Can a fluorous biphase solvent system improve a polymer immobilized heterogeneous hydrogenation catalyst?

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When diphosphine rhodium(I) hydrogenation catalysts are incorporated into organic polymers that contain a permanent pore structure, they can be utilized in fluorous biphase solvent systems, where reaction rates increase with the fluorous content of the solvent.

The application of a fluorous biphase system (FBS) to separate products from a catalyst was both an intellectual and technical achievement in catalysis research.[1] At its heart, the FBS relies on the reversible temperature dependent miscibility of per-fluorinated and nonfluorinated liquids,[2] and the solvent preferences of organic products, substrates, and catalysts that contain ligands with perfluorinated substituents. This reversible temperature dependent miscibility provides the means to separate a catalyst from its product, and as such it has been applied in a number of catalyzed reactions.[2] These methods are characterized by high turnover numbers and relatively low catalyst leaching. Moreover, fluorous solvents show gas solubilities modestly higher than typical organic solvents,[2b] a property that could lead to higher reaction rates, in for example, olefin hydrogenation and hydroformylation.

We recently reported an olefin hydrogenation catalyst that was copolymerized into the matrix of a highly cross-linked macroporous (permanent pore structure) polymer.[3] The advantage of this solid support is that it does not require polymer swelling for access to its internal volume, and should thus be compatible with any solvent system. These heterogenized catalysts have already demonstrated easy separation and efficient recyclability in polar, nonpolar, and protic organic solvents, however, they can be less active than their solution-based analogues.[4,5] The combination of higher gas solubility coupled with the ease of adapting an existing heterogeneous catalyst for use in fluorous solvents[6] (*i.e.* no synthetic modifications) suggested that the combination be examined.

For testing purposes, a cationic diphosphine hydrogenation catalyst (2 mol%) was copolymerized into an ethylene dimethacrylate-based polymer (98%) as shown in Scheme 1. These materials contain ~100 μmol Rh g^{-1} dry polymer and ~400 m^2 g^{-1} surface areas (N$_2$ BET).[3,7]

To compare the activity and longevity of $\mathbf{P_{Rh}}$ in a FBS and a typical organic solvent, we carried out a series of catalyst recycling experiments under conditions where substrate conversion was incomplete, enabling run-to-run and solvent-to-solvent comparisons. Longer reaction times always provided 100%
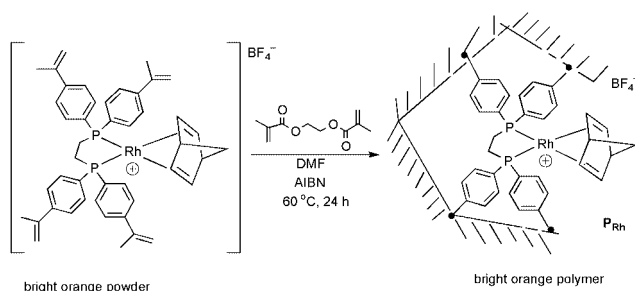
conversion to product. We examined a relatively simple hydrogenation substrate, methyl-*trans*-cinnamate **1** (Scheme 2), toluene for our organic phase, and the benchmark 1:1 perfluoromethylcyclohexane (PFMC)–toluene for our FBS.[8] In the PFMC–toluene mixture the polymer floats at the interface, while it sinks in toluene. Once monophasic (~103 °C when [**1**] = 0.2 M),[9] the polymer in the FBS floats to the surface until cooling and phase separation.[10]

Scheme 2
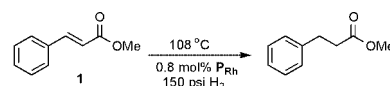
The plot in Fig. 1 charts the evolution of $\mathbf{P_{Rh}}$ activity in the hydrogenation of **1** in FBS and toluene. Each reactor was run side by side, and percentage conversions were determined after 1 h by GC after careful venting. Once an aliquot was obtained for analysis, the vessels were re-introduced into the glove box and the product/substrate removed from the catalysts. For the FBS, the organic phase was removed with a pipette and the fluorous layer washed 3 times with additional toluene (this results in some PFMC loss, *vide infra*). In the toluene case, the solution was decanted and the polymer similarly washed with toluene. Additional substrate/toluene was added under the inert atmospheric conditions, and in the fluorous case additional PFMC was added every 2–3 runs to a total volume of 2 mL.

