


Article

Functionalized Polyisobutylene and Liquid/Liquid Separations as a Method for Scavenging Transition Metals from Homogeneously Catalyzed Reactions

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Abstract: Ethanedithiol-functionalized polyisobutylene was prepared in one step by a photoinitiated thiol-ene “click” reaction starting from ethanedithiol and polyisobutylene (PIB). The functionalized oligomer product was then used as a soluble sequestrant for transition metals. This PIB-bound thioether-thiol ligand is phase selectively soluble in alkanes and it quantitatively sequesters common transition metals like Cu²⁺ and Pd²⁺ into an alkane phase, separating them from polar solvents in a biphasic liquid/liquid separation. The chelating thioether-thiol ligand was also successfully used to remove Cu and Pd transition metal catalyst residues from products in crude reaction mixtures in both azide/alkyne click reactions and cross-coupling reactions using a liquid/liquid extraction. Separation efficiencies exceeding 95% and in many cases 99% were achieved.

Keywords: polyisobutylene; homogeneous catalysis; green chemistry; chelation; sequestrant

1. Introduction

While homogeneous catalysis using transition metals is now commonly used in synthesis of most drugs and chemical intermediates [1,2], the separation of the metal catalysts from the desired products remains a problem. This issue has been addressed in a variety of ways [3,4], and the oldest approach is to use solid state sequestrants. There is an immense arsenal of ion exchange resins and functionalized inorganic supports that can sequester metals or metal catalyst residues [5–11]. These materials like ion exchange resins are insoluble and have the advantage that they are physically separable from product solutions. However, metal catalyst residues are often present with other ligands that make insoluble sequestrants less effective. In other cases, catalyst residues are present in the form of colloids that might not be as effectively sequestered by solid supported scavengers. Thus, it is not surprising that there is still ongoing work to develop better metal scavenging systems. This includes developing novel homogeneous scavenging agents. Indeed, recent reports have suggested that soluble sequestrants that can be separated by liquid/liquid or liquid/solid separations can be more effective than conventional solid sequestrants. For example, Gallagher and Vo showed that copper catalyst residue sequestration by water soluble dithiocarbamate sequestrants was more effective in large scale pharmaceutical synthesis than solid sequestrants [12]. Szczepaniak et al. reported a homogeneous isocyanate scavenger that was extremely efficient at precipitation of ruthenium catalyst residues followed by simple filtration [13]. Similarly, Baker et al. prepared a perfluorinated

ketone with temperature dependent solubility for heavy metal removal [14]. In another report, Ren et al. demonstrated that in the case of cephalosporin antibiotic synthesis, solid state scavengers had only limited success in palladium sequestration in comparison with homogeneous organosulfur scavengers [15]. Those successes and our past work where we developed phase selectively soluble polymeric ligands that immobilize transition metal catalysts suggested to us that alkane phase selectively soluble sequestrants would be practical sequestering agents too [5,6,15–22].

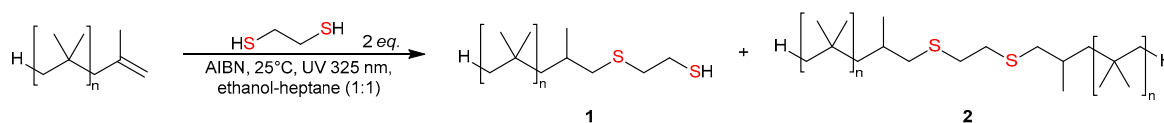
Based on that prior work, we reasoned that polyisobutylene (PIB) could be functionalized to make it a capable sequestrant. Commercially available alkene-terminated PIB oligomers have a reactivity identical to that of low molecular weight analogs that enables their efficient functionalization [23]. Moreover, if dilute heptane solution of such functional PIB were used in a liquid/liquid extraction in a water/heptane biphasic mixture, it would be expected to lead to essentially no PIB leaching to the aqueous phase. Heptane has a known solubility in water of 3.37 ppm under ambient conditions [24]. If we assume polyisobutylene solubility in heptane equal to that in water, addition of 1000 ppm solution of PIB in heptane to water would lead to ca. 3 ppb solubility of PIB in water. Since hydrocarbon solubility in water decreases dramatically with increase of molecular weight, PIB solubility in water is extremely low. Hence, its leaching in water is also negligibly low. Such quantitative phase separation was further demonstrated in our previous studies [25].

