Chiral Discrimination in Rhodium(I) Catalysis by 2,5-Disubstituted 1,3a,4,6a-Tetrahydropentalenatole Ligands—More Than Just a Twist of the Olefins?

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Supporting Information

ABSTRACT: Chiral dienes are useful ligands in a number of asymmetric transition-metal-catalyzed reactions. Here, we evaluate the efficiency of 2,5-disubstituted 1,3a,4,6a-tetrahydropentalenates as ligands to rhodium(I). 2,5-Dibenzyl and diphenyl tetrahydropentalenates were synthesized in two steps and resolved, either chromatographically, or through fractional crystallization of diastereomeric rhodium(I) salts. When evaluated in a 1,4-arylation reaction, the 2,5-dibenzyl ligand gave up to 99% ee. The use of a well-defined rhodium complex as catalyst, Cs₂CO₃ as the base, and toluene/water as solvent was found to have a pronounced beneficial effect on the selectivity of the reaction. The homologous 2,5-diphenyl ligand on the other hand proved to be highly prone to racemization/loss of chirality during catalysis. Control experiments reveal that this rearrangement proceeds via a rhodium-mediated 1,3-hydride shift. Implications for ligand design and catalysis are discussed.

INTRODUCTION

Chiral bis-macroyclic diene ligands have a broad utility in asymmetric catalysis. Exceptional levels of enantiodiscrimination have been achieved, particularly in rhodium- and iridium-catalyzed reactions, but also with metals like palladium and ruthenium. Examples are plentiful and include C–C bond forming reactions like cross-couplings, asymmetric cyclizations, hydroacylations, polymerizations, and cyclopropanations, as well as strategy-level reactions like cycloadditions. Ligands of this type have found particular use in variations of asymmetric arylation reactions.

Due to the unfunctionalized nature of most diene ligands beyond the metal-binding motif, synthesis and resolution is challenging. As a consequence, fewer ligands of this type are available compared to other ligand classes. With new applications of diene catalysts continuing to emerge, there is a need for expanding the library of efficient and readily available ligands of this type. A hydrocarbon framework with utility in this context is the 1,3a,4,6a-tetrahydropentalenene structure. With substituents at the 3 and 6 positions, this structure was independently developed as an efficient ligand in asymmetric catalysis by Laschat and Lin/Xu (Figure 1). Recently, computational studies by Kantchev have suggested that a variation on this theme, a repositioning of the steering substituents from 3,6- to 2,5-positions would significantly enhance the enantioselectivity in catalysis. In particular, ee’s in excess of 99.9% were predicted in Hayashi–Miyaura-type arylation reactions with 3b as the steering ligand. This unusually high selectivity would originate from a beneficial cooperative effect of the large torsional twist angle between the coordinating olefins (C2–C3–C6–C5) and a favorable positioning of the steering substituents for steric interactions with the enone substrates.

As part of our program for developing chiral annulene-type ligands like 2 for asymmetric catalysis, we became interested in evaluating also the 2,5-disubstituted tetrahydropentalene framework. Structures of this type are interesting, not least because the twisted olefin geometry represents a complimentary extreme to the parallel olefins of both dibenz[a,e]cyclooctatetraenes and more commonly studied norbornadiene and bicyclo[2.2.2]octa-2,5-diene-type ligands.

Moreover, tetrahydropentalenates with this pattern of substitution are intriguing from a stereochemical viewpoint as the steering substituents are positioned on a pseudoplane of symmetry in the ligand framework and mirror symmetry is broken only by the orientation of the olefins. During the preparation of this manuscript, an independent study on this topic was reported by Laschat and co-workers. In light of this study, we here present our approach to enantiomerically pure di-μ-chlorobis rhodium(I) complexes of 3a and 3b, and the evaluation of these in asymmetric catalysis. Using a well-defined rhodium complex of 3a as catalyst, up to 99% ee was achieved in a 1,4-arylation reaction, which is higher than what was previously reported. The corresponding diphenyl substituted 3b gave a modest 44% ee when evaluated in the same context. A series of control experiments reveal that a facile racemization...
of 3b via an allylic C−H insertion/olefin isomerization process during catalysis accounts for the low selectivity.

