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The Role of Regioisomeric Bicyclo[3.3.0]octa-2,5-diene Ligands in Rh Catalysis: Synthesis, Structural Analysis, Theoretical Study and Application in Asymmetric 1,2- and 1,4-Additions

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ABSTRACT: In order to study the impact of regioisomeric diene ligands on the formation and catalytic activity of Rh complexes, a series of C_2- and C_S-symmetric 2,5-disubstituted bicyclo[3.3.0]octa-2,5-dienes C_2-L and C_S-L, respectively, were synthesized from Weiss diketone by simultaneous deprotonation/electrophilic trapping of both oxo functions and the catalytic behavior was studied in the presence of $[RhCl(C_2H_4)_2]_2$. Complexes $[RhCl(C_2\text{-}L)]_2$ bearing C_2-symmetric ligands catalyzed effectively the asymmetric arylation of *N*-tosylaldimines to (*S*)-diarylamines with yields and *ee*-values up to 99%. In Hayashi-Miyaura reactions, however, the complexes showed poor catalytic activity. When complexes $[RhCl(C_S\text{-}L)]_2$ with C_S-symmetric ligand or mixtures of $[RhCl(C_2\text{-}L)]_2$ and $[RhCl(C_S\text{-}L)]_2$ were employed in 1,2-additions, racemic addition products were observed, suggesting a C=C isomerization of the diene ligands. X-ray crystal structure analysis of both Rh complexes formed from the $[RhCl(C_2H_4)_2]_2$ precursor and ligands C_2-L and C_S-L, respectively, revealed that only the C_2-symmetric ligand C_2-L coordinated to the Rh, whereas C_S-L underwent a Rh-catalyzed C=C isomerization to *rac*-C_2-L, which then gave the racemic $[RhCl(\textit{rac}\text{-}C_2\text{-}L)]_2$ complex. DFT calculations of the relative stabilities of the Rh complexes and the proposed intermediates provided a mechanistic rationale via Rh-mediated hydride transfer.

KEYWORDS: asymmetric catalysis, C-C coupling, density functional calculations, diene ligands, rhodium, X-ray diffraction

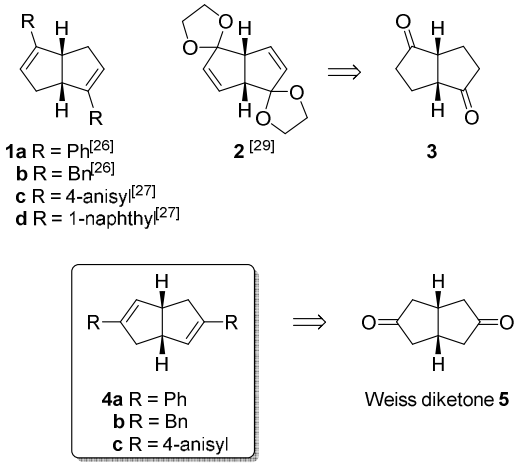
INTRODUCTION

Chiral olefin ligands have received increased attention over the last decade particularly in Rh- and Ir-catalysis, and complement the well established set of P-, P,N- and N-ligands.[1] Since the early discoveries by Hayashi,[2] Carreira[3] and Grützmacher,[4] most work has been devoted to asymmetric 1,4- and 1,2-additions.[5,6] Furthermore, the scope of diene ligands was expanded to cross couplings,[7] cyclopropanations,[8] arylative cyclizations,[9] intramolecular [4+2] cycloadditions,[10] polymerizations,[11] hydrogenations,[12] [3+2] annulations of 1,3-dienes,[13] 1,6-additions,[14] C–H alkylation of ferrocenes,[15] three-component reactions,[16] or carbene-insertions into B–H[17] and Si–H bonds.[18] In addition, practical synthetic procedures to a variety of chiral diene ligands have been developed.[19] Quantitative structure–property relationships,[20] nonlinear effects (NLE)[21] and density functional theory (DFT) calculations provided valuable mechanistic insight on catalytic 1,4-additions[22–24] and 1,2-additions.[25] However, the impact of regioisomeric dienes on the catalytic properties of the corresponding Rh-complexes has never been considered.

Previously, the groups of Laschat[26] and Lin[27] independently disclosed C_2-symmetric chiral dienes **1** with bicyclo[3.3.0]octane skeleton (Chart 1) and successfully implemented **1** in catalytic Hayashi-Miyaura reactions and nucleophilic additions to imines. The versatility of diene ligands **1** in various Rh-, Ir- and Pd-catalysis was subsequently demonstrated[6b,27,28] and their catalytic performance studied in detail. Water-soluble bicyclo[3.3.0]octa-2,5-dienes such as **2** were reported by Lin.[29] Surprisingly the corresponding regioisomeric dienes **4** (Chart 1) have not been used in catalytic reactions so far. Only diene **4a** was mentioned in a theoretical investigation by Kantchev.[22b,c] Thus, we were interested whether the different topology of the double bonds in chiral 2,5-disubstituted ligands **4** as compared to 3,6-disubstituted ligands **1** while keeping the overall C_2-symmetry would influence the catalytic behavior. In addition, a much shorter

synthesis of diene ligands **4** from Weiss diketone[30] was anticipated as compared to diene ligands **1**, which are derived from the chiral C_2-symmetrical diketone **3** requiring a considerable synthetic effort, e.g. 7 steps for (*R,R)*-diphenyl-diene (*R,R)*-**1a** and 6 steps for (*S,S*)-**1a** respectively from 1,5-cyclooctadiene.[26] In the current manuscript we not only present the synthesis of a new member of the diene ligand family and its performance in catalytic 1,4- and 1,2-additions, but provide also experimental and theoretical insight for a Rh-catalyzed C=C isomerization. The results are reported below.

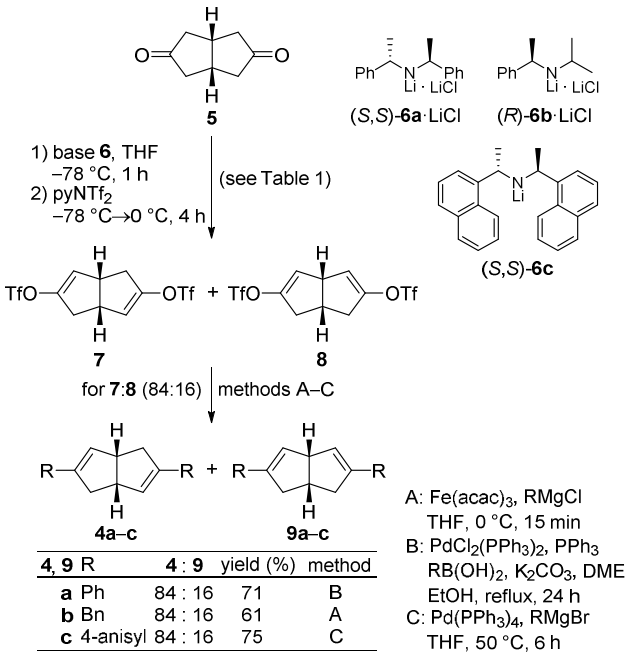
Chart 1. Known 3,6-Disubstituted Bicyclo[3.3.0]octadiene Ligands 1, 2 Derived from Diketone 3 and the C_2-Symmetric 2,5-Disubstituted Dienes 4 Derived from Weiss Diketone 5



RESULTS AND DISCUSSION

Synthesis of Ligands. A double asymmetric deprotonation of Weiss diketone **5**[30] utilizing chiral base **6** was envisaged as initial reaction in the synthesis of diene ligands **4** (Scheme 1).

Scheme 1. Synthesis of Bicyclo[3.3.0]octadiene Ligands 4 and 9



4, 9	R	4 : 9	yield (%)	method
a	Ph	84 : 16	71	B
b	Bn	84 : 16	61	A
c	4-anisyl	84 : 16	75	C

While enantioselective desymmetrizations of *meso*-ketones with chiral bases are long known[31] and sequential deprotonation/electrophilic trapping sequences for bicyclo[3.3.0]octane precursors of natural products have been reported,[32,33] the simultaneous deprotonation/electrophilic trapping of two oxo functions remained elusive.

In order to obtain racemic products as analytical reference samples, Weiss diketone **5** was deprotonated with 2.25 equiv. of KHMDS in THF at –78°C for 1 h, followed by quenching with 2-pyridyltriflimide and warming the solution to 0°C over 4 h. After workup, a (33 : 67) mixture of C_2-symmetric (**7**) and C_S-symmetric bis(enoltriflate) **8** was isolated in 49% combined yield (Table 1, entry 1). Replacing KHMDS with the chiral base (*S,S*)-**6a** · LiCl, which was generated in situ from the (*S*)-1-phenylethylamine-derived (*S*,*S*)-bis(1-phenylethyl)ammonium chloride and BuLi,[32b,33,34] inverted the ratio of regioisomers **7**, **8** in favor of the desired C_2-symmetric product **7** giving a (79 : 21) mixture in 74% (entry 2). The isomeric ratio was found to be influenced by

the addition rate of **5**, i.e. the slower its addition the higher the amount of **7**, resulting in a (89 : 11) mixture of **7** / **8** (entry 4). Neither the unsymmetric base (*R*)-**6b** · LiCl nor the sterically more demanding naphthylethylamine-derived base (*S,S*)-**6c** was capable of further decreasing the amount of the undesired regioisomer **8** (entries 5, 6).

Table 1. Preparation of Regioisomeric Bis(enoltriflates) 7 and 8 Using Various Bases

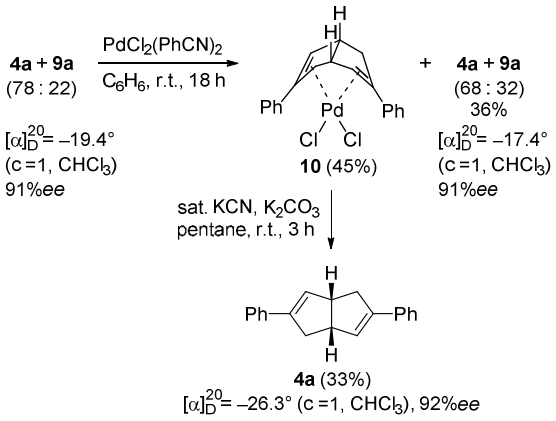
entry	base	ratio **7** : **8**[a]	yield (%)
1	KHMDS	33 : 67	49
2	(S,S)-**6a**·LiCl	79 : 21	74
3	(S,S)-**6a**·LiCl	84 : 16	62
4	(S,S)-**6a**·LiCl	89 : 11	80
5	(R)-**6b**·LiCl	71 : 29	42
6	(S,S)-**6c**	74 : 26	n.d.

[a]Determined from ^{1}H NMR spectra.

Due to the sensitivity of the enoltriflates separation of the regioisomers **7**, **8** was not considered at this stage, but cross coupling was performed with the mixture (Scheme 1). Cross coupling of a (84 : 16) mixture of enoltriflates **7** / **8** with 20 mol% of $Fe(acac)_3$ and BnMgCl following our previously described method[26,28] gave regioisomeric dibenzylated dienes **4b** and **9b** in 61% yield as a (84 : 16) mixture (method A). Suzuki cross coupling employing 10 mol% of $PdCl_2(PPh_3)_2$ and PPh_3 as a catalyst (method B)[35] yielded 71% of a (84 : 16) mixture of the corresponding phenyl-substituted ligands **4a** and **9a**, whereas Kumada coupling in the presence of 2 mol% of $Pd(PPh_3)_4$[36] provided anisyl-substituted dienes **4c** and **9c** as a (84 : 16) mixture in 75% yield (method C).

All attempts to separate the regioisomeric dienes **4** and **9** by flash chromatography failed. Therefore, we tested a method initially developed by Askani for the separation of isomeric semibullvalene precursors via Pd complexes.[37]

Scheme 2. Separation of Diene 4a from a Regioisomeric Mixture of 4a / 9a via Pd Complex and Decomplexation with KCN[36]



ee-Values were determined by HPLC on chiral stationary phases

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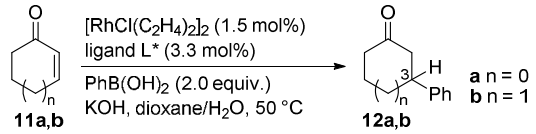
In a preliminary experiment a (78 : 22) mixture of 2,5-diphenyl-substituted regioisomers **4a / 9a** was treated with $PdCl_2(PhCN)_2$ (1 equiv.) in benzene at room temperature (Scheme 2). After 18 h, Pd-diene complex **10** precipitated as a red solid, which was isolated in 45% yield. As observed for related Pd complexes,[37] complex **10** was poorly soluble and thus characterized only by ^1H and ^{13}C NMR. According to ^1H NMR spectra the filtrate consisted of a (68 : 32) mixture of **4a** / **9a** with regioisomer **4a** as the major compound. Decomplexation of **10** with a saturated KCN solution in the presence of K_2CO_3 in pentane at room temperature[37] gave exclusively regioisomer **4a** with 92%*ee* as determined by analytical HPLC on a chiral Chiracel OJ-H column, however, only in meager 33% yield. Further attempts were therefore abandoned and we focussed on the separation of regioisomers **4** / **9** by preparative HPLC using various chiral stationary phases. With both Chiracel OJ-H and DAICEL Chiralpak IA the separation of

regioisomers **4a** / **9a** succeeded, and pure **4a** was obtained in 46% yield with >99%*ee* and **9a** in 13% yield. Regioisomeric mixture **4b** / **9b** was successfully separated on a Chiracel OJ-H phase yielding **4b** in 24% (>99%*ee*) while **9b** was not isolated. In contrast, the regioisomeric pair **4c** / **9c** could not be separated anymore.

As discussed below, the absolute configuration of ligand **4a** was assigned to be (*R,R*) by X-ray crystal structure analysis of the corresponding diene **4a** ligated Rh catalyst.[38]

Rh-catalyzed Reactions with Dienes 4, 9 as Steering Ligands. In initial experiments the application of dienes **4** and **9** as ligands in the Hayashi-Miyaura reaction with phenylboronic acid was studied in comparison with the known benchmark dienes **1a** and **1b**. As substrates cyclohex-2-en-1-one (**11a**) and cyclopent-2-en-1-one (**11b**) were chosen.[39] The results are summarized in Table 2.

