

Designing Polymers for Biphasic Liquid/Liquid Separations after Homogeneous Reactions

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Abstract:

The phase-selective solubility properties of polymer supports that could be used in thermomorphic and latent biphasic systems useful in synthesis and catalysis were evaluated using polymers tagged with either visible dyes or fluorescent probes. Heptane/DMF, heptane/90% ethanol–water, heptane/ethyl acetate, heptane/ethanol, and heptane/*tert*-butyl alcohol solvent mixtures were all studied as examples of thermomorphic or latent biphasic systems. A range of polymers including polyisobutylene (PIB), poly(*tert*-butylstyrene) (PTBS), poly(octadecyl acrylate) (PODA), and poly(octadecyl methacrylate) (PODMA) were tested for hydrophobic phase-selective solubility. The results of these studies are compared to prior work with polar and nonpolar poly(*N*-alkylacrylamide)s and polystyrene. Together with this prior work, these results show that a wide range of polymers and solvent mixtures can be used for the recycling of soluble polymer-bound catalysts, reagents, and sequestrants using either thermomorphic or latent biphasic separation strategies.

Introduction

The use of liquid/liquid biphasic systems^{1,2} and the attachment of catalysts, reagents, and sequestrants to insoluble polymeric supports³ have both been recognized as feasible methods to facilitate organic synthesis through simplified purifications and through catalyst recovery and recycling. However, such systems have limitations. For example, while liquid/liquid biphasic systems allow for simple separation of a catalyst, reagent, or sequestrant from a product, the liquid/liquid interface introduces kinetic barriers—barriers that hinder the reaction or that require the use of phase transfer catalysts. Biphasic liquid/solid systems that rely on the use of insoluble polymeric supports for the separation of a catalyst, reagent, or sequestrant from a product often sacrifice solution-like activity for a simpler separation. Nonetheless, biphasic organic/aqueous or organic/fluorous liquid/liquid systems^{4,5} and liquid/solid systems based on cross-linked resins such as those pioneered by Merrifield⁶ for peptide synthesis or by Letsinger

for oligonucleotide synthesis⁷ are both commonly used industrially and in academic laboratories. Indeed, the availability of such systems for facilitated chemical synthesis has ushered in entirely new technologies such as combinatorial chemistry.

Soluble, linear polymer-supported catalysts, reagents, and sequestrants are also known.^{8–12} Such soluble polymer-supported species often exhibit improved reactivities. Often these species are recovered by solvent precipitation or membrane filtration.^{13–15} However, solvent precipitation or membrane filtration often requires the use of additional solvent in the separation process. In some cases, these separations are not as simple, fast, selective, and as efficient as separations using an insoluble resin. Our recent work has emphasized an alternative strategy based on the fact that many linear polymers exhibit selective solubility in either polar or nonpolar solvents.¹⁶ Such phase-selective solubility can be exploited in a simple liquid/liquid separation to recover catalysts, reagents, or sequestrants on soluble polymers. Moreover, we and others have shown with select examples that soluble polymers can effect separation of catalysts from products simply and quantitatively without the introduction of significant additional solvent.^{8,11,17–21} This initial work focused on only a few such polymers and solvent mixtures. The work below uses a variety of other polymers with dye labels as catalyst surrogates and shows that many other polymers and solvent mixtures are equally suitable in such separations. These results show that it is possible to use many sorts of common polymers to design highly phase-selective polymers that are well suited for use in a variety of thermomorphic or latent biphasic solvent systems.

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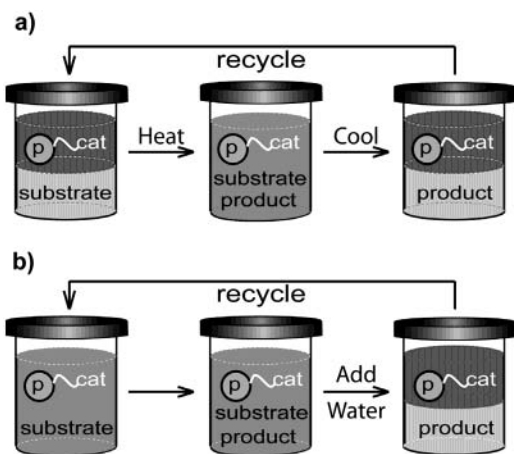


Figure 1. Separation schemes using soluble polymers that employ a monophasic reaction step and a biphasic liquid/liquid separation step: (a) nonpolar thermomorphic system where a nonpolar polymer is initially soluble exclusively in the less dense nonpolar phase of a reaction mixture that becomes miscible on heating and immiscible on cooling; (b) latent biphasic system where the solvent mixture is initially a single phase at the cusp of immiscibility during the reaction but perturbed by the addition of <10 vol % perturbant (here, water) to form a biphasic system.

Our group and others have shown that catalytic and synthetic operations performed in thermomorphic^{18,21–28} or latent biphasic^{19,20} solvent mixtures address the reactivity issues experienced with biphasic or heterogeneous reactions. In our work, we have emphasized how such systems using linear polymers as supports combine the advantages of monophasic reactions and biphasic separation of a product phase from the catalyst-, reagent-, or sequestant-containing phase (Figure 1). In either the thermomorphic or latent biphasic systems, the monophasic conditions for the reaction eliminate liquid/liquid or liquid/solid interface limitations that affect reactions in other biphasic systems. The systems we have developed do require the application of a stimulus or perturbation to induce the system to become biphasic, but this perturbant need only be mild heating or a small amount of a solvent or a salt additive.

