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Enantiomerically Pure Rhodium Complexes Bearing 1,5-Diphenyl-1,5-cyclooctadiene as a Chiral Diene Ligand. Their Use as Catalysts for Asymmetric 1,4-Addition of Phenylzinc Chloride

Asato Kina, Kazuhito Ueyama, and Tamio Hayashi*

Department of Chemistry, Graduate School of Science, Kyoto University, Sakyo, Kyoto 606-8502, Japan

thayashi@kuchem.kyoto-u.ac.jp

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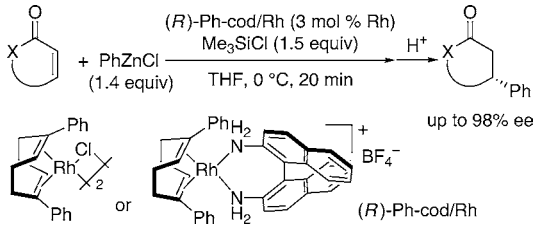
ABSTRACT



A rhodium complex coordinated with 1,5-diphenyl-1,5-cyclooctadiene (Ph-cod), [RhCl((*R*)-Ph-cod)]$_2$, was obtained enantiomerically pure through optical resolution of diastereomeric isomers [Rh(Ph-cod)((*R*)-1,1′-binaphthyl-2,2′-diamine)]BF_4. The enantiomerically pure rhodium complexes showed high catalytic activity and enantioselectivity (up to 98% ee) in the asymmetric 1,4-addition of phenylzinc chloride to α,β-unsaturated ketones and esters in the presence of chlorotrimethylsilane.

Since our first report on the preparation of a chiral diene ligand and its successful use for rhodium-catalyzed asymmetric 1,4-addition,[1] the chemistry of chiral diene ligands has been undergoing a rapid development. The chiral dienes so far reported to be effective as chiral ligands are all those based on bicyclic diene skeletons. They are bicyclo[2.2.1]hepta-2,5-diene (nbd*),[1,2] bicyclo[2.2.2]octa-2,5-diene (bod*),[3−6] bicyclo[3.3.1]nona-2,6-diene (bnd*),[7,8] and bicyclo[3.3.2]-deca-2,6-diene (bdd*)[8] (Figure 1). We have prepared C_2-symmetric chiral dienes, which are substituted with benzyl or aryl substituents one each at the two double bonds, by way of catalytic asymmetric hydrosilylation[1,2] or optical

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(4) (a) Otomaru, Y.; Okamoto, K.; Shintani, R.; Hayashi, T. *J. Org. Chem.* **2005**, *70*, 2503. (b) Shintani, R.; Kimura, T.; Hayashi, T. *Chem. Commun*. **2005**, 3213. (c) Hayashi, T.; Tokunaga, N.; Okamoto, K.; Shintani, R. *Chem. Lett*. **2005**, 1480. (d) Shintani, R.; Okamoto, K.; Hayashi, T. *Org. Lett*. **2005**, *7*, 4757.

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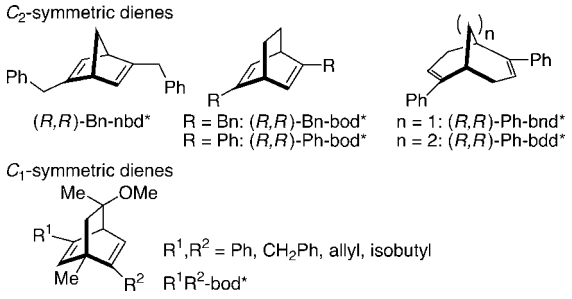


Figure 1. Chiral bicyclic diene ligands.

resolution of their intermediates[3,4] or the dienes themselves.[7,8] Carreira reported C_1-symmetric bod* ligands which are readily accessible from (−)-carvone.[6] These chiral diene ligands have been demonstrated to be highly effective, especially in rhodium-catalyzed aryl transfer reactions. High catalytic activity and/or high enantioselectivity was observed in asymmetric 1,4-addition of arylboron reagents to *N*-sulfonylarylimines[3,7] and α,*β*-unsaturated ketones, esters, amides, and aldehydes.[1,2,4,6,8] In the arylative cyclization of alkynes bearing an aldehyde or enoate moiety,[5] high chemoselectivity and high enantioselectivity was achieved by use of a chiral diene ligand.

