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Dendritic [$RuCl_2$(BINAP)(DPEN)] catalysts with 'Sandwich' multi-layer structure for asymmetric hydrogenation of simple aryl ketones

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ABSTRACT

A new kind of chiral dendritic [$RuCl_2$(BINAP)(DPEN)] catalysts with a 'Sandwich' multi-layer structure have been synthesized *via* metal coordination reactions with dendritic chiral diphosphines and dendritic chiral diamine ligands. The formation of the dendritic catalysts was confirmed by ^{31}P NMR. The catalyst performance was then investigated in the asymmetric hydrogenation of simple aryl ketones, and comparable enantioselectivities were achieved with comparison to that of the corresponding small-molecular catalyst. In addition, the recyclable property of these homogeneous catalysts was studied with the third-generation catalyst, which was reused nine times by simple solvent precipitation without any loss of enantioselectivity.

1. Introduction

Dendrimers represent a new kind of macromolecules which possess highly branched and well-defined molecular structures with nano-scale sizes. These well-defined, discrete structures can be precisely controlled at a molecular level [1,2]. The dendrimers with these favorable properties have generated considerable interests for their application in the field of supported catalysis during the past decades [3–9].

Since van Koten and co-workers reported the first example of dendritic catalyst in 1994 [10], a variety of dendritic catalysts have been reported and successfully applied in various catalytic reactions. Generally, the catalytically active sites are located at the core, the focal point, the periphery or the branches of dendrimers (Fig. 1a–d). In the case of core-functionalized dendritic catalysts [11–24], on one hand, isolation effects created by the sterically demanding dendritic wedges would be beneficial for some reactions [25], in which a bimetallic deactivation mechanism is operative. On the other hand, the core-functionalized dendritic catalysts might benefit from the local micro-environment along with desolvation effects during the penetration of substrate into the dendrimer shell, which is similar to the situation in enzyme catalysis. In addition, the solubility of the core functionalized dendritic catalysts can be well controlled by changing the surface groups, which makes the recycle of catalyst much easier by solvent precipitation. Although good catalytic results and easy catalyst separation were achieved in most cases, placing a single catalytic site at the core of a large dendrimer results in a catalytic system with low catalyst loading. Especially for the higher generation catalyst, it may result in low catalytic activity. In contrast to the core-functionalized catalysts, the active sites of the periphery-functionalized systems are located at the dendrimer surface, which are directly available to substrate in addition to a high catalyst loading [26–35]. Also, some reactions may benefit from the high local catalyst concentration created by these catalysts. But sometimes, undesired interactions between the neighboring peripheral catalytic sites may cause "negative" dendrimer effects (a bimetallic deactivation mechanism). Besides, catalyst recycling has not yet been achieved for most of these periphery-functionalized dendritic metal catalysts. Compared to the cases above, the catalysts with active sites at the branching points of dendrimer (Fig. 1d) [36–38] will offer an opportunity to combine the advantages of both. However, the metal dendritic catalysts with this topology structure are rarely reported due to the difficulties in synthesis, especially in asymmetric catalysis. Therefore, developing new types of dendritic catalysts that feature easy synthesis, high efficiency and reliable recyclability is still remaining a challenging subject.

Recently, we reported a new kind of easily available chiral BINAP-functionalized Janus dendrimers (Fig. 1e) for the Ru-catalyzed asymmetric hydrogenation of 2-arylacrylic acids [39,40]. Based on this work and for our continuing interest in the applications of functionalized organometallic dendrimers as homogeneous catalysts, herein we report the synthesis of a novel series of dendritic catalysts (Fig. 1f) of Janus type with the metal catalytic centers located at the branching points of one dendron. The dendritic catalysts are expected to provide the following advantages: (1) By introducing the peripheral Fréchet dendrons, the solubility and the molecular weight of the dendritic catalysts could be fine-tuned to facilitate catalyst synthesis and recycling

