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Polyisobutylene-Supported Phosphines as Recyclable and Regenerable Catalysts and Reagents

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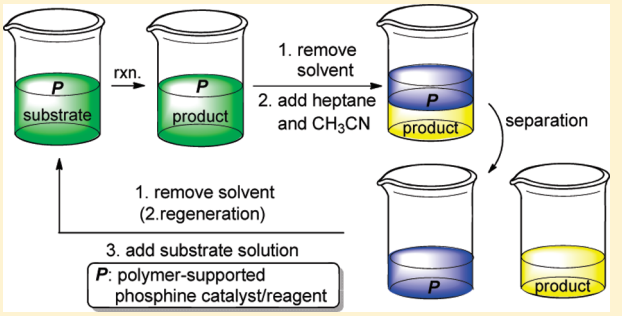
Supporting Information

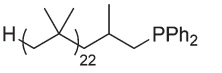
ABSTRACT: Phosphines are important as catalysts or reagents in synthesis but must be separated from products after a reaction. This report shows that polyisobutylene (PIB)-bound alkyldiaryl- and triarylphosphines are useful as catalysts in addition and allylic amination reactions or as reagents in aza-Wittig and Mitsunobu reactions. Heptane solutions of such phosphines and their oxidized byproducts can be easily separated from polar solutions of organic products, and PIB-phosphine oxides formed during a reaction can readily be reduced to PIB-phosphines for reuse.



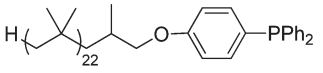
Phosphines are commonly used as reagents and catalysts in modern organic chemistry in Baylis−Hillman, Wittig, and Mitsunobu reactions.[1−8] However, a drawback of using phosphines is the difficulty of separating phosphines or their phosphine oxide byproducts from products after a reaction. For example, triphenylphosphine oxide, which is generated in Mitsunobu reactions that use triphenylphosphine as a reagent, usually has to be separated from products by chromatography. The toxicity of phosphines and phosphine oxides can also pose concerns.[9] These green chemistry issues have led to the development of several methods to facilitate product purification after reactions that use phosphines as reagents or catalysts. For example, the use of water-soluble phosphines allows phosphines or phosphine byproducts to be separated from products with an aqueous wash.[6,8] Another strategy involves attaching phosphines onto insoluble polymer supports that allow products and phosphine species to be separated by filtration.[6−8,10] Here we describe soluble phosphines that can be readily separated from polar organic products using their heptane solubility.

There have been limited studies where soluble polymers or similar phase handles have been used to support phosphine reagents or catalysts during a homogeneous reaction with a biphasic separation of phosphines or phosphine oxide byproducts after the reaction.[11,12] These strategies include using fluorous tags for fluorous biphasic separations or the use of soluble polymers like polyethylene (PE), poly(ethylene glycol) (PEG), or linear polystyrene supports. Fluorous phosphines and their byproducts can be separated from products by a thermomorphic strategy, and soluble polymer-bound phosphines and their byproduct are typically separated from products using solvent precipitation of the polymeric species. In our work, we have been exploring terminally functionalized polyisobutylene (PIB) oligomers as nonpolar phase-selective supports for ligands and catalysts. PIB supports are readily soluble in many nonpolar or modestly polar solvents but can be separated in the heptane phase of liquid/liquid biphasic mixtures after a homogeneous reaction.[13−21] As shown in the examples below, the heptane phase-selective solubility properties of PIB enable PIB-bound phosphines and phosphine oxides to be easily separated from products. Moreover, these PIB-bound species can be recovered, regenerated, and reused.

PIB-alkyldiphenylphosphine (**1**) and PIB-triarylphosphine (**2**) were synthesized by reaction of polyisobutyl bromide with either potassium diphenylphosphide or 4-(diphenylphosphino)phenol respectively using chemistry reported previously. These two PIB-supported phosphines have ^{31}P NMR spectra similar to those of their low-molecular weight analogues.[22,23]



1: PIB-$CH_2CH(CH_3)CH_2PPh_2$



2: PIB-$CH_2CH(CH_3)CH_2OC_6H_4PPh_2$

PIB-alkyldiphenylphosphine (**1**) was first examined for its use as a catalyst for methanol addition of methyl propiolate, a known reaction that generates a product mixture consisting mainly of *cis*- and *trans*-1,4 addition products (eq 1).[24] Methyl propiolate, methanol, and **1** were dissolved in heptane and allowed to react for 20 h. Acetonitrile was then added to the reaction mixture to form a biphasic mixture where **1** was in the heptane-rich phase and the products were in the polar acetonitrile phase. The heptane solution of **1** was then separated from the product phase by a gravity separation. Addition of fresh substrates to this recovered heptane phase allowed **1** to be reused. Using 20 mol % of **1** allowed **1** to be recycled for up to six cycles when care was taken to avoid adventitious oxidation of this alkyldiarylphosphine in recycling the catalyst (Table 1). However, even with careful catalyst recycling, the yield of products decreased in the last