A variety of solvents can be used in liquid/liquid separations with soluble polymer-supported catalysts. Much of our work to date has used heptane/ethanol/water mixtures under thermomorphic or latent biphasic conditions. In a thermomorphic scheme, a 10:9:1 (vol:vol:vol) heptane/ethanol/water mixture is used. This solvent mixture is biphasic at room temperature and monophasic at 70 °C but separates into two phases if allowed to cool to room temperature.²² A latent biphasic system would use ethanol and heptane but without any water or with less than 2 vol %

water present initially.²⁰ This latter 1:1 (vol:vol) heptane/ethanol mixture is monophasic at room temperature. However, perturbation of this mixture into a 10:9:1 (vol:vol:vol) heptane/ethanol/water mixture by the addition of 5 vol % water induces phase separation. A latent biphasic system is designed so that the reaction mixture is miscible and monophasic but near the miscibility/immiscibility boundary so that the addition of a small volume of water (or other perturbant) is sufficient to make the whole system biphasic.²⁰ Since hundreds of other solvent combinations are thermomorphic or can be designed to be latently biphasic, these strategies together afford one a range of possible reaction media with various solvent polarities at a range of different temperatures.²⁹

The thermomorphic and latent biphasic solvent systems are only useful if a reagent, catalyst, or sequestant can be readily separated from a product. We have emphasized in our past work and in the studies below the utility of soluble polymers in this regard. Some polar low-molecular weight species would probably work equally well. Whether macromolecules or low-molecular weight species are used, this past work and earlier work on enzymatic catalysis carried out in biphasic systems requires that the species to be recovered have a high selective solubility in one phase of the biphasic mixture if the separations are to be practical.³⁰ Nominally, this phase-selective solubility should be above 100:1. A phase-selective solubility of >500:1 would be more desirable. We also believe that designing systems where a catalyst is recovered in the nonpolar phase would be more generally useful because most organic products of interest have some polar character. Polar polymers such as poly(ethylene glycol) and poly(*N*-isopropylacrylamide) are still useful as supports.^{31,32} However, these polymer supports are only useful in reactions where the products are nonpolar. Moreover, if the reaction produces a polar byproduct, recycling will eventually be compromised because this product will gradually increase in concentration as the polar phase is recycled. Using nonpolar phase selectively soluble polymer supports for the synthesis of polar organic molecules solves these problems.^{17,18,21} We have shown that at least one class of soluble polymeric supports can be tailored to exhibit the desirable phase selectivity (often greater than 99.5%) in either polar or nonpolar solvents.¹⁶

Here we demonstrate that not only can we vary the structure of one class of polymer to control phase-selective solubility but we can also prepare a wide variety of polymers as nonpolar supports for thermomorphic or latent biphasic chemistry. Using a variety of solvent systems, the heptane phase selectively soluble polymers described here can be separated as is shown by polymers that are modified with visible dye or fluorophore probes.

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Experimental Section

All phase selectivity measurements were performed on a Cary 100 scanning UV/vis spectrophotometer or with a Fluorolog 2 spectrofluorometer. Standard curves were prepared to determine the range of dye concentrations that preserved linearity for quantitative analyses. Where necessary, samples were diluted with the appropriate solvent prior to measurement. Extinction coefficients were considered to be unaffected by solvent media, and the phase selectivity preference of a polymer was calculated as a ratio of the absorbance measured for the polymer in each phase of a system.

Previously reported as well as new thermomorphic and latent biphasic systems were studied for use in recycling systems. Heptane/DMF, heptane/90% ethanol, and heptane/ethyl acetate solvent systems were examined for reversible thermomorphic monophasic/biphasic behavior. These solvents were all biphasic cold and monophasic hot. Heptane/ethanol and heptane/*tert*-butyl alcohol solvent systems were examined as examples of latent biphasic systems where the initially monophasic system was rendered biphasic by addition of an additive (typically water).

General Procedure for Phase Selectivity Studies. Since our typical applications of polymer supports involve using soluble polymers as catalysts or as catalyst supports in thermomorphic or latent biphasic solvent systems, polymer concentrations for the phase-selective solubility studies were calculated by determining the quantity of polymer that would be necessary in a catalytic reaction if the polymer were to later be used as a catalytic support. Substrate concentrations in the range of 0.1–0.5 M would commonly require catalyst concentrations of 0.1–2 mol %. The amount of polymer necessary to support this concentration of catalyst was then tested for phase selectivity. Standard curves were first prepared to determine the concentration of dyes that preserved the linearity of the absorbance readings. The polymers were dissolved in the heptane phase and the second polar phase added after complete solvation had been obtained. If necessary, heat was applied to induce phase miscibility. Once a homogeneous solution was obtained, cooling or the necessary perturbation was applied to induce phase separation. Centrifugation with a Jouan CT422 centrifuge was applied as necessary to induce complete and timely separation. The solvent layers were then isolated and serially diluted with the predominant solvent until the absorbance reading fell within the previously determined linear range using a Cary 100 scanning UV/vis spectrophotometer or Fluorolog 2 spectrofluorometer.

Hydroxyl-Terminated Polyisobutylene (PIB–OH) (1). Borane dimethyl sulfide (8.5 mL of a 2.0 M solution in THF, 17 mmol) was added to a solution of PIB (50 g, 50 mmol). The solution was stirred for 24 h and then cooled to 0 °C prior to the addition of 40 mL of ethanol and 12 mL of 4 N NaOH. Then 8 mL of 30% H₂O₂ was added dropwise, and the oxidation was allowed to proceed for 2 h. At this point, 300 mL of H₂O was added, and the solution was extracted with hexane (5 × 100 mL). The resulting organic phase was

washed with H₂O (3 × 50 mL) and brine (1 × 50 mL). The organic phase was dried over MgSO₄, and the solvent was removed under reduced pressure. A total yield of 52 g of **1** was obtained after drying under vacuum for 24 h. ¹H NMR (300 MHz, CDCl₃, δ): 0.75–1.46 (m, 180H), 3.26–3.32 (dd, *J* = 7.5 and 10.2 Hz, 1H), 3.44–3.49 (dd, *J* = 5.4 and 10.2 Hz, 1H).