Table 2. Rhodium-Catalyzed 1,4-Addition of Phenylboronic Acid to Cyclic Enones 11



entry	enone	ligand L*	*t* (h)	prod.	yield[a] (%)	*ee* (%)
1	**11a**	(*R*,*R*)-**4a**	2	**12a**	10 (12)[b]	29 (*R*)
2	**11a**	**9a**	2	**12a**	15	0
3	**11a**	**4a**/**9a** (78:22)	2	**12a**	26	26 (*R*)
4	**11a**	(*R*,*R*)-**4b**	2	**12a**	12	47 (*R*)
5	**11a**	**4b**/**9b** (67:33)	2	**12a**	42	69 (*R*)
6	**11a**	(*R*,*R*)-**1a**	2	**12a**	88	>99 (*S*)
7	**11a**	(*R*,*R*)-**1b**	2	**12a**	82	68 (*S*)
8	**11b**	(*R*,*R*)-**4a**	2	**12b**	20 (23)[b]	12 (*R*)
9	**11b**	**9a**	2	**12b**	20 (19)[b,c]	0

10	**11b**	(*R*,*R*)-**4b**	2	**12b**	20 (25)[b,c]	41	(*R*)
11	**11b**	**4b**/**9b** (83:17)	2	**12b**	22	36	(*R*)
12	**11b**	(*R*,*R*)-**1a**	2	**12b**	78	77	(*S*)
13	**11b**	(*R*,*R*)-**1b**	2	**12b**	99 (99)[b]	79	(*S*)

[a]Isolated yield. [b]NMR yield in parentheses. The crude product was dissolved in a small volume of $CHCl_3$ and 1,3,5-trimethylbenzene (1.0 equiv. related to starting enone) was added and the mixture stirred. In its ^{1}H NMR spectrum the signal of the aromatic protons of trimethylbenzene at δ = 6.80 ppm was set to 3 as reference correlating with the amount of starting enone. Integration of the 3-H proton in the product at δ = 3.00–3.50 ppm corresponds to the percentage yield. [c]Starting **11b** was detected by ^{1}H NMR in 29% (entry 9) and 40% (entry 10)

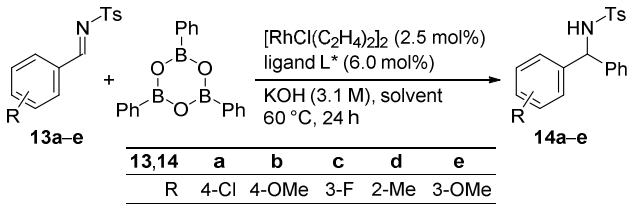
Treatment of cyclopentenone (**11a**) with phenylboronic acid in the presence of $[RhCl(C_2H_4)_2]_2$ and diphenyldiene **4a** under common Hayashi-Miyaura reaction conditions yielded 1,4-addition product 3-phenylcyclopentanone (**12a**) in only 10% with 29%*ee* in favor of the (*R*)-product (entry 1), while C_S-symmetric ligand **9a** gave **12a** in 15% yield, however, with 0% *ee* (entry 2). When 1.5 mol% of Rh precursor and a (78 : 22) ligand mixture **4a** / **9a** (3.3 mol% related to **4a**) were employed, addition product **12a** was isolated in 26% yield with 26%*ee* (entry 3). Dibenzyldiene **4b** gave comparable yield, but improved enantioselectivity (47%*ee*) of (*R*)-**12a** (entry 4). However, both yield and enantiomeric excess were increased to 42% yield and 69%*ee* (*R*) using diene mixture **4b** / **9b** (67 : 33) as ligand (entry 5). For comparison, under the used conditions $[RhCl(C_2H_4)_2]_2$ ligated with the known diene **1a** and **1b**,[26] respectively, provided product **12a** in yields up to 88% with >99%*ee* and 68%*ee* in favor of the (*S*)-enantiomer (entries 6, 7).

The Rh-catalyzed 1,4-addition of phenylboronic acid to cyclohexenone (**11b**) in the presence of diphenyldiene **4a** again proceeded with low yield (20%) and poor enantioselectivity (12%*ee*) (entry 8). The use of C_S-symmetric diphenyldiene **9a** surprisingly resulted in 20% of 3-phe-

nylcyclohexanone (**12b**) and 29% of starting material **11b** according to NMR (entry 9). Obviously catalysis is taking place either by the Rh complex generated from C_S-symmetric diene **9a** or through rearrangement of **9a** to C_2-symmetric **4a** and subsequent complexation. C_2-symmetric dibenzylated diene **4b** reacted similarly to diphenyldiene **4a** giving addition product **12b** in 20% isolated yield with 41%*ee* together with 40% of enone **11b** according to the NMR (entry 10), while the mixture of benzyldienes **4b** / **9b** (83 : 17) provided 22% of **12b** (36%*ee*) (entry 11). Again, the known ligands (*R,R*)-**1a** and (*R,R*)-**1b** were superior providing (*S*)-**12b** in 78–99% yield with 77–79%*ee* (entries 12, 13).[39] Surprisingly, acyclic non-3-en-2-one gave nearly racemic 1,4-addition product with ligand **4a** (see Scheme S2, ESI), whereas Kantchev calculated high enantioselectivities for this substrate / ligand combination.[22]

Recently Sieffert reported a detailed mechanistic study of the arylation of *N*-tosylimines by boronic acids or boroxines catalyzed by a complex of Rh/diene **1a**.[25] By this type of reaction chiral α-arylamines, prevalent building blocks for pharmaceutically relevant compounds, are accessible.[40] We therefore turned our attention to the catalytic 1,2-addition of phenylboroxine to electron poor aldimines **13**. *N*-Tosyl-(4-chloro)benzaldimine **13a** was used as substrate for reaction optimization (Table 3).

Table 3. Rhodium-Catalyzed 1,2-Addition of Phenylboroxine to *N*-Tosylimines 13 under Various Reaction Conditions



entry	**13**	ligand L*	solvent	conc. **13** (M)	**14**	yield[a] (%)	*ee* (%)
1	**13a**	(*R,R*)-**4a**	dioxane	0.125	**14a**	25 (29)	>99 (*S*)

2	**13a**	**9a**	dioxane	0.125	**14a**	– (8)	–
3	**13a**	**4c/9c** (79:21)	dioxane	0.125	**14a**	34 (40)	77 (*S*)
4	**13a**	(*R*,*R*)-**4b**	dioxane	0.125	**14a**	40 (48)	>99 (*S*)
5	**13a**	**4b/9b** (67:33)	dioxane	0.125	**14a**	40 (45)	81 (*S*)
6	**13a**	**4b/9b** (67:33)	MeOH	0.125	**14a**	60 (69)	75 (*S*)
7	**13a**	**4b/9b** (67:33)	THF	0.125	**14a**	80 (83)	84 (*S*)
8[b]	**13a**	**4b/9b** (67:33)	THF	0.125	**14a**	– (16)	–
9[c]	**13a**	**4b/9b** (67:33)	THF	0.125	**14a**	– (48)	–
10	**13a**	**4b/9b** (67:33)	THF	0.074	**14a**	– (68)	–
11	**13a**	**4b/9b** (67:33)	THF	0.18	**14a**	83 (97)	86 (*S*)
12[d]	**13a**	**4b/9b** (67:33)	THF	0.18	**14a**	– (57)	–
13[e]	**13a**	**4b/9b** (67:33)	THF	0.18	**14a**	– (71)	–
14	**13a**	(*R*,*R*)-**4b**	THF	0.18	**14a**	86 (96)	>99 (*S*)
15	**13a**	(*R*,*R*)-**4a**	THF	0.18	**14a**	9 (12)	40 (*S*)
16	**13a**	**4c/9c** (79:21)	THF	0.18	**14a**	47 (48)	76 (*S*)
17	**13b**	(*R*,*R*)-**4b**	THF	0.18	**14b**	29 (34)	97 (*S*)
18	**13c**	(*R*,*R*)-**4b**	THF	0.18	**14c**	91 (95)	99 (*S*)
19	**13d**	(*R*,*R*)-**4b**	THF	0.18	**14d**	99 (99)	98 (*S*)
20	**13e**	(*R*,*R*)-**4b**	THF	0.18	**14e**	99 (99)	97 (*S*)
21	**13a**	(*S*,*S*)-**1a**	dioxane	0.18	**14a**	85	99 (*S*)
22	**13a**	(*R*,*R*)-**1a**	THF	0.18	**14a**	90 (92)	97 (*R*)
23	**13a**	(*R*,*R*)-**1b**	THF	0.18	**14a**	79 (93)	89 (*R*)

[a]Isolated yield; yield by NMR in parenthesis. [b]At room temperature. [c]At 40 °C. [d]1 mol% of [Rh], 2 mol% of ligand. [e]3 mol% of [Rh], 7 mol% of ligand

In a first attempt, **13a** was treated with 1.2 equiv. of phenylboroxine in the presence of 3.1 M KOH, 2.5 mol% of $[RhCl(C_2H_4)_2]_2$ and 6 mol% of diphenyldiene **4a** in dioxane at 60°C for 24 h

to give 29% of the *N*-tosylamine **14a** according to reaction monitoring by NMR. After chromatography, **14a** was isolated in 25% yield albeit with exceptional enantioselectivity of >99%*ee* (entry 1). Under identical conditions the C_S-symmetric diene **9a** revealed 8% of the 1,2-adduct **14a** (entry 2), again supporting the "background catalysis" via Rh-catalyzed C=C isomerization and formation of racemic *rac*-**4a**. Conducting the reaction with dianisyldiene mixture **4c** / **9c** (67 : 33) increased the yield of **14a** to 34% with decreased *ee*-value of 77% (entry 3). When dibenzyldiene **4b** was employed the yield raised to 40% with outstanding enantioselectivity of >99%*ee* (entry 4).

In order to minimize synthetic efforts required for separation of the regioisomeric dienes **4b** / **9b**, a (67 : 33) mixture was used for the subsequent optimization studies (entries 5–13). Thus, **14a** was isolated in 40% yield but somewhat decreased enantioselectivity of 81% by using the (67 : 33) mixture of **4b** / **9b** (entry 5). Replacement of the solvent dioxane by MeOH or THF improved the yields, while *ee*-values were only little affected (entries 6, 7). A temperature reduction to 40°C or room temperature, a higher dilution (0.074 M) as well as a reduced catalyst loading of 1 mol% or 3 mol% turned out to decrease reaction rates considerably (entries 8–10, 12, 13). Optimal reaction conditions were found with an aldimine concentration of 0.18 M, THF as solvent and a catalyst loading of 5 mol% (entry 11) that were applied to pure dibenzylated diene (*R*,*R*)-**4b**, resulting in a high yield and excellent enantioselectivity (86%, >99%*ee*) in favor of (*S*)-product **14a** (entry 14). Under these conditions the arylation of **13a** in the presence of rhodium pre-catalyst with either diphenyldiene **4a** or the dianisyldiene mixture **4c** / **9c** (79 : 21) as ligand proceeded poorly with conversions below 47% and *ee*-values between 76%*ee* (entry 15) and 40%*ee* (entry 16). It should be noted that the known ligands **1a** and **1b** gave results comparable to those of diene **4b**, however, in favor of the (*R*)-congener **14a** (entries 22, 23).

Under optimized reaction conditions further aldimine substrates **13b**–**e** with varying substitution pattern were tested in the presence of dibenzyldiene (*R*,*R*)-**4b**. 4-Methoxyphenylimine **13b** yielded the corresponding diarylamine **14b** in only 29% (34% by NMR) but 97%*ee* (*S*) (entry 17). The arylation of 3-fluorophenylimine **13c**, 2-methylphenylimine **13d** as well as 3-methoxyphenylimine **13e** with phenylboroxine gave the desired products **14c**–**e** in excellent yields (91–99%) and selectivities (97–99%*ee*) for the respective (*S*)-enantiomers (entries 18–20).

These results reveal that the novel diene ligands **4** are poorly suited for catalytic 1,4-additions to enones, but complement well the asymmetric Rh-catalyzed arylation of aldimines. In particular the dibenzylated diene (*R*,*R*)-**4b** exhibited excellent catalytic activity in nucleophilic additions of phenylboroxine to *N*-tosylimines.

The rhodium-catalyzed reactions using pure C_S-symmetric ligands **9** resulted in racemic addition products. Consequently, ligand mixture of **4** / **9** may give lower *ee*-values of the products as compared to the pure C_2-symmetric ligands **4**. Such decrease of the enantioselectivity was indeed experimentally observed (see for example Table 3, entry (4) vs. (5) and entry (11) vs. (14)). The palladium complexation of tetrahydropentalene derivatives is known to proceed via isomerization of the double bond.[37] Taking this finding into account an analogous Rh-catalyzed isomerization of ligand **9a** may lead to partial racemization of regioisomer **4a** and thus decreased enantioselectivity.

The mechanistic considerations were further fueled by previous results from Nguyen,[27d,41] who successfully utilized the π–σ–π isomerization of π-allylrhodium intermediates for a catalytic dynamic kinetic asymmetric amination of allylic trichloroacetimidates. From deuteration experiments in Rh-catalyzed nucleophilic allylations of cyclic imines Lam and coworkers deduced rapid interconversion of σ-allylrhodium(I) intermediates.[6a] Very recently the same

group reported chain walking of allylrhodium species, when δ-trifluoroboryl β,γ-unsaturated esters were employed in nucleophilic allylation of cyclic imines.[42] Based on DFT calculations Hayashi proposed an 1,4-rhodium shift upon conjugate addition of arylethenylboronic acids to enones.[43] However, in neither of the reported cases an isomerization via allylrhodium species involving the diene ligand was observed. To further proof, whether C_S-symmetric dienes **9** are able to form Rh complexes, both dienes **4a** and **9a** were submitted to complexation experiments and subsequent crystallization.

X-Ray Crystal Structure Analyses of Ligands and their Rh Complexes. Fortunately, we obtained suitable single crystals of both regioisomeric C_2- and C_S-symmetric free diphenyldiene ligands **4a** and **9a** as well as their corresponding Rh complexes (Figures 1 and 2).

C_2-symmetric diene **4a** crystallized as fragment in the asymmetric unit of the acentric space group C2. The whole molecule is completed by a coupled symmetry operation of rotation and translation (–x+1, y, –z) (Figure 1a). The C1=C2 (and C1A=C2A) double bond was unambiguously identified by a distance of 1.3412(18) Å. The interplanar angle between the five-membered ring systems is 78.24(6)°, and the torsion angle between the double bonds C1–C2–C2A–C1A is 153.7(2)°. A slight envelope conformation of the ring system is evident, where the bridge atom C4 (C4A) is –0.331(2) Å out of plane.

