Comparison of 1,2-Diarylcyclopropanecarboxylates with 1,2,2-Triarylcyclopropanecarboxylates as Chiral Ligands for Dirhodium-Catalyzed Cyclopropanation and C—H Functionalization.

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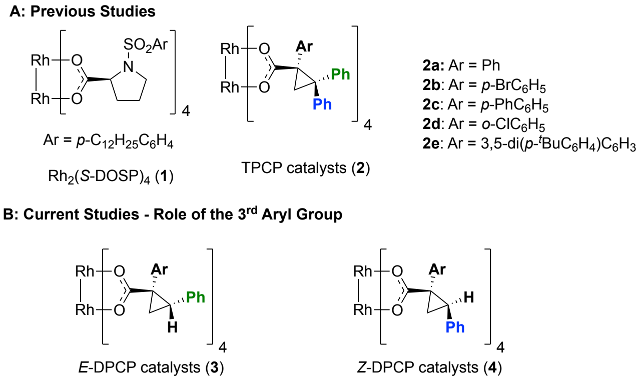
Supporting Information Placeholder

ABSTRACT: Dirhodium triarylcyclopropanecarboxylate catalysts (Rh_2TPCP_4) are sterically demanding and capable of controlling the site selectivity of C—H functionalization by means of C—H insertion with donor/acceptor carbenes. This study compares the structures and the reactivity profiles of dirhodium triarylcyclopropanecarboxylates with dirhodium diarylcyclopropanecarboxylates. The absence of the third aryl group makes the catalysts less sterically demanding and lack a well-defined preferred conformation. The catalysts have a greater tendency for inducing C—H functionalization at tertiary C—H bonds versus their triaryl counterparts but are generally not capable of achieving high levels of asymmetric induction. These studies confirm the critical requirement of having at least three substituents on the cyclopropanecarboxylate ligands in order to have well defined sterically demanding catalysts capable of high levels of asymmetric induction.

Introduction

Catalyst-controlled C—H functionalization is a research area of considerable current interest.[1-4] Controlling site selectivity in molecules with multiple C—H bonds is crucial for the chemistry to be generally useful.[5-8] The use of intramolecular reactions or directing groups as controlling elements is now well established and predictable.[6, 9-11] However, broadly selective reactions in which the control comes primarily from the catalysts is still very challenging.[1-3] We have developed an approach for site selective reactions using the dirhodium tetracarboxylate-catalyzed C—H insertion of donor/acceptor carbenes.[12, 13] The initial catalyst used in these reactions was Rh_2(*S*-DOSP)$_4$ (**1**)[14] and it results in high asymmetric induction with many substrates.[12] A breakthrough in this area was the development of dirhodium catalysts with triphenylcyclopropanecarboxylate (TPCP) ligands (**2**, Scheme 1).[15] They are sterically demanding catalysts capable of overcoming the natural electronic tendency of the carbenes to insert into tertiary C—H bonds, and by appropriate modifications, they can be tuned to select specific primary[16] or secondary[17, 18] C—H bonds. Some of the most significant Rh-TPCP catalysts developed to date are **2a-e**,[13] and they have been shown to be effective chiral catalysts in a range of carbene transformations.[19-28]

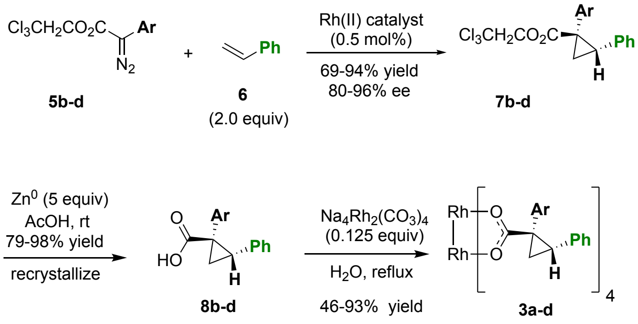


Scheme 1. Chiral dirhodium tetracarboxylate catalysts

In order to further expand the toolbox of catalysts we have developed for site selective C—H functionalization reactions,[16-18] we decided to investigate what were the key structural features of the cyclopropanecarboxylate ligands that made them so effective. For this reason, in this paper, we describe the synthesis and evaluation of dirhodium complexes with diarylcyclopropanecarboxylate ligands (Rh_2(*R*-(*E*)-DPCP)$_4$ (**3**) and Rh_2(*R*-(*Z*)-DPCP)$_4$ (**4**)), where an aryl group is *trans* or *cis* to the carboxylate group.[29] Comparison of performance of these catalysts with each other and with that of dirhodium-triarylcyclopropanecarboxylate (**2**) complex revealed the important role of the third aryl group on the site selectivity and the enantioselectivity of dirhodium tetra(cyclopropanecarboxylate)-catalyzed reactions of donor/acceptor carbenes.

Catalyst Synthesis

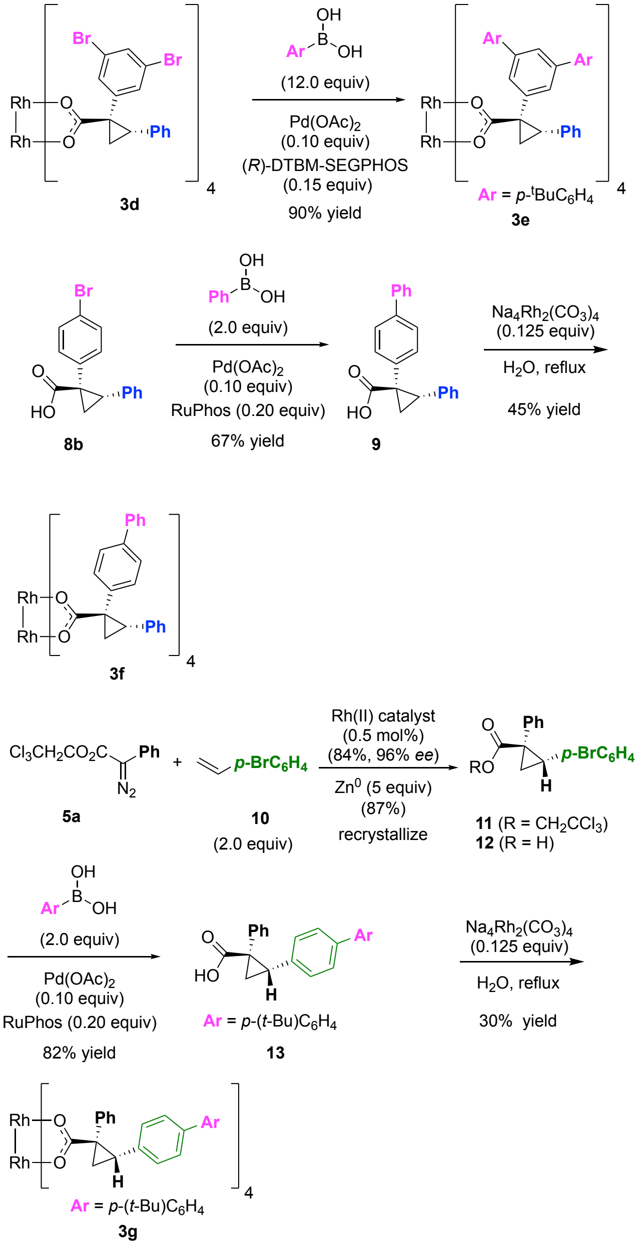
The synthesis of the (*E*)-DPCP catalysts (**3**) is relatively straightforward because the rhodium-catalyzed cyclopropanation of styrenes with aryldiazoacetates is highly diastereoselective, favoring the diastereomer with the two aryl groups arranged *cis* to each other.[15] The synthesis involves an asymmetric cyclopropanation, which can be used to introduce some of the most significant aryl groups that have been used in the triarylcyclopropanecarboxylate dirhodium catalysts. The parent catalyst, **3a** has been prepared previously.[15] The general synthetic approach to the substituted catalysts **3b-d** is summarized in Scheme 2. The cyclopropanation was conducted using 2,2,2-trichloroethyl aryldiazoacetates **5b-d** as the carbene precursor with styrene. The optimal chiral dirhodium catalyst for each cyclopropanation were identified (see supporting information for details). The cyclopropanation to form **7b-d** in 80-96% ee was conducted with a catalyst loading of 0.5 mol %, although it has been recently reported that similar cyclopropanations can be conducted using catalyst loadings as low as 0.001 mol %.[30] The 2,2,2-trichloroethyl ester in **7b-d** is easily cleaved by treatment with zinc powder in glacial acetic acid to afford the carboxylic acids **8b-d**, which can be readily enantioenriched by means of fractional crystallization. A ligand exchange with sodium rhodium carbonate generated the desired catalysts **3b-d**.



a: Ar = Ph, **b**: Ar = *p*-BrC_6H_4, **c**: Ar = *o*-BrC_6H_4, **d**: Ar = 3,5-di-BrC_6H_3

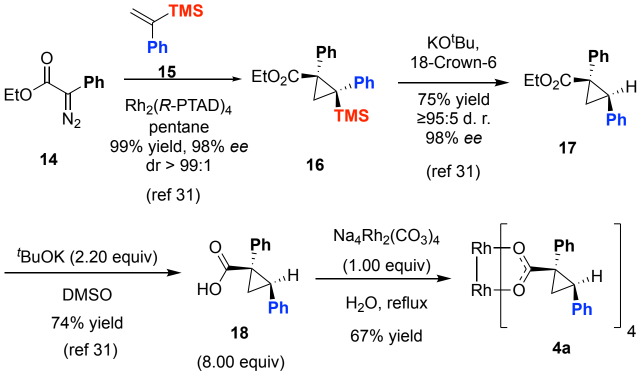
Scheme 2. Synthesis of DPCP catalysts 3a-d

More highly functionalized DPCP catalysts were obtained by combining the asymmetric cyclopropanation with a palladium-catalyzed Suzuki coupling, as illustrated in Scheme 3. The 3,5-di-(*t*-BuC_6H_4)C_6H_3 group was found to be very effective in the TPCP catalysts for site selective functionalization of the most accessible secondary C—H bonds, and it was incorporated into the DPCP catalyst by conducting an eightfold cross coupling[17] on the preformed dibromo catalyst **3d** to form **3e** in 90% yield. In the case of very large ligands, such as the carboxylate required for the formation of **3e**, it is best to do the cross-coupling on the preformed catalyst, but in the case of smaller ligands, the cross coupling can be conducted first on the carboxylic acid ligand before the ligand exchange. The biphenyl functionality in the TPCP catalyst series lead to the bulkiest catalyst to date, capable of site selective reactions at unactivated primary C—H bonds.[16] Thus, the biphenyl catalysts **3f** and **3g** were also formed, in this case with the cross-coupling reaction being conducted first on **8b** and **12** to form **9** and **13**, respectively followed by the ligand exchange.



Scheme 3. Synthesis of DPCP catalysts 3e-g

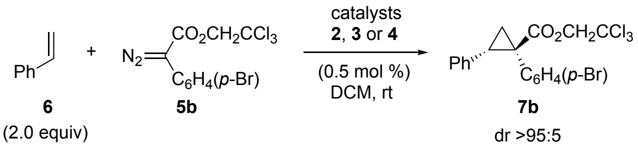
The (*Z*)-DPCP catalyst series **4** cannot be prepared directly from the cyclopropanation of styrene because the formation of the other diastereomer is strongly preferred. However, Su has shown that the Rh_2(*R*-PTAD)$_4$ catalyzed cyclopropanation of the TMS derivative **15** with ethyl phenyldiazoacetate **14** is highly diastereoselective and enantioselective, favoring the cyclopropane **16** with the 2-phenyl groups *cis* to each other.[31] Furthermore, on silyl removal the system equilibrates to form the diphenyl cyclopropane **17** with the phenyl groups trans to each other. Ester hydrolysis leads to the formation of the cyclopropanecarboxylate **18**, which is then capable of ligand exchange with sodium rhodium carbonate to form the (*Z*)-DPCP catalyst **4a**.



