Communication

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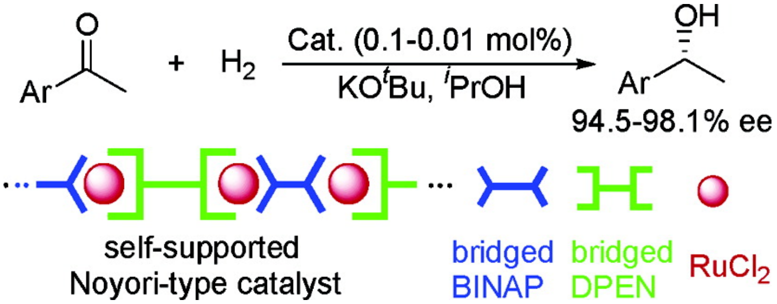

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Programmed Assembly of Two Different Ligands with Metallic Ions: Generation of Self-Supported Noyori-type Catalysts for Heterogeneous Asymmetric Hydrogenation of Ketones

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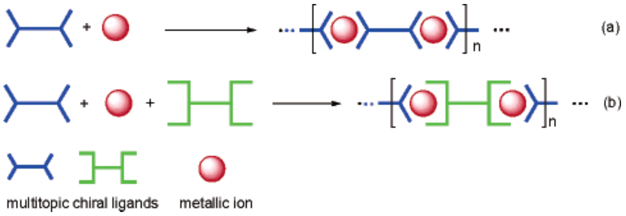
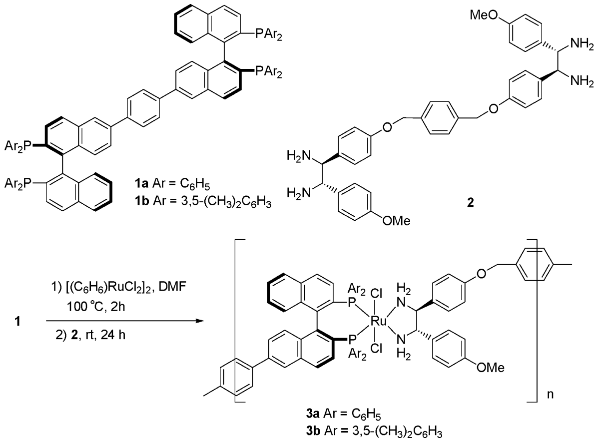
The immobilization of chiral catalysts for asymmetric reactions as one of the most promising solutions to the problems associated with the difficulties in the recovery and reuse of expensive homogeneous catalysts, as well as the product contamination caused by metal leaching, has attracted a great deal of interest recently.[1] Among various strategies for homogeneous catalyst immobilization, "self-supported" chiral catalysts exhibited some salient features, including facile preparation, remarkable stability, high density of catalytically active units, and excellent stereocontrol performance, as well as simple recovery and reuse.[2] With this strategy, chiral catalysts could be heterogenized by a homocombination of multitopic chiral ligands with metallic ions (Scheme 1a) without using any supports.

Although assembly of a chiral catalyst by heterocombination of different multitopic chiral ligands with metal ions (Scheme 1b) could, in principle, provide a viable alternative to the route in Scheme 1a, no work has been done to demonstrate the validity of this strategy. The major challenge to this goal is that a complex multispecies system would be formed when the three reacting components were mixed together. Thus, selective formation of a heteroligand complex would require the structural and coordination information stored in the ligands and metallic ion, respectively, to be sufficiently strong to dictate their coordination organization and thus direct the assembly process in a programmed way.[3] In this respect, the structural feature of Noyori's catalyst,[4] [RuCl$_2${(*R*)-BINAP}{(*R*,*R*)-DPEN}] (BINAP = 2,2′-bis(diphenylphosphino)-1,1′-binaphthyl; DPEN = 1,2-diphenylethylenediamine), may provide an excellent opportunity for generation of self-supported catalysts by the approach shown in Scheme 1b, due to the selective incorporation of a chiral diphosphine and a chiral diamine in a Ru(II) complex. In the present communication, we report our preliminary results on the generation of a self-supported Noyori-type catalyst for asymmetric hydrogenation of ketones by programmed assembly of bridged diphosphine (**1**) and diamine (**2**) ligands with Ru(II) metallic ions (Scheme 2).