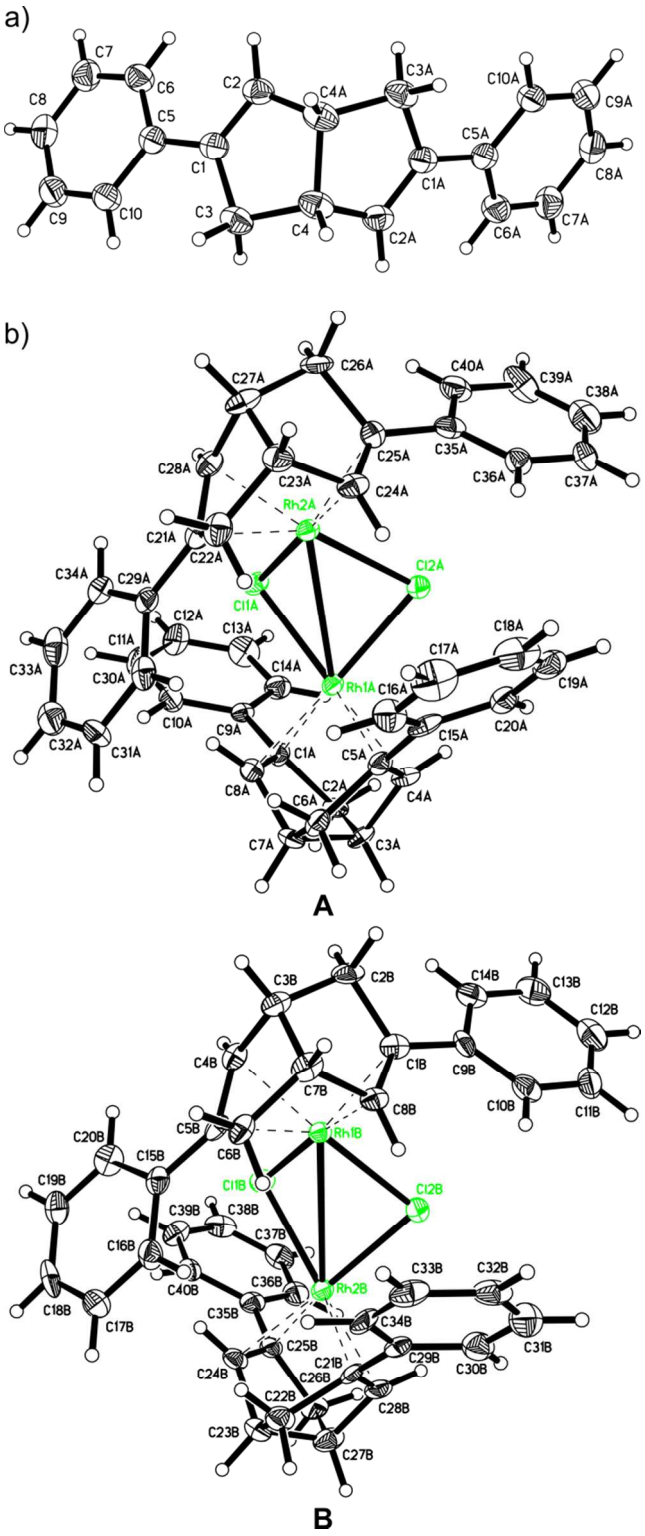


Figure 1. a) Structure of C_2-symmetric 2,5-diphenylbicyclo[3.3.0]octadiene **4a** in the solid state and b) structure of the corresponding complex $[RhCl(\mathbf{4a})]_2$ in the solid state. The complex crystallized with two independent conformers **A** and **B** in the acentric space group $P2_12_12_1$. The

absolute configuration of C_2-symmetric **4a** could be clearly determined by anomalous dispersion, characterized by the Flack x parameter of –0.03(3).[44]

The μ-chloro-bridged rhodium complex [RhCl(**4a**)]$_2$ crystallized with two independent complex conformers **A** and **B** in the acentric space group (Figure 1b). As all geometric aspects differ only very slightly in conformer **B**, only conformer **A** is discussed in detail in the following. An elongation of the double bonds with respect to the stand-alone structure of **4a** was observed. Double bond distances of 1.400(8) Å (C4A=C5A), 1.376(8) Å (C1A=C8A), 1.374(8) Å (C21A=C28A) and 1.405(9) Å (C24A=C25A) were determined.

The torsion angles between the double bonds C1A–C8A–C4A–C5A and C21A–C28A–C24A–C25A are 157.0(5)° and 156.7(5)°, respectively, which result in an equivalent orientation. The bicyclic systems of both molecules **4a** possess nearly the same interplanar angle of 77.1(3)° and 76.2(3)°. In the same way the four cyclopentyl subunits exhibit an envelope behavior with similar magnitudes of 0.56(1) to 0.60(1) Å out of plane. The Rh–Rh distance of conformer **A** is 3.0975(6) Å. It must be noted that the Rh–Rh distance in conformer **B** clearly differs and is significantly longer (3.2258(6) Å). The distance of the Rh atoms to the double bond centers of the dienes in conformer **A** are nearly identical with 2.159(6) Å and 2.155(6) Å. The distances of Rh to the phenyl atoms C9A, C15A and C29A, C35A attached to the bicycles ranged from 3.054(6) to 3.104(6) Å. The bite-angles C8A–Rh1A–C5A and C28A–Rh2–C25A are with 82.0(2)° and 83.4(2)° comparable. A similar trend was found for the angles values between Rh and the double bond atoms: 104.3(2)° for C1A–Rh1A–C5A and 103.9(2)° for C21A–Rh2A–C25A as well as 82.1(2)° for C8A–Rh1A–C4A and 81.4(2)° for C28A–Rh2A–C24A. Overall, the experimentally observed Rh–Rh distances and bite-angles are in good agreement with those reported for related Rh diene complexes.[29,45]

The crystal structure of the C_S-symmetric diene **9a** is depicted in Figure 2. Diene **9a** crystallized as racemic specimen in the centrosymmetric space group $R\bar{3}$ (Figure 2a). Both bridged cyclopentyl moieties show an ideal planar conformation. The interplanar angle of them is 60.17(7)°. The double bonds were identified by the distances of 1.365(2) Å (C2=C3) and 1.361(2) Å (C5C6). The torsion angle between the double bonds C2–C3–C5–C6 is 0.5(2)°.

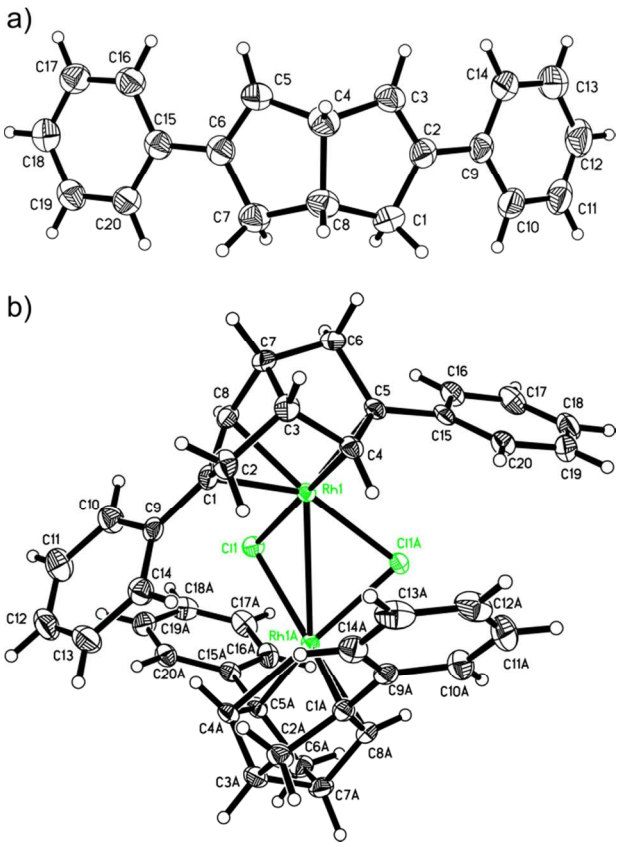


Figure 2. a) Structure of pure C_s-symmetric diene **9a** in the solid state and b) structure of the Rh complex [RhCl(*rac*-**4a**)]$_2$ in the solid state obtained from complexation of **9a**.

Complexation of pure diene **9a** resulted in a Rh complex, which crystallized as half fragment in the asymmetric unit of the centrosymmetric space group C2/c (Figure 2b). The complex will be completed by the coupled symmetry operation (2.0–x, y, 1.5–z) of rotation and translation. Surprisingly, starting C_S-symmetric diene **9a** did not act as ligand but the C_2-symmetric

regioisomer **4a**. Diphenyldiene **4a** itself is not generated by a symmetry operation as in its X-ray structure (Figure 1a). An elongation of the double bond C1=C8 by 0.038 Å as compared to C21A=C28A in [RhCl(**4a**)]$_2$ conformer **A** was observed, while the length of 1.408(3) Å for C4=C5 is comparable to that of C24A=C25A (1.405(9) Å). Moreover, the envelope conformation of the bicyclic system is pronounced, where C7 and C3 are 0.586(4) Å and 0.569(4) Å, respectively, out of plane. The interplanar angle between the bicycle is found to be 75.9(1)°, and the torsion angle between the double bonds C1–C8–C4–C5 is 156.8(2)°. The Rh–Rh distance is 3.1107(4) Å. The Rh distances to the double bond centers of C1=C8 and C4=C5 resemble (2.146(2) Å and 2.152(2) Å). The Rh1 distances to C9 and C15 of the phenyl substituent are 3.096(2) Å and 3.059(2) Å. The angles of C1–Rh1–C5 and C8–Rh1–C4 are 104.55(9)° and 82.02(9)°, respectively. The bite-angle C8–Rh1–C5 is 82.75(9)°.

The outcome that the Rh complex derived from pure C_S-symmetric ligand **9a** contained the C_2-symmetric ligand *rac*-**4a** instead of **9a** further supported the Rh-catalyzed isomerization with concomitant racemization. Consequently, the C_S-symmetric dienes **9** do not form suitable, i.e. catalytically active dimeric Rh precursor complexes.

DFT Calculations of Various Complexes of 4a and 9a. To further verify our assumption, complex [RhCl(**9a**)]$_2$ was investigated by density functional theory (DFT) using dispersion corrected hybrid and double hybrid functionals and large basis sets as detailed in the experimental part. We consider the relative stability of both [RhCl(**4a**)]$_2$ and [RhCl(**9a**)]$_2$ as well as a possible reaction mechanism to complex [RhCl(*rac*-**4a**)]$_2$. Computed complex [RhCl(**4a**)]$_2$ and experimental X-ray structure **A** are very similar (Table S2 in the Supporting Information).

A number of relevant computed energy differences are summarized in Table 4. Both isolated ligands **9a** and **4a** are very close in energy, compound **9a** is slightly less stable by 5 kJ mol^{-1}

when calculated with DFT (entry 1). This difference in energy is much more pronounced in the respective complexes, where [RhCl(**9a**)]$_2$ is by 137 kJ mol^{-1} less stable than [RhCl(**4a**)]$_2$. Hence this difference must originate from either the steric situation or the bonding situation of the complexes.

Table 4. Calculated Best Estimates of Relative Energies and Formation Energies of 4a and 9a Complexes on a COSMO/B3LYP-D3/def2-TZVP Level Corrected with B2PLYP

entry	reaction	ΔG (kJ mol^{-1})
1	**4a** → **9a**	5
2	[RhCl(**4a**)]$_2$ → [RhCl(**9a**)]$_2$	137
3	[RhCl(**4H**)]$_2$ → [RhCl(**9H**)]$_2$	105
4	[**4a**(RhCl(C_2H_4))$_2$] → [**9a**(RhCl(C_2H_4))$_2$]	66
5	2 **4a** + [RhCl(C_2H_4)$_2$]$_2$ → 4 C_2H_4 + [RhCl(**4a**)]$_2$	–141
6	2 **9a** + [RhCl(C_2H_4)$_2$]$_2$ → 4 C_2H_4 + [RhCl(**9a**)]$_2$	–13
7	**4a** + [RhCl(C_2H_4)$_2$]$_2$ → 2 C_2H_4 + [**4a**(RhCl(C_2H_4))$_2$]	–66
8	**9a** + [RhCl(C_2H_4)$_2$]$_2$ → 2 C_2H_4 + [**9a**(RhCl(C_2H_4))$_2$]	–5

To investigate the influence of the bulky phenyl groups [RhCl(**4a**)]$_2$ and [RhCl(**9a**)]$_2$ were modified by replacing the phenyl groups with hydrogen atoms, as exemplarily shown for **9a** (Figure 3). Still [RhCl(**9H**)]$_2$ is less stable than [RhCl(**4H**)]$_2$ by 105 kJ mol^{-1} (entry 3). Therefore it is not mainly the steric interaction of the phenyl groups that makes [RhCl(**9a**)]$_2$ unfavorable. Comparison of the mono complexes [4**a**(RhCl(C_2H_4))$_2$] and [9**a**(RhCl(C_2H_4))$_2$], which are assumed to be formed in a first step during complexation, once again reveals that [**9a**(RhCl(C_2H_4))$_2$] is less stable than [4**a**(RhCl(C_2H_4))$_2$] (Entry 4). Since this energy difference is about half of the energy difference between the full complexes, it is clear that ligand **9a** does not

coordinate the Rh centers as well as **4a** does. The close proximity of the two double bonds in **9a** appears to lead to a non-optimal overlap of the orbitals of the ligands and the Rh d-orbitals.

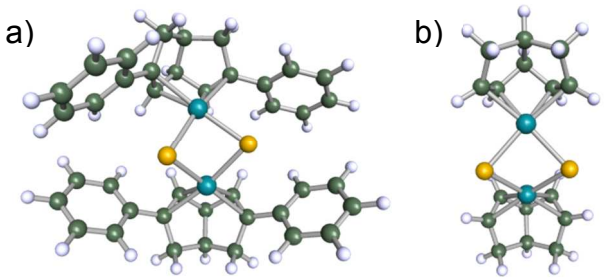
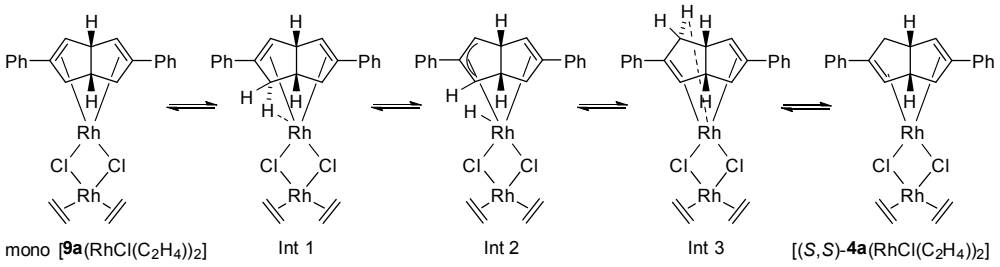


Figure 3. a) Complex [RhCl(**9a**)]$_2$ and b) truncated complex [RhCl(**9H**)]$_2$ based on DFT calculations (COSMO/B3LYP-D3/def2-TZVP).

