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Guide to Enantioselective Dirhodium(II)-Catalyzed Cyclopropanation with Aryldiazoacetates

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Abstract

Catalytic enantioselective methods for the generation of cyclopropanes has been of longstanding pharmaceutical interest. Chiral dirhodium(II) catalysts prove to be an effective means for the generation of diverse cyclopropane libraries. Rh₂(*R*-DOSP)₄ is generally the most effective catalyst for asymmetric intermolecular cyclopropanation of methyl aryldiazoacetates with styrene. Rh₂(*S*-PTAD)₄ provides high levels of enantioinduction with *ortho*-substituted aryldiazoacetates. The less-established Rh₂(*R*-BNP)₄ plays a complementary role to Rh₂(*R*-DOSP)₄ and Rh₂(*S*-PTAD)₄ in catalyzing highly enantioselective cyclopropanation of 3-methoxy-substituted aryldiazoacetates. Substitution on the styrene has only moderate influence on the asymmetric induction of the cyclopropanation.

Keywords

Asymmetric cyclopropanation; Cyclopropanes; Donor/acceptor carbenoids; Dirhodium catalysis; Phenyl diazoacetate

1. Introduction

The metal-catalyzed decomposition of diazo compounds in the presence of alkenes is a general method for the stereoselective synthesis of cyclopropanes.^{1,2} We have previously shown the rhodium-catalyzed cyclopropanation of donor/acceptor carbenoids to be effective for the enantioselective synthesis of cyclopropanes with one or more quaternary stereogenic centers.³⁻⁶ As many cyclopropyl amines are known to have significant CNS activity,^{7,8} we have initiated a program to use our cyclopropanation methodology to access novel diarylcyclopropylamines as potential therapeutic agents (Scheme 1). For the methodology to be broadly useful in drug discovery, access to a range of diarylcyclopropyl derivatives

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Supplementary Material: Detailed experimental for the compounds, HPLC traces for all chiral compounds, ¹H NMR and ¹³C NMR spectra for all new compounds are described in Supplementary data. Supplementary data associated with this article can be found in the online version.

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with high levels of enantioenrichment is required. Herein, we define the optimal catalysts for the cyclopropanation with various types of methyl aryldiazoacetates.

Three chiral dirhodium(II) catalysts were selected for this study (Figure 1). The first catalyst, $\text{Rh}_2(\text{R-DOSP})_4$, is considered to be the optimal catalyst for the reactions of donor/acceptor carbenoids when the acceptor group is a methyl ester.^{1,4} The substrate scope of $\text{Rh}_2(\text{R-DOSP})_4$ -catalyzed cyclopropanation is quite broad in terms of both the trapping agent and the donor group on the carbenoid.^{3,4,9-18} However, a detailed study on the influence of the aryl substituent of the aryldiazoacetate on $\text{Rh}_2(\text{R-DOSP})_4$ -catalyzed cyclopropanation has not been conducted. The second catalyst, $\text{Rh}_2(\text{S-PTAD})_4$, is the optimal chiral catalyst when the acceptor group in the donor/acceptor carbenoid is a phosphonate,¹⁹ trifluoromethyl,²⁰ cyano,²¹ or keto group.²² Due to the perceived superiority of $\text{Rh}_2(\text{R-DOSP})_4$ in the reactions of aryldiazoacetates, $\text{Rh}_2(\text{S-PTAD})_4$ has not been thoroughly evaluated in the reactions of this class of carbenoid precursor. The third catalyst, $\text{Rh}_2(\text{R-BNP})_4$, is an interesting catalyst of D_4 -symmetry that has been applied to a number of carbenoid reactions,²³⁻²⁷ but has not been previously evaluated in the cyclopropanation of donor/acceptor carbenoids.

2. Results and Discussion

The study began by exploring the effect of aryl substitution on the enantioselectivity in the cyclopropanation of styrene by aryldiazoacetates. The results for a series of aryldiazoacetates (**1a-l**) using the three chiral dirhodium catalysts $\text{Rh}_2(\text{R-DOSP})_4$, $\text{Rh}_2(\text{S-PTAD})_4$ and $\text{Rh}_2(\text{R-BNP})_4$ are summarized in Table 1. Excellent levels of diastereoselectivity were achieved in all cases (>95:5 dr) and the isolated yields of the cyclopropanes were generally high, ranging from 63-98%. The absolute configuration of the major isomer of the cyclopropanes is tentatively assigned as 1*S*,2*R*.²⁸ $\text{Rh}_2(\text{R-DOSP})_4$ provided high levels of enantioinduction when unsubstituted (**1a**) or 4-substituted (**1b-e**) methyl aryldiazoacetates were employed as substrates (Table 1, entries 1-5, 87-90% ee). In general, $\text{Rh}_2(\text{S-PTAD})_4$ and $\text{Rh}_2(\text{R-BNP})_4$ gave <60% ee in the cyclopropanation reactions of unsubstituted or 4-substituted aryldiazoacetates with these same substrates. The one exception, however, is the reaction of 4-methoxyphenyldiazoacetate **1e** with $\text{Rh}_2(\text{S-PTAD})_4$, which gave the cyclopropane **3e** in exceptionally high enantioselectivity (entry 5, 96% ee). $\text{Rh}_2(\text{R-DOSP})_4$ also performed well in the reactions of 2-substituted aryldiazoacetates **1f** (entry 6, 92% ee) and **1g** (entry 7, 86% ee), and moderately well with 3,4-dichlorophenyldiazoacetate **1h** (entry 8, 82% ee), confirming that $\text{Rh}_2(\text{R-DOSP})_4$ is the optimal catalyst for a range of aryldiazoacetates. The enantioselection with $\text{Rh}_2(\text{S-PTAD})_4$ is extremely variable. However, in certain cases, it provides exceptional levels of enantioselectivity, as seen in the reaction with 2-chlorophenyldiazoacetate **1f**, which generates the cyclopropane **3f** in 97% ee (entry 6).

Interestingly, $\text{Rh}_2(\text{R-DOSP})_4$ fails to provide high levels of enantioinduction when the aryldiazoacetate contains a 3-methoxy substituent (**1i-l**) (entries 9-12), especially when the ring is polysubstituted (**1i**, **k-l**). In these cases, the cyclopropanes **3i**, **k-l** are produced in 28-56% ee (entries 9, 11-12). $\text{Rh}_2(\text{S-PTAD})_4$ is an effective catalyst only in the case of 3, 4-dimethoxyphenyldiazoacetate **1i**, generating the cyclopropane **3i** in 94% ee (entry 9). In contrast, $\text{Rh}_2(\text{R-BNP})_4$ is an extremely effective catalyst with all of the 3-methoxy substituted aryldiazoacetates **1i-l**, generating the cyclopropanes **3i-l** in 88-97% ee (entries 9-12).

One of the most attractive features of $\text{Rh}_2(\text{R-DOSP})_4$ and $\text{Rh}_2(\text{S-PTAD})_4$ as chiral catalysts is that they are capable of operating at low catalyst loadings.²⁹ As $\text{Rh}_2(\text{R-BNP})_4$ was found to be the optimal catalyst for 3-methoxyaryldiazoacetate derivatives, we investigated

whether it could also operate at low catalyst loading. Reactions of aryldiazoacetate **1i**, with successively lower loadings of $\text{Rh}_2(\text{R-BNP})_4$ are summarized in Table 2. $\text{Rh}_2(\text{R-BNP})_4$ was effective at catalyzing highly enantioselective cyclopropanation with catalyst loadings of 1.0 and 0.5 mol%, providing **3i** with virtually the same level of enantioselectivity (entry 1 vs. 2, 97% ee vs. 96% ee). When the catalyst loading was decreased further to 0.1 mol% a more significant drop in the level of enantioselectivity was observed (entry 3, 91% ee). Further decreasing the catalyst loading to 0.01 mol%, however, caused a dramatic decrease in enantioinduction (entry 4, 40% ee). These results suggest that, although $\text{Rh}_2(\text{R-BNP})_4$ is capable of moderately high turnover numbers (TONs), it may not be as robust a catalyst as $\text{Rh}_2(\text{R-DOSP})_4$ or $\text{Rh}_2(\text{S-PTAD})_4$, which are capable of TONs as high as 850,000 and 1,800,000 respectively in asymmetric intermolecular cyclopropanation.²⁹

