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Magnetically Recoverable Chiral Catalysts Immobilized on Magnetite Nanoparticles for Asymmetric Hydrogenation of Aromatic Ketones

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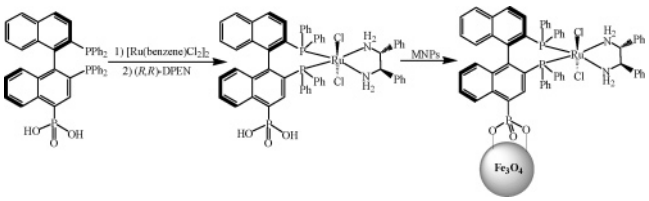
Asymmetric catalysis provides a powerful method for the synthesis of optically active molecules that serve as precursors to pharmaceutically important compounds.[1] Although numerous highly selective chiral catalysts have been developed in the past three decades, their practical applications in industrial processes are hindered by their high costs as well as difficulties in removing trace amounts of toxic metals from the organic products. To overcome these problems, many different approaches have been used to generate heterogenized asymmetric catalysts.[2] The heterogenized catalysts are, however, typically less effective than their homogeneous counterparts. There thus exists a need to develop new, innovative approaches toward the design of recoverable and reusable asymmetric catalysts.

Crystalline nanoparticles with appropriate surface coatings are readily dispersible in organic solvents. Owing to their small sizes, nanoparticles tend to have very high surface areas. Spherical nanoparticles of 10 nm diameter, for example, have a calculated surface area of 600 m^2/cm^3, which is comparable to that of many porous supports for catalyst immobilization. Nanoparticles can thus be used as novel supports to prepare "heterogenized" asymmetric catalysts that are more accessible to the reactants. Aerogel-derived nanocrystalline MgO was recently used to prepare a nanoheterogeneous catalyst for Claisen−Schmidt condensation of benzaldehydes with acetophenones to yield chalcones, which were converted to chiral epoxy ketones by subsequent asymmetric epoxidation reactions.[3] BINAP-capped Pd nanoparticles were recently shown to catalyze the asymmetric hydrosilylation of styrene to afford chiral alcohols.[4] The difficulty in recovering nanoparticle-supported asymmetric catalysts by settling or filtration, however, precludes their widespread applications.[5]

Superparamagnetic materials are intrinsically nonmagnetic but can be readily magnetized in the presence of an external magnetic field. As a result of this unique property, superparamagnetic materials have been widely used in biomedical applications, such as protein purification, cell sorting, MRI contrast enhancement, and drug targeting.[6] Recent advances in the synthesis of superparamagnetic nanoparticles facilitate their exploitation in many technological and biomedical applications.[7] Herein, we wish to report the design of novel magnetically recoverable heterogenized chiral catalysts and their applications in highly enantioselective asymmetric hydrogenation of aromatic ketones.[8]

Magnetite nanoparticles (MNPs) used for this work were synthesized by the thermal decomposition (MNP_1)[9] or by coprecipitation method (MNP_2).[10] Ruthenium(II) complex with phosphonic acid-substituted BINAP [Ru(BINAP−PO_3H_2)(DPEN)Cl_2] (**1**) was synthesized by treating [Ru(benzene)Cl_2]$_2$ with (*R*)-2,2′-bis(diphenylphosphino)-1,1′-binaphthyl-4-phosphonic acid (BINAP−PO_3H_2) followed by (*R*,*R*)-1,2-diphenylethylenediamine (DPEN) in DMF at elevated temperatures. Immobilization of **1** on MNPs was carried out by ultrasonicating a mixture of **1** and MNPs in anhydrous methanol at room temperature for 1 h.[10] The MNPs coated with **1** (designated as **1**-MNP_1 and **1**-MNP_2) were isolated by magnetic decantation and washed with methanol three times. The loading of **1** on MNPs was estimated by quantifying the amount of **1** remaining in the solution using ^{31}P NMR spectroscopy.

Scheme 1. Immobilization of Chiral Ru Catalyst on Magnetite Nanoparticles



Transmission electron microscopy (TEM) images showed slight aggregation of MNPs after immobilization of **1** (Figure 1), presumably because the [Ru(BINAP−PO_3)(DPEN)Cl_2] moieties on the MNP surfaces are less effective in preventing the aggregation of the MNPs (upon solvent evaporation) than oleic acid. Powder X-ray diffraction (XRD) patterns confirmed that both MNPs were magnetite. The average sizes of MNPs were estimated using Scherrer's equation, and they did not change upon the immobilization of **1**. The average diameter is 8.9 nm for **1**-MNP_1, while the average diameter is 6.6 nm for **1**-MNP_2. Magnetization curves measured at 300 K showed that the MNPs modified with the [Ru-

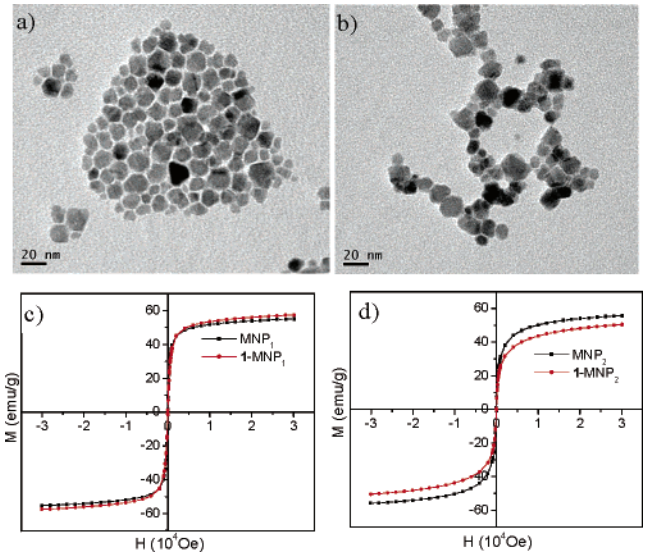


Figure 1. (a) TEM image of as-synthesized MNP_1. (b) TEM image of **1**-MNP_1. (c) Magnetization curves for MNP_1 and **1**-MNP_1 measured at 300 K. (d) Magnetization curves for MNP_2 and **1**-MNP_2 measured at 300 K.