***N,N*-Dimethyl-*p*-aminophenylazobenzoyl Chloride (2).** *N,N*-Dimethyl-*p*-aminophenylazobenzoic acid³³ (3 g, 11.14 mmol) was dissolved in 40 mL of benzene and heated to reflux. Thionyl chloride (0.8 mL, 10.97 mmol) was then added via syringe. The solution was stirred at reflux for 24 h and then filtered hot. The clear solution was cooled to room temperature. The resulting solid was filtered and dried under vacuum, yielding 1.1 g of product having mp 173–180 °C. IR (KBr, cm⁻¹): 2924, 2859, 1764, 1724, 1603, 1599, 1530, 1369, 1208, 1136, 943, 878, 838, 741, 645, 532. ¹H NMR (300 MHz, DMSO-*d*₆, δ): 3.09 (s, 6H), 6.88 (d, *J* = 9 Hz, 2H), 7.83 (d, *J* = 8.7 Hz, 2H), 7.84 (d, *J* = 9 Hz, 2H), 8.06 (d, *J* = 8.7 Hz, 2H).

Methyl Red-Labeled Polyisobutylene (PIB–MR) (3). A solution of **1** (1.8 g, 1.8 mmol) in 50 mL of toluene was allowed to react with **2** (0.5 g, 1.74 mmol) in the presence of 1 mL of pyridine. The reaction was stirred at reflux for 24 h and the solvent removed under reduced pressure. The residue was taken up in 300 mL of hexane and washed with 90% EtOH (10 × 30 mL). The organic phase was dried over MgSO₄, and the solvents were removed under reduced pressure and dried in vacuo for 24 h to give 1.67 g of (**3**) as a viscous red liquid. IR (neat, cm⁻¹): 2953, 2889, 2263, 1710, 1606, 1517, 1477, 1397, 1373, 1277, 1245, 1141, 916, 740; ¹H NMR (300 MHz, CDCl₃, δ): 0.80–1.43 (m, 180H), 2.06 (m, 1H), 3.07 (s, 6H), 4.01–4.07 (dd, *J* = 7.8 and 10.5 Hz, 1H), 4.17–4.23 (dd, *J* = 5.7 and 10.5 Hz, 1H), 6.71 (d, *J* = 9.3 Hz, 2H), 7.86 (t, *J* = 9.3 Hz, 4H), 8.17 (d, *J* = 8.7 Hz, 2H).

Bromide-Terminated Polyisobutylene (PIB–Br) (4). A solution of **1** (10 g, 10 mmol) in 100 mL of dichloromethane was cooled to 0 °C. A solution of methanesulfonyl chloride (2.3 mL, 30 mmol) and triethylamine (4.3 mL, 31 mmol) was added to the solution dropwise. The reaction was allowed to warm to room temperature and stirred for an additional 6 h. The solvent was removed under reduced pressure and the residue dissolved in 200 mL of 1:1 heptane/acetone containing LiBr (9 g, 104 mmol). The reaction mixture was heated to 80 °C for 24 h. The mixture was cooled to room temperature and added to 200 mL of hexane. The organic phase was then washed successively with H₂O (1 × 50 mL), DMF (5 × 10 mL), and again with H₂O (2 × 20 mL). After drying over Na₂SO₄, the solvent was removed under vacuum to yield 9.4 g of **4**. ¹H NMR (300 MHz, CDCl₃, δ): 0.76–1.49 (m, 180H), 3.28 (dd, *J* = 6.9 and 9.6 Hz, 1H), 3.37 (dd, *J* = 4.8 and 9.6 Hz, 1H).

Phthalimide-Terminated Polyisobutylene (PIB–phthalimide) (5). A mixture of potassium phthalimide (3.0

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g, 16.2 mmol) and **4** (9.0 g, 8.3 mmol) in xylene/DMF (150 mL/150 mL) was stirred at 160 °C for 40 h. The reaction was cooled to room temperature, and 300 mL of hexane was added. The nonpolar organic phase was isolated and washed with H₂O (3 × 40 mL) and 90% EtOH (4 × 25 mL). The organic phase was then dried over Na₂SO₄, and the solvent removed in vacuo to yield 8.5 g of **5**. ¹H NMR (300 MHz, CDCl₃, δ): 0.76–1.49 (m, 180H), 3.42 (dd, *J* = 8.1 and 13.4 Hz, 1H), 3.54 (dd, *J* = 6.6 and 13.4 Hz, 1H), 7.68 (dd, *J* = 3.0 and 5.4 Hz, 2H), 7.82 (dd, *J* = 3.0 and 5.4 Hz, 2H).

Amine-Terminated Polyisobutylene (PIB–NH₂) (6). A solution of hydrazine hydrate (18 mL, 314 mmol) and **5** (8.0 g, 6.97 mmol) in 400 mL of 1:1 ethanol/heptane was heated to reflux for 20 h. The reaction was allowed to cool to room temperature, and 50 mL of H₂O was added. The organic phase was then washed first with H₂O (3 × 40 mL) and then with 90% EtOH (4 × 25 mL). The heptane phase was dried over Na₂SO₄ and the solvent removed under vacuum to yield 7.5 g of **6**. ¹H NMR (300 MHz, CDCl₃, δ): 0.76–1.49 (m, 180H), 2.43 (dd, *J* = 7.5 and 12.4 Hz, 1H), 2.60 (dd, *J* = 5.4 and 12.4 Hz, 1H).

