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SYNTHESIS AND EVALUATION OF NOVEL DIRHODIUM(II) CARBOXYLATE CATALYSTS WITH ATROPISOMERIC BIARYL BACKBONE†

Ken Hikichi,[a] Shinji Kitagaki,[a] Masahiro Anada,[a] Seiichi Nakamura,[a] Makoto Nakajima,[a] Motoo Shiro,[b] and Shunichi Hashimoto*[a]

[a]Graduate School of Pharmaceutical Sciences, Hokkaido University, Sapporo 060-0812, Japan

[b]Rigaku Corporation, 3-9-12 Matsubara, Akishima, Tokyo 196-8666, Japan

Abstract – Three new dirhodium(II) carboxylate catalysts containing an axially dissymmetric biphenyl or binaphthyl skeleton have been synthesized and characterized. The X-Ray structure of the dirhodium(II) complex incorporating (*R*)-2'-methoxycarbonyl-6,6'-dimethyl-[1,1'-biphenyl]-2-carboxylate as bridging ligands demonstrates that the four carboxylate ligands are arranged in a C_2-symmetry-like conformation. These catalysts have been shown to provide a reasonable level of asymmetric induction in intramolecular C–H insertion of α-methoxycarbonyl-α-diazoacetamide.

In recent years, a dramatic development in dirhodium(II) complex-catalyzed, asymmetric carbene transformations of α-diazo carbonyl compounds has been recorded in a number of processes, including cyclopropanation, C–H insertion, and rearrangement or cycloaddition *via* ylide generation.[1] In this context, considerable effort continues to be devoted to the design, synthesis, and evaluation of chiral dirhodium(II) catalysts. Unique in their design are chiral bridging ligands bound to the dirhodium(II) core, which constitute one of the most fundamental factors responsible for a high level of chemical reactivity, turnover numbers, regio-, diastereo- and enantioselectivity.[1,2] Our efforts in this area have led to the development of dirhodium(II) carboxylate catalysts, which incorporate *N*-phthaloyl- or *N*-benzene-fused phthaloyl-(*S*)-amino acids as bridging ligands.[3,4] These catalysts mediate intramolecular C–H insertions of a structurally diverse array of diazo carbonyl compounds,[5-10] intermolecular Si–H insertions,[11] intermolecular 1,3-dipolar cycloadditions *via* the generation of keto-[4] or ester-carbonyl ylides,[12] and [2,3] sigmatropic rearrangement *via* the intramolecular formation of allylic[13] or propargylic oxonium ylides[14] with a maximum of 98%, 74%, 93%, and 79% ee's, respectively. In these reactions, the presence of phthalimido or benzene-fused phthalimido groups in bridging ligands has proven to be

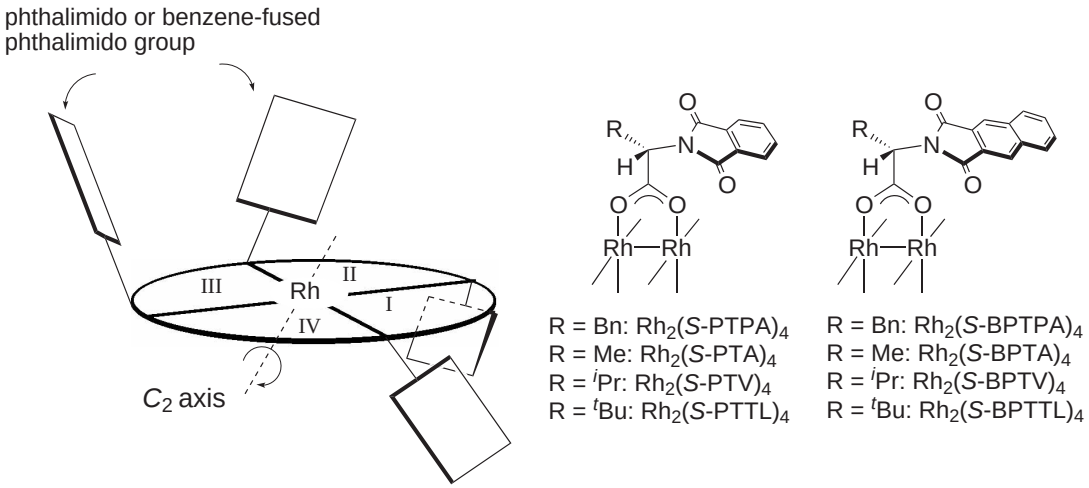


Figure 1. Schematic representation of dirhodium (II) carboxylates incorporating *N*-phthaloyl- and *N*-benzene-fused phthaloyl-(*S*)-amino acid as bridging ligands