In the actual complexation reaction [RhCl(C_2H_4)$_2$]$_2$ reacted with **4a** and **9a**, respectively. Both the reactions towards the mono complex as well as towards the full complex [RhCl(**4a**)]$_2$ are strongly exergonic (Table 4, entries 5, 7). In contrast, the formation of the analogous complexes with **9a** is slightly favored with an overall reaction energy of only –13 kJ mol^{-1} (entries 6, 8). Nevertheless, a **9a**/Rh complex can be formed under the experimental conditions. It should be noted that rhodium complexes are known for their catalytic activity in hydride transfer reactions,[46] and thus an isomerization of **9a** to *rac*-**4a** via hydride transfer seems to be reasonable. The mono complex [**9a**(RhCl(C_2H_4))$_2$] (Scheme 3) was considered as the starting point for a hydride transfer reaction, because it is a necessary intermediate in the formation of [RhCl(**9a**)]$_2$ and hydride transfers are usually fast processes.

From C_S-symmetric compound [**9a**(RhCl(C_2H_4))$_2$] two equivalent reaction paths may start, leading to the two enantiomers of [**4a**(RhCl(C_2H_4))$_2$]. A possible mechanism of this hydride transfer was determined computationally for the pathway to enantiomer [(*S*,*S*)-**4a**(RhCl(C_2H_4))$_2$] and can be described as follows (Scheme 3, Figure 4).

Scheme 3. Proposed Mechanism for the Rh-Catalyzed Isomerization of Complexed C_S-Symmetric Ligand 9a Based on DFT Calculations



As this reaction can also proceed at the opposite side in **9a** giving enantiomeric [(*R*,*R*)-**4a**(RhCl(C_2H_4))$_2$], racemization was observed

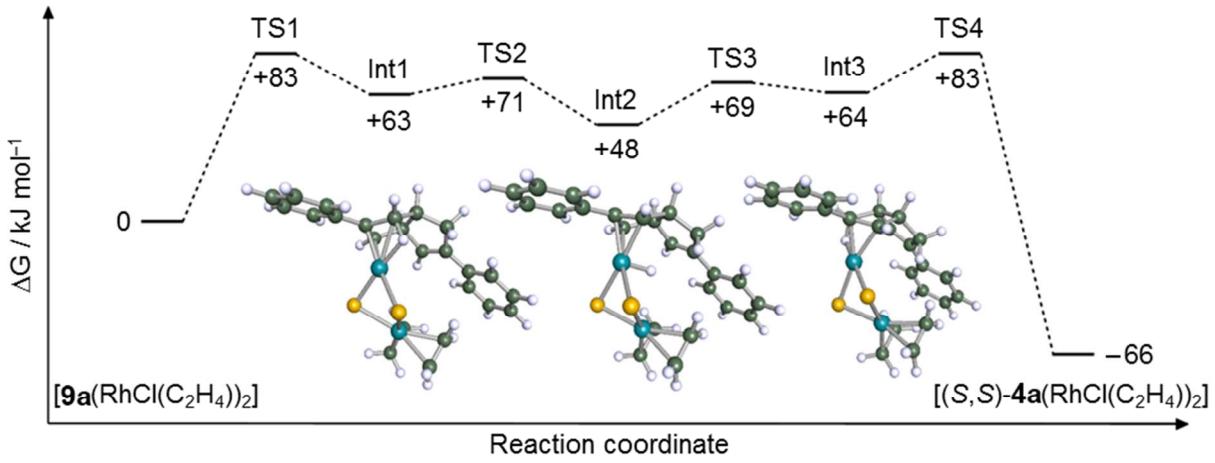


Figure 4. Computed best estimate of the Gibbs free energy profile of the proposed hydride transfer reaction on a COSMO/B3LYP-D3/def2-TZVP level corrected with B2PLYP (see computational details). An equivalent path may provide [(*R*,*R*)-**4a**(RhCl(C_2H_4))$_2$].

In the first step, proceeding via transition state TS1, one of the η^2 bonds is broken and simultanously an agostic interaction between rhodium and one of the hydrogens from the methylene bridges is formed, leading to a first intermediate (Int1). In the next transition state (TS2) a true Rh–H bond is formed, while the remaining η^2 bond is converted to an η^3 bond giving second intermediate Int2. Subsequently the hydride is shifted towards the η^3 bound carbon

on the far side of the molecule (TS3), resulting in an agostic interaction of rhodium and hydrogen, while retrieving an η^2 bond. This complex Int3 is very similar to Int1. Analogously to TS1 in the last transition state (TS4) the agostic interaction is given up in favor of a restoration of the second η^2 bond to form the complex [(*S,S*)-**4a**($RhCl(C_2H_4)$)$_2$].

If TS1 is regarded as the rate determining step of the reaction of **9a** to *rac*-**4a** at 50°C, this reaction will have an effective barrier of only 83 kJ mol^{-1}. Using transition state theory and assuming a first order reaction this leads to a half life $\tau_{0.5} \approx 3$ s of [**9a**($RhCl(C_2H_4)$)$_2$]. In contrast, a possible back reaction with an effective barrier of 149 kJ mol^{-1} will be very slow with a half life $\tau_{0.5} \approx 4 \cdot 10^3$ years of [**4a**($RhCl(C_2H_4)$)$_2$]. Therefore, in agreement with the experiment, racemization of **4a** is not expected during its complexation, while **9a** will react to *rac*-**4a**.

CONCLUSION

We provided a synthetic access to chiral C_2-symmetric bicyclo[3.3.0]octadienes **4** utilizing an enantioselective deprotonation/electrophilic trapping of Weiss diketone **5** followed by cross coupling as the key steps. When comparing the synthetic routes towards diene ligands **4** with the preparation of known ligands **1**, it should be noted that (*R,R)*-diphenyl-diene (*R,R)*-**4a** and (*R,R)*-dibenzyl-diene (*R,R)*-**4b**, respectively, were obtained in 3 steps from dimethyl acetone-1,3-di-carboxylate (i.e. the starting material for Weiss diketone **5**) in 28% and 31% overall yield (20% and 10% after HPLC) respectively. In order to access the (*S,S)*-ligands **4** the enantiomeric chiral base (*R,R*)-**6a · LiCl** can be employed. In contrast, known (*R,R)*-diphenyl-diene (*R,R)*-**1a** and its antipode (*S,S)*-**1a**, respectively, were prepared in 7 and 6 steps (5% and 11% overall) respectively from 1,5-cyclooctadiene and required large amounts of toxic lead(IV)acetate.[26] Rh-catalyzed conjugate additions of phenylboronic acid to cyclic enones **11** did not meet the expectations raised by a previous comparative DFT study,[22] giving yields of 10–42% and

enantioselectiveties up to 69%*ee*, regardless of the used diphenyl- (*R*,*R*)-**4a** or dibenzyldiene (*R*,*R*)-**4b**.

In contrast, the rhodium/dibenzyldiene **4b** complex is capable of catalyzing the nucleophilic addition of phenylboroxine to *N*-tosylimines **13** to provide the corresponding diarylamines **14** in yields of 86–99% with excellent enantioselectivities of 97–99%*ee*.

Furthermore, when mixtures of chiral C_2-symmetric diene (*R*,*R*)-**4** and achiral C_S-symmetric diene **9** were employed in the catalytic reactions, experimental evidence for a Rh-catalyzed C=C isomerization of diene **9** to *rac*-**4** was found based on optical rotations, NMR studies and X-ray crystal structure data of the Rh complexes. The finding could be supported by DFT calculation. The calculated relative energies reveal that $[RhCl(\mathbf{4a})]_2$ and even its truncated analogue $[RhCl(\mathbf{4H})]_2$ are more stable than the respective complexes with regioisomer **9a**. Furthermore, the energy difference between mono complexes $[\mathbf{4a}(RhCl(C_2H_4))_2]$ and $[\mathbf{9a}(RhCl(C_2H_4))_2]$, assumed to be the first intermediate during complexation, is about half of the energy difference between the full complexes. This indicates that ligand **9a** does not coordinate the Rh centers as **4a** does. Under contribution of Rh complexed **9a** can undergo a hydride transfer reaction which finally leads to the *rac*-**4a** ligated Rh catalyst.

Future work is necessary to figure out, which parameters govern such isomerizations also with respect to other diene ligands in order to avoid deterioration of the enantioselectivity and to obtain reliable catalysts for C–C bond formation.

EXPERIMENTAL SECTION

General. NMR spectra were recorded on a Bruker Avance 300, a Bruker Avance 400 or a Bruker Avance 500 spectrometer in $CDCl_3$ with TMS as an internal standard. Assignment of the resonances was supported by 2D experiments (COSY). IR spectra were recorded on a Bruker

FT-IR-spectrometer Vektor 22 with MKII golden gate single reflection Diamant ATR-system. Mass spectra were recorded on a Varian MAT 711 (EI, 70 eV) and a Bruker Daltonics micrOTOF_Q (ESI) with nitrogen as carrier gas. Optical rotations were measured with a Perkin-Elmer 241 polarimeter at 20 °C. Flash chromatography was performed on silica gel, grain size 40–63 μm (Fluka). Moisture-sensitive reactions were performed under nitrogen atmosphere in oven-dried glassware. All reagents were used as purchased unless otherwise noted. Solvents used for chromatography were distilled. THF was distilled from potassium/ benzophenone, CH_2Cl_2 and toluene from CaH_2. The reactions were monitored by TLC (Merck 60 F_{254} plates).

Single-crystal X-ray Structure Analyses. Analyses were performed on a Bruker kappa APEXII Duo diffractometer at 130 K. Data collection: APEX2 Software Suite; cell refinement: SAINT (both Bruker 2008). The structures were solved by using the program SHELXS 97 (Sheldrick 2008). The structures were refined by using the program SHELXL 97 (Sheldrick 2008). Molecular graphics: XP in SHELXTL-Plus (Sheldrick 2008). For details see Table S1 in the Supporting Information.

Computational Details. All calculations were carried out with the TURBOMOLE V6.6 program package.[47] The resulting structures were visualized with TmoleX 4.0.[48] Molecular geometries were optimized using density functional theory (DFT) in conjunction with the B3LYP functional[49] including dispersion effects through Grimme's D3 correction[50] with Becke-Johnson damping.[51a] Numerical integration was carried out on a m3 grid and density fitting (multipole accelerated resolution of the identity)[51b–e] was enabled to speed up the integral evaluation. For all calculations the def2-TZVP basis set[52] was used. Solvent effects were accounted for with the conductor-like screening model (COSMO)[53] using a relative dielectric constant of $\varepsilon = 2.2$ to mimic the polarity of 1,4-dioxane. Gibbs free energies *G* were calculated

for a temperature of 50°C using partition functions obtained with the rigid-rotor harmonic oscillator (RRHO) approximation. The temperature was chosen to match the experimental conditions during the ligand exchange reaction.

The Gibbs free energies computed at the B3LYP-D3/COSMO level were corrected by additional single point calculations with the double hybrid functional B2PLYP-D3.[54] The corrected energies were obtained as $G = G$(B3LYP-D3/COSMO)$-E$(B3LYP-D3)$+ E$(B2PLYP-D3), where E refers to purely electronic energies.

The following compounds were prepared according to literature procedures: **5**,[30] **6a**,[32b,33,34] **6b**,[55] **6c**,[56] phenylboroxine,[57] **13a**, **13b**,[58] **13c**,[59] **13d**,[60] **13e**.[61]

Synthesis of triflates *rac*-**7 / 8.** According to ref.,[26] to a solution of **5** (100 mg, 0.72 mmol) and 2-PyNTf$_2$ (623 mg, 1.76 mmol) in THF (3 mL) at –78 °C was added dropwise a solution of KHMDS (330 mg, 1.65 mmol) in THF, and the reaction mixture was warmed up to 0 °C over 4 h. The reaction was quenched by addition of a saturated solution of $NaHCO_3$ (10 mL). THF was removed under reduced pressure and the residue was extracted with Et_2O (3 × 20 mL). The combined organic layers were dried ($MgSO_4$) and the solvent was removed under reduced pressure. The crude product was purified by column chromatography on SiO_2 with hexanes/EtOAc (25:1) (R_f = 0.21, hexanes/EtOAc 4:1) to give a mixture of *rac*-**7** / **8** (141 mg, 0.35 mmol, 49%) as a colorless oil in an isomeric ratio *rac*-**7** / **8** = 33 : 67, which was used in the next step without further purification. The spectroscopic data of *rac*-**7** / **8** are in agreement with the (*R,R*)-**7** / **8**.

Synthesis of triflates (*R,R*)-**7 / 8.** To a solution of (*S,S*)-**6a**, generated from (*S,S*)-bis(1-phenylethyl)ammonium chloride (3.18 g, 12.1 mmol, 2.4 eq.) (or (*R*)-*N*-(1-phenylethyl)propan-2-ammonium chloride) in THF (15 mL) at –80 °C by dropwise addition of *n*-BuLi (2.5 M in hexane, 9.1 mL, 22.8 mmol, 4.5 eq.), warming the mixture to room temperature and recooling to –78 °C,[55] was added a solution of **5** (700 mg, 5.07 mmol, 1 eq.) in THF (8 mL). The reaction mixture was stirred at –78 °C for 1 h and then warmed up to –40 °C over 4 h. The reaction was quenched by addition of a saturated solution of $NaHCO_3$ (20 mL). The water layer was extracted

with Et_2O (3 × 50 mL), and the combined organic layers were dried ($MgSO_4$) and evaporated under reduced pressure. The crude product was purified by column chromatography on SiO_2 with hexanes/EtOAc (25:1) (R_f = 0.21, hexanes/EtOAc 4:1) to give (*R,R*)**-7** / **8** (1.48 g, 3.70 mmol, 74%) as yellow oil in the respective isomeric ratio (*R,R*)**-7** / **8**. The mixture was used in next steps without further purification. The NMR signals of (*R,R*)**-7** and **8** are assigned by using 2D-NMR spectorscopy. (*R,R*)**-7**: ^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) = 2.38–2.45 (m, 2H, 3-H_b, 6-H_b), 2.87–2.96 (m, 2H, 3-H_a, 6-H_a), 3.50–3.59 (m, 2H, 3'-H, 6'-H), 5.55 (d, *J* = 2.3 Hz, 2H, 1-H, 4-H); ^{13}C NMR (126 MHz, $CDCl_3$): δ (ppm) = 38.9 (C-3, C-6), 41.4 (C-3', C-6'), 119.41 (q, *J* = 320 Hz, SO_2CF_3), 120.0 (C-1, C-4), 148.8 (C-2, C-5). **8**: ^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) = 2.44–2.52 (m, 2H, 3-H_b, 4-H_b), 2.95–3.03 (m, 2H, 3-H_a, 4-Ha), 3.14–3.24 (m, 1H, 3'-H), 3.85 (d, *J* = 8.1 Hz, 1H, 6'-H), 5.66 (q, *J* = 2.3 Hz, 2H, 1-H, 6-H), ^{13}C NMR (126 MHz, $CDCl_3$): δ (ppm) = 34.6 (C-3'), 36.0 (C-3, C-4), 49.0 (C-6'), 119.41 (q, *J* = 320 Hz SO_2CF_3), (C-1, C-6), 149.6 (C-2, C-5). Isomers (*R,R*)**-7** / **8**: IR (cm^{-1}): $\tilde{\nu}$ = 1420, 1248, 1202, 1136, 895, 608; GC/MS (EI, 70 eV): *m/z* (%) = 402 (35) [M^+], 269 (67) [$M^+ - CF_3$], 227 (96), 69 (100) [CF_3]; MS (EI, 70 eV): *m/z* (%) = 402 (25) [M^+], 252 (11) [$M^+ - SO_2CF_3$], 227 (24), 163 (20), 119 (100) [C_8H_8O], 91 (55), 77 (54), 69 (70) [CF_3], 39 (16); HRMS (ESI): *m/z* calcd. for $C_{10}H_8F_6O_6S_2Na^+$: 424.9559, found: 424.9558; HRMS (EI): *m/z* calcd. for $C_{10}H_8F_6O_6S_2^+$: 401.9666, found: 401.9666.