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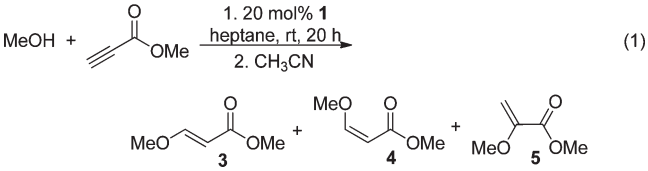
Table 1. Alcohol Addition Catalyzed by 1[a]

	yield (%)[b]			
run	*trans* (**3**)	*cis* (**4**)	*gem* (**5**)	combined yield (%)
1	64	20	6	90
2	62	18	5	85
3	68	25	3	96
4	66	22	4	92
5	59	21	3	82
6	48	15	3	65

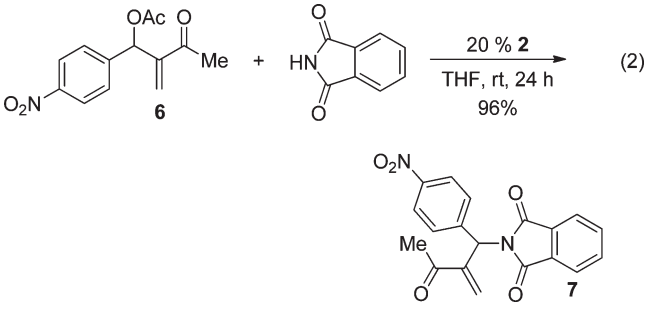
[a] The reaction was conducted using 0.2 mmol of methyl propiolate, 0.6 mmol of methanol, and 0.04 mmol of **1** in 2 mL of heptane. [b] GC yields.

cycle. ^{31}P NMR spectroscopy verified that this was the result of the adventitious oxidation of **1** to form a phosphine oxide. At this point the heptane solution of **1** could still be reused but only after reduction of the oxidized **1** (vide infra).



(1)

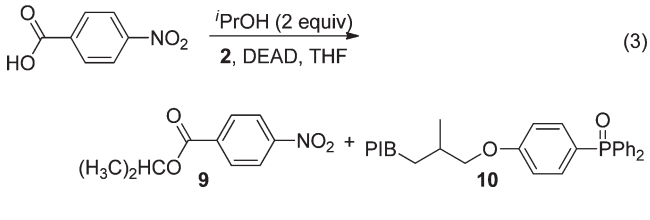
Phosphines can also function as catalysts in allylic aminations, and both **1** and **2** were examined in this chemistry (eq 2).[25] In this reaction, the allylic acetate **6**, phthalimide, and 20 mol % of **1** or **2** were allowed to react for 24 h at rt in THF. Removal of the solvent and addition of an equivolume mixture of heptane and acetonitrile to the residue afforded a biphasic mixture consisting of a heptane-rich solution of **1** or **2** and an acetonitrile solution of the product. Early experiments with **1** gave good yields of **7** in the first two cycles. However, exposure of recycled **1** to oxygen led to ca. 40% oxidation of **1** and decreased yield of product in a subsequent cycle. Using the more oxygen tolerant **2** instead of **1** lessens this problem, and the catalyst **2** was recovered and reused 5 times with yields of purified product of 96%, 95%, 93%, 94% 87%, and 54% in cycles 1−6. Oxidation of **2** can still be a problem, however, and was shown to account for the low yield in cycle 6. ^{1}H NMR spectra of residues of the heptane and acetonitrile phases showed that neither **6** nor **7** were present in the heptane phase and that no PIB-phosphine or phosphine oxide was present in the acetonitrile phase.