crucial to a high degree of enantioselection, though the secondary effect of the alkyl substituent of amino acids on enantioselectivities has yet to be elucidated. In addition, it has recently been demonstrated that the absolute stereochemical course of intramolecular C–H insertion reactions[3,6a,9a,9d] and [2,3] sigmatropic rearrangement reactions via the intramolecular formation of propargylic oxonium ylides[14] could be rationalized based on a structural model of our dirhodium(II) catalysts (Figure 1), which has been patterned after the solid-state structure of Rh_2(*S*-PTPA)$_4$, established as the bis(4-*tert*-butylpyridine) adduct by X-Ray crystallography (Figure 2).[5b] Consequently, the catalysts are considered to function in a C_2-symmetry-like fashion in these reactions with the protruding phthalimido or benzene-fused phthalimido groups aligned in a "down-down-up-up" arrangement. Taking advantage of these findings, we now set out to synthesize chiral dirhodium(II) carboxylate catalysts containing an axially dissymmetric biaryl skeleton.[15] In this design we envisaged that if the aryl group bound to the carboxylate carbon might be coplanar to the bridging carboxylate group for maximum overlap between 2*p* orbitals on them,[16] this would orient out two *ortho*-aryl rings in a pair of adjoining ligands to an axial site of each octahedral rhodium such that the axial coordination of α-diazo carbonyl compounds could be allowed. Thus, these dirhodium(II) catalysts were expected to conduct themselves in a similar C_2-symmetry-like fashion as Rh_2(*S*-PTPA)$_4$, with the *ortho*-aryl rings aligned in a "down-down-up-up" arrangement. Even though the alternative D_2-symmetry-like conformation in a "down-up-down-up" arrangement cannot be ruled out,[1g] this

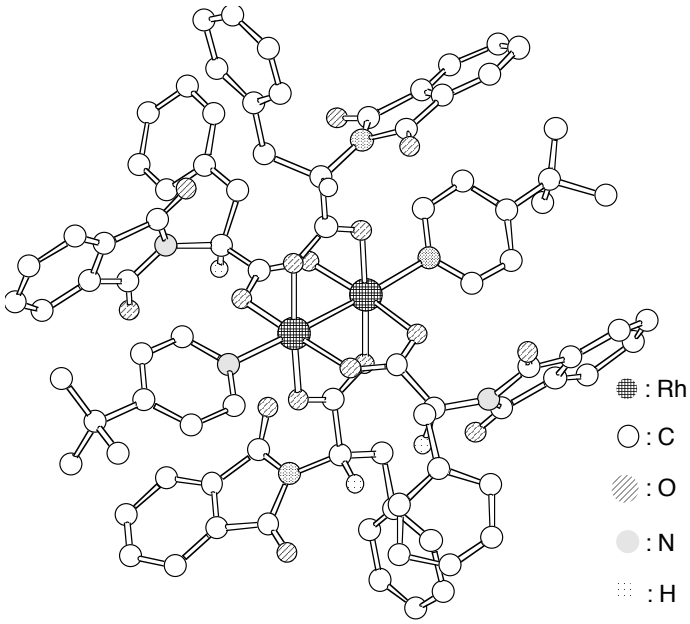
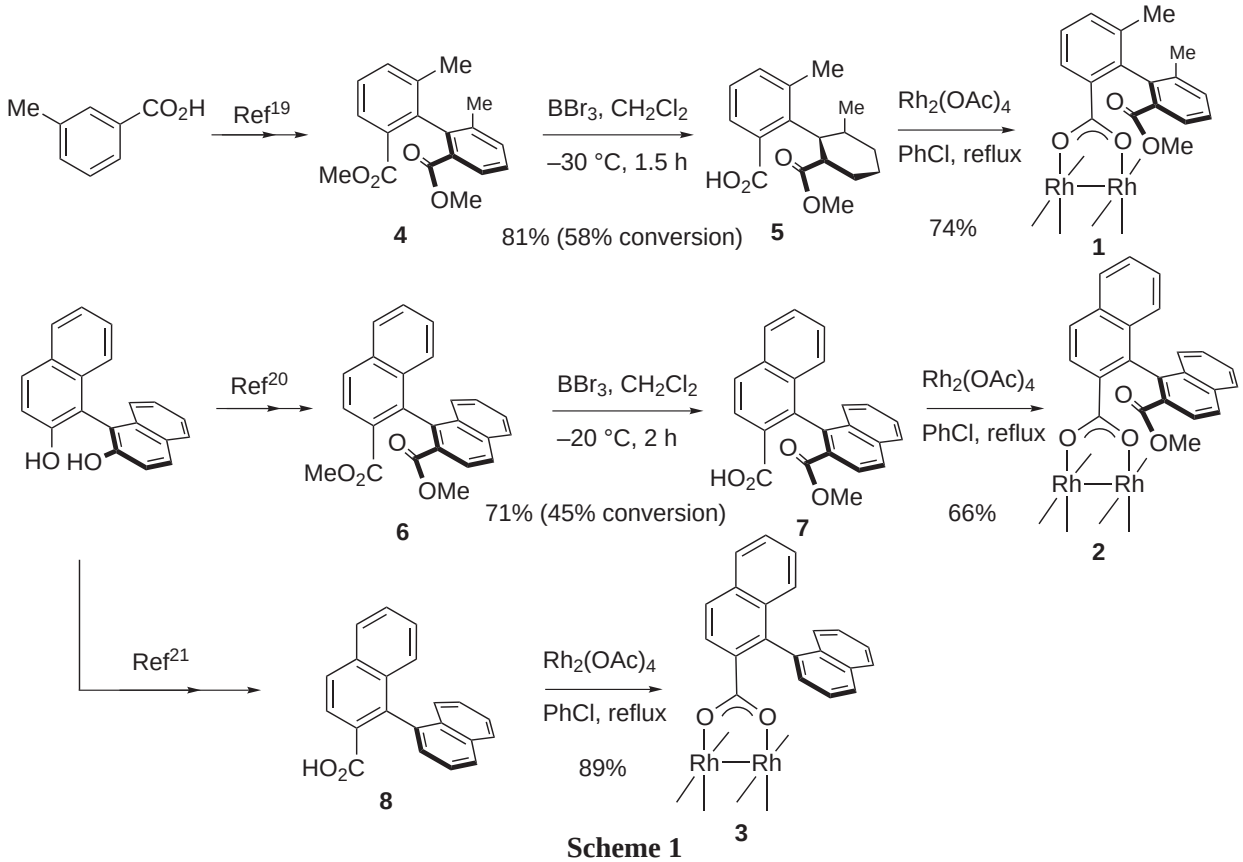