The work described below confirms that simple oligomer PIB derivatives are excellent sequestrants that quantitatively phase separate and sequester transition metals from aqueous or polar organic solutions. Readily available polyisobutylene thioether thiol was successfully utilized for the liquid-liquid extractions of transition metals such as Co^{2+} , Ni^{2+} , Cu^{2+} , Pd^{2+} and Ru^{3+} from aqueous or polar organic solutions. This functionalized PIB derivative remains efficient even in the presence of competing ligands that are typically present in crude reaction mixtures obtained in Pd catalyzed cross-coupling reactions [26–31], as well as in a Cu(I)-catalyzed alkyne azide cyclization (CuAAC) reaction [32].

2. Results and Discussion

2.1. Synthesis of Polymer-Supported Sequestrant

Dithiol-functionalized polybutadiene **1** was prepared via a green thiol-ene “click” reaction [33] using commercially available 1,2-ethanedithiol and alkene-terminated PIB Glissopal 1000 ($DP_n = 18$) as depicted in Scheme 1. Two equivalents of dithiol were used to avoid formation of undesired dimer **2** that is typical for equimolar reagent ratio (Figure S2). While others have shown that functional thiols can be attached to polyolefin oligomers with thiol-ene thermal chemistry [34], in our hands the photochemical approach described by Storey worked better [35]. Photoinitiation with 365 nm UV light of the PIB-alkene in 8 h afforded a mixture of the desired compound **1** and bis-adduct **2** (Figure S2). The desired oligomer **1** was purified and isolated as a clear viscous liquid in 92% yield and characterized by ^1H and ^{13}C -NMR spectroscopy (Figures S3 and S4). Based on the ^1H -NMR integral intensities of polyisobutylene backbone and functional chain end (Figures S1 and S3), each polymer chain contains one thiol-thioether unit per chain. SEC (Figure S5) revealed slight increase of molecular weight that is consistent with theoretical expectations, while dispersity and molecular weight distribution remain essentially the same. This allows to estimate the degree of the functionalization on the level of 0.92 mmol/g or 5.9% of sulfur by weight.



Scheme 1. Synthesis of the polymer **1**.

2.2. Determination of Sequestration Activity of **1** under Biphasic Conditions

A series of experiments were performed to determine the ability of **1** to sequester metals (in particular Cu^{2+} and Pd^{2+}) from various polar solvents including water under biphasic conditions. These initial studies involved sequestration of transition metal cations such as Co^{2+} , Ni^{2+} , Cu^{2+} , Pd^{2+} and Ru^{3+} from solutions of their salts in deionized water, methanol or acetonitrile by a heptane solution of **1**. In a typical experiment (Figure 1), a solution of sequestrant in heptane was added to the solution of CuSO_4 in water and shaken for 2 h with formation of an emulsion which separated into two distinct layer on standing. During this time, visually observed discoloration of the aqueous phase qualitatively indicated a high level of Cu^{2+} sequestration. Quantitative inductively coupled plasma optical emission spectroscopy (ICP-OES) analysis of the polar phase indicated 60-fold decrease of copper content (Table 1) that confirmed this visual observation. A control experiment with pure heptane did not result in any metal extraction based on ICP-OES analysis.

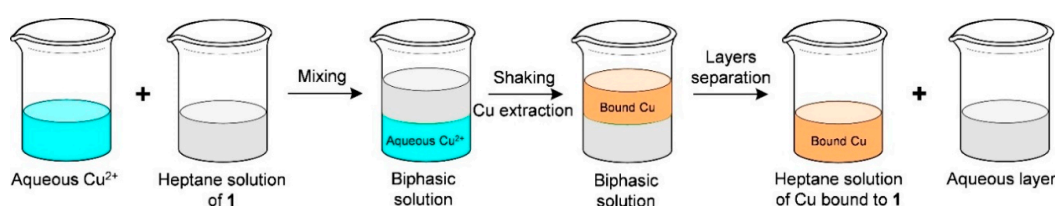


Figure 1. Schematic representation of copper sequestration from aqueous solution.

Table 1. Results of metal sequestration by **1** from model solutions under biphasic conditions.

