Catalytic Asymmetric [4 + 1] Cycloaddition of Vinylallenes with Carbon Monoxide: Reversal of the Induced Chirality by the Choice of Metal

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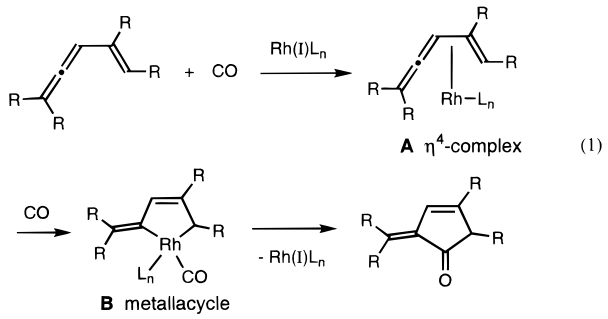
Abstract: Rhodium(I) and platinum(0) complexes having a chiral ligand, 1,2-bis(2,5-dialkylphosphorano)-benzene, effected an asymmetric carbonylative [4 + 1] cycloaddition reaction of vinylallenes. Useful levels of asymmetric induction were attained even with substrates lacking directive heteroatom functionalities. The highest enantioselectivity of 95.0% ee was achieved in the rhodium-catalyzed reaction of a vinylallene bearing an ester group. Whereas the enantioselectivities of the rhodium-catalyzed reactions were significantly affected by the substrate structures, the platinum-catalyzed reactions generally presented good enantioselectivities over 70% ee. In particular, the observed absolute configurations were opposite to those observed in the rhodium-catalyzed reactions. The reversal of the induced chirality according to the center metal employed was interpreted mechanistically.

Introduction

Carbon monoxide is an important C1 source, and transition metal-catalyzed carbonylation reactions have offered useful methods for the synthesis of various carbonyl compounds ranging from industrial processes to small scale laboratory preparations.[1] The outstanding synthetic utility of carbonylation has stimulated many attempts to develop catalytic asymmetric reactions.[2] In the past few years, major breakthroughs have been achieved in this area.[3] We have recently reported a new catalytic carbonylation reaction, i.e., [4 + 1] cycloaddition of vinylallenes with carbon monoxide (eq 1).[4,5] Asymmetric induction can potentially be achieved with a transition metal catalyst modified by a chiral ligand. This paper describes the rhodium- and platinum-catalyzed enantioselective [4 + 1] cycloaddition reactions of vinylallenes with carbon monoxide, which furnish chiral 5-substituted 2-alkylidene-3-cyclopentenones.[6] A highlight of the present study is that the absolute configurations obtained using a platinum catalyst were opposite to those observed in the rhodium-catalyzed reactions.



Rhodium-Catalyzed Asymmetric [4 + 1] Cycloaddition

The catalyst precursor for the asymmetric carbonylation of vinylallenes was prepared by treatment of a cationic complex $[Rh(cod)_2]PF_6$ (5 mol %) with a chiral diphosphine ligand (6 mol %). The resultant complex promoted the carbonylative [4 + 1] cycloaddition of vinylallenes at 60−80 °C, affording 2-alkylidene-3-cyclopentenones. Preliminary screening of a series of chiral diphosphine ligands, most of which are commercially available, validated the occurrence of asymmetric induction by the rhodium complexes. Among them, (*R*,*R*)-Me-DuPHOS [1,2-bis(2,5-dimethylphosphorano)benzene][7] was found to be the chiral ligand of choice. Interestingly, no double bond isomerization to a 5-alkylidene-2-cyclopentenone form was observed in the product when the DuPHOS ligand was used.

(1) Colquhoun, H. M.; Thompson, D. J.; Twigg, M. V. *Carbonylation: Direct Synthesis of Carbonyl Compounds*; Plenum: New York, 1991.

(2) (a) Consiglio, G. In *Catalytic Asymmetric Synthesis*; Ojima, I., Ed.; VCH: New York, 1993; pp 273−302. (b) Agbossou, F.; Carpentier, J.-F.; Mortreux, A. *Chem. Rev.* **1995**, *95*, 2485. (c) Gladiali, S.; Bayn, J. C.; Claver, C. *Tetrahedron Asymm.* **1995**, *6*, 1453.

(3) Hydroformylation: (a) Sakai, N.; Mano, S.; Nozaki, K.; Takaya, H. *J. Am. Chem. Soc.* **1993**, *115*, 7033. (b) Sperrle, M.; Consiglio, G. *J. Am. Chem. Soc.* **1995**, *117*, 12130. (c) Horiuchi, T.; Ohta, T.; Nozaki, K.; Takaya, H. *Chem. Commun.* **1996**, 155. Alternating carbonylative copolymerization: (d) Brookhardt, M.; Wagner, M. I.; Balavoine, G. G. A.; Haddou, H. A. *J. Am. Chem. Soc.* **1994**, *116*, 3641. (e) Bronco, S.; Consiglio, G.; Hutter, R.; Batistini, A.; Suter, U. W. *Macromolecules* **1994**, *27*, 4436. (f) Jiang, Z.; Sen, A. *J. Am. Chem. Soc.* **1995**, *117*, 4455. (g) Nozaki, K.; Sato, N.; Takaya, H. *J. Am. Chem. Soc.* **1995**, *117*, 9911. (h) Nozaki, K.; Sato, N.; Tonomura, Y.; Yasutomi, M.; Takaya, H.; Hiyama, T.; Matsubara, T.; Koga, N. *J. Am. Chem. Soc.* **1997**, *119*, 12779.

(4) (a) Murakami, M.; Itami, K.; Ito, Y. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 2691. (b) Murakami, M.; Itami, K.; Ito, Y. *J. Am. Chem. Soc.* **1996**, *118*, 11672. (c) Murakami, M.; Itami, K.; Ito, Y. *Organometallics* **1999**, *18*, 1326.