It is evident from the graph that the FBS yields a slightly more active catalyst than in toluene alone, and although the rate is reproducibly higher in the FBS, the absolute rate difference may not be significant as batch to batch variability exists (±20%).[11] Over the 15 runs, the catalysts completed ~1400 and ~800 turnovers in the FBS and toluene, respectively. Combining the filtrate solutions for the 15 runs and analyzing for Rh
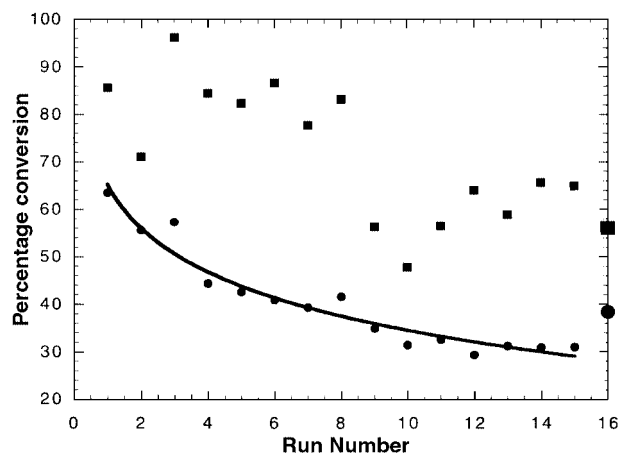

Scheme 1

Fig. 1 Catalyst recycling for the hydrogenation of **1**. FBS (■)—1:1 CF$_3$C$_6$F$_{11}$–toluene, 0.79 mol% $\mathbf{P_{Rh}}$; toluene (●)—0.76 mol% $\mathbf{P_{Rh}}$. 108 °C, 150 psi H$_2$, 1 h. For run # 16, both samples were run under identical FBS conditions.

(ICP), indicated that only minor catalyst leaching (~ 1%) occurred in both systems.

To determine if the toluene catalyst's activity was inherently lower, or if it had slightly less Rh than the FBS,[11] a 16th run was carried out in the 1:1 PFMC–toluene biphase. A 10% increase in conversion (Fig. 1) indicates that under the reaction conditions, the FBS does increase the absolute product output and thus the rate difference cannot be solely ascribed to a difference in the polymer's Rh content. Although we don't know unequivocally the reason(s) for loss of activity in the two solvents, we suspect that it comes from catalyst deactivation during the recycling process, as both systems routinely reach 10,000 turnovers in side-by-side experiments, although complete conversion was always achieved 2–3× more quickly in the FBS.[12]

It is also apparent from Fig. 1 that the run-to-run throughput of the catalyst in the FBS is not as reproducible as in toluene. Based on the mechanics of this recycle experiment, we suspected that the variability might be due to changes in the PFMC–toluene ratio. In practice, PFMC losses occurred during product extraction and washing (3×) of each run as it is slightly soluble in toluene, and the aliquots were removed at or near the reaction temperature leading to some evaporative loss (bp ~ 77 °C). Since the reactivity spikes coincided with the addition of fluorous solvent (every 2–3 runs, to 4 mL), we hypothesized that higher fluorous–organic solvent ratios might be responsible for the enhanced reactivity.

This hypothesis was tested by a series of control experiments varying the ratio of PFMC–toluene (1:3, 2:2, 3:1 and 4:0; 4 mL total volume). To eliminate batch-to-batch variability effects we measured the effect of fluorous composition in a series of recycle experiments where the same catalyst was used for each solvent ratio. Moreover, the experiments were conducted from least to most reactive to ensure that catalyst decomposition would not be misinterpreted as a decrease in activity.

