

A novel system consisting of easily recyclable dendritic Ru-BINAP catalyst for asymmetric hydrogenation†

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Received (in Cambridge, UK) 28th March 2002, Accepted 6th June 2002

First published as an Advance Article on the web 20th June 2002

Dendritic Ru-BINAP catalysts functionalized with alkyl chain at the periphery together with organic binary solvent system that exhibited phase separation induced by addition of a little water have been employed for asymmetric hydrogenation, leading to high catalytic activity and enantioselectivity as well as facile catalyst recycling.

Homogeneous asymmetric catalysis is one of the most important developments in modern chemistry over the past several decades.¹ Transition metal complexes with diphosphine ligands, such as BINAP [2,2'-bis(diphenylphosphino)-1,1'-binaphthyl], have proved to be excellent homogeneous catalysts in various asymmetric hydrogenation reactions.² As these chiral catalysts are often expensive, attempts have been made to heterogenize these catalysts so as to reuse them as often as possible. Different approaches to the heterogenization of chiral catalysts have recently been reviewed.³ These included immobilization of chiral metal complexes by anchoring the catalyst on a solid support⁴ or by using a liquid–liquid two-phase system.⁵ In most cases, however, the activity and enantioselectivity of the immobilized catalysts were lower than those of the parent homogeneous system as a result of mass transfer limitations. Recently, two new strategies—soluble polymer-supported catalyst systems⁶ and thermomorphic catalyst systems⁷—have been highlighted as new options for catalyst heterogenization so as to combine the advantages of homogeneous catalysis and heterogeneous catalysis. The unique feature of both strategies is that the catalytic reactions were carried out in homogeneous manner (one phase) under proper reaction conditions.⁸ The recovering of the thermomorphic catalyst could be realized *via* phase separation by cooling the reaction mixture (two-phase). This strategy, however, was limited to high reaction temperature and, to our knowledge, has not been applied for asymmetric catalysis.

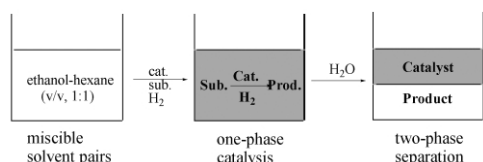
Here, we reported a novel system for highly effective asymmetric hydrogenation and liquid–liquid separation of the catalyst (Scheme 1). Our strategy⁹ relies on the following two ideas: (1) Some solvent pairs of non-polar hydrocarbons and polar light alcohols, such as hexane and pure ethanol, are completely miscible, but exhibit phase separation with the addition of a little water. (2) The chiral catalyst should have a strong phase preference under biphasic conditions. In this study, we chose BINAP as a model ligand. Taking advantage of the

unique properties and well-defined nanostructures of dendrimer,^{10,11} we modified BINAP by incorporating it onto the Fréchet-type dendrimer functionalized with alkyl chains at the periphery so as to make its metal complexes exclusively soluble in hydrocarbons at room temperature. To the best of our knowledge, such a liquid–liquid phase separating system including a dendrimer-bound chiral metal catalyst has not been previously reported.

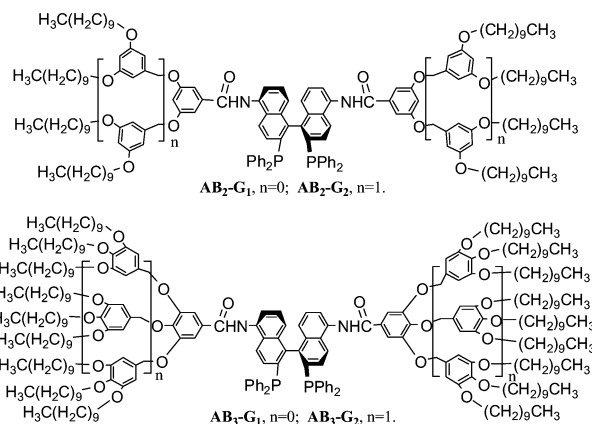
This system provided several key advantages: (a) Unlike the thermomorphic system, this binary solvent system provided complete miscibility of the phase over a broad range of reaction temperature. (b) The organic binary solvent system avoided the use of water which has often shown detrimental effect on the enantioselectivity in the asymmetric hydrogenation. (c) Upon completion of the reaction, the addition of very small amount of water (only 2.5%) could induce phase separation and provided facile catalyst recovery. (d) As compared to soluble polymer-supported asymmetric catalysis, this strategy avoided the use of large amounts of other solvents for catalyst precipitation. Consequently, this system combines the advantages of homogeneous asymmetric catalysis and the traditional two-phase catalysis: high catalytic activity and enantioselectivity, tailor-made catalyst, facile phase separation and reuse of the catalyst.

The preparation of new dendritic chiral BINAP ligands (Scheme 2) was conducted according to our recently reported procedure.^{11f} Condensation reaction of 5,5'-diamino-BINAP with the peripherally alkyl-functionalized polyether dendritic wedges with carboxy group located at the focal point in the presence of triphenylphosphite, pyridine, and calcium chloride in *N*-methyl-2-pyrrolidone at 100 °C gave the chiral dendrimer ligands in moderate reaction yield. These ligands were purified by fast column chromatography and characterized by ¹H and ³¹P NMR spectroscopy and MALDI-TOF mass spectrometry. All results are in full agreement with the compounds synthesized.

The dendritic Ru-BINAP catalysts were prepared *in situ* by the reaction of dendritic BINAP ligand with [RuCl₂(benzene)]₂



Scheme 1 Illustration of the effective and recyclable catalyst system.