## RESULTS AND DISCUSSION

At the outset, we envisioned a divergent synthesis where the steering substituents of the 2,5-disubstituted tetrahydroptalene framework would be installed by cross-coupling reactions. To this end, ditriphenyl 5 was targeted. In practice, this compound was synthesized in a single step from the commercially available Weiss ketone (4) by trapping a dienolate with N-(2-pyridyl)bis(trifluoromethanesulfonimide) (Scheme 1). After screening conditions with the aim of increasing the selectivity for the desired C2 symmetric dienolate, we found that treatment of 4 with NaHMDS, in tetrahydrofuran (THF), at 0 °C for 3 h followed by addition of the triflating reagent gave 5 and 6 in 86% yield with a useful 77/23 selectivity in favor of the desired C2-symmetric 5. The regioisomers could be chromatographically separated but were typically carried through the subsequent steps as a mixture.

A Negishi coupling with BnZnBr using the PEPPSI−IPr catalyst system then provided a mixture of 3a and 7 in a combined yield of 89%. A single-crystal X-ray diffraction (scXRD) structure of rac-3a showed that the structure adopts a folded shape similar to 1 with a pronounced 30° twist angle of the olefins (defined by the torsion C2−C3−C6−C5). The corresponding diphenyl ligand 3b was similarly synthesized using the Kumada coupling. It is noteworthy that even when using an essentially pure sample of 5 for this cross coupling, the ratio of 3b−8 was not improved beyond 83:17. Presumably, this is a result of a palladium-mediated olefin isomerization during catalysis. In contrast, the isomeric ratio of the starting materials 5 and 6 was conserved in the product distribution in the synthesis of 3a. Attempts to synthesize the corresponding 2,5-dimethyl and 2,5-disopropyl ligands under the same conditions proved unsuccessful despite extensive experimentation.

Resolution of the dibenzyl ligand 3a was then readily accomplished by high-performance liquid chromatography (HPLC) on a chiral stationary phase (Chiracel OJ-H, 250 × 10 mm, 5 μm). The (S,S)-isomer was obtained as a mixture with 7.

Ligand exchange of chlorobis(ethylene)rhodium(1) dimer with (R,R)-3a proceeded cleanly to give (R,R)-9a in 65% yield following recrystallization from chloroform/diethyl ether. Complexation of the mixture of (S,S)-3a and 7 obtained from HPLC resolution under the same conditions with an amount of rhodium corresponding to the amount of 3a provided also (S,S)-9a after recrystallization. A scXRD structure of (S,S)-9a was solved and the absolute configuration of this compound, and by extension of 3a, was established from anomalous dispersion (Flack = −0.03(3)). Structurally, a pronounced increase in the folding angle between the two five-membered rings of the ligand, resulting from coordination to the rhodium atom, is seen in 9a compared to free 3a. The torsion angle C3−C3a−C6a−C6 is reduced from 108° in 3a to 77° in 9a. This conformational change also reduces the twist angle between the coordinating olefins to 22°.

For the resolution of diphenyl ligand 3b, we employed the Grützmachers method of fractional crystallization of diastereomeric rhodium 2,2′-diamino-1,1′-binaphthyl (DABN) salts. This method could be used also for the resolution of 3a, but due to the air sensitivity of rhodium complexes with this ligand, chromatographic resolution was preferred. Thus, di-μ-chlorobis rhodium dimer rac-9b was formed as a single detected diastereomer (1H NMR spectroscopy) using a procedure similar to that of 9a. When performing the complexation from a mixture of rac-3b and 8, a complete selectivity for complexation of 3b could be achieved by using a limiting amount of the rhodium precursor. The structural assignment of rac-9b was corroborated by solving a scXRD structure.

Treatment of 9b with (+)-DABN in the presence of a silver salt then gave the cationic complex 10 as a 50:50 mixture of diastereomers in essentially quantitative yield. Pleasingly, the diastereomer with an (S,S)-configuration of the ligand had a considerably lower solubility in chlorinated solvents than the (R,R)-ligand diastereomer. Recrystallization of this mixture from chloroform/benzene, followed by trituration with chloroform, gave (S,S)-10 as a single detected diastereomer (1H NMR spectroscopy). A scXRD of this structure was solved, which...
provided a stereochemical assignment using the absolute configuration of the DABN moiety as a reference.

