Chiral Porous Hybrid Solids for Practical Heterogeneous Asymmetric Hydrogenation of Aromatic Ketones

Aiguo Hu, Helen L. Ngo, and Wenbin Lin*

Department of Chemistry, CB#3290, University of North Carolina, Chapel Hill, North Carolina 27599

Received February 24, 2003; E-mail: wlin@unc.edu

Asymmetric reduction of prochiral olefins, ketones, and imines is one of the most powerful methods for the production of optically active compounds.[1] Among these methodologies, Ru and Rh complexes of chiral chelating bisphosphines, particularly 2,2′-bis-(diphenylphosphino)-1,1′-binaphthyl (BINAP) and its derivatives, were widely used for the hydrogenation of a wide range of substrates with high chemo- and enantioselectivity.[2] However, their practical applications in industrial processes were often hindered due to high costs of both noble metals and chiral ligands as well as difficulties in removing trace amounts of toxic metals from the organic products.

Heterogenization of these highly enantioselective catalysts has proven effective in overcoming these problems. The heterogenized catalysts can potentially combine the advantages of both homogeneous and heterogeneous systems and therefore provide easily recyclable and reusable solid catalysts that have uniform and precisely engineered active sites similar to those of their homogeneous counterparts. Many heterogenization approaches have been explored, including attaching the chiral catalysts to organic polymers, dendrimers, membrane supports, and porous inorganic oxides and immobilization via biphasic systems.[3] The heterogenized catalysts afforded by these methods are, however, typically less effective than their homogeneous counterparts.

In an effort to rationally design functional hybrid solids based on organic linkers and metal nodes,[4] we have explored the synthesis of chiral porous zirconium phosphonates for applications in asymmetric catalysis. Such hybrid materials will combine the robust metal phosphonate frameworks[5] with highly enantioselective metal complexes of the pendant chiral bisphosphines[3] and will find practical applications in heterogeneous asymmetric catalysis. Herein we report the synthesis of novel chiral porous solid catalysts for practically useful enantioselective hydrogenation of unfunctionalized aromatic ketones. Remarkably, BINAP-derived porous Zr phosphonates provide enantioselectivity superior to their parent homogeneous counterpart Ru−BINAP−DPEN (DPEN is 1,2-diphenylethylenediamine) system developed by Noyori et al.[6]

Treatment of (R)-2,2′-bis(diphenylphosphino)-1,1′-binaphthyl-4,4′-bis(phosphonic acid), L_1-H_4, with [Ru(benzene)Cl$_2$]$_2$ followed by (R,R)-DPEN afforded the phosphonic acid-substituted Ru−BINAP−DPEN intermediate, which was directly reacted with Zr-(O^{t}Bu)$_4$ under reflux conditions to give chiral porous Zr phosphonate of the approximate formula Zr[Ru(L_1)(DPEN)Cl$_2$]·4H$_2$O (Zr−Ru−L_1). The solid precatalyst Zr−Ru−L_2 with a 6,6′-disubstituted BINAP was similarly prepared and also has an approximate formula of Zr[Ru(L_2)(DPEN)Cl$_2$]·4H$_2$O. These chiral porous Zr phosphonates have been characterized with a variety of techniques including TGA, adsorption isotherms, XRD, SEM, IR, and microanalysis (Scheme 1).

TGA results indicated that Zr−Ru−L_1 and Zr−Ru−L_2 lost 5.1 and 5.4% of their weights by 200 °C, respectively (expected 5.42% for loss of four water molecules). These formulations are supported