(5) For other examples of transition metal-catalyzed [4 + 1] cycloaddition of vinylallenes, see; (a) Eaton, B. E.; Rollman, B.; Kaduk, J. A. *J. Am. Chem. Soc.* **1992**, *114*, 6245. (b) Mandai, T.; Tsuji, J.; Tsujiguchi, Y.; Saito, S. *J. Am. Chem. Soc.* **1993**, *115*, 5865. (c) Sigman, M. S.; Eaton, B. E. *J. Am. Chem. Soc.* **1996**, *118*, 11783. (d) Darcel, C.; Bruneau, C.; Dixneuf, P. H. *Synlett* **1996**, 218.

(6) Preliminary communication: Murakami, M.; Itami, K.; Ito, Y. *J. Am. Chem. Soc.* **1997**, *119*, 2950.

(7) For asymmetric reactions based on DuPHOS, see: (a) Burk, M. J.; Nugent, W. A.; Harlow, R. L. *J. Am. Chem. Soc.* **1993**, *115*, 10125. (b) Burk, M. J.; Kalberg, C. S.; Pizzano, A. *J. Am. Chem. Soc.* **1998**, *120*, 4345 and references therein.

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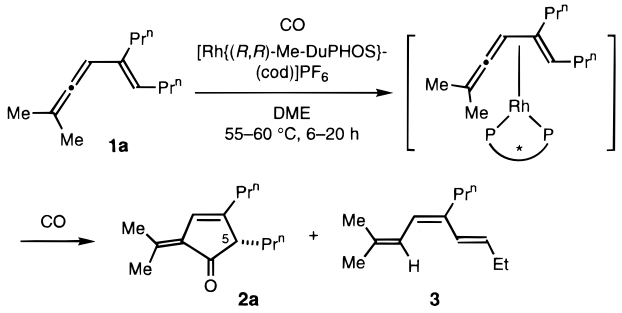
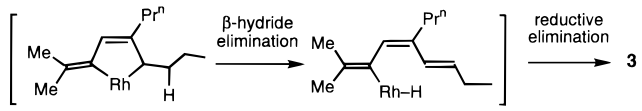
Table 1. Rhodium-Catalyzed Asymmetric [4 + 1] Cycloaddition of Vinylallene (**1a**)



entry	CO pressure (atm)	**2a** : **3**	% ee of **2a**	configuration
1	1	53:47	42.3	5*S*
2	5	97:3	64.5	5*S*
3	15	100:0	61.6	5*S*



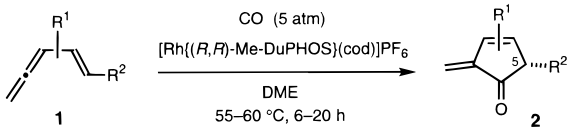
Next, the reaction conditions were examined using vinylallene (**1a**) as a model substrate (Table 1). 1,2-Dimethoxyethane (DME) gave better enantioselectivity under 1 atm of carbon monoxide than other solvents examined such as MeOH, toluene, THF, CH_2Cl_2, etc. The reaction suffered, however, from the formation of a conjugated triene (**3**),[8] which was probably formed through β-hydride elimination of the metallacyclopent-3-ene intermediate followed by reductive elimination (entry 1). Increasing the CO pressure substantially reduced the formation of **3** (entries 2 and 3). This was understood by assuming that migratory insertion of carbon monoxide is accelerated under higher CO pressure, suppressing β-hydride elimination. Moreover, the enantioselectivity was also affected by the CO pressure, and the reaction under 5 atm of CO afforded **2a** in 64.5% ee (entry 2).

The standard set of reaction conditions (5 atm of CO, in DME, 60 °C, 6−20 h) was applied to the carbonylation of various vinylallenes listed in Table 2. The ee values of the produced cyclopentenones **2** varied greatly depending on the structures of the starting vinylallenes **1**. Serious decreases in the enantioselectivity were observed when the substrate structure was slightly changed from **1a** (entry 1) to **1d** and **1e** (entries 4 and 5). Similarly, the ee value was also lowered when the cyclohexene ring of substrate **1b** (entry 2) was replaced with a cycloheptene ring (entry 7). Nevertheless, it is a formidable task to gain stereocontrol over substrates lacking directive heteroatom functionalities using transition metal complexes.[9] In this regard, it is noteworthy that useful levels of asymmetric induction were attained with substrates **1a**−**c**.

(8) No [4 + 1] cycloadduct potentially arising from **3** was detected, suggesting the superior reactivity of a vinylallene skeleton.

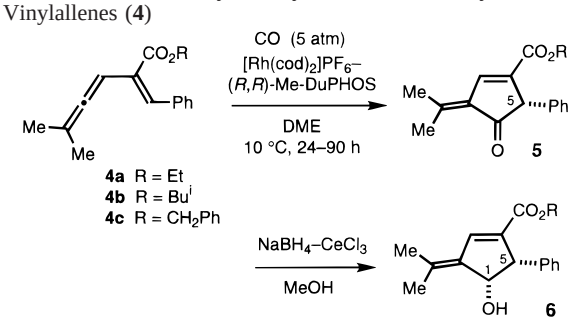
(9) For leading examples, see: (a) Jacobsen, E. N.; Markó, I.; Mungall, W. S.; Schröder, G.; Sharpless, K. B. *J. Am. Chem. Soc.* **1988**, *110*, 1968. (b) Hayashi, T.; Matsumoto, Y.; Ito, Y. *J. Am. Chem. Soc.* **1989**, *111*, 3426. (c) Zhang, W.; Loeback, J. L.; Wilson, S. R.; Jacobsen, E. N. *J. Am. Chem. Soc.* **1990**, *112*, 2801. (d) Uozumi, Y.; Hayashi, T. *J. Am. Chem. Soc.* **1991**, *113*, 9887. (e) Ohta, T.; Ikegami, H.; Miyake, T.; Takaya, H. *J. Organomet. Chem.* **1995**, *502*, 169. (f) Kondakov, D. Y.; Negishi, E. *J. Am. Chem. Soc.* **1995**, *117*, 10771.