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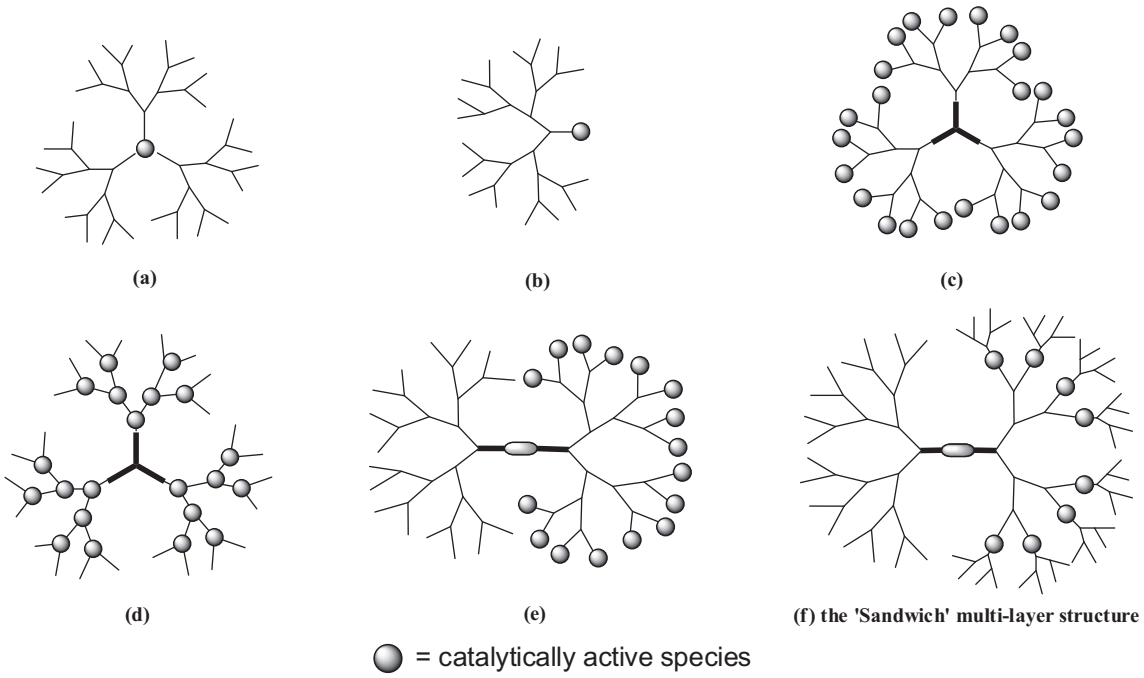


Fig. 1. Different types of dendritic catalysts.

by solvent precipitation. (2) The interactions between the catalytic sites, which often cause low catalytic activity in some cases, may be reduced due to the site-isolation effects created by the peripheral Fréchet dendrons. (3) High catalyst loading is achieved. The dendritic catalysts with 'Sandwich' multi-layer structure, in which the metal complex layer is ''cramped'' between layers of poly(aryl ether) dendrons, were applied to the asymmetric hydrogenation of simple ketones, and the recyclability of the dendritic catalyst was also studied.

