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Design of C_2-Symmetric Tetrahydropentalenes as New Chiral Diene Ligands for Highly Enantioselective Rh-Catalyzed Arylation of *N*-Tosylarylimines with Arylboronic Acids

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Most recently, impressive progress has been made in the development of chiral diene ligands for asymmetric catalysis.[1] Hayashi[2] and Carreira[3] independently reported the preparation of two types of chiral dienes with 1,4-cyclohexadiene framework and 1,5-cyclooctadiene framework. These dienes were recognized as novel efficient chiral ligands in several Rh- and Ir-catalyzed asymmetric reactions, showing even better selectivity and catalytic activity than powerful phosphine ligands.[2,3] It can be expected that the exploration of using chiral dienes with different catalytic properties in a diverse range of asymmetric transformations will be of significant interest to chemists. The design and synthesis of new chiral diene ligands have therefore been an important recent research effort.[4] We, too, were attracted by the great success of this new class of chiral ligand in asymmetric catalysis. In this Communication, we wish to report our discovery of a new type of C_2-symmetric chiral diene ligand and its successful application in the enantioselective arylation of *N*-tosylarylimines with arylboronic acids.

In Hayashi's and Carreira's work, chiral dienes are generally derived from [2.2.1]bicycloheptadiene[2a] (such as **1**, $n = 1$), [2.2.2]-bicyclooctadiene[2c,f,3a,b] (**1**, $n = 2$ and **3**), [3.3.1] bicyclononadiene[2d,g] (**2**, $n = 1$) and [3.3.2]bicyclodecadiene[2g] (**2**, $n = 2$, Figure 1). Bridged bicyclic skeleton is a common element in these molecules and plays a key role in the reaction stereocontrol. To develop new diene ligand, we are interested in the potency of using a nonbridged bicyclic [3.3.0] framework. Chiral tetrahydropentalene **4** containing a simple bicyclic backbone is carefully designed. As depicted, the two cis-fused cyclopentene rings in the molecule effect a characteristic wedge structure, which would equally provide a good chiral environment and exert excellent enantiocontrol in the reaction when the two double bonds are coordinated to the metal (**4** vs **1**, **2** and **3**, Figure 1).

As shown in Scheme 1, the designed chiral diene **4** was readily prepared in a three-step sequence from enantiomerically enriched (1*R*,3*aS*,4*R*,6*aS*)-octahydropentalene-1,4-diol[5] (**5**) in good yields. Notably, the variation of the Ar substitutents at C-3 and C-6 could be easily accomplished by the Suzuki-coupling reaction of ditriflate **7** with different arylboronic acids, suggesting that the electronic and steric properties of the ligand could be possibly tuned.

With the new chiral dienes **4a**−**c** in hand, we next evaluated them in the asymmetric arylation of *N*-tosylarylimines with arylboronic acids. Highly efficient asymmetric addition of arylboron reagents to *N*-sulfonylimines to generate chiral diarylmethylamines is a current topic of interest, and only recently have several examples of using Rh-complex catalysts been developed.[2c−d,6,7] Initial experiments were carried out by the reaction of *N*-tosylimine **8** with 4-methoxyphenylboronic acid (**9**) in the presence of chiral diene ligand **4a** (3 mol %) in acetone. Very gratifyingly, the addition product diarylmethyltosylamide **10a** was smoothly afforded with

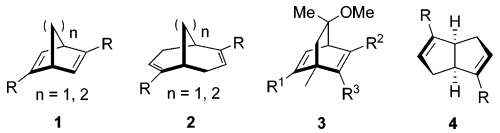
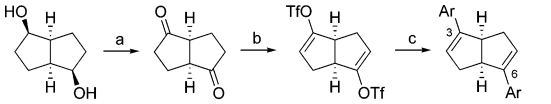


Figure 1. Hayashi's and Carreira's chiral diene ligands and our design.

Scheme 1 [a]



[a] Reagents and conditions: (a) PCC, CH_2Cl_2, 86%; (b) Tf_2O, 2,6-lutidine, CH_2Cl_2, −78 °C to room temp, 72%; (c) $ArB(OH)_2$, $Pd(PPh_3)_4$, 2N Na_2CO_3, toluene/EtOH, reflux, 90% for **4a**; 90% for **4b**; 79% for **4c**.