Scheme 4. Synthesis of (*Z*)-DPCP catalysts 4

Catalyst evaluation

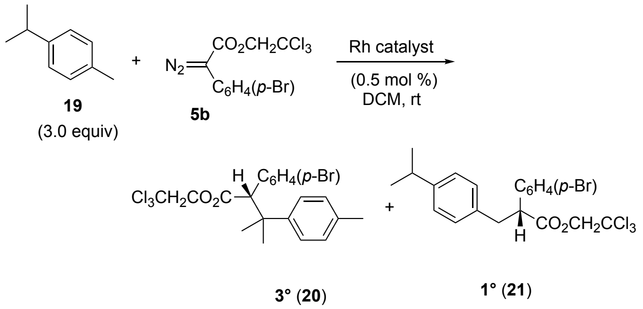
The cyclopropanation of styrene with 2,2,2-trichloroethyl 4-bromophenyldiazoacetate (**5b**) was used as a benchmark reaction to determine the effectiveness of the DPCP catalysts for asymmetric induction (Scheme 5). The cyclopropanation with the triphenylcyclopropanecarboxylate catalyst, Rh_2(*S*-TPCP)$_4$ (**2a**) was used as the reference reaction[15] because the goal of these studies was to determine how the DPCP catalysts compared with the TPCP catalysts. All of the DPCP catalysts **3** gave good yields and excellent diastereoselectivity for the *E*-cyclopropane **7b**. The high diastereoselectivity is a characteristic feature of cyclopropanation with donor/acceptor carbenes.[29] Rh_2(*S*-TPCP)$_4$ is also highly enantioselective, generating **7b** in 91% ee.[15] In contrast, the (*E*)-DPCP catalysts **3**, generated **7b** with low levels of enantioinduction (6-26% ee), even though several of the catalysts had aryl functionality that were especially effective in the TPCP class of catalysts. Interestingly, the (*Z*)-DPCP catalyst **4a** did give high asymmetric induction in the cyclopropanation (84% ee). These results indicate the aryl group cis to the carboxylate has a more significant influence on the enantioselectivity than its stereoisomeric counterpart.



Catalyst	Yield, %	ee, %
Rh_2(*S*-TPCP)$_4$ (**2a**)	**90**	**91**
3a	92	8
3b	85	14
3c	72	10
3d	77	12
3e	93	6
3f	82	26
3g	70	6
4a	**76**	**84**

Scheme 5. Asymmetric cyclopropanation of styrene

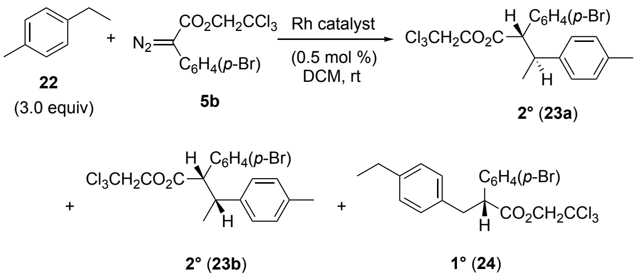
One of the most intriguing features of the Rh-TPCP catalysts is their steric influence on the approach of substrates to the metal-bound carbene. Hence, they can achieve site selective C—H functionalization of electronically less favoured but sterically more accessible C—H bonds.[13] In order to test the site-selectivity of the new DPCP catalysts, they were challenged in the reaction of the aryldiazoacetate **4b** with 4-isopropyltoluene (**19**). The C—H functionalization with the prolinate catalyst Rh_2(*S*-DOSP)$_4$ (**1**) and Rh_2(*S*-TPCP)$_4$ (**2a**) were used as the reference reactions. Rh_2(*S*-DOSP)$_4$ (**1**) is a first-generation chiral catalyst and is relatively uncrowded. In the case of isopropylbenzene the steric and electronic influences are relatively balanced and a mixture of the tertiary (**20**) and primary (**21**) products are formed.[32, 33] In contrast, the Rh_2(*S*-TPCP)$_4$ (**2a**)-catalyzed reaction results in a strong preference for the primary C—H insertion to form **21** with high asymmetric induction (93% ee).[32, 33] All of the (*E*)-DPCP catalysts **3** behave as relatively uncrowded catalysts, leading to a mixture of the primary and tertiary C—H insertion products **20** and **21**, similar to Rh_2(*S*-DOSP)$_4$ (**1**). Furthermore, the enantioselectivity for the formation of **20** is relatively modest (12-51% ee) and even lower for **21** (>5-14% ee). The (*Z*)-DPCP catalyst **4a**, however, generally demonstrates characteristics more similar to the dirhodium triarylcyclopropane Rh_2(*S*-TPCP)$_4$ **2a**. It gives a strong preference for the formation of the primary C—H insertion product **21** (90:10 r.r.), which is formed in 72% ee.



Catalyst	Yield, %	3°:1°	ee 3°, %	ee 1°, %
Rh_2(*S*-DOSP)$_4$ (**1**)	**69**	36:64	-67	**81**
Rh_2(*S*-TPCP)$_4$ (**2a**)	**85**	**<1:99**	---	**93**
3a	74	39:61	40	6
3b	87	43:57	38	14
3c	95	24:76	12	6
3d	91	56:44	51	14
3e	70	57:43	41	<5
3f	87	35:65	37	10
3g	96	34:66	47	<5
4a	**87**	**10:90**	<5	**72**

Scheme 6. Asymmetric C—H functionalization of 4-isopropyltoluene

Further evaluation of the general catalyst trends was conducted for the reaction with 4-ethyltoluene (**22**, Scheme 7). In this case, Rh_2(*S*-DOSP)$_4$ (**1**), gives predominantly the secondary C—H functionalization products **23a** and **23b** (92:8 rr)[32, 33] whereas Rh_2(*S*-TPCP)$_4$ (**2a**) gives a preference for the primary C—H insertion product **24** (81:19 rr) in 93% ee.[32, 33] The (*E*)-DPCP catalysts **3** performed slightly better than Rh_2(*S*-DOSP)$_4$ (**1**) with respect to site selectivity favouring the secondary C—H functionalization products **23a** and **23b** (93:7 to 96:4 rr). However, the enantioselectivity for the formation of the major diastereomer **23a** was low. The results of the reaction with the (*Z*)-DPCP catalyst **4a** diverged from what had been seen with 4-isopropyltoluene because in this case reaction at the secondary C—H bond was preferred, demonstrating characteristics more similar to Rh_2(*S*-DOSP)$_4$ (**1**). Both, the secondary and primary C—H functionalization products **23** and **24** were produced with moderate levels of enantioselectivity, 45% ee and 66% ee, respectively. From these experiments is can be concluded that Rh_2(*R*-(*E*)-DPCP)$_4$ catalysts (**3**) behave as relatively uncrowded catalysts and give low levels of asymmetric induction. In contrast Rh_2(*R*-(*Z*)-DPCP)$_4$ (**4**), with a phenyl group *cis* to the carboxylate, behaves much more sterically demanding and can give reasonable levels of asymmetric induction. However, neither series of DPCP catalysts come close to the TPCP catalysts in terms of high asymmetric induction and controlling reactions to occur at less hindered C—H bonds.



Catalyst	Yield, %	2°:1°	23a:23b	ee 2°, %	ee 1°, %
Rh_2(*S*-DOSP)$_4$ (**1**)	66	**92:8**	75:25	**-81**	**82**
Rh_2(*S*-TPCP)$_4$ (**2a**)	91	**19:81**	76:24	<5	**93**
3a	90	95:5	85:15	13	<5
3b	43	93:7	86:14	<5	<5
3c	62	93:7	82:18	<5	<5
3d	68	95:5	88:12	29	-23
3e	32	95:5	87:13	<5	55
3f	57	96:4	87:13	<5	<5
3g	81	95:5	85:15	13	<5
4a	87	91:9	82:18	**-45**	**66**

Scheme 7. Asymmetric C—H functionalization of 4-ethyltoluene

Structural Studies on the Rh_2(DPCP)$_4$ catalysts

Having established the general reactivity characteristics of the Rh_2(DPCP)$_4$ catalysts, the next stage of the project is to understand the structural features of these catalysts and how they relate to the Rh_2(TPCP)$_4$ catalyst. Previous extensive studies on the Rh_2(TPCP)$_4$ catalysts have established that their preferred orientation is strongly dependent on the functionality of the C1-aryl group.[13] When the C1 aryl group is unsubstituted or *para*-substituted, the most stable orientations are C_2-symmetric structures, as shown in Figure 1 for Rh_2(*S*-TPCP)$_4$ (**2a**).[34] This structure is typically 3-6 kcal mol^{-1} more stable than any other structural arrangement. The substitution pattern at the C1 aryl group can have a dramatic effect on the orientation of the ligands in the catalysts. When the catalyst is 3,5-diaryl-substituted, it adopts a D_2 symmetric structure,[17] which keeps the bulky groups as far away from each other as is possible. In contrast, an ortho-chloro substituent causes the catalyst to adopt a C_4 symmetric structure.[18]

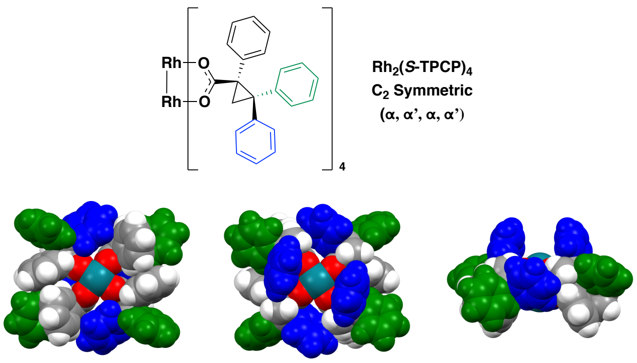


Figure 1. Preferred Conformation for Rh$_2$(S-TPCP)$_4$

X-ray structures were obtained for two of the (*E*)-DPCP catalysts **3** (see Figure 2) and shown that the parent (*E*)-Rh$_2$(DPCP)$_4$ catalyst **3a** has a D$_2$ symmetric structure, whereas the (*E*)-Rh$_2$(*3,5*-diBrDPCP)$_4$ catalyst **3d** adopts a C$_4$ symmetric structure. Although in **3a**, there does appear to be steric interference on both faces of the complex, the top face of catalysts **3d** is wide open and would not be expected to be an effective chiral catalyst.

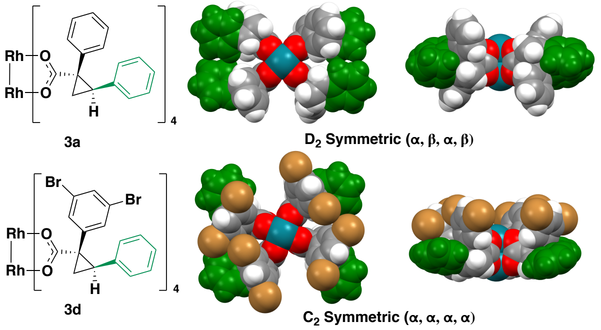


Figure 2. X-ray crystallographic structures for **3a** and **3d.** (Solvent molecules have been omitted for clarity).

Previously, our study on the Rh-TPCP series of catalysts have shown that the X-ray structures are not always the lowest energy conformation of the catalyst.[34] For example, for catalyst Rh$_2$(*S*-*p*-BrTPCP)$_4$ (**2b**), the crystal structure was reported to be D$_2$ symmetric,[15] while conformational analysis revealed that its C$_2$-symmetric structure is strongly preferred.[34] The X-ray structures of **3a** and **3d** suggested that the catalysts may be too open to have a strongly favoured specific orientation. In order to evaluate this hypothesis, here, a computational study, at the B3LYP-D3BJ/[Lanl2dz(for Rh) + [6-31(d,p)](for other atoms) level of theory (see below for more details), was conducted on the parent (*E*)-Rh$_2$(DPCP)$_4$ catalyst **3a**. As seen in Figure 3, where we presented four energetically low-lying conformations of this catalyst, all the calculated conformers of **3a** are within a 0.4 kcal/mol free energy range. These findings are consistent with the observation that these catalysts are relatively uncrowded and exhibit low levels of asymmetric induction.