2. Experimental

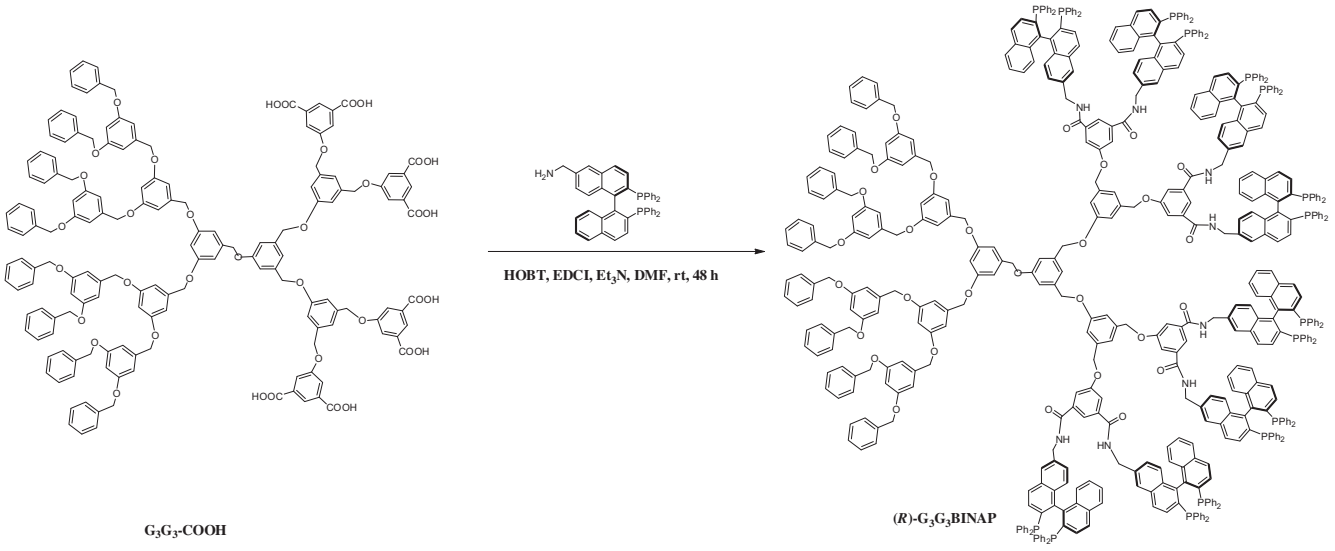
2.1. Materials and methods

Unless otherwise noted, all experiments were carried out under an inert atmosphere of dry nitrogen by using standard Schlenk-type techniques. ^{1}H, ^{31}P and ^{13}C NMR spectra were recorded on a Bruker Model Advance DMX 300 or 600 Spectrometer (^{1}H 300 MHz, ^{31}P 121 MHz and ^{13}C 75 or 150 MHz, respectively). MALDI–TOF mass spectra were obtained on a BIFLEX instrument with α-cyano-4-hydroxycinnamic acid (CCA) as the matrix. HR-ESI mass spectra were obtained on a Bruker APEX IV instrument. Elemental analyses were performed on a Carlo–Erba-1106 instrument. GC analyses were performed on a Varian CP-3800 Gas Chromatograph equipped with chiral capillary column (CP 7502).

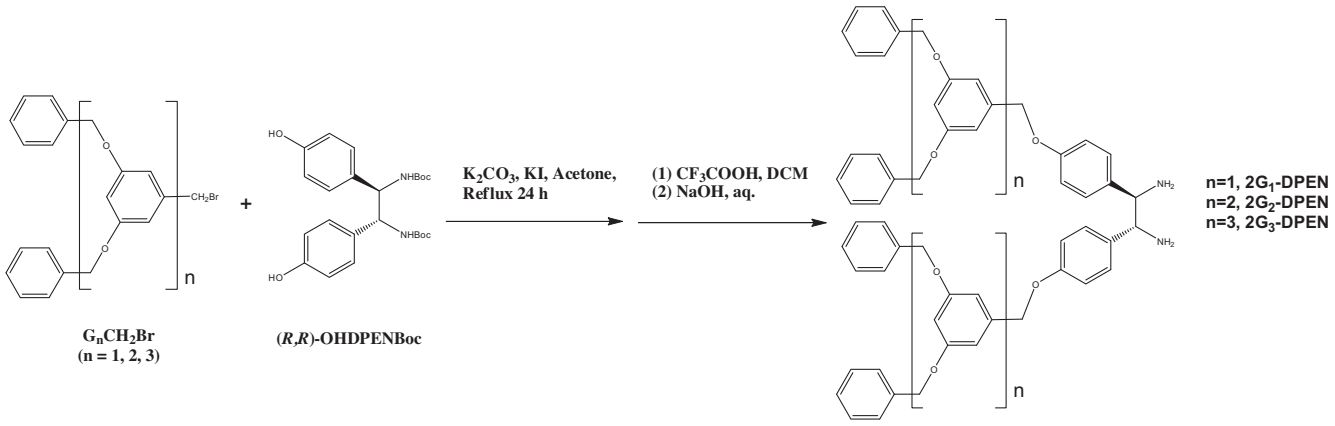
All starting materials were obtained from Aldrich, Acros or Alfa and used as received unless otherwise mentioned. The organic solvents used were dried according to published methods.

2.2. Synthesis and characterization of the dendritic diphospine ligand

(*R*)-G_3G_3BINAP was synthesized in excellent yield by coupling of G_3G_3-COOH with (*R*)-6-aminomethyl-2,2′-bis(diphenylphospha-



Scheme 1. Synthesis of dendritic diphospine ligand (*R*)-G_3G_3BINAP.



Scheme 2. Synthesis of dendritic diamine ligand (*R*,*R*)-2G$_n$DPEN.

nyl)-1,1′-binaphthyl in the presence of ethyl-*N*,*N*-dimethyl-carbodiimide and 1-hydroxybenzotriazole Scheme 1 [40].