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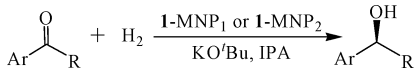
Table 1. Enantio Excess Values (% ee) for the Heterogeneous Hydrogenation of Aromatic Ketones[a]



substrate	BINAP	**1**	**1**-MNP_1	**1**-MNP_2
Ar = Ph, R = Me	83.0	87.0	87.6	81.7
Ar = 1-naphthyl, R = Me	96.9	98.0	98.0	97.6
Ar = 2-naphthyl, R = Me	75.2	84.9	87.6	82.0
Ar = 4-^{t}Bu−Ph, R = Me	94.0	94.1	95.1	91.1
Ar = 4-Me−Ph, R = Me	83.1	85.6	87.9	80.5
Ar = 4-Cl−Ph, R = Me	60.0	75.9	76.6	70.6
Ar = 4-MeO−Ph, R = Me	80.7	82.5	87.6	77.7
Ar = Ph, R = Et	85.4	89.0	88.9	86.3

[a] All of the reactions were carried out at room temperature with 0.1 mol % of catalyst and 1 mol % of KO^{t}Bu under 700 psi of hydrogen pressure in 20 h. The ee values were determined by GC on a Supelco β-Dex 120 column. All of the conversions were >99% as judged by the integrations of GC peaks.

Table 2. Results of Catalyst Reuse Experiments

	1-MNP_1		**1**-MNP_2	
run	conversion	% ee	conversion	% ee
1	100	98.0	100	97.0
4	100	98.0	100	97.6
5	92	97.5	100	97.7
6	35	96.8	100	97.8
10			100	97.7
14			99	96.7
15			35	95.1

(BINAP−PO_3)(DPEN)Cl_2] moieties are superparamagnetic (Figure 1). **1**-MNP_1 and **1**-MNP_2 have a saturation magnetization (σ_s) of 57.5 and 50.5 emu/g, respectively. These values are essentially the same as those of the as-synthesized MNPs and slightly smaller than that of bulk magnetite (92 emu/g), which is consistent with the presence of surface coatings of Ru catalysts. The modified MNPs are readily dispersible in common organic solvents and can be efficiently attracted with a small magnet (surface field of ~4000 G).

With the readily accessible surface-bound [Ru(BINAP−PO_3)-(DPEN)Cl_2] functionality, the modified MNPs have been used for the hydrogenation of aromatic ketones with high reactivity and enantioselectivity.[11] 1-Acetonaphthone was, for example, hydrogenated with 0.1 mol % of **1**-MNP_1 or **1**-MNP_2 in 2-propanol to afford α-(1-naphthyl)ethanol with complete conversion and 98.0 or 97.6% ee, respectively.[12] As shown in Table 1, a wide range of aromatic ketones were hydrogenated to their corresponding secondary alcohols in the presence of **1**-MNP_1 and **1**-MNP_2 with complete conversion. The enantiomeric excess values are significantly higher than those of the parent homogeneous catalyst [Ru(BINAP)(DPEN)-Cl_2] and comparable to those of the homogeneous counterpart **1**.[13] The supernatant (before or after hydrogenation reactions) is not active for hydrogenation of aromatic ketones, indicating heterogeneous nature of the present MNP-supported catalyst system. The MNP-supported Ru catalysts were easily recovered by decanting the reaction mixture while attracting the modified MNPs with an external magnet.[14] Pure chiral secondary alcohols obtained by magnetic decantation are free from contamination of either Ru catalyst or MNPs.

We have also successfully reused both **1**-MNP_1 and **1**-MNP_2 for asymmetric hydrogenation of 1-acetonaphthone without the deterioration of enantioselectivity. As shown in Table 2, the **1**-MNP_1 system was used for six cycles of hydrogenation without loss of enantioselectivity. The activity did not decrease for the first four runs, but began to drop for the fifth run. The **1**-MNP_2 system could be used for asymmetric hydrogenation for an impressive number of 14 times (with no deterioration of conversion and enantiomeric excess).[15]

In summary, we have designed novel magnetite nanoparticle-supported chiral Ru complexes that catalyze heterogeneous asymmetric hydrogenation of aromatic ketones with remarkably high activity and enantioselectivity. The heterogenized catalysts can be readily recycled by magnetic decantation and used for asymmetric hydrogenation for up to 14 times without loss of activity and enantioselectivity. Orthogonal nature of the present catalyst immobilization approach should allow the design of other superparamagnetic nanoparticle-supported asymmetric catalysts for a wide range of organic transformations.

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

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(12) The catalyst loading was calculated based on the amount of surface-bound [Ru(BINAP−PO_3)(DPEN)Cl_2].

(13) We have recently shown the positive effects of 4,4′-substituents on BINAP in homogeneous asymmetric hydrogenation. See: Hu. A.; Ngo, H. L.; Lin, W. *Org. Lett.* **2004**, *6*, 2937.

(14) For highly viscous reaction mixtures, equal amounts of hexane or diethyl ether were added to facilitate magnetic separation.

(15) The eventual loss of catalyst activity and enantioselectivity is probably a result of their air-sensitivity. It was not possible to completely exclude air with our current experimental setup.

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