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Enantioselective Carbonyl−Ene Reactions Catalyzed by Chiral Cationic Dirhodium(II,III) Carboxamidates

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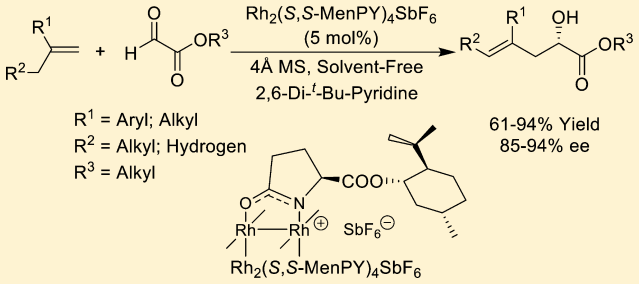
Supporting Information

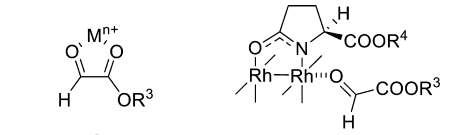
ABSTRACT: An enantioselective carbonyl−ene reaction of glyoxylate esters with 1,1-disubstituted alkenes catalyzed by chiral cationic dirhodium(II,III) carboxamidates is described. The paddlewheel dirhodium(II,III) carboxamidates having one open coordination site at each rhodium smoothly catalyze the carbonyl−ene reaction to afford homoallylic alcohol products in good isolated yields with high enantioselectivities.



The carbonyl−ene reaction,[1] which occurs with the concomitant formation of a carbon−carbon bond and a 1,5-hydrogen migration, is an alternative but more atom-economical route to homoallylic alcohols compared with the conventional carbonyl allylation strategy.[2] Numerous efforts have been devoted to the elucidation of its mechanistic profile[3] and, to a greater extent, the development of asymmetric methodologies[1a,b,g] because the resulting optically active homoallylic alcohols are ubiquitous chiral building blocks for the synthesis of biologically active compounds and natural products.[1a,b] The catalytic enantioselective carbonyl−ene reaction is particularly intriguing[1g] since the direct use of abundant and readily available carbonyl compounds and substituted alkenes as starting materials in conjunction with a chiral catalyst for the transfer of chirality dramatically enhances the practicality and sustainability of asymmetric carbonyl−ene reactions. Although organocatalysis has recently demonstrated its capacity to catalyze highly enantioselective carbonyl−ene reactions,[4] chiral metal Lewis acid catalysis has occupied a central role in advancing catalytic asymmetric carbonyl−ene reactions since the seminal work of Yamamoto.[5] Within this context, chiral metal Lewis acid complexes derived from main-group metals,[6] transition metals,[7] and lanthanides[8] have been utilized to catalyze highly stereoselective carbonyl−ene reactions.

Probably because of the low nucleophilicity of unactivated alkenes,[7e,j] the carbonyl counterpart for intermolecular carbonyl−ene reactions must be highly electrophilic.[1g] Glyoxylate esters, which join a formyl group to an ester functionality, are the most frequently used carbonyl components. The ester carbonyl group not only renders the adjacent formyl group electron-deficient but also influences the coordinating conformation that the glyoxylate ester adopts (Scheme 1). Bidentate coordination restricts rotation around the carbon−carbon bond that connects the two carbonyls and provides a more stereodefined complex that enhances the stereocontrol.

Scheme 1. Dirhodium Catalysts Use a Single Coordination Site for Complexation with Glyoxylate Esters



Indeed, most of the highly enantioselective catalytic systems developed for asymmetric carbonyl−ene reactions involving glyoxylates primarily build on this bidentate coordination pattern.[7d,f,h,k−m,8] The Ti(IV)−BINOLate catalytic system devised by Mikami represents one of the very few that arguably[9] coordinate in a monodentate fashion with glyoxylates, but few other chiral catalytic systems for carbonyl−ene reactions that may have only single-point binding from the catalyst to the carbonyl oxygen have been reported.[7a−c,i]

Dirhodium carboxamidates inherit the fundamental paddlewheel structure from dirhodium carboxylates but display more structural diversity as a result of the unsymmetrical nature of the bridging carboxamidate ligand.[10] Chiral dirhodium carboxamidates derived from cyclic amides in which the chirality of the ligand is dictated by the carbon adjacent to the nitrogen are intrinsically Lewis acidic,[10b,e] and the only electrophilic coordination site available to each rhodium resides at the axial position.[10c,e,11] Although they are purposely designed to catalyze highly diastereoselective and enantioselective electrophilic dirhodium carbene transformations,[10d,e] the rigid and tunable chiral environment surrounding each Lewis acidic rhodium center unsurprisingly translates into highly efficient chiral Lewis acid catalysts as well.[12] Equilibrium