At the onset of this study, the asymmetric induction of the cyclopropanation was not expected to be heavily influenced by the functionality on the aryldiazoacetate. Having observed considerable variation in enantioselectivity depending on the nature of the aryl group, we decided to explore the effect of modifying the substitution on the styrene. These studies were focused on $\text{Rh}_2(\text{R-BNP})_4$ -catalyzed cyclopropanation with the 3, 4-dimethoxyphenyldiazoacetate **1i** (Table 3), because $\text{Rh}_2(\text{R-BNP})_4$ had not been previously evaluated as a catalyst for this transformation. The levels of enantioselectivity in the cyclopropanation under $\text{Rh}_2(\text{R-BNP})_4$ -catalyzed conditions were found to be moderately influenced by the functionality on the styrene, as the cyclopropanes **5a-g** were obtained with uniformly high levels of enantioinduction (80-90% ee). Previous studies have shown that $\text{Rh}_2(\text{R-DOSP})_4$ -catalyzed cyclopropanation is also not especially influenced by the nature of the styrene^{3,4,9} and the $\text{Rh}_2(\text{R-DOSP})_4$ -catalyzed cyclopropanation of a range of styrenes (**4a-g**) with **1i** gave **5a-g** with modest levels of enantioselectivity (48-67% ee).

These studies reveal subtle differences in the ability of the chiral dirhodium tetracarboxylate catalysts to induce high enantioselectivity in the cyclopropanation of styrenes, as summarized in Table 4. The previous expectation that $\text{Rh}_2(\text{R-DOSP})_4$ would give high asymmetric induction for all aryldiazoacetates was found not to be true, although it was found to be the most effective catalyst for the broadest range of substituted methyl aryldiazoacetates. In spite of the fact that $\text{Rh}_2(\text{S-PTAD})_4$ is the most consistent catalyst when the acceptor group of the donor/acceptor carbenoid is modified,¹⁹⁻²² the level of enantioselectivity was found to be highly variable when aryl substitution of the aryldiazoacetate was modified. In particular, $\text{Rh}_2(\text{S-PTAD})_4$ was very effective with 2-chlorophenyl aryldiazoacetate derivative. $\text{Rh}_2(\text{R-BNP})_4$ becomes the best catalyst for 3-methoxyphenyl-substituted aryldiazoacetate derivatives. The cause for these subtle variations, at this stage, is not well understood. There is no clear steric or electronic trend to define which catalyst will perform best in a given system, which suggests the asymmetric induction may involve a combination of factors including π -stacking interactions. Computational studies are in progress to develop a rational model to explain these trends.

3. Conclusion

This study provides guidelines for choosing the optimal chiral dirhodium-(II) catalyst for cyclopropanation of aryldiazoacetates. The nature of the aryl group on the aryldiazoacetate strongly affects the asymmetric induction imparted by the three catalysts studied. Depending on the aryl substituent, $\text{Rh}_2(\text{R-DOSP})_4$, $\text{Rh}_2(\text{S-PTAD})_4$, or $\text{Rh}_2(\text{R-BNP})_4$ can be utilized to obtain the desired cyclopropane with a high level of enantioinduction. In contrast, the functionality on the styrene has only moderate influence on the level of asymmetric induction in cyclopropanation reactions. These studies set the chemical foundation for our ongoing studies to develop the rationally useful diarylcyclopropylamines, the results of which will be reported in due course.

4. Experimental Section

4.1 General

All reactions were conducted under anhydrous conditions in oven-dried glassware under an inert atmosphere of dry argon, unless otherwise stated. Hexanes, pentane, and toluene were dried by a solvent purification system (passed through activated alumina columns). All solvents were degassed by bubbling argon through the solvent for a minimum of 10 minutes prior to use. Unless otherwise noted, all other reagents were obtained from commercial sources and used as received. ^1H Nuclear Magnetic Resonance (NMR) spectra were recorded at 400 MHz or 600MHz. Data presented as follows: chemical shift (in ppm on the scale relative to ^1H 7.27 for the residual protons in CDCl_3), coupling constant (J/Hz), integration. Coupling constants were taken directly from the spectra and are uncorrected. ^{13}C NMR spectra were recorded at 100 MHz and all chemical shift values are reported in ppm on the scale, with an internal reference of ^{13}C 77.23 for CDCl_3 . Mass spectral determinations were carried out by using APCI as ionization source. Melting points are uncorrected. Infrared spectral data are reported in units of cm^{-1} . Analytical TLC was performed on silica gel plates using UV light. Flash column chromatography was performed on silica gel 60Å (230-400 mesh). Optical rotations were measured on Jasco polarimeters. Analytical enantioselective chromatographies were measured on Varian Prostar instrument and used isopropanol:hexane as gradient. Chiral HPLC conditions were determined by obtaining separation of the racemic product. $\text{Rh}_2(\text{R}/\text{S}\text{-DOSP})_4$ was employed as the catalyst in the racemic reactions. Styrene (**2**) and substituted styrenes (**4a-f**) were commercially available and purified by pushing through a silica-filled pipette prior to use. $\text{Rh}_2(\text{R}\text{-DOSP})_4$,³ $\text{Rh}_2(\text{S}\text{-PTAD})_4$,¹⁹ $\text{Rh}_2(\text{R}\text{-BNP})_4$,²³ aryldiazoacetates **1a-1**,² and styrene **4g**³⁰ were all synthesized according published procedures.

4.2 General Procedure for the Synthesis of Methyl Phenylidazoacetates³¹

The methyl arylacetate (1 equiv.) and *p*-ABSA (1.3 equiv.) were dissolved in acetonitrile and cooled to 0 °C using an ice bath under an argon atmosphere. 1, 8-Diazabicycloundec-7-ene (DBU, 1.3 equiv.) was then added to the stirring mixture over the course of 5 minutes. After the addition of the DBU, the reaction mixture continued to stir at 0 °C for an additional 15 minutes. Once this allotted time had passed, the ice bath was removed and the reaction mixture was stirred for 24 hours at room temperature. The resulting orange solution was quenched with saturated NH_4Cl and the aqueous layer was extracted with diethyl ether (3×). The organic layer was then washed with deionized H_2O to remove any residual salts. The combined organic layers were dried over MgSO_4 and filtered. The organic layer was then concentrated under reduced pressure. The residue was purified via flash chromatography on silica gel (10:1 Hexanes:EtOAc).

4.3 General Procedure for the Synthesis of Methyl Phenylcyclopropanecarboxylates with $\text{Rh}_2(\text{R}\text{-DOSP})_4$

In a 25-mL round bottom flask (Flask A) equipped with a magnetic stir bar, styrene (5 equiv.) and $\text{Rh}_2(\text{R}\text{-DOSP})_4$ (0.01 equiv.) were dissolved in dry, degassed pentane (3 mL). The reaction mixture was then degassed using vacuum/argon cycles (×3). In a separate 25-mL round bottom flask (Flask B), the methyl phenylidazoacetate (0.5 mmol, 1 equiv.) was dissolved in dry, degassed pentane (5 mL) and degassed using vacuum/argon cycles (×3). The contents in Flask B were then added to Flask A using a syringe pump for the duration of 1 hour. After the addition, the reaction mixture continued to stir for 1 additional hour. Once the allotted time had passed, the reaction mixture was concentrated under reduced pressure and purified using silica gel column chromatography (increasing gradient starting at 10:1 Hexanes:EtOAc).

4.4 General Procedure for the Synthesis of Methyl Phenylcyclopropanecarboxylates with $\text{Rh}_2(\text{S-PTAD})_4$

In a 25-mL round bottom flask (Flask A) equipped with a magnetic stir bar, styrene (5 equiv.) and $\text{Rh}_2(\text{S-PTAD})_4$ (0.005 equiv.) were dissolved in dry, degassed pentane (3 mL). The reaction mixture was then degassed using vacuum/argon cycles ($\times 3$). In a separate 25-mL round bottom flask (Flask B), the methyl phenyldiazoacetate (0.5 mmol, 1 equiv.) was dissolved in dry, degassed pentane (5 mL) and degassed using vacuum/argon cycles ($\times 3$). The contents in Flask B were then added to Flask A using a syringe pump for the duration of 1 hour. After the addition, the reaction mixture continued to stir for 1 additional hour. Once the allotted time had passed, the reaction mixture was concentrated under reduced pressure and purified using silica gel column chromatography (increasing gradient starting at 10:1 Hexanes:EtOAc).

