Rhodium-Catalyzed Asymmetric [4 + 1] Cycloaddition

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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 has stimulated many attempts to develop a catalytic asymmetric carbonylation reaction, yet only limited success has been achieved.[2] This is probably because carbon monoxide is among the most common σ-donor/π-acceptor ligands and, hence, is capable of displacing chiral auxiliaries. In the last few years, major breakthroughs have been achieved in this area.[3] We have recently reported a new rhodium(I)-catalyzed carbonylation reaction (*i.e.*, [4 + 1] cycloaddition of vinylallenes with carbon monoxide).[4] An important feature of the reaction is that η^4-coordination of a vinylallene in an *s-cis* conformation to rhodium (**A**) occurs prior to the incorporation of carbon monoxide (Scheme 1). Face-selection of the conjugated diene system can potentially be provided by a rhodium catalyst modified by a chiral ligand, leading to an enantioselective carbonylation reaction. This paper describes the first example of catalytic asymmetric [4 + 1] cycloaddition of vinylallenes with carbon monoxide which furnishes chiral 5-substituted 2-alkylidene-3-cyclopentenones with moderate to high enantioselectivity.

The catalyst precursors for the asymmetric carbonylation of vinylallenes were prepared by treatment of a cationic complex $[Rh(cod)_2]PF_6$ (5 mol %) with chiral diphosphine ligands (6 mol %), most of which are commercially available. The resultant complexes were very effective catalysts for the carbonylative [4 + 1] cycloaddition of vinylallenes at 60−80 °C, affording 2-alkylidene-3-cyclopentenone in good chemical yield. Preliminary screening of a series of chiral diphosphine ligands validated the occurrence of face-selection by the rhodium complexes, and (*R*,*R*)-Me-DuPHOS [1,2-bis(2,5-dimethylphosphorano)benzene][5] was found to be the chiral ligand of choice. Next, the solvent effect was examined using (*R*,*R*)-Me-DuPHOS in the reaction of vinylallene (**1a**) under 1 atm of carbon monoxide. 1,2-Dimethoxyethane (DME) gave the best enantioselectivity (42.3% ee, Table 1, entry 1) among tested solvents (MeOH, toluene, THF, CH_2Cl_2, etc.). The reaction suffered, however, from the formation of a conjugated triene (**3**),[6] which was probably formed through β-hydride elimination of the intermediate metallacyclopent-3-ene followed by reductive elimination (Scheme 2). It was found that increase of CO pressure suppressed the formation of **3**. This was understood in terms of acceleration of migratory insertion of carbon monoxide with metallacyclopent-3-ene (**B**) in preference to 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). Although the origin of the enantioselectivity has not been fully elucidated, the stereo-determining step at 5 atm of CO pressure appears to carry the largest bias of the enantioface differentiation.

Scheme 1

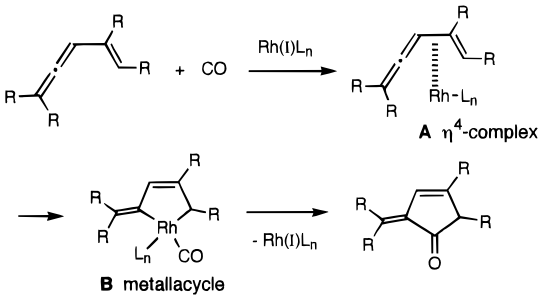
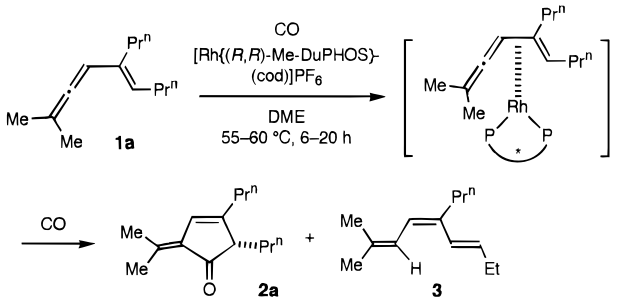
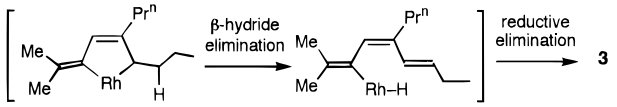