98% ee and in 75% yield, indicating the high efficiency of this novel diene ligand (Table 1, entry 1). Replacing both phenyl units (Ar) in **4a** by two more electron-rich *p*-anisyl groups (**4b**) or two more sterically bulky 1-naphthyl groups (**4c**) resulted in a significant decrease of enantioselectivity (entry 1 vs entries 2−3). When **4c** was used, the reaction proceeded very slowly (entry 3). With ligand **4a**, we further optimized the reaction conditions, and found that the yield could be improved to 85% by changing the solvent from acetone to toluene while still maintaining the excellent enantioselectivity (98%) (entry 5).

Experiments to probe the reaction generality are summarized in Table 2. A wide variety of *N*-tosylarylimines with diverse steric and electronic properties were tested to react with several arylboronic acids, affording the desired diarylmethyltosylamides with extremely high ees (98−99%). As we can find, the electronic nature of the phenyl ring of either imines or boronic acids has apparently no influence on the reaction enantioselectivity. Sterically encumbered ortho-substituted arylimines could also be successfully employed in the reaction (entries 5−7, 12 and 13). Moreover, the phenyl substitution could be extended to other aromatics, such as furanyl, thiopheneyl, or naphthyl (entries 8, 14−16, and 20). In entries 1 and 11, both enantiomers of the product were obtained by simply switching the corresponding aryl acceptor and donor, without changing the catalyst (also see entries 3 and 19, entries 4 and 18). It is noteworthy that the current catalytic system allows efficient synthesis of diarylmethylamines where both of the aryl groups are substituted phenyls or naphthyls (entries 2−8 and 18−20). The preparation of such kind of diarylmethylamines has not been extensively explored before by the direct addition of arylboronic acids to *N*-tosylarylimines.[8]

Having established that **4a** could serve as an efficient chiral diene ligand, we further explored the scope of *N*-tosylarylimine substrate using methyl 2-formylbenzoate *N*-tosylimine (**11**) as a more challenging reactant. To our delight, imine **11** containing an ortho-

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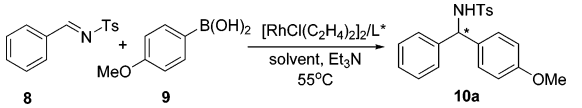
Table 1. Ligand Screening and Reaction Condition Optimization

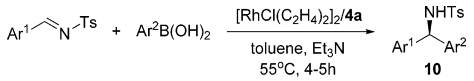


8 9 10a

entry[a]	ligand	solvent	time (h)	yield (%)[b]	ee[c]
1	**4a**	acetone	2	75	98
2	**4b**	acetone	2	79	83
3	**4c**	acetone	48	15	83
4	**4a**	THF	4	70	98
5	**4a**	toluene	4	85	98
6	**4a**	dioxane	8	75	98

[a] The reaction was carried out with 2 equiv of boronic acid **9** in the presence of 2 equiv of Et_3N, 3 mol % of $[RhCl(C_2H_4)_2]_2$ and 3.3 mol % of chiral diene **4** at 55 °C. [b] Isolated yield. [c] Determined by chiral HPLC analysis using Chiralcel OD−H column.

Table 2. Catalytic Asymmetric Arylation of *N*-Tosylarylimines with Arylboronic Acids