4.5 General Procedure for the Synthesis of Methyl Phenylcyclopropanecarboxylates with $\text{Rh}_2(\text{R-BNP})_4$

In a 25-mL round bottom flask (Flask A) equipped with a magnetic stir bar, styrene (5 equiv.) and $\text{Rh}_2(\text{R-BNP})_4$ (0.01 equiv.) were dissolved in dry, degassed toluene (3 mL). The reaction mixture was then degassed using vacuum/argon cycles ($\times 3$). In a separate 25-mL round bottom flask (Flask B), the methyl phenyldiazoacetate (0.5 mmol, 1 equiv.) was dissolved in dry, degassed pentane (5 mL) and degassed using vacuum/argon cycles ($\times 3$). The contents in Flask B were then added to Flask A using a syringe pump for the duration of 1 hour. After the addition, the reaction mixture continued to stir for 1 additional hour. Once the allotted time had passed, the reaction mixture was concentrated under reduced pressure and purified using silica gel column chromatography (increasing gradient starting at 10:1 Hexanes:EtOAc).

4.1.1. (1R,2S)-methyl 1, 2-diphenylcyclopropanecarboxylate (3a)—Title compound was prepared by general procedure and obtained as a white solid. 85% yield for $\text{Rh}_2(\text{R-DOSP})_4$; 87% yield for $\text{Rh}_2(\text{S-PTAD})_4$; 72% yield for $\text{Rh}_2(\text{R-BNP})_4$; HPLC: (Chiralcel SS-WHELK, 1% *i*-PrOH in hexane, 1.0 mL/min, 1 mg/mL, 30min, $\lambda = 254$ nm) retention times of 8.62 min (major) and 10.22 min (minor), 88% ee for $\text{Rh}_2(\text{R-DOSP})_4$; 21% ee for $\text{Rh}_2(\text{S-PTAD})_4$; 42% ee for $\text{Rh}_2(\text{R-BNP})_4$; $R_f = 0.25$ (hexane: ethyl acetate 10:1); ^1H NMR (600 MHz, CDCl_3) 7.12-7.11 (m, 3H), 7.05-7.01 (m, 5H), 6.77-6.75 (m, 2H), 3.70 (s, 3H), 3.11 (dd, $J = 7.2, 9.3$, 1H), 2.13 (dd, $J = 4.8, 9.3$, 1H), 1.88 (dd, $J = 4.8, 7.2$, 1H); ^{13}C NMR (100 MHz, CDCl_3) 174.5, 136.5, 134.9, 132.1, 128.2, 127.9, 127.2, 126.5, 52.8, 37.6, 33.3, 20.7; Data are consistent with the literature^{5,6}.

4.1.2. (1S,2R)-methyl 2-phenyl-1-(*p*-tolyl)cyclopropanecarboxylate (3b)—Title compound was prepared by general procedure and obtained as a white solid. 84% yield for $\text{Rh}_2(\text{R-DOSP})_4$; 77% yield for $\text{Rh}_2(\text{S-PTAD})_4$; 69% yield for $\text{Rh}_2(\text{R-BNP})_4$; HPLC: (Chiralcel SS-WHELK, 1% *i*-PrOH in hexane, 1.0 mL/min, 1 mg/mL, 30 min, $\lambda = 254$ nm) retention times of 10.57 min (major) and 14.13 min (minor), 87% ee for $\text{Rh}_2(\text{R-DOSP})_4$; 46% ee for $\text{Rh}_2(\text{S-PTAD})_4$; 51% ee for $\text{Rh}_2(\text{R-BNP})_4$; $R_f = 0.44$ (4:1 Hexanes:EtOAc); $[\alpha]_D^{20} + 17.2^\circ$ (c. 1, chloroform); ^1H NMR (400 MHz; CDCl_3) 7.11-7.07 (m, 3H), 6.98-6.92 (m, 4H), 6.82-6.80 (m, 2H), 3.69 (s, 3H), 3.12 (dd, $J = 9.2$ and 7.2 Hz, 1H), 2.27 (s, 3H), 2.16 (dd, $J = 9.6$ and 4.8 Hz, 1H), 1.88 (dd, $J = 7.2$ and 4.8 Hz, 1H); ^{13}C NMR (100 MHz, CDCl_3) 174.8, 136.8, 136.7, 131.9, 131.8, 128.7, 128.3, 127.9, 126.5, 52.9, 37.3, 33.4, 21.4, 20.9; IR (film): 3028, 2950, 1716, 1255; m/z (ESI) 267.1 (100%, M+H), 268.1 (20%); HRMS-ESI m/z 167.138 ($\text{C}_{18}\text{H}_{19}\text{O}_2$ requires 267.138).

4.1.3. (1S,2R)-methyl 2-phenyl-1-(4-(trifluoromethyl)phenyl)cyclopropanecarboxylate (3c)—Title compound was

prepared by general procedure and obtained as a transparent oil. 93% yield for Rh₂(*R*-DOSP)₄; 67% yield for Rh₂(*S*-PTAD)₄; 80% yield for Rh₂(*R*-BNP)₄; HPLC: (Chiralcel OD-H, 0.5% *i*-PrOH in hexanes, 1.0 mL/min, 1 mg/mL, 30 min, $\lambda = 254$ nm) retention times of 8.27 min (minor) and 10.34 min (major), 87% ee for Rh₂(*R*-DOSP)₄; 77% ee for Rh₂(*S*-PTAD)₄; 57% ee for Rh₂(*R*-BNP)₄; $R_f = 0.44$ (4:1 Hexanes:EtOAc); [α]_D²⁰: 19.1 (c. 1, chloroform); ¹H NMR (400 MHz; CDCl₃) 7.36 (d, $J = 8$ Hz, 2H), 7.12 (d, $J = 8$ Hz, 2H), 7.06 (m, 3H), 6.74 (m, 2H), 3.66 (s, 3H), 3.14 (dd, $J = 9.6$ and 7.6 Hz, 1H), 2.17 (dd, $J = 9.2$ and 5.2 Hz, 1H), 1.88 (dd, $J = 7.2$ and 5.2 Hz, 1H); ¹³C NMR (100 MHz, CDCl₃) 173.9, 139.2, 135.8, 132.4, 128.1, 126.9, 125.0, 124.9, 124.8, 124.7, 53.0, 37.2, 33.5, 20.4; IR (film): 3032, 2954, 1719, 1501, 1322, 1257; m/z (ESI) 321.1 (100%, M+H), 322.1 (21%); HRMS- m/z 321.1097 (C₁₈ H₁₆ O₂ F₃ requires 321.1097).

4.1.4. (1*S*,2*R*)-methyl 1-(4-chlorophenyl)-2-phenylcyclopropanecarboxylate

(3d)—Title compound was prepared by general procedure and obtained as a transparent oil. 87% yield for Rh₂(*R*-DOSP)₄; 71% yield for Rh₂(*S*-PTAD)₄; 89% yield for Rh₂(*R*-BNP)₄; HPLC: (Chiralcel OJ-H, 1% *i*-PrOH in hexanes, 1.0 mL/min, 1mg/mL, 30 min, $\lambda = 254$ nm) retention times of 8.62 min (minor) and 12.58 min (major), 88% ee for Rh₂(*R*-DOSP)₄; 48% ee for Rh₂(*S*-PTAD)₄; 57% ee for Rh₂(*R*-BNP)₄; $R_f = 0.56$ (4:1 Hexanes:EtOAc); [α]_D²⁰: 4.8 (c. 1, chloroform); ¹H NMR (300 MHz; CDCl₃) 7.12-7.06 (m, 5H), 6.95 (d, $J = 8.7$ Hz, 2H), 6.79-6.76 (m, 2H), 3.67 (s, 3H), 3.12(dd, $J = 9.3$ and 7.5 Hz, 1H), 2.15 (dd, $J = 9.3$ and 4.8 Hz, 1H), 1.85 (dd, $J = 7.2$ and 4.8 Hz, 1H); ¹³C NMR (100 MHz, CDCl₃) 174.1, 136.1, 133.7, 133.4, 133.2, 128.3, 128.2, 128.1, 126.8, 52.9, 36.9, 33.4, 20.6; IR (film): 3031, 2951, 1717, 1493, 1255; m/z (ESI) 287.1 (100%, M+H), 288.1 (16.42%), 289.1 (29.3%); HRMS-ESI m/z 287.0833 (C₁₇ H₁₆ O₂ Cl requires 287.0833).