Table 2. Rhodium-Catalyzed Asymmetric [4 + 1] Cycloaddition of Vinylallenes (**1**)



entry	**1**	**2**	yield / %	% e.e. configuration
1	**1a**	**2a**	87	64.5 (5*S*)
2	**1b**	**2b**	99	78.0 (5*S*)
3	**1c**	**2c**	97	74.6 (5*S*)
4	**1d**	**2d**	72	41.9 (5*S*)
5	**1e**	**2e**	98	14.8 (5*S*)
6	**1f**	**2f**	45	17.3 (5*S*)
7	**1g**	**2g**	98	10.6 (5*S*)

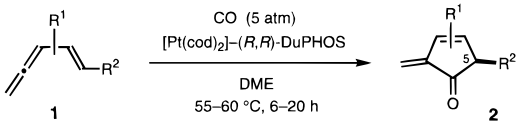
Table 3. Rhodium-Catalyzed Asymmetric [4 + 1] Cycloaddition of Vinylallenes (**4**)



6	R	yield from **4** / %	% ee	configurations
6a	Et	93	92.0	1*S*, 5*S*
6b	Bu^i	96	91.5	1*S*, 5*S*
6c	CH_2Ph	94	95.0	1*S*, 5*S*

We next examined the asymmetric carbonylation of vinylallenes (**4**) bearing an ester group (Table 3). The cycloaddition proceeded at lower temperatures giving remarkably improved selectivities. Particularly, the reaction of the benzyl ester (**4c**)

Table 4. Platinum-Catalyzed Asymmetric [4 + 1] Cycloaddition of Vinylallenes (**1**)



1 2

entry	1	2	(*R*,*R*)-DuPHOS	yield / %	% ee	configuration
1	**1a**	**2a**	Me-DuPHOS	76	74.8	5*R*
2	**1a**	**2a**	Et-DuPHOS	68	78.7	5*R*
3	**1b**	**2b**	Me-DuPHOS	81	64.1	5*R*
4	**1b**	**2b**	Et-DuPHOS	87	74.1	5*R*
5	**1d**	**2d**	Et-DuPHOS	99	76.6	5*R*
6	**1e**	**2e**	Me-DuPHOS	97	70.7	5*R*
7	**1f**	**2f**	Me-DuPHOS	98	75.8	5*R*
8	**1g**	**2g**	Me-DuPHOS	96	76.9	5*R*

at 10 °C provided **5c** with the highest enantioselectivity of 95.0% ee. Successive treatment of the cyclopentenones (**5**) with $NaBH_4-CeCl_3$[10] without isolation[11] caused exclusive 1,2-reduction of the carbonyl group to produce cis cyclopentenols (**6**) stereoselectively in high yields based on the starting vinylallenes (**4**). It is likely that hydride approached the carbonyl group from the less-hindered side of the cyclopentenone skeleton.

Platinum-Catalyzed Asymmetric [4 + 1] Cycloaddition

The use of platinum complexes as catalysts for the asymmetric [4 + 1] cycloaddition of vinylallenes was also examined (Table 4).[4c] The catalyst precursor was prepared by treatment of [Pt(cod)$_2$] (5 mol %) with (*R*,*R*)-Me-DuPHOS (or Et-DuPHOS, 6 mol %), the same ligand as used in the rhodium-catalyzed reactions. The resultant complex effectively catalyzed the carbonylative [4 + 1] cycloaddition of the vinylallene **1a** at 55 °C, affording 2-alkylidene-3-cyclopentenone (**2a**) in 76% yield (entry 1). An enantioselectivity of 74.8% ee, being better than 64.5% ee obtained in the rhodium-catalyzed reaction (Table 2, entry 1), was observed. The Pt-Et-DuPHOS complex was slightly more selective than was the Pt-Me-DuPHOS complex (entry 2). It was surprising, inter alia, that the absolute configuration of the product was opposite to that obtained in the rhodium-catalyzed reaction.[12-14] The results of the platinum-catalyzed reactions with other vinylallenes lacking heteroatom functionalities are summarized in Table 4. The reversal of the absolute configurations occurred with all vinylallenes listed.

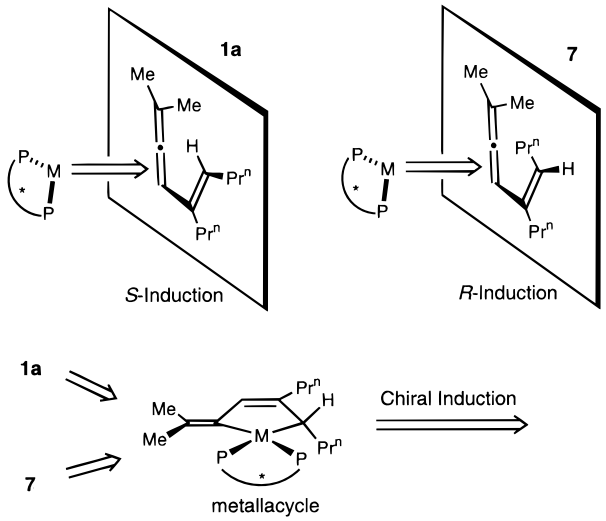


Figure 1.

Furthermore, good ee values over 70% were observed generally with the cycloaddition products. This stands in marked contrast with the rhodium case, in which the enantioselectivities were significantly affected by the substrate structures. These contrasting results indicate that a different enantiodifferentiating mechanism is operative when platinum is used as the metal catalyst instead of rhodium.

