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Preparation of chiral 7,7′-disubstituted BINAPs for Rh-catalyzed 1,4-addition of arylboronic acids

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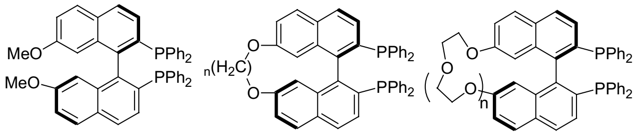
Abstract—A series of new 7,7′-disubstituted BINAPs were readily prepared starting with an asymmetric catalytic oxidative coupling. They were applied as ligands to rhodium catalyzed 1,4-addition of arylboronic acids to enones, resulting in enantioselectivities of up to 99% ee. The enantioselectivity was found to be dependent on the size of achiral substituents.

Asymmetric conjugate addition of organometallic reagents to electron-deficient olefins is one of the most versatile methods for forming carbon–carbon bonds.[1] Organozinc addition to enones in the presence of copper complexes of chiral phosphorus ligands has an impressive advance,[2] however it only provides excellent results with alkylzinc and thus suffers from the poor efficiency in reactions with arylzincs. Since the first example of highly enantioselective 1,4-addition of arylboronic acids to α,β-unsaturated carbonyl compounds catalyzed by Rh-BINAP was reported by Miyaura and co-workers,[3] it has been an attractive method for the introduction of aryl functions.[4] Although a number of bi- and monodentate ligands have been tested for this reaction, few chiral ligands show excellent stereocontrol. The use of BINAP as a ligand is most frequent.[4,5] Therefore, an active search for new efficient ligands for Rh(I) catalyzed 1,4-addition remains extremely valuable.

Recently, we developed two types of chiral oxovanadium complexes, which catalyze the oxidative coupling of 2-naphthols in very high enantioselectivity.[6] On the basis of catalytic procedures, optically pure 7,7′-disubstituted BINOLs have been prepared conveniently, and their application in catalytic phenylacetylene addition to aldehydes results in excellent enantioselectivities.[7] As a logical extension of this project, we were interested to prepare 7,7′-disubstituted 2,2′-bis(diphenylphosphino)-1,1′-binaphthyls (7,7′-disubstituted BINAPs **1a**–**e**,[8] Fig. 1) starting from optically pure 7,7′-disubstituted BINOLs, and to investigate their applications in the asymmetric catalysis. Compared with BINAP, these 7,7′-disubstituted BINAPs have their own structural features: firstly, they have two electron-donating groups at 7,7′-positions; secondly the dihedral angles of these ligands are tunable by changing the substituent size. Subtle variation of the dihedral angle and electrical density generally leads to the improvement of catalytic performance of the ligand,[9] therefore 7,7′-disubstituted BINAPs might exhibit different catalytic performance from BINAP in Rh-catalyzed 1,4-addition of arylboronic acids. Herein, we present the preparation of 7,7′-disubstituted BINAPs and their application to Rh-catalyzed highly enantioselective 1,4-addition of arylboronic acids. The dramatic influence of achiral substituents on the enantioselectivity is also be reported.



1a

1b, n=6
1c, n=8

1d, n=1
1e, n=2

Figure 1. The chiral ligands evaluated for this study.

Keywords: 7,7′-Disubstituted BINAP; 1,4-Addition; Arylboronic acids; Asymmetric catalysis.

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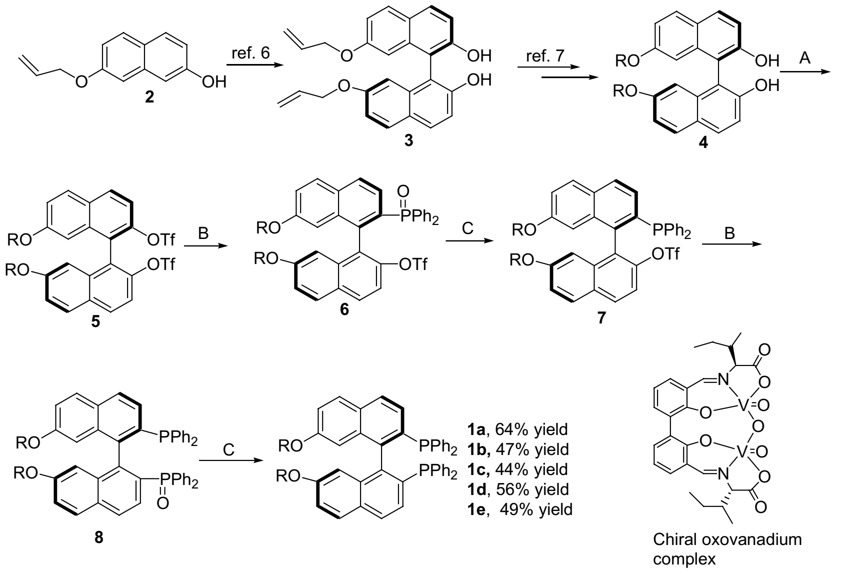
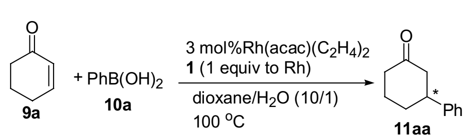