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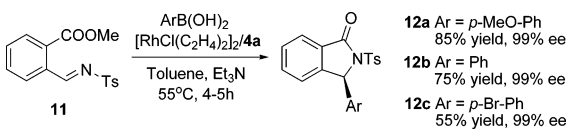
entry[a]	Ar^1	Ar^2	**10**	yield (%)[b]	ee[c,d]
1	C_6H_5	4-$MeOC_6H_4$	**10a**	85	98 (*R*)
2	4-FC_6H_4	4-$MeOC_6H_4$	**10b**	90	99 (*S*)
3	4-ClC_6H_4	4-$MeOC_6H_4$	**10c**	85	98 (*S*)
4	4-MeC_6H_4	4-$MeOC_6H_4$	**10d**	92	99 (*R*)
5	2-$MeOC_6H_4$	4-$MeOC_6H_4$	**10e**	85	99 (*S*)
6	2-MeC_6H_4	4-$MeOC_6H_4$	**10f**	93	99 (*S*)
7	2-ClC_6H_4	4-$MeOC_6H_4$	**10g**	65	99 (*S*)
8	1-naphthyl	4-$MeOC_6H_4$	**10h**	93	99 (*S*)
9	4-ClC_6H_4	C_6H_5	**10i**	81	99 (*S*)
10	4-BrC_6H_4	C_6H_5	**10j**	72	99 (*S*)
11	4-$MeOC_6H_4$	C_6H_5	**10a′**	97	99 (*S*)
12	2-MeC_6H_4	C_6H_5	**10k**	78	99 (*S*)
13	2-ClC_6H_4	C_6H_5	**10l**	56	99 (*S*)
14	1-naphthyl	C_6H_5	**10m**	88	99 (*S*)
15	2-furanyl	C_6H_5	**10n**	74	99 (*S*)
16	2-thiopheneyl	C_6H_5	**10o**	93	98 (*S*)
17	C_6H_5	4-MeC_6H_4	**10p**	81	99 (*R*)
18	4-$MeOC_6H_4$	4-MeC_6H_4	**10d′**	99	98 (*S*)
19	4-$MeOC_6H_4$	4-ClC_6H_4	**10c′**	97	99 (*R*)
20	1-naphthyl	2-naphthyl	**10q**	91	99 (*S*)

[a] The reaction was carried out with 0.5 mmol of *N*-tosylarylimine, 2 equiv of arylboronic acid in the presence of 2 equiv of Et_3N, 3 mol % of $[RhCl(C_2H_4)_2]_2$ and 3.3 mol % of chiral diene **4a** at 55 °C; see Supporting Information for details. [b] Isolated yield. [c] Determined by chiral HPLC analysis. [d] The absolute configurations of **10i**, **10a′**, **10l**, **10m**, **10p** and **10c′** were determined by comparing the optical rotation $[\alpha]_D$ with known data. Assuming an analogous reaction mechanism, the configurations of other diarylmethylamine products are assigned as indicated in the table.

Scheme 2

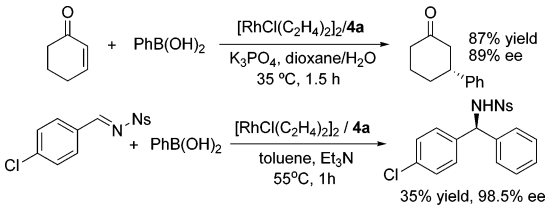


11

ester functionality was also found to be suitable substrate. Under the similar reaction conditions, **11** was subjected to the arylation with different arylboronic acid catalyzed by Rh-**4a** complex. The corresponding diarylmethyltosylamides formation followed by the in situ lactamization gave the chiral 3-substituted *N*-tosylphthalimidine products **12a**−**c** in good yields and with excellent enantioselectivities (99% ee) (Scheme 2). Chiral phthalimidines (isoindolinones) are valuable pharmacological compounds. They are usually difficult to access by catalytic asymmetric strategy.[9]

We are also currently studying on the application of this new diene ligand **4a** to other asymmetric reactions such as 1,4-addition to α,β-unsaturated ketones and arylation of *N*-nosylimines, and two very preliminary results are shown in Scheme 3.

Scheme 3



In summary, we have developed a new type of C_2-symmetric chiral diene ligand bearing a simple bicyclic [3.3.0] backbone. **4a** is proved to be a remarkably efficient ligand for asymmetric arylation of *N*-tosylarylimines using arylboronic acids instead of arylboroxines.[10] With the current catalytic system, a broad range of highly enantiomerically enriched diarylmethylamines as well as 3-aryl substituted phthalimidines could be easily prepared.

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Supporting Information Available: Experimental procedures and characterization data; copies of ^1H and ^{13}C NMR spectra and HPLC spectra. This material is available free of charge via the Internet at http://pubs.acs.org.

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