Mechanistic Interpretation

The postulated mechanism of the [4 + 1] cycloaddition is shown in eq 1. First, vinylallene in an *s-cis* conformation coordinates to a metal center beset with a chiral environment in a η^4-binding mode (**A**). Next, carbon monoxide is introduced into the coordination sphere to give a (vinylallene)(carbonyl)-metal complex, which acquires a significant contribution from a metallacyclo-3-pentene form, or actually assumes a σ^2-binding structure (**B**). Migratory insertion of the carbonyl group in the metal−carbon bond and subsequent reductive elimination of the metal catalyst produces a [4 + 1] cycloadduct. Although it might be difficult to assign concrete binding structures to the species involved in a catalytic process, it is possible to attribute the origin of the enantioselectivity to a η^4-bound form (**A**), a σ^2-bound form (**B**), or a later stage.

A comparison of the results obtained from **1a** and from its geometric isomer, (*Z*)-vinylallene (**7**), would be informative (Figure 1). If the origin of the enantioselectivity is attributed to a η^4-bound form (**A**), and if both vinylallenes approach the chiral metal center from the same face of the *s-cis* conformer, configurations induced at the 5-positions are expected to be opposite for the olefinic isomers **1a** and **7**, albeit different levels of asymmetric induction might be observed. On the contrary, there are no differences between the structural environments of the planar σ^2-bound complexes derived from **1a** and **7**. Therefore, if the origin of the enantioselectivity is attributed to a planar σ^2-bonded metallacyclopentene form (**B**) or a later stage, a comparable level of, or virtually identical asymmetric induction in the *same* direction would be expected with both **1a** and **7**.

(10) Gemal, A. L.; Luche, J.-L. *J. Am. Chem. Soc.* **1981**, *103*, 5454.

(11) The cyclopentenones (**5**) were prone to racemization, probably due to the presence of the phenyl substituent, when subjected to chromatographic isolation.

(12) For reversal of the induced chirality by the employed metal, see: (a) Kawano, H.; Ikariya, T.; Ishii, Y.; Saburi, M.; Yoshikawa, S.; Uchida, Y.; Kumobayashi, H. *J. Chem. Soc., Perkin Trans. 1* **1989**, 1571. (b) Kitamura, M.; Hsiao, Y.; Ohta, M.; Tsukamoto, M.; Ohta, T.; Takaya, H.; Noyori, R. *J. Org. Chem.* **1994**, *59*, 297. (c) Kinting, A.; Kreuzfeld, H.-J.; Abicht, H.-P. *J. Organomet. Chem.* **1989**, *370*, 343. (d) Faller, J. W.; Chase, K. J. *Organometallics* **1994**, *13*, 989. (e) Nishibayashi, Y.; Segawa, K.; Ohe, K.; Uemura, S. *Organometallics* **1995**, *14*, 5486.

(13) For reversal of the induced chirality by the presence of an additive, see: (a) Kobayashi, S.; Ishitani, H.; Hachiya, I.; Araki, M. *Tetrahedron* **1994**, *50*, 11623. (b) Desimoni, G.; Faita, G.; Invernizzi, A. G.; Righetti, P. *Tetrahedron* **1997**, *53*, 7671. (c) Ashimori, A.; Bachand, B.; Overman, L. E.; Poon, D. J. *J. Am. Chem. Soc.* **1998**, *120*, 6477.

(14) For reversal of the induced chirality by the dihydrogen pressure, see: Kuwano, R. Doctor Dissertation, Kyoto University, 1998, Chapter 2.

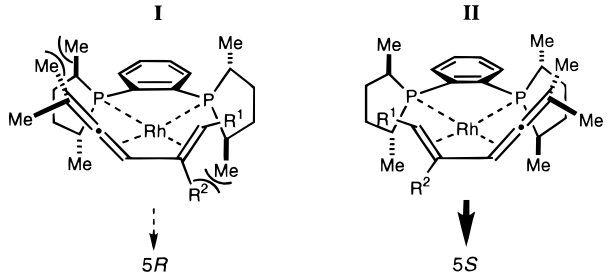


Figure 2.

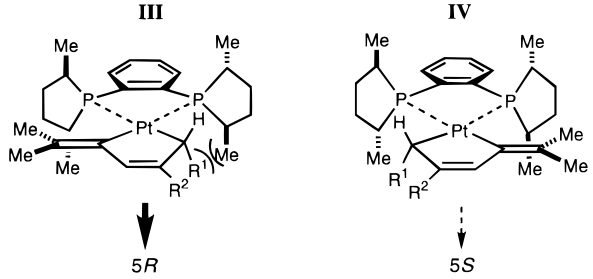
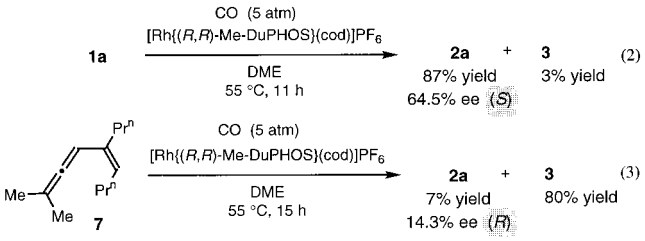
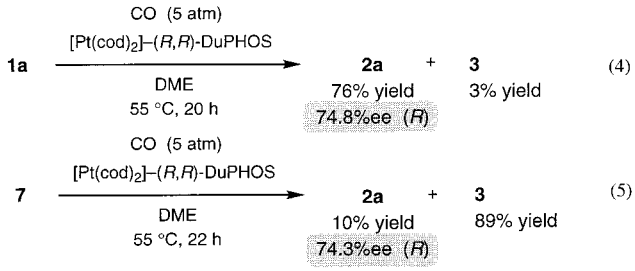


Figure 3.