Figure 2. Crystal structure of bis(4-*tert*-butylpyridine) adduct of Rh_2(*S*-PTPA)$_4$

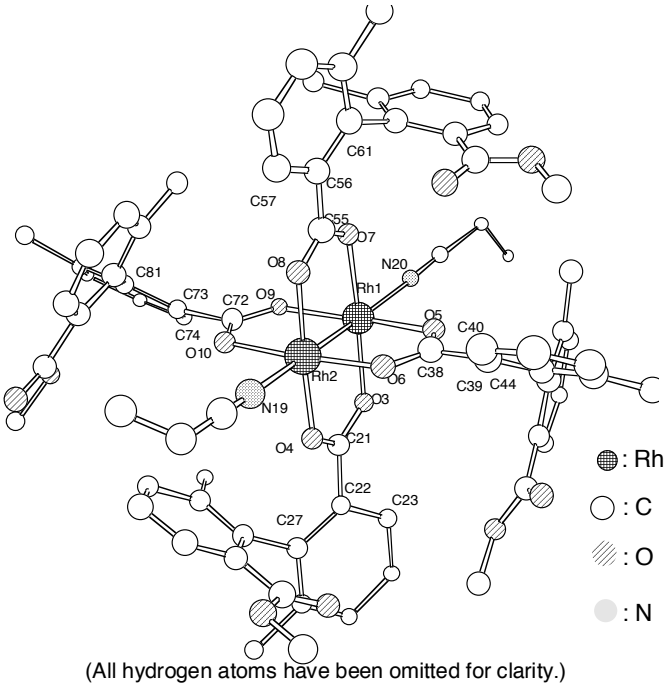
conformation seems unlikely because the two *ortho*-aryl rings directed toward each end of the molecule might prevent the axial coordination of α-diazo carbonyl compounds as well as subsequent reactions particularly in an intramolecular system. In 1997 Achiwa reported the synthesis of Rh_2(*S*-BDME)$_4$ incorporating (*S*)-6'-methoxycarbonyl-3,3'-dimethoxy-2,2',4,4'-tetramethyl-[1,1'-biphenyl]-6-carboxylate as bridging ligands and its effective use for asymmetric cyclopropanation of styrene with *d*-menthyl diazoacetate (up to 99% ee), though no explanation of the chiral environment was offered.[17] The purpose of this paper is to describe the synthesis and characterization of this class of dirhodium(II) carboxylates and their preliminary evaluation as a chiral catalyst for intramolecular C–H insertion of α-methoxycarbonyl-α-diazoacetamide.

Three new chiral dirhodium(II) carboxylate complexes (**1**-**3**) were prepared from $Rh_2(OAc)_4$ by ligand exchange reaction (chlorobenzene, 160 °C, 2–3 h)[18] with (*R*)-2'-methoxycarbonyl-6,6'-dimethyl-[1,1'-biphenyl]-2-carboxylic acid (**5**) and (*R*)-2'-methoxycarbonyl-1,1'-binaphthyl-2-carboxylic acid (**7**), which were prepared by partial hydrolysis of the corresponding known dimethyl esters (**4**[19] and **6**[20]) with BBr_3, and the known (*S*)-1,1'-binaphthyl-2-carboxylic acid (**8**),[21] respectively (Scheme 1). The HRMS (FAB)



Scheme 1

data indicated that these complexes contained four molecules of bridging carboxylate ligands. While a number of structures of chiral dirhodium(II) carboxamidate catalysts pioneered by Doyle have been determined by X-Ray crystallography,[1b] only a handful of chiral dirhodium(II) carboxylate catalysts have been crystallographically characterized. Clearly, the difficulty in making single-crystals of the latter is due to the conformational flexibility of bridging carboxylate ligands. Thus, we were pleased to find that red single-crystals of the bis(propionitrile) adduct of **1** were grown from propionitrile/hexane solution. The X-Ray structure of this complex reveals that each rhodium geometry is octahedral, with the nitrogen



(All hydrogen atoms have been omitted for clarity.)

Figure 3. Crystal structure of bis(propionitrile) adduct of **1**

Table 1. Selected Bond Lengths (Å)