Suzuki cross coupling of (*R,R*)-7 / 8 to ligands (*R,R*)-4a / 9a. $PdCl_2(PPh_3)_2$ (202 mg, 0.29 mmol, 0.1 eq.), PPh_3 (152 mg, 0.58 mmol, 0.2eq.) and K_2CO_3 (1.98 g, 14.38 mmol) were evacuated for 1 h. Then H_2O (7 mL), a solution of (*R,R*)**-7 / 8** (84 : 16) (1.16 g, 2.88 mmol, 1 eq.) in degassed 1,2-dimethoxyethane (12 mL) and a solution of $PhB(OH)_2$ (1.74 g, 14.38 mmol, 5 eq.) in EtOH (5 mL) were added, and the reaction mixture was heated at 85 °C for 24 h. After cooling to room temperature, the reaction was quenched by addition of H_2O (20 mL). The mixture was extracted with Et_2O (3 × 50 mL), the combined extracts were dried ($MgSO_4$) and the solvent was removed under reduced pressure. The residue was purified by column chromatography on SiO_2 with hexanes/Et_2O (500:1) to give (*R,R*)**-4a / 9a** (84 : 16) (526 mg, 2.04 mmol, 71%). The isomers were separated by chiral HPLC to give (*R,R*)**-4a** (243 mg, 0.94 mmol, 32%) and **9a** (59 mg, 0.22 mmol, 8%) as colorless solids. (*R,R*)**-4a**: R_f = 0.43 (hexanes/Et_2O 500:1), mp = 125–129 °C; $[\alpha]_D^{20}$ = –27.2 °(c = 1.0, $CHCl_3$, >99%*ee* *R*-enantio-

mer); ^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) = 2.70 (dq, *J* = 15.9 Hz, 2.1 Hz, 2H, 3-H_b, 6-H_b), 2.99–3.07 (m, 2H, 3-H_a, 6-H_a), 3.70–3.75 (m, 2H, 3'-H, 6'-H), 6.06 (s, 2H, 1-H, 4-H), 7.18–7.24 (m, 2H, *p*-Ar), 7.28–7.33 (m, 4H, *m*-Ar), 7.41–7.45 (m, 4H, *o*-Ar); ^{13}C NMR (126 MHz, $CDCl_3$): δ (ppm) = 38.8 (C-3, C-6), 48.6 (C-3', C-6'), 125.9 (*o*-Ar), 127.2 (*p*-Ar), 128.4 (*m*-Ar), 130.3 (C-1, C-4), 136.7 (*i*-Ar), 140.1 (C-2, C-5); IR (cm^{-1}) 2897, 2838, 1493, 1446, 907, 748, 733, 689; MS (EI): *m/z* (%): 258 (100), 243 (21), 202 (5), 179 (5), 167 (14), 155 (33), 141 (12), 129 (7), 117 (21), 103 (6), 91 (9), 77 (8), 63 (2), 51 (3), 39 (1); HRMS (EI): *m/z* calcd. for $C_{20}H_{18}^{+}$: 258.1409, found: 258.1407. **9a**: R_f = 0.43 (hexanes/Et_2O 500:1), mp = 104–106 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 2.63 (ddt, *J* = 16.0 Hz, 4.3 Hz, 2.2 Hz, 2H, 3-H_b, 4-H_b), 3.13 (ddt, *J* = 16.0 Hz, 9.3 Hz, 1.7 Hz, 2H, 3-H_a, 4-H_a), 3.24–3.35 (m, 1H, 3'-H), 4.06–4.12 (m, 1H, 6'-H), 6.18 (q, *J* = 2.1 Hz, 2H, 1-H, 6-H), 7.22 (d, *J* = 7.3 Hz, 2H, *p*-Ar), 7.27–7.34 (m, 4H, *m*-Ar), 7.40–7.46 (m, 4H, *o*-Ar); ^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 39.2 (C-3, C-4), 41.7 (C-3'), 59.5 (C-6'), 125.9 (*o*-Ar), 127.0 (C-1, C-6), 127.2 (*p*-Ar), 128.4 (*m*-Ar), 136.8 (*i*-Ar), 141.4 (C-2, C-5); IR (cm^{-1}) 2914, 1492, 1445,750, 735, 689; MS (EI): *m/z* (%): 258 (100), 243 (16), 228 (5), 215 (5), 202 (2), 189 (1), 179 (7), 167 (17), 154 (18), 141 (16), 129 (6), 115 (16)), 103 (7), 91 (11), 77 (8), 63 (2), 51 (3), 39 (1); HRMS (EI): *m/z* calcd. for $C_{20}H_{18}^{+}$: 258.1409, found: 258.1409. **Analytical HPLC of** (*R,R*)**-4a** / **9a**: DAICEL Chiracel OJ-H (250 × 4.6 mm, 5 µm), flow rate 0.7 mL min^{-1}, hexane/isopropanol (20 : 80), t_{R1} = 12.630 min (major, (*R,R*)-**4a**), t_{R2} = 17.930 min (minor, **9a**), t_{R3} = 25.41 min (minor, (*S,S*)-**4a**); HD-Separations: DAICEL Chiracel OJ-H (250 × 4.6 mm), flow rate 1 mL min^{-1}, 100% MeOH, t_{R1} = 17.132 min (major, (*R,R*)-**4a**), t_{R2} = 24.225 min (minor, **9a**); University Bonn: DIACEL Chiralpak IA (5 µm, 4,6 mm × 250 mm), flow rate 1 mL min^{-1}, MeCN/H_2O (75:25), t_{R1} = 11.55 min (major, (*R,R*)-**4a**), t_{R2} = 15.52 min (minor, **9a**).

Kumada coupling of (*R,R*)**-7 / 8 with BnMgBr to ligands** (*R,R*)**-4b / 9b.** According to ref.,[26] to a solution of (*R,R*)**-7 / 8** (84 : 16) (1.16 g, 2.88 mmol, 1 eq.) and $Fe(acac)_3$ (202 mg, 0.56 mmol, 0.2 eq.) in THF (27 mL) at 0 °C was added dropwise a solution of benzylmagnesiumchloride (2 M in THF, 2.70 mL, 5.46 mmol, 1.8 eq.). After complete addition, the reaction mixture was stirred for 15 min at 0 °C and the reaction quenched by addition of a solution of saturated NH_4Cl (20 mL). The reaction mixture was extracted with CH_2Cl_2 (3 × 20 mL). The combined organic layers were dried ($MgSO_4$) and the solvent was evaporated under reduced pressure. The crude

product was purified by column chromatography on SiO_2 with hexanes/Et_2O (500:1) to give (*R,R*)-**4b / 9b** (84 : 16) (500 mg, 1.75 mmol, 61%, R_f = 0.43 (hexanes/Et_2O 500:1) as a yellowish oil. The isomers were separated by chiral HPLC to give (*R,R*)-**4b** (210 mg, 0.69 mmol, 24%) as a colorless solid. (*R,R*)-**4b**: Mp = 46–49 °C, $[\alpha]_D^{20}$ = + 58.4 (c = 1.0, $CHCl_3$, >99%*ee* of *R*-enantiomer); ^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) = 2.00 (d, *J* = 16.3 Hz, 2H, 3-H_b, 6-H_b), 2.37–2.44 (m, 2H, 3-H_a, 6-H_a), 3.30–3.41 (s, 6H, 3'-H, 6'-H, 7-H), 5.14 (s, 2H, 1-H, 4-H), 7.13–7.21 (m, 6H), 7.25–7.30 (m, 4H); ^{13}C NMR (126 MHz, $CDCl_3$): δ (ppm) = 38.0 (C-7), 40.3 (C-3, C-6), 48.4 (C-3', C-6'), 126.0 (*p*-Ar), 128.3 (*o*-Ar), 128.9 (*m*-Ar), 130.5 (C-1, C-4), 140.2 (*i*-Ar), 141.2 (C-2, C-5). **9b**: ^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) = 1.91–1.97 (m, 2H, 3-H_b, 4-H_b), 2.49 (dd, *J* = 16.5 Hz, 9.4 Hz, 2H, 3-H_a, 4-H_a), 2.92–3.03 (m, 1H, 3'-H), 3.30–3.41 (m, 4H, 7-H), 3.64–3.72 (m, 1H, 6'-H), 5.32 (s, 2H, 1-H, 6-H), 7.12–7.30 (m, 10H, Ar-H); ^{13}C NMR (126 MHz, $CDCl_3$): δ (ppm) = 38.0 (C-7), 40.0 (C-3'), 43.2 (C-3, C-4), 58.4 (C-6'), 126.0 (Ar, *p*-Ar), 127.9 (C-1, C-6), 128.4 (*o*-Ar), 128.9 (*m*-Ar), 140.2 (*i*-Ar), 142.5 (C-2, C-5). Isomers **4b**/**9b**: IR (cm^{-1}) 2899, 2837, 1493, 696; MS (EI, 70 eV): *m/z* (%) = 286 (34) [M^+], 195 (100) [M^+– C_7H_7], 155 (10), 117 (10) [M^+– $C_7H_7C_5H_5$], 91 (43) [C_7H_7]; HRMS (ESI): *m/z* calcd. for $C_{22}H_{22}^+$: 286.1722, found: 286.1714. **Analytical HPLC**: Chiracel OJ-H (250 × 4.6 mm, 5 μm), flow rate 0.5 mL min^{-1}, hexane/isopropanol (20 : 80), t_{R1} = 16.17 min (major, (*R,R*)-**4b**), t_{R2} = 18.187 min (minor, **9b**). HD-Separations: Chiracel OJ-H (250 × 4.6 mm, 5 μm), flow rate 1 mL min^{-1}, 100% MeOH, t_{R1} = 13.919 min (major, (*R,R*)-**4b**), t_{R2} = 16.239 min (minor, **9b**).

Kumada coupling of (*R,R*)**-7 / 8 to ligand** (*R,R*)**-4c / 9c.** To a solution of $Pd(PPh_3)_4$ (15 mg, 0.01 mmol, 0.02 eq.) and (*R,R*)-**7 / 8** (84 : 16) (225 mg, 0.56 mmol, 1 eq.) in THF(4 mL) at 50 °C was added dropwise 4-methoxyphenylmagnesiumbromide (3.4 mL, 1.68 mmol, 3.0 eq., 0.5 M in THF). After complete addition, the reaction mixture was stirred for 6 h at 50 °C. The reaction was quenched by addition of a solution of saturated $NaHCO_3$ (5 mL). The mixture was extracted with Et_2O (3 × 15 mL), the combined extracts were dried ($MgSO_4$) and concentrated. The crude product was purified by column chromatography on SiO_2 with hexanes/ EtOAc (50:1) (R_f = 0.61, hexanes/EtOAc 9:1) to give (*R,R*)-**4c / 9c** (84 : 16) (134 mg, 0.42 mmol, 75%) as a colorless solid. The NMR signals of (*R,R*)-**4c** and **9c** are assigned by using 2D-NMR spectroscopy. (*R,R*)-**4c** : ^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) = 2.61–2.68 (m, 2H, 3-H_a, 6-H_a), 2.93–3.02 (m, 2H, 3-H_b, 4-H_b), 3.66–3.73 (m, 2H, 3'-H, 6'-H), 3.80 (s, 6H, OCH_3), 5.91 (d, *J* = 2.2 Hz, 2H, 1-H,

4-H), 6.80–6.86 (m, 4H, *m*-Ar), 7.32–7.39 (m, 4H, *o*-Ar);[13]C NMR (126 MHz, $CDCl_3$): δ (ppm) = 39.0 (C-3, C-6), 48.6 (C-3', C-6'), 55.4 (OCH_3), 113.8 (*m*-Ar), 127.1 (*o*-Ar), 128.3 (C-1, C-4), 129.6 (C-2, C-5), 139.4 (*i*-Ar), 158.9 (*p*-Ar). **9c**: ^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) = 2.55–2.62 (m, 2H, 3-H_a, 4-H_a), 3.05–3.13 (m, 2H, 3-H_b, 4-H_b), 3.22–3.31 (m, 1H, 3'-H), 3.80 (s, 6H, OCH_3), 4.06 (d, J = 7.7 Hz, 1H, 6'-H), 6.04 (d, J = 2.5 Hz, 2H, 1-H, 6-H), 6.80–6.86 (m, 4H, *m*-Ar), 7.32–7.39 (m, 4H, *o*-Ar);[13]C NMR (126 MHz, $CDCl_3$): δ (ppm) = 39.3 (C-3'), 41.9 (C-3, C-4), 55.4 (OCH_3), 59.4 (C-6'), 113.8 (*m*-Ar), 125.2 (C-1, C-6), 127.1 (*o*-Ar), 129.6 (C-2, C-5), 139.4 (*i*-Ar), 158.9 (*p*-Ar). Isomers **4c** / **9c**: IR (cm^{-1}) 2908, 2837, 1606, 1511, 1251, 1178, 1033, 824; MS (EI, 70 eV): *m/z* (%) = 318 (100), 303 (10), 185 (17), 171 (14), 147 (11), 121 (10); HRMS (ESI): *m/z* calcd. for $C_{22}H_{22}O_2^+$: 318.1620, found: 318.1612.

