Using Soluble Polymers in Latent Biphasic Systems
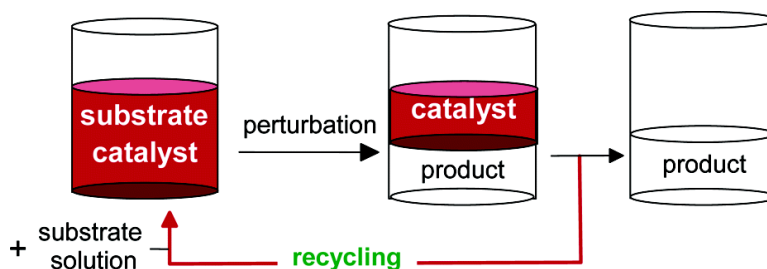
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Using Soluble Polymers in Latent Biphasic Systems

David E. Bergbreiter,* Philip L. Osburn, Thomas Smith, Chunmei Li, and
Jonathon D. Frels

*Contribution from the Department of Chemistry, Texas A&M University, P.O. Box 30012,
College Station, Texas 77842-3012*

Received January 22, 2003; E-mail: bergbreiter@tamu.edu

Abstract: A new strategy for carrying out reactions with a soluble polymer-bound reagent or catalyst is described. In this latent biphasic process, a solvent mixture at the cusp of immiscibility is prepared and used to carry out a reaction under homogeneous conditions. Then, after the reaction is complete, this mixture is perturbed by the addition of solvent or some other perturbing agent to produce a biphasic mixture. The product-containing phase is then separated under liquid/liquid conditions from the polymer-containing phase. The generality of this process is demonstrated using both dye-labeled polymers as surrogates for polymer-bound catalysts and with various polymer-bound organic and transition metal catalysts or reagents. In cases where a polymeric catalyst is used, the addition of fresh solvent and substrate reforms the original mixture allowing facile reuse of the catalyst.

Biphasic systems facilitate homogeneous catalyst recovery and reuse and are widely used in catalysis.[1] However, while biphasic conditions facilitate catalyst/product separation, multiple phases introduce kinetic barriers and make the resulting process more complex. Phase transfer catalysis and thermomorphic catalysis strategies address these issues but preserve the underlying advantages of a biphasic system.[2,3] Here, we describe another alternative, a latent biphasic system. In such a system, a solvent mixture at the cusp of immiscibility is prepared and used to carry out a reaction under homogeneous conditions. Then, after the reaction is complete, this mixture is perturbed by the addition of some perturbing agent to produce a biphasic mixture. A similar procedure was recently described as being useful with dendrimer-bound catalysts.[4] This paper describes the generality of this simple alternative strategy using linear polymers as supports. Dye-labeled polymers are used as surrogates for catalysts on polymers to test separation efficiency and catalysts on polymers are used to demonstrate feasibility of this scheme in known homogeneous catalytic reactions.

Mixtures of solvents have a spectrum of phase behavior. For example, ethanol/water or ethanol/heptane are miscible in all proportions. However, mixtures containing all three of these solvents vary in miscibility depending on the proportions of solvents used, the temperature, and the presence or absence of solutes. As an illustrative example, a 10.0:9.5:0.5 (vol:vol:vol) mixture of heptane, EtOH and H_2O is monophasic at 25 °C,
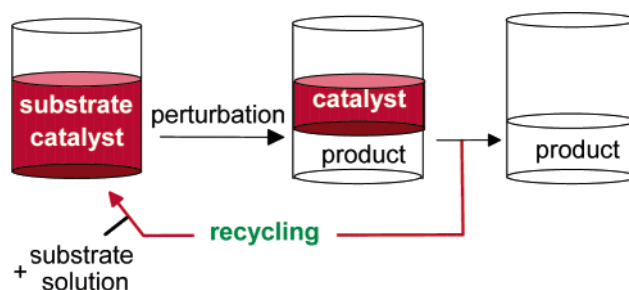

Figure 1. Latent biphasic process with a reaction occurring under monophasic conditions and separation occurring under liquid/liquid biphasic conditions after some perturbation.

but a perturbed 10.0:9.0:1.0 mixture of these solvents is biphasic at 25 °C (Figure 1). We and others have used the temperature dependence of the latter sort of mixture in thermomorphic reactions.[5-9] Here we show how addition of small amounts of another solvent or salt to the former sort of monophasic mixture that is at the cusp of miscibility (a latent biphasic system) can be used as a new way to effect a separation after a homogeneous reaction.

Although solvent mixtures can be designed to change from a monophasic system to a biphasic system by addition of a small volume of another solvent or by the addition of a small amount of some other phase perturbing agent, that fact alone is not sufficient to effect a practical separation after a homogeneous reaction. Any practical separation scheme for a catalytic reaction

(1) A recent issue of *Chem. Rev.* reviewed this topic, see: Gladysz, J. A. *Chem. Rev.* **2002**, *102*, 3215−3216 and also Baker, R. T.; Tumas, W. *Science* **1999**, *284*, 1477−1479.
(2) Goldberg, Y.; Alper, H. Phase-transfer catalysis and related systems. In *Applied Homogeneous Catalysis with Organometallic Compounds*, 2nd ed.; Cornils, B., Herrmann, W. A., Ed.; VCH: Weinheim, 2002; Vol. 2, 953−974.
(3) Bergbreiter, D. E.; Liu, Y.-S.; Osburn, P. L. *J. Am. Chem. Soc.* **1998**, *120*, 4251−4252.
(4) Deng, G.-J.; Fan, Q.-H.; Chen, X.-M.; Liu, D. S.; Chan, A. S. C. *Chem. Commun.* **2002**, 1570−1571.