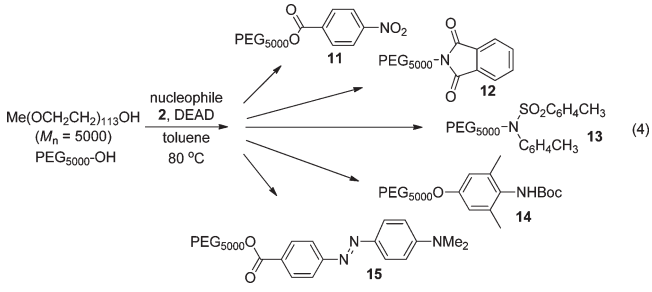
(2)

PIB-bound phosphines **1** or **2** were also used in an aza-Wittig reaction of 4-methylbenzyl azide and 4-methylbenzaldehyde to form the *N*-4-methylbenzyl aldimine **8**. The use of soluble polymeric phosphines in such chemistry is precedented in work by Mahdavi who relied on the change in solubility of the phosphine oxide-containing polymer to separate polymer from the product.[26] The use of **1** or **2** in this aza-Wittig reaction simplified separation of the product from the oxidized phosphine byproduct. After removal of the reaction solvent, the reaction mixture was redissolved in a biphasic mixture of heptane and acetonitrile to separate the acetonitrile-soluble aldimine product from the heptane soluble PIB-bound oxidized phosphine byproduct with similar yields to those reported by Mahdavi.[26]

A common reaction that uses a triarylphosphine as a reagent is the Mitsunobu reaction. PIB-triarylphosphine **2** was shown to be useful in a variety of Mitsunobu reactions with a wide range of substrates. In these cases, using the PIB-bound phosphine **2** simplified the isolation of products free of phosphine oxide byproducts. For example, when 2-propanol was allowed to react with 4-nitrobenzoic acid, the phosphine oxide **10** could be easily removed from the ester product **9** by a liquid/liquid extraction (eq 3). The ease of separation of **10** from products was also useful in functionalizing polymers. For example, when poly(ethylene glycol) monomethyl ether (M_n = 5000) was used as the alcohol substrate (eq 4), a wide range of substrates could be used as nucleophiles to provide high yields of terminally substituted poly(ethylene glycol)s. In these cases, the functionalized PEG products could be isolated by precipitation after adding the reaction mixture to cold ether. Since the PIB-bound phosphine oxide **10** and the DEAD byproduct are soluble in ether, no chromatography was required in isolation of **11**−**15**. This was in contrast to a similar experiment using triphenylphosphine to form **11**−**15**. When triphenylphosphine was used to prepare these PEG derivatives, the first precipitation of PEG led to PEG products containing ca. 20% triphenylphosphine oxide.[27] We were also able to separate **10** from the DEAD byproduct by concentrating the filtrate and redissolving the residue in a heptane/acetonitrile mixture. A liquid/liquid separation of this mixture afforded a heptane phase containing only **10** which could be reduced and reused.



(3)



(4)

The use of these PIB-bound phosphines to modify polymers via Mitsunobu chemistry was also extended to the synthesis of terminally functional polyethylene oligomers (PE_{Olig}) using phthalimide, *N*-Boc-4-amino-3,5-xylenol, or 3-(*tert*-butyl)-2,5-dihydroxybenzaldehyde as nucleophiles (eq 5) to form **16**, **17**, and **18**, respectively. These polyethylene oligomers have thermomorphic solubility and are completely insoluble in all solvents at room temperature but soluble in solvents like toluene above 70 °C. This makes functional PE_{Olig} derivatives useful as ligands for thermomorphic catalysts.[21,28−33] However, syntheses of ligands

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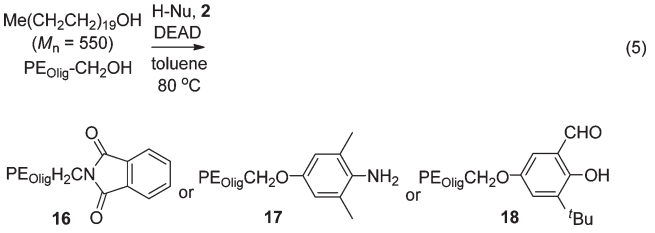
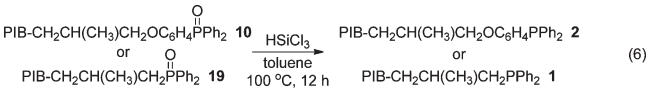
with PE_{Olig} groups can be complicated because separation techniques like chromatography are impractical and because PE oligomers are insoluble in the polar aprotic solvents often favored for nucleophilic substitution reactions. Thus, we were pleased to find that PIB-phosphine reagents are a viable alternative to ordinary phosphines in Mitsunobu reactions of hydroxyl-terminated polyethylene oligomers. For example, when a PE_{Olig} (M_n = 550) with a terminal hydroxyl group was used in Mitsunobu reactions like those in eq 5, the PE derivatives formed in a nucleophilic substitution can be isolated by filtration after cooling the reaction mixture to room temperature with complete conversion to products based on ^{1}H NMR analysis showing the change of the chemical shift of the terminal methylene group of the starting PE_{Olig}-CH_2OH.



