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Dendritic BINAP based system for asymmetric hydrogenation of simple aryl ketones

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Abstract

A series of dendritic BINAP-Ru/chiral diamine catalysts were developed for asymmetric hydrogenation of various simple aryl ketones. The resulting catalytic system showed very attractive due to very good catalytic activity and enantioselectivity as well as facile catalyst recycling. In the case of 1-acetonaphthone and 2′-methyl-acetophenone, interesting e.e. value up to 95% was observed which are comparable to the enantioselectivity reported by Noyori under similar conditions and higher than that of the heterogeneous poly(BINAP)-Ru catalyst reported by Pu and co-workers [Tetrahedron Lett. 41 (2000) 1681].

Keywords: Asymmetric hydrogenation; Dendritic catalyst; BINAP; DPEN; Chiral secondary alcohol

1. Introduction

In the recent years, the design and synthesis of effective enantioselective catalysts for hydrogenation of simple ketones have been attracting much attention, and various strategies have been introduced [1–4]. Among all the chiral catalysts reported today, the ternary catalyst system of Ru-chiral diphosphine-chiral diamine-KOH, which was described by Noyori and Ohkima [4], have been found to be the most effective catalysts for asymmetric hydrogenation of simple ketones lacking a secondary coordinating functional group. However, a major problem associated with this homogeneous catalytic system is the separation and recycling of these very expensive chiral catalysts. A practical approach is to "heterogenize" these homogeneous catalysts onto a cross-linked polymer supports. Most recently, several polymer-supported BINAP-containing catalysts have been studied in the heterogeneous asymmetric hydrogenation of simple ketones under the similar catalytic conditions reported [5,6] and by Noyori and co-workers [7]. Unfortunately, these insoluble catalytic systems often gave much lower catalytic activity and/or enantioselectivity as a result of mass transfer limitations.

The development of soluble polymer-supported chiral ligands for asymmetric catalysis has the potential to combine the advantages of homogeneous and heterogeneous catalysis [8,9]. Recently, we have developed several kinds of soluble polymer or dendrimer-supported chiral ligands [10–13]. In this paper, we reported the first example of asymmetric hydrogenation of simple ketones catalyzed by dendrimer-based chiral catalysts.

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2. Experimental

All experiments were carried out under a nitrogen atmosphere by using standard Schlenk-type techniques, or performing in a glovebox.

2.1. Materials and equipment

All solvents were dried using standard, published methods and were distilled under nitrogen atmosphere before use. Except as specified, commercial reagents were used as received without further purification. Dendritic BINAP ligands were synthesized according to our recently published method using 5,5′-diamino-2,2′-bis(diphenylphosphino)-1,1′-binaphthyls (5,5′-diamino BINAP) as starting materials [13].

NMR spectra were taken on a BRUKER Model AVDANCE DPX 300 spectrometer (300 MHz ^{1}H and 122 MHz ^{31}P) using tetramethylsilane for ^{1}H as an internal standard, 85% of H_3PO_4 in D_2O for ^{31}P as an external standard. All signals are reported in ppm unit. For high-pressure hydrogenation, 50 ml stainless autoclave equipped with a glass liner was used.

2.2. General procedure for preparation of in situ dendritic [$RuCl_2$((R)-BINAP)((R,R)-DPEN)] catalyst

[$RuCl_2$(cymene)]$_2$ (0.35 mg, 0.00057 mmol) and dendritic (*R*)-BINAP (0.0012 mmol) was stirred in dry DMF (1 ml) at 100 °C for 10 min to form a reddish brown solution. After the solution was cooled to 30 °C, (*R*,*R*)-DPEN (0.24 mg, 0.00114 mmol) was added and the mixture was stirred for further 10 h. The solvent was removed under reduced pressure to give the in situ catalyst, which was used for asymmetric hydrogenation reaction without further purification.