(5) Bergbreiter, D. E.; Osburn, P. L.; Wilson, A.; Sink, E. M. *J. Am. Chem. Soc.* **2000**, *122*, 9058−9064.
(6) Bergbreiter, D. E.; Osburn, P. L.; Frels, J. D. *J. Am. Chem. Soc.* **2001**, *123*, 11 105−11 106.
(7) Wende, M.; Meier, R.; Gladysz, J. A. *J. Am. Chem. Soc.* **2001**, *123*, 11490−11491.
(8) Mizugaki, T.; Murata, M.; Ooe, M.; Ebitani, K.; Kaneda, K. *Chem. Commun.* **2002**, 52−53.
(9) Chiba, K.; Kono, Y.; Kim, S.; Nishimoto, K.; Kitano, Y.; Tada, M. *Chem. Commun.* **2002**, 1766−1767.

requires that a catalyst selectively partition itself into one of the two phases formed after perturbation of the original monophasic system. If a catalyst were used, then it should also be possible to recycle the catalyst-containing phase through multiple reaction cycles. A phase selective solubility of at least 200:1 for the catalyst is necessary if effective separable, recyclable catalysts are to be developed. Similar considerations have been discussed previously in connection with enzymatic catalyst separations in aqueous biphasic systems and are implicitly taken into account in any extraction.[10] As shown below, such selectivity and recyclability is possible with linear polymer supports.

Results and Discussion

To test the efficacy of soluble linear polymers for separations in this latent biphasic strategy for catalyst recovery, we prepared a variety of soluble polymers containing dye labels. First we prepared poly(*N*-octadecylacrylamide) (PNODAM) containing 2 mol % of *p*-methyl red as a visually detectable surrogate for a lipophilic polymer-bound catalyst (eq 1). We first showed that this PNODAM-bound dye **2** is soluble in heptane or toluene but is insoluble in an EtOH/H_2O phase that contains >10% H_2O. We then showed that a visually homogeneous solution of this lipophilic polymer-bound dye in a mixture of 10 mL each of toluene and 95% EtOH/H_2O becomes biphasic on addition of 0.5 mL of H_2O. UV–visible analysis showed that >99.9% of the polymer-bound dye stayed in the nonpolar toluene-rich phase. Separation of this phase and addition of fresh aqueous EtOH reformed the initial monophasic mixture. Repetition of this cycle 5 times with no detectable loss of **2** in the EtOH-rich phase showed that this approach is viable as a way to recover and reuse polymeric catalysts. However, these immiscible phases have similar density that makes phase separation slow. When a 1.00:0.96:0.04 mixture (vol:vol:vol) of heptane, EtOH, and H_2O was used to form a 20 mL monophasic solution, the addition of just 10 drops of H_2O was sufficient to induce phase separation. This latter system's phases had less similar densities, making the separation cleaner, simpler, and faster. UV–visible analysis showed that >99.9% of the polymer-bound dye stayed in the nonpolar heptane-rich phase and the dye **2** was as recyclable in this heptane/EtOH–H_2O system as it was in the toluene system above.
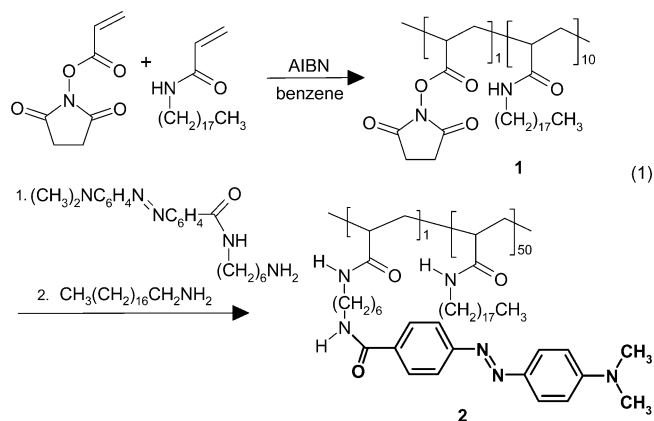
Poly(*N*-isopropylacrylamide) (PNIPAM), a polymer previously used in thermomorphic systems,[3] also showed good

separation efficiency in this heptane/EtOH–H_2O latent biphasic system. When 0.5 mL of water was added to 8 mL of a 1:1 heptane-ethanol homogeneous solution of the dansyl-labeled **3**, two phases formed. More than 99.99% of the polymer stayed in the aqueous ethanol phase based on fluorescence analysis of both the heptane-rich and EtOH-rich phases for the dansyl fluorophore. PNIPAM labeled with the *p*-methyl red azo dye described above (i.e. polymer **4**)[11] was similarly phase selectively soluble in the polar EtOH-rich phase of these heptane/EtOH–H_2O mixtures after phase separation, though the extent of phase selective solubility could only be estimated at >99.9%. These results and the PNODAM result above suggest that separation and recovery of a catalyst bound to these polyacrylamides in either a nonpolar or a polar phase of a nonpolar/polar mixture should be feasible.

