Chiral Dirhodium(II) Catalysts with Orthometalated Aryl Phosphine Ligands: Synthesis and Application for Enantioselective C−H Insertion of α-Diazo Ketones

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Racemic dirhodium(II) complexes derived from orthometalated aryl phosphines, $Rh_2(O_2CCH_3)_2(pc)_2$ (pc = orthometalated phosphine, with head-to-tail arrangement) (**1**−**7**), are isolated as pure enantiomers by conventional resolution methods. They are the first examples of dirhodium(II) chiral catalysts without chiral ligands. These compounds have been used in the cyclization of α-diazo ketones; the influence of catalyst and substrate on enantioselectivity is studied. Results are compared with those obtained for reactions catalyzed by $Rh_2(protos)_4$ and $Rh_2(protos)_2(pc)_2$ [ProtosH (**8**) = *N*-(4-methylphenylsulfonyl-L-proline] (**9**−**22**). Only catalysts **1**−**7** afford a high level of enantioselectivity in the synthesis of carbocycles from α-diazo ketones.

Introduction

The intramolecular carbon−carbon coupling by the metal-catalyzed transformation of diazocarbonyl compounds is a general strategy for the obtention of carbocycles and heterocycles.[1] While copper-based complexes, which have proved effective in cyclopropanation, have limited reactivity in C−H insertion, dirhodium(II) compounds are catalytically active across the entire spectrum of carbenoid reactions involving C−H insertion.[1,2]

The utility of this approach for ring construction is directly related to the level of selectivity of the process. Dirhodium(II) complexes have shown to be chemo-, regio-, and diastereoselective catalysts for the cyclization of different types of diazo compounds; the selectivity of the transformation depends on the nature of both the substrate and the ancillary ligands of the catalyst.[3]

A great deal of effort is presently being devoted to the development of methods that make it possible to construct both carbocycles and heterocycles with high enantioselectivities. The most active area of investigation for inducing asymmetry in C−H insertion reactions has been the design, synthesis, and evaluation of chiral Rh(II) catalysts.[4] Chiral dirhodium carboxamidates have proved particularly useful in enantioselective intramolecular C−H insertion leading to the production of heterocycles. Thus, lactones and lactams are obtained with high enantiomeric excess from alkyl diazoacetates and diazoacetamides, respectively.[5] On the other hand, chiral rhodium carboxylates provide moderate to good enantioselectivity in the cyclization of α-diazo β-keto esters,[6] α-methoxycarbonyl α-diazo acetamides,[7] and α-acetyl α-diazo acetamides.[8] Surprisingly, few examples are found in the literature dealing with asym-

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(1) (a) Doyle, M. P. *Chem. Rev.* **1986**, *86*, 919. Adams, J.; Spero, D. M. *Tetrahedron* **1991**, *47*, 1765. (b) Padwa, A.; Krumpe, K. E. *Tetrahedron* **1992**, *48*, 5385.

(2) (a) Anciaux, A. J.; Hubert, A. J.; Noels, A. F.; Petiniot, N.; Teyssié, P. *J. Org. Chem.* **1980**, *45*, 695. (b) Doyle, M. P.; Dorow, R. L.; Buhro, W. E.; Griffin, J. H.; Tamblyn, W. H.; Trudell, M. L. *Organometallics* **1984**, *3*, 44. (c) Doyle, M. P. *Recl. Trav. Chim. Pays-Bas* **1991**, *110*, 305. (d) Cai, L.; Mahmoud, H.; Han Ying *Tetrahedron: Asymmetry* **1999**, *10*, 411. (e) Gettwert, V.; Krebs, F.; Maas, G. *Eur. J. Org. Chem.* **1999**, *1213*, 3.

(3) For references on chemoselective transformations see: (a) Ceccherelli, P.; Curini, M.; Marcotullio, M. C.; Rosati, O. *Tetrahedron* **1992**, *48*, 9767. (b) Brown, D. S.; Padwa, A.; Austin, D. J.; Price, A. T.; Semones, M. A.; Doyle, M. P.; Protopopova, M. N.; Winchester, W. R.; Tran, A. *J. Am. Chem. Soc.* **1993**, *115*, 8669. (c) Padwa, A.; Austin, D. J. *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 1797. (d) Pirrung, M. C.; Morehead, A. T., Jr. *J. Am. Chem. Soc.* **1994**, *116*, 8991. (e) Moody, C. J.; Mowlen, T. J.; Marino, J. P., Jr.; Padwa, A. *J. Org. Chem.* **1994**, *59*, 2447. (f) Estevan, F.; Lahuerta, P.; Pérez-Prieto, J.; Stiriba, S.-E.; Ubeda, M. A. *Synlett* **1995**, 1121. For references on regioselective transformations see: (g) Hashimoto, S.; Watanabe, N.; Ikegami, S. *Tetrahedron Lett.* **1992**, *33*, 2709. (h) Doyle, M. P.; Westrum, L. J.; Wolthius, W. N. E.; See, M. M.; Boone, W. P.; Bagheri, V.; Pearson, M. M. *J. Am. Chem. Soc.* **1993**, *115*, 958. For references on diastereoselective transformations see: (i) Taber, D. F.; You, K. K.; Rheingold, A. L. *J. Am. Chem. Soc.* **1996**, *118*, 547. (j) Doyle, M. P.; Kalinin, A. V.; Ene, D. G. *J. Am. Chem. Soc.* **1996**, *118*, 8837.

(4) (a) McKervey, M. A. *Chem. Commun.* **1997**, 983. (b) Doyle, M. P.; Forbes, D. C. *Chem. Rev.* **1998**, *98*, 911. (c) Doyle, M. P.; Sulikowski, G. A.; Cha, K. L.; Sulikowski, M. M. *Tetrahedron: Asymmetry* **1998**, *9*, 3145.

(5) (a) Doyle, M. P.; Protopopova, M. N.; Winchester, W. R.; Daniel, K. L. *Tetrahedron Lett.* **1992**, *33*, 7819. (b) Doyle, M. P.; Dyatkin, A. B.; Protopopova, M. N.; Yang, C. L.; Miertschin, C. S.; Winchester, W. R.; Simonsen, S. H.; Lynch, V.; Ghosh, R. *Recl. Trav. Chim. Pays-Bas* **1995**, *114*, 163.

(6) (a) Hashimoto, S.; Watanabe, N.; Ikegami, S. *Synlett* **1994**, 353. (b) Ferris, L.; Haigh, D.; Moody, C. J. *Tetrahedron Lett.* **1996**, *37*, 107.

(7) Anada, M.; Watanabe, N.; Hashimoto, S. *Chem. Commun.* **1998**, 1517.

(8) Watanabe, N.; Anada, M.; Hashimoto, S.; Ikegami, S. *Synlett* **1994**, 1031.