Rh-catalyzed reaction: The [4 + 1] cycloadduct **2a** was obtained in only 7% yield from **7** along with a significant amount of the triene **3** (80%), which presumably resulted from a thermal ene reaction (eq 3).[15] With **2a** produced from **7**, a low level of asymmetric induction (14.3% ee) was observed, and that in favor of the *R* configuration. The opposite chiralities observed in the reactions of the two geometric isomers **1a** and **7** indicate that chirality is installed on a vinylallene which binds to rhodium in a η^4-fashion (**A**) rather than in a σ^2-bonded form (**B**). On the basis of η^4-binding, the stereochemical outcome was explained by assuming the following models for the formation of a vinylallene-Rh-DuPHOS complex (Figure 2). Model **I** is disfavored because of the two major repulsive steric interactions, one between the methyl group on the phosphorano ring and the R^2 group, and the other between another ligand methyl group and the substrate methyl group at the allenic terminus. Model **II** is free from such interactions, with the vinylallene fitting better to the chiral environment. The coordination depicted in Model **II** is consistent with the observed absolute stereochemistry of the product. In the case of **7**, additional steric interactions between the inward-oriented R^1 (propyl) group and the methyl group on the phosphorano ring are expected for the η^4-binding form corresponding to Model **II**. This might explain the lower enantioselectivity observed with **7**.



Pt-catalyzed reaction: While the [4 + 1] cycloadduct **2a** was obtained in only 10% yield from **7**, the enantioselectivity (74.3% ee) was essentially identical to that observed with **1a** (74.8% ee), and the *same* enantiomer was obtained as the major product (eq 5). This suggests that the binding step to give a η^4-complex leading to a planar σ^2-bonded metallacyclopentene form (**B**) is reversible and that the first irreversible step which dictates the enantioselection[16,17] lies after the establishment of a planar σ^2-bonded metallacyclopentene form (**B**) on the reaction coordinate. The following diastereomeric models are conceivable for the planar σ^2-bonded intermediate (Figure 3). Model **III** suffers from major repulsive steric interactions between the methyl group on the phosphorano ring and the R^1 group. Model **IV** is free from such interactions, and hence, is expected to be thermodynamically more stable than Model **III**. However, the 5*R* enantiomer predominantly obtained should be derived from Model **III**, the unfavorable diastereomer. This paradox in the platinum system may be attributed to the much higher reactivity of the unfavorable diastereomer toward incorporation of carbon monoxide; the enantiomers ratio is governed by the kinetic difference in the subsequent irreversible step, irrespective of the relative thermodynamic stabilities of the planar σ^2-bonded metallacyclic intermediates.[16] While the origin of this kinetic difference is still unclear, it may be postulated that incorporation of carbon monoxide by the less stable diastereomer proceeds faster in order to release the steric congestions.



Although the precise mechanisms of these unique reactions must await further studies, we presently rationalize the reversal of the induced chirality as follows; the enantiodifferentiating event with the rhodium complex occurs around a η^4-bound form (**A**) on the reaction coordinate which dictates the ultimate *S* chirality. The first irreversible step of the platinum-catalyzed reaction occurs after the establishment of a planar σ^2-bonded metallacyclopentene form (**B**). It dictates the *R* chirality under Curtin−Hammett control.

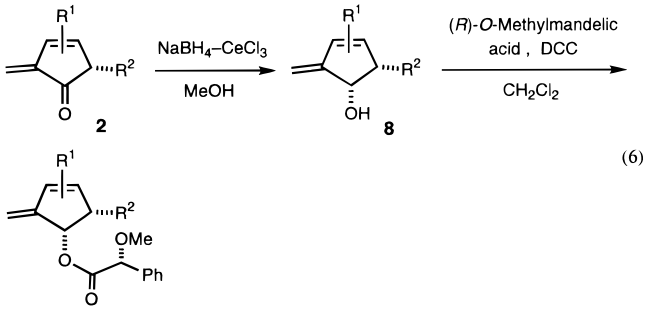
Determination of Absolute Configuration

Exclusive 1,2-reduction of the carbonyl group of the cyclopentenones (**2**) was carried out by treatment with $NaBH_4$−$CeCl_3$.[10] Similar to the in situ reduction of **5**, cis cyclopentenols (**8**) were stereoselectively produced in high yields (eq 6). The hydride approach from the less-hindered side accounts for the cis stereoselectivity. Treatment of the cis cyclopentenols (**8**) with (*R*)-*O*-methylmandelic acid in the presence of DCC (1,3-dicyclohexylcarbodiimide) afforded the corresponding *O*-methylmandelate esters. The absolute configuration of the major enantiomer of **8** was determined on the basis of the ^{1}H NMR studies.[18] The absolute configuration of **6** was determined in an analogous manner.

(15) Since the formation of **3** could not be avoided even at higher CO pressure (15 atm), it is likely that the thermal ene reaction preferentially occurred with **7**. See: Bond, D. *J. Org. Chem. Soc.* **1990**, *55*, 661 and references therein.

(16) Landis, C. R.; Halpern, J. *J. Am. Chem. Soc.* **1987**, *109*, 1746.

(17) For an exception, see: Zhang, W.; Lee, N. H.; Jacobsen, E. N. *J. Am. Chem. Soc.* **1994**, *116*, 425.



(6)

Conclusion

Asymmetric cycloaddition is a powerful tool to construct complex chiral molecules.[19] The asymmetric carbonylative [4 + 1] cycloaddition of vinylallenes documented herein adds a new promising example which achieves enantioselectivities up to 95% ee. The studies illustrate that either enantiomer of the [4 + 1] cycloadduct can be obtained with good selectivity using a single enantiomer of a chiral diphosphine ligand by appropriate choice of a metal catalyst. Although the origin of the reversal of the induced chirality according to the metal employed is only partially interpreted at this time, the ability to carry out enantioselective cycloaddition in two distinct ways enhances the synthetic utility of the present reaction.