4.1.5. (1*S*,2*R*)-methyl 1-(4-methoxyphenyl)-2-phenylcyclopropanecarboxylate

(3e)—Title compound was prepared by general procedure and obtained as a white solid. 66% yield for Rh₂(*R*-DOSP)₄; 93% yield for Rh₂(*S*-PTAD)₄; 84% yield for Rh₂(*R*-BNP)₄; HPLC: (Chiralcel OD-H, 0.7% *i*-PrOH in hexanes, 1.0 mL/min, 1 mg/mL, 30 min, $\lambda = 254$ nm) retention times of 11.97 min (major) and 17.71 min (minor), 90% ee for Rh₂(*R*-DOSP)₄; 96% ee for Rh₂(*S*-PTAD)₄; 57% ee for Rh₂(*R*-BNP)₄; $R_f = 0.39$ (4:1 Hexanes:EtOAc); [α]_D²⁰ = + 5.1° (c. 1, chloroform); ¹H NMR (400 MHz; CDCl₃) 7.10-7.07 (m, 3H), 6.95 (d, $J = 8.8$ Hz, 2H), 6.80-6.77 (m, 2H), 6.68 (d, $J = 8.8$ Hz, 2H), 3.74 (s, 3H), 3.68 (s, 3H), 3.09 (dd, $J = 9.2$ and 7.6 Hz, 1H), 2.14 (dd, $J = 9.2$ and 4.8 Hz, 1H), 1.84 (dd, $J = 7.2$ and 4.8 Hz, 1H); ¹³C NMR (100 MHz, CDCl₃) 174.9, 158.6, 136.7, 133.1, 128.3, 127.9, 127.0, 126.5, 113.4, 55.3, 52.8, 36.9, 33.4, 21.0; IR(film): 3031, 2951, 2836, 1715, 1515, 1245; m/z (ESI) 283.1(100%, M+H), 284.1 (18.7%); HRMS-ESI m/z 283.1328(C₁₈ H₁₉ O₃ requires 283.1329).

4.1.6. (1*S*,2*R*)-methyl 1-(2-chlorophenyl)-2-phenylcyclopropanecarboxylate (3f)

—Title compound was prepared by general procedure and obtained as a transparent oil. 89% yield for Rh₂(*R*-DOSP)₄; 80% yield for Rh₂(*S*-PTAD)₄; 78% yield for Rh₂(*R*-BNP)₄; HPLC: (Chiralcel OJ-H, 0.5% *i*-PrOH in hexanes, 1.0 mL/min, 1 mg/mL, 30 min, $\lambda = 254$ nm) retention times of 11.47 min (major) and 15.27 min (major), 92% ee for Rh₂(*R*-DOSP)₄; 97% ee for Rh₂(*S*-PTAD)₄; 51% ee for Rh₂(*R*-BNP)₄; $R_f = 0.43$ (4:1 Hexanes:EtOAc); [α]_D²⁰: 61.8 (c. 1, chloroform); ¹H NMR (300 MHz; CDCl₃) 7.18-7.02 (m, 7H), 6.84-6.76 (m, 2H), 3.68 (s, 3H), 3.13 (t, $J = 8.7$ Hz, 1H), 2.10 (m, 1H), 1.91 (dd, $J = 7.2$ and 5.1 Hz, 1H); ¹³C NMR (100 MHz, CDCl₃) 173.6, 137.5, 133.5, 129.6, 128.9, 128.2, 127.6, 126.6, 126.4, 52.9, 33.5, 29.9, 21.7; IR (film): 3031, 2950, 1718, 1251, 694; m/z (ESI) 287.1 (100%, M+H), 288.1 (17%), 289.1 (32%); HRMS- m/z 287.0833 (C₁₇ H₁₆ O₂ Cl requires 287.0833).

4.1.7. (1S,2R)-methyl 1-(2-methoxyphenyl)-2-phenylcyclopropanecarboxylate (3g)—Title compound was prepared by general procedure and obtained as a white solid. 92% yield for Rh₂(*R*-DOSP)₄; 87% yield for Rh₂(*S*-PTAD)₄; 69% yield for Rh₂(*R*-BNP)₄; HPLC: (SS-WHELK column, 1% *i*-PrOH in hexanes, 1.0 mL/min, 1 mg/mL, 30 min, $\lambda = 254$ nm) retention times of 11.65 min (minor) and 14.00 min (major), 86% ee for Rh₂(*R*-DOSP)₄; 80% ee for Rh₂(*S*-PTAD)₄; 27% ee for Rh₂(*R*-BNP)₄; $R_f = 0.45$ (4:1 Hexanes:EtOAc); $[\alpha]_D^{20} + 133.3^\circ$ (c. 1, chloroform); ¹H NMR (400 MHz; CDCl₃) 7.19-7.10 (m, 2H), 7.04-6.98 (m, 3H), 6.86 (td, $J = 7.6, 1.1$ Hz, 1H), 6.81-6.74 (m, 2H), 6.53 (d, $J = 8$ Hz, 1H), 3.65 (s, 3H), 3.36 (s, 3H), 3.24 (dd, $J = 9.6$ and 7.6 Hz, 1H), 1.98 (dd, $J = 9.2$ and 4.8 Hz, 1H), 1.85 (dd, $J = 7.2$ and 4.8 Hz, 1H); ¹³C NMR (100 MHz, CDCl₃) 174.7, 159.2, 137.0, 131.8, 128.9, 127.9, 127.3, 126.1, 124.1, 120.1, 110.5, 55.2, 52.7, 34.3, 32.6, 20.8; IR (film): 3030, 2950, 2835, 1716, 1496, 1242; m/z (ESI) 283.1 (100%, M+H), 284.1(19%); HRMS-ESI m/z 283.1329 (C₁₈H₁₉O₃ requires 283.1329).

4.1.8. (1S,2R)-methyl 1-(3, 4-dichlorophenyl)-2-phenylcyclopropanecarboxylate (3h)—Title compound was prepared by general procedure and obtained as a clear oil; 88% yield for Rh₂(*R*-DOSP)₄; 88% yield for Rh₂(*S*-PTAD)₄; 82% yield for Rh₂(*R*-BNP)₄; HPLC: (Chiralcel OD-H, 1% *i*-PrOH in hexane, 1 mL/min, 1 mg/mL, 30 min, $\lambda = 254$ nm) retention times of 7.54 min (minor) and 9.78 min (major), 82% ee for Rh₂(*R*-DOSP)₄; 60% ee for Rh₂(*S*-PTAD)₄; 63% ee for Rh₂(*R*-BNP)₄; $R_f = 0.23$ (Hexane:EtOAc = 7:1); $[\alpha]_D^{20} - 8.1^\circ$ (c = 1.60, CHCl₃); ¹H NMR (400 MHz, CDCl₃) 7.18-7.16 (m, 2H), 7.14-7.10 (m, 3H), 6.82-6.79 (m, 3H), 3.68 (s, 3H), 3.14 (dd, $J = 9.2, 7.6$ Hz, 1H), 2.15 (dd, $J = 9.2, 4.8$ Hz, 1H), 1.84 (dd, $J = 7.6, 5.2$ Hz, 1H); ¹³C NMR (100 MHz, CDCl₃) 173.3, 135.3, 135.2, 133.7, 131.6, 131.4, 131.2, 129.6, 128.0, 127.9, 126.8, 52.8, 36.3, 33.3, 20.2; IR (film): 2925, 1719, 1257, 1163, 695; HRMS (ESI) calcd for C₁₇H₁₃O₂Cl₂ (M-H)⁺ 319.02927 found 319.02985.

