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Stereoselectivity in metal carbene and Lewis acid-catalyzed reactions from diastereomeric dirhodium(II) carboxamidates: Menthyl *N*-acetyl-2-oxoimidazolidine-4(*S*)-carboxylates

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Abstract

The influence of a chiral menthyl group as the pendant ester substituent on the *N*-acetyl-2-oxoimidazolidine-4*S*-carboxylate ligands in chiral dirhodium(II) imidazolidinone catalysts has been examined. Significant match/mismatch influences are evident in the observed stereocontrol for carbon–hydrogen insertion reactions with diazoacetates, but these effects are minimal in cyclopropanation reactions. Steric restrictions prevent effective enantiocontrol in hetero-Diels–Alder reactions using these menthyl-substituted catalysts.

Keywords: Dirhodium(II); Metal carbene; Enantioselective; Cyclopropanation; Insertion; Hetero-Diels–Alder

1. Introduction

Recent efforts in our research have been directed toward broadening the understanding of stereochemical factors that allow a chiral catalyst to influence product configuration [1]. With catalysts whose ligand(s) have multiple stereogenic elements, configurational and conformational conditions arise that can be transmitted favorably (“matched”) or unfavorably (“mismatched”) for increased or decreased stereocontrol in product formation [2,3]. Numerous examples of this double asymmetric induction exist in catalytic hydrogenation chemistry, focusing primarily on match/mismatch effects on stereoselectivity with bidentate phosphine ligands containing multiple stereocenters [4–8]. Analogous influences have been reported for a broad selection of catalytic chemical transformations by the introduction of a binaphthyl unit into the salen ligand [9]. The strategy that we have employed is the design of multiple ligand stereocenters to control overall catalyst–reactant orientation which, in turn, influences product stereochemistry [10,11]. We recently reported that homo-ligated dirhodium(II) carboxamidates, because of their structural rigidity and their suitability as catalysts for several chemical transformations [12], provide well-defined frameworks with which to investigate catalyst-controlled multiple asymmetric induction (“match/mismatch” effects) [13]. In particular, additional stereocenters can be conveniently built on 1-acyl-2-oxoimidazolidine-4-carboxylate (“imidazolidinone”) ligands [14]. With catalysts that feature diastereomeric pairs of imidazolidinone ligands containing 2-phenylcyclopropane and *N*-benzenesulfonylproline attachments at the 1-*N*-acyl site, recognizable levels of double asymmetric induction for carbon–hydrogen insertion, cyclopropanation, and hetero-Diels–Alder cycloaddition applications were readily achieved [13].

One concern with these studies arises from prior results which demonstrated that stereoselectivity

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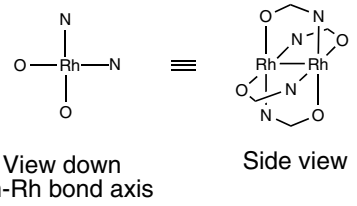
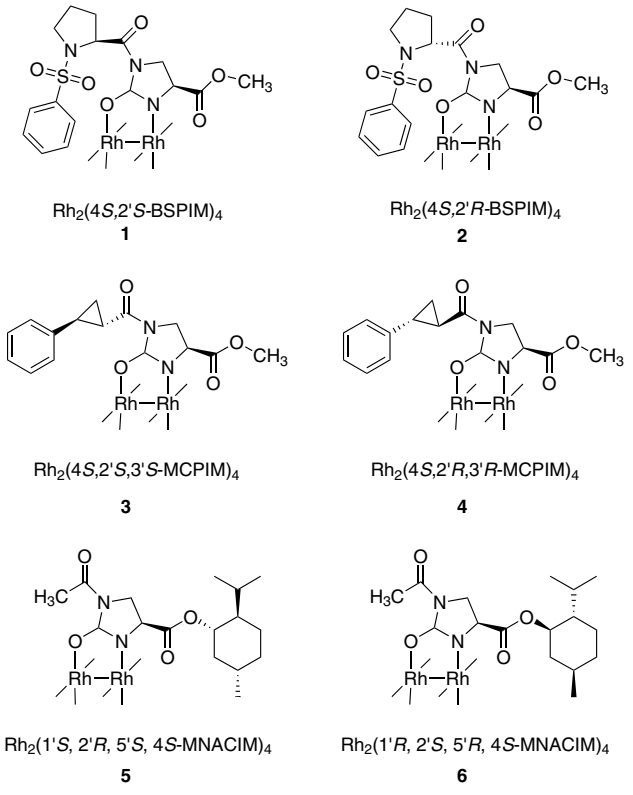