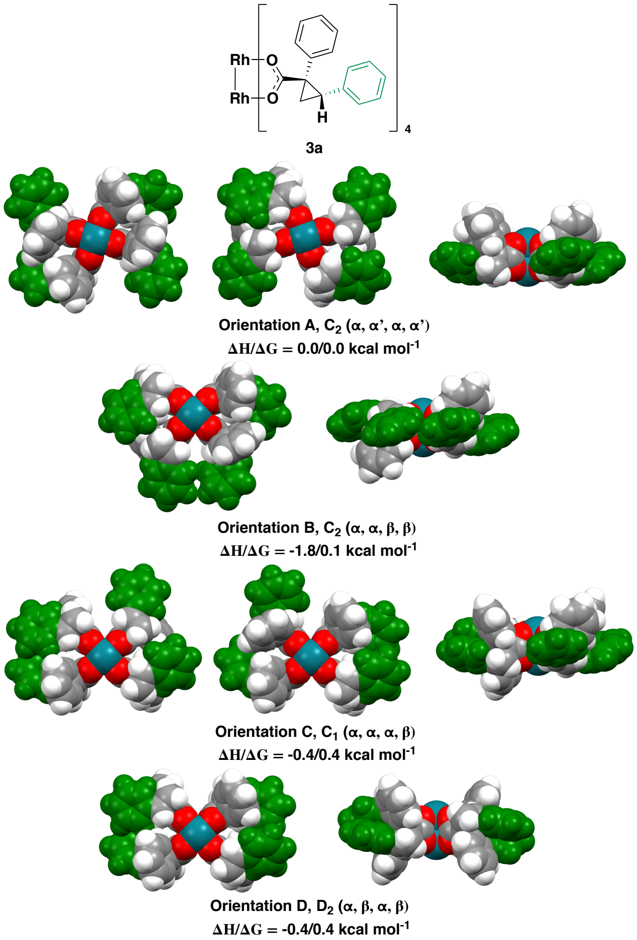


Figure 3. Calculated lower energy conformations of **3a**

Crystallization of the (*Z*)-DPCP catalyst **4a** resulted in two types of polymorphic crystals, shown in Figure 4. The two polymorphs are fairly similar, with the major difference being the dihedral angles of the C-C bond between the cyclopropane and carboxyl groups. One adopts a structure that does not have any simplifying symmetry, whereas the other adopts an α, α, β, β, i.e. C$_2$ symmetric orientation.

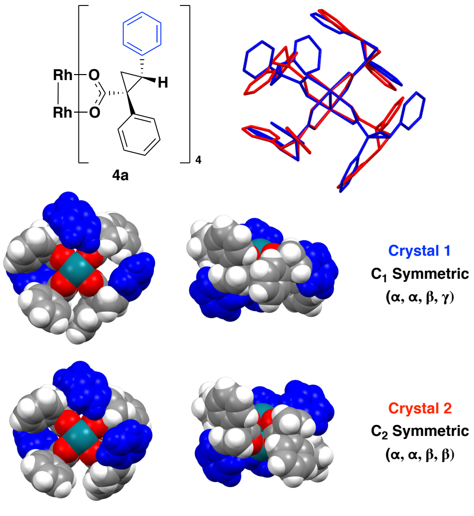
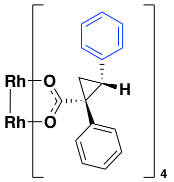
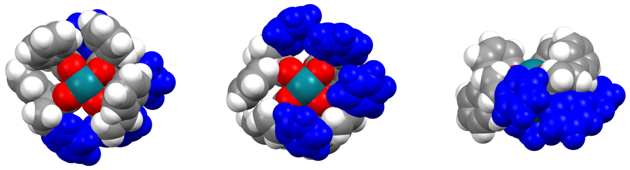


Figure 4. Two polymorphs of **4a** (Solvent molecules have been omitted for clarity.)

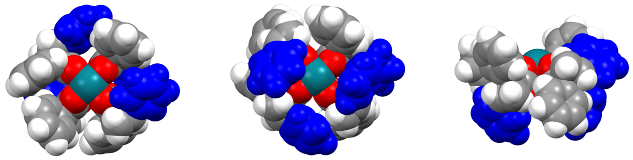
The presence of two relatively similar crystallographic structures for the (*Z*)-DPCP catalyst **4a** is an indication that this catalyst might be capable of adopting several conformations. This was confirmed through conformational analysis of **4a,** as summarized in Figure 5. These studies revealed several possible conformations within 1.0 kcal/mole of free energy interval. Even though there are several structures of similar energy, many of them have aryl groups surrounding the carbene binding site. Thus, it would be reasonable to expect **4a** to be more sterically crowded than the *E*-catalyst **3a**, which may explain why **4a** is more selective than **3a** for the primary C—H bond in isopropyltoluene and capable of moderate levels of enantioselectivity.



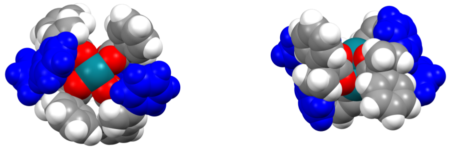
4a



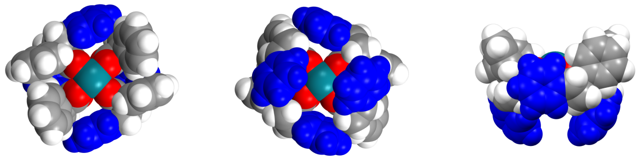
Orientation A, C_1 (α, α, β, γ)
ΔH/ΔG = 0.0/0.0 kcal mol^{-1}



Orientation B, C_1 (α, β, α, γ)
ΔH/ΔG = 0.5/0.6 kcal mol^{-1}



Orientation C, D_2 (α, β, α, β)
ΔH/ΔG = 0.3/0.6 kcal mol^{-1}



Orientation D, C_2 (α, α', α, α')
ΔH/ΔG = 0.6/1.9 kcal mol^{-1}

Figure 5. Calculated lower energy conformations of **4a**

Conclusion

This study has elucidated several factors that appear to be essential to the design of selective dirhodium cyclopropanecarboxylate catalysts. We have shown that diaryl catalysts do not perform well without a third substituent to crowd out the periphery of the catalyst, where the ligand can have only a slight influence on enantioselectivity. Without a third aryl substituent, there are many conformers energetically accessible to the cyclopropanecarboxylate catalysts, including some which place the substituent groups near the dirhodium center. These studies indicate that the most effective cyclopropanecarboxylate ligands need to have at least three additional substituents to be consistently effective in enantioselective catalysis. This feature is likely to be an important design criterion for the development of further chiral catalysts with the cyclopropanecarboxylate ligands.

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Supporting Information

The Supporting Information is available free of charge on the ACS Publications website. Expanded details of the experimental procdures, speactral data, and computational calculations. The following crystal structures have been deposited at the Cambridge Crystallographic Data Centre: **3a** (CCDC 2001026), **3d** (CCDC 2001028), **4a** – crystal 1 (CCDC 2001048), **4a** – crystal 2 (CCDC 2001276).

Competing Financial Interest

H.M.L.D. is a named inventor on a patent entitled 'Dirhodium catalyst compositions and synthetic processes related thereto' (US 8,974,428, issued March 10, 2015). The other authors declare no competing interests.

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EXPERIMENTAL SECTION

General Methods. Reagents were used as received from commercial suppliers unless otherwise stated. Styrene (**6**) was filtered through a plug of silica gel before use. All glassware was oven-dried prior to use and all reactions were performed under an inert gas (argon or nitrogen) unless otherwise stated.

Dichloromethane, toluene, hexane, pentane, and diethyl ether solvents were obtained from drying columns (Grubbs type solvent purifier) immediately prior to use. Preparative flash chromatography was performed on a Biotage MPLC system using SiliCycle SilaFlash P60 silica (normal phase, 60 Å, 40-63 µm.) ^{1}H NMR spectra were recorded on Varian Nuclear Magnetic Resonance spectrometers at nominal frequencies of 600, 500, 400 or 300 MHz. ^{13}C NMR spectra were recorded at nominal frequencies of 150, 125, 100 or 75 MHz and ^{13}C NMR spectra were obtained with complete proton decoupling. High resolution mass spectra were recorded on a Finnigan LTQ FTMS. Melting points were measured on a MEL-TEMP electrothermal apparatus and are uncorrected. FTIR spectra were collected on a Nicolet iS10 from Thermo Scientific. Optical rotations were measured on a PerkinElmer Model 341 Polarimeter. Chiral HPLC analyses using standard pressure columns were performed on Varian Prostar 210, Agilent 1100, or Agilent 1290 Infinity II instruments. All HPLC columns had dimensions of 4.6x250 mm. A corresponding racemic standard was run sequentially with every chiral analysis to verify the retention times of the major and minor enantiomers. These were prepared using either $Rh_2(OOct)_4$, $Rh_2(OAc)_4$, or a 1:1 mixture of both enantiomers of the indicated chiral catalyst. The following previously prepared compounds were prepared by literature procedures: dirhodium tetrakis[1-[[4-dodecylphenyl]sulfonyl](2*S*)-prolinate] [Rh$_2$(*S*-DOSP)$_4$] (**1**),[29] dirhodium tetrakis ((*S*)-1,2,2-triphenylcyclopropanecarboxylate) [Rh$_2$(*S*-TPCP)$_4$] (**2a**),[35] dirhodium tetrakis ((*S*)-1-([1,1'-biphenyl]-4-yl)-2,2-diphenylcyclopropane-1-carboxylate) [Rh$_2$(*S*-*p*-PhTPCP)$_4$] (**2c**),[33] dirhodium tetrakis ((1*R*,2*S*)-1,2-diphenylcyclopropane-1-carboxylate) [(*E*)-Rh$_2$(*S*-DPCP)$_4$] (**3a**).[15] 2,2,2-trichloroethyl 2-diazo-2-phenylacetate (**5a**),[36] 2,2,2-trichloroethyl 2-(4-bromophenyl)-2-diazoacetate (**5b**),[32] 2,2,2-trichloroethyl 2-(2-bromophenyl)-2-diazoacetate (**5c**),[37] 2,2,2-trichloroethyl 2-diazo-2-(3,5-dibromophenyl)acetate (**5d**),[37] 2,2,2-trichloroethyl (1*R*,2*S*)-1-(4-bromophenyl)-2-phenylcyclopropane-1-carboxylate (**7b**),[38] ethyl (1*R*,2*R*)-1,2-diphenyl-2-(trimethylsilyl)cyclopropane-1-carboxylate (**15**),[31] 2,2,2-trichloroethyl 2-(4-bromophenyl)-3-methyl-3-(p-tolyl)butanoate (**20**),[39] 2,2,2-trichloroethyl 2-(4-bromophenyl)-3-(4-isopropylphenyl)propanoate (**21**),[53] 2,2,2-trichloroethyl 2-(4-bromophenyl)-3-(p-tolyl)butanoate (**23b:23a**),[39] 2,2,2-trichloroethyl 2-(4-bromophenyl)-3-(4-ethylphenyl)propanoate(**24**),[33] methyl 2-(4-bromophenyl)-3-methyl-3-(*p*-tolyl)butanoate (**26**).[33]