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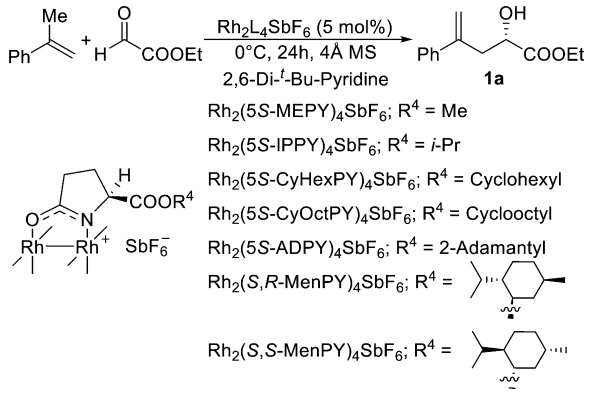
constants for aldehyde association with dirhodium(II) carboxamidates have been determined, and their superior catalytic performance in chiral Lewis acid catalysis has been adequately exemplified by the highly enantioselective hetero-Diels–Alder reactions of aromatic aldehydes with Danishefsky's diene.[12b] Mild oxidation of dirhodium(II,II) carboxamidates to their corresponding cationic dirhodium(II,III) carboxamidates by equimolar nitrosonium salts at ambient temperature strengthens their Lewis acidities and grants enhanced enantiocontrol in both hetero-Diels–Alder reactions and 1,3-dipolar cycloaddition reactions of aryl nitrones with α,β-unsaturated aldehydes.[13] Remarkably, these highly enantioselective reactions depend solely upon the use of a catalytic system that is noted for single-point association with Lewis bases. Could there be a secondary effect that facilitates the enantiocontrol? During studies of solvent effects associated with catalytic applications of chiral dirhodium(II,III) carboxamidates, the potential of using chiral cationic dirhodium(II,III) carboxamidates for Lewis acid-catalyzed reactions that do not occur with their parent dirhodium(II,II) carboxamidates was examined, and preliminary results suggested their feasibility.[14] We have undertaken a comprehensive examination of carbonyl–ene reactions of glyoxylate esters, and here we present results on catalyst screening and substrate scope for reactions catalyzed by chiral cationic dirhodium(II,III) carboxamidates.

We began our investigation with the carbonyl–ene reaction between ethyl glyoxylate and α-methylstyrene catalyzed by the chiral dirhodium(II,II) carboxamidate Rh_2(5*S*-MEPY)$_4$. However, no conversion of the starting materials was observed after extended reaction time. Switching to the more reactive catalyst Rh_2(5*S*-MEPY)$_4SbF_6$ gave evidence of the facile consumption of ethyl glyoxylate, and the carbonyl–ene reaction product **1a** was obtained in 39% isolated yield with 43% ee after 24 h at 0 °C (Table 1, entry 1). Further screening of dirhodium(II,III) carboxamidates revealed that the ester alkyl groups of the chiral pyrrolidinone ligands greatly influence the enantiocontrol in the formation of the homoallylic alcohol product. Reactions catalyzed by Rh_2(5*S*-MEPY)$_4SbF_6$ (entry 1), Rh_2(5*S*-IPPY)$_4SbF_6$ (entry 2), and Rh_2(5*S*-CyHexPY)$_4SbF_6$ (entry 3) with methyl, isopropyl, and cyclohexyl as ester alkyl groups, respectively, showed an increase in ee from 43% to 82%, but incorporation of even larger ester alkyl groups did not enhance the enantiocontrol in the reaction (entries 4 and 5). However, making use of the "matched" and "mismatched" effects between the stereogenic centers of the chiral menthyl ester group and the (5*S*)-2-oxopyrrolidine-5-carboxylate motif[10e,13–15] enabled fine-tuning of the chiral environment surrounding the Lewis acidic Rh^{3+} center and reinforced the enantiocontrol. Although Rh_2(*S*,*R*-MenPy)$_4SbF_6$ afforded the product with 70% ee (entry 6), the use of Rh_2(*S*,*S*-MenPY)$_4SbF_6$ (entry 7) gave the same compound in 94% ee (configurational match). These reactions were clean, with only reactants and product **1a** evident by NMR analyses. The role of 2,6-di-*tert*-butylpyridine was to neutralize the trace amount of acid that came from the hydrolysis of $NOSbF_6$.[14]

With the optimal catalyst in hand but with low product yield, we investigated ways to increase the product yield of the model reaction. Since conducting the reaction at higher temperature should in principle accelerate the catalytic turnover, we performed the reaction at room temperature instead of at 0 °C. Although a higher isolated yield was obtained, a decrease in enantiomeric excess from 94% to 88% was observed (Table 2, entry 2). Extending the reaction time from 24 to 168 h afforded

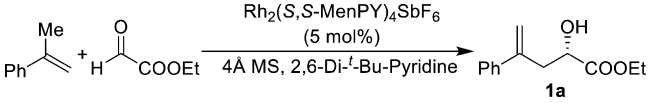
Table 1. Catalyst Screening for the Carbonyl–Ene Reaction between α-Methylstyrene and Ethyl Glyoxylate Catalyzed by Chiral Cationic Dirhodium(II,III) Carboxamidates



entry[a]	$Rh_2L_4SbF_6$	yield[b]	ee[c]
1	Rh_2(5*S*-MEPY)$_4SbF_6$	39%	43%
2	Rh_2(5*S*-IPPY)$_4SbF_6$	20%	55%
3	Rh_2(5*S*-CyHexPY)$_4SbF_6$	30%	82%
4	Rh_2(5*S*-CyOctPY)$_4SbF_6$	26%	71%
5	Rh_2(*S*-ADPY)$_4SbF_6$	33%	70%
6	Rh_2(*S*,*R*-MenPY)$_4SbF_6$	20%	70%
7	Rh_2(*S*,*S*-MenPY)$_4SbF_6$	27%	94%