Scheme 1. Dirhodium(II) carboxamidate complex in the (*cis*-2,2) configuration.

decreased with dirhodium(II) oxaimidazoline-4-carboxylates in which the pendant ester group was enlarged from methyl to either ethyl or isobutyl (with a 3-phenylpropanoyl attachment at the 1-*N*-acyl site) [15]. These experiments showed that increased levels of selectivity could not be achieved by simply increasing the steric bulk around the active site. However, decreasing the size of the 1-*N*-acyl attachment to *N*-acetyl brought about a relative increase in stereoselectivity, suggesting that a delicate balance in steric distribution around the active site of the catalyst must be achieved to maximize both selectivity and reactivity.

Dirhodium(II) carboxamidates are constructed with four bridging ligands around the dirhodium core so that two nitrogen and two oxygen donor atoms are attached to each rhodium with the composite arranged in a *cis*-2,2 fashion (Scheme 1) [12]. In the previous report [13] we examined stereocontrol in selected metal carbene and Lewis acid-catalyzed reactions with dirhodium(II) 1-acyl-2-oxaimidazolidine-4-carboxylates, in which additional stereocenters were placed in the 1-acyl site (**1/2** and **3/4** in Scheme 2). In this report we describe a set of catalysts in which the stereocenters are placed in the pendant ester group at the 4-position (**5/6** in Scheme 2) and their comparative influence on stereocontrol in the same set of reactions is discussed.



Scheme 2. Diastereomeric dirhodium(II) 1-acyl-2-oxaimidazolidine-4-carboxylates.

2. Experimental

2.1. General

^{1}H (300 or 400 MHz) and ^{13}C (75 or 100 MHz) NMR spectra were recorded on Varian Unity 300 or Bruker DRX 400 instruments, respectively. Chemical shifts are reported in parts per million (ppm, δ) downfield from internal standard Me_4Si in $CDCl_3$, unless otherwise noted. High-resolution mass spectra were measured on JEOL SX102a, Bruker Reflex-III MALDI/TOF, and JEOL HX110A spectrometers. Desert Analytics in Tucson, AZ, performed elemental analyses. Melting points were measured on a Meltemp 3.0 apparatus. Optical rotations were measured on a Jasco DIP-1000 digital polarimeter. Enantiomeric excesses were determined on a Varian 3800 gas chromatograph, Hewlett Packard 5890 gas chromatograph, or Hewlett Packard 1100 series HPLC with Chiraldex GC or Chiralcel HPLC columns and conditions as noted for each compound.

Reagents were obtained from Acros or Aldrich Chemical Company and used without further purification (unless otherwise noted). Dichloromethane, acetonitrile, and chlorobenzene were dried by distillation over calcium hydride. Diazoacetates were prepared from the commercially available alcohols by literature procedure [16], except for ethyl diazoacetate, which was commercially available. Danishefsky's diene was distilled prior to use.

2.2. Synthesis of (1'S,2'R,5'S)-menthyl 3-benzyloxycarbonyl-2-oxoimidazolidine-4(S)-carboxylate (**12**)

A 250 mL round bottom flask was charged with 3-benzyloxycarbonyl-2-oxoimidazolidine-4(*S*)-carboxylic acid **11** (10.0 g, 37.8 mmol), 4-dimethylaminopyridine (0.114 g, 9.40 mmol), (1*S*,2*R*,5*S*)-(+)-menthol (5.90 g, 37.8 mmol), and 150 mL dichloromethane and cooled to 0 °C. A solution of *N*,*N*′-dicyclohexylcarbodiimide (9.78 g, 47.3 mmol) in 30 mL of dichloromethane was added over 30 min via syringe pump. After stirring for 5 days at room temperature, the white urea precipitate was removed by filtration, and the resulting yellow filtrate was concentrated under reduced pressure to