Experimental Section[20]

Materials. [Rh(cod){(*R*,*R*)-Me-DuPHOS}]PF_6 was prepared from [Rh(cod)$_2$]PF_6[21] by a method analogous to that reported for [Rh(cod)-{(*R*,*R*)-Me-DuPHOS}]OTf.[7a]

(6*S*)-8-Isopropylidenebicyclo[4.3.0]non-1(9)-en-7-one (2b). A mixture of [Rh(cod){(*R*,*R*)-Me-DuPHOS}]PF_6 (4.5 mg, 6.8 μmol) and **1b** (20.0 mg, 135 μmol) in DME (3 mL) under 5 atm of CO in an autoclave was stirred in an oil bath at 58 °C for 9 h. After the mixture was cooled, the solvent was removed under vacuum. The residue was subjected to preparative thin-layer chromatography (silica gel, ether:hexane = 1:10) to afford **2b** (23.5 mg, 99%): oil, $[\alpha]^{20}_D$ +57.7 (*c* 1.24, $CHCl_3$), 78.0% ee [HPLC, CHIRALPAK AS (4.6ϕ × 250 mm), 0.5 mL/min, hexane, (*R*) t_1 = 19.3 min, (*S*) t_2 = 22.9 min]. ^{1}H NMR δ 0.80−1.50 (m, 4 H), 1.80−2.40 (m, 3 H), 1.92 (s, 3 H), 2.22 (s, 3 H), 2.45−2.70 (m, 2 H), 6.36 (s, 1 H); ^{13}C{^{1}H} NMR δ 20.0, 23.5, 25.3, 27.3, 28.9, 29.8, 52.8, 122.6, 133.4, 140.6, 145.0, 208.3; MS *m*/*e* 176 (M^+). Anal. Calcd for $C_{12}H_{16}O$: C, 81.77; H, 9.15. Found: C, 81.92; H, 9.38.

The following rhodium-catalyzed asymmetric [4 + 1] cycloaddition reactions producing **2** were carried out according to the preceding procedure for **2b**. The platinum-catalyzed reactions were carried out analogously except that the catalyst was prepared in situ from [Pt(cod)$_2$] (5 mol %) and (*R*,*R*)-Me-DuPHOS (or Et-DuPHOS, 6 mol %).

(5*S*)-4,5-Dipropyl-2-isopropylidene-3-cyclopentenone (2a). Oil. 64.5% ee [HPLC, CHIRALCEL OD-H (4.6ϕ × 250 mm), 0.5 mL/min, hexane, (*S*) t_1 = 15.8 min, (*R*) t_2 = 19.6 min]. ^{1}H NMR δ 0.86 (t, *J* = 7.1 Hz, 3 H), 0.96 (t, *J* = 7.3 Hz, 3 H), 1.05−1.40 (m, 2 H), 1.40−1.65 (m, 3 H), 1.70−1.90 (m, 1 H), 1.91 (s, 3 H), 2.10−2.25 (m, 2 H), 2.22 (s, 3 H), 2.76 (t, *J* = 4.4 Hz, 1 H), 6.46 (d, *J* = 1.4 Hz, 1 H); ^{13}C{^{1}H} NMR δ 15.3, 15.6, 19.9, 21.2, 21.6, 24.6, 32.0, 33.5, 55.1, 127.4, 134.8, 141.1, 146.3, 210.2; HRMS *m*/*e* calcd for $C_{14}H_{22}O$ 206.1670, found 206.1655.

(6*S*)-2,3-Benzo-8-isopropylidenebicyclo[4.3.0]non-1(9)-en-7-one (2c). Oil. $[\alpha]^{20}_D$ −19.6 (*c* 1.30, $CHCl_3$), 74.6% ee [HPLC, CHIRALCEL OD-H (4.6ϕ × 250 mm), 0.5 mL/min, hexane−^{i}PrOH (250:1), (*R*) t_1 = 26.6 min, (*S*) t_2 = 29.7 min]. ^{1}H NMR NMR δ 1.45−1.70 (m, 1 H), 2.05 (s, 3 H), 2.31 (s, 3 H), 2.40−2.53 (m, 1 H), 2.90−3.14 (m, 3 H), 7.00 (d, *J* = 2.3 Hz, 1 H), 7.12−7.28 (m, 3 H), 7.60−7.70 (m, 1 H); ^{13}C{^{1}H} NMR δ 20.5, 23.8, 24.3, 30.0, 51.5, 122.1, 123.9, 126.4, 128.1, 129.4, 131.4, 134.6, 137.2, 139.0, 143.2, 206.9; HRMS *m*/*e* calcd for $C_{16}H_{16}O$ 224.1201, found 224.1199.

(5*R*)-4,5-Diethyl-2-isopropylidene-3-cyclopentenone (2d). Oil. $[\alpha]^{20}_D$ −77.9 (*c* 1.40, $CHCl_3$), 76.6% ee [HPLC, CHIRALCEL OD-H (4.6ϕ × 250 mm), 0.5 mL/min, hexane, (*S*) t_1 = 15.0 min, (*R*) t_2 = 17.1 min]. ^{1}H NMR δ 0.72 (t, *J* = 7.4 Hz, 3 H), 1.13 (t, *J* = 7.4 Hz, 3 H), 1.51−1.75 (m, 2 H), 1.80−2.00 (m, 1 H), 1.91 (s, 3 H), 2.10−2.35 (m, 1 H), 2.21 (s, 3 H), 2.76 (t, *J* = 4.5 Hz, 1 H), 6.48 (d, *J* = 1.5 Hz, 1 H); ^{13}C{^{1}H} NMR δ 9.5, 11.6, 20.2, 21.4, 23.2, 23.5, 55.0, 125.7, 134.0, 140.0, 146.4, 209.2; HRMS *m*/*e* calcd for $C_{12}H_{18}O$ 178.1358, found 178.1372.