Ligand Synthesis. 2,2,2-trichloroethyl (1*R*,2*S*)-1-(2-bromophenyl)-2-phenylcyclopropane-1-carboxylate (7c). A round bottom flask was charged with anhydrous pentane (60 mL), styrene (**6**) (10.6 g, 101 mmol, 5.0 equiv) and Rh$_2$(*R*-PTAD)$_4$ (160 mg, 102 µmol, 0.5 mol %). The flask was placed under an argon atmosphere, and then the mixture was cooled to 0 °C using an ice bath. 2,2,2-trichloroethyl 2-(2-bromophenyl)-2-diazoacetate (**5c**, 7.6 g, 20 mmol, 1.0 equiv) dissolved in anhydrous pentane (100 mL) was introduced dropwise to the stirred mixture. After the addition was complete the mixture was stirred under argon for an additional 2 h 30 min. Then, volatiles were removed on a rotary evaporator, and the crude product was purified by flash column chromatography on normal phase silica gel (0-10% EtOAc / hexanes.) to give 5.8 g of the desired product as a colorless oil (79% yield.) Chiral HPLC (OD-H, 1.0 mL / min, 0.5% i-PrOH / hexanes, λ = 254 nm, rt 15.0 min (major) 21.0 (minor); 80% ee. $[\alpha]_D^{20}$ – 36.1 (c 1.00, CHCl$_3$). IR (neat): 3089, 3064, 3034, 2952, 1735, 1238, 1154, 810, 745, 716, 695 cm^{-1}. The ^{1}H NMR and ^{13}C{1H} NMR spectra of this compound showed that this compound exists as a mixture of rotational isomers at room temperature. The signals converged when the spectra were collected at 85 °C. ^{1}H NMR (500 MHz, toluene-d8) δ 7.24 (d, J = 7.9 Hz, 1H), 7.02 – 6.89 (m, 4H), 6.86 (t, J = 7.8 Hz, 1H), 6.79 – 6.73 (m, 2H), 6.71 (td, J = 7.7, 1.7 Hz, 1H), 4.61 (d, J = 11.9 Hz, 1H), 4.52 (d, J = 11.9 Hz, 1H), 3.47 (t, J = 8.6 Hz, 1H), 2.33 – 2.20 (m, 1H), 1.85 (dd, J = 7.6, 5.3 Hz, 1H). ^{13}C{1H} NMR (126 MHz, toluene-d8) δ 170.3, 135.6, 134.4, 133.5, 132.7, 128.6, 128.2, 128.1, 127.4, 126.5, 126.3, 95.2, 74.6, 38.3, 34.2, 22.4. HRMS (APCI) m/z: [M+H]$^+$ (Pos.) calcd for $C_{18}H_{15}O_2{}^{79}Br^{35}Cl_3$ 446.9316; found 446.9317. Further enantioenrichment was performed at the next step of the synthesis.

2,2,2-trichloroethyl (1*R*,2*S*)-1-(3,5-dibromophenyl)-2-phenylcyclopropane-1-carboxylate (7d). A round-bottom flask was charged with Rh$_2$(*S*-*p*-PhTPCP)$_4$ (**2c**, 50.0 mg, 28.3 µmol, 0.5 mol %), styrene (**6**) (2.95 g, 28.3 mmol, 5.0 equiv), and anhydrous DCM (57 mL). A dropping funnel was attached to the flask, and the apparatus was purged with argon for 10 min. A solution of 2,2,2-trichloroethyl 2-diazo-2-(3,5-dibromophenyl)acetate (**5d**, 2.55 g, 5.66 mmol, 1.0 equiv) in DCM (45 mL) was introduced dropwise over 2 h with moderate stirring at room temperature. The mixture was then concentrated *in vacuuo* to afford 4.05 g of a thick green oil. The desired product was separated from the crude mixture by flash column chromatography on normal phase silica gel (50 g, 0-5% EtOAc / hexanes.) to give 2.52 g of 2,2,2-trichloroethyl (1*R*,2*S*)-1-(3,5-dibromophenyl)-2-phenyl-cyclopropane-1-carboxylate as a colorless solid after drying under high vacuum (85% yield). mp 91.0-93.0 °C (from EtOAc). Chiral HPLC: OD-H column, 0.5 mL/min, 0.5 % i-PrOH in hexanes, λ = 230 nm. rt 14.5 min (major) 18.3 min (minor); 89% ee. $[\alpha]^{20}_{D}$ +2.8 (c = 1.00, $CHCl_3$). IR (solid): 3069, 3030, 2950, 1721, 1583, 1553, 1254, 1235, 1161, 1116, 721, 697 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.41 (t, J = 1.8 Hz, 1H), 7.19 – 7.09 (m, 4H), 6.88 – 6.79 (m, 2H), 4.84 (d, J = 11.9 Hz, 1H), 4.61 (d, J = 11.9 Hz, 1H), 3.22 (dd, J = 9.4, 7.5 Hz, 1H), 2.26 (dd, J = 9.4, 5.4 Hz, 1H), 1.98 (dd, J = 7.5, 5.4 Hz, 1H). ^{13}C{1H} NMR (75 MHz, $CDCl_3$) δ 170.9, 137.8, 134.5, 133.9, 133.0, 128.2, 128.1, 127.3, 121.9, 94.8, 74.5, 36.3, 34.3, 19.9. HRMS (APCI) [M+H]$^+$ (Pos.) calcd for $C_{18}H_{14}O_2{}^{79}Br_2{}^{35}Cl_3$ 524.8421; found 524.8424. Further enantioenrichment was performed at the next step of the synthesis.

(1*R*,2*S*)-1-(4-Bromophenyl)-2-phenylcyclopropane-1-carboxylic acid (8b). A 20 mL scintillation vial was charged with 2,2,2-trichloroethyl (1*R*,2*S*)-1-(4-bromophenyl)-2-phenylcyclopropane-1-carboxylate (**7b**, 110 mg, 0.28 mmol, 1.00 equiv), obtained in 96% *ee* using Rh_2(*S*-*p*-PhTPCP)$_4$ (**2c**) as the catalyst[4]), zinc dust (80.2 mg, 1.38 mmol, 5.00 equiv), and acetic acid (2.50 mL). The mixture was stirred at room temperature for 18 h. Then, it was partitioned between EtOAc/H_2O. The aqueous phase was extracted with an additional portion of EtOAc, and then dried with $MgSO_4$. The EtOAc solution was filtered and concentrated under vacuum to afford the crude product as a colorless solid. Further purification was achieved with flash column chromatography (10-50% Et_2O/hexanes), which yielded 72 mg of the pure product as a colorless solid (82% yield). A racemic precipitate crystallized from a hexanes solution of this material. It was filtered and the eluent was evaporated to afford the enantiopure product (>99% ee) as a colorless solid (41 mg, 57% recovery.) mp 72.5-75.0 °C. Chiral HPLC: AD-H, 1.0 mL/min, 5.0% i-PrOH / hexanes, λ = 230 nm. rt 10.0 min (minor) 11.4 min (major); >99% ee. $[\alpha]^{20}_{D}$ – 6.7 (c = 1.00, $CHCl_3$.) IR (solid): 3030, 2924, 2852, 2589, 1681, 1488, 1420, 1280, 1264, 1012, 907, 731, 711, 695 cm^{-1}. ^{1}H NMR (600 MHz, benzene-d6) δ 6.99 (d, J = 8.1 Hz, 2H), 6.81 – 6.71 (m, 3H), 6.53 (d, J = 8.0 Hz, 2H), 6.43 (dd, J = 7.0, 2.6 Hz, 2H), 3.07 (t, J = 8.3 Hz, 1H), 1.92 (dd, J = 9.3, 5.0 Hz, 1H), 1.43 (dd, J = 7.4, 5.0 Hz, 1H). ^{13}C{1H} NMR (126 MHz, DMSO-d6) δ 174.5, 136.6, 135.5, 134.3, 130.7, 128.5, 128.2, 126.7, 120.2, 37.0, 32.4, 19.0. HRMS (APCI) m/z: [M+H]$^+$ (Pos.) calcd for $C_{16}H_{14}O_2{}^{79}Br$ 317.0172; found 317.0165.

(1*R*,2*S*)-1-(2-bromophenyl)-2-phenylcyclopropane-1-carboxylic acid (8c). To a round bottom flask was added: 2,2,2-trichloroethyl (1*S*,2*R*)-1-(2-bromophenyl)-2-phenylcyclopropane-1-carboxylate (**7c**, 5.80 g, 12.9 mmol, 1.0 equiv), glacial acetic acid (100 mL) and zinc dust (4.2 g, 64.5 mmol, 5.0 equiv) The mixture was stirred at room temperature for 4 days. Then, it was diluted with water (1 L) and extracted with three portions of EtOAc. The pooled organic phase was backwashed with DI water and then dried over $MgSO_4$. The resulting filtrate was concentrated *in vacuuo* to afford a colorless solid. The product was purified by flash column chromatography on silica gel (normal phase, 10-60% EtOAc / hexanes) to afford 1.88 g of the desired product as a colorless solid (46% yield.) To prepare the enantiopure product from this material (>99% ee) it was recrystallized from EtOH/hexanes (recrystallization recovery 733 mg, 40%). mp 99-102 °C (from CH_2Cl_2). Chiral HPLC: AD-H, 1.0 mL/min, 1.0% i-PrOH / hexanes, λ = 254 nm. rt 47.9 min (major) 51.2 min (minor); >99% ee. $[\alpha]^{20}_{D}$ +56 (c = 0.29, EtOH.) IR (solid): 3383, 2971, 2542, 1677, 1426, 1287, 1027, 973, 947, 763, 743, 695 cm^{-1}. The ^{1}H NMR and ^{13}C{1H} NMR spectra of this compound showed that this compound exists as a mixture of rotational isomers at room temperature. The signals converged when the spectra were collected at 85 °C. ^{1}H NMR (500 MHz, toluene-d8) δ 11.81 (s, 1H), 7.19 – 7.08 (m, 1H), 6.87 – 6.77 (m, 4H), 6.74 (s, 1H), 6.64 – 6.49 (m, 3H), 3.31 (s, 1H), 2.07 – 1.87 (m, 1H), 1.71 – 1.59 (m, 1H). ^{13}C{1H} NMR (126 MHz, toluene-d8) δ 178.3, 135.7, 134.6, 133.5, 132.7, 128.5, 128.2, 127.8, 127.3, 126.4, 126.2, 38.3, 34.3, 22.6. HRMS (APCI) m/z: [M+H]$^+$ (Pos.) calcd for $C_{16}H_{14}O_2{}^{79}Br$ 317.0172; found 317.0171.

(1*R*,2*S*)-1-(3,5-dibromophenyl)-2-phenylcyclopropane-1-carboxylic acid (8d). 2,2,2-Trichloroethyl (1*R*,2*S*)-1-(3,5-dibromophenyl)-2-phenylcyclopropane-1-carboxylate (**7d**, 2.80 g, 5.3 mmol, 1.0 equiv) was treated with zinc dust (1.74 g, 26.5 mmol, 5.0 equiv) and acetic acid (44 mL). The mixture was stirred at room temperature for 18 h. Then, it was extracted with EtOAc (2x100 mL). The organic phase was separated and dried over $MgSO_4$. Filtration of the mixture and evaporation of solvent *in vacuuo* afforded 1.96 g of (1*R*,2*S*)-1-(3,5-dibromophenyl)-2-phenylcyclopropane-1-carboxylic acid (93% yield.) The product was enantioenriched by crystallization from EtOAc (recrystallization recovery 1.23 g, 70%). mp 218-219 °C (from EtOAc). Chiral HPLC: AD-H, 1.0 mL/min, 1.0% i-PrOH in hexanes, λ = 230 nm. rt 21.4 min (major) 19.0 min (minor), >99% *ee*. $[\alpha]^{20}_{D}$ +12.6 (c = 0.387, EtOH.) IR (solid): 3069, 3030, 2950, 1720, 1553, 1254, 1235, 811, 721, 697 cm^{-1}. ^{1}H NMR (600 MHz, DMSO-d6) δ 12.70 (s, 1H), 7.49 (d, J = 1.8 Hz, 1H), 7.16 (d, J = 1.8 Hz, 2H), 7.08 (t, J = 7.4 Hz, 2H), 7.03 (t, J = 7.2 Hz, 1H), 6.93 – 6.86 (m, 2H), 3.02 (dd, J = 9.1, 7.3 Hz, 1H), 2.10 (dd, J = 7.3, 5.3 Hz, 1H), 1.87 (dd, J = 9.1, 5.3 Hz, 1H). ^{13}C{1H} NMR (151 MHz, DMSO-d6) δ 173.8, 140.7, 136.1, 134.1, 132.1, 128.6, 128.2, 126.9, 121.6, 36.6, 32.7, 18.8. HRMS (APCI) m/z: [M+H]$^+$ (Pos.) calcd for $C_{16}H_{13}O_2{}^{79}Br_2$ 394.9277; found 394.9278.