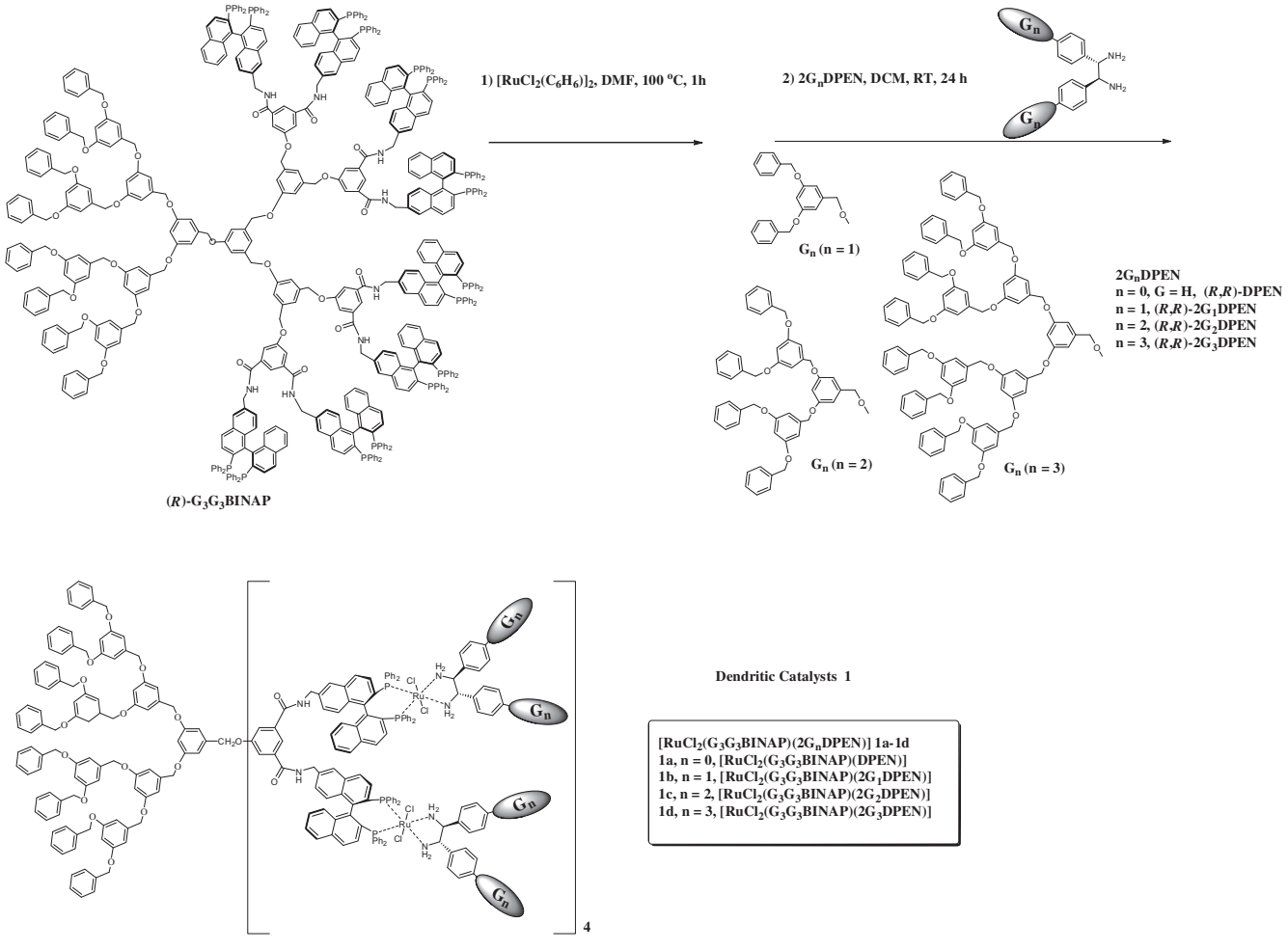
2.3. Synthesis and characterization of the dendritic diamine ligands

According to the reported convergent method [41], the dendritic diamine ligands (*R*,*R*)-2G$_n$DPEN were prepared from (*R*,*R*)-2G$_n$DPENBoc after treatment with trifluoroacetic acid (Scheme 2). (*R*,*R*)-2G$_n$DPENBoc were readily synthesized in very good yields by coupling of the corresponding Fréchet-type dendrons G$_n$CH$_2$Br [42] with chiral (*R*,*R*)-OHDPENBoc (For details, see the Supporting Information).