Entry	Metal	Solvent	Time/h	Contents/ppm ¹		Sequestration Efficiency/%
				Initial	Final	
1	Co	water	4	26.0	17.4	33.1
2		water ²	4	26.0	2.64	89.8
3	Ni	water	4	26.0	17.9	31.2
4		water ²	4	26.0	3.72	85.7
5	Cu	water	2	21.6	0.360	98.3
6		MeOH	2	14.4	0.0250	99.8
7	Ru	water	4	26.0	1.02	96.1
8		water ²	4	26.0	0.0200	99.9
9	Pd	water	2	500	0.270	99.9
10		water	0.25	22.5	0.120	99.5
11		water ²	1.5	26.8	0.0250	99.9
12		CH ₃ CN	0.25	50.0	2.90	94.2
13		CH ₃ CN	1.5	50.0	0.160	99.7

¹ 6 eq. of **1** were used for extraction. ² pH = 10.0.

According to the results in Table 1, oligomer **1** demonstrates good to excellent sequestration efficiency for a variety of transition metals under biphasic conditions. The best results were obtained for copper, palladium and ruthenium ions (Table 1, entries 5–13). In case of Co^{2+} and Ni^{2+} cations, sequestration efficiency for neutral solutions was modest but it significantly increased under basic conditions. The same trend was observed for other metals. This observation can be explained by formation of poorly soluble metal hydroxides with enhanced affinity to sequestrant **1**. Although 99.5% of palladium was absorbed from water solution in only 15 min, sequestration from acetonitrile required extended times to achieve the same efficiency. This result is attributed to competitive complexation of Pd^{2+} cation by acetonitrile.

2.3. Competitive Sequestration of Palladium Solutions Containing Other Ligands

Inspired by these results, we investigated whether a heptane solution of **1** could competitively sequester palladium species from polar organic solutions in the presence of other ligands that are

commonly used in catalytic reactions. According to ICP-OES results (Table 2, initial Pd contents 50 ppm) high levels of Pd were sequestered by **1** in 4 h in most cases. Sequestration efficiency tended to increase with time and generally exceeded 96% except for samples where Pd was complexed by P(*o*-Anisyl)₃, P(*o*-Tolyl)₃, RuPhos, DPPF and Hermann's ligand. Even in those cases *ca.* 90–95% of Pd could be removed with **1** if the extraction time was increased.

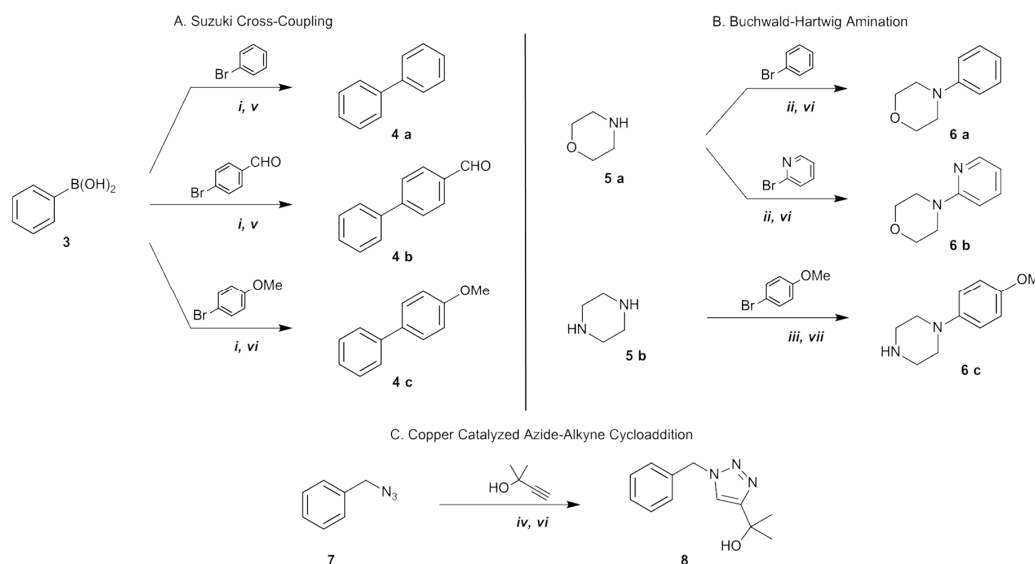
Table 2. Results of competitive sequestration of palladium complexes from acetonitrile solutions.