(1*R*,2*S*)-1-([1,1'-Biphenyl]-4-yl)-2-phenylcyclopropane-1-carboxylic acid (9). A round bottom flask was charged with phenylboronic acid (1.77 g, 14.5 mmol, 2.0 equiv), RuPhos (677 mg, 1.45 mmol, 0.20 equiv), tribasic potassium phosphate (3.59 g, 16.9 mmol, 2.33 equiv), and palladium(II) acetate (162.8 mg, 0.73 mmol, 0.10 equiv). A reflux condenser was attached to the flask, and the apparatus was purged with argon as a solution of (1*R*,2*S*)-1-(4-bromophenyl)-2-phenylcyclopropane-1-carboxylic acid (**8b**, 2.30 g, 7.25 mmol, 1.0 equiv), in degassed 1,4-dioxane (21 mL) was introduced. The mixture was stirred at 100 °C for 16 h (oil bath). After cooling to room temperature, the mixture was then passed through a plug of silica gel with 20% MeOH/DCM. The filtrate was concentrated under vacuum, yielding 5.43 g of an orange solid. 1.51 g of the desired product was obtained from this mixture after flash chromatography on silica (0-38% EtOAc/hexanes) as a colorless solid (67% yield.) An additional recrystallization from toluene was conducted at this stage (recrystallization recovery 1.34 g, 89%). mp 201.5-203.0 °C (from toluene). Chiral HPLC: AD-H, 0.5 mL/min, 5.0% i-PrOH / hexanes, λ = 230 nm. rt 25.7 min (minor) 29.7 min (major); >99% ee. $[\alpha]^{20}_D$ + 46 (c = 0.287, EtOH.) IR (neat): 3215, 3031, 1680, 1488, 1418, 1286, 1263, 974, 758, 728 cm^{-1}. ^{1}H NMR (500 MHz, DMSO-d6) δ 12.49 (s, 1H), 7.57 (d, J = 7.7 Hz, 2H), 7.52 – 7.36 (m, 5H), 7.31 (q, J = 8.0, 7.4 Hz, 1H), 7.11 (d, J = 8.0 Hz, 2H), 7.04 (dt, J = 15.5, 7.1 Hz, 3H), 6.90 (d, J = 7.5 Hz, 2H), 3.14 – 3.00 (m, 1H), 2.04 (dd, J = 7.3, 5.0 Hz, 1H), 1.96 (dd, J = 9.2, 4.9 Hz, 1H). ^{13}C{^{1}H} NMR (126 MHz, DMSO-d6) δ 174.8, 140.1, 138.5, 137.0, 135.1, 132.7, 129.3, 128.6, 128.1, 127.7, 126.9, 126.6, 126.0, 37.2, 32.5, 19.3. HRMS (APCI) m/z: [M+H]$^+$ (Pos.) calcd for $C_{22}H_{19}O_2$ 315.1380; found 315.1377.

2,2,2-Trichloroethyl (1*R*,2*S*)-2-(4-bromophenyl)-1-phenylcyclopropane-1-carboxylate (11) Rh_2(*S*-p-PhTPCP)$_4$ (**2c**, 53.6 mg, 30.4 µmol, 0.2 mol %), pentane (90 mL), and 4-bromostyrene (**10**) (7.79 g, 42.7 mmol, 2.8 equiv) were combined in a round bottom flask. The flask was cooled to 0 °C using an ice bath, and then a solution of 2,2,2-trichloroethyl 2-diazo-2-phenylacetate (**5a**, 2.22 g, 15.2 mmol, 1.0 equiv) in pentane (120 mL) was added dropwise via an addition funnel. After the addition was completed, the mixture was stirred for 1 h and then concentrated to a green oil *in vacuuo*. The oil was subjected to flash column chromatography (2% EtOAc / hexanes,) affording the desired product as a colorless solid (2.86 g, 84% yield) mp 68.0-69.0 °C (from CH_2Cl_2). Chiral HPLC: OD-H, 1.0 mL/min, 1.0% i-PrOH / hexanes, λ = 230 nm. rt 38.5 min (major) 71.7 min (minor); 95% ee. $[\alpha]^{20}_D$ – 15.2 (c = 1.00, $CHCl_3$.) IR (solid): 3086, 3031, 2950, 1739, 1492, 1239, 1151, 1050, 830, 808, 709, 701 cm^{-1}. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.22 – 7.08 (m, 5H), 7.04 (dd, J = 6.6, 3.0 Hz, 2H), 6.63 (d, J = 8.2 Hz, 2H), 4.81 (d, J = 11.9 Hz, 1H), 4.62 (d, J = 11.8 Hz, 1H), 3.14 (dd, J = 9.3, 7.3 Hz, 1H), 2.26 (dd, J = 9.3, 5.2 Hz, 1H), 1.93 (dd, J = 7.4, 5.2 Hz, 1H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$) δ 171.8, 134.9, 133.2, 131.9, 130.9, 129.6, 127.9, 127.5, 120.5, 94.9, 74.4, 37.3, 33.1, 20.5. Further chiral purification was performed during the next step of the synthesis. HRMS (APCI) m/z: [M+H]$^+$ (Pos.) calcd for $C_{18}H_{15}O_2{}^{79}Br^{35}Cl_3$ 446.9316; found 446.9317.

(1*R*,2*S*)-2-(4-bromophenyl)-1-phenylcyclopropane-1-carboxylic acid (**12**). A round bottom flask was charged with 2,2,2-trichloroethyl (1*R*,2*S*)-2-(4-bromophenyl)-1-phenylcyclopropane-1-carboxylate (**11**, 2.30 g, 5.1 mmol, 1.0 equiv), acetic acid (45 mL) and zinc dust (1.71 g, 25.5 mmol, 5.0 equiv.) The mixture was stirred at room temperature for 36 h. Then, the mixture was diluted with water (200 mL) and extracted with ethyl acetate (3x150 mL). The pooled organic phase was backwashed with water (2x150 mL) and then dried with $MgSO_4$. The mixture was gravity filtered, and the filtrate was concentrated under vacuum, affording 1.42 g of the title compound as a colorless solid (87% yield.) To prepare the enantiopure product from this material (>99% ee,) it was recrystallized from hexanes (recrystallization recovery 1.11 g, 78%). mp 232.0-232.5 °C (from CH_2Cl_2). Chiral HPLC: AS-H, 1.0 mL/min, 1.0% i-PrOH / hexanes, λ = 230 nm. rt 9.1 min (major) 19.8 min (minor); >99% ee. $[\alpha]^{20}_D$ – 43.5 (c = 1.00, $CHCl_3$) IR (solid): 3022, 2834, 2548, 1678, 1491, 1435, 1293, 710, 698 cm^{-1}. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.20 – 7.08 (m, 5H), 7.05 – 6.96 (m, 2H), 6.66 – 6.56 (m, 2H), 3.09 (dd, J = 9.3, 7.4 Hz, 1H), 2.18 (ddd, J = 9.4, 5.1, 0.9 Hz, 1H), 1.88 (dd, J = 7.3, 5.1 Hz, 1H). ^{13}C{^{1}H} NMR (126 MHz, DMSO-d6) δ 174.6, 136.7, 135.5, 132.1, 130.9, 130.6, 127.9, 127.1, 119.6, 37.6, 31.7, 19.3. HRMS (APCI) m/z: [M+H]$^+$ (Pos.) calcd for $C_{16}H_{14}O_2{}^{79}Br$ 317.0172; found 317.0171.

(1*R*,2*S*)-2-(4'-(*tert*-Butyl)-[1,1'-biphenyl]-4-yl)-1-phenylcyclopropane-1-carboxylic acid (13). To a round-bottom flask was added: (1*R*,2*S*)-2-(4-bromophenyl)-1-phenylcyclopropane-1-carboxylic acid (**12**, 200 mg, 0.63 mmol, 1.0 equiv), (4-(*tert*-butyl)phenyl)boronic acid (224.5 mg, 1.26 mmol, 2.0 equiv), RuPhos (58.8 mg, 0.12 mmol, 0.20 equiv), palladium(II) acetate (14.2 mg, 63.0 µmol, 0.10 equiv), potassium phosphate tribasic (312 mg, 1.47 mmol, 2.33 equiv) and 1,4-dioxane (1.8 mL, pre-degassed with a 15 min argon sparge.) The mixture was heated at 100 °C for 16 h (oil bath), and then partitioned between EtOAc (50 mL) and 1 M aqueous HCl. The EtOAc extract was dried over $MgSO_4$. Filtration and concentration of the filtrate liquid afforded 437 mg of a green oil. The components of the oil were separated by flash column (0-5% CH_3OH/CH_2Cl_2) to afford 191 mg of the desired product as a colorless solid (82% yield) mp 234-235 °C (from CH_2Cl_2). Chiral HPLC: AD-H, 0.5 mL/min, 5.0% i-PrOH / hexanes, λ = 230 nm. rt 21.5 min (minor) 25.8 min (major); >99% ee. $[\alpha]^{20}_{D}$ + 10 (c = 1.00, EtOH.) IR (solid): 3055, 3031, 2962, 2926, 2866, 2588, 1678, 1280, 972, 817, 698 cm^{-1}. ^1H NMR (600 MHz, $CDCl_3$) δ 7.45 – 7.36 (m, 4H), 7.29 (t, J = 7.3 Hz, 2H), 7.15 – 7.09 (m, 3H), 7.05 (dt, J = 7.0, 3.9 Hz, 2H), 6.79 (d, J = 8.0 Hz, 2H), 3.18 (dd, J = 9.3, 7.4 Hz, 1H), 2.21 (dd, J = 9.3, 5.0 Hz, 1H), 1.95 (dd, J = 7.5, 5.0 Hz, 1H), 1.30 (s, 9H). $^{13}C\{1H\}$ NMR (126 MHz, $CDCl_3$) δ 180.4, 150.2, 139.0, 137.6, 134.8, 134.0, 132.0, 128.4, 128.1, 127.9, 127.4, 126.5, 126.2, 125.7, 37.4, 34.7, 34.5, 33.8, 31.4, 21.0. HRMS (APCI) m/z: $[M+H]^+$ (Pos.) calcd for $C_{26}H_{27}O_2$ 371.2006; found 371.2002.

