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Using Soluble Polymers to Enforce Catalyst-Phase-Selective Solubility and as Antileaching Agents to Facilitate Homogeneous Catalysis**

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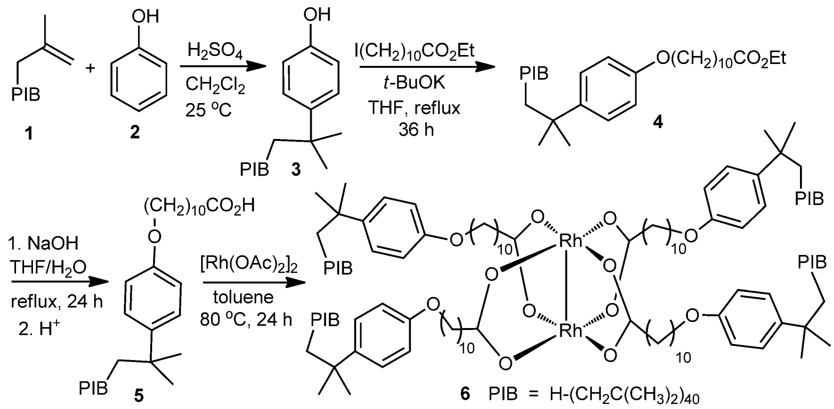
Abstract: *The enforced phase-selective solubility of polyisobutylene (PIB)-bound Rh^{II} catalysts in biphasic heptane/acetonitrile mixtures can be used not only to recycle these catalysts but also to minimize bimolecular reactions with ethyl diazoacetate. When cyclopropanation and O–H insertion reactions are carried out with PIB-bound Rh^{II} catalysts either with or without addition of an unfunctionalized hydrocarbon polymer cosolvent, dimer by-product formation is suppressed even without slow syringe pump addition of the ethyl diazoacetate. This suppression of by-product formation is shown to be due to increased phase segregation of the soluble polymer-bound catalyst and the ethyl diazoacetate reactant. These studies also reveal that added hydrocarbon polymer cosolvents can function as antileaching agents, decreasing the already small amount of a soluble polymer-bound species that leaches into a polar phase in a biphasic mixture during a liquid/liquid separation step.*

Soluble polymer supports are useful tools in homogeneous catalysis.[1] This work shows that the enforced phase-selective solubility of polyisobutylene (PIB)-supported catalysts can be used to both recycle catalysts and to suppress by-product formation involving the bimolecular reaction of a polar-phase-soluble reactant. Such effects are enhanced using added hydrocarbon polymer cosolvents that can serve as antileaching agents.

Rhodium(II) carboxylates have been used as catalysts in cyclopropanation, C–H insertion, X–H (X = O, N, S) insertion, and aromatic cycloaddition reactions of diazo compounds.[2] Both soluble supported catalysts we developed and insoluble supported catalysts others have used are recyclable in these processes.[3,4] However, all these catalysts require slow addition of the diazo substrate with a syringe pump because of the facile and exothermic Rh^{II}-catalyzed dimerization of the diazo reactant.[5] Here we describe how a soluble polymer's phase-selective solubility segregates the Rh^{II} catalyst and diazo reactant in nonpolar and polar phases of a biphasic heptane/CH_3CN mixture enabling both catalyst recycling and suppression of dimer formation without syringe pump addition of the N_2CHCO_2Et. This is possible because the low solubility of the diazo reactant in the heptane-catalyst-containing phase lowers the bimolecular rate of dimer formation more than the rate of cyclopropanation or O–H insertion. We further show that adding an unfunctionalized hydrocarbon polymer to the heptane phase of a heptane/polar solvent biphasic mixture further limits both dimer formation and leaching of PIB-bound species into the polar phase of a heptane/polar solvent biphasic mixture. These results suggest new roles for soluble polymers or oligomers as supports or as cosolvents in catalysis where soluble polymer supports recycle catalysts,[6] suppress undesired side reactions, and reduce leaching of heptane-soluble polymer-bound species.