To complete the synthesis of 9b, (S,S)-3b was first released from 10 by treatment with 1,5-cyclooctadiene (COD). A ligand exchange with chlorobis(ethylene)rhodium dimer then provided (S,S)-9b in good yield. Attempts to convert (S,S)-10 directly into (S,S)-9b by treatment with HCl proved unsuccessful. Instead, a mixture of 3b and 8 was recovered in a 79:21 ratio. Surprisingly, 3b obtained using this method was found to be essentially racemic.

To investigate whether this isomerization was Brønsted acid-catalyzed, the ligand was refluxed with p-toluene sulfonic acid in THF/D2O for 24 h. No isomerization or deuterium incorporation electrospray ionization mass spectrometry (ESI-MS) was observed in this experiment, which implies that the isomerization was indeed mediated by rhodium.

A comparison between the solid-state structure of rac-9b and 9a revealed a highly similar binding geometry: the olefin twist torsion in 9b was 23° and the folding angle between the rings, 78°. In terms of stability, crystalline 9b could be handled in air without visible deterioration. Complex 9a, on the other hand, was found to be prone to aging and was best prepared freshly or stored in a glovebox to prevent deterioration over time.

With access to both targeted catalysts 9a and 9b, we turned to evaluate their respective catalytic properties. For this purpose, the rhodium-catalyzed 1,4-addition of boronic acids to cyclohexenone was selected as a suitable benchmark reaction. The dibenzyl ligand complex 9a system was first evaluated under a series of commonly employed conditions for this transformation (Table 1). Previous work achieved 41% ee, 25% yield, in this reaction by in situ complexation of 3a to rhodium and using KOH as the base.19 We found that the combination of preformed 9a as a catalyst together with Cs2CO3 in toluene/water gave up to 99% ee. This constitutes synthetically relevant levels of selectivity and is a significant enhancement compared to what was previously reported. It seems likely that the key factor behind this difference is the use of a well-defined preformed catalyst, but the performance of the system is clearly also dependent on the precise reaction conditions.22 The observed level of selectivity with 9a is

Scheme 1. Synthesis of Enantiomerically Pure Catalysts 9a and 9b

(a) A 92:8 mixture of 5 and 6 was used as starting material; (b) yield given for the shown diastereomer. See Supporting Information for details; (c) thermal ellipsoids shown at 30% probability. Hydrogen atoms, noncoordinating counter ions, and solvate molecules are omitted for clarity; (d) the stereochemical descriptor refers to the configuration of the diene ligand.
with HCl (vide infra) was suggestive of a rhodium-mediated facile isomerization/racemization of source. This surprisingly low selectivity combined with the outcome nor did a switch to an aryl zinc reagent as the phenyl conditions and reagents neither signi

in the same reaction (Scheme 2). Variations of the reaction homologous diphenyl ligand complex a good compromise (Table 1, entry 1).

and yield, the use of a boroxine as the aryl source appears to be noteworthy also as it supersedes the performance of 3,6-ba
determined by HPLC on a chiral stationary phase. The major product enantiomer was (R)-11a. a Determined by 1H NMR spectroscopy using CH2Br2 as internal standard. b 0.5 equiv of base was used. DCE: 1,2-dichloroethane; IPA: isopropyl alcohol.