(1*R*,2*R*)-1,2-diphenylcyclopropane-1-carboxylic acid (**18**). A 25 mL round bottom flask was charged with ethyl (1*R*,2*R*)-1,2-diphenylcyclopropane-1-carboxylate (**17**, 208 mg, 0.78 mmol, 1.0 equiv)[31] and dimethyl sulfoxide (10 mL) The stirring was turned on, and then solid potassium *tert*-butoxide (193 mg, 1.72 mmol, 2.2 equiv) was added, which caused the mixture to turn dark green. After 53 h, the reaction was quenched by pouring into saturated aqueous NH_4Cl (excess) The mixture was acidified to pH 1 via the addition of 4 M aqueous HCl solution, and then extracted with CH_2Cl_2 (2x100 mL). The pooled organic phase was dried over Na_2SO_4, and then filtered. Concentration of the liquid phase *in vacuuo* yielded the crude product as a green oil. The material was further purified by flash column chromatography (0-17% EtOAc/hexanes) to yield 136 mg of a colorless solid (73% yield.) Recrystallization from hexanes afforded the enantiopure substance (recrystallization recovery 99 mg, 73%). mp 98.0-99.5 °C (from hexanes). Chiral HPLC: AD-H, 1.0 mL/min, 5% i-PrOH / hexanes. rt 15.26 min (minor), 23.1 min (major). ee >99%. $[\alpha]_D^{20}$ + 254.1 (c 1.98, EtOH). FTIR: 3027, 2955, 2921, 1689, 1497, 1448, 1418, 1308, 1223, 695 cm^{-1}. ^1H NMR (300 MHz, methanol-d4) δ 7.59 – 7.47 (m, 2H), 7.47 – 7.03 (m, 8H), 5.05 (s, 1H), 2.85 (t, J = 8.3 Hz, 1H), 2.28 (dd, J = 7.6, 4.8 Hz, 1H), 1.55 (dd, J = 9.0, 4.8 Hz, 1H). $^{13}C\{1H\}$ NMR (75 MHz, methanol-d4) δ 173.0, 140.9, 136.7, 129.9, 128.9, 127.9, 127.7, 126.8, 126.3, 48.5, 48.3, 48.0, 47.7, 47.4, 47.1, 46.8, 38.0, 32.8, 17.6. HRMS (ESI) m/z: $[M+H]^+$ (Pos.): calcd for $C_{16}H_{15}O_2$ 239.1067; found 239.1065.

Catalyst Synthesis. Dirhodium tetrakis ((1*R*,2*S*)-1,2-diphenyl-cyclopropanecarboxylate) (**3a**). This compound was prepared following the literature procedure.[15] An X-ray quality crystal of the material was grown by vapor diffusion with toluene/hexane. The spectral data for the sample were consistent with the previously reported data.[15] ^1H NMR (400 MHz, CDCl3) δ 7.13 – 7.01 (m, 6H), 6.96 – 6.89 (m, 2H), 6.76 – 6.68 (m, 2H), 2.96 (dd, J = 9.2, 7.1 Hz, 1H), 2.04 (dd, J = 9.2, 4.8 Hz, 1H), 1.76 (dd, J = 7.2, 4.8 Hz, 1H).

Dirhodium tetrakis((1*R*,2*S*)-1-(4-bromo)phenyl-2-phenyl-cyclopropanecarboxylate) (**3b**). A 100 mL round bottom flask equipped with a magnetic stirbar and reflux condenser was charged with (1*R*,2*S*)-1-(4-bromophenyl)-2-phenylcyclopropane-1-carboxylic acid (**8b**, 1.60 g, 5.0 mmol, 8.0 equiv), sodium rhodium carbonate 2.5 hydrate (360 mg, 0.631 mmol, 1.0 equiv), and water (35 mL). The flask was purged with argon and heated to reflux (oil bath). The reaction mixture stirred at reflux for 48 h, and then it was transferred to a separatory funnel and extracted with EtOAc (3x 35 mL). The combined organic layers were washed three times with saturated aqueous $NaHCO_3$ solution, followed by 10% aqueous NaOH (3x20 mL,) and then brine (20 mL). The organic extracts were dried with $MgSO_4$, filtered, and concentrated under vacuum. The resulting material was subjected to chromatographic purification (100:1 toluene/MeCN) to afford the desired product as a green solid (755 mg, 81% yield). mp 180-188 (dec.) ^1H NMR (500 MHz, $CDCl_3$) δ 7.24 (d, J = 8.1 Hz, 2H), 7.11 (d, J = 6.2 Hz, 3H), 6.84 – 6.65 (m, 4H), 2.92 (t, J = 8.2 Hz, 1H), 2.01 (dd, J = 9.3, 4.9 Hz, 1H), 1.79 – 1.67 (m, 1H). $^{13}C\{1H\}$ NMR (126 MHz, $CDCl_3$) δ 191.4, 136.2, 134.4, 133.3, 130.8, 128.0, 127.8, 126.6, 121.1, 38.9, 33.2, 19.7. IR (Solid): 3086, 3061, 3028, 2979, 1685, 1577, 1491, 1401, 1319, 1011, 774, 763 cm^{-1}. HRMS (ESI) *m/z*: $[M+H]^+$ (Pos.) calcd for $C_{64}H_{48}O_8Br_4Rh_2$ 1465.8187; found 1465.8196.

Dirhodium tetrakis((1*R*,2*S*)-1-(2-bromophenyl)-2-phenylcyclopropanecarboxylate) (**3c**). A round bottom flask was charged with (1*R*,2*S*)-1-(2-bromophenyl)-2-phenylcyclopropane-1-carboxylic acid (**8c**, 400 mg, 1.26 mmol, 8.0 equiv), sodium rhodium carbonate 2.5 hydrate (91.9 mg, 0.16 mmol, 1.0 equiv), and degassed, deionized water (10 mL). A condenser was attached to the flask, and the mixture was heated at reflux under argon for 3 days (oil bath). Then, the mixture was poured directly into saturated aqueous $NaHCO_3$ solution (50 mL) and vigorously stirred for 30 min. After bubbling had ceased, the resulting mixture was frozen and lyophilized to dryness, affording a colorless to green solid. The solid was treated with dichloromethane (100 mL) and sonicated for 5 minutes. The resulting mixture was filtered using a fritted glass funnel, and the solid was extracted two additional times in the same manner. The pooled filtrate liquid afforded 268 mg of a green oil after concentration under vacuum. This material was then subjected to flash column chromatography (0-3% MeCN/toluene) affording 120.4 mg of the desired product as a green solid after lyophilization from C_6H_6 (52% yield.) mp 247-250 °C (dec.) The NMR spectra of this compound showed a mixture of rotational isomers at room temperature. The NMR spectra were collected at 85 °C to resolve the signals. ^1H NMR (500

MHz, Toluene-d8) δ 7.29 (s, 1H), 6.91 (dq, J = 13.8, 7.2 Hz, 4H), 6.80 (d, J = 7.4 Hz, 2H), 6.70 (t, J = 7.8 Hz, 1H), 3.40 (s, 1H), 1.93 (s, 1H), 1.64 (s, 1H). ^{13}C{^{1}H} NMR (126 MHz, Toluene-d8) δ 189.5, 136.9, 133.4, 133.0, 129.4, 128.6, 128.5, 128.3, 127.8, 126.6, 126.5, 41.1, 33.7, 30.3, 22.4. IR (solid): 3061, 3030, 2955, 2923, 2853, 1586, 1398, 1321, 1025, 748 cm^{-1}. HRMS (ESI) *m/z*: $[M+H]^+$ (Pos.) calcd for $C_{64}H_{48}O_8Br_3{}^{81}BrRh_2$ 1467.8167; found 1467.8202.

Dirhodium tetrakis((1*R*,2*S*)-1-(3,5-dibromophenyl)-2-phenylcyclopropanecarboxylate) (3d). A round bottom flask was charged with (1*R*,2*S*)-1-(3,5-dibromophenyl)-2-phenylcyclopropane-1-carboxylic acid (**8d**, 1.00 g, 2.52 mmol, 8.0 equiv), sodium rhodium carbonate 2.5 hydrate (184 mg, 0.320 mmol, 1.0 equiv), and degassed, deionized water (20 mL). The mixture was heated at a bath temperature of 100 °C (oil bath) under an atmosphere of argon with moderate stirring. After 68 h, the mixture was cooled to room temperature and extracted with ethyl acetate (3x100 mL). The pooled organic phase was washed with saturated aqueous $NaHCO_3$ solution (3x100 mL,) followed by 10% aqueous NaOH (3x100 mL,) and then brine (100 mL). The organic phase was dried over Na_2SO_4, and then gravity filtered. The filtrate liquid was concentrated *in vacuuo*, affording 991 mg of a dark green solid. Purification by flash column chromatography (0-10% EtOAc/hexanes) afforded 296 mg of the desired product as a dark green solid (52% yield.) An X-ray quality crystal was grown by vapor diffusion from toluene/hexane containing trace acetonitrile. mp 205-210 (dec., from EtOAc). ^{1}H NMR (400 MHz, CDCl3) δ 7.41 (td, J = 1.8, 0.7 Hz, 1H), 7.17 – 7.07 (m, 3H), 6.98 (dd, J = 1.8, 0.8 Hz, 2H), 6.73 (dd, J = 6.7, 2.9 Hz, 2H), 3.05 – 2.92 (m, 1H), 2.02 (dd, J = 9.2, 5.1 Hz, 1H), 1.80 (dd, J = 7.3, 5.2 Hz, 1H) ^{13}C{^{1}H} NMR (100 MHz, CDCl3) δ 191.0, 139.2, 135.2, 133.4, 132.6, 128.1, 127.9, 126.9, 121.9, 38.5, 33.7, 29.7, 19.6. IR (solid): 3063, 3029, 2923, 2852, 1581, 1552, 1393, 1304, 741 cm^{-1}. HRMS (ESI) m/z: $[M+H]^+$ (Pos.) calcd for $C_{64}H_{44}O_8Br_6{}^{81}Br_2Rh_2$ 1781.4567; found 1781.4607.

Dirhodium tetrakis((1*R*,2*S*)-1-(3,5-di-(4-*tert*-butyl)phenyl)-2-phenylcyclopropanecarboxylate) (3e). A 4 mL screw-cap vial was charged with dirhodium tetrakis ((1*R*,2*S*)-1-(3,5-dibromophenyl)-2-phenylcyclopropane-caroxylate) (**3d**, 38.2 mg, 21.4 µmol, 1.0 equiv), (4-*tert*-butyl)phenylboronic acid (45.7 mg, 0.26 mmol, 12.0 equiv), (*R*)-(-)-DTBM-SEGPHOS (3.8 mg, 3.20 µmol, 0.15 equiv), palladium(II) acetate (0.5 mg, 2 µmol, 0.1 equiv), tribasic potassium phosphate (72.6 mg, 0.34 mmol, 16.0 equiv), and degassed 1,4-dioxane (0.42 mL). The vial was purged with argon before and during the addition of the solvent, and immediately sealed thereafter. Parafilm was used as a precaution to seal the mixture from atmospheric gases. The mixture was heated at 100 °C for 16 h (oil bath). At the end of the heating period, it was dry-loaded onto silica gel and subjected to flash column chromatography (0-6% EtOAc/hex). 43.0 mg of the desired product was obtained from the column as a green solid after drying under high vacuum (90% yield). mp 198-200 °C (dec., from EtOAc). ^{1}H NMR (300 MHz, CDCl3) δ 7.52 (t, J = 1.7 Hz, 1H), 7.41 – 7.23 (m, 8H), 7.13 (d, J = 1.7 Hz, 2H), 7.11 – 6.99 (m, 3H), 6.82 – 6.66 (m, 2H), 2.94 (dd, J = 9.2, 7.1 Hz, 1H), 2.18 – 2.04 (m, 1H), 1.76 (dd, J = 7.1, 4.8 Hz, 1H), 1.32 (s, 15H). ^{13}C{^{1}H} NMR (75 MHz, CDCl3) δ 191.56, 150.02, 140.63, 138.26, 137.01, 136.21, 129.56, 128.15, 127.78, 126.75, 126.05, 125.53, 124.30, 39.58, 34.44, 33.39, 31.34, 29.73. IR (Solid): 3087, 3054, 3029, 2960, 2927, 2903, 2866, 1580, 1399, 1362, 1269, 1114, 831. HRMS (ESI) m/z: $[M+H]^+$ (Pos.) calcd for $C_{144}H_{148}O_8Rh_2$ 2210.9279; found 2210.9240.