Synthesis of the ligand *rac*-4a. a) According to ref.,[26] $CeCl_3 \cdot 7\ H_2O$ (1.51 g, 4.05 mmol) was heated for 1.5 h at 110 °C to remove H_2O. Then dry THF (7 mL) was added and the suspension was stirred for 1 h prior to be cooled to –78 °C. PhLi (2.40 mL, 4.05 mmol, 1.8 M in dibutylether) was added and the suspension was stirred for a further 1 h at –78 °C. After dropwise addition of a solution of **5** (200 mg, 1.45 mmol) in THF (2 mL), the reaction mixture was warmed up to –40 °C over 6 h. The reaction was quenched by addition of H_2O (10 mL). The mixture was extracted with EtOAc (3 × 15 mL) and the combined organic layers were dried ($MgSO_4$). The solvent was removed under reduced pressure and the crude product was purified by column chromatography on SiO_2 with hexanes/EtOAc (4:1→1:1) (R_f = 0.26, hexanes/EtOAc 1:1) to give a 72 : 28 product mixture of (2*RS,3aRS*,5*SR*,6a*SR*)-2,5-diphenyloctahydropentalene-2,5-diol : (3a*SR*,5*SR*,6a*RS*)-5-hydroxy-5-phenylhexahydropentalen-2-one (383 mg, 1.02 mmol, 69%) as a colorless solid. The product was used in the next step without further purification. The NMR-signals are assigned by using 2D-NMR spectorscopy. (2*RS,3aRS*,5*SR*,6a*SR*)-**2,5-diphenyloctahydropentalene-2,5-diol**: ^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) = 2.28 (dd, J = 14.2 Hz, 3.0 Hz, 4H, 1-H_a, 3-H_a, 4-H_a, 6-H_a), 2.46–2.55 (m, 4H, 1-H_b, 3-H_b, 4-H_b, 6-H_b), 2.87–2.96 (m, 2H, 3′-H, 6′-H), 3.64 (s, 2H, O*H*), 7.21–7.27 (m, 1H, *p*-Ar), 7.29–7.35 (m, 2H, *m*-Ar), 7.46–7.51 (m, 2H, *o*-Ar); ^{13}C NMR (126 MHz, $CDCl_3$): δ (ppm) = 43.1 (C-3′, C-6′), 49.1 (C-1, C-3, C-4, C-6), 85.6 (C-2, C-5), 125.2 (*o*-Ar), 126.8 (*p*-Ar), 128.2 (*m*-Ar), 147.0, (*i*-Ar). (3a*SR*,5*SR*,6a*RS*)-**5-hydroxy-5-phenylhexahydropentalen-2-one**: ^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) = 1.94–2.01 (m, 2H, 4-H_a, 6-H_a), 2.38–2.45 (m, 4H, 3-H_b, 4-H_b, 1-H_b, 3-H_b), 2.58–2.66 (m, 2H, 1-H_a, 3-H_a), 3.06–3.14 (m, 2H, 3′-H, 6′-H), 3.64 (s, 1H, O*H*), 7.21–7.27 (m, 2H, *p*-Ar),

7.29–7.35 (m, 2H, *m*-Ar), 7.42–7.46 (m, 1H, *o*-Ar); ^{13}C NMR (126 MHz, $CDCl_3$): δ (ppm) = 38.2 (C-3′, C-6′), 46.4 (C-1, C-3), 49.2 (C-4, C-6), 84.7 (C-5), 124.9 (*o*-Ar), 127.2 (*p*-Ar), 128.4 (*m*-Ar), 145.7 (*i*-Ar), 221.0 (C-2).

b) According to the literature,[62] to a solution of (2*RS,3aRS*,5*SR*,6a*SR*)-2,5-diphenylocta-hydropentalene-2,5-diol / (3a*SR*,5*SR*,6a*RS*)-5-hydroxy-5-phenylhexahydropentalen-2-one (150 mg, 0.51 mmol) in dry $CHCl_3$ (3 mL) was added dropwise TMSCl (0.30 mL, 2.05 mmol) and the reaction mixture stirred for 2 h at room temperature. The reaction was quenched by addition of brine (5 mL) and the aqueous layer was extracted with CH_2Cl_2 (3 × 10 mL). The combined organic layers were dried ($MgSO_4$) and concentrated. The crude product was purified by column chromatography on SiO_2 with hexanes/Et_2O (500:1→20:1) to give *rac*-**4a** (105 mg, 0.41 mmol, 80%, isomeric ratio 66 : 34, R_f = 0.60, hexanes/EtOAc 500:1) and **5-phenyl-3,3a,4,6a-tetrahydropentalen-2-one** (15 mg, 0.08 mmol, 16%, R_f = 0.17, hexanes/EtOAc 20:1) as a color-less solid. The spectroscopic data of *rac*-**4a** are in accordance with those of (*R,R*)-**4a**. (3a*SR*,5*SR*,6a*RS*)-**5-phenyl-3,3a,4,6a-tetrahydropentalen-2-one**: ^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) = 2.10 (ddd, *J* = 18.2 Hz, 6.7 Hz, 1.5 Hz, 1H, 3-H_a,), 2.30–2.38 (m, 1H, 1-H_a), 2.47–2.67 (m, 3H, 1-H_a, 3-H_a, 6-H_b), 3.04–3.19 (m, 2H, 6-H_a), 3.56–3.65 (m, 1H, 3′-H), 6.00–6.08 (m, 1H, 4-H), 7.23–7.27 (m, 1H, *p*-Ar), 7.31–7.35 (m, 2H, *o*-Ar), 7.39–7.44 (m, 2H, *m*-Ar); ^{13}C NMR (126 MHz, $CDCl_3$): δ (ppm) = 37.5 (C-6′), 40.6 (C-6) 42.9, 45.0, 46.9 (C-3′), 125.8 (*m*-Ar), 127.6 (*p*-Ar), 128.4 (*o*-Ar), 128.6 (C-4), 135.9 (C-5), 142.1 (*i*-Ar), 219.8 (C-2); IR (cm^{-1}) 3032 (s), 2899, 1734, 1154, 756, 693; MS (EI): *m/z* (%) = 198 (100) [M^+], 183 (4) [M^+–O], 169 (4), 155 (94) [M^+–C_2H_2O], 141 (28) [M^+-C_3H_4O], 128 (14), 115 (17) [M^+–C_5H_6O], 102 (3) [M^+–C_6H_8O], 91 (9), 77 (8) [M^+–C_8H_9O], 65 (2) [M^+–C_3H_4O-C_6H_5], 51 (3), 39 (2); HRMS (EI): *m/z* calcd. for $C_{14}H_{14}O$: 198.1045, found: 198.1043.

Synthesis of ligand *rac*-4b. As described above for (*R,R*)-**4b**, from **5** (116 mg, 0.29 mmol, 1 eq.), yield: 53 mg, 0.19 mmol, 65%, yellowish oil. The isomeric ratio of *rac*-**4b / 9b** remained unchanged during the reaction. The spectroscopic data are in accordance with those of (*R,R*)-**4b**. HPLC: Chiracel OJ-H (250 × 4.6 mm, 5 μm), flow rate 0.5 mL min^{-1}, hexane/isopropanol (20:80), t_{R1} = 15.133 min (minor, *S,S*-**4b**), t_{R2} = 16.17 min (minor, *R,R*-**4b**), t_{R3} = 18.187 min (major, **9b**).

General procedure for the asymmetric rhodium-catalyzed 1,4-addition of phenylboronic

acid to cyclic 11 (GP1). A solution of $[RhCl(C_2H_4)_2]_2$ (2.92 mg, 0.008 mmol, 3 mol% [Rh]) and the respective ligand (0.017 mmol, 3.3 mol%) in degassed dioxane (2 mL) was stirred at room temperature for 15 min. Then a degassed 1.5 M solution of KOH (167 µL, 0.25 mmol) was added, and the mixture was stirred for a further 10 min. After addition of the respective enone (0.5 mmol) and $PhB(OH)_2$ (122 mg, 1.0 mmol), the reaction mixture was stirred at 50 °C for 2 h. The reaction mixture was then quenched with a saturated solution of NH_4Cl (5 mL) and extracted with Et_2O (3 × 15 mL). The combined organic layers were dried ($MgSO_4$), the solvent was removed under reduced pressure and the residue purified by column chromatography with hexanes/ Et_2O.

3-Phenylcyclopentan-1-one (**12a**). Flash chromatography (hexanes/Et_2O 15:1); R_f = 0.29 (hexanes/Et_2O 10:1); ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 1.90–2.07 (m, 1H, 4-H_a), 2.24–2.39 (m, 2H, 2-H_a, 5-H_a), 2.39–2.53 (m, 2H, 4-H_b, 5-H_b), 2.62–2.72 (m, 1H, 2-H_b), 3.36–3.51 (m, 1H, 3-H), 7.22–7.28 (m, 3H, *o*-Ar, *p*-Ar), 7.32–7.38 (m, 2H, *m*-Ar); ^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm) = 31.2 (C-4), 38.9 (C-5), 42.2 (C-3), 45.8 (C-2), 126.7 (*o*-Ar, *p*-Ar), 128.7 (*m*-Ar), 143.1 (*i*-Ar), 218.5 (C-1). Spectroscopic data are in accordance with those in the literature.[26] GC: Bondex UN-α+β 50 °C |1′|10 °C min^{-1} |100 °C |2′| 1 °C min^{-1}| 120 °C, R_{t1} = 38.840 min (*R*-enantiomer), R_{t2} = 39.493 min (*S*-enantiomer).

3-Phenylcyclohexan-1-one (**12b**). Flash chromatography (hexanes/Et_2O 15:1); R_f = 0.27 (hexanes/Et_2O 10:1); ^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm) = 1.70–1.95 (m, 2H, 5-H), 2.05–2.21 (m, 2H, 4-H)), 2.31-2.65 (m, 4H, 2-H, 6-H), 2.95–3.08 (m, 1H, 3-H), 7.19–7.26 (m, 3H, *o*-Ar, *p*-Ar), 7.30–7.37 (m, 2H, *m*-Ar); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) = 25.6 (C-5), 32.8 (C-4), 41.2 (C-6), 44.8 (C-3), 49.0 (C-2), 126.6 (*p*-Ar), 126.7 (*o*-Ar), 128.7 (*m*-Ar), 144.3 (*i*-Ar), 211.1 (C-1). Spectroscopic data are in accordance with those in the literature.[26] GC: Bondex UN-α+β 40 °C | 1′ | 2.5 °C min^{-1} |120 °C | 1 °C min^{-1} | 120 °C, R_{t1} = 54.480 min (*R*-enantiomer), R_{t2} = 55.105 min (*S*-enantiomer).

General procedure for the racemic rhodium-catalyzed 1,2-addition of phenylboroxine to *N*-tosylimines 13 (GP2). Under nitrogen atmosphere $[RhOH(cod)]_2$ (5.7 mg, 7.5 µmol, 5 mol% [Rh]) was dissolved in degassed dioxane (4 mL) and stirred at room temperature for 10 min. Then degassed H_2O (0.1 mL), the respective **13** (0.5 mmol, 1 eq.) and phenylboroxine (187 mg, 0.6 mmol, 1.2 eq.) were added and the reaction mixture was strirred at 60 °C for 24 h. The

reaction mixture was allowed to cool to room temperature and filtered over a small pad of silica (pre-treated with MeOH, EtOAc as eluent). The filtrate was concentrated under reduced pressure and the residue was purified by column chromatography on SiO_2 with hexanes/EtOAc (10:1 → 4:1, 1% Et_3N).

General procedure for the rhodium-catalyzed asymmetric 1,2-addition of phenylboroxine to *N*-tosylimines 13 (GP3). A solution of $[RhCl(C_2H_4)_2]_2$ (1.94 mg, 0.005 mmol, 5 mol% [Rh]) and the respective ligand (3.44 mg, 0.01 mmol, 6 mol%) in dry THF was stirred at room temperature for 15 min. Then a degassed 3.1 M solution of KOH (13 μL, 0.04 mmol) was added, and the mixture was stirred for a further 10 min. After addition of the respective **13** (0.2 mmol) and phenylboroxine (75 mg, 0.24 mmol), the reaction mixture was stirred at 60 °C for 24 h. The reaction mixture was allowed to cool to room temperature and filtered over a small pad of silica (pre-treated with MeOH, EtOAc as eluent). The filtrate was concentrated under reduced pressure and the residue was purified by column chromatography on SiO_2 with hexanes/EtOAc (10:1 → 4:1, 1% Et_3N).

N-[(4-Chlorophenyl)(phenyl)methyl]-4-methylbenzenesulfonamide (**14a**). GP2: 151 mg, 0.41 mmol, 82%; GP3: 64 mg, 0.17 mmol, 86%; >99 %*ee*, R_f = 0.48 (hexanes/EtOAc 4:1); $[\alpha]_D^{20}$ = –5.8 (c = 1.0, $CHCl_3$, >99 %*ee* *R*-enantiomer); ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 2.39 (s, 3H, C*H*$_3$), 5.25 (d, *J* = 7.2 Hz, 1H, N*H*), 5.53 (d, *J* = 7.2 Hz, 1H, N-C*H*), 7.01–7.08 (m, 4H, *m*′′-Ar, *m*-Ar), 7.11–7.23 (m, 7H, *o*′′-Ar, *p*′′-Ar, *o*-Ar, *m*′-Ar), 7.51–7.58 (m, 2H, *o*′-Ar); ^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 21.5 (*C*H$_3$), 60.8 (N-*C*H), 127.2 (*o*′-Ar), 127.3 (*m*′′-Ar), 127.9 (*p*′′-Ar), 128.6 (*o*′′-Ar), 128.7 (*o*-Ar), 128.8 (*m*′-Ar), 129.4 (*m*′-Ar), 133.5 (*i*-Ar), 137.2 (*i*′-Ar), 139.0 (*p*-Ar), 140.1 (*i*′′-Ar), 143.4 (*p*-Ar). Spectroscopic data are in accordance with those in the literature.[63] Separation: Chiracel OD-H, hexane/isopropanol (93:7), flow rate 1.0 mL min^{-1}, λ = 254 nm, R_{t1} = 16.536 min (major, *S*-enantiomer), R_{t1} = 21.944 min (minor, *R*-enantiomer).