4.1.9. (1S,2R)-methyl 1-(3, 4-dimethoxyphenyl)-2-phenylcyclopropanecarboxylate (3i)—Title compound was prepared by general procedure and obtained as a white solid. 74% yield for Rh₂(*R*-DOSP)₄; 70% yield for Rh₂(*S*-PTAD)₄; 93% yield for 1 mol% Rh₂(*R*-BNP)₄; 83% yield for 0.5 mol% Rh₂(*R*-BNP)₄; 80% yield for 0.1 mol% Rh₂(*R*-BNP)₄; 73% yield for 0.01 mol% Rh₂(*R*-BNP)₄; HPLC: (Chiralcel OD-H, 6% *i*-PrOH in hexane, 1 mL/min, 1 mg/mL, 30 min, $\lambda = 254$ nm) retention times of 13.99 min (minor) and 17.97 min (major), 56% ee for Rh₂(*R*-DOSP)₄; 94% ee for Rh₂(*S*-PTAD)₄; 97% ee for 1 mol% Rh₂(*R*-BNP)₄; 96% ee for 0.5 mol% Rh₂(*R*-BNP)₄; 91% ee for 0.1 mol% Rh₂(*R*-BNP)₄; 40% ee for 0.01 mol% Rh₂(*R*-BNP)₄; $R_f = 0.20$ (hexane: ethyl acetate 4:1); mp 88-89°C; $[\alpha]_D^{20} + 28.4^\circ$ (c = 1.51, CHCl₃); ¹H NMR (400 MHz, CDCl₃) 7.09-7.07 (m, 3H), 6.81-6.79 (m, 2H), 6.69 (m, 2H), 6.36 (s, 1H), 3.81 (s, 3H), 3.68 (s, 3H), 3.56 (s, 3H), 3.08 (dd, $J = 9.2, 7.6$ Hz, 1H), 2.14 (dd, $J = 9.2, 4.4$ Hz, 1H), 1.84 (dd, $J = 7.6, 4.8$ Hz, 1H); ¹³C NMR (100 MHz, CDCl₃) 174.5, 147.8, 136.4, 127.9, 127.7, 127.2, 126.3, 123.9, 115.3, 110.2, 55.5, 52.6, 36.9, 33.1, 20.8; IR (film): 2924, 1716, 1518, 1455, 1434, 1413, 1341, 1229, 1208, 1177; HRMS (ESI) calcd for C₁₉H₂₁O₄ (M+H)⁺ 313.14398 found 313.14332.

4.1.10. (1S,2R)-methyl 1-(3-methoxyphenyl)-2-phenylcyclopropanecarboxylate (3j)—Title compound was prepared by general procedure and obtained as a yellow oil. 78% yield for Rh₂(*R*-DOSP)₄; 72% yield for Rh₂(*S*-PTAD)₄; 82% yield for Rh₂(*R*-BNP)₄; HPLC: (Chiralcel OD-H, 0.7% *i*-PrOH in hexane, 1 mL/min, 1 mg/mL, 30 min, $\lambda = 254$ nm), retention times of 9.50 min (major) and 11.38 min (minor), 79% ee for Rh₂(*R*-DOSP)₄; 16% ee for Rh₂(*S*-PTAD)₄; 88% ee for Rh₂(*R*-BNP)₄; $R_f = 0.25$ (hexane: ethyl acetate 9:1); $[\alpha]_D^{20} + 21.1^\circ$ (c = 1.25, CHCl₃); ¹H NMR (400 MHz, CDCl₃) 7.09-7.03 (m, 4H), 6.81-6.79 (m, 2H), 6.69-6.63 (m, 2H), 6.53-6.52 (m, 1H), 3.67 (s, 3H), 3.59 (s, 3H), 3.12

(dd, $J=9.6, 7.2$ Hz, 1H), 2.12 (dd, $J=9.2, 4.8$ Hz, 1H), 1.87 (dd, $J=7.6, 5.2$ Hz, 1H); ^{13}C NMR (100MHz, CDCl_3) 174.2, 158.8, 136.4, 136.2, 128.5, 127.9, 127.7, 126.3, 124.4, 117.5, 112.9, 55.0, 52.6, 37.3, 33.1, 20.6; IR (film): 2925, 1717, 1602, 1454, 1239, 697; HRMS (ESI) calcd for $\text{C}_{18}\text{H}_{19}\text{O}_3$ (M+H) $^+$ 283.13344 found 283.13288.

4.1.11. (1S,2R)-methyl 1-(3, 5-dimethoxyphenyl)-2-phenylcyclopropanecarboxylate (3k)—Title compound was prepared by general

procedure and obtained as a yellow oil. 85% yield for $\text{Rh}_2(\text{R-DOSP})_4$; 85% yield for $\text{Rh}_2(\text{S-PTAD})_4$; 69% yield for $\text{Rh}_2(\text{R-BNP})_4$; HPLC: (Chiralcel OD-H, 6% *i*-PrOH in hexane, 1 mL/min, 1 mg/mL, 30 min, $\lambda=254$ nm) retention times of 7.33 min (major) and 9.07 min (minor), 28% ee for $\text{Rh}_2(\text{R-DOSP})_4$; 3% ee for $\text{Rh}_2(\text{S-PTAD})_4$; 92% ee for $\text{Rh}_2(\text{R-BNP})_4$; $R_f=0.31$ (hexane: ethyl acetate 5:1); $[\alpha]_D^{20}+33.7^\circ$ ($c=1.1$, CHCl_3); ^1H NMR (400 MHz, CDCl_3) 7.10-7.08 (m, 3H), 6.82 (dd, $J=7.2, 2.4$ Hz, 2H), 6.24 (t, $J=2.4$ Hz, 1H), 6.15 (d, $J=2.4$ Hz, 2H), 3.68 (s, 3H), 3.56 (s, 6H), 3.08 (dd, $J=9.2, 7.2$ Hz, 1H), 2.10 (dd, $J=9.2, 4.8$ Hz, 1H), 1.84 (dd, $J=7.2, 4.8$ Hz, 1H); ^{13}C NMR (100 MHz, CDCl_3) 174.4, 160.1, 137.2, 136.6, 128.2, 128.0, 126.6, 110.4, 99.8, 55.4, 52.9, 37.7, 33.3, 20.9; IR(film): 2951, 2840, 1715, 1594, 1456, 1425, 1260, 1203, 1151, 1046, 715, 692; HRMS (APCI) calcd for $\text{C}_{19}\text{H}_{21}\text{O}_4$ (M+H) $^+$ 313.14344 found 313.14348.

4.1.12. (1S,2R)-methyl 2-phenyl-1-(3, 4, 5-trimethoxyphenyl)cyclopropanecarboxylate (3l)—Title compound was prepared by

general procedure and obtained as a yellow oil. 98% yield for $\text{Rh}_2(\text{R-DOSP})_4$; 95% yield for $\text{Rh}_2(\text{S-PTAD})_4$; 63% yield for $\text{Rh}_2(\text{R-BNP})_4$; HPLC: (Chiralcel OD-H, 6% *i*-PrOH in hexane, 1 mL/min, 1 mg/mL, 30 min, $\lambda=254$ nm), retention times of 10.78 min (minor) and 11.79 min (minor), 34% ee for $\text{Rh}_2(\text{R-DOSP})_4$; 9% ee for $\text{Rh}_2(\text{S-PTAD})_4$; 90% ee for $\text{Rh}_2(\text{R-BNP})_4$; $R_f=0.20$ (hexane: ethyl acetate 5:1); $[\alpha]_D^{20}+17.5^\circ$ ($c=2.02$, CHCl_3); ^1H NMR (400 MHz, CDCl_3) 7.09-7.07 (m, 3H), 6.81-6.78 (m, 2H), 6.16 (s, 2H), 3.76 (s, 3H), 3.69 (s, 3H), 3.59 (s, 6H), 3.07 (dd, $J=9.2, 7.2$ Hz, 1H); 2.14 (dd, $J=9.6, 4.8$ Hz, 1H), 1.82 (dd, $J=7.6, 5.2$ Hz, 1H); ^{13}C NMR (100 MHz, CDCl_3) 174.2, 152.3, 136.5, 130.3, 128.0, 127.7, 126.4, 109.4, 60.7, 55.9, 52.6, 37.4, 33.1 20.8; IR (film): 2925, 1716, 1587, 1413, 1258, 1235, 1153, 1124; HRMS (ESI) calcd for $\text{C}_{20}\text{H}_{23}\text{O}_4$ (M+H) $^+$ 345.14852 found 345.14853.