[a]Reactions were performed on a 0.5 mmol scale of ethyl glyoxylate with 5.0 equiv of α-methylstyrene in toluene, except for the reaction catalyzed by Rh_2(5*S*-MEPY)$_4SbF_6$, which was conducted in dichloromethane because of its limited solubility in toluene. [b]Isolated yields. [c]Determined by HPLC analysis using a chiral stationary phase.

Table 2. Further Optimization of the Reaction Conditions



entry	temp	time	yield[c]	ee[d]
1[a]	0 °C	24 h	27%	94%
2[a]	rt	24 h	42%	88%
3[a]	0 °C	168 h	90%	94%
4[b]	0 °C	72 h	81%	94%

[a]Reactions were performed on a 0.5 mmol scale of ethyl glyoxylate with 5.0 equiv of α-methylstyrene in toluene. [b]The reaction was carried out with 10.0 equiv of α-methylstyrene as the solvent. [c]Isolated yields; unreacted starting material remained. [d]Determined by HPLC analysis using a chiral stationary phase.

the final product in 90% isolated yield with 94% ee (entry 3). Surprisingly, the allylic alcohol product **1a** provided only modest inhibition of the rate of conversion. We hypothesized that performing the reaction under solvent-free conditions would further increase the reaction rate. As expected, running the reaction neat resulted in a significant increase in the reaction rate. Moreover, an identical enantiomeric excess was obtained under solvent-free conditions with 10.0 equiv of α-methylstyrene as the solvent. Under the optimized conditions, the carbonyl–ene reaction of ethyl glyoxylate with α-methylstyrene catalyzed by Rh_2(*S*,*S*-MenPY)$_4SbF_6$ afforded the desired product in 81% isolated yield with 94% ee at 0 °C after 72 h (entry 4).

Having established the optimized reaction conditions for the carbonyl–ene reaction between ethyl glyoxylate and α-

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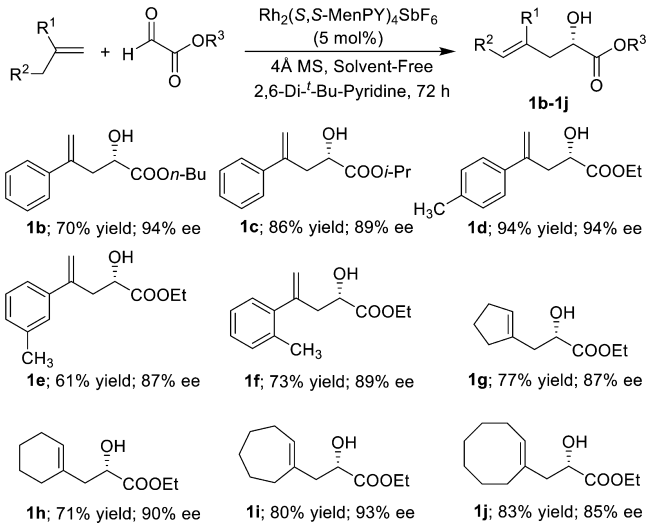
methylstyrene, we explored the substrate scope with representative alkenes and glyoxylates using $Rh_2(S,S\text{-MenPY})_4SbF_6$ as the catalyst (Scheme 2). For the carbonyl−ene

Scheme 2. Substrate Scope of the Enantioselective Carbonyl−Ene Reaction Catalyzed by $Rh_2(S,S\text{-MenPy})SbF_6$[a]



[a]Reactions were performed on a 0.5 mmol scale of glyoxylate ester with 10.0 equiv of the corresponding alkene as the solvent. Isolated yields are reported. The enantiomeric excesses were determined by HPLC analysis using a chiral stationary phase.

reaction of α-methylstyrene with different glyoxylate esters, a 70% isolated product yield with 94% ee was obtained with *n*-butyl glyoxylate, and a higher yield of 86% but a lower 89% ee was obtained for the product derived from isopropyl glyoxylate. For reactions of various α-methylstyrene derivatives with ethyl glyoxylates, a methyl substituent can be tolerated at the *ortho*, *meta*, or *para* position on the phenyl ring of the α-methylstyrene, and all of the substrates examined afforded the ene reaction products in good yields (61−94%) with high enantiomeric excesses (87−94% ee). In addition, the carbonyl−ene reaction of ethyl glyoxylate with methylene cycloalkanes bearing five- to eight-membered rings were investigated. Interestingly, although similar product yields were obtained, an increase in enantioselectivity for the carbonyl−ene products was observed, from 87% ee for methylenecyclopentane to 93% ee for methylenecycloheptane. However, a decrease in enantioselectivity to 85% ee was obtained for methylenecyclooctane (Scheme 2). Attempts to replace the glyoxylate with phenylglyoxal by employing the same catalytic system under the optimum reaction conditions were unsuccessful, probably because of competing coordination of the ketone carbonyl of phenylglyoxal with the dirhodium catalyst.