(5*R*)-4,5-Dibutyl-2-isopropylidene-3-cyclopentenone (2e). Oil. $[\alpha]^{20}_D$ −75.4 (*c* 1.22, $CHCl_3$), 70.7% ee [HPLC, CHIRALPAK AS (4.6ϕ × 250 mm), 0.5 mL/min, hexane, (*R*) t_1 = 10.5 min, (*S*) t_2 = 12.7 min]. ^{1}H NMR δ 0.85 (t, *J* = 7.3 Hz, 3 H), 0.93 (t, *J* = 6.7 Hz, 3 H), 1.00−1.85 (m, 10 H), 1.91 (s, 3 H), 2.10−2.30 (m, 2 H), 2.22 (s, 3 H), 2.77 (t, *J* = 4.4 Hz, 1 H), 6.46 (d, *J* = 1.5 Hz, 1 H); ^{13}C{^{1}H} NMR δ 14.2, 14.2, 20.2, 22.8, 23.3, 23.6, 27.6, 28.4, 29.5, 30.1, 54.1, 126.3, 133.9, 140.1, 145.5, 209.2; HRMS *m*/*e* calcd for $C_{16}H_{26}O$ 234.1982, found 234.1981.

(5*R*)-4,5-Diethyl-2-(1-ethylpropylidene)-3-cyclopentenone (2f). Oil. $[\alpha]^{20}_D$ −72.9 (*c* 1.20, $CHCl_3$), 74.8% ee [HPLC, CHIRALCEL OD-H (4.6ϕ × 250 mm), 0.5 mL/min, hexane, (*S*) t_1 = 11.9 min, (*R*) t_2 = 13.3 min]. ^{1}H NMR δ 0.72 (t, *J* = 7.5 Hz, 3 H), 1.02 (t, *J* = 7.5 Hz, 3 H), 1.07 (t, *J* = 7.6 Hz, 3 H), 1.13 (t, *J* = 7.4 Hz, 3 H), 1.54−1.73 (m, 1 H), 1.78−1.96 (m, 1 H), 2.10−2.40 (m, 4 H), 2.55−2.83 (m, 3 H), 6.48 (d, *J* = 1.6 Hz, 1 H); ^{13}C{^{1}H} NMR δ 9.5, 11.6, 12.9, 13.3, 21.5, 23.3, 24.1, 27.8, 55.0, 125.5, 132.8, 146.8, 151.8, 209.1; HRMS *m*/*e* calcd for $C_{14}H_{22}O$ 206.1670, found 206.1667.

(7*R*)-9-Isopropylidenebicyclo[5.3.0]dec-1(10)-en-9-one (2g). Oil. $[\alpha]^{20}_D$ −144.3 (*c* 1.92, $CHCl_3$), 76.9% ee [HPLC, CHIRALCEL OD-H (4.6ϕ × 250 mm), 0.5 mL/min, hexane, (*S*) t_1 = 20.6 min, (*R*) t_2 = 22.1 min]. ^{1}H NMR δ 1.40−1.55 (m, 3 H), 1.55−1.85 (m, 4 H), 1.91 (s, 3 H), 1.90−2.20 (m, 1 H), 2.21 (s, 3 H), 2.45−2.60 (m, 2 H), 2.75−2.90 (m, 1 H), 6.40−6.50 (m, 1 H); ^{13}C{^{1}H} NMR δ 20.1, 23.4, 28.0, 28.6, 30.2, 30.9, 31.7, 56.3, 126.0, 133.7, 139.8, 147.4, 208.5; HRMS *m*/*e* calcd for $C_{13}H_{18}O$ 190.1358, found 190.1366.

(4*Z*,6*E*)-2-Methyl-5-propyl-2,4,6-nonatriene (3). Oil. ^{1}H NMR δ 0.92 (t, *J* = 7.3 Hz, 3 H), 1.04 (t, *J* = 7.4 Hz, 3 H), 1.40−1.59 (m, 2 H), 1.77 (s, 3 H), 1.83 (s, 3 H), 2.10−2.26 (m, 4 H), 5.77 (dt, *J* = 15.5, 6.7 Hz, 1 H), 6.02 (d, *J* = 11.6 Hz, 1 H), 6.27 (d, *J* = 11.6 Hz, 1 H), 6.52 (d, *J* = 15.5 Hz, 1 H); ^{13}C{^{1}H} NMR δ 14.1, 14.4, 18.3, 22.6, 26.7, 36.9, 120.6, 123.2, 125.2, 132.4, 134.6, 135.6.

General Procedure for the Synthesis of 5 and 6. After the asymmetric [4 + 1] cycloaddition reactions of **4** were carried out according to the procedure for **2b**, the [4 + 1] cycloadducts **5a**−**c** were isolated by passing the reaction mixture through a short pad of silica gel. The cycloadducts **5a**−**c** thus isolated were subsequently subjected to reduction with $NaBH_4$/$CeCl_3$ in MeOH to give **6a**−**c**.

(5*S*)-4-(Ethoxycarbonyl)-2-isopropylidene-5-phenyl-3-cyclopentenone (5a). Oil. ^{1}H NMR δ 1.16 (d, *J* = 7.1 Hz, 3 H), 2.15 (s, 3 H), 2.32 (s, 3 H), 4.06−4.22 (m, 2 H), 4.28 (d, *J* = 1.6 Hz, 1 H), 7.10−7.20 (m, 2 H), 7.20−7.40 (m, 3 H), 7.90 (d, *J* = 1.6 Hz, 1 H); ^{13}C{^{1}H} NMR δ 14.3, 21.3, 24.6, 58.4, 60.7, 127.3, 127.8, 128.8, 132.7, 132.8, 137.2, 141.5, 154.8, 164.6, 202.5; HRMS *m*/*e* calcd for $C_{17}H_{18}O_3$ 270.1255, found 270.1252.