(5)

Trichlorosilane can be used to reduce phosphine oxides to phosphines. However, our experience is that using trichlorosilane to reduce phosphine oxides to phosphines is experimentally complicated because of separation problems involving the solid siliceous side products produced after an aqueous workup. For example, these byproducts make reduction of an insoluble polymer-bound phosphine oxide and reduction of PEG-bound phosphine oxides experimentally difficult. However, this is not the case with phosphine oxides formed in reactions of **1** or **2**. Since PIB is soluble in a nonpolar solvent, we could carry out reduction of phosphine oxides **10** or **19** with trichlorosilane in toluene and easily separate the toluene solution of **1** or **2** from the silicon-containing byproducts formed in an aqueous workup (eq 6). Removal of toluene after reduction of **10** or **19** produced **2** or **1** based on ^{31}P NMR spectroscopy. The regenerated phosphines **1** and **2** could be reused in all the catalytic and stoichiometric reactions described above with reactivity equivalent to freshly prepared **1** and **2**.



(6)

In summary, PIB-bound alkyldiphenylphosphine **1** and triarylphosphine **2** were synthesized and examined as catalysts and reagents. The PIB-bound alkyldiphenylphosphine **1** can be used as a catalyst and recycled/reused in methanol addition of methyl propiolate and the PIB-bound triarylphosphine **2** can be used as a reusable catalyst in allylic amination. Both PIB-bound phosphines **1** and **2** can be used as reagents in aza-Wittig and Mitsunobu reactions where the nonpolar phase selective solubility of the phosphine oxide byproducts facilitates product purification. Finally, the phosphine oxides **10** and **19** formed either by adventitious oxidation or in the course of a stoichiometric reaction can be separated as heptane solutions and can easily be recycled by reduction with trichlorosilane.

EXPERIMENTAL SECTION

Vinyl-terminated polyisobutylene (Glissopal 1300) with an M_n value of 1300 Da and hydroxyl-terminated polyethylene (Unilin 550) with an M_n of 550 were obtained from BASF and Baker-Hughes, respectively. All other reagents were purchased from commercial sources and used without further purification unless otherwise stated. ^{1}H and ^{13}C NMR spectra were recorded on a 500 or 300 MHz spectrometer. Chemical shifts (δ) were reported in ppm relative to residual proton resonances in $CDCl_3$, C_6D_6, or acetone-d_6. ^{31}P NMR spectra were recorded on a 300 MHz spectrometer, and chemical shifts were referenced to external 85% H_3PO_4 at room temperature. Coupling constants (J values) are reported in hertz (Hz), and spin multiplicities are indicated by the following symbols: s (singlet), d (doublet), t (triplet), dd (doublet of doublet), and m (multiplet). All reactions were carried out under a nitrogen atmosphere unless otherwise noted. Compounds **1**,[22] **6**,[25] polyisobutyl bromide,[13] 4-(diphenylphosphino)phenol,[34] 4-methylbenzyl azide,[35] and 3-*tert*-butyl-5-hydroxysalicylaldehyde[36] were prepared according to literature procedures.

Polyisobutyltriarylphosphine (PIB-$CH_2OC_6H_4PPh_2$) (2). To a 250-mL round-bottomed flask equipped with a magnetic stirrer and a reflux condenser were added polyisobutyl bromide (11.0 g, 8.5 mmol), 4-(diphenylphosphino)phenol (2.50 g, 9.0 mmol), and Cs_2CO_3 (5.54 g, 17.0 mmol). The apparatus was first flushed with N_2, and then heptane (50 mL) and DMF (50 mL) were added. The flask was immersed in an oil bath regulated at 100 °C, and the reaction mixture was stirred for 12 h. At this point, the reaction mixture was allowed to cool to rt and was transferred to a separation funnel. The heptane phase was separated and washed with H_2O (50 mL × 2), 90% aqueous ethanol (50 mL), and acetonitrile (50 mL × 2) and dried over anhydrous $MgSO_4$. The solvent was removed under reduced pressure to give a crude product that was then purified by silica gel column chromatography (hexanes/CH_2Cl_2 = 4:1) to afford a colorless, viscous liquid (8.62 g, 5.5 mmol, 65% yield): ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.76−1.82 (m, 182 H), 1.97−2.11 (m, 1 H), 3.61−3.68 (m, 1 H), 3.79 (dd, J = 8.8, 5.6 Hz, 1 H), 6.87−6.92 (m, 2 H), 7.25−7.37 (m, 12 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 20.4, multiple peaks between 29 and 33, 35.9, multiple peaks between 37 and 39, 49.6, 56.7, 58.2, 58.8, multiple peaks between 59 and 60, 74.2, 114.8 (d, J = 8.4 Hz), 126.9 (d, J = 6.3 Hz), 128.4 (d, J = 6.8 Hz), 128.5, 133.4 (d, J = 19.0 Hz), 135.6 (d, J = 21.5 Hz), 137.8 (d, J = 10.1 Hz), 160.1; ^{31}P NMR (121 MHz, $CDCl_3$) δ −6.5.