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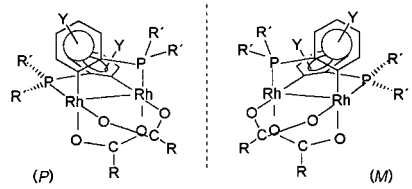
metric induction in the transformation of α-diazo ketones.[9,10] The transformation of these substrates mediated by dirhodium carboxylates and carboxamidates has been extensively studied, and very efficient and selective processes have been observed this way.[1−3] However, the achievement of a high level of enantioselectivity in the synthesis of carbocycles from α-diazo ketones remains a challenge, as the best reported ee's are below 30%.[4,10,11] This enantiocontrol dependence on the type of diazo compound has been attributed to several factors: conformational influence of carbonyl alignment of the metal carbene intermediate and differences in the stability of oxocarbenes and in constraints to reach the transition state.[11]

Dirhodium(II) complexes derived from orthometalated aryl phosphines, $Rh_2(O_2CCH_3)_2(pc)_2$ (pc = orthometalated aryl phosphine, with head-to-tail arrangement), are readily prepared by thermal reaction of $Rh_2(O_2CCH_3)_4$ and aryl phosphines.[12] They were shown to be regio- and chemoselective catalysts in the transformation of α-diazo ketones.[13] On the other hand, these rhodium compounds have backbone chirality, and the complex with formula $Rh_2(O_2CCF_3)_2[(C_6H_4)P(C_6H_5)_2]_2$ has been isolated as pure enantiomers by conventional resolution methods.[14] They are the first examples of dirhodium(II) chiral catalysts without chiral ligands and have shown to induce moderate asymmetry in the cyclization of 5-phenyl-1-diazo-2-pentanone. In the present paper we report the synthesis of chiral complexes of general formula $Rh_2(O_2CCF_3)_2(pc)_2$ (**1**−**7**) (Figure 1) and the scope and limitations of these catalysts for enantioselective C−H insertion reactions of α-diazo ketones. The only remarkable example of enantiocontrol in aliphatic C−H insertion of diazo ketones is that reported by McKervey et al.[9] They have used proline-derived Rh(II) catalysts in cyclization of 2-diazo-1-(2-alkoxyphenyl)propan-1-ones to give six-membered oxygen heterocycles. For that reason we also used one of those catalysts, the $Rh_2(protos)_4$ [ProtosH (**8**) = *N*-(4-methylphenylsulfonyl-L-proline], for purposes of comparison of enantiocontrol in the C−H insertion reaction of the diazo compounds studied by us (**23**, **25**, **27**, **29**, and **31**). Results were also compared with those obtained for $Rh_2(protos)_2(pc)_2$ (**9**−**22**). Only catalysts **1**−**7** afforded this cyclization with moderate to high enantioselectivity. However, $Rh_2(protos)_4$ promoted the intramolecular Buchner reaction of the diazo-5-aryl-2-pentanones, similarly to the literature result with dirhodium(II) acetate. In the case of 1-diazo-5-cyclohexyl-2-pentanone (**31**), $Rh_2(protos)_4$ gave rise to its cyclization with high yield but low ee (8%). Thus, heretofore dirhodium catalysts with general formula $Rh_2(O_2CCF_3)_2(pc)_2$ are the catalysts of choice to accomplish such transformations.



Rh(II)	Phosphine	RCOO	R′	Y
1	$(C_6H_5)_3P$	CF_3COO	C_6H_5	H
2	$(p\text{-}CH_3C_6H_4)_3P$	CF_3COO	$p\text{-}CH_3C_6H_4$	CH_3
3	$(m\text{-}CH_3C_6H_4)_3P$	CF_3COO	$m\text{-}CH_3C_6H_4$	CH_3
4	$[3,5\text{-}(CH_3)_2C_6H_3]_2(C_6H_5)P$	CF_3COO	$3,5\text{-}(CH_3)_2C_6H_3$	H
5	$\{p\text{-}[C(CH_3)_3]C_6H_4\}_3P$	CF_3COO	$p\text{-}[C(CH_3)_3]C_6H_4$	$C(CH_3)_3$
6	$(p\text{-}FC_6H_4)_3P$	CF_3COO	$p\text{-}FC_6H_4$	F
7	$(CH_3)_2(C_6H_4)P$	CF_3COO	CH_3	H
(P)-9 **(M)-10**	$(C_6H_5)_3P$	Protos	C_6H_5	H
(P)-11 **(M)-12**	$(p\text{-}CH_3C_6H_4)_3P$	Protos	$p\text{-}CH_3C_6H_4$	CH_3
(P)-13 **(M)-14**	$(m\text{-}CH_3C_6H_4)_3P$	Protos	$m\text{-}CH_3C_6H_4$	CH_3
(P)-15 **(M)-16**	$[3,5\text{-}(CH_3)_2C_6H_3]_2(C_6H_5)P$	Protos	$3,5\text{-}(CH_3)_2C_6H_3$	H
(P)-17 **(M)-18**	$\{p\text{-}[C(CH_3)_3]C_6H_4\}_3P$	Protos	$p\text{-}[C(CH_3)_3]C_6H_4$	$C(CH_3)_3$
(P)-19 **(M)-20**	$(p\text{-}FC_6H_4)_3P$	Protos	$p\text{-}FC_6H_4$	F
(P)-21 **(M)-22**	$(CH_3)_2(C_6H_4)P$	Protos	CH_3	H

Figure 1. List of Rh(II) catalysts with orthometalated aryl phosphine ligands.

Results

Synthesis of Rhodium Complexes. Rh(II) complexes of general formula $Rh_2(O_2CR)_2(pc)_2$ (**1**−**7**) were prepared by a modified method first published by Cotton et al.[12] These compounds are inherently chiral and are obtained as a racemic mixture of the (*P*) and (*M*) enantiomers (Figure 1). We have recently published the separation of pure enantiomers of compound **1**;[14] the racemic mixture of the compound $Rh_2(O_2CCH_3)_2[(C_6H_4)P(C_6H_5)_2]_2 \cdot 2HO_2CCH_3$ was transformed into two diastereoisomers by replacement of the acetate groups by chiral carboxylates (Protos). Both proline derivatives were separated by column chromatography, and the pure enantiomers were obtained via ligand exchange with trifluoroacetic acid (Scheme 1). The same strategy was used to obtain the enantiomerically pure compounds **2**−**7**. For all the compounds, the enantiomer arising from the first eluted diastereoisomer was the dextrorotatory isomer and was assigned the (*M*)-configuration by correlation of the sign of the rotation of polarized light with the known structure of **(*M*)-1**.

(9) McKervey et al. have achieved good levels of enantioselectivity in cyclization of 2-diazo-1-(2-alkoxyphenyl)propan-1-ones to give six-membered oxygen heterocycles by using chiral carboxylates: Ye, T.; Fernandez-Garcia, C.; McKervey, M. A. *J. Chem. Soc., Perkin Trans. 1* **1995**, 1373.

(10) Müller, P.; Polleux P. *Helv. Chim. Acta* **1994**, *77*, 645.