Dansyl-Labeled Polyisobutylene (PIB–Dansyl) (7). A solution of dansyl chloride (0.337 g, 1.25 mmol), **6** (0.5 g, 0.5 mmol), and triethylamine (3.0 mL, 0.42 mmol) in 20 mL of chloroform was refluxed for 24 h. The solvent was removed under reduced pressure and the residue taken up 100 mL of hexane and washed with 90% EtOH (3 × 20 mL). The organic phase was dried over MgSO₄, the solvents were removed under reduced pressure, and the product dried in vacuo for 24 h to give 0.40 g of **7** as a light yellow liquid. ¹H NMR (300 MHz, CDCl₃, δ): 0.77–1.39 (m, 180H), 2.54–2.62 (m, 1H), 2.73–2.82 (m, 1H), 2.86 (s, 6H), 4.54 (t, *J* = 6.3 Hz, 1H), 7.17 (d, *J* = 7.5 Hz, 1H), 7.52 (m, 2H), 8.29 (m, 2H), 8.51 (d, *J* = 8.4 Hz, 1H).

Dansyl-Labeled Poly(*tert*-butylstyrene) (PTBS–Dansyl) (9). A mixture of *N*-propyl-5-dimethylaminonaphthalene-1-sulfonamide (**8**)³⁴ (0.0833 g, 0.285 mmol) and potassium *tert*-butoxide (0.317 g, 0.283 mmol) in 15 mL of dry DMA was placed in a flame-dried flask. The reaction was stirred under argon for 1 h before the dropwise addition of a solution of 10:1 poly(*tert*-butylstyrene)-*c*-poly(vinyl benzyl chloride) (PTBS–VBC) (1.0041 g, 0.57 mmol) in 5 mL of DMA. An additional 5 mL of DMA was added via syringe, and the reaction was allowed to stir overnight. The reaction was determined complete by phenolphthalein indicator and titration with standardized HCl. The mixture was extracted with hexanes (3 × 20 mL), washed with DMF (5 × 50 mL), and concentrated under reduced pressure. The polymer was taken back up into ether and washed with water (3 × 50 mL). The organic phase was dried over MgSO₄ and the ether removed under reduced pressure. The polymer was then dissolved in 3 mL of chloroform, precipitated into 500 mL of methanol, filtered, and dried in vacuo. ¹H NMR (300 MHz, CDCl₃, δ): 0.3–2.5 (m, 254H), 2.91 (br s, 6H), 3.13 (br s, 2H), 4.2–4.8 (br m, 4H), 6.00–7.28 (br m, 100H), 7.55 (br m, 2H), 8.18 (br s, 1H), 8.5 (br s, 1H), 8.36 (br s, 1H).

General Procedure for Synthesis of Octadecyl Acrylates (12 and 13). A 500-mL three-necked round-bottomed flask with stir bar, addition funnel, and condenser was charged with octadecanol (31.427 g, 110.37 mmol), *N,N*-dimethylaniline (10 mL, 86.32 mmol), and 60 mL of dichloromethane. The mixture was warmed to dissolve the alcohol, and a solution of acryloyl chloride (11 mL, 130 mmol) in 50 mL of dichloromethane was added dropwise. Following addition, the reaction was gently refluxed overnight. The mixture was cooled and alternately washed with water and 10% HCl. The organic phase was dried over MgSO₄, concentrated under reduced pressure, and dried in vacuo to give 35.09 g of **12** as a viscous oil (95%). ¹H NMR (300 MHz, CDCl₃, δ): 0.88 (t, *J* = 7.8 Hz, 3H), 1.25 (s, 28H), 1.55–1.75 (m, 4H), 4.14 (t, *J* = 6.9 Hz, 2H), 5.80 (dd, *J* = 1.8 and 10.5 Hz, 1H), 6.11 (dd, *J* = 10.5 and 17.4 Hz, 1H), 6.39 (dd, *J* = 1.8 and 17.4 Hz, 1H). Octadecyl methacrylate (**13**) ¹H NMR (300 MHz, CDCl₃, δ): 0.80 (t, *J* = 6.6 Hz, 3H), 1.18 (s, 28H), 1.4–1.7 (m, 4H), 1.85 (t, *J* = 0.9 and 1.5 Hz, 3H), 4.05 (t, *J* = 6.9 Hz, 2H), 5.45 (q, *J* = 1.5 and 1.8 Hz, 1H), 6.01 (dd, *J* = 0.9 and 1.8 Hz, 1H).

Amine-Terminated *p*-Methyl Red (14). *p*-Methyl red (7.89 g, 29.3 mmol) was suspended in 225 mL of dichloromethane. To this suspension was added carbonyldiimidazole (10.0 g, 61.67 mmol), resulting in a rapid emission of CO₂. The mixture was stirred at ambient temperature for 4 h, and the starting material was observed to dissolve to form a bright red homogeneous solution. This solution was transferred to an addition funnel and added dropwise over 3 h to a solution of 1,6-hexanediamine (13.6 g, 117 mmol) in 200 mL of dichloromethane. After the addition, the resulting solution was allowed to stir for 24 h at room temperature. The reaction was filtered, and the filtrate was washed with water (10 × 60 mL), dried over MgSO₄, and dried in vacuo to yield 8.57 g of **14** as a red solid (80%). ¹H NMR (300 MHz, CDCl₃, δ): 1.25 (m, 4H), 1.60–1.67 (m, 4H), 2.69 (t, *J* = 6.6 Hz, 2H), 3.10 (s, 6H), 3.47 (q, *J* = 6.3 Hz, 2H), 6.21 (t, *J* = 6 Hz, 2H), 6.76 (d, *J* = 9 Hz, 2H), 7.86 (s, 4H), 7.89 (d, *J* = 9 Hz, 1H).

