80 mL of freshly distilled THF. CH_3MgBr (3.3 mL, 10 mmol) was added via syringe. The solution was heated to reflux and stirred for 2 h, and $\text{Ni}(\text{dppp})\text{Cl}_2$ (27 mg, 0.05 mmol) was added. The mixture was stirred for 1 h, and then the reaction was quenched with methanol. The solid polymer was washed with methanol by using a Soxhlet extractor. The polymer then was dissolved by Soxhlet extraction with chloroform, the chloroform was removed, and the residue was dried under vacuum to yield 1.51 g of 98% head-to-tail coupled poly(3-bromohexylthiophene) with 61% yield. ^1H NMR (δ , CDCl_3): 6.95 (s, 1H), 3.40 (t, 2H), 2.80 (t, 2H), 1.88 (m, 2H), 1.70 (m, 2H), 1.51 (m, 4H). Anal. Calcd for $\text{C}_{10}\text{SH}_{13}\text{Br}$: C, 48.9; H, 5.3; S, 13.1; Br, 32.65. Found: C, 49.02; H, 5.43; S, 13.11; Br, 32.74. ($M_n = 26430$ and $\text{DP} = 1.6$ by GPC.)

Synthesis of 2,5-Poly(3-(2(4,4-dimethyloxazolin-2-yl)heptyl)thiophene), 3. To a three-necked 100 mL round-bottom flask was added freshly dried 2,4,4-trimethyloxazoline (2.26 g, 20 mmol), and 30 mL of dry THF was added via syringe. The flask was cooled to -70°C , and the solution was stirred for 10 min. *n*-BuLi (7.2 mL, 18 mmol) was added dropwise via syringe to the solution. The solution was stirred for 2 h. Poly(3-bromohexylthiophene) (0.49 g, 2 mmol) was dissolved in 30 mL of dry THF. The polymer solution was transferred to oxazoline lithium salt solution via cannula, and the addition was completed in 30 s. The cooling bath was removed, and the mixture was stirred for 1 h and quenched in hexane. The solid polymer was washed with hexane by using a Soxhlet extractor. Thus, 519 mg of polymer was obtained with 93% yield. ^1H NMR (δ , CDCl_3): 6.95 (s, 1H), 3.88 (s, 2H), 2.80 (t, 2H), 2.25 (t, 2H), 1.70 (m, 2H), 1.40 (m, 8H), 1.22 (s, 6H). ($M_n = 28790$ and $\text{DP} = 1.5$ by GPC.)

Synthesis of HT-2,5-Poly(3-hexyl azide thiophene), 4. To a three-necked 100 mL round-bottom flask equipped for stirring was added poly(3-bromohexylthiophene) (490 mg, 2 mmol), 100 mL of DMF was added, and the solution was heated to reflux. Sodium azide (1.3 g, 20 mmol) was added in one portion, and the mixture was stirred overnight at reflux temperature of DMF. The reaction was quenched in methanol. The solid polymer was washed with methanol by using a Soxhlet extractor. Thus, 330 mg polymer was obtained in 80% yield. ^1H NMR (δ , CDCl_3): 6.95 (s, 1H), 3.25 (t, 2H), 2.80 (t, 2H), 1.51 (m, 8H). ($M_n = 25290$ and $\text{DP} = 1.6$ by GPC.)

Synthesis of HT-2,5-Poly(3-hexylthiolacetate thiophene), 5. To a three-necked 100 mL round-bottom flask equipped for stirring was added poly(3-bromohexylthiophene) (490 mg, 2 mmol); 50 mL of dry THF was added, and the solution was heated to reflux. Potassium thiolacetate (1.14 g, 10 mmol) was added in one portion, and the mixture was stirred overnight at reflux temperature of THF. The reaction was quenched in methanol. The solid polymer was washed with methanol by using a Soxhlet extractor. Thus, 430 mg

polymer was obtained in 93% yield. ^1H NMR (δ , CDCl_3): 6.95 (s, 1H), 2.80 (t, 2H), 2.50 (t, 2H), 0.51 (m, 8H). (M_n = 25380 and DP = 1.6 by GPC.)

Synthesis of HT-2,5-Poly(3-octanic acid thiophene), 6.

A sample of 2,5-poly(3-(2(4,4-dimethyloxazolin-2-yl)heptyl)-thiophene) (278 mg, 1 mmol) was dissolved in 3 N HCl (60 mL) in a 300 mL one-neck round-bottom flask and heated to reflux for 12 h. The solid was filtered, rinsed with H_2O , and dried to recover the product in 86% yield. ^1H NMR (δ , pyridine): 7.09 (s, 1H), 2.67 (t, 2H), 2.20 (t, 2H), 1.49 (m, 4H), 1.09 (m, 6H). Anal. Calcd for $\text{C}_{12}\text{H}_{16}\text{SO}_2$: C, 64.3; H, 7.14; O, 14.3; N, 0, Br, 0 (C:O = 4.5:1). Found: C, 62.16; H, 7.27; O, 13.08; N, 0 Br, 0 (C:O = 4.7:1).

Synthesis of HT-2,5-Poly(3-hexylamine thiophene), 7.

To a three-necked 100 mL round-bottom flask equipped for stirring was added poly(3-hexyl azide thiophene) (400 mg, 2 mmol), and then 30 mL of dry THF was added via syringe. Lithium aluminum hydride in THF solution (2 mL, 4 mmol) was injected via syringe, and the solution was stirred for 30 min and quenched in 3 M HCl(aq). The precipitate was filtered and dried under vacuum, and 340 mg of polymer was obtained in 94% yield. ^1H NMR (δ , tetrahydrofuran): 6.95 (s, 1H), 2.80 (t, 2H), 2.52 (t, 2H), 1.32 (m, 8H). Anal. Calcd for $\text{C}_{10}\text{H}_{16}\text{NS}$: C, 65.9; H, 8.79; S, 17.6; N, 7.6 (C:N = 8.7). Found: C, 47.56; H, 6.87; S, 12.15; N, 5.23 (C:N = 9.1). M_n = 24820 and DP = 1.6 by GPC.

Synthesis of HT-2,5-Poly(3-hexylthiol thiophene), 8.

To a three-necked 100 mL round-bottom flask equipped for stirring was added poly(3-hexylthiolacetatethiophene) (230 mg, 1 mmol), and 50 mL of dry THF was added via syringe. Lithium aluminum hydride in THF solution (5 mL, 5 mmol) was injected via syringe, and the solution was stirred for 30 min and quenched in methanol. The solid polymer was washed with methanol by using a Soxhlet extractor. Thus, 180 mg of polymer was obtained in 91% yield. ^1H NMR (δ , tetrahydro-

furan): 6.95 (s, 1H), 2.80 (t, 2H), 2.52 (q, 2H), 1.32 (m, 8H). Anal. Calcd for $\text{C}_{10}\text{H}_{14}\text{S}_2$: C, 60.0; H, 7.0; S, 32.3 (C:S = 1.86). Found: C, 58.1; H, 7.2; S, 29.5 (C:S = 1.96). M_n = 20938 and DP = 1.6 by GPC.

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