Pd complex	Contents/ppm ¹		Efficiency/%	
	in 4 h	in 12 h	in 4 h	in 12 h
(PPh ₃) ₂ Pd(OAc) ₂	0.620	0.39	98.8	99.2
P(<i>o</i> -Anisyl) ₃) ₂ Pd(OAc) ₂	6.36	3.17	87.3	93.7
P(<i>o</i> -Tolyl) ₃) ₂ Pd(OAc) ₂	6.03	1.94	87.9	96.1
(PCy ₃) ₂ Pd(OAc) ₂	0.610	0.560	98.8	98.9
(RuPhos) ₂ Pd(OAc) ₂	9.24	2.01	81.5	96.0
(DPPF)Pd(OAc) ₂	10.2	2.67	79.5	94.7
(DPEPhos)Pd(OAc) ₂	2.08	1.02	95.8	98.0
(XPhos)Pd(OAc) ₂	0.820	0.440	98.4	99.1
Pd ₂ (dba) ₃	2.65	1.47	97.3	98.5
(C ₆ H ₅ CN) ₂ PdCl ₂	0.430	0.430	99.3	99.1
(CH ₃ CN) ₂ PdCl ₂	0.310	0.190	99.4	99.6
Herrmann's catalyst	8.05	5.19	83.9	89.6

¹ 6 eq. of **1** were used for extraction.

2.4. Biphasic Sequestration of Pd and Cu from Products of Catalytic Reactions

As noted in the introduction, metal sequestration and separation from products is especially important in catalytic reactions where the catalysts end up in a product phase. Our results in Tables 1 and 2 suggest that the soluble polymer bound sequesterant **1** should be useful in these cases. To explore this question, we studied the use of **1** for removal of the Pd residues from Suzuki cross-coupling and Buchwald-Hartwig amination reactions (Scheme 2). Similar studies were also carried out for a CuAAC reaction.



Scheme 2. Model Pd and Cu catalyzed reactions. *i*) 1 eq. ArBr, 0.025 eq. Pd(OAc)₂, 0.05 eq. P(*o*-Anisyl)₃, 2 eq. K₂CO₃, toluene, 110 °C, 12 h; *ii*) 1.05 eq. ArBr, 0.01 eq. Pd(OAc)₂, 0.02 eq. RuPhos, 1.2 eq. *t*-BuONa, neat, 110 °C, 12 h; *iii*) 0.9 eq. ArBr, 0.01 eq. Pd₂(dba)₃, 0.015 eq. *rac*-BINAP, 1.5 eq. *t*-BuONa, toluene/THF, 100 °C, 12 h; *iv*) 1 eq. alkyne, 0.15 eq. CuSO₄·5H₂O, 0.45 eq. sodium ascorbate, DCM/H₂O, 25 °C, 3 h; *v*) **1**, MeOH/heptane; *vi*) **1**, DCM/heptane/MeOH; *vii*) **1**, acetonitrile/heptane.

Reaction of phenyl boronic acid **3** with different substituted bromoarenes under typical coupling conditions using 2.5 mol% of Pd(OAc)₂ afforded biaryls **4a–c** in toluene (Scheme 2). The crude products **4a** and **4b** (dark brown) contained 275 ppm of Pd as measured by ICP-OES. However, when the crude products were dissolved in MeOH and shaken for 4 h with a 6-fold excess of **1** in a heptane solution, complete discoloration of the MeOH phase was observed as depicted in Figure 2. Quantitative ICP-OES analysis of the treated product showed that the Pd concentration decreased by 99.9 % (Table 3). However, in the case of the reaction leading to **4c**, the Pd recovery under the same biphasic conditions was not as efficient due to its poor solubility. A separate experiment where **1** was allowed to interact with the crude product mixture under homogeneous conditions led to three order of magnitude decrease of Pd contents. In this case the crude **4c** was mixed with 6-fold excess of **1** in DCM and stirred at ambient temperature for 2 h. After solvent removal, the desired 4-methoxybisphenyl **4c** was isolated by liquid-liquid fractionation in MeOH-heptane 1:1 (*v/v*) mixture.



Figure 2. Qualitative visual photographs showing the results of Pd sequestration from crude compounds **4a,b**.