afford an orange oil. Ethyl acetate (100 mL) was added, and the solution was washed with aqueous solutions of 1 M HCl (50 mL), saturated $NaHCO_3$ (50 mL), and deionized water (100 mL). The combined organics were dried over anhydrous $MgSO_4$. The resulting solution was filtered, concentrated, and purified by column chromatography (SiO_2; ethyl acetate: hexanes = 2:1) to yield 8.39 g of **12** as a white solid (20.8 mmol, 55% yield). ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.37–7.27 (comp, 5H), 6.20 (br s, 1H), 5.26 (d, J = 12.5 Hz, 1H), 5.19 (d, J = 12.5 Hz, 1H), 4.74–4.66 (comp, 2H), 3.74 (t, J = 9.9 Hz, 1H), 3.37 (dd, J = 8.9, 3.8 Hz, 1H), 1.73–1.67 (m, 1H), 1.80–1.59 (comp, 4H), 1.49–1.30 (comp, 2H), 1.13–0.92 (comp, 2H), 0.89 (d, J = 7.3 Hz, 3H), 0.82 (d, J = 6.8 Hz, 3H), 0.70 (d, J = 7.1 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 169.2, 155.7, 150.9, 135.1, 128.4, 128.3, 128.0, 76.2, 68.0, 55.9, 46.6, 40.8, 40.3, 34.0, 31.3, 26.0, 22.9, 21.9, 20.7, 15.8. M.p. 114–115 °C. $[\alpha]_D^{24} = -13.6$ (c 0.1, CH_2Cl_2). HRMS for $C_{22}H_{31}N_2O_5^+$. Theoretical: 403.2233. Found: 403.2242.

2.3. Synthesis of (1′S,2′R,5′S)-menthyl 1-acetyl-3-benzyloxycarbonyl-2-oxoimidazolidine-4(S)-carboxylate (*13*)

A 100 mL round bottom flask was charged with (1′*S*,2′*R*,5′*S*)-menthyl 3-benzyloxycarbonyl-2-oxoimidazolidine-4(*S*)-carboxylate **12** (5.00 g, 12.4 mmol), 4-dimethylaminopyridine (0.15 g, 1.24 mmol), pyridine (2.00 mL, 25.0 mmol), and 50 mL dichloromethane. The reaction vessel was equipped with a condenser, flushed with nitrogen, and cooled to 0 °C. Acetyl chloride (1.06 g, 14.9 mmol) was added over 30 min via syringe pump, and the resulting solution was then stirred at 0 °C for 30 min. The system was then heated to reflux for 18 h to afford an orange solution. An additional 100 mL of dichloromethane was added, and the organic solution was then washed with aqueous solutions of cold 1 M HCl (2 × 30 mL), saturated $NaHCO_3$ (30 mL), and saturated brine (30 mL). The solution was dried over anhydrous $MgSO_4$, filtered, and concentrated to an orange foam, which was purified via column chromatography (SiO_2; ethyl acetate: hexanes 1:1) to yield 4.20 g of **13** (9.42 mmol, 76% yield) as a white powder. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.38–7.29 (comp, 5H), 5.27 (s, 2H), 4.69 (dt, J = 11.0, 4.4 Hz, 1H), 4.63 (dd, J = 10.4, 3.8 Hz, 1H), 3.97 (dd, J = 11.9, 10.4 Hz, 1H), 3.77 (dd, J = 11.9, 3.8 Hz, 1H), 2.53 (s, 3H), 1.90–1.85 (m, 1H), 1.74 (m, J = 6.9 Hz, 1H), 1.70–1.60 (comp, 3H), 1.50–1.33 (comp, 2H), 1.07–0.91 (comp, 2H), 0.89 (d, J = 4.4 Hz, 3H), 0.83 (d, J = 4.4 Hz, 3H), 0.70 (d, J = 6.8 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 170.7, 168.9, 150.9, 149.5, 134.7, 128.8, 128.3, 128.1, 77.6, 69.0, 52.6, 46.8, 42.4, 40.5, 34.1, 31.5, 26.2, 24.1, 23.1, 22.1, 20.9, 16.0. M.p. 98–99 °C. $[\alpha]_D^{23} = +25.7$ (c 0.1, CH_2Cl_2). HRMS for $C_{24}H_{33}N_2O_6^+$. Theoretical: 445.2339. Found: 445.2335.