While it is abundantly clear that the introduction of an appropriately sized ester on the carboxamidate ligand and the "matched effect" of multiple stereogenic centers collectively contribute to the highly enantioselective outcomes that have been observed, an additional organizing element that is induced by coordination of the formyl carbonyl to the electrophilic Rh^{3+} center could be fundamental to understanding the enantiocontrol in these reactions. A formyl C−H···O hydrogen-bonding interaction from the aldehydic C−H bond to the catalyst, which was first introduced by Corey[16] and later incorporated in dirhodium Lewis acid catalysis by Hashimoto,[17] represents a secondary effect that operates cooperatively with the primary formyl oxygen−Rh^{3+} complexation and occurs with the most stereoelectronically accessible oxygen (Figure 1a). These two

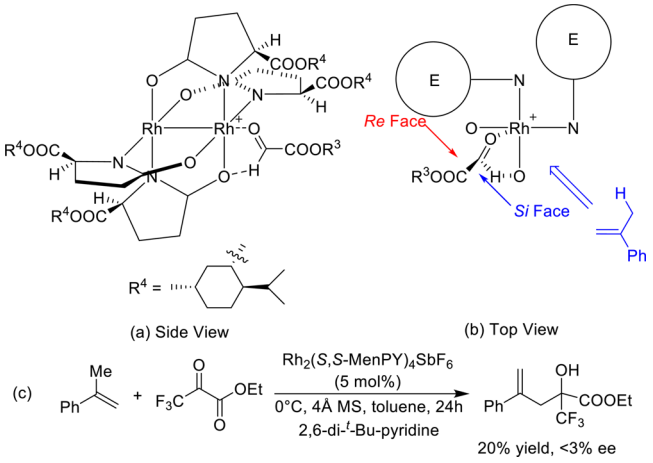


Figure 1. Stereocontrol model. (a) Side view and proposed coordination pattern of glyoxylate with $Rh_2(S,S\text{-MenPY})_4^+$. (b) Top view and approaching direction of α-methylstyrene. (c) The lack of a formyl C−H···O hydrogen-bonding interaction results in diminished enantiocontrol in the ketone−ene reaction catalyzed by dirhodium carboxamidates.

interactions contribute concurrently, leaving the *Re* face of the glyoxylate shielded by the bulky ester group and the *Si* face open for the access by the alkene (Figure 1b). This rationale is corroborated by the absolute configuration of the final product, which was determined to be *S* by comparison of optical rotation data with literature values.[7m] Moreover, although $Rh_2(S,S\text{-MenPY})_4SbF_6$ promoted the ketone−ene reaction between highly reactive ethyl trifluoropyruvate and α-methylstyrene, the enantiomeric excess for the reaction product was less than 3% (Figure 1c); this result is also consistent with the coordination model proposed for glyoxylates, since evidently the formyl C−H···O hydrogen-bonding interaction is not applicable.

In conclusion, we have reported that chiral cationic dirhodium(II,III) carboxamidates catalyze highly enantioselective carbonyl−ene reactions of glyoxylate esters. Consistent with the reactivity of glyoxylate esters and high enantiocontrol that have been achieved, the donor−acceptor association of glyoxylate esters on the face of the dirhodium catalyst presents a compelling explanation for the results obtained and for other dirhodium-catalyzed reactions that are specific to glyoxylates.[18]

EXPERIMENTAL SECTION

General Information. Experiments involving moisture- and/or air-sensitive components were performed in oven-dried glassware under a positive pressure of nitrogen using freshly distilled solvents. Commercial reagents were used without further purification. Thin-layer chromatography (TLC) was carried out using silica gel 60 F254 plates. The chromatograms were analyzed using a UV lamp (254 nm) or by development with cerium ammonium molybdate (CAM). Liquid chromatography was performed using a forced flow (flash chromatography) of the indicated system on silica gel (230−400 mesh). ^1H and ^{13}C NMR spectra were recorded on a 400 MHz spectrophotometer using $CDCl_3$ as the solvent. Chemical shifts for ^1H NMR spectra are reported as δ in units of parts per million downfield from $SiMe_4$ (δ 0.00) and relative to the signal of chloroform-*d* (δ 7.26, singlet). Multiplicities are given as s (singlet); d (doublet); t (triplet); q

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(quartet); dd (doublet of doublets); ddd (doublet of doublets of doublets); dddd (doublet of doublets of doublets of doublets); dt (doublet of triplets); tt (triplet of triplets); m (multiplet), or comp (composite). The number of protons (*n*) for a given resonance is indicated by *n*H. Coupling constants (*J*) are reported in hertz. Chemical shifts for ^{13}C NMR spectra are reported as δ in units of parts per million downfield from $SiMe_4$ (δ 0.0) and relative to the signal of chloroform-*d* (δ 77.0, triplet). Enantioselectivities were determined by HPLC analysis employing a chiral column at 25 °C. Optical rotation was measured using a polarimeter equipped with a sodium vapor lamp (λ = 589 nm); concentration is denoted as *c* and was calculated as grams per deciliter (g/100 mL). The absolute configurations of **1a**−**h** were determined by comparison with specific rotation data of the known compounds. The absolute configurations of **1i** and **1j** were assigned as *S* by assuming that the reactions proceeded through a similar enantiocontrol mode. High-resolution mass spectrometry (HRMS) was performed on a TOF-ESI mass spectrometer using CsI as the internal standard.