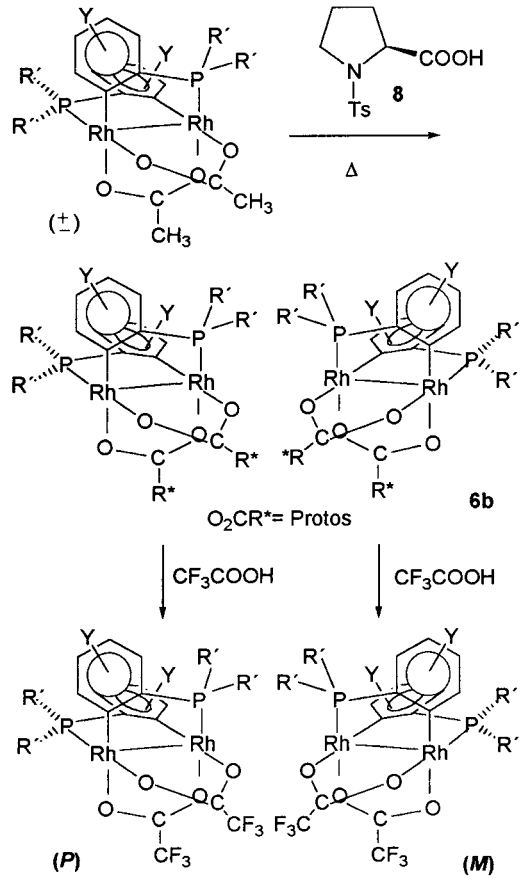
(11) (a) Doyle, M. P.; Eismont, M. Y.; Zhou, Q. L. *Russ. Chem. Bull.* **1997**, *46*, 955. (b) Müller, P.; Maitrejean, E. *Collect. Czech. Chem. Commun.* **1999**, *64*, 1807.

(12) Chakravarty, A. R.; Cotton, F. A.; Tocher, D. A.; Tocher, J. H. *Organometallics* **1985**, *4*, 8.

(13) (a) Estevan, F.; Lahuerta, P.; Pérez-Prieto, J.; Sanaú, M.; Stiriba, S.-E.; Ubeda, M. A. *Organometallics* **1997**, *16*, 880. (b) Estevan, F.; Lahuerta, P.; Pérez-Prieto, J.; Pereira, I.; Stiriba, S. E. *Organometallics* **1998**, *17*, 3442.

(14) Taber, D. F.; Malcolm, S. C.; Bieger, S. K.; Lahuerta, P.; Stiriba, S.-E.; Pérez-Prieto, J.; Sanaú, M.; Monge, M. A. *J. Am. Chem. Soc.* **1999**, *121*, 860.

Scheme 1

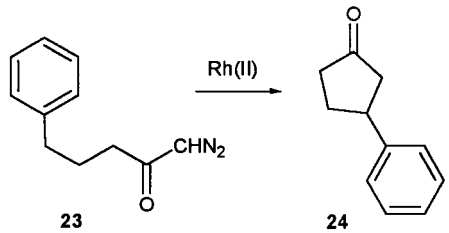


Asymmetric Catalysis. Diazo compounds were prepared from the corresponding acid by reaction with methyl chloroformate, followed by treatment with freshly prepared diazomethane.[15]

Catalytic reactions were performed by addition of the dirhodium(II) complex (1 mol %) to an anhydrous dichloromethane solution containing the diazo compound. The mixture was refluxed for 1 h (unless otherwise indicated). After cooling, the solution was filtered through a short plug of silica gel to remove catalyst, the solvent was evaporated under reduced pressure, and the crude product was analyzed by ^1H and ^{13}C NMR. The products were separated by HPLC chromatography, and the ee values were based on GC analysis with a 2,3-di-*O*-acetyl-6-*O*-*tert*-butyldimethylsilyl beta CDX column.

We examined the influence of substituent adjacent to the target C−H bond on enantioselectivity. The first substrate used was **23**; we expected that electron-withdrawing character of the phenyl group would decrease the electron density of the adjacent C−H bond, rendering it reluctant to attack by the electrophilic rhodium−carbene species.[16] We expected that if this particular C−H insertion was governed by electronic factors, the lowering of reactivity could improve the selectivity of the process. Addition of chiral catalysts **1**−**7** to diazo compound **23** resulted in the production of ketone **24** in good yields. In the case of catalysts **4** and **5** the reaction was very slow and needed 48 h to be complete. The enantiocontrol in the C−H insertion reaction obtained with these catalysts was up to 54% ee. The absolute stereochemistry of compound **24** formed from the (*M*)-series of Rh(II) catalysts **1**−**6** was stablished as (*S*) by correlation of the sign of polarized light with that of the known enantiomer.[6a,17] The reversal of enantiomer preference was observed for catalyst **7**; thus, **(*R*)-24** was the major isomer when using **(*M*)-7**. On the other hand, the reaction of diazo compound **23** catalyzed by $Rh_2(protos)_4$ afforded only the aromatic cycloaddition product.[18] Diastereoisomers **(*P*)-9** and **(*M*)-10** were also tested, but only dimerization and water/solvent insertion products were observed (Table 1).

Table 1. C−H Insertion Results for Diazo Ketone 23[a]



Rh(II)	C−H insertion yield (%)	**24** % ee	
(M)-1	80	45	(*S*)
(M)-2	73	54	(*S*)
(M)-3	78	40	(*S*)
(M)-4	65	17	(*S*)
(M)-5	68	48	(*S*)
(M)-6	64	32	(*S*)
(M)-7	68	51	(*R*)
(P)-9	0		
(M)-10	0		
$Rh_2(protos)_2$	0		

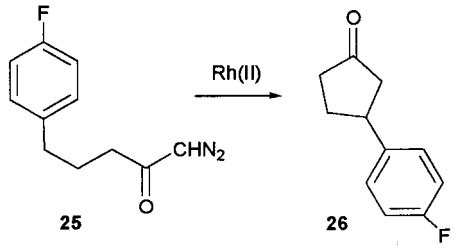
[a] The reaction mixture was refluxed in dichloromethane for 1 h except for catalysts **4** and **5** (48 h).

Afterward, we reasoned that if a decreased rate at the C−H insertion step was associated with an enhacement of the selectivity, much higher enantioselectivity could be achieved by appending electron-withdrawing substituents to phenyl group. Then, we studied the behavior of chiral Rh(II) catalysts in the transformation of diazo compounds **25** and **27**. The results are summarized in Tables 2 and 3. In general, enantiomeric excess increased for each catalyst compared to the results obtained for diazo compound **23**. An exception was the catalyst **7**, for which lower enantiocontrol in the cyclization of diazo with *p*-halo-substituted aryl groups and the reversal of enantiomer preference was found.