2.4. Synthesis of (1′S,2′R,5′S)-menthyl 1-acetyl-2-oxoimidazolidine-4(S)-carboxylate (*14*)

A 100 mL round bottom flask was charged with (1′*S*,2′*R*,5′*S*)-menthyl 1-acetyl-3-benzyloxycarbonyl-2-oxoimidazolidine-4(*S*)-carboxylate **13** (3.00 g, 6.75 mmol) and 30 mL ethyl acetate and placed under argon. A small amount of palladium black (~5.0 mg, 0.047 mmol) was added and the solution was flushed with hydrogen from a balloon, stirring overnight at room temperature. The mixture was subsequently filtered through Celite and concentrated under reduced pressure. The resulting off-white solid was purified by column chromatography (SiO_2; ethyl acetate:hexanes 3:2) to afford a white solid, which was recrystallized by slow evaporation of a dichloromethane/hexanes solution to afford 1.62 g of **14** as colorless crystals (5.33 mmol, 79% yield), m.p. 77–78 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 5.48 (s, 1H), 4.75 (dt, J = 11.0, 4.4 Hz, 1H), 4.22 (dd, J = 10.0, 4.9 Hz, 1H), 4.13 (dd, J = 11.5, 10.0 Hz, 1H), 4.01 (dd, J = 11.5, 4.9 Hz, 1H), 2.48 (s, 3H), 1.96 (m, 1H), 1.77 (m, J = 7.0 Hz, 1H), 1.71–1.63 (comp, 3H), 1.53–1.36 (comp, 2H), 1.09–0.92 (comp, 2H), 0.89 (dd, J = 6.7, 3.3 Hz, 6H), 0.90 (d, J = 3.3 Hz, 3H), 0.88 (d, J = 3.4 Hz, 3H), 0.73 (d, J = 6.8 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 170.5, 169.7, 155.3, 76.7, 49.7, 46.8, 44.9, 40.6, 34.0, 31.4, 26.2, 23.4, 23.1, 21.9, 20.8, 16.0. $[\alpha]_D^{23} = +110.6$ (c 0.1, CH_2Cl_2). HRMS for $C_{16}H_{27}N_2O_4^+$. Theoretical: 311.1971. Found: 311.1967. Anal. Calc. for $C_{16}H_{26}N_2O_4$: C, 61.95; H, 8.45; N, 9.03. Found: C, 62.11; H, 8.60; N, 9.20%.

2.5. Synthesis of dirhodium(II) tetrakis[(1′S,2′R,5′S)-menthyl 1-acetyl-2-oxoimidazolidine-4(S)-carboxylate], Rh_2(1′S,2′R,5′S,4S-MNACIM)$_4$(*5*)

A 25 mL two-neck round bottom flask equipped with a stirbar, Soxhlet extractor, and condenser was flame-dried and assembled while still warm under a flow of argon, utilizing teflon tape to seal all joints. A cellulose extraction thimble filled with an oven-dried mixture of sodium carbonate and sand (2:1) and capped with glass wool was placed in the Soxhlet extractor during assembly. Dirhodium(II) acetate (270 mg, 0.611 mmol) was added though the open neck, along with (1′*S*,2′*R*,5′*S*)-menthyl 1-acetyl-2-oxoimidazolidine-4(*S*)-carboxylate (**14**) (1.50 g, 4.83 mmol) and 15 mL chlorobenzene. The side neck was sealed with a fresh septum, and the reaction solution was heated to reflux. The progress of ligand exchange was monitored by TLC using Merck CN F_{254} plates in 97:3 methanol:acetonitrile. Heating was stopped when no further change was observed (approx. 16 h total heating time). The solution was

concentrated and purified via column chromatography on reverse phase Bakerbond® CN resin (1 × anhydrous THF, 1 × anhydrous ethyl acetate), with the first purple band collected. The desired (2,2-*cis*)-isomer **5** was isolated as 405 mg of a purple powder (0.281 mmol, 46% yield). Attempts to crystallize the powder were unsuccessful. ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.77–4.67 (comp, 4H), 4.12 (dd, J = 10.7, 4.8 Hz, 2H), 4.00–3.82 (comp, 6H), 3.56 (dd, J = 11.5, 2.8 Hz, 2H), 3.47 (dd, J = 11.5, 4.8 Hz, 2H), 2.30 (s, 6H), 2.27 (s, 6H), 2.21–2.15 (comp, 4H), 1.96 (s, 6H), 1.94 (comp, 2H), 1.84 (m, J = 6.8 Hz, 4H), 1.77–1.40 (comp, 16H), 1.23–1.04 (comp, 7H), 1.01 (d, J = 6.4 Hz, 6H), 0.99–0.94 (comp, 3H), 0.92 (d, J = 6.4 Hz, 6H), 0.91 (d, J = 6.8 Hz, 6H), 0.88 (d, J = 6.8 Hz, 6H), 0.73 (d, J = 7.2 Hz, 6H), 0.69 (d, J = 7.2 Hz, 6H). ^{13}C NMR (100 MHz, CD_3CN): δ 174.8, 173.6, 169.1, 169.0, 166.3, 165.8, 76.2, 74.7, 60.1, 60.0, 48.7, 48.4, 48.2, 48.1, 43.0, 42.4, 35.1, 34.9, 32.3, 32.2, 27.2, 27.1, 24.1, 24.0, 23.6, 23.2, 22.8, 22.5, 21.1, 21.0, 16.5. $[\alpha]_D^{24} = -210.6$ (c 0.1, CH_3CN). HRMS for $CsRh_2C_{64}H_{100}N_8O_{16}^+$. Theoretical: 1575.4336. Found: 1575.4451. Anal. Calc. for $Rh_2C_{66}H_{103}N_9O_{16}$: C, 53.40; H, 6.99; N, 8.49. Found: C, 53.25; H, 7.14; N, 8.31%.