Scheme 1
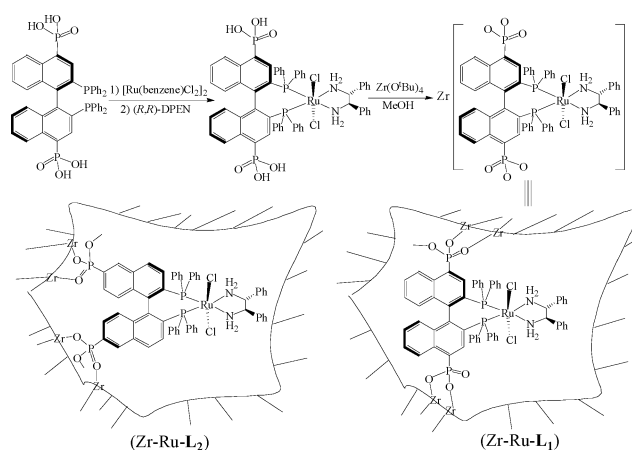
by the microanalysis results. The IR spectra exhibit strong and broad peaks at 950−1150 cm^{-1} for the P−O stretches and intense and broad O−H stretching vibrations at ∼3350 cm^{-1} for the H$_2$O solvates. N$_2$ adsorption measurements (Figure 1) indicate that both Zr−Ru−L_1 and Zr−Ru−L_2 are highly porous with rather wide pore size distributions. Zr−Ru−L_1 exhibits a total BET surface area of 328 m^2/g with a microporous surface area of 60 m^2/g and a pore volume of 0.65 cm^3/g (by BJH method). Zr−Ru−L_2 exhibits a total BET surface area of 400 m^2/g with a microporous surface area of 81 m^2/g and a pore volume of 0.98 cm^3/g (by BJH method). SEM images show that both solids are composed of submicrometer particles, while PXRD indicates that both solids are amorphous.

With the built-in Ru−BINAP−DPEN moieties, porous solids of Zr−Ru−L_1 and Zr−Ru−L_2 exhibited exceptionally high activity and enantioselectivity in hydrogenation of aromatic ketones. Acetophenone was hydrogenated to 1-phenylethanol with complete
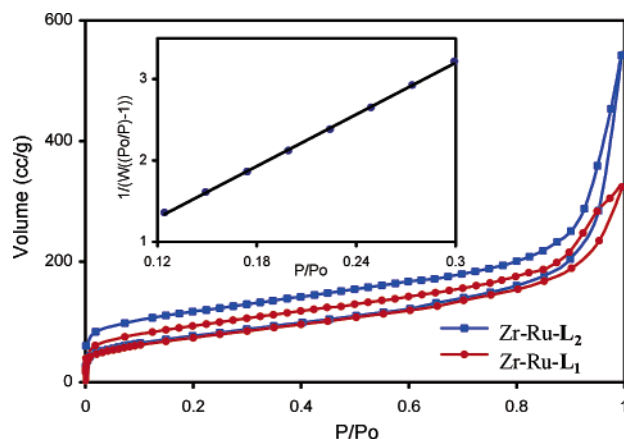

Figure 1. N$_2$ adsorption isotherms for Zr−Ru−L_1 and Zr−Ru−L_2 at 77 K. The inset shows BET plot for Zr−Ru−L_1 in the mesoporous region.

Table 1. Heterogeneous Asymmetric Hydrogenation of Aromatic Ketones[a]

substrate	solid loading (%)	KO^{t}Bu (%)	Zr–Ru–L$_1$ ee (%)	Zr–Ru–L$_2$ ee (%)
Ar = Ph, R = Me	0.1	1	96.3 (97.1)[b]	79.0 (81.3)[b]
Ar = 2-naphthyl, R = Me	0.1	1	97.1	82.1
Ar = 4′-^{t}Bu-Ph, R = Me	0.1	1	99.2	91.5
Ar = 4′-MeO-Ph, R = Me	0.1	1	96.0	79.9
Ar = 4′-Cl-Ph, R = Me	0.1	1	94.9	59.3
Ar = 4′-Me-Ph, R = Me	0.1	1	97.0	79.5
Ar = Ph, R = Et	0.1	1	93.1	83.9
Ar = Ph, R = cyclo-Pr	0.1	1	90.6	–
Ar = 1-naphthyl, R = Me	0.1	1	99.2	95.8
	0.02	0.4	98.9	
	0.005	0.02	98.8 (70)[c]	
	0.005	0.02	98.6[d]	

[a] All of the reactions were carried out in 20 h, and the ee values were determined by GC on a Supelco β-Dex 120 column. The absolute configurations of the products are identical to those obtained by the Ru–(R)-BINAP–(R,R)-DPEN catalyst. All the conversions were >99% as judged by the integrations of GC peaks. [b] Homogeneous reactions. [c] 70% conversion. [d] 40 h reaction time.