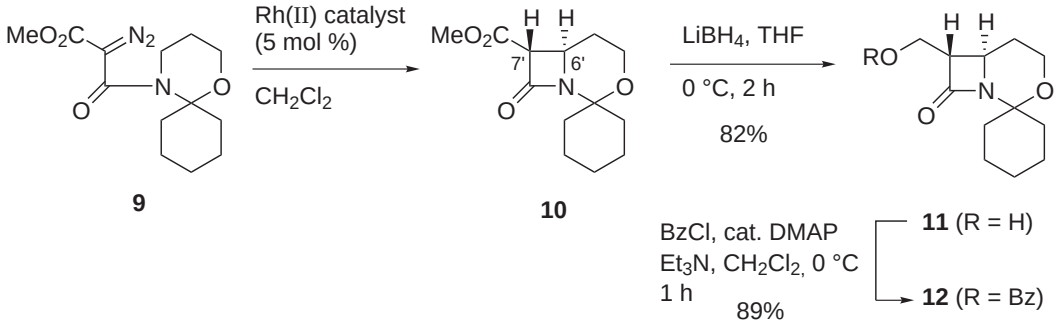
Rh1-Rh2	2.398	Rh2-O4	1.996
Rh1-O3	2.034	Rh2-O6	2.028
Rh1-O5	2.008	Rh2-O8	2.031
Rh1-O7	2.081	Rh2-O10	2.088
Rh1-O9	2.030	Rh2-N20	2.245
Rh1-N19	2.246		

Table 2. Selected Torsion Angles (°)

O3-C21-C22-C23	24.251
O4-C21-C22-C27	28.193
O5-C38-C39-C44	30.349
O6-C38-C39-C40	35.098
O7-C55-C56-C61	12.679
O8-C55-C56-C57	13.563
O9-C72-C73-C74	33.240
O10-C72-C73-C78	45.360

atom of propionitrile coordinated to each axial site (Figure 3). The Rh–Rh bond distance (2.398 Å, Table 1) is comparable to that found in Rh_2(*S*-PTPA)$_4$·(4-*tert*-butylpyridine)$_2$ (2.407 Å).[5b] It is noteworthy that the aromatic rings bound to the carboxylate carbon atoms deviate from each carboxylate plane by average values of 13.1°, 26.2°, 32.7°, and 39.3°, respectively (Table 2), which probably minimizes steric repulsion between the *ortho*-aryl groups.[22] Interestingly, although the crystal structure suffers from considerable distortion, it has been shown that the 2-methoxycarbonyl-6-methylphenyl groups at the *ortho* position align in a "down-down-up-up" arrangement.

With new chiral dirhodium(II) carboxylates (**1**-**3**) in hand, we then explored intramolecular C–H insertion of □-methoxycarbonyl-□-diazoacetamide (**9**), which leads to the key azetidin-2-one intermediate for the synthesis of 1-unsubstituted carbapenem antibiotics (Scheme 2). In this system, we previously achieved enantioselectivities greater than 90% with the use of dirhodium(II) carboxylate catalysts incorporating *N*-phthaloyl-(*S*)-amino acids as bridging ligands.[9b] The sense and extent of enantioselection in this reaction were determined by HPLC (Daicel Chiralcel OJ) after conversion of the product (**10**) *via* alcohol (**11**) into benzoate (**12**).



Scheme 2

The results are summarized in Table 3, where the previous results[9b] are also presented for comparison. The reaction under the influence of catalysts (**1**-**3**) was found to provide *trans*-azetidin-2-one derivative

Table 3. Enantioselective Intramolecular C–H Insertion Reaction of α-Methoxycarbonyl-α-diazoacetamide (**9**) Catalyzed by Chiral Dirhodium(II) Carboxylates

Entry	Rh(II) catalyst	Temp. (°C)	Time (h)	Yield (%)[a]	Ee (%)[b]	Confign
1	**1**	23	24	58	50	6'*R*,7'*R*
2	**2**	23	36	62	52	6'*R*,7'*R*
3	**3**	23	18	71	52	6'*R*,7'*R*
4	Rh_2(*S*-PTPA)$_4$	0	3	89	90	6'*R*,7'*R*
5	Rh_2(*S*-PTA)$_4$	0	2	94	96	6'*R*,7'*R*
6	Rh_2(*S*-PTV)$_4$	0	3	86	92	6'*R*,7'*R*
7	Rh_2(*S*-PTTL)$_4$	0	4	85	93	6'*R*,7'*R*

a) Isolated yield.
b) Determined by HPLC analysis (Daicel Chiralcel OJ) after conversion to benzoate (**12**).

(**10**) in 58-71% yields with the same sense of asymmetric induction as observed with our standard catalysts. Somewhat surprisingly, all these catalysts displayed highly uniform levels of enantioselection (50–52% ee), regardless of whether the ester group is attached or not (Entry 2 vs. 3). Although they are less efficient than our standard catalysts for this reaction in terms of catalytic activity, product yield, and enantioselectivity (Entries 1–3 vs. 4–7), the same sense of asymmetric induction as found with the well-characterized Rh_2(*S*-PTPA)$_4$ suggests that the catalysis might take place through the C_2-symmetry-like conformation of their catalysts as designed.

In summary, we have demonstrated that new chiral dirhodium(II) carboxylate catalysts containing an atropisomeric biaryl skeleton, synthesized patterned after the solid-state structure of Rh_2(*S*-PTPA)$_4$, display a reasonable level of catalytic performance in intramolecular C–H insertion of α-methoxycarbonyl-α-diazoacetamide. Further studies are in progress to determine the scope of these complexes as chiral catalysts for a range of rhodium(II)-carbene transformations.