Table 3. Results of palladium/copper sequestration from model reaction mixtures.

Substrate	Metal Concentration/ppm ¹		Sequestration Efficiency/%
	Crude	Treated	
4a	275	0.170	99.9
4b	275	0.180	99.9
4c	275	0.230	99.9
6a	171	1.25	99.3
6b	246	0.130	99.9
6c	290	63.2 ²	78.2 ²
	290	9.01 ³	96.9 ³
8	727	0.300	99.9

¹ 6 eq. of **1** were used for extraction. ² pH = 10.0. ² at 25 °C; ³ at 80 °C.

Bromobenzene and 2-bromopyridine were successfully coupled to morpholine under neat conditions using 1 mol% of Pd(OAc)₂ and RuPhos as a ligand to afford compounds **6a** and **6b**. Again, a high level of removal of the Pd residues from the final product was achieved under biphasic conditions. A third example of this reaction that led to formation of N-(4-anisyl)piperazine **6c** was slightly less successful and afforded only 63% Pd sequestration at ambient temperature. As was true for the methoxybisphenyl **4c** example above, this poor sequestration efficiency was presumed to result from the modest solubility of the crude product in the solvent mixture. In this case, heating the biphasic mixture of acetonitrile solution of the product **6c** and heptane solution of **1** at 80 °C for 4 h led to 96.9% sequestration of the Pd catalyst residue.

An azide-alkyne “click” reaction between benzyl azide **7** and dimethyl ethynyl carbinol in the presence of 15 mol% of Cu led to formation of triazole **8**. Copper sequestration afforded a nearly 2500-fold reduction of residual Cu amount in the reaction product (Table 3), an extraction efficiency that is more than 99.9 %.

2.5. ^1H -NMR Spectroscopic Studies of the Mode of Pd-chelation by **1**

^1H -NMR spectroscopy titration of **1** with palladium acetate was used to better understand the complexation of **1** to Pd^{2+} (Figure 3). Complexation of Pd^{2+} to **1** led to a change in the chemical shift of methylene groups adjacent to the sulfur atoms as well as to the significant signal broadening. Signals of ligand **1** were detected up to 1:2 ratio of $[\text{Pd}^{2+}]:[\textbf{1}]$, while saturation was achieved at the equimolar $[\text{Pd}^{2+}]:[\textbf{1}]$ ratio. At this stage, new signal of acetate protons appeared. It's shifted upfield from δ 2.10 ppm to 2.00 ppm that corresponds to free palladium acetate [36]. Based on these observations we suggest chelation of Pd^{2+} with both coordination sites similarly to thioglycolic acid [37].

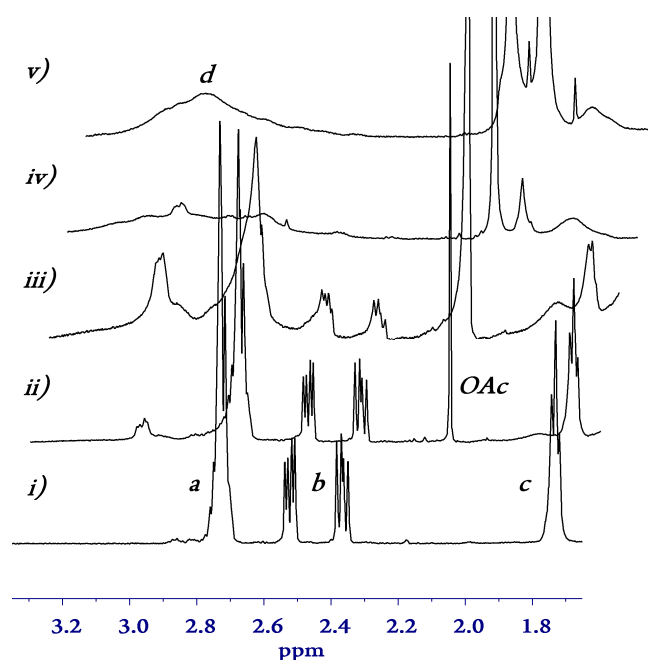
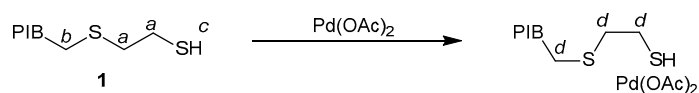


Figure 3. Results of ^1H -NMR spectroscopic titration of **1** with $\text{Pd}(\text{OAc})_2$. See Scheme 3 for signal assignment. Quantities of $\text{Pd}(\text{OAc})_2$: i) 0 eq.; ii) 0.2 eq.; iii) 0.5 eq.; iv) 1 eq.; v) 2 eq.