We believe that the most effective way to recover catalysts in a latent biphasic reaction is to recover them in the nonpolar phase of a nonpolar/polar mixture. This is illustrated by the examples of catalysis described below. However, it might be desirable to use polar/polar solvent mixtures in other situations. To test the generality of linear polymers in latent biphasic separations, we have also briefly explored the use of linear polymers in this circumstance too.
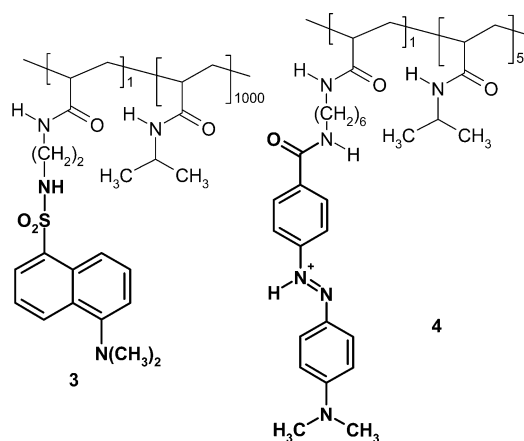
The polar solvent mixture we examined was a mixture of *tert*-butyl methyl ether (TBME), ethanol and water. First, we prepared a miscible mixture of these solvents using 10 mL of TBME, 6 mL of EtOH, and 4 mL of H_2O. PNIPAM labeled with methyl red (**4**) dissolved in this mixture. On addition of 2.5 mL of water to this homogeneous solution, a biphasic mixture formed. The dye labeled polymer **4** was exclusively in the TBME-rich layer at that point.

PNIPAM was phase selectively soluble in one phase of the perturbed latently biphasic TBME/EtOH/H_2O mixture. We reasoned it should be possible to design a polymer that is phase selectively soluble in either phase as was the case for the PNIPAM/PNODAM polymers used in heptane/aqueous EtOH mixtures above. This required a more polar polymer than PNIPAM. A candidate more polar polymer, poly(*N*-acrylethanolamide) **6**, was prepared by reaction of an active ester polymer, poly(*N*-acryloxysuccinimide) (PNASI),[12] with a mix-

(10) Pollak, A.; Whitesides, G. M. *J. Am. Chem. Soc.* **1976**, *98*, 289–291.

(11) Bergbreiter, D. E.; Case, B. L.; Liu, Y.,-S.; Caraway, J. W. *Macromolecules* **1998**, *31*, 6053–6062.

(12) (a) Mammen, M.; Dahmann, G.; Whitesides, G. M. *J. Med. Chem.* **1995**, *38*, 4179–4190. (b) Batz, H. G.; Franzmann, G.; Ringsdorf, H. *Angew. Chem., Int. Ed. Engl.* **1972**, *11*, 1103–1104.

ture of ethanolamine and an amine-derivative of *p*-methyl red (eq 2). As was true in the examples above, the methyl red indicator dye was incorporated both to serve as a surrogate for a catalyst and as a convenient UV−visible label for the polymer.


5 (2)

6
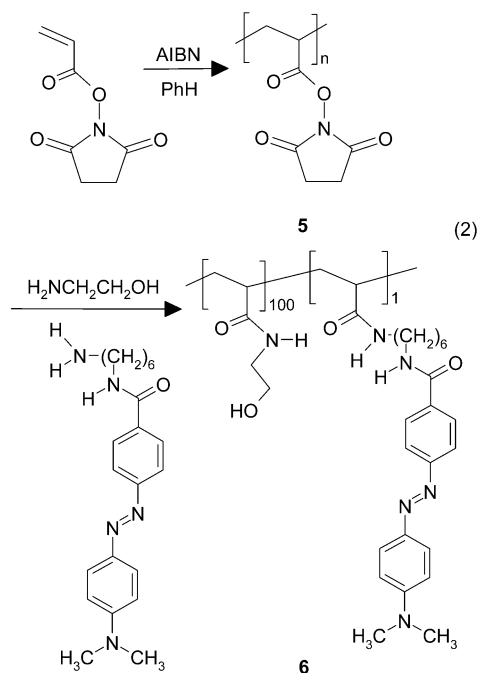
The dye-labeled polymer poly(*N*-acrylethanolamide) (PNAEAM, **6**) (20 mg) was first dissolved in 6 mL of ethanol. Heating was used to speed dissolution, but the polymer was soluble in ethanol at room temperature. Then an approximately 4 mL portion of water was added. The polymer stayed in solution. Finally, 10 mL of TBME was added to form an orangish transparent solution. This latently biphasic system was then perturbed into a biphasic state by the addition of 2.5 mL of water. The denser orangish water-rich phase and less dense TBME-rich phase thus formed separated readily in less than five minutes. Once separation occurred, the polymer-bound azo dye was recovered as an aqueous solution by simple liquid/liquid separation.

Catalysis was not studied in this TBME/EtOH/H$_2$O system. However, recycling the polymer bound azo dye was feasible. This recycling was followed both visually and by UV−visible spectroscopy. First, the less dense TBME-rich layer from the first cycle described above was separated from the H$_2$O-rich phase and analyzed by UV−visible spectroscopy. A small absorbance due to the dye (<3% of the original dye) was detected in this first cycle in the TBME rich phase. Then, 10 mL of fresh pure TBME was added to the denser bottom layer (the H$_2$O-rich, polymer-bound dye-containing phase) along with 4 mL of ethanol. These additions of solvent reformed a single miscible orangish homogeneous solution that was visually indistinguishable from the starting solution. Water addition to form a biphasic system, separation, analysis of the TBME-rich phase for **6** and reforming of the miscible solution by further addition of TBME and EtOH was then carried out for several cycles. Less than 1% of the polymer **6** was lost in the TBME phase in cycles 2−5 as determined by UV−visible spectroscopy.