table 1. Catalytic Performance of 9a in 1,4-Arylation of Cyclohexenone

| entry | base | boronic acid derivative | solvent | ee (%) | yield (%) |
|-------|------|-------------------------|---------|--------|----------|
| 1     | Cs2CO3 | (PhBO)3 | PhMe/H2O | 97     | 92       |
| 2     | Cs2CO3 | PhB(OH)3 | PhMe/H2O | 99     | 56       |
| 3     | Cs2CO3 | PhBF3K | PhMe/H2O | 88     | 44       |
| 4     | Cs2CO3 | phenylpinacol boronic ester | PhMe/H2O | 94     | 71       |
| 5     | Cs2CO3 | PhB(OH)3 | dioxane/H2O | 91     | 63       |
| 6     | Cs2CO3 | PhB(OH)3 | DCE/IPA | 92     | 67       |
| 7     | Cs2CO3 | 4-F-PhB(OH)3 | PhMe/H2O | 98     | 64       |
| 8     | Cs2CO3 | 4-MeO-PhB(OH)3 | PhMe/H2O | 92     | 81       |
| 9     | Cs2CO3 | 2-MePhB(OH)3 | PhMe/H2O | 87     | 31       |
| 10    | K2PO4 | PhB(OH)3 | dioxane/H2O | 80     | 63       |
| 11    | KOH | PhB(OH)3 | dioxane/H2O | 61     | 63       |
| 12    | iBuOK (PhBO)3 | PhMe/H2O | 97     | 82       |

"In all entries, 10% v/v of the protic co-solvent was used. b Determined by HPLC on a chiral stationary phase. The major product enantiomer was (R)-11a. c Determined by 1H NMR spectroscopy using CH2Br2 as internal standard. d 0.5 equiv of base was used. DCE: 1,2-dichloroethane; IPA: isopropyl alcohol.

noteworthy also as it supersedes the performance of 3,6-diphenyl 1,3a,4a,6-tetrahydropentalenes 1 in the same reaction (91% ee).

Good results were obtained in this reaction with electron-rich and electron-deficient boronic acids. The sterically more demanding 2-toluenoboronic acid on the other hand gave lower yield and a selectivity below 90% ee (Table 1, entries 7–9). On the balance between operational simplicity, selectivity, and yield, the use of a boroxine as the aryl source appears to be a good compromise (Table 1, entry 1).

The major product enantiomer of 11a showed an (R)-configuration in all entries using (R,R)-9a as the catalyst, which follows the predictions of ref 13 and the Hayashi’s quadrant model for related diene-ligand structures (see Supporting Information for details). 15

In stark contrast to the excellent enantioselectivity of 9a, the homologous diphenyl ligand 9b gave a modest 44% ee in the same reaction (Scheme 2). Variations of the reaction conditions and reagents neither significantly improved this outcome nor did a switch to an aryl zinc reagent as the phenyl source. This surprisingly low selectivity combined with the facile isomerization/racemization of 9b upon treatment of 10 with HCl (vide infra) was suggestive of a rhodium-mediated isomerization of the ligand also during catalysis. 23

To prove this possibility, we conducted a series of control experiments. First, we explored the possibility that the ligand was released from rhodium during catalysis. We were however not able to induce a ligand exchange of 9b even with large excess of cyclohexenone or phenyl boronic acid. Moreover, no free ligand could be detected in the reaction mixture during catalytic experiments with this complex (thin-layer chromatography (TLC) control and 1H NMR spectroscopy of the crude reaction mixture).

A catalytic experiment was then conducted wherein the water was replaced for D2O (Scheme 3, entry a). In this experiment, the ligand was also released from rhodium by addition of COD to the reaction mixture after full conversion of the starting materials was reached. From this experiment, 3b and 8 were obtained in a 28:72 ratio in favor of the meso-ligand. Moreover, no deuterium incorporation into the ligand framework could be detected by 1H NMR spectroscopy or ESI-MS, which suggested that isomerization is a purely intramolecular 1,3-hydride shift mediated by the metal center. When conducting similar experiments, but excluding individual components of the catalytic mixture, only trace isomerization was seen (Scheme 3, entries b–d). Finally, 9b was found to not isomerize spontaneously when dissolved in organic solvents and was also unable to catalyze the isomerization of free 3b, even under mild heating (50 °C).

Combined, our interpretation of these experiments is that isomerization/racemization of 3b occurs during catalysis following the general mechanism outlined in Scheme 4. Additional experiments are however needed to identify the precise nature of the intermediate(s) capable of triggering the apparent C–H insertion/hydride 1,3-migration.

Given such processes are facilitated by increased electron density on the metal center, 24 it seems reasonable that intermediates like rhodium-oxa-allyl- and/or rhodium-phenyl complexes are the culprits. The higher susceptibility toward isomerization of 3b compared to 3a is attributed to the inductive electron-withdrawing nature of the phenyl substituent, which weakens the allylic C–H bond, thus making it more electrophilic.