2.6. General procedure for the catalytic decomposition of diazoacetates

A flame-dried 25 mL round bottom flask, equipped with a condenser and a stirbar, was charged with the catalyst (0.004 mmol, 1 mol%) and flushed with nitrogen. Dichloromethane (5.0 mL) was added via syringe, and the reaction vessel was heated to 35 °C. The diazoacetate (0.40 mmol) was weighed into an oven-dried vial (previously flushed with nitrogen). Dichloromethane (2.0 mL) was added to the diazo compound and the resulting solution was added over 2 h to the refluxing catalyst solution via syringe pump. After addition was complete, the solution was heated at reflux for an additional hour and then filtered through a silica plug (eluting with dichloromethane) to remove the catalyst. The resulting solution was concentrated under reduced pressure and the various products were purified by column chromatography. Enantio- and diastereoselectivities were measured (prior to chromatographic purification) by gas chromatography utilizing a chiral GC column as previously reported [17–20]. Yields were determined by weight of isolated product after chromatography.

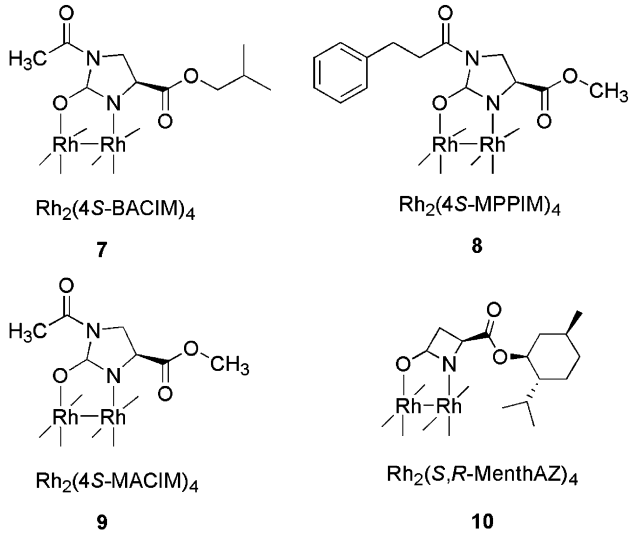
2.7. General procedure for hetero-Diels–Alder reactions

An oven-dried vial containing a stirbar was charged with the dirhodium(II) carboxamidate catalyst (0.002 mmol, 1.0 mol%) and the aldehyde (5.0 eq, 1.0 mmol). Dichloromethane (1.0 mL) and the Danishefsky diene (1.0 eq, 0.20 mmol) were added and the vial was capped, sealed with parafilm, and stirred overnight. The following day 3 drops of trifluoroacetic acid were added and the solution was stirred for 30 min. The product was then purified by column chromatography and analyzed by HPLC for enantioselectivity according to the literature procedure [21]. Yields were determined by weight of isolated product after chromatography.