Scheme 3. Tentative Pd chelation.

3. Materials and Methods

3.1. General

All the reactions were performed using standard Schlenk techniques under a dry argon atmosphere. Products were purified with flash chromatography on Merck silica gel (particle size 230–400 mesh, porosity 60 Å).

NMR spectra were recorded on a Bruker Avance II 400 (Bruker, Zurich, Switzerland, strength of the magnetic field is 9.4 T, operating frequencies are 400 MHz for ^1H and 100 MHz for ^{13}C) or Bruker Avance II 600 (Bruker, Zurich, Switzerland, strength of the magnetic field is 14.1 T, operating frequencies are 600 MHz for ^1H and 150 MHz for ^{13}C) spectrometers in CDCl_3 at 298 K. Chemical shifts

are expressed in parts per million with chloroform signals as internal reference ($\delta = 7.26$ ppm in ^1H and 77.16 ppm in ^{13}C -NMR). In case of polymer solutions, relaxation delay was increased to 10 s to optimize the accuracy of integration.

Number-average molar mass (M_n) and dispersity (D) values of the polymer samples were determined by SEC. Analyses were conducted on a system composed of Waters 515 HPLC pump (Waters S.A.S., Saint-Quentin En Yvelines, France), Agilent 1260 Autosampler (Agilent Technologies France, Les Ulis, France), Varian ProStar 500 column valve module (Agilent Technologies France, Les Ulis, France), set of three Waters columns (Styragel Guard Column, 20 μm , 4.6 mm \times 30 mm, Styragel HR3, 5 μm , 7.8 mm \times 300 mm and Styragel HR4E, 5 μm , 7.8 mm \times 300 mm) and Wyatt Optilab rEX differential refractive index detector (Wyatt Technology France, Toulouse, France) using tetrahydrofuran as an eluent at a flow rate of 1.0 mL min^{-1} (35 $^\circ\text{C}$). The column system was calibrated with PMMA standards (ranging from 1.120 to 138.600 kg mol^{-1}) using the Landau-Kuhn-Mark-Houwink-Sakurada equation [38]. Prior to injection, samples were diluted to a concentration of 5 mg mL^{-1} and filtered through 0.45 μm Nylon syringe filters.

Metal concentrations were measured using a Thermo Scientific iCAP 6000 Series inductively coupled plasma – optical emission spectrometer (ICP-OES, Thermo Fisher Scientific, Waltham, MA, USA) equipped with autosampler (ASx 260). Standard deviations (SD), limits of detection (LOD) and limits of quantification (LOQ) are listed in Table S1, calibration curves are depicted in Figures S6–S10.

Aqueous solutions were analyzed with ICP-OES without additional sample treatment. Organic solutions were dried under reduced pressure, remaining solids were mixed with concentrated nitric acid (2 mL) in a glass vial and heated for 24 h at 100 $^\circ\text{C}$. If sample was not completely digested, concentrated sulfuric acid (2 mL) was added and heating was continued at 120 $^\circ\text{C}$ for 24 h. Obtained solutions were cooled to room temperature and adjusted with 4% aqueous nitric acid to initial volume prior to ICP-OES analysis.

Alkene terminated polyisobutylene (PIB, Glissopal[®] 1000) was received as a gift from BASF and used as is. All other reagents and solvents were commercially supplied by Sigma Aldrich and used without further purification, unless otherwise stated.

3.2. Synthesis of ((2-mercaptoethyl)thio)polyisobutylene 1

Thermal initiation. PIB (10.0 g, 10 mmol), 1,2-ethanedithiol (1.67 mL, 20 mmol) and appropriate initiator (1.0 mmol, 164 mg of AIBN or 146 mg of DTBP) were dissolved in 140 mL of heptane-ethanol 1:1 (*v/v*) mixture, degassed by three freeze-pump-thaw cycles and stirred at 25 or 70 $^\circ\text{C}$ for 24 or 48 h (Table 4, entries 1–4).