EXPERIMENTAL

General. Melting points were determined on a Büchi 535 digital melting point apparatus and are uncorrected. Optical rotations were measured on a JASCO DIP-370 digital polarimeter at the sodium D line (589 nm). IR spectra were recorded on a Jasco FT/IR-5300 spectrophotometer and absorbance bands are reported in wavenumber (cm^{-1}). ^{1}H NMR spectra were recorded on JEOL JNM-EX 270 (270 MHz) or JEOL JNM-AL 400 (400 MHz) spectrometers. Chemical shifts are reported relative to internal standard (tetramethylsilane; δ_H 0.00 or $CDCl_3$; δ_H 7.26). Data are presented as follows: chemical shift (δ, ppm), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad), coupling constant, integration and assignment. ^{13}C NMR spectra were recorded on JEOL JNM-EX 270 (67.8 MHz) or JEOL JNM-AL 400 (100 MHz) spectrometers. The following internal reference was used: $CDCl_3$ (δ 77.0). EIMS spectra were obtained on a JEOL FAB-mate spectrometer, operating with an ionization energy of 70 eV. FABMS spectra were obtained on a JEOL JMS-HX 110 spectrometer. Column chromatography was carried out on Merck Kieselgel 60 (60–200 μm) or Kanto silica gel 60 N (63–210 μm) unless otherwise stated. Analytical thin layer chromatography (TLC) was carried out on Merck Kieselgel 60 F_{254} plates with visualization by ultraviolet, anisaldehyde stain solution or

phosphomolybdic acid stain solution. Analytical high performance liquid chromatography (HPLC) was performed on a JASCO PU-1580 intelligent HPLC pump with Jasco UV-1575 intelligent UV/VIS detector. Detection was performed at 254 nm. Chiralcel OD and OJ columns (0.46 cm × 25 cm) from Daicel were used. Retention times (t_R) and peak ratios were determined with Shimadzu C-R6A chromatopac integrator.

All non aqueous reactions were carried out in flame-dried glassware under Ar atmosphere unless otherwise noted. Reagents and solvents were purified by standard means. CH_2Cl_2 was distilled from P_2O_5 and then CaH_2. THF was distilled from Na/benzophenone ketyl.

Methyl hydrogen (*R*)-6,6'-dimethyl-[1,1'-biphenyl]-2,2'-dicarboxylate (5). Boron tribromide (1.2 mL, 12.7 mmol) was added to a solution of dimethyl (*R*)-6,6'-dimethyl[1,1'-biphenyl]-2,2'-dicarboxylate (**4**)[19] [$[\alpha]_D^{25}$ –54.6° (*c* 1.97, benzene), >99% ee,[23] 1.23 g, 4.13 mmol] in CH_2Cl_2 (100 mL) at –30 °C. After 1.5 h of stirring at this temperature, the reaction was quenched with water and the whole was extracted with EtOAc (200 mL). The organic layer was washed with water and brine, and dried over Na_2SO_4. Filtration and evaporation *in vacuo* followed by column chromatography (silica gel, 10:1 $CHCl_3$/MeOH) provided **5** (613 mg, 52%) as a white solid, along with unreacted **4** (517 mg, 42%). Further recrystallization of **5** from benzene–hexane afforded colorless fine needles (553 mg); mp 96–97 °C; Rf = 0.35 (30:1 CH_2Cl_2/MeOH); $[\alpha]_D^{31}$ –19.8° (*c* 1.45, $CHCl_3$); IR ($CHCl_3$) ν: 3023, 1721 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$) δ 1.86 (s, 3H, ArC*H*$_3$), 1.89 (s, 3H, ArC*H*$_3$), 3.62 (s, 3H, CO_2CH_3), 7.28–7.37 (m, 2H, Ar*H*), 7.39–7.46 (m, 2H, Ar*H*), 7.76–7.86 (m, 2H, Ar*H*); ^{13}C NMR (67.8 MHz, $CDCl_3$) δ 19.93, 52.02, 127.08, 127.12, 127.51, 127.98, 129.34, 129.52, 133.78, 133.96, 136.39, 136.73, 140.49, 140.67, 168.43, 171.23; HRMS (EI) calcd for $C_{17}H_{16}O_4$ (M^+) 284.1049, found 284.1052; Anal. Calcd for $C_{17}H_{16}O_4$: C, 71.82; H, 5.67. Found: C, 71.84; H, 5.83.

Dirhodium(II) tetrakis[(*R*)-2'-methoxycarbonyl-6,6'-dimethyl-[1,1'-biphenyl]-2-carboxylate] (1). A mixture of $Rh_2(OAc)_4$·2MeOH (156 mg, 0.31 mmol) and (*R*)-**5** (522 mg, 1.84 mmol) in chlorobenzene (20 mL) was heated at reflux with vigorous stirring, while the solvent was distilled off at a rate such that 5 mL of the solvent was removed per an hour. After completion of the reaction (2 h) was confirmed by TLC analysis, the deep green mixture was cooled to room temperature, and the whole was partitioned between EtOAc (60 mL) and saturated aq. $NaHCO_3$ (30 mL). The organic layer was successively washed with water and brine, and dried over Na_2SO_4. Filtration and evaporation *in vacuo* followed by column chromatography (silica gel, 2.5:1 hexane/EtOAc) afforded bis(ethyl acetate) adduct of **1** (398 mg) as a green solid, which was recrystallized from THF–hexane to give bis(tetrahydrofuran) adduct of **1** (304 mg, 74%) as green needles: mp > 250 °C; Rf = 0.16 (3:1 hexane/EtOAc); $[\alpha]_D^{25}$ –52.8° (*c* 0.021, $CHCl_3$); IR ($CHCl_3$) ν: 1719, 1570 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.47 (s, 12H, ArC*H*$_3$), 1.69 (s, 12H, ArC*H*$_3$), 1.88–1.91 (m, 8H, C*H*$_2$ of THF), 3.14 (s, 12H, CO_2CH_3), 3.73 (br-s, 8H, C*H*$_2$O of THF), 7.12 (m, 4H, Ar*H*), 7.21 (m, 4H, Ar*H*), 7.27 (m, 4H, Ar*H*), 7.37 (m, 4H, Ar*H*), 7.42 (m, 4H, Ar*H*), 7.80 (m, 4H, Ar*H*); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.00, 20.07, 25.56 (THF), 51.57, 68.36 (THF), 125.85, 126.13, 127.01, 127.70, 129.83, 131.12, 132.14, 133.04, 135.55, 136.50, 139.14, 141.53, 167.87, 184.61; HRMS