2.4. Synthesis and characterization of the dendritic catalysts with 'Sandwich' multi-layer structure

2.4.1. General procedure for the synthesis of dendritic catalysts

According to the reported method [39], (*R*)-G$_3$G$_3$BINAP (30.0 mg, 1.0 equiv) and [RuCl$_2$(C$_6$H$_6$)]$_2$ (7.7 mg, 4.0 equiv) were placed in a Schlenk flask, and the mixture was stirred under argon



Scheme 3. Synthesis of dendritic catalysts with 'Sandwich' multi-layer structure.

at 100 °C in DMF (2 mL) for 0.5 h. Then, DMF was removed under reduces pressure, and dendritic diamine (*R*,*R*)-2G$_n$DPEN (1.0 equiv) was added to the reaction mixture. After stirring in DCM (2 mL) for another 24 h, DCM was removed and methanol (4 mL) was added to the mixture, and the catalyst was precipitated to afford the dendritic catalyst [RuCl$_2$(G$_3$G$_3$BINAP)(2G$_n$DPEN)] as a brown solid.

[RuCl$_2$(G$_3$G$_3$BINAP)(DPEN)]:
Yield 22.3 mg, 95%. ^{31}P NMR (121 MHz, CDCl$_3$) δ = 43.6.
[RuCl$_2$(G$_3$G$_3$BINAP)(2G$_1$DPEN)]:
Yield 61.7 mg, 95%. ^{31}P NMR (121 MHz, CDCl$_3$) δ = 45.4.
[RuCl$_2$(G$_3$G$_3$BINAP)(2G$_2$DPEN)]:
Yield 93.0 mg, 97%. ^{31}P NMR (121 MHz, CDCl$_3$) δ = 45.6, 46.0.
[RuCl$_2$(G$_3$G$_3$BINAP)(2G$_3$DPEN)]:
Yield 137.0 mg, 97%. ^{31}P NMR (121 MHz, CDCl$_3$) δ = 45.5, 45.7.

2.5. General procedure for hydrogenation reactions

To a 10 mL glass-lined stainless steel reactor with a magnetic stirring bar was added substrate (1.0 mmol), the above prepared catalyst [RuCl$_2$(G$_3$G$_3$BINAP)(2G$_n$DPEN)] (1.0×10^{-3} mmol), *t*-BuOK (2.5 mg, 0.02 mmol) and 2 mL of *i*-PrOH/DCM (1:1, *v*/*v*). The autoclave was closed and was pressurized with H_2 to 45 atm. The mixture was stirred at 20 °C for 48 h. After careful venting of hydrogen, conversion and ee values were determined by GC with a chiral capillary column.

2.6. General procedure for the catalyst recycling using [RuCl$_2$(G$_3$G$_3$BINAP)(2G$_3$DPEN)] as catalyst

To a 10 mL glass-lined stainless steel reactor with a magnetic stirring bar was added substrate (2.0 mmol), the above prepared catalyst RuCl$_2$[(G$_3$G$_3$BINAP)(2G$_3$DPEN)] (2.0×10^{-3} mmol), *t*-BuOK (5.0 mg, 0.04 mmol) and 4 mL of *i*-PrOH/DCM (1:1, *v*/*v*). The autoclave was closed and was pressurized with H_2 to 45 atm. The mixture was stirred at 20 °C for 36–72 h. After careful venting of hydrogen, most of the solvent was removed under reduced pressure. Then, methanol was added, and the catalyst was precipitated and collected *via* filtration. The recovered catalyst was reused in the next catalytic cycle directly without further purification. The methanol layer was used to determine the conversion and enantioselectivity of the reduced product by chiral GC analysis.

3. Results and discussion

3.1. Synthesis and characterization of the dendritic catalysts with 'Sandwich' multi-layer structure

As illustrated in Scheme 3, series of dendritic catalysts **1a**–**1d** with 'Sandwich' multi-layer structure were prepared *via* metal coordination reactions with [RuCl$_2$(C$_6$H$_6$)]$_2$, dendritic chiral diphosphine (*R*)-G$_3$G$_3$BINAP and dendritic chiral diamine ligands (*R*,*R*)-2G$_n$DPEN in nearly quantitative yields according to the published method [43]. The complete coordination was confirmed by ^{31}P NMR spectroscopy. As shown in Fig. 2, signals were found only around δ = 44 ppm for all dendritic catalysts. The chemical shift of dendritic ligand (*R*)-G$_3$G$_3$BINAP at δ = −16.6 ppm had completely disappeared after the coordination reactions.