Recently, Grützmacher reported [Rh((*R*)-Ph-dbcot)(MeCN)$_2$]-OTf as a new type of chiral diene−rhodium complex, where Ph-dbcot stands for 5-phenyldibenzo[*a*,*e*]cyclooctene (Figure 2).[9] This chiral rhodium complex, obtained in an enantio-

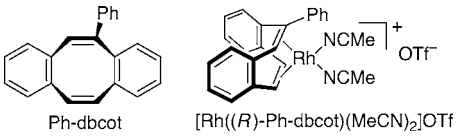


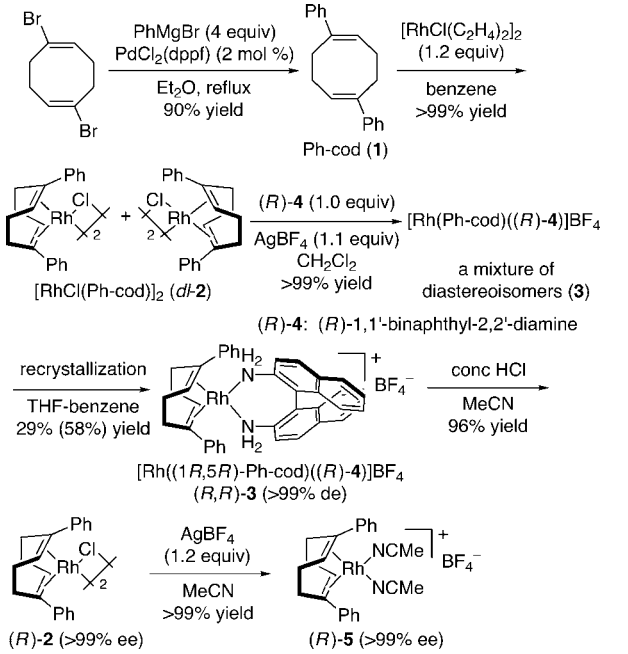
Figure 2. Grützmacher's chiral diene−rhodium complex.

merically pure form through optical resolution of a mixture of diastereomeric rhodium complexes coordinated with the diene and (*R*)-1,1′-binaphthyl-2,2′-diamine, was used as a catalyst for asymmetric reactions including asymmetric 1,4-addition of phenylboronic acid. This chiral diene complex is very different from those of the chiral bicyclic dienes such as substituted bod* in that the chirality of the prochiral diene Ph-dbcot is generated and fixed on coordination to a metal.[10] Unfortunately, the Ph-dbcot/rhodium catalyst was not so enantioselective as other chiral diene−rhodium catalysts probably due to its C_1-symmetric structure lacking a substituent on one of the two double bonds.

Here, we report our studies on the chiral diene−rhodium complexes where the diene is not chiral but prochiral until its coordination to a metal. We chose 1,5-diphenyl-1,5-cyclooctadiene (**1**, Ph-cod) as a prochiral diene because 1,5-cyclooctadiene (cod) is well-known to coordinate to late transition metals forming stable chlelate diene−metal complexes[11] and the diene **1** is expected to form C_2-symmetric chiral diene moiety on coordination to a metal. The chiral environment brought about by the enantioface-selective coordination of the diene **1** turned out to be very powerful, giving rise to high enantioselectivity in the rhodium-catalyzed asymmetric 1,4-addition of a phenylzinc reagent to α,*β*-unsaturated ketones and esters.