### CONCLUSIONS

In summary, we have evaluated the potential of 2,5-disubstituted 1,3a,4a,6-tetrahydropentalenes to induce asymmetry in rhodium(I) catalysis. The results show that with an appropriate choice of steering substituents, here benzyl groups, this ligand class is highly capable of biasing catalytic reactions like the Hayashi–Miyaura 1,4 arylations with up to 99% ee. A diphenyl-substituted ligand of the same type on the other hand proved to be highly prone to loss of chirality/enantiomeric purity during catalysis through a rhodium-mediated isomerization. This behavior emphasizes the propensity of rhodium(I)
to insert into allylic C−H bonds of diene ligands as an important consideration in the design of novel ligands of this type for transition-metal catalysis. On a more general note, such intermediates are commonly invoked as catalyst decomposition pathways, but are perhaps deserving of more consideration also as intermediates in highly efficient catalyst systems: both as off-cycle intermediates and to generate alternative catalytically competent species through rearrangement of the ligand structure. This study also exemplifies that purely theoretical predictions are useful inspirational tool for discovery. It is however equally clear that computational approaches are still limited when it comes to capturing the full complexity of a catalytic system. Without experimental verification, alternative reaction pathways such as the here described ligand racemization, and the dependence of enantioselectivity on solvent, base, and phenyl reagent are easily overlooked.

Finally, we envision that the efficiency in catalysis, simple synthesis, and straightforward resolution of dibenzyl ligand 3b will serve as inspiration for further refined ligands, and moreover ligands of this type will find use in chemical synthesis and coordination chemistry. Such investigations are ongoing in our laboratory and will be reported in due course.

**EXPERIMENTAL SECTION**

**General Information.** Air- and moisture-sensitive reagents, solvents, and solutions were transferred via syringe or stainless-steel cannula under a dry argon atmosphere. Commercial reagents and solvents were used as received without further purification unless otherwise noted. Cyclohexene was distilled using a Hickman still prior to use. CH2Cl2, diethyl ether, THF, toluene, n-hexane, and acetonitrile were obtained from a dry solvent dispense system. Commercially available metal salts were stored and handled in an argon-filled glovebox. Bicyclo[3.3.0]octane-3,7-dione (4) was synthesized following a procedure by Weiss and co-workers.20b 1H NMR signals were reported in chemical shifts downfield from SiMe4 using the respective residual solvent peak as internal standard (chloroform = 7.26 ppm; CD2Cl2 = 5.30 ppm; MeCN = 1.94 ppm) and listed as follows: chemical shifts (δ, ppm), multiplicity, coupling constant(s) in Hz, and integration. 13C NMR signals were reported in chemical shifts downfield from SiMe4, using the respective residual solvent peak as internal standard. (CDCl3 = 77.16 ppm; CD2Cl2 = 53.84 ppm; MeCN-d3 = 118.3 ppm). Unless otherwise indicated, all products for which yields are given were >95% pure by 1H NMR spectroscopy and TLC (where applicable).