Table 4. Conditions used for the synthesis of polymer 1.

Entry	$t/^\circ\text{C}$	Initiator	Time/h	Conversion/%
1	70	AIBN	24	100
2	70	DTBP	24	100
3	25	AIBN	48	50
4	25	DTBP	48	20
5	25	UV	8	100

Photoinitiation. PIB (10.0 g, 10 mmol), 1,2-ethanedithiol (1.67 mL, 20 mmol) and AIBN (1.0 mmol, 164 mg) were dissolved in 140 mL of heptane-ethanol 1:1 (*v/v*) mixture, degassed by three freeze-pump-thaw cycles and stirred at room temperature with irradiation at 365 nm for 8 h (Table 4, entry 5).

Reaction mixture workup. After the reaction was complete, deionized water (10 mL) was added to the solution with formation of biphasic system. The heptane layer was washed twice with 90% ethanol (2 \times 50 mL), dried over anhydrous Na_2SO_4 and concentrated under reduced pressure.

Crude product was subjected to chromatography, eluting with heptane-ethyl acetate 4:1 (v:v) mixture, that afforded desired **1** as a colorless oil.

¹H-NMR (600 MHz, CDCl₃, 298 K, δ): 2.77–2.69 (m, 4H; CH₂S(CH₂)₂SH), 2.52 (dd, ¹J = 12.4, ³J = 5.4 Hz, 1H; CH₂S(CH₂)₂SH), 2.37 (dd, ³J = 12.3, ³J = 8.0 Hz, 1H; CH₂S(CH₂)₂SH), 1.75–1.71 (m, 1H; CH(CH₃)CH₂S), 1.54–1.33 (m, 38H; PIB-CH₂), 1.21–0.99 (m, 120H; PIB-CH₃). ¹³C{¹H} NMR (150 MHz, CDCl₃, 298 K, δ): 59.7, 59.6, 59.4, 59.0, 58.4, 57.1, 52.7, 42.4, 38.3, 38.2, 38.0, 37.9, 37.0, 36.2, 32.7, 32.6, 31.4, 31.3, 31.2, 30.9, 29.7, 29.4, 29.3, 25.0, 22.7.

3.3. General Procedure for Metal Sequestration from Polar Solvents

CuSO₄·5H₂O (98.2 mg), Co(NO₃)₂·6H₂O (123.5 mg), NiSO₄·6H₂O (112.0 mg) or RuCl₃ (51.3 mg) were dissolved in deionized water (50 mL) to obtain 500 ppm solutions. Pd(OAc)₂ (52.7 mg) was dissolved in water-acetonitrile 4:1 (v/v) mixture. These solutions were further diluted with appropriate solvent to prepare the final metal solutions (Table 1).

Stock solution of **1** in heptane with 0.1 M concentration (1 mmol of **1** in 10 mL of solution) was prepared by adjusting 1.09 g of polymer with heptane to 10 mL. Amount of this stock solution was calculated according to the formula:

$$V_{stock} = \frac{0.6 \times x_{Metal}(\text{ppm})}{M_{w\ Metal}(\text{g} \cdot \text{mol}^{-1})} (\text{mL})$$

Calculated volume was adjusted with heptane to 10 mL and used for the sequestration (*vide infra*). Such ligand concentration affords 6-fold excess of **1** compared to extracted metal.

The chelation was typically performed by shaking metal solutions (10 mL) with 10 mL of heptane solution of **1** at room temperature. After separation of layers, polar solution was analyzed with ICP-OES.

3.4. Procedures for Model Pd and Cu Catalyzed Reactions

i. A screw-cap vial equipped with a magnetic stir bar was charged with appropriate aryl bromide (0.81 mmol), phenylboronic acid **3** (100 mg, 0.82 mmol), Pd(OAc)₂ (4.6 mg, 2 mmol), P(*o*-Anisyl)₃ (14.5 mg, 4 mmol), K₂CO₃ (226.6 mg, 1.64 mmol) and toluene (3 mL). The reaction mixture was stirred at 110 °C for 12 h, cooled down and diluted with 6 mL of diethyl ether-water 1:1 (v/v) mixture. Then organic phase was separated and concentrated under reduced pressure yielding a crude product that was further subjected to metal sequestration.