A diagonally substituted cyclic diene, 1,5-diphenyl-1,5-cyclooctadiene (**1**, Ph-cod), was obtained in a high yield by the palladium-catalyzed cross-coupling[12] between phenylmagnesium bromide and 1,5-dibromo-1,5-cyclooctadiene, which is accessible from 1,5-cyclooctadiene by bromination with bromine followed by dehydrobromination with potassium *tert*-butoxide.[13] Treatment of diene **1** with [RhCl(ethylene)$_2$]$_2$ in benzene brought about ligand substitution giving a quantitative yield of racemic [RhCl(Ph-cod)]$_2$ (*dl*-**2**). Optical resolution of the Ph-cod complex *dl*-**2** was conducted according to the Grützmacher's method[9] (Scheme 1). Thus, *dl*-**2** was treated with (*R*)-1,1′-binaphthyl-2,2′-

Scheme 1. Preparation of Ph-cod (**1**) and Its Rhodium Complexes



diamine (*R*)-**4** and $AgBF_4$ in dichloromethane to give [Rh(Ph-cod)((*R*)-1,1′-binaphthyl-2,2′-diamine (**4**))]BF_4 (**3**), which

(9) Läng, F.; Breher, F.; Stein, D.; Grützmacher, H. *Organometallics* **2005**, *24*, 2997.

(10) It has been well-documented that coordination of prochiral alkenes to a metal with either of their enantiotopic faces generates chirality on the alkene moiety. As a pioneering work: Paiaro, G.; Panunzi, A. *J. Am. Chem. Soc.* **1964**, *86*, 5148.

(11) For a example of the cod/rhodium complexes: Ibers, J. A.; Snyder, R. G. *J. Am. Chem. Soc.* **1962**, *84*, 495.

(12) Hayashi, T.; Konishi, M.; Kobori, M.; Kumada, M.; Higuchi, T.; Hirotsu, K. *J. Am. Chem. Soc.* **1984**, *106*, 158.

(13) Detert, H.; Rose, B.; Mayer, W.; Meier, H. *Chem. Ber.* **1994**, *127*, 1529.

is a mixture of diastereomeric isomers in a ratio of one to one. Fractional crystallization of the diastereomeric mixture from tetrahydrofuran and benzene gave 29% yield (58% yield based on one diastereomer) of one of the diastereomeric isomers **3**. ^{1}H NMR showed that its diastereomeric purity is >99% and the complex keeps its purity in solution at room temperature for a week, indicating that the dissociation of the diene causing epimerization is not taking place. Removal of the chiral diamine (*R*)-**4** by the reaction with concd hydrochloric acid in acetonitrile gave enantiomerically pure [RhCl(Ph-cod)]$_2$ (**2**), whose absolute configuration was determined to be (1*R*,5*R*) by its X-ray crystal analysis (vide infra). We will denote its configuration (*R*) hereafter for simplicity. Cationic complex [Rh((*R*)-Ph-cod)(MeCN)$_2$]BF$_4$ ((*R*)-**5**) was also prepared from the chloro-bridge dimer, [RhCl((*R*)-Ph-cod)]$_2$ ((*R*)-**2**), by abstraction of the chloride with AgBF$_4$ in acetonitrile. The retention of the >99% enantiomeric purity during these transformations was confirmed by the reaction of (*R*)-**2** with (*R*)-**4** and AgBF$_4$, which gave back the diastereomerically pure complex [Rh((*R*)-Ph-cod)((*R*)-**4**)]BF$_4$ ((*R*,*R*)-**3**) in a quantitative yield.

