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Thermomorphic Rhodium(I) and Palladium(0) Catalysts

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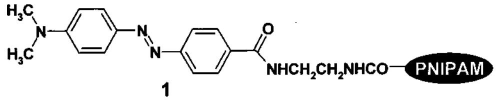
Applications of polymer-supported chemistry in synthesis and catalysis continue to enjoy a resurgence of interest.[1−3] Combinatorial chemistry and the desire to develop new more environmentally friendly processes that minimize waste have both increased interest in separation processes where polymer supports are useful.[4] While conventional cross-linked Merrifield's polymer supports can be separated by simple filtration, non-cross-linked soluble polymer supports are typically isolated by solvent precipitation,[5] membrane filtration,[6] or heating above polymer's LCST.[7,8] Here we describe a new system where a soluble polymer-supported catalyst is used that combines attractive features of biphasic and homogeneous catalysis. This chemistry uses a solvent system that changes thermally from biphasic to monophasic and a polymeric ligand that prefers one phase under biphasic conditions. When a substrate (product) is preferentially soluble in the opposite phase, repetitive reactions proceed in excellent synthetic yield with facile catalyst/product separation at the biphasic stage.

Biphasic catalysis is a strategy that has become increasingly employed in synthesis since the discovery of phase transfer catalysis over 30 years ago.[9] Recent work in fluorous phase chemistry has increased interest in biphasic systems that can combine the activity of homogeneous catalysis with the simplicity of product isolation seen in a biphasic system.[10−12] Another expression of this concept is to use a system that itself reversibly changes from being biphasic to monophasic as a function of temperature, a thermomorphic system. Many solvent pairs exhibit varying miscibility as a function of temperature.[13a−d] Fully thermomorphic behavior has also been noted in some catalytic sytems.[10,14] Here we describe a general approach that uses a polymer support as a general tool in this sort of temperature-induced phase-changing process. In the resulting thermomorphic system, a soluble polymer's strong phase preference under biphasic conditions leads to a general way to effect quantitative isolation of a polymer-bound catalyst.

Our approach to thermomorphic catalyst systems has its roots in our prior work with soluble poly(*N*-isopropylacrylamide) (PNIPAM) supports.[8,15] Catalysts or substrates on PNIPAM can be readily recovered either by heating (water) or by solvent precipitation but are comparable in reactivity to their low molecular weight analogues when dissolved in water or an organic solvent.

Pure ethanol and heptane are completely miscible at 25 °C. Addition of a polymer such as PNIPAM does not affect this miscibility. However, addition of as little as 10% water (v/v) to the ethanol phase induces phase separation. Our work with this system began with the realization that heating to 70 °C was sufficient to make this system miscible. Cooling reformed the initial biphasic system. We realized that the addition of reagent that was exclusively soluble in one phase at 25 °C would lead to a useful and potentially general scheme for catalyst/product/reagent separation. This realization was confirmed by simple experiments with the polymer-supported dye **1**. When this dye was added to a 2:1 (v:v) 90% aqueous ethanol/heptane mixture, the aqueous ethanol phase was bright red. The heptane phase was colorless. On heating to 70 °C, the mixture became monophasic with the dye distributed throughout the solution. Cooling regenerated the original biphasic system with **1** being exclusively in the aqueous ethanol phase.



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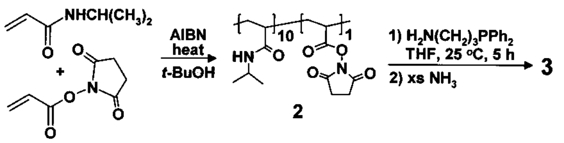
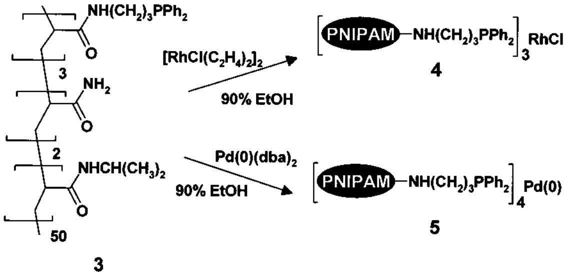
To use these systems in catalysis, we prepared a PNIPAM−phosphine **3** from the known copolymer **2** using a reported procedure (eq 1).[8] The product of this chemistry was a water-soluble polymer-bound phosphine with a 50:2:3 (^{1}H NMR spectroscopy) ratio of the *N*-isopropyl, $-NH_2$ and *N*-(3-diphenylphosphino)propyl groups. This polymeric phosphine was then complexed with Rh(I) or Pd(0) as shown in eq 2.