Dirhodium tetrakis((1*R*,2*S*)-1-([1,1'-biphenyl]-4-yl)-2-phenylcyclopropane-1-carboxylate) (3f). (1*R*,2*S*)-1-([1,1'-biphenyl]-4-yl)-2-phenylcyclopropane-1-carboxylic acid (**9**, 1.0 g, 3.18 mmol, 8.0 equiv) and sodium rhodium carbonate 2.5 hydrate (232 mg, 0.40 mmol, 1.0 equiv) were combined in a round bottom flask with degassed, deionized water (25 mL). A reflux condenser was attached to the flask, and the mixture was heated at 100 °C (oil bath) for 2 days with moderate stirring. Then the mixture was poured into saturated aqueous $NaHCO_3$ solution (100 mL) and stirred for 30 min. After bubbling had ceased, the mixture was frozen and lyophilized to dryness, affording a faintly green solid. The solid was treated with toluene (120 mL) and sonicated for 5 min. The mixture was filtered and the solid phase was extracted two additional times in the same manner. Concentration of the filtrate under high vacuum afforded 854 mg of a dark green solid. The material was purified by flash column chromatography (0-1% MeCN/toluene.) to afford 362 mg of compound **3f** after lyophilization from C_6H_6 (45% yield.) mp 145-150 °C (dec.) ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.49 – 7.42 (m, 2H), 7.38 – 7.33 (m, 2H), 7.33 – 7.26 (m, 3H), 7.09 – 7.00 (m, 3H), 7.00 – 6.94 (m, 2H), 6.77 (dd, J = 7.4, 2.2 Hz, 2H), 2.97 (dd, J = 9.3, 7.2 Hz, 1H), 2.09 (dd, J = 9.3, 4.8 Hz, 1H), 1.81 (dd, J = 7.2, 4.8 Hz, 1H). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 191.8, 140.8, 139.3, 137.0, 134.7, 132.2, 128.8, 128.1, 127.9, 127.2, 127.0, 126.4, 126.2, 39.4, 33.3, 20.0. IR (Solid): 3085, 3057, 3028, 2923, 2852, 1578, 1497, 1487, 1397, 1321, 1094, 975, 761, 736 cm^{-1}. HRMS (ESI) *m/z*: $[M+H]^+$ (Pos.) calcd for $C_{88}H_{68}O_8Rh_2$ 1458.3019; found 1458.3054.

Dirhodium tetrakis((1*R*,2*S*)-1-phenyl-2-(4-tert-butyl)phenyl-cyclopropanecarboxylate) (3g). A round bottom flask was charged with (1*R*,2*S*)-2-(4'-(tert-butyl)-[1,1'-biphenyl]-4-yl)-1-phenylcyclopropane-1-carboxylic acid (**13**, 130 mg, 0.35 mmol, 8.0 equiv), sodium rhodium carbonate 2.5 hydrate (25.6

mg, 44 µmol, 1.0 equiv), and degassed, deionized water (2.76 mL). The mixture was stirred at reflux under an argon atmosphere for 41 h. Then, the mixture was treated with saturated aqueous $NaHCO_3$ solution (100 mL) and the aqueous phase was lyophilized to dryness. The resulting salty green residue was extracted with 5% acetonitrile in toluene (3x50 mL). The organic phase was filtered and concentrated to dryness in vacuuo, affording 101 mg of a dark green oil. The oil was subjected to flash column chromatography (0-3% MeCN/toluene,) to afford 34.3 mg of the desired product **3g** as a green solid. (30% yield.) mp 100-110 °C (dec., from C_6H_6) ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.50 – 7.40 (m, 4H), 7.33 (d, J = 8.2 Hz, 2H), 7.15 – 7.08 (m, 3H), 7.03 – 6.94 (m, 2H), 6.78 (d, J = 8.2 Hz, 2H), 3.09 – 2.93 (m, 1H), 2.13 – 2.07 (m, 1H), 1.81 (dd, J = 7.1, 4.8 Hz, 1H), 1.38 – 1.33 (m, 9H). ^{13}C{1H} NMR (75 MHz, $CDCl_3$) δ 191.7, 150.1, 138.5, 137.6, 135.9, 135.5, 131.8, 128.3, 127.7, 126.8, 126.4, 126.1, 125.6, 39.7, 34.5, 32.9, 31.4, 20.2. IR (solid): 3056, 3028, 2953, 2923, 2864, 1581, 1499, 1395, 1321, 821 cm^{-1}. HRMS (ESI) *m/z*: $[M+H]^+$ (Pos.) calcd for $C_{104}H_{100}O_8Rh_2$ 1682.5523; found 1682.5556.

Dirhodium tetrakis ((1*R*,2*R*)-1,2-diphenylcyclopropane-1-carboxylic acid) (**4a**). A 10 mL round bottom flask equipped with a reflux condenser was charged with a magnetic stirbar, (1*R*,2*R*)-1,2-diphenylcyclopropane-1-carboxylic acid (**18**, 99 mg, 0.42 mmol, 8.0 equiv), sodium rhodium carbonate (30.3 mg, 52.0 µmol, 1.0 equiv) and degassed, deionized water (3.3 mL). The mixture was heated at an oil bath temperature of 100 °C for 4 d with vigorous stirring. At the end of the heating period, the mixture was partitioned between CH_2Cl_2 (100 mL) and saturated aqueous $NaHCO_3$ solution (100 mL). The organic phase was separated and washed with 5 additional 25 mL aliquots of saturated $NaHCO_3$ solution. Then, the CH_2Cl_2 phase was dried over Na_2SO_4 and filtered. Concentration *in vacuuo* afforded 58.3 mg of the crude product as a green residue. The desired product was separated from the mixture by flash column chromatography (24 g SiO_2, 0-16% EtOAc / hexanes,) which afforded 45.7 mg of the desired product as a green solid after lyophilization from C_6H_6 (76% yield.) mp 224.0-225.5 (dec.) ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33 – 7.19 (m, 6H), 7.14 – 7.07 (m, 2H), 7.01 (dd, J = 7.8, 1.7 Hz, 2H), 2.55 (t, J = 8.6 Hz, 1H), 1.72 (dd, J = 8.0, 4.7 Hz, 1H), 1.28 (dd, J = 9.3, 4.6 Hz, 1H). ^{13}C{1H} NMR (75 MHz, $CDCl_3$) δ 188.6, 141.7, 136.4, 130.1, 129.2, 127.8, 127.7, 126.7, 126.2, 39.8, 34.1, 20.4. FTIR: 3057, 3026, 1578, 1494, 1401, 1244, 1030, 979, 770, 726, 694 cm^{-1}. HRMS (ESI) m/z: $[M+H]^+$ (Pos.) calcd for $C_{64}H_{52}O_8NaRh_2$ 1177.1665; found 1177.1685.

General Procedures. General Procedure 1: Cyclopropanation of Styrene. A 10 mL vial was charged with styrene (**6**, 55.9 mg, 0.54 mmol, 2.0 equiv), the dirhodium catalyst (1.3 µmol, 0.5 mol %) and dichloromethane (1.0 mL). To this mixture was added a solution of 2,2,2-trichloroethyl 2-(4-bromophenyl)-2-diazoacetate (**5b**, 100 mg, 0.27 mmol, 1.0 equiv) in DCM (2.5 mL) over 2 h using a syringe pump. After the addition had completed, the mixture was concentrated to dryness under vacuum, and the crude product thus obtained was subjected to column chromatography (12 g SiO_2, 0-5% EtOAc/hexanes,) affording 2,2,2-trichloroethyl (1*R*,2*S*)-1-(4-bromophenyl)-2-phenylcyclopropane-1-carboxylate (**7b**) as a colorless solid in the indicated yield. The ee determination was made directly on the cyclopropanation products using chiral HPLC (OJ-H, 1.0 mL/min, 1.0% i-PrOH / hexanes, λ = 230 nm. rt 7.9 min (major) 12.5 min (minor)). Positive ee values indicate that the drawn enantiomer is formed. Negative ee values indicate that the opposite enantiomer is formed.

General Procedure 2: C—H Insertion into 4-Isopropyltoluene. A 10 mL vial equipped with a magnetic stir bar was charged with the dirhodium catalyst (1.0 µmol, 0.5 mol %,) dichloromethane (1.0 mL), and 4-isopropyltoluene (**19**, 81 mg, 0.60 mmol, 3.0 equiv). The vial was held under an argon atmosphere, and the mixture was heated to reflux (oil bath). Then, a solution of 2,2,2-trichloroethyl 2-(4-bromophenyl)-2-diazoacetate (**5b**, 75 mg, 0.20 mmol, 1.0 equiv) in dichloromethane (2.5 mL) was introduced over 1.5 h via syringe pump with stirring on. After 12-16 h at 40 °C (oil bath), the contents of the vial were concentrated *in vacuuo*, and the crude mixture was analyzed by ^{1}H NMR. The ratio of primary insertion product to tertiary insertion product was determined by the relative integration of the 2,2,2-trichloroethyl methylene doublets at 4.68 ppm (primary) and 4.43 ppm (tertiary). The yield represents the combined yield of the regiosiomeric products after purification by chromatography. The enantiomeric excess values were determined via reduction to the corresponding primary alcohols. Chiral HPLC: AD-H, 1.0 mL/min, 3.0% i-PrOH / hexanes, λ = 230 nm, rt 22.3 min (as drawn) and 44.6 min.

General Procedure 3: C—H Insertion into 4-Ethyltoluene. A 10 mL vial equipped with a magnetic stir bar was charged with the dirhodium catalyst (1.0 µmol, 0.5 mol %,) dichloromethane (1.0 mL,) and 4-ethyltoluene (**22**, 72 mg, 0.60 mmol, 3.0 equiv.) The vial was held under an argon atmosphere, and the mixture was heated to reflux (oil bath). Then, a solution of 2,2,2-trichloroethyl 2-(4-bromophenyl)-2-diazoacetate (**5b**, 75 mg, 0.20 mmol, 1.0 equiv) in dichloromethane (2.5 mL) was introduced over 1.5 h via syringe pump with stirring on. After 12-16 h at 40 °C (oil bath), the contents of the vial were concentrated *in vacuuo*, and the crude mixture was analyzed by ^{1}H NMR. The diastereomeric ratio of **23a** and **23b** was determined by integration of the methyl doublets at 1.40 ppm and 1.02 ppm. The primary/secondary insertion ratio (**23a** + **23b**:**24**) was determined by integration of the benzylic methine protons at 3.94 ppm (primary insertion) and 3.80 ppm (secondary insertion, including the overlapping signals from both diastereomers.). The yield represents the combined yield of the regioisomeric products after purification by chromatography. The enantiomeric excess values were determined via reduction to the corresponding primary alcohols. Chiral HPLC: AD-H, 0.80 mL/min, 1.0% i-PrOH / hexanes, λ = 230 nm, rt 54.7 min (as drawn) and 44.6 min. All reactions gave predominantly the (2S,3S)/(2R,3R) diastereomer for insertion into the secondary site. The absolute configuration is assigned by analogy to related literature assignments.[41]

Reduction of C—H Functionalization Products to Alcohols for ee Determination. A round bottom flask was charged with the analyte mixture (1.0 equiv) and anhydrous tetrahydrofuran (0.1 molar with respect to the analyte mixture). The flask was cooled to 0 °C using an ice bath, and then a solution of lithium aluminum hydride (1.0 equiv) in tetrahydrofuran (1.0 M in $LiAlH_4$) was added dropwise via syringe with magnetic stirring engaged. The mixture warmed to room temperature with the cooling bath over the course of 3-4 h. After stirring for 12-17 h, the contents of the flask were poured onto sodium sulfate decahydrate (50 g / mmol analyte) and stirred for 10-30 min. Then, the mixture was filtered through coarse paper, washing with diethyl ether (300 mL / mmol analyte). The filtrate was concentrated under vacuum to afford a crude product. The alcohols were purified by flash column chromatography (0-15% EtOAc / hexanes for 4-isopropyltoluene-derived products or 0-30% EtOAc/hexanes for 4-ethyltoluene-derived products). Following purification, chiral HPLC was used to determine the enantiomeric excess values for these materials. The following methods were used to analyze the mixtures: 4-isopropyltoluene: Chiralpak AD-H, 1.0 mL/min, 3.0% i-PrOH / hexanes, λ = 230 nm. 4-ethyltoluene: Chiralpak AD-H, 0.80 mL/min, 1.0% i-PrOH / hexanes, λ = 230 nm. For the mixtures containing the C-H functionalization products of 4-ethyltoluene, flash column purification was effective for removing the minor diastereomer **23b**, which showed a slight overlap with the major diastereomer **23a** in the HPLC analysis. The enantiomeric excess observed for the alcohol derivatives was assumed to be equal to that of the C-H insertion reactions. Racemic standards for the alcohol products were prepared as described below. The standards were run concurrently with each analysis to validate the HPLC method.