The X-ray crystal structure of [RhCl((*R*)-Ph-cod)]$_2$ ((*R*)-**2**), which contains a CH_2Cl_2 solvent molecule, is shown in Figure 3. The complex adopts the chloro-bridge dimeric

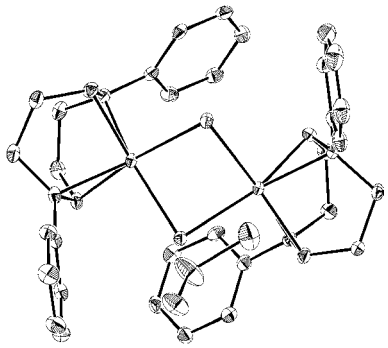
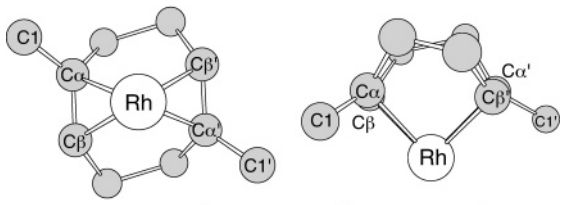


Figure 3. ORTEP illustration of [RhCl((*R*)-Ph-cod)]$_2$·CH_2Cl_2 ((*R*)-**2**) with thermal ellipsoids drawn at the 50% probability level. Hydrogens are omitted for clarity.

structure, two rhodium atoms and two chlorine atoms forming a folded diamond shape. Two double bonds of the Ph-cod ligand coordinate to one rhodium atom in a chelate coordination manner. Absolute configuration (1*R*,5*R*) of the coordinated diene was determined by the Flack parameter.[14] Figure 4 shows the structure of the diene−rhodium moiety of [RhCl((*R*)-Ph-cod)]$_2$ ((*R*)-**2**) and selected bond distances and angles around the rhodium atom. The two phenyl substituents on the double bond are situated at the second and fourth quadrants in a C_2 fashion, thereby constructing a good chiral environment around the rhodium center. The distance between rhodium and the carbon bonded to phenyl (Rh−Cα = 2.14 Å) is longer than that between rhodium and unsubstituted carbon (Rh−Cβ = 2.09 Å). Two double

(14) Flack, H. D. *Acta Crystallogr.* **1983**, *A39*, 876.



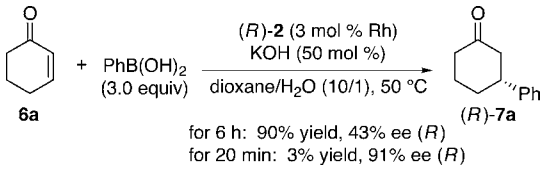
Rh-C1 = 3.03 Å, Rh-Cα = 2.14 Å, Rh-Cβ = 2.09 Å
∠C1-Rh-C1' = 149°, ∠Cα-Rh-Cα' = 93°
∠Cβ-Rh-Cβ' = 93°, ∠Cα-Cβ/Cα'-Cβ' = 9.4°
bite angle of the diene coordination = 89°

Figure 4. Selected bond distances and angles for [RhCl(*R*)-Ph-cod)]$_2$ (*R*)-**2**.

bonds (Cα═Cβ and Cα'═Cβ') of the Ph-cod **1** are not parallel to each other but twisted by 9.4°. As a result, the whole structure of the 1,5-cyclooctadiene moiety is not in a higher symmetry than C_2. This twisted coordination manner of Ph-cod **1** is similar to that of Ph-bnd*, whose basic skeleton is bicyclo[3.3.1]nona-2,6-diene.[8]

The enantiomerically pure rhodium complexes, (*R*)-**2**, (*R*,*R*)-**3**, and (*R*)-**5**, were first examined for their catalytic activity and enantioselectivity in the asymmetric addition of phenylboronic acid to 2-cyclohexenone (**6a**)[15,16] (Scheme 2).