The total volume of the recovered H$_2$O-rich phase in each of the 4 subsequent cycles was not substantially different from the volume of the H$_2$O-rich phase in the first cycle because 2.5 mL of H$_2$O was being added every cycle to induce phase separation.

The absorbance in the TBME (top) layers through five cycles was as follows; cycle 1−0.108 at 421 nm; cycle 2−0.034 at 426 nm; cycle 3−0.022 at 422 nm; cycle 4−0.037 at 423 nm; cycle 5−0.011 at 426 nm. The absorbance of the polymer-bound dye containing layer was generally too high to measure without dilution (*A* > 3.5). Qualitatively, it was the same shade of orange through each cycle. The loss of some material in cycles 1 through 5 may be due to low molecular weight PNAEAM present in the sample of **6** used. The PNASI precursor used to prepare **6** was polydisperse since it was derived from a standard radical polymerization. Although the polymer **6** was not directly analyzed, the PNASI used to prepare the PNAEAM was characterized indirectly. This was accomplished by allowing the common PNASI precursor polymer to react with isopropylamine to form PNIPAM. The PNIPAM so prepared (and by inference the PNASI) had a PDI of 1.89 and an M_n of 1.8×10^5 Da based on GPC analysis. In prior experiments using a PEG-bound dye as a surrogate for a PEG-bound catalyst in a thermomorphic system,[5] we noted that it can be necessary to extract low concentrations of less phase selectively soluble polymer from a polydisperse sample in a liquid/liquid extractor if a >99.5% recovery of a polymer is to be achieved. This was not done in this case prior to the use of **6** in this latent biphasic system, whereas recovery of PNAEAM was >99.5% by cycle 5.

The studies above with dye-labeled polymers show that a latent biphasic strategy can effect separations. Studies with catalysts bound to phase selectively heptane-soluble polymer supports show the utility of this latent biphasic chemistry in known catalytic reactions. Three reactions were studied. The first was Heck catalysis using an SCS-Pd(II) catalyst we described previously (eq 3).[5] Catalyst **7** is soluble at 25 °C in a miscible 1:1 heptane-dimethylacetamide (DMA) mixture along with acrylic acid, iodobenzene and Et$_3$N. After a homogeneous reaction (120 °C for 12 h), cooling to 25 °C formed a biphasic mixture of **7** and the Heck product due to formation of triethylammonium iodide. Isolation of the heptane phase containing **7** and addition of a fresh amount of DMA, substrates, and base to this heptane solution allowed us to recycle this catalyst.


7

(3)