Preparation of Authentic Racemic Sample of Reduced 20. 2-(4-bromophenyl)-3-methyl-3-(p-tolyl)butan-1-ol (25). This compound was prepared according to the general reduction procedure with methyl 2-(4-bromophenyl)-3-methyl-3-(*p*-tolyl)butanoate (**26**, 99 mg, 1.00 equiv, 0.27 mmol), prepared by the literature prodcedure.[33] 84 mg of the pure product was obtained as a colorless oil (92% yield). IR (film): 3569, 3350, 2967, 2929, 2888, 1513, 1488, 1407, 1386, 1364, 1074, 1026, 1009, 818, 771, 728 cm^{-1}. Chiral HPLC: AD-H, 1.0 mL/min, 3.0% i-PrOH / hexanes, λ = 230 nm, rt 22.3 min (as drawn) and 44.6 min. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.41 (d, J = 8.1 Hz, 2H), 7.18 (d, J = 8.0 Hz, 2H), 7.13 (d, J = 8.1 Hz, 2H), 6.97 (d, J = 8.2 Hz, 2H), 3.83 (t, J = 10.6 Hz, 1H), 3.75 (s, 1H), 3.07 (dd, J = 10.3, 4.6 Hz, 1H), 2.35 (s, 3H), 1.28 (d, J = 8.1 Hz, 3H), 1.21 (s, 3H), 0.98 (s, 1H). ^{13}C{1H} NMR (126 MHz, $CDCl_3$) δ 144.5, 138.5, 135.6, 131.7, 131.1, 128.8, 126.2, 120.8, 62.7, 59.0, 39.7, 28.9, 24.4, 20.9. HRMS (ESI) m/z: [M+Na]$^+$ (Pos.) calcd for $C_{18}H_{21}O^{79}Br^{23}Na$ 355.0668; found 355.0668.

Reduction of 21 to Generate Authentic Racemic Sample 27. 2-(4-bromophenyl)-3-(4-isopropylphenyl) propan-1-ol (27). 2,2,2-trichloroethyl 2-(4-bromophenyl)-3-(4-isopropylphenyl)propanoate (**21**, 63 mg, 0.13 mmol, 1.00 equiv)[40] was dissolved in CH_2Cl_2 (10 mL) in a 20 mL scintillation vial, and the solution was cooled to -78 °C using a bath of dry ice in acetone. Then, diisobutylaluminum hydride (190 mg, 1.3 mmol, 10.0 equiv) in CH_2Cl_2 (1.3 mL, 1.0 M) was introduced dropwise via syringe. The mixture was stirred for 14 h, during which time the vial gradually warmed to room temperature with the cooling bath. At the end of the stir period, the vial was cooled to 0 °C in an ice bath and the reaction was quenched via the addition of methanol (1 mL). The mixture was concentrated under vacuum to a colorless solid. The solid was washed with diethyl ether (3x10 mL) and filtered through silica gel (10 g), washing with additional diethyl ether (100 mL). Concentration of the filtrate liquid afforded 24 mg of product **27** as a colorless oil (55% yield). IR (film): 3568, 3340, 2958, 2923, 2869, 1513, 1488, 1072, 1009, 819 cm^{-1}. Chiral HPLC: AD-H, 1.0 mL/min, 3.0% i-PrOH / hexanes, λ = 230 nm, rt 13.5 min (as drawn) and 15.6 min. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.44 (d, J = 8.3 Hz, 2H), 7.16 – 7.07 (m, 4H), 7.01 (d, J = 7.9 Hz, 2H), 3.76 (qd, J = 10.9, 6.2 Hz, 2H), 3.05 (td, J = 7.3, 5.4 Hz, 1H), 2.98 (dd, J = 13.7, 7.4 Hz, 1H), 2.86 (ddd, J = 13.6, 10.8, 7.2 Hz, 2H), 1.36 (s, J = 6.6 Hz, 1H), 1.23 (d, J = 6.9 Hz, 6H). ^{13}C{1H} NMR (126 MHz, $CDCl_3$) δ 146.7, 141.3, 136.7, 131.6, 129.8, 128.9, 126.4, 120.5, 66.2, 49.6, 38.1, 33.7, 24.0. HRMS (ESI) m/z: [M+Na]$^+$ (Pos.) calcd for $C_{17}H_{19}O^{79}Br^{23}Na$ 355.0668; found 355.0670.

Reduction of **23a/23b** to Generate Authentic Racemic Samples **28** and **29**. 2,2,2-trichloroethyl (2*S*,3*S*)-2-(4-bromophenyl)-3-(p-tolyl)butanoate (28) and 2,2,2-trichloroethyl (2*S*,3*R*)-2-(4-bromophenyl)-3-(*p*-

tolyl)butanoate (**29**) The standard reduction procedure was used to reduce a 42:58 mixture of **23a**:**23b** (400 mg, 0.86 mmol), prepared via a published procedure.[39] Flash column chromatography on silica gel (0-30% EtOAc/hexanes) gave complete resolution of the two diastereomers **28** and **29**. 94 mg (34% yield) of compound **28** were obtained as a colorless oil. IR (film): 3568, 3339, 3021, 2962, 2921, 2875, 1514, 1487, 1453, 1406, 1375, 1073, 1052, 1010, 817 cm^{-1}. Chiral HPLC: AD-H, 0.80 mL/min, 1.0% i-PrOH / hexanes, λ = 230 nm, rt 54.7 min (as drawn) and 44.6 min. ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.35 – 7.28 (m, 2H), 6.97 (d, J = 7.7 Hz, 2H), 6.85 (dd, J = 11.7, 8.0 Hz, 4H), 3.96 (dt, J = 9.7, 4.3 Hz, 1H), 3.86 (dd, J = 10.9, 8.2 Hz, 1H), 3.11 (p, J = 7.2 Hz, 1H), 2.99 (td, J = 8.2, 5.1 Hz, 1H), 2.26 (s, 3H), 1.32 (d, J = 7.0 Hz, 3H). ^{13}C{1H} NMR (126 MHz, CDCl$_3$) δ 141.1, 139.8, 135.5, 131.2, 130.7, 128.7, 127.7, 120.3, 64.7, 54.2, 41.1, 21.0, 20.0. HRMS (ESI) m/z: $[M+Na]^+$ (Pos.) calcd for $C_{17}H_{19}O^{79}Br^{23}Na$ 341.0512; found 341.0507. 128 mg of compound **29** were also obtained in 47% yield as a colorless crystalline solid. mp 98.0-99.0 °C (from CHCl$_3$). IR (solid): 3463, 3020, 2954, 2927, 2895, 2870, 1514, 1485, 1375, 1072, 1055, 1008, 819, 723 cm^{-1} Chiral HPLC: AD-H, 0.80 mL/min, 1.0% i-PrOH / hexanes, λ = 230 nm, rt 53.0 min (The enantiomeric pair for the minor diastereomer **29** showed no resolution under these conditions, and the retention time is reported for identification purposes only. Enantiomeric excess values were not determined for this minor product. It was removed by column chromatography prior to analysis.) ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.52 – 7.47 (m, 2H), 7.20 – 7.16 (m, 2H), 7.15 (s, 4H), 3.61 – 3.46 (m, 2H), 2.99 – 2.79 (m, 2H), 2.35 (s, 3H), 1.02 (d, J = 6.6 Hz, 3H). ^{13}C{1H} NMR (126 MHz, CDCl$_3$) δ 142.1, 140.9, 136.1, 131.7, 130.3, 129.4, 127.1, 120.6, 65.8, 55.1, 42.0, 21.0, 20.9. A single crystal of adequate size was grown from CHCl$_3$/hexanes to confirm the relative configuration of this compound using X-ray crystallography. HRMS (ESI) m/z: $[M+Na]^+$ (Pos.) calcd for $C_{17}H_{19}O^{79}Br^{23}Na$ 341.05115; found 341.0506.

Reduction of 24 to Generate Authentic Racemic Sample 30. 2-(4-bromophenyl)-3-(4-ethylphenyl)propan-1-ol (30). 2,2,2-Trichloroethyl 2-(4-bromophenyl)-3-(4-ethylphenyl)propanoate[33] (**24**, 60 mg, 0.13 mmol, 1.0 equiv) was dissolved in CH$_2$Cl$_2$ (10 mL). The flask was cooled to -78 °C using a bath of dry ice in acetone, and then a solution of diisobutylaluminum hydride (92 mg, 0.65 mmol, 5.0 equiv) in CH$_2$Cl$_2$ (0.65 mL, 1.0 M) was introduced dropwise via syringe. The mixture was stirred for 17 h, during which time the flask warmed to room temperature with the cooling bath. Then, the flask was cooled to 0 °C and the reaction was quenched via the addition of methanol (1 mL). The mixture was concentrated to a colorless solid under vacuum. The solid was washed with ethyl acetate (3x10 mL) and then filtered through silica gel (15 g) with 100% ethyl acetate (100 mL). Concentration of the filtrate liquid afforded 34 mg of **30** as a colorless oil (82% yield). IR (solid): 3569, 3321, 3020, 2962, 2926, 2870, 1514, 1487, 1406, 1073, 1010, 822, 731 cm^{-1}. Chiral HPLC: AD-H, 0.80 mL/min, 1.0% i-PrOH / hexanes, λ = 230 nm, rt 57.9 min (as drawn) and 69.2 min. ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.43 (d, J = 8.1 Hz, 2H), 7.08 (dd, J = 10.1, 8.0 Hz, 4H), 6.99 (d, J = 7.8 Hz, 2H), 3.77 (dd, J = 11.0, 6.3 Hz, 2H), 3.10 – 3.02 (m, 1H), 2.98 (dd, J = 13.6, 7.3 Hz, 1H), 2.84 (dd, J = 13.6, 7.6 Hz, 1H), 2.60 (q, J = 7.6 Hz, 2H), 1.33 (d, J = 6.9 Hz, 1H), 1.21 (t, J = 7.6 Hz, 3H). ^{13}C{1H} NMR (126 MHz, CDCl$_3$) δ 142.1, 141.2, 136.6, 131.6, 129.8, 128.9, 127.8, 120.5, 66.2, 49.7, 38.1, 28.4, 15.5. HRMS (ESI) m/z: $[M+Na]^+$ (Pos.) calcd for $C_{17}H_{19}O^{79}Br^{23}Na$ 341.0512; found 341.0506.

Computational Procedures. All presented computational data were obtained at the B3LYP-D3BJ/BS1 level of theory, which contains B3LYP functional[42-44] and dispersion-correction (at the Grimme's empirical (D3) level[45] with the Becke-Johnson (BJ) damping[46-48]). Here, BS1 is a basis set including Lanl2dz for Rh and 6-31G(d,p) for all other atoms. For Rh, we used the Hay-Wadt effective core potential.[49-51] Frequency analysis was used to characterize each minimum with zero imaginary frequency. Bulk solvent effects were incorporated for all calculations at the conductor-like polarizable continuum model (C-PCM).[52, 53] Dichloromethane was used as the solvent because this is the common solvent for these carbene reactions. The calculated thermodynamic data are reported as ΔH/ΔG at the 298.15K temperature and 1 atm pressure conditions. All the calculations were performed with the Gaussian 09 suite of programs.[54]

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