Materials. Ethyl glyoxylate (~50% in toluene) was purified according to the reported method.[18] *n*-Butyl and isopropyl glyoxylate were prepared by the literature method[19] and freshly distilled prior to use. Commercially available alkenes were distilled prior to use. Methylenecycloheptane and methylenecyclooctane were prepared by known methods.[20] $NOSbF_6$ used for the oxidation of dirhodium(II,II) carboxamidates to the corresponding dirhodium(II,III) carboxamidates was used as received.

Preparation of Chiral Dirhodium(II,II) Carboxamidates. Rh_2(5*S*-MEPY)$_4$,[21] Rh_2(5*S*-IPPY)$_4$,[14] Rh_2(*S*,*S*-MenPY)$_4$,[13] and Rh_2(*S*,*R*-MenPY)$_4$[14] were prepared and analyzed according to literature methods. The chiral pyrrolidinone ligands cyclohexyl (5*S*)-2-oxopyrrolidine-5-carboxylate, cyclooctyl (5*S*)-2-oxopyrrolidine-5-carboxylate, and 2-adamantyl (5*S*)-2-oxopyrrolidine-5-carboxylate were prepared by the previously reported procedure using the corresponding alcohols.[14] The preparation of chiral dirhodium(II,II) catalysts followed the general procedure reported previously.[14]

Cyclohexyl (5S)-2-Oxopyrrolidine-5-carboxylate. 1.65 g, 78% isolated yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 5.94 (br s, 1H), 4.83−4.80 (m, 1H), 4.20 (ddd, *J* = 8.5, 3.4, 0.5 Hz, 1H), 2.53−2.45 (m, 1H), 2.40−2.34 (comp, 2H), 2.26−2.17 (m, 1H), 1.86−1.83 (comp, 2H), 1.74−1.71 (comp, 2H), 1.58−1.52 (m, 1H), 1.46−1.26 (comp, 5H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 177.8, 171.4, 74.1, 55.6, 31.4, 29.3, 25.2, 24.9, 23.6. $[\alpha]_D^{23}$ = −1.3 (*c* 2.20, $CHCl_3$). HRMS (ESI$^+$): calcd for $C_{11}H_{18}NO_3$ ([M + H]$^+$) 212.1287, found 212.1290.

Cyclooctyl (5S)-2-Oxopyrrolidine-5-carboxylate. 1.82 g, 76% isolated yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 5.95 (br s, 1H), 5.01 (tt, *J* = 8.2, 4.3 Hz, 1H), 4.19 (ddd, *J* = 8.7, 4.2, 0.5 Hz, 1H), 2.51−2.41 (m, 1H), 2.41−2.29 (comp, 2H), 2.24−2.15 (m, 1H), 1.81−1.51 (comp, 14H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 178.0, 171.6, 77.2, 56.0, 31.8, 29.6, 27.4, 27.4, 23.2, 23.2. $[\alpha]_D^{23}$ = +2.0 (*c* 2.00, $CHCl_3$). HRMS (ESI$^+$): calcd for $C_{13}H_{22}NO_3$ ([M + H]$^+$) 240.1600, found 240.1605.

2-Adamantyl (5S)-2-Oxopyrrolidine-5-carboxylate. 2.19 g, 83% isolated yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 6.09 (br s, 1H), 4.99 (br s, 1H), 4.26 (ddd, *J* = 7.6, 5.2, 0.5 Hz, 1H), 2.55−2.43 (m, 1H), 2.41−2.30 (comp, 2H), 2.29−2.20 (m, 1H), 2.03−1.57 (comp, 14H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 178.2, 171.8, 79.0, 56.1, 37.6, 36.7, 36.2, 32.2, 32.2, 32.2, 29.7, 27.5, 27.3, 25.5. $[\alpha]_D^{23}$ = −4.5 (*c* 1.00, $CHCl_3$). HRMS (ESI$^+$): calcd for $C_{15}H_{22}NO_3$ ([M + H]$^+$) 264.1600, found 264.1603.

Dirhodium(II) Tetrakis[cyclohexyl (5S)-2-oxopyrrolidine-5-carboxylate] [Rh$_2$(5S-CyHexPY)$_4$]. 639 mg, 61% isolated yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 4.77−4.74 (comp, 4H), 4.19−4.16 (comp, 2H), 4.11−4.08 (comp, 2H), 2.70−2.54 (comp, 4H), 2.36−1.30 (comp, 52H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 187.6, 187.5, 174.7, 174.1, 73.9, 72.9, 67.0, 66.9, 31.6, 31.6, 25.9, 25.4, 25.4, 25.2, 24.0, 23.9, 23.7, 23.6. $[\alpha]_D^{23}$ = −122.6 (*c* 0.23, MeOH). HRMS (ESI$^+$): calcd for $C_{44}H_{65}N_4O_{12}Rh_2$ ([M + H]$^+$) 1047.2709, found 1047.2715.