2.3. Standard procedure for asymmetric hydrogenation reaction and catalyst recycling

In a typical experiment, the 50 ml glass-lined stainless autoclave with a magnetic stirring bar was charged with 0.00114 mmol dendritic [$RuCl_2$((*R*)-BINAP)((*R*,*R*)-DPEN)] complex, 0.0046 mmol *t*-C_4H_9OK, 0.57 mol aryl ketone and 5 ml of 2-propanol/toluene = 1:1 (v/v). The autoclave was closed and was pressurized with H_2 to 40 atm. The mixture was stirred with a magnetic stirrer under the H_2 pressure for 20 h. After the H_2 was vented, most of the solvent was removed under reduced pressure and dry methanol (2 ml) was added. The dendritic catalyst was quantitatively precipitated and used for the next catalytic cycle. The methanol solution containing the reduced product was used for GC analysis. Enantioselectivity excesses were measured by GC analysis using a chiral column.

3. Results and discussion

Four dendritic BINAP ligands (*R*)-**1**(**a**–**d**, generation 1–4; Fig. 1) were synthesized by condensation of (*R*)-5,5′-diamino-BINAP(*R*)-**2** with the Frechet-type polyether dendrons with carboxyl group located at the focal point according to our recently published method [13], respectively. For the purpose of comparison, a model compound of small molecule (*R*)-**3** was also synthesized by reacting (*R*)-**2** with benzoyl chloride in the presence of pyridine in dichloromethane [8]. The ruthenium catalysts were prepared in situ according to the Noyori's protocol. For example, the third generation dendritic Ru-BINAP pre-catalyst was prepared by reacting the dendritic BINAP ligand ((*R*)-**1c**) with [$RuCl_2$(cymene)]$_2$ at 100 °C in a DMF-toluene (1:1, v/v) mixture for 10 min, followed by treatment with 1 equivalent of (*R*, *R*)-1,2-diphenylethylenediamine (*R*, *R*)-DPEN **4** at room temperature for 10 h. The resulting dendritic catalyst showed a predominate ^{31}P NMR signal at 46.8 ppm, which was very close to the corresponding parent BINAP complex (47.4 ppm) [14]. The Ru complexes of other dendritic BINAP ligands (**1a**, **1b** and **1d**) and the model ligand (*R*)-**3** were also prepared with the similar method and used in the catalytic reactions without further purification.

With the catalysts in hand, our initial efforts were aimed at probing the asymmetric induction of these catalysts using acetophenone as a typical substrate. A 2-propanol–toluene mixture was chosen as solvent because the dendritic catalysts are insoluble in neat 2-propanol. Various generations of these dendritic Ru-BINAP catalysts were tested, and showed highly effective in the hydrogenation of acetophenone with the experimental results summarized in Table 1. As compared with the model catalyst, (*R*)-**3**-Ru, only slightly low enantioselectivity was observed (entries 1–5). The size of the dendritic wedges showed little