(1)



(2)

Catalysis in a thermomorphic system was studied by using hydrogenation of 1-octadecene and 1-dodecene. GC experiments showed that the K_D for 1-octadecene in an 1:1 (v:v) mixture of 90% aqueous ethanol and heptane (defined as $[(C_{18}H_{36})_{\text{heptane}}]/[(C_{18}H_{36})_{90\%\ \text{EtOH}}]$) was >1000. We estimate that K_D for the catalyst **4** was <1:500. Thus, no detectable hydrogenation occurred at 22 °C (biphasic conditions). However, hydrogenation did occur when this biphasic mixture was heated to 70 °C (monophasic conditions). As Figure 1 shows, catalyst **4** and $(PPh_3)_3RhCl$ (**6**) have comparable activity at 70 °C. However, while the PNIPAM-bound catalyst **4** was completely insoluble

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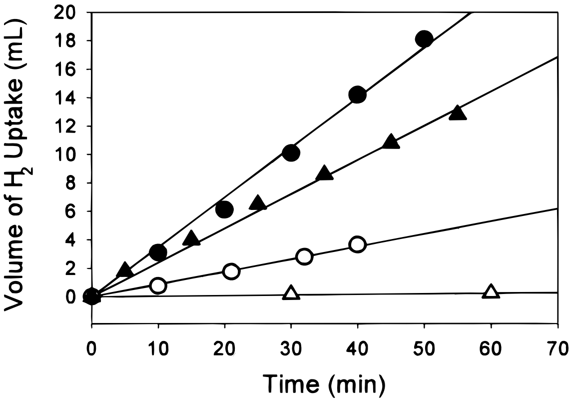


Figure 1. Plot of Rh(I)-catalyzed hydrogenations in 1:1 (v/v) 90% EtOH/heptane for Wilkinson's catalyst and $(PNIPAM\text{-}PPh_2)_3RhCl$ (**4**) at 70 °C (closed circle, closed triangle, respectively) and 22 °C (open circle, open triangle, respectively).

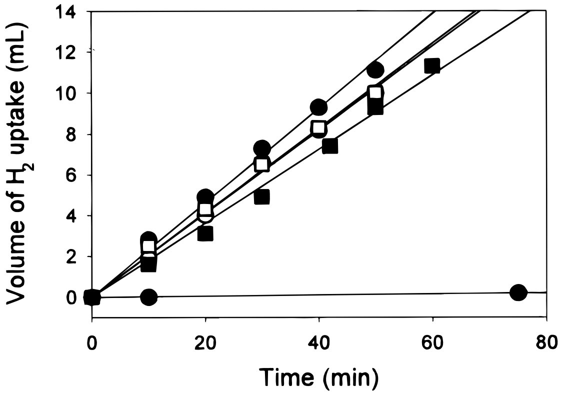
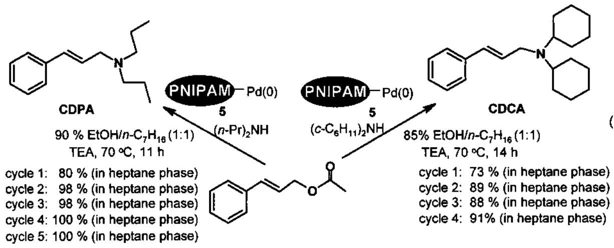


Figure 2. Recycling of PNIPAM-bound Rh(I) catalyst (**4**). The catalyst was used four times (first, ●; second, ○; third, ■; fourth, □) by cooling the miscible hot solution, separating the ethanol/water and heptane phases after cooling, and then adding fresh heptane/octadecene to the original ethanol/water phase

in heptane and thus inactive and separable at 22 °C, **6** had modest activity (ca. one-sixth of the rate at 70 °C) due to its having some solubility in the heptane phase at 22 °C (separate experiments with **6** and heptane alone confirmed that **6** is soluble in heptane).