Diazo compound **29** allowed us to study the influence on the enantioselectivities of an electron-donating substituent (OMe) in the para position of the phenyl group. As expected, with catalysts **1**−**6**, lower enantiocontrol was achieved (ee's 7−36%) compared with the transformation of diazo compound **23** (ee's 17−54%). Inter-

(15) Boer, Th.; Backer, H. J. In *Organic Synthesis*; Rabjohn, N. Ed.; Wiley: New York, 1963; Vol. IV, p 250.
(16) Taber, D. F.; Ruckle, R. E., Jr. *J. Am. Chem. Soc.* **1986**, *108*, 7686.
(17) Paquette, L. A.; Gilday, J. P.; Ra, C. S. *J. Am. Chem. Soc.* **1985**, *109*, 6858.
(18) Similarly, rhodium(II) acetate catalyzes the intramolecular Buchner reaction of diazo compound **23** to produce the bicyclo[5.4.0]-undecane system: Kennedy, M.; McKervey, M. A.; Maguire, A. R.; Tuladhar, S. M.; Twohig, M. F. *J. Chem. Soc., Perkin Trans 1* **1990**, 1047.

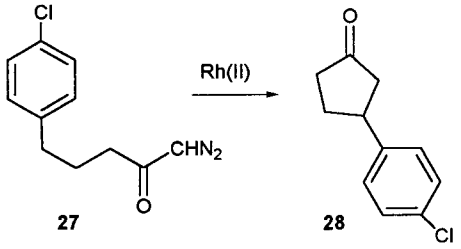
Table 2. C−H Insertion Results for Diazo Ketone 25[a]



Rh(II)	C−H insertion yield (%)	**26** % ee	
(M)-1	68	60	(*S*)
(M)-2	61	58	(*S*)
(M)-4	44	40	(*S*)
(M)-5	18	60	(*S*)
(M)-6	61	36	(*S*)
(M)-7	70	36	(*R*)

[a] The reaction mixture was refluxed in CH_2Cl_2 for 1 h except for catalysts **4** and **5** (48 h).

Table 3. C−H Insertion Results for Diazo Ketone 27[a]



Rh(II)	C−H insertion yield (%)	**28** % ee	
(M)-1	87	65	(*S*)
(M)-2	74	59	(*S*)
(M)-3	87	73	(*S*)
(M)-4	63	57	(*S*)
(M)-5	no reaction		
(M)-6	54	46	(*S*)
(M)-7	54	33	(*R*)

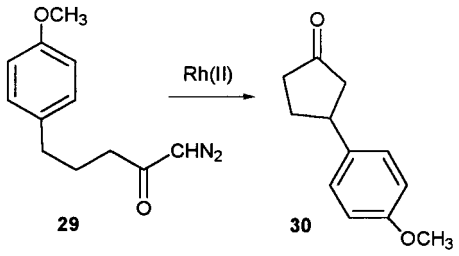
[a] The reaction mixture was refluxed for 1h except forcatalysts **4** and **5** (48 h).

estingly, catalyst **7** led to similar enantiomeric excess in both diazo compounds (56% compared to 51%), but, once again, the observed enantiomeric preference is opposite of that found with all the others (Table 4).

Diazo compound **31**, containing a cyclohexyl group in place of the phenyl one, was used to examine if the steric factors could be dominant in the control of the enantioselectivity of the insertion process. In this case, two products were obtained; the secondary insertion product with a five-membered ring, **32**, and the tertiary insertion product with a six-membered ring, **33** (Table 5). It is well documented the preference for five-membered-ring cyclization for diazo compounds with freely rotating aliphatic side chains,[19] but a more nucleophilic tertiary C−H bond allowed the six-membered cyclization to be competitive in the reactions catalyzed by Rh(II) compounds **1**−**5**. Catalysts **6** and ***(P)*-9** were unreactive

(19) (a) Doyle, M. P.; Dyatkin, A. B.; Roos, G. H. P.; Cañas, F.; Pierson, D. A.; Van Basten, A.; Müller, P.; Polleaux, P. *J. Am. Chem. Soc.* **1994**, *116*, 4507. (b) Wang, P.; Adams, J. *J. Am. Chem. Soc.* **1994**, *116*, 3296. (c) Taber, D. F.; Amedio, J. C., Jr.; Raman, K. *J. Org. Chem.* **1988**, *53*, 2984.

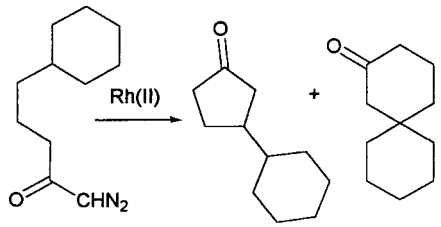
Table 4. C−H Insertion Results for Diazo Ketone 29[a]



Rh(II)	C−H insertion yield (%)	**30** % ee	
(M)-1	86	22	(*S*)
(M)-2	75	7	(*S*)
(M)-3	74	28	(*S*)
(M)-4	87	3	(*S*)
(M)-5	78	30	(*S*)
(M)-6	78	36	(*S*)
(M)-7	95	56	(*R*)

[a] The reaction mixture was refluxed in CH_2Cl_2 for 1 h except for catalysts **4** and **5** (48 h).

Table 5. C−H Insertion Results for Diazo Ketone 31[a]



Rh(II)	C−H insertion yield (%)[a]	32:33 yield (%)	**32** % ee	
(M)-1	71	40:31	66	(*S*)
(M)-2	74	30:44	74	(*S*)
(M)-3	82	37:45	47	(*S*)
(M)-4	54	25:29	44	(*S*)
(M)-5	73	30:44	57	(*S*)
(M)-6	0			
(M)-7	99	80:19	9	(*R*)
(P)-9	0			
Rh_2(protos)$_4$	99	83:16	8	(*R*)

[a] The reaction mixture was refluxed in CH_2Cl_2 for 1 h except for catalysts **4** and **5** (48 h).

toward cyclization. Interestingly, catalyst **7** and Rh_2(protos)$_4$ showed high regioselectivity with predominance of the five-membered-ring cyclization product **32** (Table 5). Additionally, the enantiocontrol in cyclization of **31** achieved with catalysts **1**−**5** was moderate to good (range 44−74%), while less than 10% ee was obtained with catalyst **7** and Rh_2(protos)$_4$. Once again, catalyst **7** showed reversal of enantiomer preference relative to all the other Rh(II) dimers with orthometalated aryl phosphine ligands tested. These data confirmed that the auxiliary ligands of these catalysts influence both the regioselectivity and the enantioselectivity of the C−H insertion reaction.

As the above results indicate, catalyst- and substrate-dependent enantioselectivities are observed for cyclization of α-diazo ketones catalyzed by orthometalated Rh(II) (Figure 2). Finally, access to both enantiomers of **24**, **26**, **28**, **30**, and **32** can be achieved with the use of the (*P*) or (*M*) forms of the catalyst.