4.1.13. (1S,2R)-methyl 1-(3,4-dimethoxyphenyl)-2-(m-

tolyl)cyclopropanecarboxylate (5a)—Prepared by general procedure with methyl 2-diazo-2-(3,4-dimethoxyphenyl)acetate (118 mg, 0.5 mmol, 1 equiv), 2-methylstyrene (148 mg, 1.25 mmol, 2.5 equiv), and $\text{Rh}_2(\text{R-BNP})_4$ (4 mg, 0.0025 mmol, 0.005 equiv). The remaining residue was purified on silica gel eluting with hexanes: ethyl acetate (5:1) to afford a yellow/green oil (114 mg, 76 % yield). $R_f=0.12$ (hexane: ethyl acetate 5:1); $[\alpha]_D^{20}+28.7^\circ$ ($c=1.23$, CHCl_3); ^1H NMR (400 MHz, CDCl_3) 7.11 (d, $J=7.6$ Hz, 1H), 7.00 (t, $J=7.6$ Hz, 1H), 6.83 (t, $J=7.6$ Hz, 1H), 6.63 (m, 2H), 6.42 (d, $J=7.6$ Hz, 1H), 6.34 (s, 1H), 3.77 (s, 3H), 3.71 (s, 3H), 3.57 (s, 3H), 3.11 (dd, $J=9.2, 7.6$ Hz, 1H), 2.51 (s, 3H), 2.06 (dd, $J=9.2, 5.0$ Hz, 1H), 1.99 (dd, $J=7.6, 5.0$ Hz, 1H); ^{13}C NMR (100 MHz, CDCl_3) 174.9, 147.9, 137.8, 134.7, 129.7, 127.8, 126.7, 126.0, 125.8, 123.7, 114.7, 110.3, 55.7, 55.6, 52.8, 36.0, 31.2, 20.2, 19.5; IR (film): 2951, 1713, 1516, 1463, 1435, 1251, 1140, 1026, 740; HRMS (APCI) calcd for $\text{C}_{20}\text{H}_{23}\text{O}_4$ (M+H) $^+$ 327.15909 found 327.15909; HPLC: (Chiralcel OD-H, 3% *i*-PrOH in hexane, 1 mL/min, 1 mg/mL, 30 min, $\lambda=254$ nm) retention times of 17.81 min (minor) and 19.31 min (major), 90% ee for $\text{Rh}_2(\text{R-BNP})_4$, 64% ee for $\text{Rh}_2(\text{R-DOSP})_4$.

4.1.14. (1S,2R)-methyl 1-(3,4-dimethoxyphenyl)-2-(p-

tolyl)cyclopropanecarboxylate (5b)—Prepared by general procedure with methyl 2-

diazo-2-(3,4-dimethoxyphenyl)acetate (118 mg, 0.5 mmol, 1 equiv), 4-methylstyrene (148 mg, 1.25 mmol, 2.5 equiv), and $\text{Rh}_2(\text{R-BNP})_4$ (4 mg, 0.0025 mmol, 0.005 equiv). The remaining residue was purified on silica gel eluting with hexanes: ethyl acetate (5:1) to afford a yellow/green oil (147 mg, 90% yield). $R_f = 0.12$ (hexane: ethyl acetate 5:1); $[\alpha]_D^{20} +27.7^\circ$ ($c = 1.24$, CHCl_3); $^1\text{H NMR}$ (400 MHz, CDCl_3) 6.88 (d, $J = 8.0$ Hz, 2H), 6.69-6.67 (m, 4H), 6.37 (s, 1H), 3.81 (s, 3H), 3.67 (s, 3H), 3.57 (s, 3H), 3.05 (dd, $J = 9.2, 7.6$ Hz, 1H), 2.22 (s, 3H), 2.11 (dd, $J = 9.2, 4.8$ Hz, 1H), 1.80 (dd, $J = 7.6, 4.8$ Hz, 1H); $^{13}\text{C NMR}$ (100 MHz, CDCl_3) 174.7, 147.9, 136.0, 133.5, 128.6, 128.0, 127.6, 124.1, 115.5, 110.3, 55.7, 55.6, 52.7, 36.9, 33.1, 21.0, 20.9; IR (film): 2951, 1714, 1589, 1516, 1435, 1413, 1341, 1315, 1250, 1228, 1155, 1027; HRMS (APCI) calcd for $\text{C}_{20}\text{H}_{23}\text{O}_4$ ($\text{M}+\text{H}$)⁺ 327.15909 found 327.15909; HPLC: (Chiralcel OD-H, 3% *i*-PrOH in hexane, 1 mL/min, 1 mg/mL, 30 min, $\lambda = 254$ nm) retention times of 17.3 min (minor) and 20.1 min (major), 88% ee for $\text{Rh}_2(\text{R-BNP})_4$, 67% ee for $\text{Rh}_2(\text{R-DOSP})_4$.

4.1.15. (1S,2R)-methyl 1-(3,4-dimethoxyphenyl)-2-(4-methoxyphenyl)cyclopropanecarboxylate (5c)—Prepared by general procedure with methyl 2-diazo-2-(3,4-dimethoxyphenyl)acetate (118 mg, 0.5 mmol, 1 equiv), 4-methoxystyrene (168 mg, 1.25 mmol, 2.5 equiv), and $\text{Rh}_2(\text{R-BNP})_4$ (4 mg, 0.0025 mmol, 0.005 equiv). The remaining residue was purified on silica gel eluting with hexanes: ethyl acetate (5:1) to afford an off-white solid (137 mg, 80% yield). $R_f = 0.20$ (hexane: ethyl acetate 3:1); mp 123-125°C; $[\alpha]_D^{20} +33.1^\circ$ ($c = 1.4$, CHCl_3); $^1\text{H NMR}$ (400 MHz, CDCl_3) 6.73-6.61 (m, 6H), 6.41 (s, 1H), 3.81 (s, 3H), 3.70 (s, 3H), 3.67 (s, 3H), 3.60 (s, 3H), 3.03 (dd, $J = 9.2, 7.6$ Hz, 1H), 2.10 (dd, $J = 9.2, 4.8$ Hz, 1H), 1.76 (dd, $J = 7.6, 4.8$ Hz, 1H); $^{13}\text{C NMR}$ (100 MHz, CDCl_3) 175.1, 158.6, 148.3, 129.5, 128.9, 127.9, 124.6, 115.9, 113.7, 110.7, 56.1, 55.6, 53.1, 37.1, 33.2, 21.3; IR (film): 2952, 1714, 1611, 1589, 1515, 1463, 1437, 1413, 1341, 1248, 1228, 1177, 1153; HRMS (APCI) calcd for $\text{C}_{20}\text{H}_{22}\text{O}_5$ ($\text{M}+\text{H}$)⁺ 342.14618 found 342.14589; HPLC: (Chiralcel OD-H, 5% *i*-PrOH in hexane, 1 mL/min, 1 mg/mL, 30 min, $\lambda = 254$ nm) retention times of 19.2 min (minor) and 22.9 min (major), 90% ee for $\text{Rh}_2(\text{R-BNP})_4$, 62% ee for $\text{Rh}_2(\text{R-DOSP})_4$.