Recycling experiments were performed by using 1-dodecene as a substrate. When **4** was dissolved in a 1:1 (v:v) mixture of 90% aqueous ethanol and heptane, no 1-dodecene hydrogenation occurred at 22 °C. After heating to 70 °C, hydrogenation commenced as shown in Figure 2. After cooling to 22 °C, the heptane phase was separated from the 90% aqueous ethanol phase containing **4**. GC analysis at this stage showed dodecane product had indeed been formed. Then a fresh portion of 1-dodecene in heptane was added and the rate was again measured on heating to 70 °C. The results of four cycles of hydrogenation/separation shown in Figure 2 show that within experimental error no catalyst activity was lost. We have further looked for Rh in the heptane phase after recycling. We found that there was no residual homogeneous hydrogenation activity in the separated heptane phase at 70 °C by adding more substrate and H_2. This result also indicates that the PNIPAM-supported catalyst can be fully recovered under this biphasic condition. In contrast to these results, recycling of **6** was not successful since some **6** was dissolved in the heptane phase.

The results of hydrogenations with α-olefins and **4** demonstrate the idea of thermomorphic catalysis. Further experiments with the Pd(0) catalyst **5** in the coupling of dicyclohexylamine and dipropylamine to cinnamyl acetate (eq 3) illustrate the generality of this idea. In addition, these experiments illustrate limitations of using thermomorphic systems in a single cycle and some potential advantages of the PNIPAM polymer ligands. The reactions in eq 3 used the same protocol described above. As was true in hydrogenations, the product in these reactions was isolated by simple removal of the heptane phase. Evaporation of solvent yielded ^{1}H NMR pure product allylic amines. However, the yields in the first cycle in these allylic substitutions were not as high as when the same reactions were carried out in a single solvent (e.g. in THF) because of product solubility in the aqueous ethanol (K_D(CDCA) = 3 and K_D(CDPA) = 2.1). Thus, in a single cycle some product was lost to the aqueous ethanol phase—a limitation if thermomorphic conditions were used in a nonrepetitive process. However, yields in cycles 2, 3, and 4 improve significantly since the aqueous ethanol phase was saturated with product allylic amine in the first cycle. Thus, in the context of using a recyclable catalyst in multiple cycles, the loss of product in the first cycle is inconsequential.



(3)

A second intriguing feature of the Pd(0) reactions is that these reactions were carried out with 85% aqueous EtOH. Prior studies had shown that 85% aqueous EtOH and heptane are not miscible at any temperature below 100 °C. However, when the polymeric Pd(0) catalyst **5** was used, 85% aqueous EtOH and heptane phases did become miscible. In these cases, the polymeric catalyst is evidently serving two roles. It both isolates and separates the Pd(0) catalyst at 22 °C into the aqueous EtOH phase and it promotes miscibilization of the solvent mixture at 70 °C.

In summary, a new thermomorphic system for homogeneous catalysis is described using two solvent systems whose miscibility is temperature dependent. In the specific examples shown, a soluble polymer ligand with a strong phase preference ensures that the catalyst ends up in one phase at low temperature, thus facilitating catalyst separation from product. This idea is a general approach to recover a catalyst, reagent, or product under biphasic conditions. There are many other solvent mixtures whose miscibility changes with temperature, and this approach should be useful in these systems. We have emphasized the use of a PNIPAM ligand to effect phase discrimination for a catalyst at low temperature. However, we note that other ligands such as water-soluble phosphines may be similarly useful.

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Supporting Information Available: Experimental details (3 pages, print/PDF). See any current masthead page for ordering information and Web access instructions.

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