1,3a,4,6a-Tetrahydropentalene-2,5-diyl Bis-(trifluoromethanesulfonate) (5). Sodium bis(trimethylsilyl) amide (7.0 mL, 2M in THF, 14.0 mmol) was diluted with THF (100 mL) and the resulting solution was cooled to 0 °C. A solution of bicyclo[3.3.0]octane-3,7-dione (4) (643 mg, 4.65 mmol) in THF (50 mL) was then added over 5 min. The resulting mixture was stirred for 4 h at 0 °C, before a solution of N-(2-pyridyl)bis(trifluoromethanesulfonimide) (5.0 g, 14.0 mmol) in THF (20 mL) was added in one portion. The reaction mixture was allowed to warm up to room temperature over 3 h during which a color change from yellow to dark brown was observed. The reaction mixture was then diluted with n-heptane (300 mL) and washed with HCl (3 × 200 mL, 1M aq) and brine (200 mL). The organic phase was separated, dried using a phase separator, and concentrated under reduced pressure. The residues were purified by flash chromatography (12.5% EtOAc/heptane) to give 5 and 6 (ratio 77:23) as a pale-yellow oil (1.61 g, 86%). Analytical data for ditriflate 5. Rf: 0.57 in 25% EtOAc/heptane (stains yellow with KMnO4 stain);
Fourier transform infrared (FTIR) (neat): 2936 (w), 2868 (w), 1419 (s), 1200 (s) cm⁻¹; ¹H NMR (CDCl₃, 400 MHz) δ: (major) 5.55 (d, J = 1.6 Hz, 2H), 3.58–3.53 (m, 2H), 2.96–2.88 (m, 2H), 2.42 (ddd, J = 16.5, 4.4, 2.8 Hz, 2H); (minor) 5.66 (dd, J = 4.4, 2.1 Hz, 2H), 3.90–3.81 (m, 1H), 3.26–3.13 (m, 1H), 3.03–2.98 (m, 2H), 2.52–2.44 (m, 2H) ppm; ¹³C NMR (CDCl₃, 101 MHz) δ: (major) 148.8, 120.0, 118.6 (q, J = 14.3 Hz, 2H), 3.35 (d, J = 7.9 Hz, 1H), 3.36 (br s, 4H), 3.05 (m, 2H), 2.52 (m, 2H) ppm; ¹³C NMR (MeCN-d₃): (major) 148.8, 120.0, 118.6 (q, J = 14.3 Hz, 2H), 3.35 (d, J = 7.9 Hz, 1H), 3.36 (br s, 4H), 3.05 (m, 2H), 2.52 (m, 2H) ppm; HRMS-ESI (m/z): [M + Na]⁺ Calcd for C₇₇H₃₇F₆O₆S₂Na 424.9564; found: 424.9569.

To a stirred clear yellow solution of PEPPSI–IPr (67.6 mg, 0.08 mmol) and LiBr (346 mg, 3.98 mmol) in THF (30 mL) was added a 2,5-Diphenyl-1,3a,4,6a-tetrahydropentalene (rac-3a) (0.40 g, 0.29 mmol) in CH₂Cl₂ (20 mL). The reaction was stirred for 4 days, then filtered through celite and concentrated under reduced pressure. The residues were purified by flash chromatography (0–3% EtOAc/heptane) to give 3a and 7 (ratio 93:7) as a colorless oil (70 mg, 89% yield). ¹H NMR (CDCl₃, 400 MHz) δ: 7.52–7.45 (m, 4H), 7.40–7.31 (m, 4H), 7.30–7.23 (m, 2H), 6.11 (d, J = 1.0 Hz, 2H), 3.88–3.78 (m, 2H), 3.14–3.02 (m, 2H), 2.74 (dd, J = 15.9, 1.3 Hz, 2H); (minor) 7.52–7.45 (m, 4H), 7.40–7.31 (m, 4H), 7.30–7.23 (m, 2H), 6.24 (q, J = 2.2 Hz, 2H), 4.15 (d, J = 6.6 Hz, 1H), 3.40–3.29 (m, 1H), 3.19 (dd, J = 16.0, 9.3 Hz, 2H), 2.73–2.63 (m, 2H) ppm; ¹³C NMR (CDCl₃, 101 MHz) δ: (major) 140.0, 136.6, 130.3, 128.3, 127.1, 125.9, 48.6, 38.7; (minor) 141.4, 136.7, 128.7, 127.2, 127.0, 125.8, 59.4, 41.7, 39.1 ppm; FTIR (neat): 3048 (w), 2909 (w), 2845 (w), 1492 (m) cm⁻¹; HRMS-ESI (m/z): [M + H]⁺ Calcd for C₁₆H₁₆BrCl 295.0526; found: 295.0525.