A PIB-supported heptane-soluble Rh^{II} catalyst was prepared as shown in Scheme 1. This route to a $[(PIB_{2300}\text{-}CO_2)_2Rh]_2$ catalyst was more convenient for multigram syntheses than a previous one.[3c] Using PIB_{2300} as the starting



Scheme 1. Synthesis of a PIB_{2300}-bound carboxylic acid and its use in the formation of a PIB_{2300}-bound Rh^{II} catalyst.

material,[7] the ester **4** was prepared and hydrolyzed to form **5** which was used to form the Rh catalyst **6** by ligand exchange with $[Rh(OAc)_2]_2$ in toluene at 80 °C. The product **6** was a viscous oil which was characterized by UV/Vis spectroscopy. A Rh loading of 0.167 mmol g^{-1} in **6** was determined based on the absorbance at 588 nm (λ_{max}) of a known amount of **6** in EtOH/toluene and the ε of $[Rh(OAc)_2]_2$ in this same solvent mixture ($\varepsilon = 260\,M^{-1}cm^{-1}$, $\lambda_{max} = 587$ nm). These spectral data are comparable to the reported data for $[Rh(OAc)_2]_2$ in

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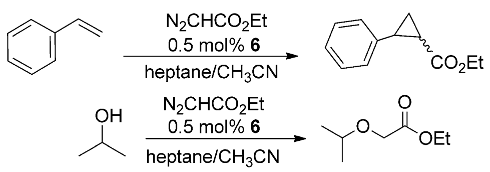
octanol ($\lambda_{max} = 585$ nm, $\varepsilon = 298\,\text{M}^{-1}\,\text{cm}^{-1}$).[8] The green PIB_{2300}-bound Rh^{II} carboxylate complex was visually insoluble in CH_3CN.

The studies in this paper make use of the phase-selective solubility of **6** and the fact that N_2CHCO_2Et is relatively insoluble in heptane versus CH_3CN to facilitate cyclopropanation and O–H insertion catalytic reactions of **6** (Scheme 2).



Scheme 2. N_2CHCO_2Et reactions catalyzed by the PIB-bound Rh carboxylate catalyst **6** in a biphasic heptane/CH_3CN solvent mixture at 25 °C.

We first confirmed that the PIB-bound Rh complex **6** was effective in cyclopropanation of styrene in CH_2Cl_2 using syringe pump addition of N_2CHCO_2Et to minimize the maleate/fumarate dimer formation (Table 1). This reaction produced a 71 % yield of the 2-phenyl-1-cyclopropylcarboxylic acid ester as a 67/33 *trans*/*cis* mixture with 2.3 % of the carbene dimer. These results are comparable to previous results with soluble polymer-bound Rh^{II} catalysts that used syringe pump addition of the N_2CHCO_2Et to suppress carbene dimer formation.[3a,c] Next, we examined **6** as a recyclable catalyst for cyclopropanation of styrene with N_2CHCO_2Et under biphasic conditions without the use of a syringe pump. The reaction was carried out in a heptane/CH_3CN biphasic system at room temperature using 0.5 mol % of **6**. In this case, most of the N_2CHCO_2Et was in the CH_3CN phase. Under these conditions, **6** was successfully reused affording the cyclopropanation product in 66, 67, and 74 % yield (as a ca. 67/33 *trans*/*cis* mixture) in cycles 1–3. The yield of dimer by-product was 7.7, 7.1, and 6.7 % for these same three cycles (as a 61/39 *Z*/*E* mixture). The catalyst **6** was recycled by separating the heptane phase containing **6** from the CH_3CN product phase and reusing the heptane solution in another cycle. The average yield of the isolated cyclopropanation product was 65 %/cycle. These results show that phase isolation of a PIB-bound Rh^{II} catalyst from N_2CHCO_2Et suppresses the dimerization of diazo substrates while still affording typical products in a reasonable time frame.