Scheme 2

† Electronic supplementary information (ESI) available: synthesis details, partition coefficients of dendritic BINAP ligands and their Ru complexes, hydrogenation and recycling procedure. See <http://www.rsc.org/suppdata/cc/b2/b203117e/>

in DMF at 100 °C for 20 min. Their catalytic efficiency was evaluated by choosing asymmetric hydrogenation of 2-acrylic acids, 2-phenylacrylic acid **1** and 2-[*p*-(2-methylpropyl)phenyl]acrylic acid **2**, as the model reactions. All dendritic Ru-BINAP complexes were tested, and complete conversions of **1** or **2** were obtained with high enantioselectivities in 4 h. The preliminary results are summarized in Table 1. The dendritic catalysts showed similar enantio-selectivity to Ru-BINAP. The high catalytic activity and enantioselectivity were probably due to the homogeneous nature of the reaction. The number of the alkyl end groups of the dendritic wedges slightly influenced the reaction performance and the results depended on the solubility of the dendrimer in hexane.

As shown in Table 1, similar enantioselectivities were obtained by using a mixture of ethanol/hexane in a different ratio as solvent (entries 3–5). However, when using a mixture of ethanol/hexane/H₂O (1 : 1 : 0.05) as solvent, much lower conversion and enantioselectivity were obtained in the hydrogenation of **2** (entries 13 vs 14). This profound solvent effect was mainly due to phase separation upon the addition of a little water, which thus resulted in mass transfer limitations.

Another unique feature of this system was the facile catalyst recycling *via* liquid–liquid biphasic separation technique. It was found that these dendrimers with an alkyl-functionalized periphery preferred to dissolve in a non-polar solvent system. In the case of the second-generation dendrimer ligands **AB₂-G₂** and **AB₃-G₂**, more than 99% of their Ru complexes could be extracted to the non-polar hexane phase in a n-hexane/ethanol (2.5% H₂O) biphasic system. For example, upon completion of the catalytic hydrogenation of **2**, a small amount of water (2.5%) was added to the reaction mixture to induce phase separation. The hexane layer, which contained the catalyst **AB₂-G₂-Ru** (about 99.3% of catalyst was recovered), was separated and reused in the next round of reaction. The recovered catalyst gave

Table 1 Dendritic Ru-BINAP catalysed asymmetric hydrogenation and catalyst recycling^a

1: R = i-Bu; 2: R = H

Entry	Sub.	Ligand	H ₂ (atm)	Time (h)	^b Conv. (%)	^b E.e. (%)
1	1	(<i>R</i>)-BINAP	80	4	100	87
2	1	AB₂-G₁	80	4	100	88
3	1	AB₂-G₂	80	4	100	87
4 ^c	1	AB₂-G₂	80	4	100	86
5 ^d	1	AB₂-G₂	80	4	100	85
6	1	AB₃-G₁	80	4	100	88
7	1	AB₃-G₂	80	4	100	84
8	2	(<i>R</i>)-BINAP	80	4	100	89
9	2	AB₂-G₁	80	4	100	90
10	2	AB₂-G₂	80	4	100	90
11	2	AB₃-G₁	80	4	100	90
12	2	AB₃-G₂	80	4	100	89
13	2	AB₃-G₁	80	2.5	95	91
14 ^e	2	AB₃-G₁	80	2.5	38	80
15	2	AB₂-G₂ (run 1) ^f	50 (80)	2	72 (94)	84 (90)
16	2	AB₂-G₂ (run 2) ^f	50 (80)	2	70 (93)	84 (90)
17	2	AB₂-G₂ (run 3) ^f	50 (80)	2	69 (93)	81 (89)
18	2	AB₂-G₂ (run 4) ^f	50 (80)	2	68 (91)	82 (89)

^a Reaction conditions: sub./cat. = 100 (mol/mol); NEt₃/sub. = 3:2 (mol/mol); rt. ^b Based on GC analysis. The absolute configuration of product is (*R*). ^c A mixture of hexane/ethanol = 2:3 (v/v) was used as solvent. ^d A mixture of hexane/ethanol = 3:2 (v/v) was used as solvent. ^e Hydrogenation was carried out under two-phase condition by using a mixture of hexane/ethanol/H₂O = 1:1:0.05 (v/v) as solvent. ^f Hydrogenation was carried out under 50 and 80 atm H₂ using recovered catalyst.

similar conversions in 2 h reaction times under 50 or 80 atm H₂ with only slight loss of enantioselectivity over at least three cycles (entries 15–18). In order to further demonstrate the recovery of the catalyst, the colorless ethanol layer which contained the reduced product was further used to catalyse the hydrogenation of **1** under the same reaction conditions, but did not, however, give any hydrogenated product.

In conclusion, peripherally alkyl-functionalized dendritic Ru-BINAP catalysts have been synthesized and employed for asymmetric hydrogenation using a mixture of ethanol/hexane as reaction medium. The combination of chiral dendritic catalyst and organic biphasic system provided high catalytic activity and enantioselectivity as well as efficient and easy catalyst recycling. Since light alcohols (*e.g.* ethanol and methanol) have been found to be the best solvents for most asymmetric hydrogenation reactions, this system can be extended to other chiral phosphine-containing catalysts. Thus, this strategy will lead to a general method of separating products from homogeneous catalysts and recovering the chiral catalysts by simple liquid–liquid biphasic separation. The investigation of other hydrogenation reactions and the extension of this strategy to other chiral diphosphine systems are in progress.

We thank National Natural Science Foundation of China (projects 20132010 and 29904009), CMS, Chinese Academy of Sciences, and The Hong Kong Polytechnic University ASD Fund for financial support of this study.

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