The plot in Fig. 2 clearly shows that the 1 h conversion increases with increasing fluorous content, suggesting that the 'noise' in Fig. 1 is actually due to small changes in the volume fraction of PFMC in the FBS. This trend is unusual as homogeneous catalysts typically become *less reactive* as the fluorous content of the solvent increases.[13] Several possibilities are *a priori* possible: (1) changes in H_2 diffusion rates under mass transport limited conditions. The possibility that H_2 diffusion from gas to solution is slower than catalysis, and sensitive to fluorous content has been eliminated by showing that under similar homogeneous conditions, a doubling and tripling of the soluble catalyst, $[(dppe)Rh(nbd)^+ B(Ar_f)_4^-]$ leads to a doubling and tripling of product turnover.[14] Thus, H_2 diffusion through the meniscus occurs faster than does catalysis.[15] (2) Increasing substrate concentration in the polymer phase with increasing fluorous content (a fluorophobic effect). For example, model experiments show that 80 mg of blank EDMA polymer will lower the [decane] in PFMC from 75 to 50
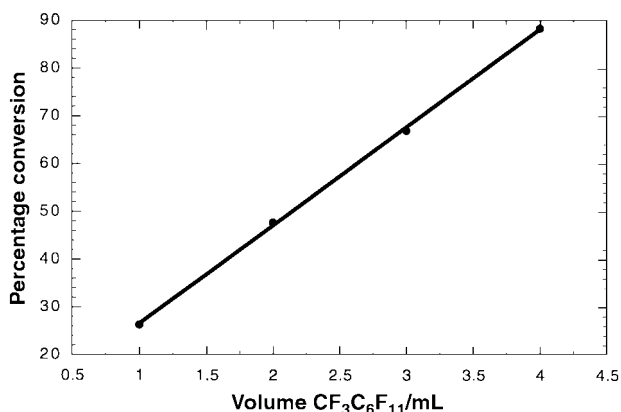
mM. To compensate for the decrease, the [decane] in the polymer phase must be ~ 600 mM. A similar effect leading to higher local substrate concentration in the catalyst containing polymer phase could lead to the observed rate accelerations. Experiments to assess the probability that these or other effects are responsible for this unusual rate acceleration are underway.

Although the polymer catalyst P_{Rh} does not suffer from the problem of catalyst/product separation of typical solution catalysts, the FBS does engender some useful and interesting properties to these immobilized catalysts. Chief among these is an increase in activity that directly correlates with the fluorous content of the solvent. The ease of utilizing a catalyst designed for use in organic solvents to operate in fluorous solvents is also noteworthy.

Notes and references

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5 The polymer's interior pores are essentially unstirred therefore access to the catalyst sites is controlled by passive diffusion processes.

6 For an alternative approach using fluorous soluble polymeric ligands, see: W. Chen, L. Xu and J. Xiao, *Chem. Commun.*, 2000, **10**, 830; D. E. Bergbreiter, J. G. Franchina and B. L. Case, *Org. Lett.*, 2000, **2**, 393

7 B. P. Santora, M. R. Gagné, K. G. Moloy and N. S. Radu, *Macromolecules*, 2001, **34**, 658.

8 In a typical run ~ 80 mg of polymer (~ 100 μmol Rh g⁻¹) and 150 mg of **1** were used along with 4.0 mL of toluene or 2.0 mL toluene and 2.0 mL PFMC. The Fischer–Porter vessel was emmersed into a pre-equilibrated oil bath, and when monophasic, the vessel was charged and vented 3× with 150 psi H_2 and charged to the final pressure.

9 The consolute temperate rises above 108 °C when concentrations of **1** are greater than 1 M.

10 The polymer sinks in the 25% v/v fluorous solution, while it floats to the surface for the 50, 75 and 100% PFMC experiments.

11 Analysis of different physical sections of the polymer monolith by AA indicates that Rh is *not* evenly distributed in the matrix (±20%). Crushing and mixing macroscopically homogenizes the Rh, however, this makes the reported recycling experiments more cumbersome, and was avoided.

12 In a typical high turnover experiment ~ 5 mg of polymer (0.01 mol%) and 800 mg of **1** were subjected to the same conditions listed in ref. 8. To minimize evaporative loss of solvent, aliquots to measure reaction progress were taken approximately every 24 h. After 40 h the toluene typically completes ~ 2300 turnovers, while the FBS completes ~ 9000; both systems do eventually show complete conversion.

13 D. Rutherford, J. J. J. Julliette, C. Rocaboy, I. T. Horváth and J. A. Gladysz, *Catal. Today*, 1998, **42**, 381; B. Richter, A. L. Spek, G. van Koten and B. Deelman, *J. Am. Chem. Soc.*, 2000, **122**, 3945.

14 These experiments were carried out with 25, 50 and 66% fluorous content (0.5, 1.0 and 1.5 mol% catalyst). Differences in activity as a function of fluorous content varied less than 10%, with absolute rates being similar to polymer rates.

15 At this time we cannot rule out the possibility that H_2 diffusion *from solution to polymer* is sensitive to fluorous content.

Fig. 2 Hydrogenation of **1** at different $CF_3C_6F_{11}$–toluene ratios (4 mL total volume, 0.76 mol% P_{Rh}, 106 °C, 150 psi H_2, 1 h).