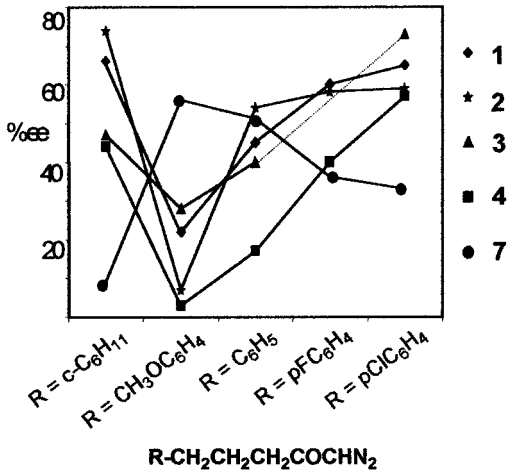
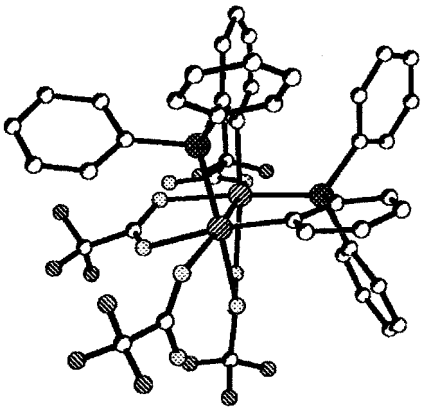
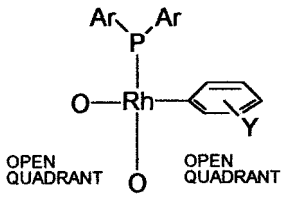


Figure 2. Dependence of asymmetric induction yield on α-diazo ketone substituents in the C−H insertion catalyzed by Rh(II) dimers with orthometalated aryl phosphine ligands.

Scheme 2



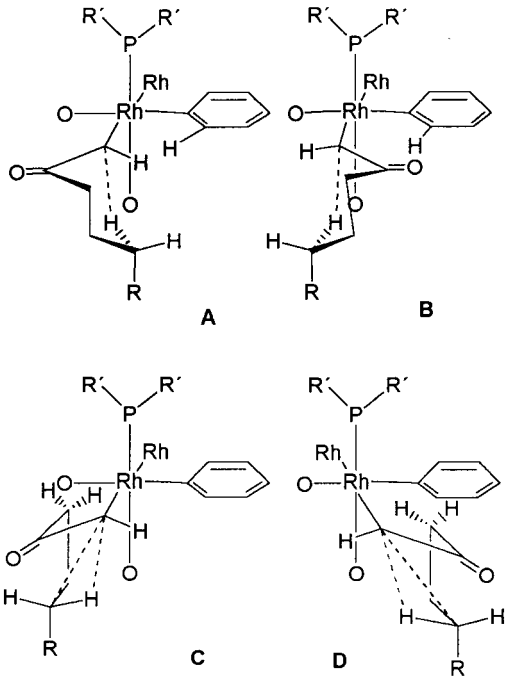


Discussion

Asymmetric induction in the C−H insertion indicates involvement of a metal carbene complex in the product-forming step. In that case, the ligand configuration around the Rh atom should have a direct influence on the selectivity of the process. The X-ray molecular structure of compound **(*P*)-1**, viewed down the rhodium−rhodium axis, reveals that the four quadrants around the metal atom have different sterical congestion. In particular, the two quadrants next to the Rh−P bond are more sterically hindered because of aryl groups attached to P (Scheme 2).

Considering the reaction of the diazo compound **23** catalyzed by (***P***)-**1**, four transition structures (**A**, **B**, **C**, and **D** in Scheme 3), in which the ketone chain occupies one of the two open quadrants, can be depicted. The transition structures **A** and **B**, with the carbonyl group "syn" to the metal carbene bond, must be favored

Scheme 3



compared to **C** and **D**, as the repulsive interaction of the hydrogen atoms in C_α with the carbonyl group is avoided.[20] Thus, the intermediate metal carbene should undergo C−H insertion mainly by one of the two favored transition states **A** and **B**, each one leading to a different ketone enantiomer, (*R*) and (*S*), respectively. To account for the observation that the (*P*)-series of dirhodium catalysts **1**−**6** yield (*R*) cyclopentanones with moderate to high ee's values, the transition state **A** must be somewhat favored; the repulsive interaction between the keto group and the metalated aryl group might be the origin of the lower stability of transition state **B**. The above-described studies of the cyclization of diazo compounds **23**, **25**, **27**, and **29** mediated by catalysts **1**−**6** showed the enantioselectivity dependence upon the electronic nature of the substituent at the insertion site. Thus, in less nucleophilic carbon−hydrogen bonds cyclization should occur at a shorter distance from the enantiocontrolling chiral Rh center, leading to an increase of asymmetric induction yield.

That steric effects can also play an important role was evidenced in the cyclization of the most nucleophilic diazo compound **31**; the relative increase of enantiocontrol in the formation of ketone **32** could agree with the higher preference of the bulky cyclohexyl group, compared to the phenyl group, to occupy an equatorial position in the proposed transition state.

Catalyst **7** deserves separate consideration from the other orthometalated Rh(II) compounds tested. That catalyst contains PMe_2Ph, a more basic and less bulky phosphine, thus leading to less electrophilic and less sterically crowded metal carbene. The lower electrophilicity will result in a closer approach of the interacting moieties and should contribute to an increase of enantiocontrol, while the second factor will tend to decrease

(20) Doyle has suggested this alignment in α-diazo ketones to explain the relative inefficiency of chiral dirhodium carboxamidates for asymmetric cyclization of diazoketones compared to diazoacetates and diazoacetamides (see ref 11).

the asymmetric induction yield. The fact that cyclization of diazo compound **31** mediated by catalyst **7** occurs with only a 9% ee points to the second effect being the predominant one.

Moreover, other results point to the unusual behavior of catalyst **7**: the reversal of asymmetric induction and unexpected substituent effects on enantioselectivity yield found for the series of diazo compounds **23**, **25**, **27**, **29**. Finding an explanation for these results is not straightforward.

Conclusion

A family of chiral Rh(II) dimers with orthometalated aryl phosphine ligands have been synthesized, and their use for enantioselective cyclization of α-diazo ketones has been explored. (*M*) and (*P*) forms of each Rh(II) dimer induced identical enantiocontrol in cyclization of α-diazo ketones to give the (*S*) and (*R*) cyclopentanones, but with opposite ee values, supporting the generally accepted idea that the catalytic reaction occurs via a dirhodium−carbenoid species and also confirming that degradation to an achiral rhodium catalyst is not a major competing pathway. The enantioselectivity found with most of them are higher than that provided with chiral carboxamides and carboxylates. Theretofore dirhodium(II) complexes with orthometalated aryl phosphine ligands have proven to be the most effective catalysts in enantioselective carbon−hydrogen insertion of α-diazo ketones.