(1*S*,5*S*)-4-(Ethoxycarbonyl)-2-isopropylidene-5-phenyl-3-cyclopentenol (6a). Oil. $[\alpha]^{20}_D$ +68.2 (*c* 3.99, $CHCl_3$), 92.0% ee [HPLC, SUMICHIRAL OA-2500I (4.0ϕ × 250 mm), 1.0 mL/min, hexane−$ClCH_2CH_2Cl$−EtOH (500:20:1), (1*S*,5*S*) t_1 = 31.9 min, (1*R*,5*R*) t_2 = 37.2 min]. ^{1}H NMR (400 MHz) δ 1.057 (d, *J* = 6.4 Hz, 1 H), 1.063 (t, *J* = 7.1 Hz, 3 H), 1.95 (s, 6 H), 3.93−4.19 (m, 2 H), 4.37 (dd, *J* = 7.7, 1.8 Hz, 1 H), 5.01 (dd, *J* = 7.7, 6.4 Hz, 1 H), 7.12−7.16 (m, 2 H), 7.20−7.33 (m, 3 H), 7.46 (d, *J* = 1.8 Hz, 1 H); ^{13}C{^{1}H} NMR δ 14.0, 21.3, 22.0, 54.7, 60.0, 72.5, 127.1, 128.4, 129.1, 135.7, 136.9, 138.6, 139.7, 140.7, 165.2; HRMS *m*/*e* calcd for $C_{17}H_{20}O_3$ 272.1411, found 272.1427.

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(5*S*)-4-(Isobutyloxycarbonyl)-2-isopropylidene-5-phenyl-3-cyclopentenone (5b). Oil. ^{1}H NMR (300 MHz) δ 0.71 (d, J = 6.9 Hz, 3 H), 0.72 (d, J = 6.9 Hz, 3 H), 1.71−1.86 (m, 1 H), 2.14 (s, 3 H), 2.31 (s, 3 H), 3.78 (dd, J = 10.5, 6.3 Hz, 1 H), 3.93 (dd, J = 10.5, 6.6 Hz, 1 H), 4.26 (d, J = 1.5 Hz, 1 H), 7.10−7.35 (m, 5 H), 7.93 (d, J = 1.5 Hz, 1 H); ^{13}C{^{1}H} NMR (75 MHz) δ 18.71, 18.74, 21.1, 24.3, 27.6, 58.3, 70.6, 127.2, 127.7, 128.7, 132.5, 132.7, 137.1, 141.6, 154.7, 164.7, 202.4; HRMS *m*/*e* calcd for $C_{19}H_{22}O_3$ 298.1568, found 298.1561.

(1*S*,5*S*)-4-(Isobutyloxycarbonyl)-2-isopropylidene-5-phenyl-3-cyclopentenol (6b). Oil. $[\alpha]^{20}_D$ +50.0 (*c* 3.52, $CHCl_3$), 91.5% ee [HPLC, SUMICHIRAL OA-2500I (4.0ϕ × 250 mm), 1.0 mL/min, hexane−$ClCH_2CH_2Cl$−EtOH (500:20:1), (1*S*,5*S*) t_1 = 27.8 min, (1*R*,5*R*) t_2 = 33.2 min]. ^{1}H NMR δ 0.69 (d, J = 6.7 Hz, 6 H), 1.10 (d, J = 6.2 Hz, 1 H), 1.61−1.80 (m, 1 H), 1.96 (s, 6 H), 3.71 (dd, J = 10.7, 6.4 Hz, 1 H), 3.85 (dd, J = 10.7, 6.6 Hz, 1 H), 4.39 (br d, J = 7.3 Hz, 1 H), 5.12 (dd, J = 7.3, 6.2 Hz, 1 H), 7.15−7.18 (m, 2 H), 7.20−7.35 (m, 3 H), 7.51 (d, J = 1.8 Hz, 1 H); ^{13}C{^{1}H} NMR (75 MHz) δ 18.7, 21.2, 21.9, 27.6, 54.7, 70.3, 72.7, 127.2, 128.5, 129.1, 135.8, 137.1, 138.6, 139.8, 141.0, 165.5; HRMS *m*/*e* calcd for $C_{19}H_{24}O_3$ 300.1724, found 300.1714.

(5*S*)-4-(Benzyloxycarbonyl)-2-isopropylidene-5-phenyl-3-cyclopentenone (5c). Oil. ^{1}H NMR δ 2.14 (s, 3 H), 2.32 (s, 3 H), 4.31 (d, J = 1.6 Hz, 1 H), 5.05 (d, J = 12.7 Hz, 1 H), 5.22 (d, J = 12.7 Hz, 1 H), 7.00−7.20 (m, 4 H), 7.20−7.40 (m, 6 H), 7.96 (d, J = 1.6 Hz, 1 H); ^{13}C{^{1}H} NMR δ 21.0, 24.3, 58.2, 66.1, 127.2, 127.7, 127.9, 128.4, 128.7, 132.2, 132.4, 135.8, 136.9, 142.0, 155.1, 164.2, 202.1; HRMS *m*/*e* calcd for $C_{22}H_{20}O_3$ 332.1411, found 332.1424.

(1*S*,5*S*)-4-(Benzyloxycarbonyl)-2-isopropylidene-5-phenyl-3-cyclopentenol (6c). Oil. $[\alpha]^{20}_D$ +64.8 (*c* 3.55, $CHCl_3$), 95.0% ee [HPLC, two SUMICHIRAL OA-4500 columns (4.6ϕ × 250 mm) connected in series, 1.0 mL/min, hexane−$ClCH_2CH_2Cl$−EtOH (500:20:1), (1*S*,5*S*) t_1 = 37.3 min, (1*R*,5*R*) t_2 = 40.1 min]. ^{1}H NMR δ 1.10 (d, J = 6.1 Hz, 1 H), 1.97 (s, 6 H), 4.43 (dd, J = 6.7, 1.9 Hz, 1 H), 4.97 (d, J = 12.7 Hz, 1 H), 5.00−5.15 (m, 1 H), 5.15 (d, J = 12.7 Hz, 1 H), 6.95−7.10 (m, 2 H), 7.15−7.40 (m, 8 H), 7.56 (d, J = 1.9 Hz, 1 H); ^{13}C{^{1}H} NMR δ 21.2, 22.0, 54.7, 65.8, 72.6, 127.3, 127.7, 127.8, 128.3, 128.7, 129.2, 135.3, 136.1, 137.0, 139.2, 139.8, 141.6, 165.1; HRMS *m*/*e* calcd for $C_{22}H_{22}O_3$ 334.1568, found 334.1552.

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