(FAB) calcd for $C_{68}H_{60}O_{16}Rh_2$ (MH^+) 1338.1991, found 1338.2009; Anal. Calcd for $C_{68}H_{60}O_{16}Rh_2 \cdot 2THF$: C, 61.54; H, 5.16. Found: C, 61.22; H, 5.22.

Crystallographic analysis of bis(propionitrile) adduct of 1. A red prismatic crystal with approximate dimensions of 0.40 × 0.05 × 0.03 mm, prepared by recrystallization of bis(tetrahydrofuran) adduct of **1** from a propionitrile/hexane solution, was sealed in a glass capillary. All measurements were made on a Rigaku RAXIS-IV Imaging Plate diffarctometer with graphite monochromated Mo-Kα radiation.
Crystal Data: Formula $C_{74}H_{70}N_2O_{16}Rh_2$, Formula Weight 1449.18, Monoclinic System, Space Group $P2_1$ (#4), a 10.3834(2) Å, b 25.696(1) Å, c 13.3540(6) Å, β 102.506(2)°, V 3478.5(2) $Å^3$, Z 2, D_{calc} 1.383 g/cm^3, μ 5.4 cm^{-1}, Lp Corrections applied, Absorption Corrections not applied, $2\theta_{max}$ 50.3°. The structure was solved by direct methods[24] and refined by full-matrix least-squares techniques.[25]
Final R, Rw and goodness of fit indicator were 0.049 for 5137 reflections with $I>2\sigma(I)$, 0.121 for 5446 reflections of positive intensity and 1.09 for 5446 reflections, respectively. The final atomic parameters will be deposited with the Cambridge Crystallographic Data Centre.

Methyl hydrogen (*R*)-1,1'-binaphthyl-2,2'-dicarboxylate (7). Boron tribromide (0.55 mL, 5.80 mmol) was added to a solution of dimethyl (*R*)-1,1'-binaphthyl-2,2'-dicarboxylate (**6**)[20] [$[\alpha]_D^{25}$ +20.5° (*c* 0.99, MeOH), >99% ee,[26] 708 mg, 1.91 mmol] in CH_2Cl_2 (50 mL) at –20 °C. After 2 h of stirring at this temperature, the reaction was quenched with water, and the whole was extracted with EtOAc (200 mL). The organic layer was washed with water and brine, and dried over Na_2SO_4. Filtration and evaporation *in vacuo* followed by column chromatography (silica gel, 10:1 toluene/EtOAc → 10:1 $CHCl_3$/MeOH) provided **7** (242 mg, 36%) as a white solid, along with unreacted **6** (389 mg, 55%). Further recrystallization from benzene–hexane afforded colorless needles (215 mg); mp 199 °C; Rf = 0.40 (30:1 CH_2Cl_2/MeOH); $[\alpha]_D^{22}$ +43.7° (*c* 1.07, $CHCl_3$); IR ($CHCl_3$) ν: 1723, 1281, 1246, 754 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$) δ 3.43 (s, 3H, CO_2CH_3), 6.95–6.99 (m, 2H, Ar*H*), 7.08–7.25 (m, 2H, Ar*H*), 7.40–7.54 (m, 2H, Ar*H*), 7.84–8.17 (m, 6H, Ar*H*); ^{13}C NMR (67.8 MHz, $CDCl_3$) δ 52.01, 125.73, 126.15, 126.72, 127.22, 127.66, 127.80, 127.87, 127.94, 132.78, 132.85, 134.86, 135.00, 139.78, 140.27, 167.64, 171.25; HRMS (EI) calcd for $C_{23}H_{16}O_4$ (M^+) 356.1048, found 356.1059.

Dirhodium(II) tetrakis[(*R*)-2'-methoxycarbonyl-1,1'-binaphthyl-2-carboxylate] (2). By the same procedure as that described for **1**, **2** was prepared from $Rh_2(OAc)_4 \cdot 2MeOH$ (117 mg, 0.23 mmol) and (*R*)-**7** (493 mg, 1.38 mmol). Column chromatography (silica gel, 2.5:1 hexane/EtOAc) followed by recrystallization from EtCN–hexane provided bis(propionitrile) adduct of **2** (264 mg, 66%) as purple needles: mp > 250 °C; Rf = 0.15 (3:1 hexane/EtOAc); $[\alpha]_D^{25}$ +183° (*c* 0.021, $CHCl_3$); IR ($CHCl_3$) ν: 1717, 1701, 1597 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.37 (t, *J* = 7.6 Hz, 6H, CH_3CH_2CN), 2.42 (q, *J* = 7.6 Hz, 4H, CH_3CH_2CN), 2.94 (s, 12H, CO_2CH_3), 6.48 (m, 4H, Ar*H*), 6.70 (m, 4H, Ar*H*), 6.78 (m, 4H, Ar*H*), 7.04 (m, 4H, Ar*H*), 7.23–7.28 (m, 8H, Ar*H*), 7.35 (m, 4H, Ar*H*), 7.67 (m, 4H, Ar*H*), 7.79 (m, 4H, Ar*H*), 7.88 (m, 4H, Ar*H*), 8.07 (m, 4H, Ar*H*), 8.17 (m, 4H, Ar*H*); ^{13}C NMR (100 MHz, $CDCl_3$) δ 10.56 (EtCN), 11.23 (EtCN), 51.80, 119.37 (EtCN), 125.52, 125.90, 125.96, 126.09, 126.56, 127.02, 127.12, 127.31,