Scheme 1. Schematic Representation of Strategies for the Generation of Self-Supported Enantioselective Heterogeneous Catalysts



Scheme 2



As shown in Scheme 2, both bridged BINAP **1** and diamine **2** were designed to possess 1,4-phenylene and a 1,4-phenylenebismethoxy linkers, which were assembled at the 6-position of the corresponding 1,1′-binaphthyl backbone or at the 4′-position of the (*S*,*S*)-DPEN derivative, respectively, to avoid the intramolecular interaction of two chiral units. The self-supported catalysts (**3a**−**b**) were prepared by reacting bridged BINAP ligands (**1a**,**b**) with [(C$_6$H$_6$)RuCl$_2$]$_2$ in DMF at 100 °C, followed by the treatment of the resulting reddish brown solution with 1 equiv of bridged DPEN **2** at room temperature. After removal of the solvent under vacuum, the resulting solids were washed with 2-propanol three times to afford catalysts **3a**,**b** as pale brown solids in nearly quantitative yields. Elemental C/H/N/Cl/P and Ru analyses, FT-IR, and ^{31}P CP/MAS showed that the composition of the resulting solids was consistent with the structure of **3** as expected. SEM images showed that the solids were composed of micrometer particles (ca. 1 μm), and the powder X-ray diffraction (PXD) indicated they were noncrystalline solids.

The self-supported catalyst **3** was then submitted to the catalysis of the hydrogenation of acetophenone (**4a**). As shown in Table 1, catalyst **3a** promoted the hydrogenation of acetophenone (**4a**) to afford **5a** with 78.2% ee (entry 1). This level of enantioselectivity is comparable to that observed in the homogeneous catalysis using [RuCl$_2${(*R*)-BINAP}{(*R*,*R*)-DPEN}] (∼80% ee of **5a**) under similar conditions.[4b] Inspired by this initial result, catalyst **3b**, which contains di(3,5-xylyl)phosphino moieties in the BINAP units, was then employed for the hydrogenation of **4a**. The enantioselectivity of the reaction was remarkably enhanced to 97.4% with complete conversion of **4a** (entry 2). In contrast, the catalysis of hydrogenation of **4a** using the homogeneous counterparts resulted in the formation of **5a** in relatively lower enantioselectivity (95.5−96.4%) (entries 3 and 4 versus 2). The enantioselectivity of the reaction under the catalysis of the self-supported catalyst generated using **1b** and the enantiomer of **2** dropped significantly, indicating a mismatched case of ligand combination (entry 5). All of these facts

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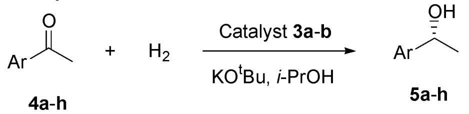
Table 1. Enantioselective Hydrogenation of Aromatic Ketones **4a−h** under the Catalysis of **3a,b**[a]



entry	catalyst	Ar in **4**	ee (%) of **5**[b]
1	**3a**	Ph (a)	78.2 (*R*)
2	**3b**	Ph (**a**)	97.4 (*R*)
3	*c*	Ph (**a**)	95.5 (*R*)
4	*d*	Ph (**a**)	96.4 (*R*)
5	*e*	Ph (**a**)	30.5 (*R*)
6	**3b**	1-naphthyl (**b**)	98.1 (*R*)
7	**3b**	2-naphthyl (**c**)	94.5 (*R*)
8	**3b**	4′-F−Ph (**d**)	96.2 (*R*)
9	**3b**	4′-Cl−Ph (**e**)	96.9 (*R*)
10	**3b**	4′-Br−Ph (**f**)	97.2 (*R*)
11	**3b**	4′-Me-Ph (**g**)	97.5 (*R*)
12	**3b**	4′-MeO−Ph (**h**)	96.2 (*R*)
13	**3b**[f]	Ph (**a**)	95.2 (*R*)