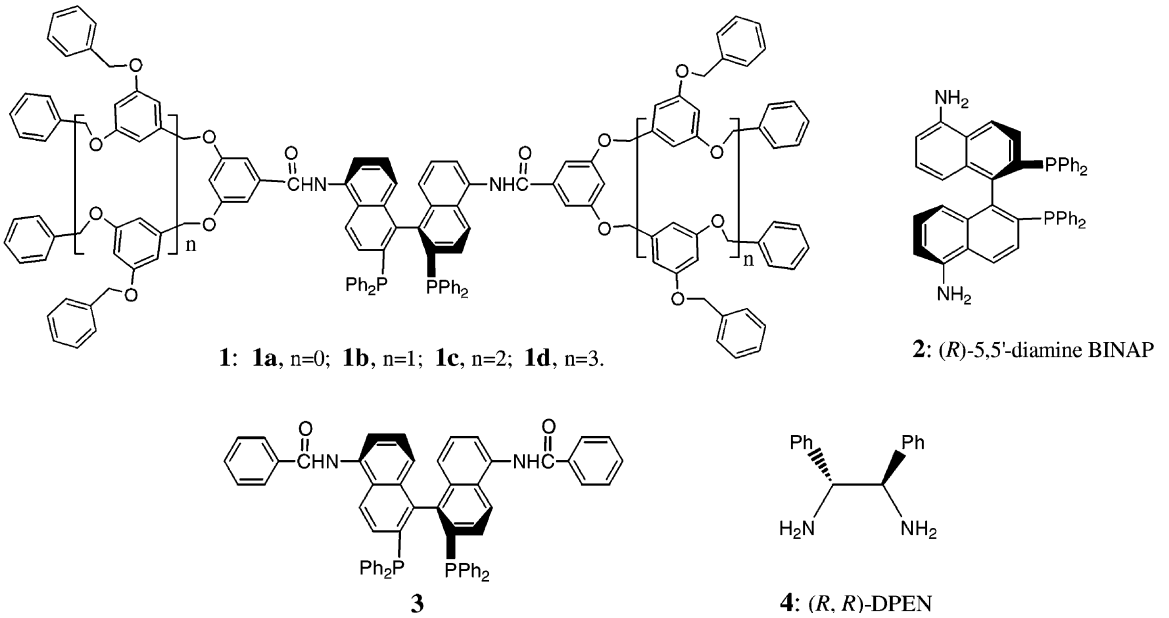
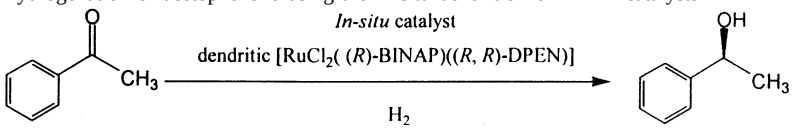


Fig. 1.

influence on the enantioselectivity. The match of the steric environment of the chiral diamine with that of the chiral dendritic BINAP ligand is important for achieving high enantioselectivity, which is consistent with Noyori's observation. For example, combination of (*R*,*R*)-DPEN and [$RuCl_2$((*R*)-**1c**)(cymene)] resulted in 75% e.e. upon hydrogenation of acetophenone, while the mismatching combination of (*S*,*S*)-DPEN and [$RuCl_2$((*R*)-**1c**)(cymene)] gave only 50% e.e. (entry 4 versus entry 6 in Table 1). Most interestingly,

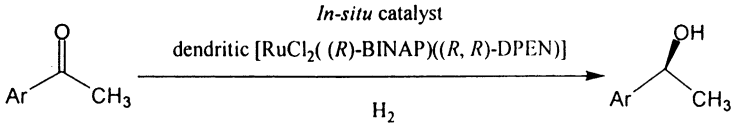
Table 1
Hydrogenation of acetophenone using the in situ dendritic Ru-BINAP catalysts[a]

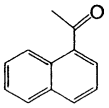
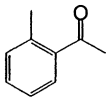
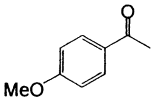
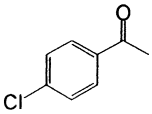


Entry	Ligand	Conversion[b] (%)	E.e.[b] (%)
1	(*R*)-**3**/(*R*,*R*)-**4**	100	78
2	(*R*)-**1a**/(*R*,*R*)-**4**	100	78
3	(*R*)-**1b**/(*R*,*R*)-**4**	100	75
4	(*R*)-**1c**/(*R*,*R*)-**4**	100	75
5[c]	(*R*)-**1d**/(*R*,*R*)-**4**	100	74
6	(*R*)-**1c**/(*S*,*S*)-**4**	100	50
7	(*R*)-BINAP/(*S*,*S*)-**4**	100	30
8	(*R*)-BINAP/(*R*,*R*)-**4**	100	80

[a] Unless otherwise stated reactions were carried out at room temperature using 0.6 mmol of ketones in 5 ml 2-propanol/toluene = 1:1 (v/v) for 20 h; acetophenone:ligand:Ru:DPEN:*t*-C_4H_9OK = 500:1.1:1:1:4 (mol ratio); H_2 pressure = 40 atm.
[b] Determined by chiral GC analysis. The absolute configuration of the product is (*S*).
[c] A mixture of 2-propanol/toluene = 2:3 (v/v) was used as solvent.