127.41, 127.54, 127.90, 128.70, 132.54, 132.75, 133.77, 134.24, 136.79, 139.86, 167.80, 184.05; HRMS (FAB) calcd for $C_{92}H_{60}O_{16}Rh_2$ (M^+) 1626.1991, found 1626.1980; Anal. Calcd for $C_{92}H_{60}O_{16}Rh_2 \cdot 2EtCN$: C, 67.75; H, 4.06; N, 1.61. Found: C, 67.38; H, 4.31; N, 1.48.

Dirhodium(II) tetrakis[(*S*)-1,1'-binaphthyl-2-carboxylate] (3). By the same procedure as that described for **1**, **3** was prepared from $Rh_2(OAc)_4 \cdot 2MeOH$ (140 mg, 0.28 mmol) and (*S*)-1,1'-binaphthyl-2-carboxylic acid (**8**)[21] [$[\alpha]_D^{23}$ –36.3° (*c* 1.05, $CHCl_3$), >99% ee,[27] 496 mg, 1.66 mmol]. Column chromatography (silica gel, 4:1 $CHCl_3$/EtOAc) followed by recrystallization from CH_2Cl_2–EtCN provided tris(propionitrile) adduct of **3** (400 mg, 89%) as purple needles: mp > 250 °C; Rf = 0.22 (3:1 hexane/EtOAc); $[\alpha]_D^{25}$ –71.8° (*c* 0.030, $CHCl_3$); IR ($CHCl_3$) ν: 3061, 3007, 1595 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.27 (t, *J* = 7.6 Hz, 9H, C*H*$_3$CH$_2$CN), 2.33 (q, *J* = 7.6 Hz, 6H, CH$_3$C*H*$_2$CN), 6.37 (m, 4H, Ar*H*), 6.86 (m, 4H, Ar*H*), 6.92 (m, 4H, Ar*H*), 7.09–7.15 (m, 8H, Ar*H*), 7.23 (m, 4H, Ar*H*), 7.30 (m, 4H, Ar*H*), 7.40 (m, 4H, Ar*H*), 7.47 (m, 4H, Ar*H*), 7.68 (m, 8H, Ar*H*), 7.82–7.86 (m, 8H, Ar*H*); ^{13}C NMR (100 MHz, $CDCl_3$) δ 10.39 (EtCN), 11.22 (EtCN), 119.21 (EtCN), 124.86, 125.21, 125.95, 126.03, 126.13, 126.41, 126.99, 127.14, 127.42, 127.73, 127.81, 132.35, 132.49, 132.63, 133.70, 136.72, 137.07, 186.65; HRMS (FAB) calcd for $C_{84}H_{52}O_8Rh_2$ (M^+) 1394.1773, found 1394.1741; Anal. Calcd for $C_{84}H_{52}O_8Rh_2 \cdot 3EtCN$: C, 71.59; H, 4.33; N, 2.69. Found: C, 71.54; H, 4.58; N, 3.02.

Typical procedure for the intramolecular C–H insertion reaction (Table 1, Entry 3). Tris(propionitrile) adduct of **3** (28.0 mg, 0.018 mmol, 5 mol %) was added in one portion to a stirred solution of **9**[28] (100 mg, 0.36 mmol) in CH_2Cl_2 (3 mL) at 23 °C. After 18 h of stirring at this temperature, the solvent was removed *in vacuo* and the residue was passed through column chromatography (silica gel, 3:1 hexane/EtOAc) to provide methyl (6'*R*,7'*R*)-8'-oxospiro[cyclohexane-1,2'-[3]oxa[1]azabicyclo[4.2.0] octane]-7'-carboxylate (**10**) (62 mg, 71%) as a purple oil; ^1H NMR (400 MHz, $CDCl_3$) δ 1.38–2.00 (m, 11H, C*H*$_2$), 2.30 (m, 1H, C*H*$_2$), 3.65 (d, *J* = 1.4 Hz, 1H, C7'-*H*), 3.78 (s, 3H, CO$_2$C*H*$_3$), 3.83–3.94 (m, 3H, C4'-*H*$_2$ and C6'-*H*). Although the ^1H NMR spectrum of this oil was consistent with structure (**10**),[9b] further spectral data were not recorded since it contained few amounts of Rh(II) complex (**3**). This material was used without further purification.