3.2. Asymmetric hydrogenation of simple aryl ketones catalyzed by the dendritic catalysts

Noyori's [RuCl$_2$(BINAP)(DPEN)] complex is a highly effective and enantioselective catalyst for the asymmetric hydrogenation of simple ketones [44,45]. Therefore, we chose simple aryl ketones

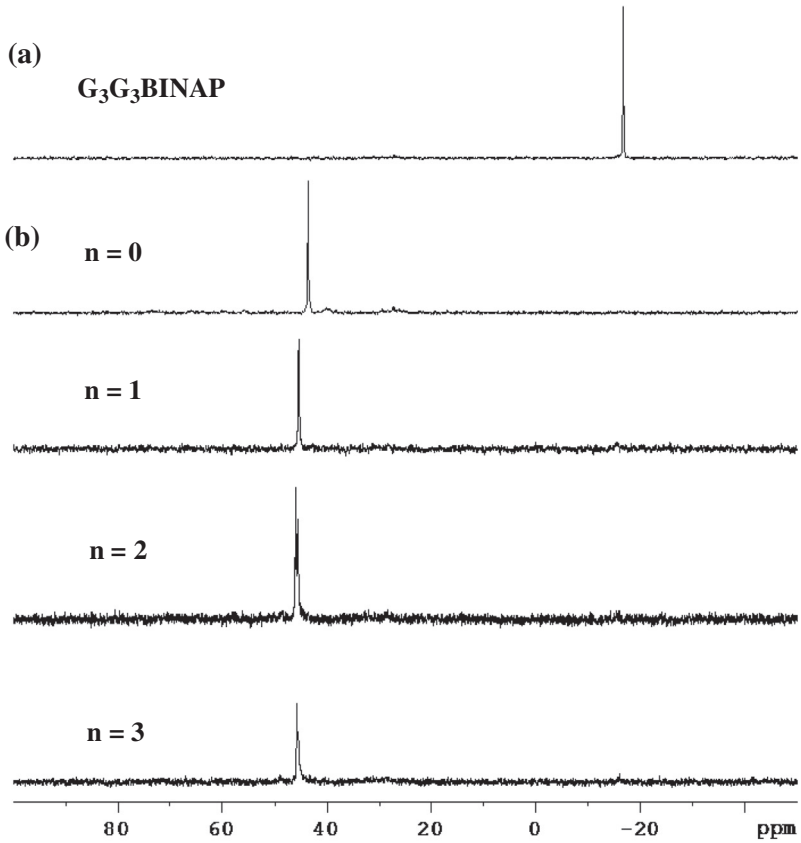
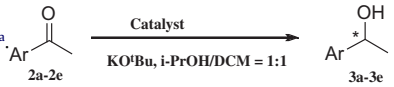


Fig. 2. ^{31}P NMR spectra (CDCl$_3$): (a) (*R*)-G$_3$G$_3$BINAP ligand; and (b) Dendritic catalysts [RuCl$_2$(G$_3$G$_3$BINAP)(2G$_n$DPEN)].

Table 1
Asymmetric hydrogenation of simple aryl ketones catalyzed by the dendritic catalysts[a].



Entry	Catalyst	Ar	Conv.[b] (%)	Ee[b] (%)
1	**1a**	Ph (a)	>99	79
2	**1b**	Ph (a)	>99	80
3	**1c**	Ph (a)	>99	80
4	**1d**	Ph (a)	>99	80
5	**1a**	2-Cl–Ph (b)	>99	92
6	**1b**	2-Cl–Ph (b)	>99	92
7	**1c**	2-Cl–Ph (b)	>99	92
8	**1d**	2-Cl–Ph (b)	>99	92
9	**1a**	4-MeO–Ph (c)	>99	82
10	**1b**	4-MeO–Ph (c)	>99	82
11	**1c**	4-MeO–Ph (c)	>99	80
12	**1d**	4-MeO–Ph (c)	>99	80
13	**1a**	1-naphthyl (d)	>99	93
14	**1b**	1-naphthyl (d)	>99	93
15	**1c**	1-naphthyl (d)	>99	93
16	**1d**	1-naphthyl (d)	>99	93
17	**1a**	2-naphthyl (e)	>99	72
18	**1b**	2-naphthyl (e)	>99	72
19	**1c**	2-naphthyl (e)	>99	72
20	**1d**	2-naphthyl (e)	>99	71