Dirhodium(II) Tetrakis[cyclooctyl (5S)-2-oxopyrrolidine-5-carboxylate] [Rh$_2$(5S-CyOctPY)$_4$]. 927 mg, 80% isolated yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 4.90−4.88 (comp, 4H), 4.12−3.99 (comp, 4H), 3.72−3.65 (comp, 4H), 2.60−1.53 (comp, 68H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 187.7, 187.6, 174.5, 174.0, 76.3, 75.4, 66.0, 66.1, 31.8, 31.7, 31.6, 31.4, 31.3, 27.2, 27.0, 27.0, 25.7, 25.6, 25.4, 25.2, 23.3, 23.1, 22.9, 22.8. $[\alpha]_D^{23}$ = −117.5 (*c* 0.26, MeOH). HRMS (ESI$^+$): calcd for $C_{52}H_{81}N_4O_{12}Rh_2$ ([M + H]$^+$) 1159.3961, found 1159.3965.

Dirhodium(II) Tetrakis[2-adamantyl (5S)-2-oxopyrrolidine-5-carboxylate] [Rh$_2$(5S-ADPY)$_4$]. 866 mg, 69% isolated yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 4.91−4.88 (comp, 4H), 4.26−4.23 (comp, 2H), 4.09−4.06 (comp, 2H), 2.28 (br, 4H), 2.32−1.50 (comp, 68H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 187.8, 187.7, 174.5, 174.9, 77.2, 66.5, 66.4, 37.5, 37.3, 36.4, 36.3, 32.1, 32.0, 31.9, 31.8, 31.6, 31.5, 27.3, 27.2, 27.1, 27.0, 26.2, 25.7. $[\alpha]_D^{23}$ = −70.6 (*c* 0.22, *i*-PrOH). HRMS (ESI$^+$): calcd for $C_{60}H_{81}N_4O_{12}Rh_2$ ([M + H]$^+$) 1255.3961, found 1255.3970.

General Procedure A for Carbonyl−Ene Reactions Catalyzed by in Situ-Generated Chiral Dirhodium(II,III) Carboxamidates in Toluene or Dichloromethane. A 10 mL Schlenk flask charged with a magnetic stir bar and 4 Å molecular sieves (300 mg) was placed under high vacuum and heated to dryness using a Bunsen burner. After the flask was cooled to room temperature, Rh_2(*S*,*S*-MenPy)$_4$ (33.8 mg, 0.025 mmol), 2,6-di-*tert*-butylpyridine (22 μL, 0.10 mmol), and 1.0 mL of solvent (toluene or dichloromethane) were added under a flow of nitrogen. The resulting green solution was stirred for 10 min before $NOSbF_6$ (6.6 mg, 0.025 mmol) was added. The solution was allowed to stir for additional 30 min, during which time the color gradually turned from green to deep red. The alkene (2.5 mmol) was added to the catalyst solution, and the mixture was stirred for 10 min at 0 °C, after which ethyl glyoxylate (0.5 mmol) was added. The resulting solution was stirred at 0 °C for specified times. The reaction mixture was concentrated and directly loaded onto a silica gel column (hexanes and ethyl acetate as eluent) to isolate the product.

General Procedure B for Carbonyl−Ene Reactions Catalyzed by in Situ-Generated Chiral Dirhodium(II,III) Carboxamidates under Solvent-Free Conditions. A 10 mL Schlenk flask charged with a magnetic stir bar and 4 Å molecular sieves (300 mg) was placed under high vacuum and heated to dryness using a Bunsen burner. After the flask was cooled to room temperature, Rh_2(*S*,*S*-MenPy)$_4$ (33.8 mg, 0.025 mmol), 2,6-di-*tert*-butylpyridine (22 μL, 0.10 mmol), and dichloromethane (0.5 mL) were added under a flow of nitrogen. The resulting green solution was stirred for 10 min before $NOSbF_6$ (6.6 mg, 0.025 mmol) was added. The solution was allowed to stir for additional 30 min, during which time the color gradually turned from green to deep red. Then the dichloromethane was removed under high vacuum, and 5.0 mmol of the alkene was added to the catalyst solution. The mixture was stirred for 10 min at 0 °C, and ethyl glyoxylate (0.5 mmol) was added. The resulting solution was stirred at 0 °C for 72 h. The reaction mixture was concentrated under vacuum and directly loaded onto a silica gel column (hexanes and ethyl acetate as eluent) to isolate the product.