We attribute the low amount of dimer formation under biphasic conditions to two factors: the enforced phase-selective solubility of **6** in the heptane phase of the heptane/CH_3CN biphasic mixture and the relatively low concentration of N_2CHCO_2Et in the catalyst-rich heptane phase. The low concentration of catalyst in the CH_3CN phase, in which there is a high concentration of N_2CHCO_2Et, slows dimer formation in CH_3CN whereas the low concentration of N_2CHCO_2Et in heptane slows what would otherwise be a fast bimolecular dimer reaction in the catalyst-rich heptane phase. This control of an unwanted bimolecular reaction in a liquid/liquid biphasic system has been reported in isolated instances in other chemistry. For example, Collins et al. have shown that pseudobiphasic conditions facilitate macrocyclization under conditions, in which a bimolecular oligomerization is suppressed.[9]

In addition to cyclopropanation, rhodium carbenoids generated from diazo compounds are also used to insert a carbene equivalent in X–H bonds. This reaction can also be effected by phase-segregated catalyst **6** in a heptane/CH_3CN biphasic mixture without the need for syringe pump addition of N_2CHCO_2Et to suppress maleate/fumarate dimer formation. As shown in Table 2, **6** was successfully recovered and reused through three cycles of an O–H insertion into isopropyl alcohol affording the product in a 63 % average yield/cycle. The average yield of dimers was 6.6 %, a result similar to that obtained using syringe pump addition with **6** as a catalyst in monophasic CH_2Cl_2.

Our hypothesis is that the small amount of dimer formed results either from minimal catalyst **6** leaching into the N_2CHCO_2Et-rich CH_3CN phase, from a lowered N_2CHCO_2Et concentration in the heptane phase, or from a combination of these scenarios. Thus we could further reduce by-product formation either by reducing the leaching of **6** into CH_3CN or

Table 1: Results for the styrene cyclopropanation reaction catalyzed by **6** using biphasic conditions to effect the N_2CHCO_2Et dimerization suppression.[a]

Polyolefin Cosolvent	Cycle	Yield [%][b]	Dimer Yield [%][b,c]
CH_2Cl_2 as solvent[d]	–	71[e]	2.3
none	1	66	7.7
none	2	67	7.1
none	3	74	6.7
PIB_{2300}[f]	1	61	3.8
PIB_{2300}[f]	2	58	4.5
PIB_{2300}[f]	3	64[g]	5.4

[a] 2 mmol scale reactions with 0.5 mol % of **6** and 20 mmol of styrene at 25 °C using a 5 mL/15 mL mixture of heptane/CH_3CN. [b] Yields are based on ^{1}H NMR spectroscopy. [c] A mixture of maleate/fumarate products. [d] Syringe pump addition was used to suppress N_2CHCO_2Et dimerization in this CH_2Cl_2 monophasic reaction. [e] Yield of isolated product. [f] PIB_{2300} was added as a cosolvent. [g] Combining the products of three cycles in which PIB was present afforded 0.67 g of the cyclopropanation product.

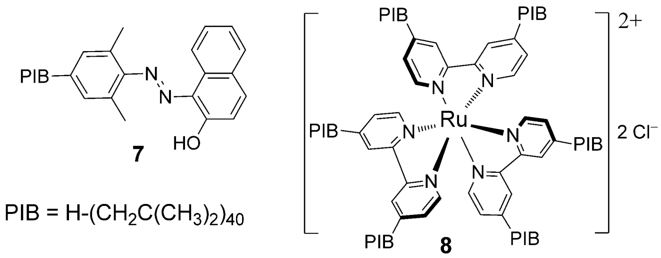
Table 2: Results of O–H insertion of isopropyl alcohol catalyzed by **6** using biphasic conditions to effect the N_2CHCO_2Et dimerization suppression.[a]

Cycle	Yield [%][b]	Dimer Yield [%][c]
1	72	6.4
2	66	6.8
3	51	6.6
–[d]	65	4.1
–[e]	66	2.6