General Procedure for Alkyne Addition. Methyl propiolate (17.8 μL, 0.2 mmol), **1** (0.0548 g, 0.04 mmol), MeOH (24.3 μL, 0.6 mmol), and heptane (2 mL) were added to a 10-mL flask equipped with a magnetic stirrer. The mixture was stirred for 20 h, at which time acetonitrile (2 mL) was added to reaction mixture to form a biphasic mixture. The polar phase was removed from the flask and analyzed by GC using 1,4-dichlorobenzene as an internal standard. Recycling experiments involved addition of methyl propiolate (17.8 μL, 0.2 mmol) and MeOH (24.3 μL, 0.6 mmol) to the heptane solution of **1** for the next cycle.

General Procedure for Allylic Amination. Phthalimide (0.0589 g, 0.4 mmol), **2** (0.062 g, 0.04 mmol), **6** (0.0527 g, 0.2 mmol), and THF (2 mL) were added to a 10-mL flask equipped with a magnetic stirrer, and the reaction mixture was stirred at rt for 24 h. At this point, the solvent was removed under reduced pressure, and heptane (5 mL) and acetonitrile (5 mL) were added to reaction flask to form a biphasic mixture. The polar acetonitrile phase was removed from the flask. The acetonitrile was removed under reduced pressure to give a crude product which was then purified by silica gel column chromatography (CH_2Cl_2) to afford **7** as a white solid: ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.41 (s, 3 H), 5.75 (s, 1 H), 6.43 (s, 1 H), 6.51 (s, 1 H), 7.55 (d, J = 8.8 Hz), 7.70−7.75 (m, 2 H), 7.79−7.84 (m, 2 H), 8.18 (d, J = 8.8 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 25.9, 53.0, 123.5, 123.8, 129.3, 129.5, 131.4, 134.3, 144.6, 144.9, 147.4, 167.7, 197.7; mp 154−156 °C (lit.[25] mp 137−139 °C). In recycling experiments, the heptane of the remaining nonpolar phase was removed under reduced pressure, and 2 mL of a THF solution containing **6** (0.0527 g, 0.2 mmol) and phthalimide (0.0589 g, 0.4 mmol) was added to the reaction flask for the next cycle.

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General Procedure for Aza-Wittig Reaction. The phosphine **1** (6.03 g, 4.4 mmol) or **2** (6.86 g, 4.4 mmol) in THF (40 mL) was added to a 100-mL round-bottomed flask equipped with a magnetic stirrer. A 10-mL THF solution containing 1-(azidomethyl)-4-methylbenzene (0.59 g, 4.0 mmol) and 4-methylbenzaldehyde (0.48 g, 4.0 mmol) was added to the reaction flask. The reaction mixture was stirred at rt for 24 h at which time the evolution of bubbles had ceased. The solvent was removed under reduced pressure, and heptane (100 mL) and acetonitrile (20 mL) were added. The heptane phase was separated and washed with acetonitrile (20 mL × 5), and then the heptane was removed under reduced pressure. The residue from the heptane phase was analyzed by ^{1}H and ^{31}P NMR spectroscopy, which showed that the residue was the PIB-phosphine oxide **19** or **10**. The acetonitrile phases were combined, and the solvent was removed under reduced pressure to give a white solid which was purified by recrystallization from MeOH to give **8** as white plates (0.875 g, 3.9 mmol, 98% yield): ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.34 (s, 3 H), 2.39 (s, 3 H), 4.77 (s, 2 H), 7.13−7.18 (m, 2 H), 7.19−7.25 (m, 4 H), 7.65−7.69 (m, 2 H), 8.34 (s, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.1, 21.5, 64.8, 127.9, 128.2, 129.1, 129.3, 133.6, 136.3, 136.5, 141.0, 161.7; mp 84−86 °C (lit.[37] mp 83.5−84.5 °C).