General Procedure for the Synthesis of *p*-Methyl Red-Labeled Acrylamides (15 and 16). A solution of **14** (1.82 g, 5 mmol) and triethylamine (2 mL, 14 mmol) in 50 mL of dichloromethane was added to a 100-mL round-bottomed flask. Acryloyl chloride (0.60 mL, 7.09 mmol) was then added dropwise via syringe. The reaction was allowed to stir for 24 h at room temperature before the mixture was transferred to a separatory funnel and the organic phase was washed with water. The organic phase was set aside, and the aqueous phase was washed with dichloromethane until the dichloromethane was colorless. The organic phases were combined, washed with water (3 × 50 mL), and dried over MgSO₄. The solvent was removed under reduced pressure, and the product was dried in vacuo to give 1.95 g of **15** as a red solid (96.5%). ¹H NMR (300 MHz, CDCl₃, δ): 1.30–1.7 (m, 8H), 3.11 (s, 6H), 3.34 (q, *J* = 6.6 Hz, 2H), 3.46 (q, *J* = 6.6 Hz, 2H), 5.61 (dd, *J* = 2.1 and 10.2 Hz, 1H), 5.8

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(br t, 1H), 6.28 (dd, $J = 2.1$ and 17 Hz, 1H), 6.10 (dd, $J = 10.2$ and 17 Hz, 1H), 6.39 (br t, 1H), 6.76 (d, $J = 9$ Hz, 2H), 7.88 (m, 6H). Methyl red-labeled methacrylamide **16** ^1H NMR (300 MHz, CDCl_3 , δ): 1.2–1.70 (m, 8H), 1.97 (s, 3H), 3.11 (s, 6H), 3.33 (q, $J = 6.9$ Hz, 2H), 3.48 (q, $J = 6.3$ Hz, 2H), 5.31 (s, 1H), 5.68 (s, 1H), 5.9 (br t, 1H), 6.40 (br t, 1H), 6.76 (d, $J = 9.3$ Hz, 2H), 7.88 (m, 6H).

General Procedure for the Synthesis of Methyl Red-Labeled Poly(octadecyl acrylate)s (17 and 18). Benzene (50 mL) was added to a 100-mL three-necked round-bottomed flask and degassed by bubbling N_2 for 3 h. The benzene was then cooled to -78 °C. Then **12** (2.50 g, 7.7 mmol), **15** (0.108 g, 1.26 mmol), and AIBN (0.0188 g, 0.114 mmol) were added to this solid, and any air that was introduced into the flask was removed under vacuum. The flask was flushed with N_2 , and the reaction mixture was allowed to warm and melt. The polymerization occurred when the mixture was heated to reflux with stirring over 48 h. After this period of time, the solution was concentrated under reduced pressure, and the residue was dissolved in 100 mL of hexane. The hexane solution was washed first with DMF until the DMF washings were no longer colored and finally with water (3×50 mL). The water–DMF phases were washed with hexane to remove any polymer. The combined hexane phases were then concentrated under reduced pressure, and the resulting product was dissolved in a minimum amount of chloroform (approximately 10 mL). Addition of this solution to 400 mL of methanol precipitated the product polymer which was isolated by filtration and dried in vacuo to yield 0.7664 g of **17** as a bright yellow solid (31%). ^1H NMR (300 MHz, CDCl_3 , δ): 0.88 (t, $J = 7.8$ Hz, 90H), 1.25 (br s, 900H), 1.5–1.65 (br m, 60H), 3.10 (s, 6H), 4.03 (br t, 60H), 5.5 (br s, 1H), 6.18 (br s 1H), 7.9 (br s, 2H). GPC analysis was carried out in THF using polystyrene standards: $M_n = 8236$, $M_w = 15157$, PDI = 1.84. Methyl red-labeled poly(octadecyl methacrylate) (**18**) was prepared similarly. ^1H NMR (300 MHz, CDCl_3 , δ): 0.88 (t, $J = 6.5$ Hz, 90H), 1.26 (br s, 900H), 1.61 (br s, 90H), 1.65–1.95 (br m, 60H), 3.10 (s, 6H), 3.92 (br t, 60H), 5.55 (br s, 1H), 6.1 (br s, 1H), 7.9 (br s, 2H). GPC analysis of **18** was carried out in THF using polystyrene standards: $M_n = 6668$, $M_w = 12567$, PDI = 1.88.

