Communication

Synthesis of Dendritic BINAP Ligands and Their Applications in Asymmetric Hydrogenation†

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A new type of chiral dendritic ligands with 2,2′-bis(diphenylphosphino)-1,1′-binaphthyl (BINAP) located at the focal point of the dendrimer has been synthesized through the condensation reaction of 5-amino BINAP and Fréchet-type poly (aryl ether) dendrons with carboxyl groups as the linker in high reaction yields, respectively. The ruthenium complexes of these dendritic ligands were found to be very efficient catalysts in asymmetric hydrogenation of 2-phenylacrylic acids as well as facile catalyst recycling.

Keywords asymmetric hydrogenation, dendritic catalyst, BINAP, homogeneous catalysis

Dendrimers are highly branched macromolecules that have precisely defined molecular structures with nanoscale size. Since the pioneering work of van Koten *et al.* reported in 1994,[1] dendritic catalysts have become a subject of intensive research.[2,3] Although a number of dendritic catalysts have been described, so far, relatively few reports on asymmetric catalysis employing chiral dendritic catalysts are available.[3]

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.[4] Most recently, chiral metal complexes with diphosphine ligand employed at the periphery[5,6] or incorporated in the core[7,8] of the dendrimer have been reported. Such novel dendritic catalysts have shown high catalytic activity and enantioselectivity as well as facile catalyst recycling. However, chiral diphosphine ligand located at the focal point of the dendrimer has not been reported so far. Such kind of dendritic catalyst suffers from less steric effect of the dendritic wedge as compared with the metal-cored dendrimer. It is thus expected that this type of dendritic catalyst may provide similar catalytic efficiency as the corresponding parent catalyst. We report here, for the first time, the synthesis of chiral dendritic ligands with BINAP located at the focal point of the dendrimer.

The synthesis of dendritic BINAP ligands was outlined in Scheme 1. Firstly, the key intermediate, 5-amino BINAP (*R*-**1**) was synthesized via three-step reactions from BINAPO for the first time.[9] Polyether dendritic wedges **5** (**5a**, $n=0$; **5b**, $n=1$; **5c**, $n=2$) with carboxyl group located at the focal point were synthesized by the convergent-growth approach introduced by Hawker and Fréchet.[10] Finally, the dendritic BINAP ligands **6** (**6a**, $n=0$; **6b**, $n=1$; **6c**, $n=2$) were synthesized by condensation of the dendrons **5** with *R*-**1** in the presence of triphenylphosphite, pyridine and calcium chloride in *N*-methyl-2-ketopyrrolidine (NMP) at 110 ℃ with high reaction yields, respectively. These ligands were purified by fast column chromatography and characterized by ^{1}H NMR, ^{31}P NMR and MALDI-TOF mass spectra.[11] All results are in full agreement with the proposed structures.