93% yield
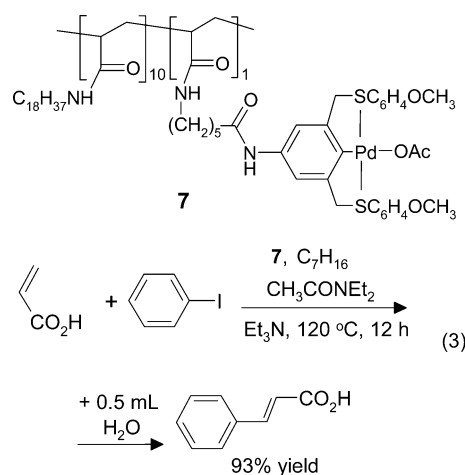
The generality of this latent biphasic approach in homogeneous catalyst recovery was shown using a polymer-bound trifunctional base catalyst **8** (eq 4) as a DMAP analog[13] in acylation of 2,6-dialkylphenols by (Boc)$_2$O in either a 1:1 heptane-aqueous EtOH or a 1:1 heptane-DMF system (eq 5). Yields in this chemistry gradually increased from cycle to cycle as the heptane-rich phase became saturated in the product carbonate. Yields through 6 cycles for R = −H were 59%, 80%, 95%, 99%, 99%, and 99% and for R = −CH$_3$ were 35%, 66%, 89%, 99%, 99%, and 99% when a heptane/ethanol system was used. A similar experiment was also carried out using 2,6-diisopropylphenol in a heated thermorphic heptane/DMF mixture. In this latter case, the product yields (from the DMF-rich phase) were 44%, 57%, 76%, 90%, 98%, 99%, and 99% through the first seven cycles. In the first two of these cases, the initially monophasic reaction mixture was perturbed to be biphasic by the addition of 10 vol % H$_2$O. The heptane phase so formed was then recycled by addition of fresh EtOH (or DMF), substrate and (Boc)$_2$O. Heptane was added as needed to replace heptane lost in the EtOH- or DMF-rich phases. In all three of these series, the polymeric catalyst used was labeled with a methyl red label. The absence of detectable dye-labeled polymer in any of the cycles in either the polar EtOH-rich or DMF-rich phases indicated quantitative separation of the catalyst into the nonpolar heptane-rich phase.
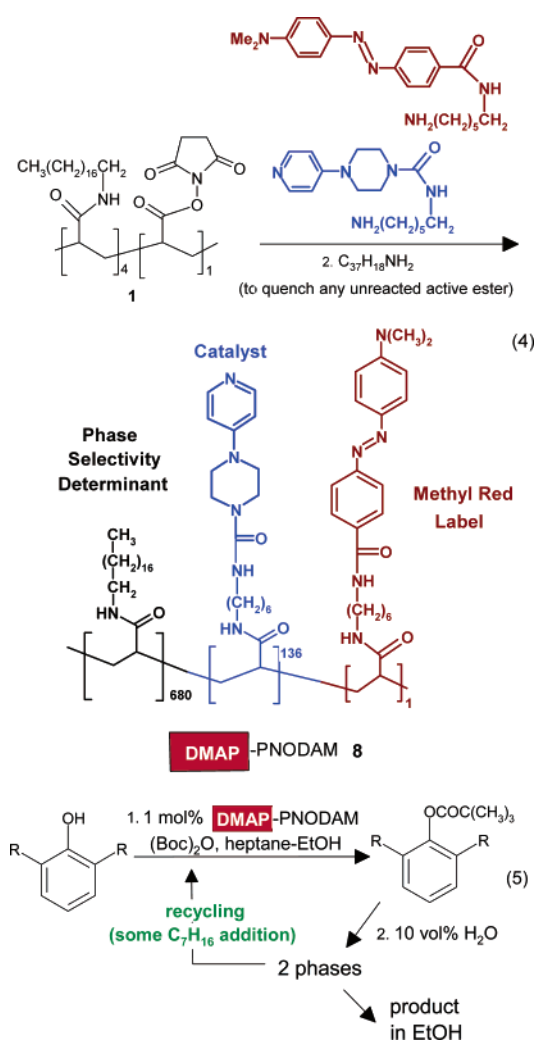
Any phase selectively soluble polymer support should work in this latent biphasic strategy. To show this, a third example of catalyst recycling under latent biphasic conditions used another nonpolar phase-soluble polymer as a support for a Lewis acid catalyst. This polymer has not been used before as a soluble polymer support, but it is similar to a material we used earlier to support hydrogenation catalysts.[14] This new polymer (**9**) was prepared by an alternating copolymerization of the commercially available monomers, octadecyl vinyl ether and maleic anhydride.[15] Post polymerization amidation of the anhydride groups of this copolymer with a 1:1 mixture of octadecylamine and morpholine produced an amic acid-containing polymer that had a 10:1 (mole:mole) mixture of secondary and tertiary amides. Heating induced imidization of the secondary amide-acids of this amic acid-containing polymer to produce a terpolymer containing *N*-octadecylmaleimide and octadecylvinyl ether repeating units with a ca. 10% loading of unimidized amic acids derived from the secondary amine morpholine. Ion exchange of some of the protons of these remaining carboxylic acid groups of these remaining amic acids with silver acetate produced an Ag(I)-polymer **5** that was then used as a heptane-soluble Lewis acid (eq 6).
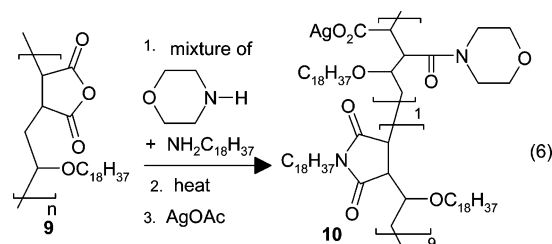
This Ag(I)-polymer **10** as well as **7**[16] both catalyze atom efficient oxazoline formation from ethyl isocyanoacetate and benzaldehyde (eq 7) under latent biphasic conditions. Recycling studies however only used the polymer-bound Ag(I) catalyst **10** since it was a more readily available catalyst.
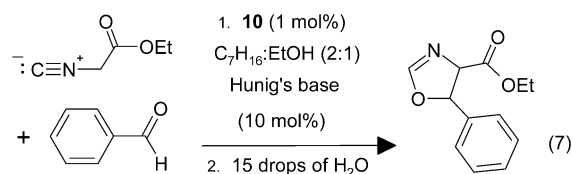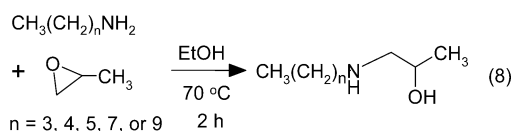

Recycling **10** proved to be simple and effective. After 20 mL of a miscible 1:1 (vol:vol) EtOH-heptane solution containing **10** (215 ppm Ag(I)) was used for oxazoline formation (overnight in a flask shielded from light), the catalyst **10** was quantitatively recovered as a heptane phase by the addition of 15 drops of water. Recycling **10** proved to be possible and involved addition of 10 mL of fresh EtOH, 5 mL of heptane and fresh reagents. Analysis of the polar phase showed traces of Ag(I) (0.44, 0.18, and 0.14 ppm Ag(I) in cycles 1−3, respectively) in the recovered EtOH-rich phase. The origin of this <0.11% loss of Ag(I) per cycle is uncertain. It may reflect loss of polymer to the other phase since this value is at the UV−visible detection limit for

(13) Bergbreiter, D. E.; Osburn, P. L.; Li, C. *Org. Lett.* **2002**, *4*, 737−740.
(14) Bergbreiter, D. E.; Liu, Y.-S. *Tetrahedron Lett.* **1997**, *38*, 3703−3706.
(15) Culberston, B. M. In *Encyclopedia of Polymer Science and Engineering*; Kroschwitz, J., Ed.; Wiley & Sons: New York, 1987; Vol. 9, p 225.
(16) Gimenez, R.; Swager, T. M. *J. Mol. Catal. A: Chem.* **2001**, *166*, 265−273.

a dye-labeled analogue of **10**. Alternatively, this could reflect low but variable Ag(I) leaching due to glassware contamination by ppb levels of anionic surfactants. Indeed, a repetition of this experiment with more cycles but with ordinary glassware (glassware that had been used and washed with phosphate-containing detergents) showed a larger and more variable average loss of <0.15% of the starting Ag(I)/cycle (0.59, 0.05, 0.58, 0.20, 0.20 ppm Ag(I) in cycles 1−5).