[a] All reactions were carried out at 25 °C under 40 atm pressure of H$_2$ at a substrate concentration of 1.5 M with substrate/catalyst/KO^{t}Bu = 1000:1:20 for 20 h. The conversions of the substrates were determined by ^{1}H NMR to be >99%. [b] Determined by chiral GC. The absolute configuration of the products was determined by the sign of optical rotation. [c] Catalyst: [RuCl$_2${(*S*)-3,5-XylBINAP}{(*S*,*S*)-1,2-bis-(4-methoxyphenyl)ethylenediamine}]. [d] Catalyst: [Ru$_2$Cl$_4${**1b**}{(*S*,*S*)-1,2-bis-(4-methoxyphenyl)ethylenediamine}$_2$]. [e] Catalyst: [RuCl$_2${**1b**}{(*R*,*R*)-**2**}. [f] Substrate/catalyst/KO^{t}Bu = 10000:1:20.

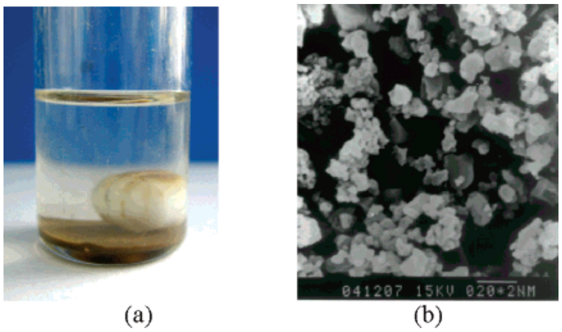


Figure 1. (a) Self-supported chiral Ru(II) catalyst **3b** (pale brown solids at the bottom of the reactor) in 2-propanol. (b) SEM image of the self-supported Ru catalyst **3b**. The scale bar indicates 2 μm.

demonstrated the synergistic impact of the supramolecular architecture of the assemblies on their catalytic behaviors. Furthermore, the catalyst **3b** was used to catalyze the hydrogenation of a series of aromatic ketones, **4b−h**, affording the corresponding secondary alcohols (**5b−h**) with excellent enantioselectivities (entries 6−12). Moreover, acetophenone (**4a**) could also be hydrogenated at a reduced catalyst loading (0.01 mol % of **3b**) to give 1-phenylethanol with complete conversion and 95.2% ee (entry 13). The TOF under this circumstance is calculated to be ∼500 h^{-1}, which illustrated the high activity of the assembled solid catalyst.

Table 2. Recycling and Reuse of the Self-Supported Catalyst **3b** in Enantioselective Hydrogenation of **3c**[a]

run	1	2	3	4	5	6	7
conv (%)	>99	>99	>99	>99	>99	>99	97
ee (%)	97.4	97.6	97.3	96.5	95.6	96.1	95.4

[a] All of the reactions were carried out under the experimental conditions of entry 2 in Table 1.

The self-supported catalyst **3b** has proven to be completely insoluble in 2-propanol, as shown in Figure 1a. The inductively coupled plasma (ICP) spectroscopic analysis of the supernatant of the catalyst indicated that no detectable Ru leached into the organic phase (<0.1 ppm). When the supernatant of catalyst **3b** in 2-propanol was used as catalyst, the hydrogenation of acetophenone (**4a**) did not occur at all. This experiment unambiguously demonstrated the heterogeneous nature of the present catalytic system. On the basis of this finding, the recovery and the reusability of catalyst **3b** were then examined in the hydrogenation of **4a**. After the completion of the hydrogenation, the separation of the catalyst and product (Ru leaching in product <0.1 ppm) could be achieved by simple filtration under Ar atmosphere. The separated solid catalyst was recharged with solvent, base, and substrate again for the next run of hydrogenation. As shown in Table 2, the self-supported catalyst could be reused for seven cycles of hydrogenation without obvious loss of enantioselectivities and catalytic activities.