4.1.16. (1S,2R)-methyl 1-(3,4-dimethoxyphenyl)-2-(4-nitrophenyl)cyclopropanecarboxylate (5d)—Prepared by general procedure with methyl 2-diazo-2-(3,4-dimethoxyphenyl)acetate (118 mg, 0.5 mmol, 1 equiv), 4-nitrostyrene (186 mg, 1.25 mmol, 2.5 equiv), and $\text{Rh}_2(\text{R-BNP})_4$ (4 mg, 0.0025 mmol, 0.005 equiv). The remaining residue was purified on silica gel eluting with hexanes: ethyl acetate (5:1) to afford yellow oil (168 mg, 94% yield). $R_f = 0.28$ (hexane: ethyl acetate 3:1); $[\alpha]_D^{20} +15.5^\circ$ ($c = 1.07$, CHCl_3); $^1\text{H NMR}$ (400 MHz, CDCl_3) 7.94 (d, $J = 8.8$ Hz, 2H), 6.92 (d, $J = 8.8$ Hz, 2H), 6.67 (d, $J = 8.2$ Hz, 1H), 6.61 (dd, $J = 8.2, 2.0$ Hz, 1H), 6.43 (d, $J = 2.0$ Hz, 1H), 3.81 (s, 3H), 3.69 (s, 3H), 3.62 (s, 3H), 3.16 (dd, $J = 9.2, 7.6$ Hz, 1H), 2.22 (dd, $J = 9.2, 5.4$ Hz, 1H), 1.91 (dd, $J = 7.6, 5.4$ Hz, 1H); $^{13}\text{C NMR}$ (100 MHz, CDCl_3) 173.9, 148.5, 145.1, 128.7, 126.2, 124.2, 123.0, 115.0, 110.6, 55.9, 55.8, 53.0, 38.4, 32.6, 29.8, 21.8; IR (film): 2924, 1717, 1597, 1515, 1463, 1415, 1342, 1229, 1206, 1156, 1141; HRMS (APCI) calcd for $\text{C}_{19}\text{H}_{20}\text{O}_6\text{N}_1$ ($\text{M}+\text{H}$)⁺ 358.12851 found 358.12836; HPLC: (Chiralcel OD-H, 6% *i*-PrOH in hexane, 1 mL/min, 1 mg/mL, 60 min, $\lambda = 254$ nm) retention times of 30.4 min (minor) and 41.0 min (major), 80% ee for $\text{Rh}_2(\text{R-BNP})_4$, 50% ee for $\text{Rh}_2(\text{R-DOSP})_4$.

4.1.17. (1S,2R)-methyl 1-(3,4-dimethoxyphenyl)-2-(4-trifluoromethyl)phenyl)cyclopropanecarboxylate (5e)—Prepared by general procedure with methyl 2-diazo-2-(3,4-dimethoxyphenyl)acetate (118 mg, 0.5 mmol, 1 equiv), styrene (215 mg, 1.25 mmol, 2.5 equiv), and $\text{Rh}_2(\text{R-BNP})_4$ (4 mg, 0.0025 mmol, 0.005 equiv). The remaining residue was purified on silica gel eluting with hexanes: ethyl acetate (6:1) to afford a yellow oil (171 mg, 90% yield); $R_f = 0.24$ (hexane: ethyl acetate

4:1); [α]²⁰_D +16.5° (c = 1.6, CHCl₃); ¹H NMR (400 MHz, CDCl₃) 7.33 (d, *J* = 8.2 Hz, 2H), 6.88 (d, *J* = 8.2 Hz, 2H), 6.70-6.65 (m, 2H), 6.35 (s, 1H), 3.81 (s, 3H), 3.68 (s, 3H), 3.56 (s, 3H), 3.11 (t, 1H), 3.12 (dd, *J* = 9.2, 7.2 Hz, 1H), 2.18 (dd, *J* = 9.2, 4.8 Hz, 1H), 1.85 (dd, *J* = 7.2, 4.8 Hz, 1H); ¹³C NMR (100 MHz, CDCl₃) 174.5, 148.7, 148.6, 141.5, 128.7, 127.0, 124.8, 124.7, 124.6, 124.3, 115.6, 110.9, 56.1, 53.2, 38.0, 33.0, 21.7; IR (film): 2954, 1718, 1517, 1465, 1437, 1414, 1324, 1252, 1230, 1210, 1193; HRMS (APCI) calcd for C₂₀H₁₉F₃O₄ (M+H)⁺ 380.12300 found 380.12251; HPLC: (Chiralcel OD-H, 6% *i*-PrOH in hexane, 1 mL/min, λ = 254 nm) retention times of 12.6 min (minor) and 15.6 min (major), 90% ee for Rh₂(*R*-BNP)₄, 63% ee for Rh₂(*R*-DOSP)₄.

4.1.18. (1*S*,2*R*)-methyl 2-(4-chlorophenyl)-1-(3,4-dimethoxyphenyl)cyclopropanecarboxylate (5f)—Prepared by general procedure with methyl 2-diazo-2-(3, 4-dimethoxyphenyl)acetate (118 mg, 0.5 mmol, 1 equiv), 4-chlorostyrene (173 mg, 1.25 mmol, 2.5 equiv), and Rh₂(*R*-BNP)₄ (4 mg, 0.0025 mmol, 0.005 equiv). The remaining residue was purified on silica gel eluting with hexanes: ethyl acetate (6:1) to afford clear oil (123 mg, 89% yield). *R_f* = 0.30 (hexane: ethyl acetate 3:1); [α]²⁰_D +13.4° (c = 1.2, CHCl₃); ¹H NMR (400 MHz, CDCl₃) 7.04 (d, *J* = 8.4 Hz, 2H), 6.72-6.63 (m, 4H), 6.38 (d, *J* = 1.6 Hz, 1H), 3.81 (s, 3H), 3.67 (s, 3H), 3.61 (s, 3H), 3.04 (dd, *J* = 9.2, 7.2 Hz, 1H), 2.13 (dd, *J* = 9.2, 4.8 Hz, 1H), 1.78 (dd, *J* = 7.2, 4.8 Hz, 1H); ¹³C NMR (100 MHz, CDCl₃) 174.4, 148.2, 148.2, 135.4, 132.3, 129.4, 128.0, 127.0, 124.2, 115.4, 110.5, 55.9, 55.8, 52.8, 37.2, 32.6, 21.2; IR (film): 2951, 1715, 1589, 1517, 1496, 1435, 1413, 1371, 1341, 1307, 1228, 1177, 1155, 1139; HRMS (APCI) calcd for C₁₉H₁₉ClO₄ (M+H)⁺ 346.09664 found 346.09632; HPLC: (Chiralcel OD-H, 5% *i*-PrOH in hexane, 1 mL/min, λ = 254 nm) retention times of 14.9 min (minor) and 18.5 min (major), 89% ee for Rh₂(*R*-BNP)₄, 67% ee for Rh₂(*R*-DOSP)₄.