Polyisobutyltriarylphosphine oxide (PIB-$CH_2OC_6H_4P$-(O)Ph_2) (10): ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.65−1.90 (m, 182 H), 1.93−2.00 (m, 1 H), 3.60−3.68 (m, 1 H), 3.77 (dd, J = 8.7, 5.7 Hz, 1 H), 6.85−6.98 (m, 2 H), 7.32−7.42 (m, 4 H), 7.42−7.50 (m, 2 H), 7.50−7.59 (m, 2 H), 7.59−7.69 (m, 4 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 20.3, multiple peaks between 28 and 33, 35.7, multiple peaks between 37 and 39, 49.4, 56.5, multiple peaks between 58 and 60, 74.1, 114.4 (d, J = 13.1 Hz), 123.0 (d, J = 110.6 Hz), 128.2 (d, J = 12.0 Hz), 131.5 (d, J = 2.3 Hz), 131.9 (d, J = 9.8 Hz), 133.0 (d, J = 104.2 Hz), 133.7 (d, J = 11.2 Hz), 162.0 (d, J = 2.6 Hz); ^{31}P NMR (121 MHz, $CDCl_3$) δ 29.3.

Polyisobutyldiphenylphosphine oxide (PIB-$CH_2P(O)Ph_2$) (19): ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.65−1.80 (m, 182 H), 2.01−2.12 (m, 1 H), 2.18 (ddd, J = 15.0, 11.7, 9.2 Hz, 1 H), 2.32 (ddd, J = 15.0, 10.3, 4.0 Hz, 1 H), 7.38−7.56 (m, 6 H), 7.69−7.82 (m, 4 H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 24.6, multiple peaks between 29 and 33, 36.2, multiple peaks between 37 and 40, 55.5, 55.6, 57.0, multiple peaks between 58 and 60, 128.5 (d, J = 11.7 Hz), 130.6 (d, J = 8.9 Hz), 130.8 (d, J = 9.3 Hz), 131.5 (d, J = 2.7 Hz), 131.5 (d, J = 2.9 Hz), 133.5 (d, J = 97.2 Hz), 134.3 (d, J = 97.3 Hz); ^{31}P NMR (121 MHz, $CDCl_3$) δ 31.5.

General Procedure for Mitsunobu Reactions. Alcohol (0.4 mmol), nucleophile (0.8 mmol), **2** (1.25 g, 0.8 mmol), and toluene (4 mL) were added to a 25-mL round-bottomed flask equipped with a magnetic stirrer. DEAD (126 μL, 0.8 mmol) was added to reaction mixture. The flask was immersed in an oil bath regulated at 80 °C, and the reaction mixture was stirred for 15 h. In the case of eq 3, the reaction was carried out in THF at rt using 4-nitrobenzoic acid (0.0668 g, 0.4 mmol) as the limiting reagent. Workup procedures varied as follows. For eq 3, the solvent was removed under reduced pressure and a mixture of heptane (40 mL) and acetonitrile (40 mL) was added to the reaction residue. The heptane phase containing **2** and its phosphine oxide byproduct **10** was separated from the acetonitrile phase and was washed with acetonitrile (10 mL × 4). The acetonitrile solutions were combined and the solvent was removed under reduced pressure to give a crude product which was purified by silica gel column chromatography (hexanes/CH_2Cl_2 = 4:1) to afford isopropyl 4-nitrobenzoate **9** as a white solid (0.0795 g, 0.38 mmol, 95% yield): ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.39 (d, J = 6.2 Hz, 6 H), 5.28 (hept, J = 6.2 Hz, 1 H), 8.17−8.22 (m, 2 H), 8.25−8.29 (m, 2 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.8, 69.7, 123.4, 130.6, 136.2, 150.4, 164.1; mp 104−106 °C (lit.[38] mp 104−106 °C).

Workup for the reactions yielding polymeric products was slightly different. For eq 4, the reaction mixture was cooled to rt and then added, in a dropwise fashion, to ice-cold Et_2O (50 mL). The product PEG polymer precipitate was isolated and characterized by ^{1}H and ^{13}C NMR spectroscopy. Concentrating the filtrate solutions, addition of heptane (15 mL) and acetonitrile (15 mL), followed by separation and washing of the heptane phase led to a heptane solution that contained a mixture of **2** and **10** based on ^{1}H and ^{31}P NMR spectroscopy. This mixture could be reduced and reused as described below.