Table 2
Hydrogenation of aryl ketones using the in situ dendritic [$RuCl_2$((*R*)-BINAP)((*R*,*R*)-DPEN)] catalysts[a]



Entry	Ketones	E.e.[b] (%)				
		(*R*)-**3**	(*R*)-**1a**	(*R*)-**1b**	(*R*)-**1c**	(*R*)[c]-**1d**
1[d]		96	95	95	95	93
2[d]		95	92	94	94	92
3		79	77	74	74	74
4		58	58	56	55	55

[a] Unless otherwise stated reactions were carried out at room temperature using 0.6 mmol of aryl ketones in 5 ml 2-propanol/toluene = 1:1 (v/v); aryl ketone:ligand:Ru:diamine:*t*-C_4H_9OK = 500:1.1:1:1:4 (mol ratio); H_2 pressure = 40 atm. All catalytic reaction reached 100% conversions were obtained in 20 h.

[b] Determined by chiral GC analysis. The absolute configuration of the product is (*S*).

[c] When using (*R*)-**1d** as ligand, a mixture of 2-propanol/toluene = 2:3 (v/v) was used as solvent.

[d] Reactions were carried out at 50 °C.

the mismatching dendritic catalyst gave higher enantioselectivity than the corresponding mismatching BINAP-Ru catalyst (50% versus 30% e.e., entries 7 and 8 in Table 1).

The new dendrimer-based catalytic system was also used for asymmetric hydrogenation of other simple aryl ketones. As shown in Table 2, the dendritic catalysts exhibited very good enantioselectivity for the hydrogenation of certain aryl ketones. With increase of generation of the dendrimers, only slightly decrease of enantioselectivity was observed. Hydrogenation of 1-acetonaphthone and 2′-methyl-acetophenone catalyzed by dendritic catalyst, for example (*R*)-**1c**-Ru catalyst, gave 95 and 94% e.e., respectively, which are comparable to the enantioselectivities reported by Noyori under similar conditions, and higher than that of the heterogeneous poly(BINAP)-Ru catalyst reported by Pu and co-workers (95% versus 92% and 94% versus 91% e.e.) [6].

An important feature of the design of soluble dendrimer-based catalyst is the easy and reliable separation of the chiral catalyst. The high generations of the dendrimer are expected to achieve quantitative recovery of the catalyst from the reaction mixtures based on the large molecular size and different solubility in various organic solvents. In this study, for example, the third generation catalyst [$RuCl_2$((*R*)-**1c**)((*R*,*R*)-**4**)] was used to carry out the recycling experiment. Upon the completion of the reaction, methanol was added to the reaction mixture and the catalyst was quantitatively precipitated and recovered via filtration. The recovered catalyst was reused for at least two cycles with similar enantioselectivity (as shown in Table 3).

In summary, we have developed a new, recoverable and highly effective dendritic Ru-BINAP/chiral diamine catalyst system for asymmetric hydrogenation of simple ketones. It was demonstrated that the use of soluble dendrimer-based catalyst might combine the

Table 3
Hydrogenation of acetophenone catalyzed by [$RuCl_2$((*R*)-**1c**)((*R*,*R*)-**4**)]: recycling of the dendritic catalyst[a]

Entry	Use	Conversion[b] (%)	E.e.[b] (%)
1	First	100	75
2	Second	100	74
3	Third	100	72
4	Fourth	47	68

[a] Reactions were carried out at room temperature using 0.6 mmol of acetophenone in 5 ml 2-propanol/toluene = 1:1 (v/v) for 20 h; acetophenone:ligand:Ru:DPEN:*t*-C_4H_9OK = 500:1.1:1:1:4 (mol ratio); H_2 pressure = 40 atm.

[b] Determined by chiral GC analysis. The absolute configuration of the product is (*S*).

advantages of homogeneous and heterogeneous catalysis. The use of these recoverable dendritic BINAP ligands in other transformations is in progress.

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