Table 1. Effect of CO Pressure



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

Scheme 2



The standard set of the reaction conditions (5 atm of CO, in DME, 60 °C, 6−14 h) was next applied to carbonylation of a variety of vinylallenes, producing cyclopentenones **2** with moderate to good enantioselectivity in high isolated yield (Table 2). It is a formidable task to gain stereocontrol over a substrate lacking directive heteroatom functionalities using transition metal complexes.[7] In this regard, it is noteworthy that a useful level of asymmetric induction was attained with these substrates, as listed in Table 2.

Finally, carbonylation of vinylallenes (**4**) bearing an ester group was examined. The cycloaddition proceeded at lower temperatures giving remarkably improved selectivities, and

(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*, 2485−2506. (c) Gladiali, S.; Bayn, J. C.; Claver, C. *Tetrahedron: Asymmetry* **1995**, *6*, 1453−1474.

(3) Hydroformylation: (a) Sakai, N.; Mano, S.; Nozaki, K.; Takaya, H. *J. Am. Chem. Soc.* **1993**, *115*, 7033−7034. (b) Sperrle, M.; Consiglio, G. *J. Am. Chem. Soc.* **1995**, *117*, 12130−12136. Alternating carbonylative copolymerization: (c) Brookhardt, M.; Wagner, M. I.; Balavoine, G. G. A.; Haddou, H. A. *J. Am. Chem. Soc.* **1994**, *116*, 3641−3642. (d) Bronco, S.; Consiglio, G.; Hutter, R.; Batistini, A.; Suter, U. W. *Macromolecules* **1994**, *27*, 4436−4440. (e) Jiang, Z.; Sen, A. *J. Am. Chem. Soc.* **1995**, *117*, 4455−4467. (f) Nozaki, K.; Sato, N.; Takaya, H. *J. Am. Chem. Soc.* **1995**, *117*, 9911−9912.

(4) (a) Murakami, M.; Itami, K.; Ito, Y. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 2691−2693. (b) Murakami, M.; Itami, K.; Ito, Y. *J. Am. Chem. Soc.* **1996**, *118*, 11672−11673.

(5) For asymmetric reactions based on DuPHOS, see: Burk, M. J.; Wang, Y. M.; Lee, J. R. *J. Am. Chem. Soc.* **1996**, *118*, 5142−5143 and references cited therein.

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

(7) For leading examples, see: (a) Jacobsen, E. N.; Markó, I.; Mungall, W. S.; Schröder, G.; Sharpless, K. B. *J. Am. Chem. Soc.* **1988**, *110*, 1968−1970. (b) Hayashi, T.; Matsumoto, Y.; Ito, Y. *J. Am. Chem. Soc.* **1989**, *111*, 3426−3428. (c) Zhang, W.; Loeback, J. L.; Wilson, S. R.; Jacobsen, E. N. *J. Am. Chem. Soc.* **1990**, *112*, 2801−2803. (d) Uozumi, Y.; Hayashi, T. *J. Am. Chem. Soc.* **1991**, *113*, 9887−9888. (e) Ohta, T.; Ikegami, H.; Miyake, T.; Takaya, H. *J. Organomet. Chem.* **1995**, *502*, 169−176. (f) Kondakov, D. Y.; Negishi, E. *J. Am. Chem. Soc.* **1995**, *117*, 10771−10772.