Results and Discussion

We have reported several examples of nonpolar phase selectively soluble polymers including recent reports of poly(*tert*-butylstyrene) and polyisobutylene. The goal of this work was to study these polymer supports and other supports in a variety of solvent systems. Since the goal of this article was to evaluate the generality of separations under thermomorphic or latently biphasic systems in various media with various polymers, our synthetic efforts focused on the development of routes to polymers that are designed so that we can incorporate dyes or fluorophores that would serve as easily traceable surrogates for a polymer-bound catalyst, reagent, or sequestant. The resulting labeled soluble polymers were then each examined for phase selectivity within several solvent systems. The soluble polymeric supports studied here

Table 1. Phase-selective solubility for polyisobutylene oligomers in heptane/polar solvent systems

polymer	polar solvent	phase selectivity in nonpolar solvent (%)
PIB–MR 1000	90% ethanol– H_2O	99.60
PIB–dansyl 1000	90% ethanol– H_2O	99.70
PIB–MR 1000	EtOAc	93.75
PIB–MR 1000	<i>t</i> -BuOH	99.42
PIB–MR 2300	90% ethanol– H_2O	99.70
PIB–dansyl 2300	90% ethanol– H_2O	99.60
PIB–MR 2300	EtOAc	92.86
PIB–MR 2300	<i>t</i> -BuOH	98.59

Table 2. Phase-selective solubility for poly(*tert*-butylstyrene) in heptane/polar solvent systems

polymer	polar solvent	phase selectivity in nonpolar solvent (%)
PTBS–dansyl	90% ethanol– H_2O	99.99
PTBS–dansyl	100% ethanol	99.99
PTBS–dansyl	DMF	99.98
PTBS–dansyl	EtOAc	0.10
PTBS–dansyl	<i>t</i> -BuOH	99.98

Table 3. Phase selective solubility for poly(octadecyl acrylate)s in heptane/polar solvent systems

polymer	polar solvent	phase selectivity in nonpolar solvent (%)
PODA–MR	DMF	-
PODA–MR	90% ethanol– H_2O	>99.95
PODMA–MR	DMF	-
PODMA–MR	90% ethanol– H_2O	>99.95

Table 4. Previously reported phase-selective solubility values for polar phase-soluble polymer supports¹⁶

polymer	solvent system	phase selectivity in nonpolar solvent (%)
PNIPAM–MR ^a	heptane/ DMF	<0.1
PNIPAM–dansyl ^b	heptane/ DMF	<0.001
PNIPAM–MR ^a	heptane/ 90% ethanol– H_2O	<0.01
PNIPAM–dansyl ^b	heptane/ 90% ethanol– H_2O	<0.01
PNIPAM–MR ^{a,c}	$\text{Et}_3\text{N}/\text{H}_2\text{O}$	>99.9 (Et_3N phase)
PNIPAM–dansyl ^{b,c}	$\text{Et}_3\text{N}/\text{H}_2\text{O}$	>99.9 (Et_3N phase)
PEG ₅₀₀₀ –MR ^d	heptane /90% ethanol– H_2O	<0.1

^a Methyl red-labeled poly(*N*-isopropyl acrylamide) was used as the polymer.¹⁶ ^b Dansyl-labeled poly(*N*-isopropyl acrylamide) was used as the polymer.¹⁶ ^c A 1:1 (vol:vol) mixture of triethylamine and water produces a solvent mixture that is monophasic at room temperature but biphasic when warmed.¹⁶ ^d Methyl red-labeled poly(ethylene glycol) with a $M_n = 5000$ was used as the polymer.¹⁶

included polyisobutylene (PIB), poly(*tert*-butylstyrene) (PTBS), poly(octadecyl acrylate) (PODA), and poly(octadecyl methacrylate) (PODMA), and the results for these polymer supports were compared with similar results for phase selectively soluble poly(*N*-alkylacrylamide)s and polystyrene in Tables 1–5.^{16–18,35,36}

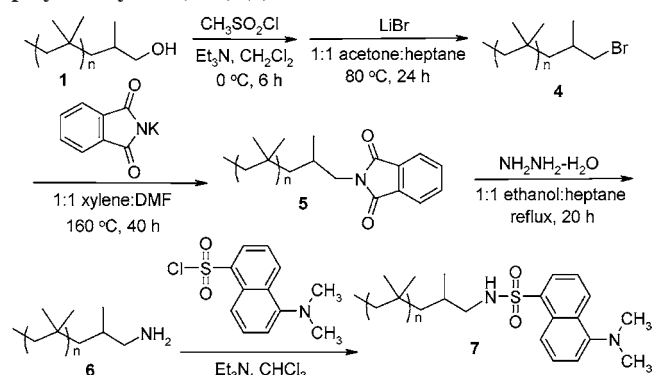
Polyisobutylene (PIB) oligomers labeled with *p*-methyl red dye for UV/vis spectroscopic analysis and with a dansyl

Table 5. Previously reported phase-selective solubility values for nonpolar phase-soluble polymer supports^{16,35,36}

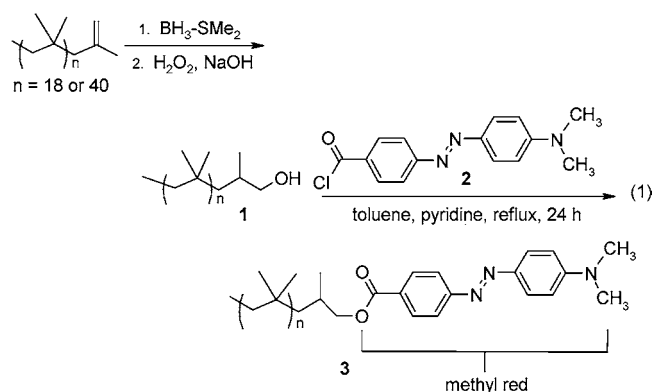
polymer	solvent system	phase selectivity in nonpolar solvent (%)
PNODAM-MR ^a	heptane/ DMF	> 99.99
PNODAM-dansyl ^b	heptane/DMF	> 99.99
PNODAM-dansyl ^b	heptane/ 90% ethanol-H ₂ O	> 99.99
PS-MR ^c	2:1 toluene/ 75% ethanol-H ₂ O	99.5
<i>d</i>	FC-77 ^e /THF	> 99.9
<i>d</i>	FC-77 ^e /H ₂ O	> 99.9

^a Methyl red-labeled poly(*N*-octadecylacrylamide) was used as the polymer.¹⁶ ^b Dansyl-labeled poly(*N*-octadecylacrylamide) was used as the nonpolar polymer.¹⁶ ^c Methyl red-labeled poly(styrene) with $M_n = 21000$ was used as the soluble polymer.³⁵ ^d Methyl red-labeled polyacrylate polymers containing Teflon "pony-tails," were used as the nonpolar fluorophilic phase soluble polymer. In this case, the solvents mixtures did not become miscible under any conditions examined although miscibility of fluorophilic and organic phases is known.^{36,38} ^e FC-77 is a fluorinated cyclic ether with formula C₈F₁₆O.