*Ethyl (S)-2-Hydroxy-4-phenylpent-4-enoate (**1a**).* 89 mg, 81% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.44−7.39 (comp, 2H), 7.36−7.30 (comp, 2H), 7.30−7.25 (m, 1H), 5.39 (s, 1H), 5.21 (s, 1H), 4.30−4.23 (m, 1H), 4.15−4.00 (comp, 2H), 3.05 (dd, 1H, *J* = 14.4, 4.4 Hz), 2.84 (dd, 1H, *J* = 14.4, 7.6 Hz), 2.75 (d, 1H, *J* = 6.3 Hz), 1.23 (t, 3H, *J* = 7.6 Hz). HPLC (AD-H, 98.5% hexanes, 1.5% *i*-PrOH, 1.0 mL/min, 254 nm): 94% ee, 25.8 min (major), 28.3 min (minor). $[\alpha]_D^{23}$ = +18.3 (*c* 1.00, $CHCl_3$). The compound had been fully characterized previously.[6a] The absolute configuration was determined to be *S* by comparison of specific rotation data with those for the known compounds[7m] [literature result: *R* configuration, 98% ee, $[\alpha]_D^{25}$ = −19.49 (*c* 0.99, $CHCl_3$)].

*1-Butyl (S)-2-Hydroxy-4-phenylpent-4-enoate (**1b**).* 87 mg, 70% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.45−7.43 (m, 2H), 7.39−7.34 (m, 2H), 7.32−7.29 (m, 1H), 5.43 (d, *J* = 1.1 Hz, 1H), 5.24 (d, *J* = 1.1 Hz, 1H), 4.31−4.26 (m, 1H), 4.14−3.99 (m, 2H), 3.10 (ddd, *J* = 14.6, 3.6, 1.0 Hz, 1H), 2.86 (ddd, *J* = 14.6, 7.6, 1.0 Hz, 1H), 2.80 (d, *J* = 4.7 Hz, 1H), 1.65−1.58 (m, 2H), 1.43−1.34 (m, 2H), 0.99−0.94 (t, *J* = 7.6 Hz, 3H). HPLC (OJ-H, 95% hexanes, 5% *i*-PrOH, 1.0 mL/min, 254 nm): 94% ee, 8.5 min (major), 10.6 min (minor). The compound had been fully characterized previously.[6a]

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*Isopropyl (S)-2-Hydroxy-4-phenylpent-4-enoate (**1c**).* 101 mg, 86% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.47−7.39 (m, 2H), 7.38−7.31 (m, 2H), 7.31−7.26 (m, 1H), 5.39 (d, J = 1.2 Hz, 1H), 5.21 (dd, J = 2.3, 1.2 Hz, 1H), 4.99 (hept, J = 6.3 Hz, 1H), 4.23 (ddd, J = 7.7, 6.2, 4.6 Hz, 1H), 3.06 (ddd, J = 14.5, 4.5, 1.0 Hz, 1H), 2.80 (ddd, J = 14.5, 7.8, 0.9 Hz, 1H), 2.71 (d, J = 6.2 Hz, 1H), 1.23 (d, J = 6.3 Hz, 3H), 1.21 (d, J = 6.3 Hz, 3H). HPLC (OJ-H, 95% hexanes, 5% *i*-PrOH, 1.0 mL/min, 254 nm): 89% ee, 8.7 min (major), 11.5 min (minor). The compound had been fully characterized previously.[6a]

*Ethyl (S)-2-Hydroxy-4-p-tolylpent-4-enoate (**1d**).* 110 mg, 94% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.32 (d, J = 8.2 Hz, 2H), 7.14 (d, J = 8.5 Hz, 2H), 5.37 (d, J = 1.4 Hz, 1H), 5.16 (d, J = 1.1 Hz, 1H), 4.35−4.22 (m, 1H), 4.22−3.96 (m, 2H), 3.05 (ddd, J = 14.4, 4.5, 1.1 Hz, 1H), 2.82 (ddd, J = 14.4, 7.7, 0.9 Hz, 1H), 2.68 (d, J = 6.3 Hz, 1H), 2.34 (s, 3H), 1.28−1.21 (t, J = 7.1 Hz, 3H). HPLC (OJ-H, 95% hexanes, 5% *i*-PrOH, 1.0 mL/min, 254 nm): 94% ee, 13.5 min (major), 18.0 min (minor). The compound had been fully characterized previously.[6a]

*Ethyl (S)-2-Hydroxy-4-m-tolylpent-4-enoate (**1e**).* 72 mg, 61% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.25−7.17 (m, 3H), 7.14−7.06 (m, 1H), 5.38 (d, J = 1.4 Hz, 1H), 5.19 (d, J = 1.1 Hz, 1H), 4.31−4.23 (m, 1H), 4.19−3.99 (m, 2H), 3.05 (ddd, J = 14.4, 4.5, 1.0 Hz, 1H), 2.83 (ddd, J = 14.4, 7.7, 0.9 Hz, 1H), 2.69 (d, J = 6.2 Hz, 1H), 2.36 (s, 3H), 1.24 (t, J = 7.1 Hz, 3H). HPLC (IA, 98% hexanes, 2% *i*-PrOH, 1.0 mL/min, 254 nm): 87% ee, 15.6 min (minor), 16.3 min (major). The compound had been fully characterized previously.[6a]