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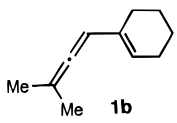
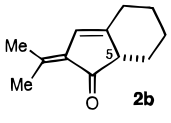
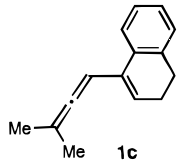
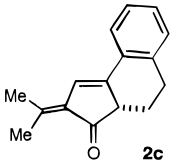
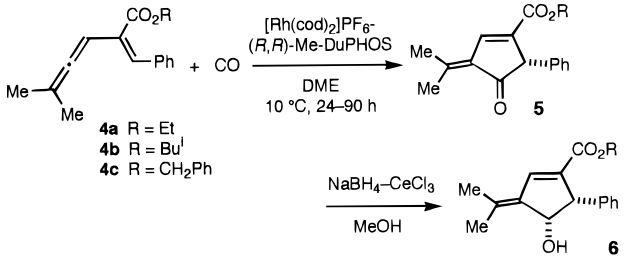
Table 2. Asymmetric [4 + 1] Cycloaddition of Vinylallenes (**1**)

entry	1	2	yield / %	% e.e.[a]
1	**1a**	**2a**	87	64.5 (5*S*)
2	 **1b**	 **2b**	99	78.0 (5*S*)
3	 **1c**	 **2c**	97	74.6 (5*S*)

[a] Enantioselectivity was determined by chiral HPLC analysis.

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



6	R	yield from **4** (%)	% ee[a]
6a	Et	93	92.0
6b	Bu^i	96	91.5
6c	CH_2Ph	94	95.0

[a] Enantioselectivity was determined by chiral HPLC analysis.

particularly, the reaction of the benzyl ester (**4c**) at 10 °C provided **5** with the highest enantioselectivity of 95.0% ee (Table 3). Successive treatment of the cyclopentenones (**5**) with $NaBH_4-CeCl_3$[8] caused exclusive 1,2-reduction of the carbonyl group to produce *cis*-cyclopentenols (**6**) stereoselectively, probably via the hydride approach from the less-hindered side, in high yield based on the starting vinylallenes (**4**). The absolute configuration of the major enantiomer given by (*R*,*R*)-DuPHOS

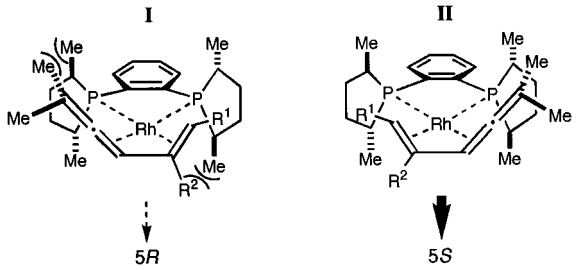


Figure 1.

was determined to be *S* by the ^1H NMR study of the *O*-methyl mandelate ester[9] derived from **6**.

We have found that a vinylallene having a substituent at the vinylic terminus coordinates to rhodium(I) in a η^4-fashion.[4] On the basis of η^4-binding, the stereochemical outcome was explained by assuming the following models for the formation of a vinylallene−rhodium complex (Figure 1). 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 these 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.

Asymmetric cycloaddition is a powerful tool to construct complex chiral molecules.[10] The asymmetric carbonylative [4 + 1] cycloaddition documented herein adds a new promising example which achieves enantioselectivities up to 95% ee. The optimal selectivity is commensurate with those accomplished in precedent highly effective systems like chiral Lewis acid-promoted Diels−Alder type [4+2] cycloaddition.

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Supporting Information Available: Experimental details and characterization for **2**, **3**, **5**, and **6** (3 pages). See any current masthead page for ordering and Internet access instructions.

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(8) Gemal, A. L.; Luche, J.-L. *J. Am. Chem. Soc.* **1981**, *103*, 5454−5459.

(9) Trost, B. M.; Belletire, J. L.; Godleski, S.; Baldwin, J. J.; Christy, M. E.; Ponticello, G. S. *J. Org. Chem.* **1986**, *51*, 2370−2374. The absolute configurations of **2a**−**d** also proved to be *S* according to the analogous derivatization and ^1H NMR studies.

(10) (a) Lautens, M.; Klute, W.; Tam, W. *Chem. Rev.* **1996**, *96*, 49−92. (b) Ojima, I.; Tzamarioudaki, M.; Li, Z.; Donovan, R. J. *Chem. Rev.* **1996**, *96*, 635−662.