For eq 5, a slightly different workup procedure was used. In the case of synthesis of **16** and **17**, the crude product PE_{Olig} product precipitated on cooling. In the case of **17**, this crude product was dissolved in toluene at 80 °C and was allowed to react with methanesulfonic acid for 1 h. After neutralization with triethylamine, the reaction mixture was cooled and the product aniline was isolated by filtration. In the case of **18**, the initial PE_{Olig} precipitate appeared to be an adduct of the aldehyde with the diethyl hydrazine-1,2-dicarboxylate based on the appearance of two $-OCH_2CH_3$ groups in the ^{1}H NMR spectrum of this initial adduct. This product was not further characterized but was simply hydrolyzed by dissolving it in toluene, adding *p*-TsOH, and adding triethylamine and water to the 80 °C toluene solution of the PE_{Olig} product. Most of the water was removed from this mixture by pipet. Cooling formed an isolable precipitate of the desired PE_{Olig}-modified salicylaldehyde derivative which was characterized by ^{1}H and ^{13}C NMR spectroscopy and was identical to the PE_{Olig} derivative of salicylaldehyde prepared previously.[21]

Poly(ethylene glycol) 4-Nitrobenzoate (11). The product was isolated as a white powder (0.245 g, 0.048 mmol, 95% yield): ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.36 (s, 3 H), 3.46−3.88 (m, 450 H), 4.49−4.53 (m, 2 H), 8.20−8.24 (m, 2 H), 8.26−8.30 (m, 2 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 58.8, 64.7, 67.2, 68.7, multiple peaks between 69 and 74, 123.3, 130.6, 135.2, 150.3, 164.4.

***N*-Poly(ethylene glycol)phthalimide (12).** The product was isolated as a white powder (0.242 g, 0.047 mmol, 94% yield): ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.36 (s, 3 H), 3.46−3.91 (m, 452 H), 7.69−7.74 (m, 2 H), 7.80−7.86 (m, 2 H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 36.9, 58.7, 67.1, 67.6, multiple peaks between 68 and 74, 122.9, 131.8, 133.7, 167.9.

4-Methyl-*N*-(4-methylphenyl)-*N*-poly(ethylene glycol)-benzenesulfonamide (13). The product was isolated as a white powder (0.244 g, 0.047 mmol, 93% yield): ^{1}H NMR (500 MHz, $CDCl_3$): δ 2.33 (s, 3 H), 2.42 (s, 3 H), 3.37 (s, 3 H), 3.47−3.80 (m, 452 H), 6.89−6.94 (m, 2 H), 7.06−7.11 (m, 2 H), 7.21−7.25 (m, 2 H), 7.47−7.51 (m, 2 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 20.8, 21.3, 49.9, 58.7, multiple peaks between 64 and 76, 127.4, 128.4, 129.0, 129.3, 135.1, 136.5, 137.6, 143.0.

***N*-Boc-2,6-dimethyl-4-poly(ethylene glycol)aniline (14).** The product was isolated as a white powder (0.241 g, 0.046 mmol, 92% yield): ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.48 (s, 9 H), 3.36 (s, 3 H), 3.44−3.84 (m, 450 H), 4.03−4.09 (m, 2 H), 6.59 (s, 2 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 18.2, 28.0, 58.6, 63.8, multiple peaks between 66 and 76, 79.0, 113.5, 126.8, 136.8, 153.7, 156.6.

Poly(ethylene glycol) 4-(4-(dimethylamino)phenylazo)-benzoate (15). The product was isolated as an orange powder (0.237 g, 0.045 mmol, 90% yield): ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.10 (s, 6 H), 3.35 (s, 3 H), 3.42−3.88 (m, 450 H), 4.40−4.52 (m, 2 H), 6.72−6.81 (m, 2 H), 7.80−7.97 (m, 4 H), 8.08−8.16 (m, 2 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 40.1, 40.2, 58.8, 64.0, multiple peaks between 65 and 76, 111.3, 121.7, 125.5, 129.8, 130.4, 134.4, 152.7, 155.6, 166.0.

***N*-Polyethylphthalimide (16)[30].** The product was isolated as a white powder (0.25 g, 0.37 mmol, 99% yield): ^{1}H NMR (500 MHz, C_6D_6, 70 °C) δ 0.91 (t, J = 6.58 Hz, 5 H), 1.20−1.49 (brs, 140 H), 1.64 (m, 2 H), 3.58 (t, J = 6.81 Hz, 2 H), 6.96 (m, 2 H), 7.49 (m, 2 H); ^{13}C NMR (125 MHz, C_6D_6, 70 °C) δ 12.2, 22.6, 26.8, 28.5, 29.1, 29.3, 29.7, 31.8, 37.8, 122.6, 132.6, 132.9, 167.6.