A final example of latent biphasic chemistry is the use of the polymer **9** as a selective primary amine sequestrant. Earlier work using a similar polymer as a support for phosphine ligands had noted that similar maleic anhydride copolymers do not readily react with 2° amines.[14] Thus, we expected **4** would be effective as a selective sequestrant for 1° amines.

This heptane-soluble sequestrant was used to remove excess amine used in a propylene oxide alkylation of amines to form ethanolamines (eq 8). In this reaction, excess 1° amine was used to minimize over alkylation. Addition of **9** then consumed the excess 1° amine and perturbation of the resulting heptane-EtOH solution separated the product 2° amine from the scavenger resin and the sequestered 1° amine. A series of reactions used 2 equiv of butyl-, amyl-, hexyl-, octyl-, or decylamine as the substrates using ethanol as the solvent. After heating to 70 °C for 2 h, the mixture was cooled to room temperature, and a heptane solution of 3 equiv of **9** was added to form a homogeneous heptane-EtOH mixture. The excess amine was consumed within 1 min. after addition by this solution of **9**. Addition of H_2O (the added water was 10% of the total volume) then produced two phases. Any 1° amine was at that point bound to the polymer and sequestered in the heptane phase. The polar phase containing the hydroxylamine products was then separated. A limitation of this chemistry was that the products derived from the more hydrophobic amine substrates have some heptane solubility. In those cases, high yields of product can only be obtained if the heptane solution is extracted with aqueous EtOH (the polymer exclusively remains in the heptane phase even after the extractions).

$$CH_3(CH_2)_nNH_2$$

support for a reagent or catalyst can be designed to be selectively soluble in a particular phase, products can partition to either phase. In a repetitive process like the phenyl carbonate synthesis described above, this problem will be of minimal consequence as the recycled phase will eventually be saturated in product. In other cases, extraction of the recycled phase might be necessary to obtain a high isolated yield of a product in a single cycle. This problem is a general problem with any biphasic liquid/liquid separation strategy. Finally, it should be recognized that reactions carried out in this way involve a mixed solvent—mixed solvent conditions will not always mirror conventional chemistry carried out in a single pure solvent.

The results here show that this latent biphasic approach is an alternative to more standard biphasic chemistry using soluble and insoluble polymers since polymers can be designed to have large distribution coefficients and phase selective solubility. While dendrimers can be used similarly, these sorts of soluble polymers are not needed to ensure efficient recovery or separation of a polymer-bound catalyst or reagent. The addition of a low volume percent of a third solvent or the addition of a phase perturbing agent should also be useful in more normal biphasic reactions such as fluorous biphasic chemistry where solvent or ligand/catalyst loss is a problem.

Experimental Section

All reagents and solvents were obtained from commercial sources and used without further purification unless otherwise specified. ^{1}H NMR spectra were recorded on Varian VXR-300 or Unity p300 spectrometers at 300 MHz. Chemical shifts are reported in ppm with chloroform (7.27 ppm) as an internal standard.

Tests of Polymer Separability/Recovery in the Toluene−Ethanol−Water System. A sample of poly(*N*-octadecylacrylamide) containing 1 or 2 mol % of *p*-methyl red as a dye label (**2**) was prepared according to a reported procedure[6] and dissolved in a mixture of 10 mL of toluene and 10 mL of 86% EtOH−H_2O. Addition of 0.5 mL of water (2.5% of the total volume) to the solution resulted in layer separation with the dye-labeled polymer visually residing in the upper toluene-rich layer. Analysis by UV−visible spectroscopy showed the polymer had >1500:1 preference for the toluene layer.

Tests of Polymer Separability/Recovery in the Heptane−Ethanol−Water System. A sample of the dye-labeled poly(*N*-octadecylacrylamide) **2** was dissolved in 20 mL of a solution containing equal portions of heptane and 96% EtOH−H_2O. Addition of 9−10 drops of water produced a biphasic mixture. As in the toluene−aqueous ethanol system above, this dye-labeled PNODAM polymer was exclusively soluble in the heptane layer. UV−visible spectroscopy showed that the phase selective solubility was >1500:1. Similar experiments with a dansyl-labeled PNIPAM (**3**) or a methyl red-labeled PNIPAM (**4**) had **3** or **4** staying exclusively in the polar EtOH-rich phase. The necessary PNIPAM derivatives were prepared by reaction of an amine derivative of dansyl or methyl red[17] with a PNIPAM-NASI copolymer using a previously described procedure.[11]

***N*-Octadecylacrylamide.** Octadecylamine (26.7 g) was suspended in 500 mL of CH_2Cl_2. Then 16.9 mL of triethylamine was added, and the mixture was cooled to 0 °C using an ice−water bath. Dropwise addition of 50 mL of a CH_2Cl_2 solution containing 8.9 mL of acryloyl chloride to the amine suspension and stirring at room temperature for 1 h yielded a solution of the product monomer. To isolate the monomer, the CH_2Cl_2 was removed under reduced pressure and the residue was taken up in 250 mL of chloroform, washed with water and brine, dried over sodium sulfate and filtered. The filtrate was concentrated and the