N-[(4-Methoxyphenyl)(phenyl)methyl]-4-methylbenzenesulfonamide (**14b**). GP2: 86 mg, 0.22 mmol, 73%; GP3: 21 mg, 0.05 mmol, 29%, >97 %*ee*, R_f = 0.29 (hexanes/EtOAc 4:1); $[\alpha]_D^{20}$ = –19.33 (c = 1.0, $CHCl_3$, >97 %*ee* *S*-enantiomer); ^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) = 2.38 (s, 3H, C*H*$_3$), 3.75 (s, 3H, OC*H*$_3$), 5.03 (d, *J* = 6.9 Hz, 1H, N*H*), 5.52 (d, *J* = 6.9 Hz, 1H, N-C*H*), 6.70–6.76 (m, 2H, *m*-Ar), 6.96–7.02 (m, 2H, *o*-Ar), 7.07–7.17 (m, 4H, *o*′′-Ar, *m*′-Ar), 7.17–7.23

(m, 3H, *m''*-Ar, *p''*-Ar), 7.53–7.58 (m, 2H, *o'*-Ar); ^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 21.5 (CH_3), 55.3 (OCH_3), 60.8 (C-NH), 113.9 (*m*-Ar), 127.2 (*o'*-Ar), 127.3 (*o''*-Ar), 127.5 (*p''*-Ar), 128.5 (*m''*-Ar), 128.6 (*o*-Ar), 129.3 (*m'*-Ar), 132.7 (*i'*-Ar), 137.4 (Ar), 140.7 (*i''*-Ar), 143.1 (Ar), 159.0 (*i*-Ar). Spectroscopic data are in accordance with those in the literature.[64] Separation: Chiracel OD-H, hexane/isopropanol (85:15), flow rate 1.0 mL min^{-1}, λ = 254 nm, R_{t1} = 12.781 min (major, *S*-enantiomer), R_{t2} = 18.534 min (minor, *R*-enantiomer).

N-[(3-Fluorophenyl)(phenyl)methyl]-4-methylbenzenesulfonamide (**14c**). GP2: 109 mg, 0.31 mmol, 61%, GP3: 65 mg, 0.18 mmol, 91%; >99%*ee*, R_f = 0.28 (hexanes/EtOAc 4:1); $[\alpha]_D^{20}$ = + 9.3 (c = 1.0, $CHCl_3$, >99%*ee* *S*-enantiomer); ^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) = 2.38 (s, 3H, C*H*$_3$), 5.10 (d, *J* = 7.1 Hz, 1H, N*H*), 5.55 (d, *J* = 7.0 Hz, 1H, C*H*-N), 6.78–6.82 (m, 1H, 4-H), 6.86–6.91 (m, 1H, 6-H), 6.91–6.95 (m, 1H, 5-H), 7.03–7.08 (m, 2H, *o'*-Ar), 7.13–7.24 (m, 6H, 2-H, *m*-Ar, *m'*-Ar, *p*-Ar), 7.57 (d, *J* = 8.3 Hz, 2H, *o*-Ar); ^{13}C NMR (126 MHz, $CDCl_3$): δ (ppm) = 21.5(*C*H$_3$), 60.9 (*C*H-N), 114.3 (C-6), 114.5 (C-4), 123.0 (C-5), 127.2 (*o*-Ar), 127.3 (*o'*-Ar), 127.9 (*p'*-Ar), 128.7 (*m'*-Ar), 129.4 (*m*-Ar), 130.0 (*i*-Ar), 137.2 (C-2), 140.0 (*i'*-Ar), 143.0 (C-1), 143.5 (*p*-Ar), 162.75 (C-3). Spectroscopic data are in accordance with those in the literature.[64] Separation: Chiracel OJ-H, hexane/isopropanol (90:10), flow rate 1.0 mL min^{-1}, λ = 254 nm, R_{t1} = 27.258 min (minor, *R*-enantiomer), R_{t1} = 29.688 min (major, *S*-enantiomer).

N-[(2-Methylphenyl)(phenyl)methyl]-4-methylbenzenesulfonamide (**14d**). GP2: 128 mg, 0.36 mmol, 73%; GP3: 70 mg, 0.2 mmol, >99%; 98%*ee*, R_f = 0.29 (hexanes/EtOAc 4:1), $[\alpha]_D^{20}$ = + 8.3 (c = 1.0, $CHCl_3$, 98%*ee* *S*-enantiomer); ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 2.16 (s, 3H, 7-H), 2.36 (s, 3H, 8-H), 5.06 (d, *J* = 7.0 Hz, 1H, N*H*), 5.80 (d, *J* = 7.0 Hz, 1H, C*H*-N), 7.02–7.14 (m, 8H, 3-H, 4-H, 5-H, 6-H, *m*-Ar, *m'*-Ar), 7.16–7.21 (m, 3H, *o'*-Ar, *p'*-Ar), 7.52–7.57 (m, 2H, *o*-Ar); ^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 19.4 (C-7), 21.5 (C-8), 58.1 (*C*-NH), 126.2 (Ar), 127.1 (Ar), 127.2 (Ar), 127.5 (Ar), 128.5 (Ar), 129.3 (*m*-Ar), 130.7 (C-3), 135.5 (C-1), 137.5 (*i*-Ar), 138.3 (C-2), 140.0 (*i'*-Ar), 143.1 (*p*-Ar). Spectroscopic data are in accordance with those in the literature.[64] Separation: Chiracel OD-H, hexane/isopropanol (90:10), flow rate 1.0 mL min^{-1}, λ = 254 nm, R_{t1} = 9.905min (minor, *R*-enantiomer), R_{t2} = 12.857 min (major, *S*-enantiomer).

N-[(3-Methoxyphenyl)(phenyl)methyl]-4-methylbenzenesulfonamide (**14e**). GP2: 20 mg, 0.05 mmol, 11%, GP3: 78 mg, 0.2 mmol, >99%; >99%*ee*, R_f = 0.37 (hexanes/EtOAc 4:1), $[\alpha]_D^{20}$ =

–2.57 (c = 1.0, $CHCl_3$, >99 %*ee* *S*-enantiomer); ^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) = 2.37 (s, 3H, C$H_{3,\ Ts}$), 3.68 (s, 3H, OCH_3), 5.08 (d, *J* = 7.0 Hz, 1H, N*H*), 5.53 (d, *J* = 7.0 Hz, 1H, N-C*H*), 6.61 (s, 1H, 2-H), 6.68 (d, *J* = 7.7 Hz, 1H, 6-H), 6.73 (dd, *J* = 8.2 Hz, 2.6 Hz, 1H, 4-H), 7.08–7.16 (m, 5H, *m*-Ar, *m*′-Ar, 5-H), 7.17–7.24 (m, 3H, *o*′-Ar, p′-Ar), 7.54–7.59 (m, 2H, *o*-Ar); ^{13}C NMR (126 MHz, $CDCl_3$): δ (ppm) = 21.5 (*C*H_3), 55.1 (O*C*H_3), 61.3 (*C*-NH), 113.0 (C-4), 113.1 (C-2), 119.7 (C-6), 127.2 (*o*-Ar), 127.3 (C-5), 127.6 (*p*′-Ar), 128.6 (*o*′-Ar), 129.4 (*m*′-Ar), 129.6 (*m*-Ar), 137.4 (*i*-Ar), 140.4 (*i*′-Ar), 142.0 (C-1), 143.2 (*p*-Ar), 159.7 (C-3). Spectroscopic data are in accordance with those in the literature.[64] Separation: Chiracel OD-H, hexane/iso-propanol (95:5), flow rate 0.8 mL min^{-1}, λ = 254 nm, R_{t1} = 39.935 min (minor, *R*-enantiomer), R_{t2} = 43.279 min (major, *S*-enantiomer).

Rhodium complex with ligand 4a. Following a literature procedure,[65] $[RhCl(C_2H_4)_2]_2$ (23 mg, 0.06 mmol, 1 eq.) and (*R,R*)-**4a** (31 mg, 0.12 mmol, 2 eq.) were dissolved in degassed dioxane at 50 °C for 4 h. The reaction mixture was allowed to cool to room temperature and the solvent was removed under reduced pressure. The residue was recrystallized from hexanes and CH_2Cl_2 to give the complex $[RhCl((R,R)\text{-}\mathbf{4a})_2]_2$ (30 mg, 0.03 mmol, 64%) as red-brown crystals, which were suitable for X-ray crystal structure analysis. ^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) = 1.74–1.80 (m, 4H, 3-H_b, 6-H_b, 3'-H, 6'-H), 3.06 (d, *J* = 13.0 Hz, 2H, 3-H_b, 6-H_b), 3.68 (s, 2H, 1-H, 4-H), 7.21–7.26 (m, 4H, Ar), 7.28–7.48 (m, 6H, Ar); ^{13}C NMR (126 MHz, $CDCl_3$): δ (ppm) = 43.8 (C-3, C-6), 46.1 (C-3', C-6'), 72.3 (C-1, C-4), 72.4 (C-1, C-4), 99.4 (*i*-Ar), 99.5 (*i*-Ar), 127.4 (*m*-Ar), 127.6 (*o*-Ar), 129.0 (*p*-Ar), 141.5 (C-2, C-5); IR (cm^{-1}) 2920, 2832, 1444, 1289, 909, 841, 759, 731, 690, 570.

Rhodium complex with ligand 9a. As described above for (*R,R*)-**4a**, from $[RhCl(C_2H_4)_2]_2$ (23 mg, 0.06 mmol, 1 eq.) and *rac*-**9a** (31 mg, 0.12 mmol, 2 eq.) to give the complex (23 mg, 0.03 mmol, 49%) as red-brown crystals. The spectroscopic data were in accordance to those of complex $[RhCl(rac\text{-}\mathbf{4a})_2]_2$. Thus, isomerization of the double bond has taken place.

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI:

Analytical data (NMR, HPLC, GC), X-ray diffraction data as well as background computational details (pdf).

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Notes

The authors declare no competing financial interest.

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REFERENCES

(1) Reviews: (a) Defieber, C.; Grützmacher, H.; Carreira, E. M. *Angew. Chem. Int. Ed.* **2008**, *47*, 4482–4501; *Angew. Chem.* **2008**, *120*, 4558–4579. (b) Johnson, J. B.; Rovis, T. *Angew. Chem. Int. Ed.* **2008**, *47*, 840–871; *Angew. Chem.* **2008**, *120*, 852–884. (c) Müller, D.; Alexakis, A. *Chem. Commun.* **2012**, *48*, 12037–12049.(d) Maksymowicz, R. M.; Bissette, A. J.; Fletcher, S. P. *Chem. Eur. J.* **2015**, *21*, 5668–5678.

(2) Hayashi, T.; Ueyama, K.; Tokunaga, N.; Yoshida, K. *J. Am. Chem. Soc.* **2003**, *125*, 11508–11509.

(3) Fischer, C.; Defieber, C.; Suzuki, T.; Carreira, E. M. *J. Am. Chem. Soc.* **2004**, *126*, 1628–1629.

(4) Maire, P.; Deblon, S.; Breher, F.; Geier, J.; Böhler, C.; Rüegger, H.; Schönberg, H.; Grützmacher, H. *Chem. Eur. J.* **2004**, *10*, 4198–4205.

(5) (a) Zhou, B.; So, C. M.; Lu, Y.; Hayashi, T. *Org. Chem. Front.* **2015**, *2*, 127–132. (b) Dou, X.; Lu, Y.; Hayashi, T. *Angew. Chem. Int. Ed.* **2016**, *55*, 6739–6743; *Angew. Chem.* **2016**, *128*, 6851–6855. (c) Wu, C.-Y.; Yu, Y.-N.; Xu, M.-H. *Org. Lett.* **2017**, *19*, 384–387.

(6) (a) Luo, Y.; Hepburn, H. B.; Chotsaeng, N.; Lam, H. W. *Angew. Chem. Int. Ed.* **2012**, *51*, 8309–8313; *Angew. Chem.* **2012**, *124*, 8434–8438. (b) Chen, C.-C.; Gopula, B.; Syu, J.-F.; Pan, J.-H.; Kuo, T.-S.; Wu, P.-Y.; Henschke, J. P.; Wu, H.-L. *J. Org. Chem.* **2014**, *79*, 8077–8085. (c) Yasukawa, T.; Kuremoto, T.; Miyamura, H.; Kobayashi, S. *Org. Lett.* **2016**, *18*, 2716–2718. (d) Nishimura, T.; Nagai, T.; Takechi, R.; Ebe, Y. *Synthesis* **2016**, *48*, 2612–2618. (e) Li, R.; Wen, Z.; Wu, N. *Org. Biomol. Chem.* **2016**, *14*, 11080–11084.

(7) Zhang, S.-S.; Wang, Z.-Q.; Xu, M.-H.; Lin, G.-Q. *Org. Lett.* **2010**, *12*, 5546–5549.

(8) (a) Nishimura, T.; Takiguchi, Y.; Maeda, Y.; Hayashi, T. *Adv. Synth. Catal.* **2013**, *355*, 1374–1382. (b) Nishimura, T.; Maeda, Y.; Hayashi, T. *Angew. Chem. Int. Ed.* **2010**, *49*, 7324–7327; *Angew. Chem.* **2010**, *122*, 7482–7485.

(9) (a) Shintani, R.; Okamoto, K.; Otomaru, Y.; Ueyama, K.; Hayashi, T. *J. Am. Chem. Soc.* **2005**, *127*, 54–55. (b) Johnson, T.; Choo, K.-L.; Lautens, M. *Chem. Eur. J.* **2014**, *20*, 14194–14197. (c) Serpier, F.; Flamme, B.; Brayer, J.-L.; Folléas, B.; Darses, S. *Org. Lett.* **2015**, *17*, 1720–1723.

(10) Shintani, R.; Sannohe, Y.; Tsuji, T.; Hayashi, T. *Angew. Chem. Int. Ed.* **2007**, *46*, 7277–7280; *Angew. Chem.* **2007**, *119*, 7415–7418.

(11) (a) Ichikawa, Y.; Nishimura, T.; Hayashi, T. *Organometallics* **2011**, *30*, 2342–2348. (b) Nishimura, T.; Ichikawa, Y.; Hayashi, T.; Onishi, N.; Shiotsuki, M.; Masuda, T. *Organometallics* **2009**, *28*, 4890–4893.

(12) (a) Punniyamurthy, T.; Mayr, M.; Dorofeev, A. S.; Bataille, C. J. R.; Gosiewska, S.; Nguyen, B.; Cowley, A. R.; Brown, J. M. *Chem. Commun.* **2008**, 5092–5094. (b) Aikawa, K.; Takahayashi, Y.; Kawauchi, S.; Mikami, K. *Chem. Commun.* **2008**, 5095–5097. (c) Liu, Y.; Du, H. *J. Am. Chem. Soc.* **2013**, *135*, 6810–6813.