ii. A screw-cap vial equipped with a magnetic stir bar was charged with appropriate aryl bromide (1.05 mmol), morpholine **5a** (87.1 mg, 1 mmol), Pd(OAc)₂ (4.5 mg, 2 mmol), RuPhos (37.0 mg, 4 mmol), and *t*-BuONa (115.0 mg, 1.2 mmol). The reaction mixture was stirred at 110 °C for 12 h, cooled down and diluted with 6 mL of DCM-water 1:1 (v/v) mixture. Then organic phase was separated, adjusted to 10 mL volume with DCM and subjected to metal sequestration.

iii. Solution of piperazine **5b** (100 mg, 1.18 mmol), Pd₂(dba)₃ (8.9 mg, 0.011 mmol) and *rac*-BINAP (10 mg, 0.016 mmol) in toluene (2 mL) was mixed with 4-bromoanisole (0.134 mL, 1.07 mmol) and suspension of *t*-BuONa (154 mg, 1.6 mmol) in THF (1 mL) in a screw-cap vial. Obtained mixture was heated to 100 °C for 12 h, cooled down and diluted with 6 mL of ethyl acetate-water 1:1 (v/v) mixture. After separation of organic phase, aqueous solution was extracted with additional 3 mL of ethyl acetate. Combined organic layers were washed with brine and concentrated under reduced pressure yielding a crude product that was further subjected to metal sequestration.

iv. Solution of benzyl azide **7** (84.1 mg, 1 mmol), 2-methyl-3-butyn-2-ol (84.1 mg, 1 mmol), sodium ascorbate (90 mg, 0.45 mmol) and CuSO₄·5H₂O (38.0 mg, 0.15 mmol) in 5 mL of DCM-water 1:1 (v/v) mixture was stirred at 25 °C for 6 h. Then it was diluted with same solvent mixture to 15 mL, organic phase was separated and subjected to metal sequestration.

3.5. Pd and Cu sequestration from Model Reaction Mixtures

v: Crude product was dissolved in methanol (10 mL) and shaken with solution of **1** in heptane (10 mL) at 25 °C for 4 h.

vi: Crude DCM solution (10 mL) was mixed with solution of **1** (10 mL) and stirred at 25 °C for 4 h. Then it was concentrated under reduced pressure, diluted with heptane (5 mL) and extracted three times with methanol.

vii: Crude product was dissolved in acetonitrile (10 mL) and was shaken with solution of **1** (10 mL) at 25 °C or 80 °C for 4 h.

Methanol or acetonitrile solutions obtained after the phase separation were concentrated under reduced pressure yielding desired products. Metal contents were determined with ICP-OES after digestion as described above.

4. Conclusions

In conclusion, the results discussed above show that a heptane soluble PIB-bound thioether thiol sulfur metal scavenger that is easy to synthesize from inexpensive commercially available starting materials is highly effective at removing metals from aqueous or polar organic solutions under biphasic conditions. In many cases, this sequestering agent removes >99% of the metal from the aqueous or polar organic phase. This soluble oligomer scavenging agent is successful at metal sequestration even when there are other ligands present and can be used for the treatment of crude reactions mixtures of catalytic reactions where the metal is visually present in colloidal form. Studies to explore the recyclability of these sequestrants and to develop other analogs are ongoing.

Supplementary Materials: The following are available online at <http://www.mdpi.com/2076-3417/9/1/120/s1>, Table S1. Standard deviations, limits of detection and limits of quantification for ICP-OES; Figure S1. ¹H-NMR spectrum of the starting alkene terminated PIB; Figure S2. ¹H-NMR spectrum of mixture of **1** and **2**; Figure S3. ¹H-NMR spectrum of ((2-mercaptoethyl)thio)polyisobutylene **1**; Figure S4. ¹³C{¹H} NMR spectrum of ((2-mercaptoethyl)thio)polyisobutylene **1**; Figure S5. SEC traces of PIB before and after functionalization; Figure S6. ICP-OES calibration curves for Co; Figure S7. ICP-OES calibration curves for Cu; Figure S8. ICP-OES calibration curves for Ni; Figure S9. ICP-OES calibration curves for Pd; Figure S10. ICP-OES calibration curves for Ru.

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