conversion and 96.3% ee in 2-propanol with 0.1 mol % loading of Zr–Ru–L$_1$ solid. This level of enantioselectivity is significantly higher than that observed for the parent Ru–BINAP–DPEN homogeneous catalyst which typically gives ~80% ee for the hydrogenation of acetophenone under similar conditions.[6a–b] In comparison, the Zr–Ru–L$_2$ solid gives 79.0% ee for the hydrogenation of acetophenone under the same conditions. As Table 1 shows, the Zr–Ru–L$_1$ solid has also been used to catalyze a series of other aromatic ketones with uniformly and remarkably high ee's of 90.6–99.2% and complete conversions. Although the Zr–Ru–L$_2$ solid is also highly active for the hydrogenation of aromatic ketones, the enantioselectivity of Zr–Ru–L$_2$ is modest and similar to that of parent Ru–BINAP–DPEN homogeneous catalyst.[7]

Aromatic ketones can also be hydrogenated with much lower catalyst loading. For example, with only 0.02 mol % solid loading of Zr–Ru–L$_1$, 1-acetonaphthone can be hydrogenated with complete conversion and 98.9% ee in 20 h. When the solid loading was decreased to 0.005 mol %, it took longer reaction time (40 h) for the hydrogenation of 1-acetonaphthone to complete (98.6% ee). The TOF is calculated to be ~500 h^{-1} at complete conversion and ~700 h^{-1} at 70% conversion.[8]

We have also successfully reused both the Zr–Ru–L$_1$ and Zr–Ru–L$_2$ systems for asymmetric hydrogenation of 1-acetonaphthone without the deterioration of enantioselectivity. As shown in Table 2, the Zr–Ru–L$_1$ system was used for eight cycles of hydrogenation without any loss of enantioselectivity. The activity did not decrease for the first six runs, but began to drop at the seventh run. This loss of activity may not reflect the intrinsic instability of the Zr–Ru–L$_1$ solid catalyst. The catalyst recycling and reuse experiments were conducted without rigorous exclusion of air, and the oxygen sensitivity of the ruthenium hydride complexes may have contributed to the loss of activity after multiple runs. Direct

Table 2. Recycling and Reuse of Zr–Ru–L$_1$ Solid Catalyst for Hydrogenation of 1-Acetonaphthone[a]

run	1	2	3	4	5	6	7	8
ee (%)	99.0	99.0	99.1	99.0	99.0	99.2	99.1	99.0
conversion (%)	100	100	100	100	100	100	95	85

[a] The reactions were carried out with 0.1 mol % solid loading and 1% KO^{t}Bu under 700 psi H$_2$ pressure for 20 h.

current plasma spectroscopic studies indicated that less than 0.2% of Ru metal has leached into the organic product for each round of hydrogenation. We have also reused the Zr–Ru–L$_2$ system for hydrogenation of 1-acetonaphthone three times with complete conversions and enantioselectivity of 96.3, 95.7, and 94.7%, respectively.

In summary, we have designed and synthesized novel chiral porous Zr phosphonates containing Ru–BINAP–DPEN moieties. The Zr–Ru–L$_1$ solid catalyzes heterogeneous asymmetric hydrogenation of aromatic ketones with practically useful, remarkably high activity and enantioselectivity (up to 99.2% ee). These solid catalysts can be readily recycled and reused without the loss of activity and enantioselectivity. The tunability of such a molecular building-block approach promises to lead to other practically useful heterogeneous asymmetric catalysts.

Supporting Information Available: Experimental procedures and 10 figures (PDF). This material is available free of charge via the Internet at http://pubs.acs.org.

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(7) We believe that very different ee values observed for the Zr–Ru–L$_1$ and Zr–Ru–L$_2$ systems are a result of the substituent effects on BINAP. The ee values similar to those listed in Table 1 have been observed for homogeneous Ru–L$_1$–DPEN and Ru–L$_2$–DPEN systems.
(8) Under identical conditions, we have obtained a TOF of 1725 h^{-1} (69% conversion) and 1250 h^{-1} (complete conversion) for the homogeneous Ru–(R)-BINAP–(R,R)-DPEN catalyst.

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