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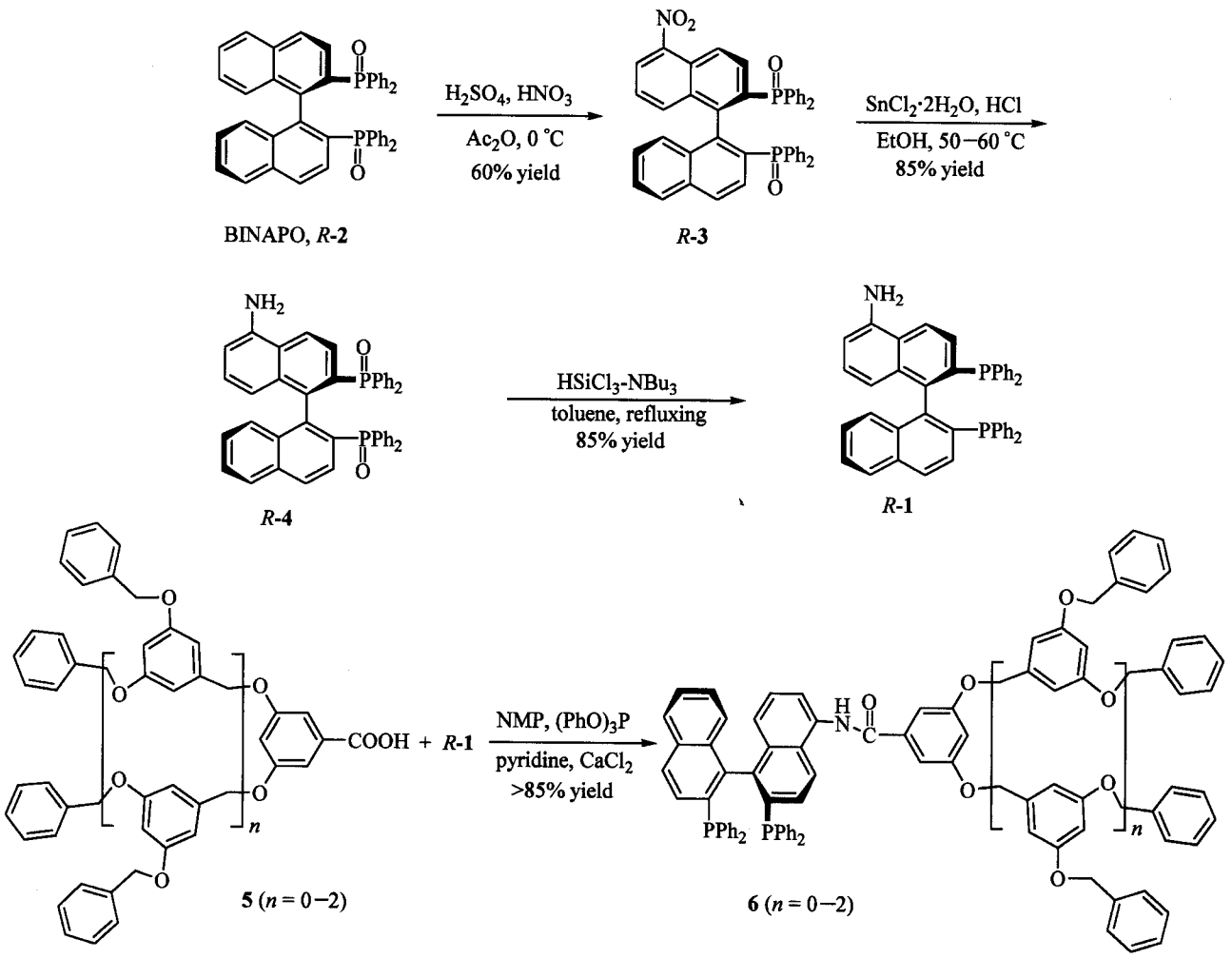
Received May 30, 2002; revised August 30, 2002; accepted September 3, 2002.

Project supported by the National Natural Science Foundation of China (Nos. 20132010 and 29904009) and Chinese Academy of Sciences.

†Dedicated to Professor HUANG Yao-Zeng on the occasion of his 90th birthday.

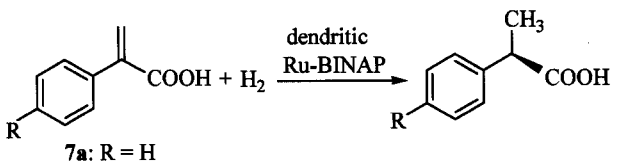
Scheme 1



The dendritic Ru-BINAP catalysts were prepared *in situ* via reaction of dendritic BINAP ligand with $[RuCl_2(benzene)]_2$ in DMF at 100 ℃ for 10 min.[12] Their catalytic efficiency was evaluated by choosing asymmetric hydrogenation of 2-phenylacryclic acid (**7a**) and 2-[*p*-(2-methylpropyl)phenyl]acrylic acid (**7b**), as the model reactions. All dendritic Ru-BINAP complexes were tested, and complete conversions of **7a** or **7b** were obtained with high enantioselectivities in 5 h with preliminary results summarized in Table 1. All dendritic catalysts showed similar enantioselectivity as compared to the parent Ru-BINAP catalyst. The importance of the attachment of dendrimer, on the other hand, is the easy and reliable separation of the chiral BINAP ligands due to their different solubilities in various organic solvents. For example, upon completion of the reaction, methanol was added to the reaction mixture and the catalyst Ru(*R*-**6c**) was quantitatively precipitated and recovered via filtration. The recovered catalyst was reused for at least three cycles with the same enantioselectivity (Entries 9—11 and 12—15).

In summary, we have developed a new type of chiral dendritic ligand with diphosphine ligand located at the focal point of the dendrimer. The dendritic BINAP ligands have been synthesized based on the mono substituted BINAP derivative *R*-**1** which was synthesized for the first time. The ruthenium complexes of these dendritic ligands were found to be very efficient catalysts in asymmetric hydrogenation of 2-phenylacryclic acid as well as facile catalyst recycling. Further applications of these dendritic BINAP ligands to other reactions is currently in progress.