Scheme 1. Preparation of a dansyl fluorophore-labeled polyisobutylene (PIB) (7)



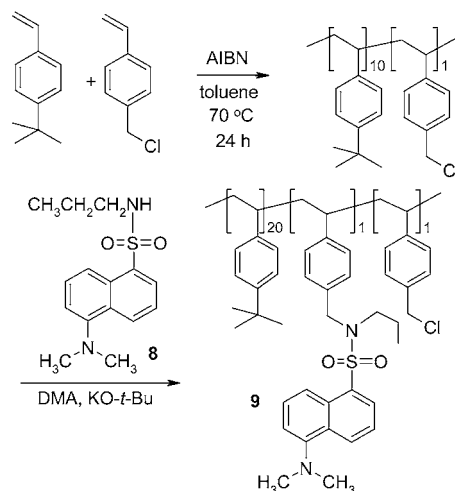
fluorophore for fluorescence spectroscopic analyses were prepared from alkene-terminated polyisobutylene oligomers ($n = 18$ or $n = 40$) using the chemistry shown in eq 1 and Scheme 1.



This chemistry where a terminal functional group was introduced and tagged with a dye is analogous to chemistry used earlier by us in modifying polyethylene oligomers and has been used by us to prepare polyisobutylene oligomers with terminal catalysts or ligands.^{18,37} These PIB oligomers are nonpolar analogues of PEG. They are very soluble at

(35) Bergbreiter, D. E.; Frels, J. D.; Heuze, K. *React. Funct. Polym.* **2001**, *49*, 249–254.

Scheme 2. Synthesis of fluorescently labeled poly(*tert*-butylstyrene) 9



room temperature in appropriate solvents or solvent mixtures. Unlike PEG they are not separable as solids but are separable in liquid/liquid systems as discussed below.

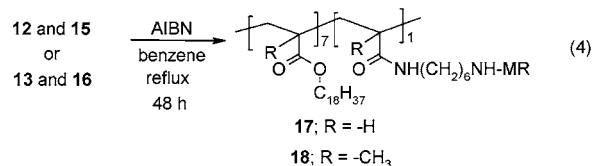
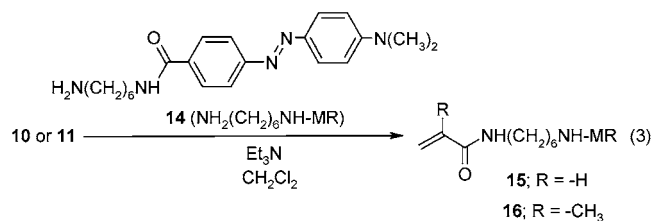
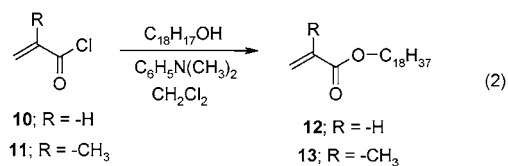
Poly(*tert*-butylstyrene) polymers with UV-visible tags have been prepared, and their phase selectivity has been described previously.¹⁷ Poly(*tert*-butylstyrene) polymers with fluorescent tags can also be prepared by nucleophilic substitution of the chloride of a poly(*tert*-butylstyrene-*c*-poly(vinyl benzyl chloride) copolymer with *N*-propyl-5-dimethylaminonaphthalene-1-sulfonamide (**8**) (Scheme 2).³⁴

Suitable nonpolar phase selectively soluble polymer supports can also be made by polymerization of labeled nonpolar monomers. This is the strategy we used earlier with poly(*N*-octadecylacrylamide)s. This same strategy in this work has been used to prepare nonpolar phase selectively soluble acrylate polymers. These octadecyl acrylate and octadecyl methacrylate polymers were prepared by copolymerization of a dye-labeled acrylamide monomer and octadecyl acrylate or octadecyl methacrylate, respectively. The acrylates were obtained by reaction of acryloyl chloride (**10**) and methacryloyl chloride (**11**) with octadecanol (eq 2). The dye-labeled monomers were acquired by reaction of the methyl red-labeled amine with either acryloyl chloride or methacryloyl chloride (eq 3). Radical copolymerization of these dye labeled acrylamides and the acrylates then produced methyl red-labeled poly(octadecyl acrylate) (**17**) or methyl red-labeled poly(octadecyl methacrylate) (**18**) (eq 4).