Conclusions

This latent biphasic strategy should be a general way to carry out homogeneous reactions and separate and recover catalysts, reagents or products by biphasic separation. However, it is important to recognize that this approach like any approach has some limitations. First, it is unlikely that any of the polymers described here would be suitable for all reactions. A specific reaction may require a different polymer—a polymer without N−H bonds for example. Second, because hundreds of different solvent mixtures might be used, it would presumably be necessary to test the phase selective solubility of a polymer with the specific solvents that are to be used. Third, the solvent mixtures used should be different in density in their biphasic state. Fourth, loss of solvent in the recovered/reused phase can occur. This problem can be minimized by using a second phase that is presaturated with this solvent. Fifth, although the polymer

(17) Bergbreiter, D. E.; Franchina, J. G.; Kabza, K. *Macromolecules* **1999**, *32*, 4993−4998.

residue was taken up in 100 mL of acetone with warming. After the addition of 80 mL of acetone, the mixture was allowed to sit at room temperature in the dark to crystallize. The product was isolated by filtration and had mp 70−71 °C (lit[18] 74.5−75.1 °C); ^{1}H NMR (CDCl$_3$) δ 6.3 (d, 15.4 Hz, 1H), δ 6.1 (dd, J = 10.2, 15.4 Hz, 1H), 5.6 (d, 10.2 Hz, 1H), 3.3 (q, 6.9 Hz, 2H), 1.5 (t, 6.9 Hz, 2H), 1.3 (bs, 30H), 0.9 (t, 6.6 Hz, 3H).

Poly(*N*-octadecylacrylamide-*co*-NASI) (PNODAM-NASI) (10:1). Benzene (50 mL) was degassed with N$_2$ for 30 min. Then octadecyl-acrylamide (4.5 g, 13.9 mmol) and *N*-acryloxysuccinimide (0.24 g, 1.39 mmol) were added. The reaction mixture was warmed to 80 °C and a solution of AIBN (12.6 mg, 0.077 mmol) in 2 mL of benzene was added. The reaction mixture was stirred at 80 °C under nitrogen for 36 h, at which point the solvent was removed and the residue was taken up in 30 mL of chloroform. The product was isolated by solvent precipitation by slow addition of this solution into 150 mL of cold methanol to give 4.1 g (87%) of a white powder. IR (KBr, cm^{-1}) 1812, 1783, 1737, 1654, 1542. ^{1}H NMR (CDCl$_3$) δ 3.1 (br s, 20H), 2.8 (br s, 4H), 1.5 (br s, 27H), 1.2 (br s, 395H), 0.8 (br t, 30H). Polymers with different monomer ratios were obtained similarly using different feed ratios of monomers.

Dye-labeled PNODAM-supported DAAP Catalyst. A sample of a 4:1 PNODAM-PNASI copolymer (4 g) prepared as described above was dissolved in chloroform and first allowed to react with 50 mg of amine-terminated methyl red[14] at room-temperature overnight. Then 500 mg of the amine-terminated DAAP catalyst[15] in chloroform was added. After overnight stirring, a final portion of 1 g of *N*-octadecyl-amine was added to quench any remaining active esters. After overnight stirring, 3.7 g of the red polymer product was isolated by methanol precipitation. The polymer was characterized by UV−visible spectroscopy (λ_{max} = 419 nm in heptane). Based on GPC analysis (DMF, 0.01 M LiBr, TOSOH BIOSEP column) of an analogously prepared PNIPAM polymer, the molecular weight (M_n) of this product and the PDI were 800,000 Da and 1.9, respectively.

Acylation Using PNODAM-Supported DAAP Catalyst. An equimolar mixture of 1 mmol of the substituted phenol and 1.02 mol of Boc anhydride was dissolved in 10 mL of ethanol. Then 10 mL of a heptane solution containing 97 mg of the PNODAM-supported DAAP catalyst (1 mol %) was added and the mixture was stirred for 30 min. Phase separation was achieved by the addition of 1.5 mL of water, and the aqueous ethanol phase was concentrated and extracted with dichloromethane to obtain the product. The heptane phase was recovered and mixed with fresh substrate solution in ethanol for the next catalytic cycle.

Poly(maleic anhydride-*c*-octadecyl vinyl ether) (PMAOVE). Maleic anhydride was recrystallized from benzene before use. In a typical copolymerization, maleic anhydride (3.3 g, 33.7 mmol) and octadecyl vinyl ether (10 g, 33.7 mmol) were dissolved in 30 mL of benzene. The reaction flask was then evacuated and backfilled with N$_2$ 5 times. After heating the resulting solution to 60 °C, 2 mL of a toluene solution of benzoyl peroxide (10 mg, 0.041 mmol) was added to initiate the polymerization. After 20 h at 60 °C, the reaction mixture was diluted with 40 mL of ether and poured into 900 mL of acetone to provide a white powder. This precipitate was isolated by filtration and dried to yield 10.5 g (79%) of the desired product polymer. ^{1}H NMR (CDCl$_3$) δ 3.7−3.2 (br s, 2H), 1.7−1.2 (br m, 37H), 0.9 (t, 6.6 Hz, 3H). IR (KBr, cm^{-1}) 1859, 1781, 1724, 1465. GPC analysis of a N-benzyl imide derivative of this product showed it had M_n = 730 000 and M_w = 1 950 000.