[a] Reaction conditions: **2** (1.0 mmol) in 2 mL solvent (*i*-PrOH/CH_2Cl_2, 1:1, *v*/*v*), S/C/KO^{t}Bu = 1000/1/20, 45 atm of H_2, stirred at 20 °C for 48 h.
[b] The conversion and ee values were determined by chiral GC analysis.

as the substrates for the hydrogenation study to inspect the catalytic properties of these synthesized dendritic catalysts. As illustrated in Table 1, quantitative conversions and 79–80% ees of **3a** were obtained when dendritic catalysts **1a**–**1d** were used in the hydrogenation of acetophenone (**2a**), which are comparable to that observed in the same reaction using small molecular [$RuCl_2$(BINAP)(DPEN)] catalyst [42]. This also means that the generation of the surface Fréchet dendrons had no obvious effect on catalytic enantioselectivity. Afterwards, other simple aryl ketones (**2b**–**2e**) were investigated in the hydrogenation study. Excellent results were also achieved in most cases.

3.3. The recovery performance of the dendritic catalyst *1d*

Taking advantage of the physical characteristics of polyether Janus dendrimer and the surface Fréchet dendrons, we finally investigated the recovery and reuse of these dendritic catalysts with 'Sandwich' multi-layer structure by using solvent precipitation method. Dendritic catalyst **1d** bearing the third generation Fréchet dendrons at the surface was expected to have the best recovery performance, and therefore, was selected to be tested in this study, and the asymmetric hydrogenation of **2b** was chosen as the standard reaction. As shown in Table 2, after the completion of the hydrogenation reactions, the catalyst was easily precipitated by the addition of methanol. Then the recovered catalyst was directly used in the next catalytic cycle. It was found that similar enantioselectivities and full conversions were obtained within 36 h before the third catalytic run. From the third to the seventh catalytic run, prolonged reaction time was needed in order to achieve full conversion. To investigate the activity of the recovered dendritic catalyst, TOF was determined after 24 h of reaction in each cycle, showing gradually decrease from the fifth run. However, an obvious loss of activity was found at the eighth catalytic run. The decreased catalytic activity might be caused by catalyst oxidation during the recycling processes. On the contrary, the high enantioselectivity was maintained for the whole catalyst recycling study.

Table 2
Catalyst recycling in the hydrogenation of **2b** with **1d** as catalyst.[a]

Run	1	2	3	4	5	6	7	8	9
Time (h)	36	36	48	48	48	48	48	48	72
Conv. (%)	99	98	99	99	99	99	99	60	80
TOF[b] (h^{-1})	26	27	27	26	23	17	16	5	6
Ee (%)	92	91	91	92	92	92	92	91	92

[a] Reaction conditions: **2b** (308 mg, 2.0 mmol), 4 mL solvent (*i*-PrOH/CH_2Cl_2, 1:1, *v*/*v*), S/C/KO^{t}Bu = 1000/1/20, 45 atm of H_2, stirred at 20 °C.
[b] TOF determined after 24 h of reaction in each catalytic cycle.

4. Conclusion

In summary, we have developed an efficient approach for the synthesis of a new type of dendritic catalysts with 'Sandwich' multi-layer structure. The resulting dendritic catalysts of different generation were purified using solvent precipitation method at the end of the coordination reaction with metal precursor, Janus dendritic diphosphine and dendritic diamines, and they were successfully applied to the asymmetric hydrogenation of simple aryl ketones. Similar enantioselectivities were obtained as compared to the corresponding small molecular catalyst. Moreover, the dendritic catalyst could be recycled nine times without obvious loss of enantioselectivity.

Acknowledgement

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Appendix A. Supplementary material

Experimental procedures, characterization data for all dendritic ligands and catalysts, descriptions of stereochemical assignments, and copies of NMR (^1H, ^{13}C and ^{31}P) and MS spectra for all compounds reported in the text. Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.ica.2013.05.035.

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