Scheme 1. Preparation of chiral 7,7′-disubstituted BINAPs **1a**–**e**. Reagents and conditions: (A) Tf_2O, pyridine, dichloromethane, 0 °C, 3 h (>99%); (B) $Ph_2P(O)H$ (2 equiv), 5 mol% $Pd(OAc)_2$, 5 mol% dppb, $^iPr_2NEt$, DMSO, 100 °C, 8 h; (C) Cl_3SiH, $^iPr_2NEt$, toluene, 110 °C, 10 h (44–64% overall yields of four steps from **5**).

Starting with an asymmetric oxidative coupling of 7-alloxyl-2-naphthol (**2**) in the presence of 5 mol% chiral oxovanadium catalyst, optically pure 7,7′-binaphthols **4** were readily prepared according to the known procedure developed by this group (Scheme 1).[6,7] The synthetic approach to 7,7′-disubstituted BINAP **1** from 7,7′-disubstituted BINOLs **4** followed the reported procedures (Scheme 1).[10] The reactions of **4** with trifluoromethane sulfonic anhydride (Tf_2O) in the presence of pyridine in CH_2Cl_2 provided **5** in quantitative yields. Monophosphinylation of **5** with two equivalents of diphenylphosphine oxide in the presence of 5 mol% of a palladium complex, in situ generated from palladium acetate and 1,4-bis(diphenylphosphino)butane (dppb), gave compounds **6**, which were subsequently reduced into **7** with trichlorosilane (Cl_3SiH). The reactions of **7** with diphenylphosphine oxide under similar conditions, for the preparations of **6** from **5** furnished **8**. Compounds **8** were reduced with Cl_3SiH again to afford the desired chiral ligands **1a**–**e**. Although the synthetic route looks long, the purification of each of the intermediates **6**–**8** was usually unnecessary and thus the chiral ligands **1** were obtained conveniently in 44–64% overall yields.

For screening the catalytic efficiency of chiral ligands **1**, a model reaction of cyclohexenone with phenylboronic acid was performed under conditions developed by Hayashi and co-workers[3,11] As shown in Table 1, the size of the achiral substituent on the ligand has an obvious influence on the enantioselectivity, thus subtle alteration of achiral substituents leads to a significantly different catalytic performance (entries 1–5). **1a** has two more methoxyl groups at its 7,7′-positions than BINAP, but gave a much lower enantioselectivity of 36% ee (entry 1). Varying the ring size of the 7,7′-substituents on the ligands, which are shown as **1b**–**e**, leads to significantly different results (entries 2–5). Among these ligands, **1d** gave the best level of enantioselectivity of 97% ee (entry 4), same as that observed with BINAP.[3] However, a much lower enantioselectivity of 38% ee was provided by **1e** (entry 5), which has a bigger achiral crown ether substituent than **1d**. Because crown ethers are easy to coordinate with some metal ions,[12] we reasoned that the complexation of metal ions with the crown ether moiety of ligand **1e** could produce some difference in its catalytic performance.[13] Indeed **1e**, as a ligand, showed an increased enantioselectivity by more than 10% ee by the addition of KF, NaF and LiF as guests into the reaction solution (entries 6–8). Although the difference are not significant, the results imply that the supramolecular effect on the stereocontrol exist in the cases where ligands bearing achiral crown ether substituents. The dramatic difference of the enantioselectivity

Table 1. Asymmetric 1,4-addition of phenylboronic acid to cyclohexenone catalyzed by ligands **1**–Rhodium(I) complexes



Entry	BINAPs	Additive	Time (h)	Yield (%)[a]	Ee (%)[b]
1	**1a**	—	5	92	36
2	**1b**	—	5	83	33
3	**1c**	—	5	94	46
4	**1d**	—	5	99	97
5	**1e**	—	5	89	38
6	**1e**	LiF[c]	5	80	51
7	**1e**	NaF[c]	5	73	49
8	**1e**	KF[c]	5	81	52
9	**1d**	—	5	92	97
10	**1d**	—	8	75	92

[a] Isolated yield based on cyclohexenone.

[b] Determined by HPLC and the absolute configuration is *R*.

[c] The ratio of additive to **1e** = 1.2:1.