PMAOVE Substituted with Octadecylamine and Morpholine. PMAOVE (1 g, 2.5 mmol) was dissolved in 50 mL of CH$_2$Cl$_2$ and allowed to react with a mixture of octadecylamine (1.36 g, 5.0 mmol) and morpholine (442 mg, 5.0 mmol) in 25 mL of CH$_2$Cl$_2$. The reaction

was stirred overnight. An acidic ion-exchange resin, Amberlyst-15 (4 g), was added to the reaction and the mixture was shaken overnight to remove any unreacted amines. The resin was filtered and washed with CHCl$_3$. The filtrate was freed of solvent under reduced pressure to yield the product amic acid-containing polymer as a solid (IR stretches at 1716, 1641, 1575, and 1467 cm^{-1}). This polymer was then dissolved in 250 mL of toluene and heated at reflux overnight using a Dean−Stark trap to remove water. The product solution was then concentrated under reduced pressure to yield a solid that was dissolved in 100 mL of CH$_2$Cl$_2$. The solvent was removed under reduced pressure using a rotary evaporator to give 1.1 g (65%) of a light yellow solid. ^{1}H NMR (CDCl$_3$) δ 3.3−3.5 (br s, 2.2H), 2.8 (br s, 1H), 1.4−1.6 (br s, 2H), 1.1−1.4 (br s, 27H), 0.83 (t, 6.6 Hz, 3H). IR (KBr, cm^{-1}) 1772, 1700, 1465, 1382.

PMOAVE-Silver Salt (10). The polymer prepared as described above (500 mg, 0.0795 mmol) was dissolved in 70 mL of heptane and added to 30 mL of EtOH. Silver acetate (132 mg, 0.795 mmol) was added to the reaction as a solid. The reaction was stirred at room temperature in the dark for 48 h. Water (10 mL) was added to the reaction to separate the layers. The mixture was transferred to a separatory funnel and the aqueous layer was removed. The organic layer was filtered and dried to give 400 mg (79%) of a dark yellow powder. IR (KBr, cm^{-1}) 1698, 1646, 1585.

Latent Biphasic Heck Catalysis. The catalyst used and the procedure used was identical to the normal thermomorphic procedure previously described with the difference being that the starting solution was a single phase.[6]

Latent Biphasic Oxazoline Synthesis. The polymeric Ag(I) catalyst **10** prepared above (125 mg, 0.02 mmol of Ag) was dissolved in 20 mL of heptane. Benzaldehyde (212 mg, 2 mmol), ethyl isocyanoacetate (226 mg, 2 mmol), and Hunig's base (35 μL, 0.2 mmol) were dissolved in 10 mL EtOH containing 1 mmol dodecane as an internal standard. The alcoholic solution was then added to the solution of the polymer to form a homogeneous system. The reaction was protected from light and stirred at room-temperature overnight. At this point, 15 drops ($\sim$600 mg) of water were added to induce separation of the layers. The lower layer was removed and stored for metal analysis. A fresh solution of reagents in ethanol was added to the reaction flask containing the heptane solution of **10**. An additional 5 mL of heptane was added to regenerate a new solution of substrate, catalyst and solvents that could be used in a subsequent reaction cycle.

Sequestration of Primary Amines by a Heptane-Soluble Polymer Under Latent Biphasic Conditions. In a typical reaction, 2 mmol of a primary amine and 70 μL of propylene oxide (1 mmol) were dissolved in 10 mL of ethanol and heated at 70 °C for 2 h. Then 10 mL of a heptane solution of 1.25 g of the polymer sequestrant PMAOVE (3 mmol) was added to this solution. After stirring 10 min, this miscible mixture of product, sequestered excess amine and polymer was induced to phase separate into two phases by the addition of 1.5 mL of water. While sequestration of primary amines in the heptane-soluble polymer was quantitative, the amino alcohol products from longer chain amines (e.g., octylamine) had some solubility in the heptane phase. In these cases, the nonpolar phase was extracted with aqueous ethanol to completely recover the product. Yields of amino alcohol products were typically in the range of 80−95% (GC yields). The absence of any contaminating primary amine in the amino alcohol product was verified by GC chromatography using dodecane as an internal standard.

Synthesis of PNAEAM. PNASI (1 g, 5.9 mmol of active ester) was first prepared following a literature procedure.[12a] This reactive ester polymer was then dissolved in 30 mL of dry DMF with heating. To this solution was added 22 mg (0.059 mmol) of amine-terminated methyl red.[17] This solution was stirred for 4 h. Then amino ethanol (1 g, 16.4 mmol) was added and the reaction stirred at room temperature. During this time a white precipitate formed. The reaction was allowed to stir overnight. The mixture was transferred to a centrifuge tube and centrifuged for about an hour. The red supernatant was removed with

(18) Roy, R.; Tropper, F. D.; Romanowska, A. *J. Chem. Soc., Chem. Commun.* **1992**, 1611−1613.

a pipet and the solvent was removed under vacuum. The resulting red solid was dissolved in 20 mL ethanol with heating. This dissolution was also slow. The red solution was added dropwise via pipet to 150 mL of hexane to form an orange powder. The powder was isolated by filtration. While on the filter, the solid started to become tacky, possibly from water in the air, so the solid was transferred to a vial and dried under vacuum to give 460 mg of an orange solid. This product was characterized by ^{1}H NMR spectroscopy but the spectrum was of poor quality with broad peaks. ^{1}H NMR (DMSO-d_6) δ 7.4−7.7 (br m, 1 H), 4.8−5.1 (br m, 1 H), 3.0−3.4 (br m, 5 H), 1.8−2.1 (br m, 1 H), 1.2−1.4 (br m, 2 H).

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