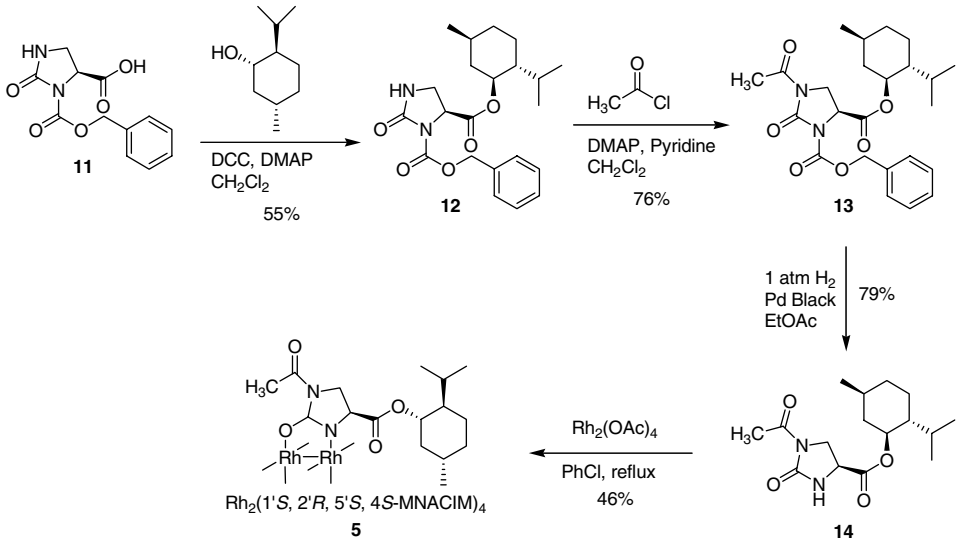
3. Results and discussion

While "match/mismatch" effects have been observed in metal carbene and Lewis acid-catalyzed reactions with imidazolidinone catalysts having chiral *N*-acyl attachments [13,21–23], the same attention has not been given to those that incorporate stereogenic centers on the ester moiety. In earlier results from several catalytic applications, higher levels of selectivity were obtained with dirhodium(II) tetrakis[2′-methyl-1′-propyl 1-acetyl-2-oxoimidazolidine-4(*S*)-carboxylate] Rh_2(4*S*-BACIM)$_4$ (**7**, Scheme 3) [15] than with the imidazolidinone catalysts that generally provide the highest levels of stereocontrol: Rh_2(4*S*-MPPIM)$_4$ (**8**) and dirhodium(II) tetrakis[methyl 1-acetyl-2-oxoimidazolidine-4(*S*)-carboxylate], Rh_2(4*S*-MACIM)$_4$ (**9**) [24]. These results suggested that the *N*-acetyl group should be preferable if the size of the pendant ester group is increased. In choosing the identity of this ester group, the high selectivities shown by another dirhodium(II) catalyst, Rh_2(*S*,*R*-MenthAZ)$_4$ (**10**) in asymmetric intermolecular cyclopropanation reactions [25], pointed to the menthyl ester as a logical choice.

The synthesis of the (−)-menthyl ester of the *N*-acetyl-2-oxaimidazolidine-4(*S*)-carboxylate ligand has been reported, and the subsequent preparation of



Scheme 3. Imidazolidinone-ligated dirhodium(II) catalysts.



Scheme 4. Synthesis of imidazolidinone-ligated $Rh_2(1'S, 2'R, 5'S, 4S\text{-MNACIM})_4$.

$Rh_2(1'R,2'S,5'R,4S\text{-MNACIM})_4$ (**6**) has been previously described [26]. The synthesis of the diastereomer of **5**, $Rh_2(1'S,2'R,5'S,4S\text{-MNACIM})_4$ (**5**), proceeded in an identical fashion (Scheme 4). The *d*-menthyl ester **12** was formed through a DCC coupling with (+)-menthol and the 4(*S*)-imidazolidinone carboxylic acid **11** to afford the white solid **12** in 55% yield. The *N*-acetyl group was then attached in the presence of DMAP and pyridine to afford the protected ligand **13** in 76% yield. Exposure to heterogeneous hydrogenation conditions produced the ligand $1'S,2'R,5'S,4S$-HMNACIM (**14**) in 79% yield after recrystallization. Catalyst **5** was generated by ligand exchange with rhodium acetate to produce a red powder in 46% yield. Attempts to obtain X-ray quality crystals of **5** have thus far been unsuccessful.

However, the structure of **6** [26] (Fig. 1) exemplifies the general features of this ligand design. In the depiction presented in Fig. 1, only the attachments on the ligands that are closest to the front rhodium are shown. Thus, there are two chiral menthyl-carboxylate attachments on adjacent quadrants around the rhodium