To a dark red solution of (S,S)-bis((R,R)-(+)-1,1′-dinaphtyl-2,2′-diamine)[Rh((S,S)-1,1′-dinaphtyl-2,2′-diamine)] +SF₆⁻ (Irrs-CN⁺) (0.40 g, 0.46 mmol) in CH₂Cl₂ (30 mL) was added a dark red solution of (R,R)-9b (0.41 g, 0.39 mmol) in CH₂Cl₂ (20 mL). The reaction was stirred for 18 h in the dark. The precipitate was removed by filtration through celite eluting with CH₂Cl₂. The filtrate was concentrated under reduced pressure to give a quantitative yield of 10 as a mixture of diastereomers. Recrystallization from chloroform/benzene and sequential washing with chloroform afforded diastereomically pure (S,S)-10 as dark red rods (547 mg, 47%). Optical rotation: [α]D²⁰ = +752 (c = 0.5, CH₂Cl₂); FTIR (neat): 3301 (w), 2921 (w), 2830 (w), 1756 (m), 1707 (s), 1645 (m), 1599 (m), 1512 (m), 1448 (m), 1439 (m), 1384 (m), 1350 (s), 1310 (m), 1295 (m), 1291 (m), 1273 (m), 1257 (m), 1159 (m) cm⁻¹; HRMS-ESI (m/z): [M – Cl]⁺ Calcd for C₉₀H₇₂BrCl⁺ 581.4917; found: 581.4918.

To a stirred clear yellow solution of PEPPSI–IPr (196 mg, 0.29 mmol) and LiBr (67.6 mg, 0.10 mmol) in CH₂Cl₂ (20 mL) was added a mixture of (R,R)-3a (1.05 g, 1.33 mmol), AgSbF₆ (0.91 g, 2.65 mmol), (R)-(−)-1,1′-binaphtyl-2,2′-diamine (0.76 g, 2.65 mmol) dissolved in CH₂Cl₂ (30 mL) and then stirred for 18 h in the dark. The precipitate was removed by filtration through celite eluting with CH₂Cl₂. The filtrate was concentrated under reduced pressure to give a quantitative yield of 10 as a mixture of diastereomers. Recrystallization from chloroform/benzene and sequential washing with chloroform afforded diastereomically pure (S,S)-10 as dark red rods (547 mg, 47%). Optical rotation: [α]D²⁰ = +752 (c = 0.5, CH₂Cl₂); FTIR (neat): 3301 (w), 2921 (w), 2830 (w), 1756 (m), 1707 (s), 1645 (m), 1599 (m), 1512 (m), 1448 (m), 1439 (m), 1384 (m), 1350 (s), 1310 (m), 1295 (m), 1291 (m), 1273 (m), 1257 (m), 1159 (m) cm⁻¹; HRMS-ESI (m/z): [M – Cl]⁺ Calcd for C₉₀H₇₂BrCl⁺ 581.4917; found: 581.4918.
was added directly to a silica-gel column and eluted with 0–3% EtOAc/heptane. The product containing fractions were pooled and concentrated under reduced pressure to give (S,S)-3b as colorless microcrystalline needles (82.0 mg, 70%). Optical rotation: \([\alpha]_D^{25} = +54^\circ\) (c = 0.5, CHCl_3); mp: 136.8–137.8 °C (microcrystalline needles, open capillary).

Chloro((S,S)-9b)rhodium(I) Dimer ((S,S)-9b). To chlorobis-(ethylene)rhodium dimer (55 mg, 0.14 mmol) was added a solution of (ethylene)rhodium dimer (73 mg, 0.28 mmol) in CH_2Cl_2 (10 mL). The resulting mixture was stirred for 24 h, then filtered through celite, and concentrated under reduced pressure. Washing the resulting amorphous solid with n-hexane, followed by concentration under reduced pressure afforded (S,S)-9b as a red powder (83.4 mg, 75%). Optical rotation: \([\alpha]_D^{25} = +136^\circ\) (c = 0.5, CHCl_3).

General Procedure for Catalytic 1,4-Addition of Boronic Acid Derivatives to Cyclohexanone. A septum-capped vial, equipped with a magnetic stirring bar, was charged with the indicated amount of base and boronic acid derivative. The vial was transferred to a glovebox, charged with catalyst (2 mol %) and sealed. Degassed organic solvent and protic co-solvent (10% v/v) were consecutively added, followed by the enone. The reaction mixture was then stirred under heating (50 °C) until completion (TLC analysis). Filtration through a short pad of silica/MgSO_4, followed by concentration under reduced pressure and purification by silica-gel chromatography (EtOAc/heptane) afforded analytically pure ketones 11a–d.

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