(13) (a) Nishimura, T.; Yasuhara, Y.; Hayashi, T. *J. Am. Chem. Soc.* **2007**, *129*, 7506–7507. (b) Hatano, M.; Nishimura, T. *Angew. Chem. Int. Ed.* **2015**, *54*, 10949–10952; *Angew. Chem.* **2015**, *127*, 11099–11102.

(14) (a) Nishimura, T.; Noishiki, A.; Hayashi, T. *Chem. Commun.* **2012**, 973–975. (b) Nishimura, T.; Yasuhara, Y.; Sawano, T.; Hayashi, T. *J. Am. Chem. Soc.* **2010**, *132*, 7872–7873.

(15) Shibata, T.; Shizuno, T. *Angew. Chem. Int. Ed.* **2014**, *53*, 5410–5413; *Angew. Chem.* **2014**, *126*, 5514–5517.

(16) Ma, X.; Jiang, J.; Lv, S.; Yao, W.; Yang, Y.; Liu, S.; Xia, F.; Hu, W. *Angew. Chem. Int. Ed.* **2014**, *53*, 13136–13139; *Angew. Chem.* **2014**, *126*, 13352–13355.

(17) Chen, D.; Zhang, X.; Qi, W.-Y.; Xu, B.; Xu, M.-H. *J. Am. Chem. Soc.* **2015**, *137*, 5268–5271.

(18) Chen, D.; Zhu, D.-X.; Xu, M.-H. *J. Am. Chem. Soc.* **2016**, *138*, 1498 – 1501.

(19) (a) Luo, Y.; Carnell, A. J. *J. Org. Chem.* **2010**, *75*, 2057–2060. (b) Boyd, W. C.; Crimmin, M. R.; Rosebrugh, L. E.; Schomaker, J. M.; Bergman, R. G.; Toste, F. D. *J. Am.*

Chem. Soc. **2010**, *132*, 16365–16367. (c) Abele, S.; Inauen, R.; Spielvogel, D.; Moessner, C. *J. Org. Chem.* **2012**, *77*, 4765–4773. (d) Herrera, A.; Linden, A.; Heinemann, T. W.; Brachvogel, R.-C.; von Delius, M.; Dorta, R. *Synthesis* **2016**, *48*, 1117–1121. (e) Mariz, R.; Briceño, A.; Dorta, R.; Dorta, R. *Organometallics* **2008**, *27*, 6605–6613.

(20) Luo, Y.; Berry, N. G.; Carnell, A. J. *Chem. Commun.* **2012**, *48*, 3279–3281.

(21) (a) Kina, A.; Iwamura, H.; Hayashi, T. *J. Am. Chem. Soc.* **2006**, *128*, 3904–3905. (b) Pollice, R.; Schnürch, M. *Chem. Eur. J.* **2016**, *22*, 5637–5642.

(22) (a) Kantchev, E. A. B. *Chem. Commun.* **2011**, *47*, 10969–10971. (b) Kantchev, E. A. B. *Chem. Sci.* **2013**, *4*, 1864–1875. (c) Qin, H.-L.; Chen, X.-Q.; Shang, Z.-P.; Kantchev, E. A. B. *Chem. Eur. J.* **2015**, *21*, 3079–3086.

(23) Gosiewska, S.; Raskatov, J. A.; Shintani, R.; Hayashi, T.; Brown, J. M. *Chem. Eur. J.* **2012**, *18*, 80–84.

(24) Hayashi, T.; Takahashi, M.; Takaya, Y.; Ogasawara, M. *J. Am. Chem. Soc.* **2002**, *124*, 5052–5058.

(25) Sieffert, N.; Boisson, J.; Py, S. *Chem. Eur. J.* **2015**, *21*, 9753–9768.

(26) Helbig, S.; Sauer, S.; Cramer, N.; Laschat, S.; Baro, A.; Frey, W. *Adv. Synth. Catal.* **2007**, *349*, 2331–2337.

(27) (a) Wang, Z.-Q.; Feng, C.-G.; Xu, M.-H.; Lin, G.-Q. *J. Am. Chem. Soc.* **2007**, *129*, 5336-5337. (b) Wang, Z.-Q.; Feng, C.-G.; Zhang, S.-S.; Xu, M.-H.; Lin, G.-Q. *Angew. Chem. Int. Ed.* **2010**, *49*, 5780–5783; *Angew. Chem.* **2010**, *122*, 5916–5919. (c) Zhang, S.-S.; Wang, Z.-Q.; Xu, M.-H.; Lin, G.-Q. *Org. Lett.* **2010**, *12*, 5546–5549. (d) Zhang, Q.; Stockdale, D. P.; Mixdorf, J. C.; Topczewski, J. J.; Nguyen, H. M. *J. Am. Chem. Soc.* **2015**, *137*, 11912–11915. (e) Zhang, Y.-F.; Chen, D.; Chen, W.-W.; Xu, M.-H. *Org. Lett.* **2016**, *18*, 2726–2729.

(28) Helbig, S.; Axenov, K. V.; Tussetschläger, S.; Frey, W.; Laschat, S. *Tetrahedron Lett.* **2012**, *53*, 3506–3509.

(29) Feng, C.-G.; Wang, Z.-Q.; Shao, C.; Xu, M.-H.; Lin, G.-Q. *Org. Lett.* **2008**, *10*, 4101–4104.

(30) (a) Kubiak, G.; Cook, J. M.; Weiss, U. *J. Org. Chem*. **1984**, *49*, 561–564. (b) Bertz, S. H.; Cook, J. M.; Gawish, A.; Weiss, U. *Org. Synth.* **1986**, *64*, 27–38.

(31) Reviews: (a) Cox, P. J.; Simpkins, N. S. *Tetrahedron: Asymm*etry **1991**, *2*, 1–26. (b) O'Brien, P. *J. Chem. Soc., Perkin Trans. 1* **1998**, 1439–1457. (c) O'Brien, P. *J. Chem. Soc., Perkin Trans. 1*, **2001**, 95–113.

(32) (a) Leonard, J.; Ouali, D.; Rahman, S. K. *Tetrahedron Lett*. **1990**, *31*, 739–742. (b) Vaulont, I.; Gais, H.-J.; Reuter, N.; Schmitz, E.; Ossenkamp, R. K. L. *Eur. J. Org. Chem*. **1998**, 805–826. (c) Lerm, M.; Gais, H.-J.; Cheng, K.; Vermeeren, C. *J. Am. Chem. Soc*. **2003**, *125*, 9653–9667. (d) Kramp, G. J.; Kim, M.; Gais, H.-J.; Vermeeren, C. *J. Am. Chem. Soc*. **2005**, *127*, 17910–17920. (e) Kim, M.; Gais, H.-J. *J. Org. Chem*. **2006**, *71*, 4642–4650. (f) van de Sande, M.; Gais, H.-J. *Chem. Eur. J*. **2007**, *13*, 1784–1795.

(33) (a) Lutz, V.; Baro, A.; Fischer, P.; Laschat, S. *Eur. J. Org. Chem.* **2010**, 1149–1157. (b) Lutz, V.; Park, N.; Rothe, C.; Krüger, C.; Baro, A.; Laschat, S. *Eur. J. Org. Chem.* **2013**, 761–771.

(34) (a) Overberger, C. G.; Marullo, N. P.; Hiskey, R. C. *J. Am. Chem. Soc*. **1961**, *83*, 1374–1378. (b) van de Sande, M. *Dissertation*, RWTH Aachen, **2006**.

(35) Jacks, T. E.; Belmont, D. T.; Briggs, C. A.; Horne, N. M.; Kanter, G. D.; Karrick, G. L.; Krikke, J. J.; McCabe, R. J.; Mustakis, J. G.; Nanninga, T. N.; Risedorph, G. S.; Seamans, R. E.; Skeean, R.; Winkle, D. D.; Zennie, T. M. *Org. Process Res. Dev.* **2004**, *8*, 201–212.

(36) Lepifre, F.; Clavier, S.; Bouyssou, P.; Coudert, G. *Tetrahedron* **2001**, *57*, 6969–6975.

(37) Askani, R.; Kirsten, R.; Dugall, B. *Tetrahedron* **1981**, *37*, 4437–4444.

(38) CCDC-1567523 (**4a**), CCDC-1567524 (**9a**), CCDC-1567526 (**4a**/Rh complex) and CCDC-1567527 (**9a**/Rh complex) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

(39) Additionally, 1,4-additions to chromone were tested. For details see Scheme S1, ESI.

(40) (a) Schmidt, F.; Stemmler, R. T.; Rudolph, J.; Bolm, C. *Chem. Soc. Rev.* **2006**, *35*, 454–470. (b) Marques, C. S.; Burke, A. J. *ChemCatChem* **2011**, *3*, 635–645. (c) Kobayashi, S.; Mori, Y.; Fossey, J. S.; Salter, M. M. *Chem. Rev.* **2011**, *111*, 2626–2704.

(41) (a) Arnold, J. S.; Nguyen, H. M. *J. Am. Chem. Soc.* **2012**, *134*, 8380–8383. (b) Arnold, J. S.; Cizio, G. T.; Heitz, D. R.; Nguyen, H. M. *Chem. Commun.* **2012**, *48*, 11531–11533. (c) Arnold, J. S.; Nguyen, H. M. *Synthesis* **2013**, *45*, 2101–2108. (d) Arnold, J. S.; Mwenda, E. T.; Nguyen, H. M. *Angew. Chem. Int. Ed.* **2014**, *53*, 3688–3692; *Angew. Chem.* **2014**, *126*, 3762–3766.

(42) Martínez, J. I.; Smith, J. J.; Hepburn, H. B.; Lam, H. W. *Angew. Chem. Int. Ed.* **2016**, *55*, 1108–1112; *Angew. Chem.* **2016**, *128*, 1120–1124.

(43) Sasaki, K. ; Hayashi, T. *Tetrahedron: Asymmetry* **2012**, *23*, 373–380.

(44) Flack, H. D. *Acta Cryst.* **1983**, *A39*, 876–881.

(45) Shintani, R.; Ichikawa, Y.; Takatsu, K.; Chen, F.-X.; Hayashi, T. *J. Org. Chem.* **2009**, *74*, 869–873.

(46) (a) Zassinovich, G.; Mestroni, G.; Gladiali, S. *Chem. Rev.* **1992**, *92*, 1051–1069. (b) Yip, S. Y. Y.; Aïssa, C. *Angew. Chem.* **2015**, *127*, 6974–6977; *Angew. Chem. Int. Ed.* **2015**, *54*,

6870–6873. (c) Yang, X.-H.; Dong, V. M. *J. Am. Chem. Soc.* **2017**, *139*, 1774–1777. (d) Cruz, F. A.; Zhu, Y.; Tercenio, Q. D.; Shen, Z.; Dong, V. M. *J. Am. Chem. Soc.* **2017**, *139*, 10641–10644.

(47) Turbomole V6.6 2014, a development of University of Karlsruhe and Forschungszentrum Karlsruhe GmbH, 1989–2007, TURBOMOLE GmbH, since 2007; available from http://www.turbomole.com.

(48) Steffen, C.; Thomas, K.; Huniar, U.; Hellweg, A.; Rubner, O.; Schroer, A. *J. Comput. Chem.* **2010**, *31*, 2967–2970.

(49) (a) Becke, A. D. *J. Chem. Phys.* **1993**, *98*, 5648–5652. (b) Lee, C.; Yang, W.; Parr, R. G. *Phys. Rev. B* **1988**, *37*, 785–789. (c) Miehlich, B.; Savin, A.; Stoll, H.; Preuss, H. *Chem. Phys. Lett.* **1989**, *157*, 200–206.

(50) Grimme, S.; Antony, J.; Ehrlich, S.; Krieg, H. *J. Chem. Phys.* **2010**, *132*, 154104-1–154104-19.

(51) (a) Grimme, S.; Ehrlich, S.; Goerigk, L. *J. Comput. Chem.* **2011**, *32*, 1456–1465. (b) Weigend, F. *Phys. Chem. Chem. Phys.* **2006**, *8*, 1057–1065. (c) Sierka, M.; Hogekamp, A.; Ahlrichs, R. *J. Chem. Phys.* **2003**, *118*, 9136–9148. (d) Eichkorn, K.; Treutler, O.; Öhm, H.; Häser, M.; Ahlrichs, R. *Chem. Phys. Lett.* **1995**, *242*, 652–660. (e) Eichkorn, K.; Weigend, F.; Treutler, O.; Ahlrichs, R. *Theor. Chem. Acc.* **1997**, *97*, 119–124.

(52) Weigend, F.; Ahlrichs, R. *Phys. Chem. Chem. Phys.* **2005**, *7*, 3297–3305.

(53) Klamt, A.; Schüürmann, G. *J. Chem. Soc. Perkin Trans. 2* **1993**, 799–805.

(54) Grimme, S. *J. Chem. Phys.* **2006**, *124*, 034108-1–034108-16

(55) C. M. Cain, R. P. C. Cousins, G. Coumbarides, N. S. Simpkins, *Tetrahedron* **1990**, *46*, 523–544

(56) H. Yamada, T. Kawate, A. Nishida, M. Nakagawa, *J. Org. Chem.* **1999**, *64*, 8821–8828.

(57) Y. Huang, T. Hayashi, *J. Am. Chem. Soc.* **2015**, *137*, 7556–7559; b) T. Hayashi, T. Senda, Y. Takaya, M. Ogasawara, *J. Am. Chem. Soc.* **1999**, *121*, 11591–11592.

(58) M. Barbarotto, J. Geist, S. Choppin, F. Colobert, *Tetrahedron: Asymmetry* **2009**, *20*, 2780–2787.

(59) G.-X. Li, J. Qu, *Chem. Commun.* **2012**, *48*, 5518–5520.

(60) J. T. Reeves, M. D. Visco, M. A. Marsini, N. Grinberg, C.A. Busacca, A. E. Mattson, C. H. Senanayake, *Org. Lett.* **2015**, *17*, 2442–2445.

(61) J. L. García Ruano, J. Alemán, M. Belén Cid, A. Parra, *Org. Lett.* **2005**, *7*, 179–182.

(62) S. Helbig, *Dissertation*, Universität Stuttgart, 2010.

(63) N. Tokunaga, Y. Otomaru, K. Okamoto, K. Ueyama, R. Shintani, T. Hayashi, *J. Am. Chem. Soc.* **2004**, *126*, 13584–13585.

(64) G.-Z. Zhao, G. Sipos, A. Salvador, A. Ou, P. Gao, B. W. Skelton, R. Dorta, *Adv. Synth. Catal.* **2016**, *358*, 1759–1766.

(65) C.-G. Feng, Z.-Q. Wang, P. Tian, M.-H. Xu, G.-Q. Lin, *Chem. Asian J.* **2008**, *3*, 1511–1516.

Graphical Abstract (Table of contents)