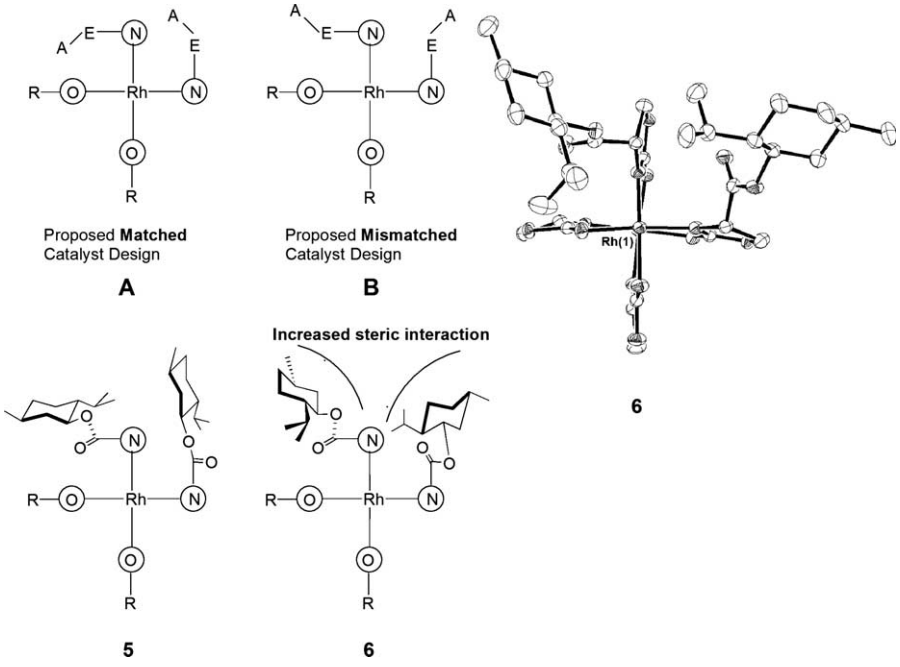
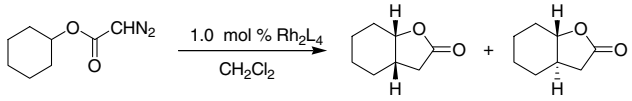


Fig. 1. Configurational depictions of "matched" (**A**, complex **5**) and "mismatched" (**B**, complex **6**) dirhodium(II) 1-*N*-acetyl-2-oxaimidazolidine-4(*S*)-carboxylates, together with the front view of **6** showing only the attachments that are closest to the front rhodium [26].

Table 1
Intramolecular carbon–hydrogen insertion reactions of cyclohexyl diazoacetate



15 16 17

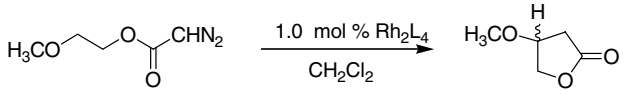
Catalyst	Overall yield	Ratio of **16**:**17**	**16** (% ee)	**17** (% ee)
$Rh_2(1'S,2'R,5'S,4S\text{-MNACIM})_4$ (**5**)	80%	100:0	95	NA
$Rh_2(1'R,2'S,5'R,4S\text{-MNACIM})_4$ (**6**)	71%	79:21	84	68

center, and two achiral *N*-acetyl substituents lie in the remaining two quadrants. The positioning of the menthyl groups can be aligned with the carboxylate group (structure **A** in Fig. 1) or stereochemically opposed to the configuration of the carboxylates (structure **B** in Fig. 1). With its configurational 1′-*S*/4-*S* match, catalyst **5** has the appearance of **A** and **6**, then, has the appearance of **B**.

To understand the selectivity differences between catalysts **5** and **6**, a selection of substrates was subjected to each of the two catalysts under standard reaction conditions (1 mol% catalyst loading). With cyclohexyl diazoacetate **15** (Table 1) catalyst **5** exhibited complete diastereocontrol for carbon–hydrogen insertion, and the enantiomeric excess for *cis* stereoisomer **16** was the highest value seen for these reactions [12]. In contrast, neither diastereoselectivity nor enantioselectivities were high using catalyst **6**.

A similar outcome is seen in the C–H insertion reactions of cyclopentyl diazoacetate **18** (Table 2), although with lower enantiomeric excess for **19** than observed with either $Rh_2(4S\text{-MACIM})_4$ (89% ee) [17] or $Rh_2(4S\text{-MPPIM})_4$ (93% ee) [18]. With 2-methoxy-1-ethyl diazoacetate **20** (Table 3) [19] the difference in product enantiomeric excess between catalysts **5** and **6** is substantial. Overall, the configurational influence of the menthyl group on the *N*-acetyl-2-oxoimidazolidine-4-carboxylate ligands in dirhodium-catalyzed C–H insertion reactions is high, and appreciable match/mismatch effects are present.

Table 3
Intramolecular carbon–hydrogen insertion reactions of 2-methoxy-1-ethyl diazoacetate



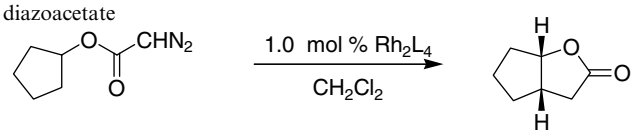
20 21

Catalyst	Overall yield of **21**	% ee
$Rh_2(1'S,2'R,5'S,4S\text{-MNACIM})_4$ (**5**)	66%	93
$Rh_2(1'R,2'S,5'R,4S\text{-MNACIM})_4$ (**6**)	75%	55

In contrast to carbon–hydrogen insertion reactions, the two diastereomeric catalysts show minimal difference in stereoselectivity for cyclopropanation reactions. With methallyl diazoacetate **22** (Table 4) enantioselectivity using catalysts **5** and **6** for intramolecular cyclopropanation is comparable to that with $Rh_2(4S\text{-MPPIM})_4$ [18] (89% ee) or $Rh_2(4S\text{-MACIM})_4$ [20] (78% ee), respectively. In addition, there is virtually no difference between results with **5** and **6** in either diastereoselectivity or enantioselectivity for intermolecular cyclopropanation of styrene with ethyl diazoacetate **24** (Table 5).