In all cases the solvent systems were first visually tested for their ability to separate into biphasic systems. Equivolume mixtures of heptane/DMF and heptane/90% aqueous ethanol achieve miscibility when heated above 70 °C and reversibly become immiscible on cooling. The triethylamine water systems become biphasic on heating—this mixture has an upper critical solution temperature. The toluene/75% aqueous

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(37) Bergbreiter, D. E.; Blanton, J. R.; Chandran, R.; Hein, M. D.; Huang, K. J.; Treadwell, D. R.; Walker, S. A. *J. Polym. Sci., Part A: Polym. Chem.* **1989**, *27*, 4205–4226.



ethanol mixture is like the heptane/90% aqueous ethanol mixture in that it is biphasic at 25 °C and a single phase at 70 °C. In the case of the heptane/ethyl acetate mixture, the solvents are miscible at 25 °C but form a biphasic system upon cooling to -78 °C. This behavior of immiscibility below room temperature has not been exploited in synthesis but is common for many common solvent mixtures.²⁹ For the latent biphasic mixtures, the heptane/ethanol mixture can be perturbed by the addition of 5 vol % water to induce phase separation, while the heptane/*tert*-butyl alcohol mixture only becomes biphasic on addition of 60 vol % of a 1:1 methanol/water mixture.

Phase selectivity studies were performed on each polymer using a variety of solvent systems (see Tables 1–3). For the polyisobutylene oligomers (Table 1), heptane selectivity for all solvent systems was high. In many cases it was >99.5%. A lower 93% phase-selective solubility was seen in the heptane/ethyl acetate mixture. Little variation was seen with the PIB oligomer's M_n . Both oligomers have comparable phase-selective solubility. The poly(*tert*-butylstyrene (PTBS) dansyl derivative's heptane phase selectivity was excellent (>99.9%) in all solvent mixtures except for the ethyl acetate/heptane mixture (Table 2). In that latter case, the dansyl derivative **9** had a 99.9% phase-selective solubility in the ethyl acetate phase. Methyl red-labeled PODA and PODMA (**17** and **18**, respectively) were examined for phase selectivity in heptane/90% ethanol and heptane/DMF thermomorphic systems (Table 3). The dye concentration present in the polar phase of both systems fell below the detection limit of the UV/vis spectrophotometer. In the case of the heptane/DMF system, both PODA-MR and PODMA-MR were observed to precipitate out of the heptane layer following phase separation. While these polymers are heptane soluble and soluble in the heated miscible mixture of heptane and DMF, the heptane phase after cooling is a heptane-rich phase that contains some DMF. Evidently there is enough DMF present to make both **17** and **18** insoluble. Thus, no value was listed for the phase-selective solubility of these polymers in the heptane phase of a heptane/DMF mixture. These polymers might potentially be useful in solid/liquid separations after

a monophasic reaction or in liquid/liquid phase separations of polymer-bound catalysts. Reasonable agreement in the measured phase-selective solubility between the dansyl- and methyl red-labeled polymers provides evidence that both methyl red and dansyl labeling are effective and accurate methods to assay the polymer concentration in a given solvent.

The heptane phase-selective solubility for the polyisobutylene support in 90% ethanol-H₂O systems (>99.5%) marks these systems as good candidates for recycling of PIB-bound catalysts. The polyisobutylene support in the *tert*-butyl alcohol/heptane system also provides reasonable phase-selective solubility in the nonpolar phase. Interestingly, lower-molecular weight PIB₁₀₀₀-MR oligomer exhibits a higher phase selectivity than the higher-molecular weight PIB₂₃₀₀-MR. This initially unexpected result is a consequence of the fact that these selectivity tests used polymers with dye loadings that were supposed to correspond to catalyst concentrations of 20 mol %—concentrations that required roughly twice the amount of polymer in the case of the 2300 molecular weight oligomer. Due to the terminal functionalization of the PIB oligomers, the dye loading decreases as the oligomer weight increases, and accurate selectivity tests require increasing the amount of polymer to maintain the concentration of catalyst surrogate. Thus, while a higher-molecular weight PIB oligomer may improve the phase preference and recyclability of the polymer-bound catalyst, an increase in molecular weight is not always desirable if an increased quantity of polymer would be required to obtain a sufficient catalyst concentration for typical catalytic reactions.

Both the methyl red-labeled poly(octadecyl acrylate) and poly(octadecyl methacrylate) have excellent heptane solubility. For both polymers **17** and **18**, the dye concentration present in the 90% ethanol-H₂O phase was below the detection limit of the UV/vis spectrophotometer. This result indicates a minimum heptane selectivity of >99.9% for both **17** and **18**. These results are indicative that both **17** and **18** may serve as viable nonpolar supports for catalysts, reagents, or substrates in heptane/90% ethanol-H₂O thermomorphic systems. These results parallel earlier results for fluorinated acrylate polymers labeled with methyl red and with catalysts.^{27,38–41} However, the observation that these polymers precipitate in the nonpolar heptane-rich phase of a thermomorphic heptane/DMF system shows that it is important that solubilities be examined in real systems where the nonpolar phase contains some of the polar solvent and some product, too.

Conclusions

Polymeric supports can be designed for high solubility and phase-selective solubility in both thermomorphic and latent biphasic systems. Simple organic transformations show

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that common linear polymers can be designed to serve as highly hydrophobic soluble supports suitable for potential recycling of catalysts. Using dye and fluorophore labels as surrogates for catalysts or ligands, we have shown that such modifications can be completed either before or after polymerization. These supports can be easily tracked for phase-selective solubility in thermomorphic or latent biphasic systems by using "catalyst surrogates" such as dyes like *p*-methyl red for UV/vis analysis or dansyl derivatives for analysis by fluorescence spectroscopy. We have shown that phase-selective solubility values of >99.5% can typically be achieved in the nonpolar phase of mixtures of various polar and nonpolar solvents with heptane. These new soluble

supports should thus be suitable for liquid/liquid separation in thermomorphic or latent biphasic systems for the recovery and recycling of catalysts or reagents.

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