Experimental Part

Commercially available $Rh_2(O_2CCH_3)_4{\cdot}(MeOH)_2$ was purchased from Pressure Chemical Co. Racemic Rh(II) complexes with orthometalated aryl phosphine ligands, $Rh_2(O_2CCH_3)_2[(C_6H_4)P(C_6H_5)_2]_2{\cdot}(HO_2CCH_3)_2$,[13a] $Rh_2(O_2CCH_3)_2[(p\text{-}CH_3C_6H_3)P(p\text{-}CH_3C_6H_4)_2]_2{\cdot}(O_2CCH_3)_2$,[21] $Rh_2(O_2CCH_3)_2[(C_6H_4)P(CH_3)_2]_2{\cdot}(HO_2CCH_3)_2$,[13a] $Rh_2(O_2CCH_3)_2[(m\text{-}CH_3C_6H_3)P(m\text{-}CH_3C_6H_4)_2]_2{\cdot}(HO_2CCH_3)_2$,[22] $Rh_2(O_2CCH_3)_2[(p\text{-}FC_6H_3)P(p\text{-}FC_6H_4)_2]_2{\cdot}(HO_2CCH_3)_2$,[13a] *N*-*p*-tolylsulfonyl-L-proline (ProtosH),[23] and 1-diazo-5-phenyl-2-pentanone,[24] were prepared according to literature procedures. Data for cyclopentanones[25] and spiro[5.5]undecan-3-one (**33**)[26] were coincident with those previously reported. ^1H, ^{13}C, and ^{31}P NMR spectra were recorded on a Bruker AC-200 FT spectrometer as solutions in $CDCl_3$ unless specified otherwise. ^{19}F NMR spectra were determined on a Bruker AC-250 FT spectrometer. Chemical shifts are reported in ppm. The coupling constants (*J*) are in hertz (Hz). All Rh(II) compounds show ^{31}P NMR spectra corresponding to an AA'XX' system. Analysis was provided by Centro Microanalisis Elemental, Universidad Complutense de Madrid. Column chromatography was performed on silica gel (70−230 mesh). Solvent mixtures are volume/volume mixtures, unless specified otherwise. Organic chemicals were purchased from Aldrich Chemical Co. CH_2Cl_2 was distilled from CaH_2 under argon immediately before use. All reactions were carried out in flame-dried glassware under argon atmosphere. Optical rotations were measured on a Perkin-Elmer 241 polarimeter at the Na-D line in 10 cm quartz cuvettes. The ee values were based on GC analysis with a 2,3-di-*O*-acetyl 6-*O*-*tert*-butyldimethylsilyl beta CDX column.

Synthesis of $Rh_2(O_2CCH_3)_2[(C_6H_4)P(m\text{-xylyl})_2]_2{\cdot}(HO_2CCH_3)_2$. The compound was prepared from $Rh_2(O_2CCH_3)_4{\cdot}(MeOH)_2$ (170 mg, 0.34 mmol) and $PhP(m\text{-xylyl})_2$ (217 mg, 0.68 mmol) in an manner analogous to that for the other dirhodium(II) complexes with orthometalated aryl phosphine ligands,[13a] yielding 265 mg (0.25 mmol, 73%) of purple product. Eluents for column chromatography: CH_2Cl_2/hexane/acetic acid, 40:20:1. $^{31}P\{^1H\}$ NMR: δ 17.3. ^1H NMR: δ 1.30 (s, 6H), 1.99 (s, 12H), 2.17 (s, 6H), 2.29 (s, 12H), 6.39 (m, 6H), 6.72 (m, 4H), 6.80 (m, 2H), 7.00 (m, 2H), 7.15 (m, 2H), 7.20 (m, 2H), 7.44 (q, $J = 5.1$ Hz, 2H). $^{13}C\{^1H\}$ NMR: δ 21.5, 21.7, 22.6, 22.9, 121.7−147.9 (aromatic signals), 166.1 (m), 179.4, 181.4. Anal. Calcd for $C_{52}H_{58}O_8P_2Rh_2$: C, 57.90; H, 5.42. Found: C, 58.41; H, 5.72.

Synthesis of $Rh_2(O_2CCH_3)_2[(p\text{-}^tBuC_6H_3)P(p\text{-}^tBuC_6H_4)_2]_2{\cdot}(HO_2CCH_3)_2$. $Rh_2(O_2CCH_3)_4{\cdot}(MeOH)_2$ (115 mg, 0.23 mmol) and $P(p\text{-}^tBuC_6H_4)_3$ (195 mg, 0.45 mmol) were refluxed in 30 mL of a mixture of toluene/acetic acid (3:1) for 2 h. After evaporation to dryness, the crude product was chromatographed (silica gel, hexane, 2 × 30 cm). Elution with CH_2Cl_2/hexane/acetic acid (50:25:1) afforded a purple band, which was collected and evaporated to dryness.Yield: 60%. $^{31}P\{^1H\}$ NMR: δ 18.1. ^1H NMR: δ 1.02 (s, 18H), 1.14 (s, 6H), 1.26 (s, 18H), 1.33 (s, 18H), 2.15 (s, 6H), 6.39 (t, $J = 8.6$ Hz, 2H), 6.82 (m, 6H), 7.10 (dd, $J = 8.4$ and 1.8 Hz, 4H), 7.14 (dd, $J = 3.7$ and 1.7 Hz, 2H), 7.42 (dd, $J = 8.4$ and 1.7 Hz, 4H), 7.58 (t, $J = 8.6$ Hz, 4H). $^{13}C\{^1H\}$ NMR: δ 21.8, 22.7, 31.2, 31.3, 34.6, 34.8, 34.9, 119.3−152.2 (aromatic signals), 165.2 (m), 178.3, 181.5. Anal. Calcd for $C_{68}H_{90}O_8P_2Rh_2$: C, 62.67; H, 6.96. Found: C, 63.03; H, 7.01.

General Procedure for the Synthesis of Diastereoisomers. To a solution of $Rh_2(O_2CCH_3)_2(pc)_2{\cdot}(HO_2CCH_3)_2$ (0.52 mmol) in toluene was added ProtosH (1.11 g, 4.14 mmol) and the mixture refluxed for 2 h using a Soxhlet with a sodium carbonate trap (2 g). The solvent was evaporated and the crude product was dissolved in acetone with sodium carbonate (550 mg) to eliminate the excess of ProtosH. The mixture was stirred at room temperature for 1 h. The resulting green solution was concentrated and transferred to a column of chromatography (silica gel/hexane 50 × 2.5 cm) to separate both diastereoisomers.

$Rh_2(Protos)_2[(C_6H_4)P(C_6H_5)_2]_2{\cdot}(H_2O)_2$. Diastereoisomers were separated using a dichloromethane/diethyl ether, 50:3, mixture as eluent.

First Diastereoisomer (*M*). Yield: 80%. $^{31}P\{^1H\}$ NMR: δ 19.4. ^1H NMR: δ 0.66 (m, 2H), 0.84 (m, 2H), 0.93 (m, 4H), 2.31 (s, 6H), 2.83 (m, 2H), 3.19 (m, 2H), 3.61 (bs, 4H), 4.19 (m, 2H), 6.56 (t, $J = 7.4$ Hz, 2H), 6.63 (t, $J = 7.4$ Hz, 2H), 6.70−6.81 (m, 8H), 6.98 (t, $J = 6.3$ Hz, 4H), 7.15 (m, 6H), 7.30 (m, 6H), 7.74 (m, 8H). $^{13}C\{^1H\}$ NMR: δ 21.5, 24.5, 31.1, 49.3, 63.5, 121.2−144.2 (aromatic signals), 165.1 (m), 181.4, 181.5. $[\alpha]^{20}_D$ −318.8 (*c* 0.138, CH_3CN). Anal. Calcd for $C_{60}H_{60}N_2O_{10}P_2Rh_2S_2$: C, 55.39; H, 4.65. Found: C, 55.05; H, 4.71.