The data obtained for hetero-Diels–Alder reactions between the Danishefsky diene **27** and both 4-nitrobenzaldehyde **28** (Table 6) or its thiophene analog **30** (Table 7) show that the menthyl ester prohibits effective stereoselective cycloaddition. This observation is consistent with recent understanding of the steric demands from the catalyst [21]. In contrast, under the same conditions,

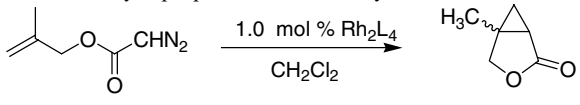
Table 2
Intramolecular carbon–hydrogen insertion reactions of cyclopentyl diazoacetate



18 19

Catalyst	Overall yield of **19**	% ee
$Rh_2(1'R,2'S,5'R,4S\text{-MNACIM})_4$ (**5**)	79%	77
$Rh_2(1'S,2'R,5'S,4S\text{-MNACIM})_4$ (**6**)	84%	33

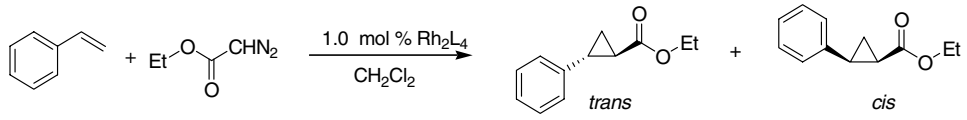
Table 4
Intramolecular cyclopropanation of methallyl diazoacetate



22 23

Catalyst	Overall yield of **23**	% ee
$Rh_2(1'S,2'R,5'S,4S\text{-MNACIM})_4$ (**5**)	70%	83
$Rh_2(1'R,2'S,5'R,4S\text{-MNACIM})_4$ (**6**)	62%	73

Table 5
Intermolecular cyclopropanation of styrene with ethyl diazoacetate



24 **25** **26**

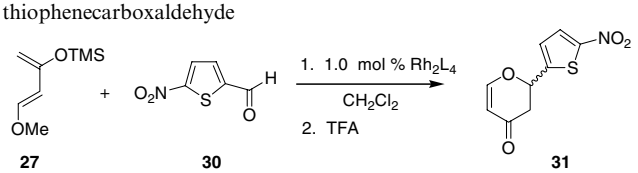
Catalyst	Overall yield	Ratio of **25**:**26**	**25** (% ee)	**26** (% ee)
$Rh_2(1'S,2'R,5'S,4S\text{-MNACIM})_4$ (**5**)	61%	49:51	43	28
$Rh_2(1'R,2'S,5'R,4S\text{-MNACIM})_4$ (**6**)	56%	47:53	45	46

Table 6
Hetero-Diels–Alder reaction of the Danishefsky diene with 4-nitrobenzaldehyde

27 **28** **29**

Catalyst	Overall yield of **29**	% ee
$Rh_2(1'S,2'R,5'S,4S\text{-MNACIM})_4$ (**5**)	43%	0
$Rh_2(1'R,2'S,5'R,4S\text{-MNACIM})_4$ (**6**)	77%	15

Table 7
Hetero-Diels–Alder reaction of the Danishefsky diene with 5-nitro-2-thiophenecarboxaldehyde



27 **30** **31**

Catalyst	Overall yield of **31**	% ee
$Rh_2(1'S,2'R,5'S,4S\text{-MNACIM})_4$ (**5**)	56%	10
$Rh_2(1'R,2'S,5'R,4S\text{-MNACIM})_4$ (**6**)	85%	31

use of $Rh_2(4S\text{-MPPIM})_4$ (**8**) produced **29** and **31** in 95% and 94% ee, respectively [13]. Clearly, the bulky menthyl group of the catalyst is limiting access of the Danishefsky diene to the coordinated aldehyde, either to distort the catalytic transition state away from optimal selectivity or to increase the relative importance of the uncatalyzed pathway.

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