In conclusion, we have demonstrated a new approach for generation of self-supported chiral catalysts by programmed assembly of two different multitopic ligands with metallic ions. The self-supported heterogeneous Noyori-type catalysts are comparable to those of their homogeneous counterpart in terms of both activity and enantioselectivity, although several excellent organic polymer-supported Ru(II) catalysts have been reported.[5] This type of catalyst can be readily recovered and reused with the retention of high enantioselectivity and activity. Further studies on the simplification of the synthetic procedures of multitopic ligands and the impact of a spacer in the multitopic ligands on both the structure of assemblies and their catalytic performance are underway in this laboratory.

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Supporting Information Available: Experimental procedures for ligand and catalyst preparation, PXD image of catalyst **3b**, and chiral GC analysis of the products. This material is available free of charge via the Internet at http://pubs.acs.org.

References

(1) (a) de Vos, D. E.; Vankelecom, I. F. J.; Jacobs, P. A. In *Chiral Catalyst Immobilization and Recycling*; Wiley-VCH: Weinheim, Germany, 2000. (b) Song, C. E.; Lee, S. *Chem. Rev.* **2002**, *102*, 3495. (c) Fan, Q.; Li, Y.-M.; Chan, A. S. C. *Chem. Rev.* **2002**, *102*, 3385. (d) Pu, L. *Chem. Rev.* **1998**, *98*, 2405.

(2) For a highlight, see: (a) Dai, L.-X. *Angew. Chem., Int. Ed.* **2004**, *43*, 5726. For leading references, see: (b) Seo, J. S.; Whang, D.; Lee, H.; Jun, S. I.; Oh, J.; Jeon, Y. J.; Kim, K. *Nature* **2000**, *404*, 982. (c) Takizawa, S.; Somei, H.; Jayaprakash, D.; Sasai, H. *Angew. Chem., Int. Ed.* **2003**, *42*, 5711. (d) Guo, H.; Wang, W.; Ding, K. *Tetrahedron Lett.* **2004**, *45*, 2009. (e) Wang, X.; Ding, K. *J. Am. Chem. Soc.* **2004**, *126*, 10524. (f) Hu, A.; Ngo, H. L.; Lin, W. *J. Am. Chem. Soc.* **2003**, *125*, 11490. (g) Hu, A.; Ngo, H. L.; Lin, W. *Angew. Chem., Int. Ed.* **2003**, *42*, 6000.

(3) Lehn, J.-M.*Chem.*−*Eur. J.* **2000**, *6*, 2097−2102.

(4) For a review, see: (a) Okuma, T.; Kitamura, M.; Noyori, R. *Angew. Chem., Int. Ed.* **2001**, *40*, 40. For leading references, see: (b) Ohkuma, T.; Ooka, H.; Hashiguchi, S.; Ikariya, T.; Noyori, R. *J. Am. Chem. Soc.* **1995**, *117*, 2675. (c) Ohkuma, T.; Ooka, H.; Ikariya, T.; Noyori, R. *J. Am. Chem. Soc.* **1995**, *117*, 10417. (d) Doucet, H.; Ohkuma, T.; Murata, K.; Yokozawa, T.; Kozawa, M.; Katayama, E.; England, A. F.; Ikariya, T.; Noyori, R. *Angew. Chem., Int. Ed.* **1998**, *37*, 1703. (e) Ohkuma, T.; Koizumi, M.; Doucet, H.; Pham, T.; Kozawa, M.; Murata, K.; Katayama, E.; Yokozawa, T.; Ikariya, T.; Noyori, R. *J. Am. Chem. Soc.* **1998**, *120*, 13529.

(5) For immobilized Noyori's catalysts, see: (a) Ohkuma, T.; Takeno, H.; Honda, Y.; Noyori, R. *Adv. Synth. Catal.* **2001**, *343*, 369. (b) Li, X.; Chen, W.; Hems, W.; King, F.; Xiao, J. *Org. Lett.* **2003**, *5*, 4559. (c) Itsuno, S.; Tsuji, A.; Takahashi, M. *Tetrahedron Lett.* **2003**, *44*, 3825.

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