Second Diastereoisomer (*P*). Yield: 70%. $^{31}P\{^1H\}$ NMR: δ 18.7. ^1H NMR: δ 0.80−1.45 (m, 8H), 2.31 (s, 6H), 2.95 (m, 2H), 3.10 (m, 2H), 3.38 (bs, 4H), 4.10 (m, 2H), 6.58−6.76 (m, 5H), 6.90 (t, $J = 7.1$ Hz, 2H), 7.00 (m, 1H), 7.10−7.19 (m, 3H), 7.34 (bs), 7.62 (m), 7.72 (d, $J = 8.0$ Hz). $^{13}C\{^1H\}$ NMR: δ 21.4, 24.4, 29.7, 49.0, 62.8, 120.8−144.0 (aromatic signals), 164.5 (m), 181.4, 181.5. $[\alpha]^{20}_D$ −60.7 (*c* 0.140, CH_3CN).

$Rh_2(protos)_2[(p\text{-}CH_3C_6H_3)P(p\text{-}CH_3C_6H_4)_2]_2{\cdot}(H_2O)_2$. Diastereoisomers were separated using a dichloromethane/hexane/diethyl ether, 30:20:3, mixture as eluent.

First Diastereoisomer (*M*). Yield: 87%. $^{31}P\{^1H\}$ NMR: δ 16.0. ^1H NMR: δ 0.72 (m, 2H), 0.8−1.0 (m, 6H), 1.81 (s, 6H), 2.23 (s, 6H), 2.24 (s, 6H), 2.30 (s, 6H), 2.87 (m, 2H), 3.19 (m, 2H), 4.09 (bs, 4H), 4.19 (m, 2H), 6.42 (bs, 2H), 6.60 (m, 6H), 6.80 (d, $J = 7.2$ Hz, 2H), 7.13 (t, $J = 8.0$ Hz, 6H), 7.66 (t, $J = 10$ Hz, 4H), 7.75 (d, $J = 8.4$ Hz, 2H). $^{13}C\{^1H\}$ NMR: δ 21.0,

(21) Lahuerta, P.; Payá, J.; Pellinghelli, M.; Tiripicchio, A. *Inorg. Chem.* **1992**, *31*, 1224.
(22) Lahuerta, P.; Martinez-Mañez, R.; Payá, J.; Peris, E. *Inorg. Chem. Acta* **1990**, *173*, 99.
(23) Cupps, T. S.; Boutin, R. H.; Rapoport, H. *J. Org. Chem.* **1985**, *50*, 3972.
(24) Kennedy, M.; McKervey, M. A.; Maguire, A. R.; Tuladhar, S. M.; Twohig, M. F. *J. Chem. Soc., Perkin Trans. 1* **1990**, 1047.
(25) Barnhart, R. W.; Wang, X.; Noheda, P.; Bergens, S. H.; Whelan, J.; Bosnich, B. *J. Am. Chem. Soc.* **1994**, *116*, 1821.
(26) Ruppert, J. F.; White, J. D. *J. Am. Chem. Soc.* **1981**, *103*, 1808.

21.1, 21.4, 21.6, 24.2, 29.4, 49.1, 62.2, 121.7−142.9 (aromatic signals), 165.0 (m), 181.1, 181.2. $[\alpha]^{20}_D$ −36 (*c* 0.05, $CHCl_3$).

Second Diastereoisomer (*P*). Yield: 74%.$^{31}P\{^1H\}$ NMR: δ 15.8. ^1H NMR: δ 0.72 (m, 2H), 0.8−1.0 (m, 6H), 1.81 (s, 6H), 2.23 (s, 6H), 2.24 (s, 6H), 2.30 (s, 6H) 2.87 (m, 2H), 3.19 (m, 2H), 4.09 (s, 4H), 4.19 (m, 2H), 6.24 (bs, 2H), 6.57 (m, 6H), 6.78 (m, 4H), 7.10 (d, J = 8.0 Hz, 2H), 7.15 (d, J = 9.0 Hz, 4H), 7.66 (t, J = 8.3 Hz, 4H), 7.71 (d, J = 8.1 Hz, 2H). $^{13}C\{^1H\}$ NMR: δ 20.9, 21.1, 21.2, 21.5, 24.1, 29.5, 48.8, 62.8, 122.0−142.7 (aromatic signals), 163.3 (m), 181.5, 181.6. $[\alpha]^{20}_D$ −249 (*c* 0.05, $CHCl_3$).

Rh_2(protos)$_2$[(*m*-$CH_3C_6H_3$)P(*m*-$CH_3C_6H_4$)$_2$]$_2$·(H_2O)$_2$. Diastereoisomers were separated by chromatography using a dichloromethane/diethyl ether, 50:3, mixture as eluent.

First Diastereoisomer (*M*). Yield: 80%. $^{31}P\{^1H\}$ NMR: δ 18.9. ^1H NMR: δ 0.59 (m, 2H), 0.91 (m, 6H), 1.95 (s, 6H), 2.08 (s, 6H), 2.31 (m, 10H), 2.83 (m, 2H), 3.19 (m, 2H), 3.56 (s, 6H), 4.15 (m, 2H), 6.22 (d, J = 11.1 Hz, 2H), 6.45 (m, 4H), 6.61 (m, 2H), 6.90−7.01 (m, 6H), 7.12 (m, 8H), 7.55 (m, 4H), 7.73 (d, J = 8.1 Hz, 2H). $^{13}C\{^1H\}$ NMR: δ 20.5, 21.1, 21.4, 21.5, 29.5, 49.1, 63.2, 127.0−144.3 (aromatic signals), 160.3 (m), 181.2. $[\alpha]^{20}_D$ +42 (*c* 0.012, $CHCl_3$).

Second Diastereoisomer (*P*). Yield: 70%. $^{31}P\{^1H\}$ NMR: δ 17.9. ^1H NMR: δ 1.03 (m, 6H), 1.32 (m, 2H), 1.95 (s, 6H), 2.08 (s, 6H), 2.32 (s, 6H), 2.36 (s, 4H), 2.99 (m, 4H), 3.22 (s, 6H), 3.95 (m, 2H), 6.23 (d, J = 11.1 Hz, 2H), 6.49 (m, 6H), 6.87 (m, 2H), 6.97 (m, 4H), 7.16 (m, 6H), 7.27 (m, 2H), 7.55 (m, 4H), 7.69 (d, J = 8.4 Hz, 4H). $^{13}C\{^1H\}$ NMR: δ 20.7, 21.1, 21.4, 21.7, 24.3, 29.4, 48.9, 62.8, 127.1−144.0 (aromatic signals), 158.2 (m), 180.2. $[\alpha]^{20}_D$ −600 (*c* 0.012, $CHCl_3$). Anal. Calcd for $C_{66}H_{72}N_2O_{10}P_2Rh_2S_2$: C, 57.23; H, 5.24; N, 2.02. Found: C, 57.44; H, 5.64; N, 2.03.