2,6-Dimethyl-4-polyethylaniline (17). The product was isolated as a light brown powder (0.25 g, 0.37 mmol, 99% yield): ^{1}H NMR

(500 MHz, C_6D_6, 70 °C) δ 0.91 (t, J = 6.58 Hz, 5H), 1.20−1.49 (brs, 164 H), 1.72 (m, 2 H), 1.94 (s, 6 H), 3.82 (t, J = 6.74 Hz, 2 H), 6.66 (s, 2 H); ^{13}C NMR (125 MHz, C_6D_6, 70 °C) δ 14.0, 22.5, 26.1, 28.9, 29.2, 29.3, 29.7, 31.9, 34.8, 68.0, 103.0, 114.0, 136.5, 157.0.

3-*tert*-Butyl-5-polyethylsalicylaldehyde (18)[21]. The product was isolated as a light orange powder (0.25 g, 0.33 mmol, 90% yield): ^{1}H NMR (500 MHz, C_6D_6, 70 °C) δ 0.91 (t, J = 6.58 Hz, 5 H), 1.30−1.49 (brs, 230 H), 1.71 (m, 1 H), 3.71 (t, J = 6.26 Hz, 2 H), 6.43 (d, J = 1.9 Hz, 1 H), 7.26 (d, J = 3.06 Hz, 1H), 9.38 (s, 1H), 11.87 (s, 1 H); ^{13}C NMR (125 MHz, C_6D_6, 70 °C) δ 13.9, 22.5, 26.1, 28.9, 29.2, 29.3, 29.7, 31.9, 34.8, 68.6, 113.1, 120.1, 123.9, 139.9, 151.7, 155.9, 196.0.

***N*-Boc-4-amino-3,5-xylenol.** To a 100-mL round-bottomed flask equipped with a magnetic stirrer was added 4-amino-3,5-xylenol (5.0 g, 45.8 mmol) and acetone (46 mL). The suspension was stirred under N_2. Upon dissolution, Boc_2O (11.0 g, 50.4 mmol) was added to reaction flask, and the reaction mixture was stirred for 24 h at rt. After this time, the solvent was removed under reduced pressure. To the solid residue was added hexanes (150 mL), and the product was isolated by filtration as a light brown powder (8.0 g, 33.7 mmol, 74% yield) which was used without further purification: ^{1}H NMR (300 MHz, acetone-d_6) δ 1.44 (s, 9H), 2.18 (s, 6H), 6.50 (s, 2H), 7.21 (bs, 1H), 8.11 (bs, 1H); ^{13}C NMR (75 MHz, acetone-d_6) δ 17.7, 27.8, 78.0, 114.3, 127.0, 137.3, 154.4, 155.5. IR (neat, cm^{-1}) 3306, 3200, 2945, 1680, 1599, 1500, 1483, 1443; HRMS calcd for $[C_{13}H_{18}NO_3]^-$ 236.1287, found 236.1290; mp 165 °C dec.

General Procedure for PIB-phosphine Oxide Reduction. PIB-phosphine oxide **10** or **19** (4.4 mmol), triethylamine (12.3 mL, 88 mmol), and degassed toluene (80 mL) were added to a 250-mL round-bottomed flask equipped with a magnetic stirrer and a reflux condenser. Trichlorosilane (4.4 mL, 44 mmol) was added to reaction flask dropwise using a syringe. The reaction flask was then immersed in an oil bath regulated at 100 °C, and the reaction mixture was stirred for 12 h. At this time, the system was allowed to cool to rt, and hexanes (50 mL) and saturated aqueous Na_2CO_3 (100 mL) were added to reaction mixture. The mixture was then filtered through a pad of Celite which was then washed with an additional portion of hexanes (100 mL). The combined filtrate was transferred to a separation funnel. The organic layer was separated, washed with H_2O (50 mL) and brine (50 mL), and then dried over anhydrous $MgSO_4$. The solvents were evaporated under reduced pressure to give a viscous liquid which was shown to be **2** or **1** based on ^{1}H and ^{31}P NMR spectroscopy.

■ ASSOCIATED CONTENT

Supporting Information. Procedures for reactions using regenerated **1** and **2** and NMR spectra of selected compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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