Scheme 2. Asymmetric 1,4-Addition of Phenylboronic Acid to 2-Cyclohexenone (**6a**)



for 6 h: 90% yield, 43% ee (*R*)
for 20 min: 3% yield, 91% ee (*R*)

The chloro-bridge dimer (*R*)-**2** (3 mol % of Rh) catalyzed the reaction at 50 °C to give 90% yield of 3-phenylcyclohexanone (**7a**) after the reaction time of 6 h. However, the enantiomeric purity of **7a** thus obtained was not so high as we expected, being only 43% ee (*R*). Fortunately, it turned out that the enantiomeric purity of the 1,4-addition product **7a** is strongly dependent on the progress of the reaction, the higher % ee at the lower conversion. For example, the reaction stopped after 20 min reaction time gave (*R*)-**7a** of 91% ee, although the yield was only 3%. We reasoned that the lower % ee at higher conversion would be caused by racemization of the catalyst under the reaction conditions, which takes place probably by dissociation of the diene **1** from rhodium and recoordination on the other enantioface.

To realize the high chemical yield and high enantioselectivity at the same time, we looked for a reaction system where

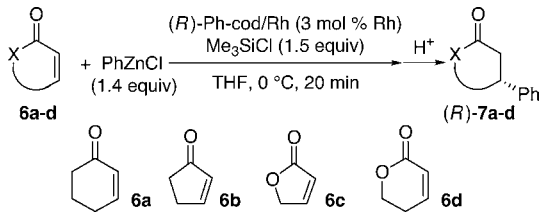
(15) For reviews: (a) Hayashi, T.; Yamasaki, K. *Chem. Rev.* **2003**, *103*, 2829. (b) Fagnou, K.; Lautens, M. *Chem. Rev.* **2003**, *103*, 169.

(16) For leading references: (a) Sakai, M.; Hayashi, H.; Miyaura, N. *Organometallics* **1997**, *16*, 4229. (b) Takaya, Y.; Ogasawara, M.; Hayashi, T.; Sakai, M.; Miyaura, N. *J. Am. Chem. Soc.* **1998**, *120*, 5579. (c) Hayashi, T.; Takahashi, M.; Takaya, Y.; Ogasawara, M. *J. Am. Chem. Soc.* **2002**, *124*, 5052.

the asymmetric 1,4-addition proceeds rapidly under catalysis by the chiral diene−rhodium complexes, hopefully, rapidly enough for the reaction to be completed before the catalyst racemization becomes a serious problem. It was found that the addition of phenylzinc chloride in the presence of chlorotrimethylsilane is very rapid,[17] the 1,4-addition to 2-cyclohexenone (**6a**) being completed within 20 min at 0 °C. Thus, to a solution of 3 mol % of the rhodium catalyst (*R*)-**2** in THF were added at 0 °C chlorotrimethylsilane (1.5 equiv) and phenylzinc chloride (1.4 equiv) in THF successively, and the mixture was stirred at the same temperature for 20 min. Hydrolysis with 3 N HCl[18] gave 89% yield of the 1,4-addition product **7a**, which is an *R* isomer of 81% ee (entry 1 in Table 1). Higher enantioselectivity was observed in the asymmetric addition to 2-cyclopentenone (**6b**). The chloro-bridge dimer (*R*)-**2** catalyzed the asymmetric addition of phenylzinc chloride to **6b** efficiently to give a high yield of (*R*)-3-phenylcyclopentanone (**7b**) of 87% ee (entry 2). Use of cationic rhodium complex, (*R*,*R*)-**3**, which bears the chiral diamine ligand (*R*)-**4** and Ph-cod ligand with *R* configuration, brought about a slightly better result, (*R*)-**7b** of 90% ee being obtained in 92% yield (entry 3). The reaction catalyzed by (*R*)-**5**, which is also a cationic rhodium complex but does not contain the diamine (*R*)-**4**, gave the product (*R*)-**7b** of the same enantiomeric purity (90% ee) (entry 4), indicating that the diamine (*R*)-**4** on the complex (*R*,*R*)-**3** does not affect the enantioselectivity probably because the diamine is free from rhodium during the catalytic reaction. The very low enantioselectivity (14% ee) observed for the reaction catalyzed by a 1:1 mixture of diastereoisomers (*R*,*R*)-**3** and (*S*,*R*)-**3** (entry 5) may support the dissociation of diamine **4** from rhodium at a stereocontrolling step. The present asymmetric 1,4-addition system which consists of the Ph-cod/rhodium catalyst, phenylzinc chloride, and chlorotrimethylsilane, is particularly effective for cyclic α,β-unsaturated esters. The addition to five-membered ring lactone **6c** and to six-membered ring lactone **6d** gave the corresponding 1,4-phenylation products with 96% ee and 98% ee, respectively (entries 6 and 7)