Table 1 Asymmetric hydrogenation of 2-phenylacryclic acids (**7**) catalyzed by dendritic Ru-BINAP and Ru-BINAP [a]



7a: R = H
7b: R = *i*-Bu

Entry	Substrate	Ligand	*ee* (%)[b]	Config.
1	**7a**	*R*-BINAP	93.3	*R*
2	**7a**	*R*-**6a**	93.3	*R*
3	**7a**	*R*-**6b**	93.4	*R*
4	**7a**	*R*-**6c**	93.5	*R*
5	**7b**	*R*-BINAP	90.0	*R*
6	**7b**	*R*-**6a**	90.2	*R*
7	**7b**	*R*-**6b**	91.0	*R*
8	**7b**	*R*-**6c**	90.8	*R*
9	**7a**	*R*-**6c** (run 1)	93.0	R
10	**7a**	*R*-**6c** (run 2)[c]	93.0	*R*
11	**7a**	*R*-**6c** (run 3)[c]	93.1	*R*
12	**7b**	*R*-**6c** (run 1)	91.3	*R*
13	**7b**	*R*-**6c** (run 2)[c]	91.2	*R*
14	**7b**	*R*-**6c** (run 3)[c]	91.2	*R*
15	**7b**	*R*-**6c** (run 4)[c]	89.7	*R*

[a]Hydrogenations were carried out in 0.06 mol/L solution of **7** in methanol-toluene (1:1, *V/V*) under the following reaction conditions: *in-situ* catalyst, [Ru(benzene)Cl_2]$_2$ + **6** or *R*-BINAP; substrate/catalyst, 100 (mol/mol); NEt_3/substrate, 2:1 (mol/mol); H_2, 8.08×10^7 Pa; temperature, 15 ℃. [b] Based on chiral GC analysis; all reactions reached 100% conversion in 5 h. [c] Recovered catalyst was used.

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9 *R*-**1**: $[\alpha]_D^{15}$ + 112.8 (*c* 0.50, CH_2Cl_2); ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 4.13 (s, 2H), 6.37 (d, J = 6.3 Hz, 1H), 6.67 (d, J = 5.7 Hz, 1H), 6.78—6.90 (m, 3H), 7.02—7.21 (m, 20H), 7.34—7.45 (m, 3H), 7.81—7.89 (m, 3H); ^{31}P NMR ($CDCl_3$) δ: −13.85, −13.81 (J = 12 Hz); MS *m/z* (ESI): 637.9 (M expected 637.69).

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11 *R*-**6a**: $[\alpha]_D^{15}$ + 104.5 (*c* 0.50, CH_2Cl_2); ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 5.15 (s, 4H), 6.72—7.24 (m, 28H), 7.32—7.60 (m, 12H), 7.81—7.96 (m, 4H), 8.18 (s, 1H); ^{31}P NMR ($CDCl_3$) δ: −13.94, −13.76 (J = 12 Hz); MS *m/z* (MALDI-TOF): 954.4 (M expected 954.04), other major peak at 768.4 (M − $HPPh_2$).

R-**6b**: $[\alpha]_D^{15}$ + 52.4 (*c* 0.50, CH_2Cl_2); ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 5.01—5.10 (m, 12H), 6.60—6.72 (m, 6H), 6.74—7.22 (m, 28H), 7.28—7.65 (m, 22H), 7.84—7.95 (m, 4H), 8.16 (s, 1H); ^{31}P NMR ($CDCl_3$) δ: −14.04, −13.66 (J = 12 Hz); MS *m/z* (MALDI-TOF): 1378.3 (M expected 1378.52), other major peak at 1192.3 (M − $HPPh_2$).

R-**6c**: $[\alpha]_D^{15}$ + 17.2 (*c* 0.50, CH_2Cl_2); ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 4.98—5.05 (m, 28H), 6.58—6.69 (m, 18H), 6.75—7.20 (m, 28H), 7.28—7.53 (m, 42H), 7.83—7.96 (m, 4H), 8.15 (s, 1H); ^{31}P NMR ($CDCl_3$) δ: −14.54, −13.06 (J = 12 Hz); MS *m/z* (MALDI-TOF): 2226.3 (M expected 2227.50), other major peak at 2040.2 (M − $HPPh_2$).

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(E0205301 ZHAO, X. J.; LING, J.)