*Ethyl (S)-2-Hydroxy-4-o-tolylpent-4-enoate (**1f**).* 86 mg, 73% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.21−7.10 (m, 4H), 5.34 (dd, J = 2.9, 1.3 Hz, 1H), 5.04 (dd, J = 1.8, 0.5 Hz, 1H), 4.19−4.13 (m, 1H), 4.13−3.93 (m, 2H), 2.90 (dddd, J = 14.4, 4.1, 1.3, 0.7 Hz, 1H), 2.82−2.65 (m, 2H), 2.33 (s, 3H), 1.20 (t, J = 7.1 Hz, 3H). HPLC (OJ-H, 95% hexanes, 5% *i*-PrOH, 1.0 mL/min, 254 nm): 89% ee, 9.2 min (major), 10.9 min (minor). The compound had been fully characterized previously.[6a]

*Ethyl (S)-3-(Cyclopent-1-en-1-yl)-2-hydroxypropanoate (**1g**).* 71 mg, 77% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 5.52 (br s, 1H), 4.35−4.28 (m, 1H), 4.24 (qd, J = 7.1, 1.2 Hz, 2H), 2.74 (d, J = 5.0 Hz, 1H), 2.61 (dd, J = 15.1, 3.6 Hz, 1H), 2.50 (dd, J = 15.4, 7.4 Hz, 1H), 2.40−2.18 (m, 4H), 1.88 (p, J = 7.4 Hz, 2H), 1.30 (t, J = 7.1 Hz, 3H). Chiral HPLC (OD-H, 98% hexanes, 2% *i*-PrOH, 1.0 mL/min, 210 nm): 87% ee, 7.8 min (major), 9.2 min (minor). The compound had been fully characterized previously.[6a]

*Ethyl (S)-3-(Cyclohex-1-en-1-yl)-2-hydroxypropanoate (**1h**).* 70 mg, 71% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 5.52 (s, 1H), 4.28−4.18 (m, 3H), 2.67 (d, J = 6.4 Hz, 1H), 2.44 (dd, J = 14.0, 3.9 Hz, 1H), 2.27 (dd, J = 13.9, 8.0 Hz, 1H), 1.99 (m, 4H), 1.64−1.52 (m, 4H), 1.28 (t, J = 7.1 Hz, 3H). Chiral HPLC (IA, 95% hexanes, 5% *i*-PrOH, 1.0 mL/min, 210 nm): 90% ee, 13.0 min (major), 14.1 min (minor). The compound had been fully characterized previously.[6a]

*Ethyl (S)-3-(Cyclohept-1-en-1-yl)-2-hydroxypropanoate (**1i**).* 85 mg, 80% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 5.65 (t, J = 6.4 Hz, 1H), 4.24−4.18 (m, 1H), 4.21 (q, J = 7.1 Hz, 2H), 2.62 (d, J = 5.7 Hz, 1H), 2.47 (dd, J = 13.6, 4.5 Hz, 1H), 2.29 (dd, J = 13.6, 7.8 Hz, 1H), 2.16−2.06 (comp, 4H), 1.74−1.69 (comp, 2H), 1.51−1.44 (comp, 4H), 1.29 (t, J = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 174.7, 139.5, 130.8, 69.3, 61.4, 45.3, 32.9, 32.4, 28.4, 27.0, 26.5, 14.2. HPLC (IA, 95% hexanes, 5% *i*-PrOH, 1.0 mL/min, 210 nm): 93% ee, 12.1 min (major), 12.9 min (minor). $[\alpha]_D^{23}$ = −18.6 (c 0.9, $CHCl_3$). HRMS (ESI$^+$): calcd for $C_{12}H_{21}O_3$ ($[M + H]^+$) 213.1491, found 213.1498.

*Ethyl (S,E)-3-(Cyclooct-1-en-1-yl)-2-hydroxypropanoate (**1j**).* 94 mg, 83% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 5.49 (t, J = 8.2 Hz, 1H), 4.30−4.25 (m, 1H), 4.24 (q, J = 7.1 Hz, 2H), 2.60 (d, J = 5.8 Hz, 1H), 2.52 (dd, J = 13.4, 3.4 Hz, 1H), 2.28 (dd, J = 14.4, 8.8 Hz, 1H), 2.19 (m, 2H), 2.13 (comp, 2H), 1.54−1.48 (comp, 8H), 1.30 (t, J = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 174.7, 135.7, 128.4, 69.2, 61.3, 42.2, 29.7, 28.5, 28.4, 26.4, 26.3, 26.1, 14.1. HPLC (IA, 95% hexanes, 5% *i*-PrOH, 1.0 mL/min, 210 nm): 85% ee, 8.1 min (major), 8.7 min (minor). $[\alpha]_D^{23}$ = −15.9 (c 1.23, $CHCl_3$). HRMS (ESI$^+$): calcd for $C_{13}H_{23}O_3$ ($[M + H]^+$) 227.1647, found 227.1650.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Copies of ^{1}H and ^{13}C NMR spectra for new compounds and chiral HPLC analyses. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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