(6'*R*,7'*S*)-7'-Hydroxymethylspiro[cyclohexane-1,2'-[3]oxa[1]azabicyclo[4.2.0]octan]-8'-one (**11**). A solution of **10** (50 mg, 0.19 mmol) in THF (1 mL) was added dropwise to a solution of $LiBH_4$ (10 mg, 0.45 mmol) in THF (2 mL) at 0 °C. After 2 h of stirring at this temperature, the reaction was quenched with water (2 mL). The whole was poured into an ice-cooled, two-layer mixture of EtOAc (30 mL) and water (10 mL), and the layers were separated. The organic layer was washed with brine, and dried over Na_2SO_4. Filtration and concentration *in vacuo* followed by column chromatography (silica gel, 1:1 EtOAc/hexane → EtOAc) afforded **11** (36 mg, 82%) as a white solid; mp 79–82 °C; Rf = 0.32 (EtOAc); $[\alpha]_D^{25}$ +9.72° (*c* 0.84, $CHCl_3$) [lit.,[9b] mp 89–90 °C (^{i}PrOH-hexane), $[\alpha]_D^{25}$ +17.7° (*c* 1.03, $CHCl_3$) for (6'*R*,7'*S*)-**11**]; IR (Nujol) ν: 3409, 1732 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$) δ 1.39–1.97 (m, 11 H, C*H*$_2$), 2.32 (m, 1H, C*H*$_2$), 2.96 (ddd, *J* = 1.6, 5.8, 6.1 Hz, 1H, C7'-*H*), 3.53 (ddd, *J* = 1.6, 4.7, 11.1 Hz, 1H, C6'-

H), 3.81–4.01 (m, 4H, C4'-H_2 and CH_2OH); ^{13}C NMR (67 MHz, $CDCl_3$) □ 21.83, 22.01, 25.11, 30.24, 30.55, 35.04, 46.56, 57.99, 59.21, 60.34, 85.10, 165.01; HRMS (EI) calcd for $C_{12}H_{19}NO_3$ (M^+) 225.1365, found 225.1384; Anal. Calcd for $C_{12}H_{19}NO_3$: C, 63.98; H, 8.50; N, 6.22. Found: C, 63.84; H, 8.48; N, 6.24.

(6'*R*,7'*S*)-8'-Oxospiro[cyclohexane-1,2'-[3]oxa[1]azabicyclo[4.2.0]octan]-7'-ylmethyl benzoate (**12**). Benzoyl chloride (50 mg, 0.36 mmol) was added to a solution of **11** (20 mg, 0.089 mmol), DMAP (1.2 mg, 0.01 mmol), and Et_3N (100 mg, 0.99 mmol) in CH_2Cl_2 (0.5 mL) at 0 °C. After 1 h of stirring at this temperature, the reaction was quenched with crushed ice, and the whole was partitioned between EtOAc (20 mL) and water (5 mL). The organic layer was washed with saturated aqueous $NaHCO_3$ and brine, and dried over Na_2SO_4. Filtration and evaporation *in vacuo* followed by column chromatography (silica gel, 4:1 hexane/EtOAc) afforded **12** (26 mg, 89 %) as a colorless oil; Rf = 0.23 (3:1 hexane/EtOAc); $[□]_D^{24}$ +6.34° (*c* 0.86, $CHCl_3$); IR (film) □: 3061, 2940, 1728 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$) □ 1.41–2.00 (m, 11H, CH_2), 2.37 (m, 1H, CH_2), 3.18 (ddd, *J* = 2.1, 4.1, 5.9 Hz, 1H, C7'-*H*), 3.60 (ddd, *J* = 2.1, 4.6, 10.8 Hz, 1H, C6'-*H*), 3.84–3.89 (m, 2H, C4'-H_2), 4.57 (dd, *J* = 5.9, 11.9 Hz, 1H, CH_2OBz), 4.67 (dd, *J* = 4.1, 11.9 Hz, 1H, CH_2OBz), 7.44 (m, 2H, Ar*H*), 7.58 (m, 1H, Ar*H*), 8.01 (m, 2H, Ar*H*); ^{13}C NMR ($CDCl_3$) □ 21.96, 22.10, 25.18, 30.37, 30.73, 35.19, 47.44, 57.58, 57.95, 61.33, 85.36, 128.41, 129.65, 130.08, 133.24, 163.25, 166.29; HRMS(EI) calcd for $C_{19}H_{23}NO_4$ (M^+) 329.1627, found 329.1639. The enantiomeric excess of **12** was determined to be 52% by HPLC with a Chiralcel OJ column (12:1 hexane/*i*-PrOH, 1.0 mL/min): t_R=15.4 min for major enantiomer; t_R=19.4 min for minor enantiomer.

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27. The homochirality of the methyl ester obtained by treatment of **8** with diazomethane was confirmed by comparison of retention time in HPLC (Chiralcel OD column, 9:1 hexane/*i*-PrOH, 1.0 mL/min) with the racemic sample: t_R =13.0 min for (*S*)-enantiomer; t_R =15.4 min for (*R*)-enantiomer.
28. Methyl □-diazo-□-oxo-1-oxa-5-azaspiro[5.5]undecane-5-propanoate (**9**) was prepared from 3-amino-1-propanol by the following sequence: (1) cyclohexanone, toluene, reflux, 6 h, then MeO_2CCH_2COCl, *N*,*N*-dimethylaniline, 0 °C, 1.5 h, 84%; (2) 4-$AcNHC_6H_4SO_2N_3$, DBU, MeCN, 0 °C, 3 h, 93%.