[a] 2 mmol scale reactions with 0.5 mol % of **6** and 20 mmol of styrene at 25 °C using a 5 mL/15 mL mixture of heptane/CH_3CN. [b] Average ^{1}H NMR spectroscopy yields of product from two independent runs. [c] NMR yield of the by-product (a ca. 60/40 *Z*/*E* mixture). [d] An O–H insertion reaction carried out in the presence of added unfunctionalized PIB. [e] An O–H insertion carried out in CH_2Cl_2 adding N_2CHCO_2Et with a syringe pump.

by further reducing the concentration of N_2CHCO_2Et in the heptane phase.

The first scheme we explored was to add unfunctionalized PIB cosolvent to the heptane phase. The premise was that addition of unfunctionalized PIB would competitively saturate the CH_3CN phase, thereby reducing the amount of **6** in that phase. Since there was no visually apparent leaching of **6** into CH_3CN, we tested this idea by examining how added hydrocarbon polymer cosolvents reduced the leaching of two chromogenic PIB derivatives **7** and **8** that had visible leaching.



The first study of the antileaching effect of added hydrocarbon cosolvents used the PIB_{2300} bound azo dye **7**.[10] In a thermomorphic mixture containing 3 g of heptane and 3 g of CH_3OH, **7** has a small but detectable solubility in CH_3OH at 25 °C with an absorbance of 0.36 at 492 nm. Replacing 1 g of the heptane with 1 g of a polypropylene polymer[11] decreased the leaching of **7** by ca. 30 % (the dye absorbance in CH_3OH was 0.25). Using 3 g of this same polypropylene polymer and 3 g of CH_3OH as the solvent mixture, the concentration of **7** in the CH_3OH phase dropped by over 50 % (the absorbance of **7** in CH_3OH was 0.16) (Figures 2S and 3S in the Supporting Information). Studies with a chromogenic PIB-bound Ru bipyridine complex **8** used previously as a photoredox catalyst[12] showed that the antileaching effect of added hydrocarbon copolymers on soluble PIB-bound dyes also affects PIB-bound metal complex leaching. Dissolving **8** in a thermomorphic heptane/ethanol/DMF (4/2/3 vol/vol/vol) system forms a monophasic solution at 90 °C that becomes biphasic on cooling to 25 °C. Reheating and adding 0.4 g of PIB_{2300} to the hot monophasic mixture and cooling this solvent mixture to reform a biphasic mixture at 25 °C drastically decreased the leaching of **8** into the polar phase (Figure 1).

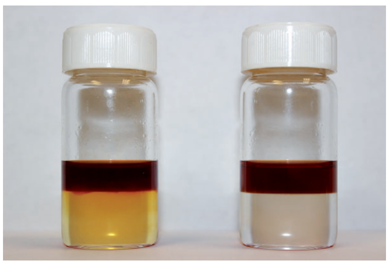


Figure 1. Antileaching effect of PIB_{2300} for the Ru bipyridine complex **8** in a heptane/ethanol/DMF solvent system; no PIB (left) or 0.45 g of added PIB_{2300} in 4 mL of a heptane phase containing 80 mg of **8** (right).

^1H NMR spectroscopy experiments (see the Supporting Information) determined the amount of leaching of the added copolymer into the polar phase. Based on a quantitative analysis using the ^{13}C satellite peaks of the CH_3OH or DMF and the methyl peaks of the added hydrocarbon cosolvent,[13] this leaching corresponds to less than 7.5×10^{-4} M copolymer in the polar phase.

The results of experiments in which PIB was added as a cosolvent to reduce by-product formation in cyclopropanation and O−H insertion are listed in Tables 1 and 2. In cyclopropanation, average dimer yields through three cycles of a catalytic reaction decreased from 7.4 % without any addition of PIB to 4.6 % with PIB_{2300} as the cosolvent. Similar results for dimer formation were obtained with PIB_{2300} as the cosolvent in O−H insertions (Table 2). The reduction of dimer formation linearly correlated with the amount of added PIB. PIB_{1000} was comparable in effect to PIB_{2300} (see Figure 1S in the Supporting Information). A small decrease in the cyclopropanation product yield was also noted.