4.1.19. (1*S*,2*R*)-methyl 2-(3,4-dichlorophenyl)-1-(3,4-dimethoxyphenyl)cyclopropanecarboxylate (5g)—Methyl 2-diazo-2-(3, 4-dimethoxyphenyl)acetate (2.7g, 11.6 mmol, 1 equiv) in 153 mL dry and degassed toluene was added by syringe pump over 2 h to a solution of 1, 2-dichloro-4-vinylbenzene (2.4 g, 13.9 mmol, 1.2 equiv) and Rh₂(*R*-BNP)₄ (92.2 mg, 0.06 mmol, 0.005 equiv) in 77 mL toluene. After addition, the solution was allowed to stir overnight and toluene was removed *in vacuo*. The remaining residue was purified on silica gel (hexane:ethyl acetate 5:1) to afford a clear oil (3.2 g, 72% yield for Rh₂(*R*-BNP)₄ [enantiomer shown above]; 2.3g, 52% yield for Rh₂(*S*-BNP)₄) *R_f* = 0.17 (hexane: ethyl acetate 5:1); [α]²⁰_D +4.1° (c = 1.03, CHCl₃) for Rh₂(*R*-BNP)₄; [α]²⁰_D -6.9° (c = 1.05, CHCl₃) for Rh₂(*S*-BNP)₄; ¹H NMR (600 MHz, CDCl₃) 7.10 (d, *J* = 9.0 Hz, 1H), 7.01 (d, *J* = 2.4 Hz, 1H), 6.69 (d, *J* = 9.0 Hz, 1H), 6.63 (dd, *J* = 9.0, 2.4 Hz, 1H), 6.51 (dd, *J* = 9.0, 2.4 Hz, 1H), 6.44 (d, *J* = 1.8 Hz, 1H), 3.82 (s, 3H), 3.67 (s, 3H), 3.66 (s, 3H), 3.02 (dd, *J* = 9.0, 7.2 Hz, 1H), 2.13 (dd, *J* = 9.0, 5.1 Hz, 1H), 1.78 (dd, *J* = 7.2, 5.1 Hz, 1H); ¹³C NMR (100 MHz, CDCl₃) 174.1, 148.4, 148.3, 137.4, 131.9, 130.5, 130.4, 129.7, 127.0, 126.6, 124.2, 115.2, 110.6, 55.9, 55.8, 52.9, 37.4, 32.1, 21.1; IR (film): 2951, 2836, 1716, 1559, 1516, 1413, 1229, 1178, 1137, 1027, 764; HRMS awaiting results; HPLC: (Chiralcel OD-H, 5% *i*-PrOH in hexane, 1 mL/min, λ = 254 nm) retention times of 15.4 min (minor) and 17.9 min (major), 86% ee for Rh₂(*R*-BNP)₄; retention times of 15.3 min (major) and 19.7 min (minor) 85% ee for Rh₂(*S*-BNP)₄, 48% ee for Rh₂(*R*-DOSP)₄.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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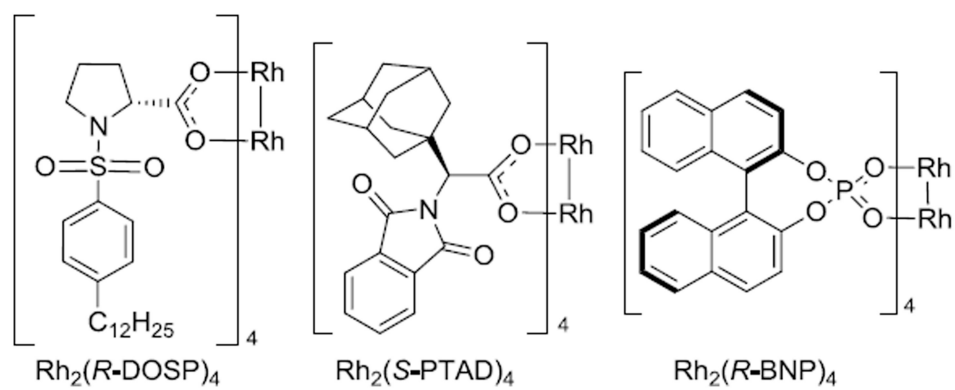
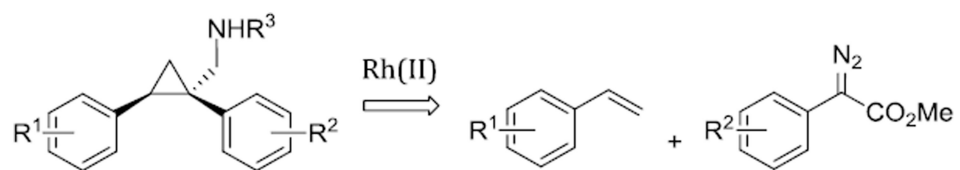


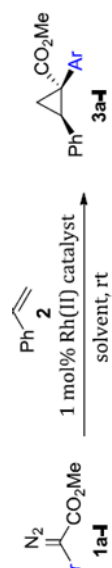
Figure 1. Dirhodium(II) catalysts used in this study



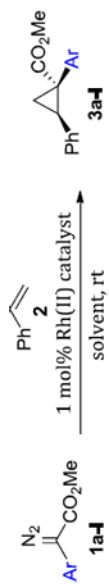
Scheme 1. Route to cyclopropyl amines from aryldiazoacetates

Table 1

Examination of the influence of substitution on aryldiazoacetate



entry	Ar	Rh ₂ (S-DOSP) ₄ ^d	Rh ₂ (S-PTAD) ₄ ^d	Rh ₂ (R-BNP) ₄ ^b	product	yield (%)	ee (%)	yield (%)	ee (%)	yield (%)	ee (%)
1		85	88	21 ^b	72	42					
2		84	87	77 ^c	46 ^c	51					
3		93	87	67 ^c	80	57					
4		87	88	71 ^c	48 ^c	57					
5		66	90	93 ^c	84	57					
6		89	92	80 ^c	78	51					



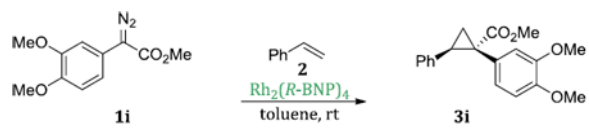
entry	Ar	Rh₂ (S-DOSP)₄^a		Rh₂ (S-PTAD)₄^a		Rh₂ (R-BNP)₄^b		
		product	yield (%)	ee (%)	yield (%)	ee (%)	yield (%)	Ee (%)
7		3g	92	86	87 ^c	80 ^c	69	27
8		3h	88 ^b	82 ^b	88 ^b	60 ^b	82	63
9		3i	74	56	70 ^c	94 ^c	93	97
10		3j	78 ^b	79 ^b	72 ^b	16 ^b	82	88
11		3k	85 ^{b,c}	28 ^{b,c}	85 ^{b,c}	3 ^{b,c}	69 ^c	92 ^c
12		3l	98 ^b	34 ^b	95 ^b	9 ^b	63	90

^a pentane,

^b toluene,

^c 0.5 mol% catalyst loading

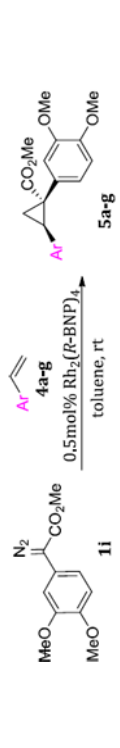
Table 2
Examination of Rh₂ (R-BNP)₄ Loading

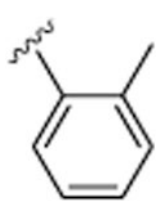
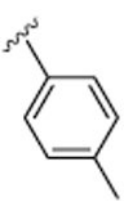
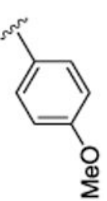
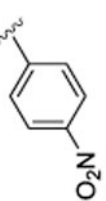
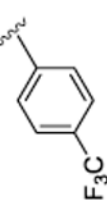


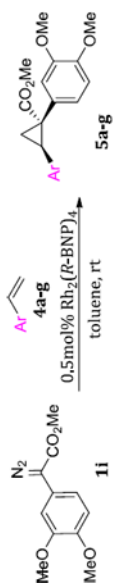
entry	catalyst loading (mol%)	reaction time(h)	yield (%)	ee (%)
1	1	1	93	97
2 ^a	0.5	1	83	96
3	0.1	12	80	91
4	0.01	17	73	40

^a2.5 equiv. styrene used

Table 3

Substrate Scope of Styrene with $\text{Rh}_2(\text{R-BNP})_4$


entry	Ar	product	yield (%)	ee(%)	yield (%)	Ee(%)
1		5a	76	90	47	64
2		5b	90	88	50	67
3		5c	80	90	82	62
4		5d	94	80	28	50
5		5e	90	90	19	63



entry	Ar	Rh ₂ (R-BNP) ₄		Rh ₂ (R-DOSP) ₄		
		product	yield (%)	ee (%)	yield (%)	Ee (%)
6		5f	81	89	49	67
7		5g	72	86	79	48

Table 4
A Guide to Chiral Dirhodium-(II) Catalyzed Cyclopropanation

Ar	catalyst	yield (%)	ee(%)
 R=H, Cl R'=H, alkyl, Cl, OMe	Rh ₂ (<i>R</i> -DOSP) ₄	66-93	82-92
 R=Cl, OMe	Rh ₂ (<i>S</i> -PTAD) ₄	80-87	80-97
 R=H, OMe	Rh ₂ (<i>R</i> -BNP) ₄	63-93	88-97