In summary, we have succeeded in the preparation of enantiomerically pure rhodium complexes to which 1,5-diphenyl-1,5-cyclooctadiene (**1**, Ph-cod) coordinates with one of the enantiotopic faces. The chiral diene−rhodium complexes were found to show high catalytic activity and high enantioselectivity (up to 98% ee) in the asymmetric 1,4-addition of phenylzinc chloride to α,β-unsaturated ketones and esters in the presence of chlorotrimethylsilane. The high enantioselectivity demonstrates that the Ph-cod ligand constructs efficient chiral surroundings around the rhodium and keeps its coordination to rhodium during the catalytic reaction.

Table 1. Rhodium-Catalyzed Asymmetric Addition of Phenylzinc Chloride to Cyclic Enones and Enoates **6** in the Presence of $ClSiMe_3$ Catalyzed by Rh/Ph-cod Complexes[a]



entry	substrate	catalyst (3 mol % of Rh)	yield (%) of **7**[b]	% ee[c]
1	**6a**	(*R*)-**2**	89	81 (*R*)
2	**6b**	(*R*)-**2**	89	87 (*R*)
3	**6b**	(*R*,*R*)-**3**	92	90 (*R*)
4	**6b**	(*R*)-**5**	80	90 (*R*)
5	**6b**	(*R*,*R*)-**3**/(*S*,*R*)-**3** (1/1)	91	14 (*R*)
6[d]	**6c**	(*R*,*R*)-**3**	86	96 (*R*)
7	**6d**	(*R*,*R*)-**3**	99	98 (*R*)

[a] The reaction was carried out with substrate **6** (0.30 mmol), PhZnCl (0.42 mmol), $ClSiMe_3$ (0.45 mmol), and a catalyst (9.0 μmol Rh, 3.0 mol % Rh) in 1.0 mL of THF at 0 °C for 20 min, unless otherwise noted. [b] Isolated yield of **7** after acidic hydrolysis followed by silica gel chromatography. [c] Determined by HPLC analysis with a chiral stationary phase column: Chiralcel OD-H for **7a**, Chiralcel OB-H for **7b**, Chiralpak AD-H for **7c**, and Chiralcel OG for **7d**. [d] Carried out with **6c** (0.30 mmol), PhZnCl (0.60 mmol), $ClSiMe_3$ (0.63 mmol), rhodium catalyst (6.0 mol % of Rh) in THF (1.0 mL) at 30 °C for 1 h.

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Supporting Information Available: Experimental procedures and spectroscopic data. This material is available free of charge via the Internet at http://pubs.acs.org.

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(17) Rhodium-catalyzed 1,6-addition of arylzinc reagents to dienones has been reported to be accelerated by the addition of chlorotrimethylsilane: Hayashi, T.; Yamamoto, Y.; Tokunaga, N. *Angew. Chem., Int. Ed.* **2005**, *44*, 4224.

(18) Before hydrolysis, the 1,4-addition product is formed as a silyl enol ether, 3-phenyl-1-(trimethylsilyloxy)cyclohex-1-ene. The formation of silyl enol ether as the 1,4-addition product has been reported in the rhodium-catalyzed asymmetric 1,4-addition of an aryltitanate reagent in the presence of chlorotrimethylsilane: Tokunaga, N.; Yoshida, K.; Hayashi, T. *Proc. Natl. Acad. Sci. U.S.A.* **2004**, *101*, 5445.