The addition of PIB cosolvent could reduce by-product formation either by lowering the leaching of **6** into CH_3CN or by reducing the concentration of N_2CHCO_2Et in the heptane phase. The decrease in yield for the cyclopropanation product suggested the latter explanation. This was confirmed by analyses showing that the N_2CHCO_2Et concentration in heptane decreased from 5.0×10^{-3} to 3.2×10^{-3} to 2.5×10^{-3} M as the amount of added PIB in heptane increased from 0 to 0.07 to 0.22 M.

Suppression of dimer formation due to a lowered concentration of **6** in the N_2CHCO_2Et-rich CH_3CN phase is an alternative explanation for decreased dimer by-product in experiments where PIB is added as a cosolvent. However, studies of the dimerization of N_2CHCO_2Et by $[Rh(OAc)_2]_2$ or **6** under monophasic and biphasic conditions showed that a lowered concentration of **6** in the CH_3CN phase was less important than a decrease in the N_2CHCO_2Et concentration in heptane in accounting for the effect of added PIB. N_2CHCO_2Et in CH_2Cl_2 quantitatively dimerizes with 0.5 mol % of either $[Rh(OAc)_2]_2$ or **6** at 25 °C within 10 min.

Other experiments showed that reaction of N_2CHCO_2Et with $[Rh(OAc)_2]_2$ in CH_3CN only proceeds to 16 % after 10 h at 25 °C. Thus, even if **6** were to leach into the CH_3CN phase, it would not produce much dimer. While added PIB cosolvent could decrease leaching of **6** into CH_3CN, the antileaching effect of PIB is not the primary reason for the lower dimer by-product formation upon PIB cosolvent addition.

In summary, this report describes new roles for soluble polymer-bound catalysts and soluble polymers in homogeneous catalysis. Using a recyclable Rh^{II} cyclopropanation/O−H insertion catalyst as an example, we show how the phase-enforced solubility of a polymer support can suppress the undesired bimolecular dimerization reaction of ethyl diazoacetate in a heptane/CH_3CN biphasic reaction mixture without recourse to the use of syringe pump addition to maintain a low ethyl diazoacetate concentration. We show that adding a hydrocarbon polymer as a cosolvent further suppresses the formation of by-products from ethyl diazoacetate dimerization. These experiments also show that added hydrocarbon polymers in biphasic nonpolar/polar liquid/

liquid solvent mixtures act as antileaching agents. This effect of hydrocarbon polymer cosolvents could be a general and inexpensive way to minimize the leaching of precious catalysts or ligands during liquid/liquid biphasic separations.

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Communications

Polymers as Antileaching Agents

Y. Liang, M. L. Harrell,
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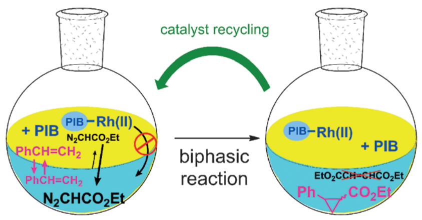
Using Soluble Polymers to Enforce Catalyst-Phase-Selective Solubility and as Antileaching Agents to Facilitate Homogeneous Catalysis



Suppression of by-product: In biphasic heptane/CH_3CN mixtures, heptane-soluble polyisobutylene (PIB)-bound Rh^{II} cyclopropanation and O–H insertion catalysts form only modest amounts of the undesired carbene dimer. It was shown that the phase isolation of these catalysts is enhanced by the addition of a polyolefin oligomer cosolvent, which acts as antileaching agent and minimizes the leaching of the PIB-bound species into the polar phase in liquid/liquid separations.