Rh_2(protos)$_2$[(C_6H_4)P(*m*-xylyl)$_2$]$_2$·(H_2O)$_2$. Diastereoisomers were separated by chromatography using a dichloromethane/diethyl ether, 100:3, mixture as eluent.

First Diastereoisomer (*M*). Yield: 71%. $^{31}P\{^1H\}$ NMR: δ 18.0. ^1H NMR: δ 0.6 (m, 2H); 0.8−1.0 (m, 6H), 2.03 (s, 12H), 2.25 (s, 12H), 2.32 (s, 6H), 2.87 (m, 2H), 3.21 (m, 2H), 3.72 (s, 4H), 4.19 (m, 2H), 6.34 (d, J = 10.8 Hz, 4H), 6.58 (t, J = 8.5 Hz, 4H), 6.71 (t, J = 7.3 Hz, 2H), 6.80 (m, 4H), 6.91 (s, 2H), 7.14 (d, J = 8.3 Hz, 4H), 7.30 (d, J = 10.6 Hz, 4H), 7.75 (d, J = 8.3 Hz, 4H). $^{13}C\{^1H\}$ NMR: δ 21.3, 21.4, 24.3, 29.4, 49.1, 63.2, 120.5−145.2 (aromatic signals), 165.4 (m), 181.1, 181.2. $[\alpha]^{20}_D$ −15 (*c* 0.05, $CHCl_3$).

Second Diastereoisomer (*P*). Yield: 74%. $^{31}P\{^1H\}$ NMR: δ 16.6. ^1H NMR: δ 0.95−1.15 (m, 6H), 1.35−1.45 (m, 2H), 2.01 (s, 12H), 2.30 (m, 18H), 2.93−1.02 (m, 4H), 3.24 (s, 4H), 4.03 (m, 2H), 6.32 (d, J = 10.6 Hz, 4H), 6.60 (m, 4H), 6.73 (m, 6H), 6.98 (s, 2H), 7.13 (d, J = 7.9 Hz, 4H), 7.30 (d, J = 10.6 Hz, 4H), 7.70 (d, J = 8.4 Hz, 4H). $^{13}C\{^1H\}$ NMR: δ 21.2, 21.4, 21.5, 24.3, 30.9, 49.0, 62.8 (d, J = 3.2 Hz), 120.7−144.7 (aromatic signals), 164.5 (m), 181.2, 181.3. $[\alpha]^{20}_D$ −265 (*c* 0.05, $CHCl_3$).

Rh_2(protos)$_2$[(*p*-^{t}BuC_6H_3)P(*p*-^{t}BuC_6H_4)$_2$]$_2$.(H_2O)$_2$. A solution of $Rh_2(O_2CCH_3)_2$ [(*p*-^{t}BuC_6H_3)P(*p*-^{t}BuC_6H_4)$_2$]$_2$·$(HO_2CCH_3)_2$ (440 mg, 0.34 mmol) and ProtosH (727 mg, 2.70 mmol) in 30 mL of toluene was refluxed for 5 h. Between the reflux condenser and the reaction flask was a Soxhlet extractor with a 1:1 mixture of sand and Na_2CO_3 to absorb the liberated acetic acid. After 5 h, the solvent was evaporated to yield a purple oil. After NMR had confirmed the presence of two diastereomers, the mixture was chromatographed (silica gel, hexane, 2 × 30 cm). Elution with dichloromethane/hexane/diethyl ether/ProtosH (30 mL:20 mL:3 mL:25 mg) afforded two green bands, which were collected separately and evaporated to dryness. To exchange the axial ProtosH for H_2O, the powdered diastereoisomers were stirred in an aqueous solution of Na_2CO_3 until the color was deeply violet. The two diastereoisomers were filtered off, redissolved in CH_2Cl_2, and evaporated to dryness.

First Diastereoisomer (*M*). Yield: 58%. $^{31}P\{^1H\}$ NMR: δ 15.3. ^1H NMR: δ 0.8−1.3 (m, 8H), 1.08 (s, 18H), 1.22 (s, 18H), 1.24 (s, 18H), 2.31 (s, 6H), 2.89 (q, J = 8.3 Hz, 2H), 3.20 (s, 4H), 3.31 (m, 2H), 4.27 (d, J = 6.4 Hz, 2H), 6.39 (t, J = 8.6 Hz, 2H), 6.60 (t, J = 8.8 Hz, 4H), 6.74 (d, J = 8.1 Hz, 2H), 6.93 (d, J = 8.1 Hz, 4H), 7.14 (d, J = 7.3 Hz, 6H), 7.31 (d, J = 8.1 Hz, 4H), 7.49 (t, J = 8.6 Hz, 4H), 7.85 (d, J = 7.8 Hz, 4H). $^{13}C\{^1H\}$ NMR: δ 21.4, 24.5, 29.7, 31.0, 31.1, 31.2, 34.4, 34.5, 34.9, 48.9, 63.1, 118.6−151.7 (aromatic signals), 163.7 (m), 181.1. $[\alpha]^{20}_D$ +74 (*c* 0.05, $CHCl_3$). Anal. Calcd for $C_{84}H_{108}N_2O_{10}P_2Rh_2S_2$: C, 61.61; H, 6.65; N, 1.71. Found: C, 62.12; H, 6.52; N, 1.35.

Second Diastereoisomer (*P*). Yield: 54%. $^{31}P\{^1H\}$ NMR: δ 15.4. ^1H NMR: δ 0.8−1.1 (m, 6H), 1.16 (s, 18H), 1.23 (s, 18H), 1.27 (s, 18H), 1.60 (m, 2H), 2.34 (s, 6H), 2.85 (s, 4H), 3.03 (m, 2H), 3.19 (m, 2H), 4.18 (m, 2H), 6.40 (t, J = 9.0 Hz, 2H), 6.58 (dd, J = 10.3 and 8.6 Hz, 4H), 6.74 (d, J = 8.1 Hz, 2H), 6.87 (d, J = 8.6 Hz, 4H), 7.17 (d, J = 8.3 Hz, 4H), 7.28 (m, 6H), 7.38 (t, J = 8.6 Hz, 4H), 7.77 (d, J = 8.3 Hz, 4H). $^{13}C\{^1H\}$ NMR: δ 21.4, 24.5, 29.6, 31.1, 31.2, 31.3, 34.4, 34.5, 34.6, 48.8, 63.0, 118.6−151.7 (aromatic signals), 163.6 (m), 181.1. $[\alpha]^{20}_D$ −176 (*c* 0.05, $CHCl_3$).

Synthesis of Rh_2(protos)$_2$[(*p*-FC_6H_3)P(*p*-FC_6H_4)$_2$]$_2$·(H_2O)$_2$. The two diastereoisomers were separated using a mixture of eluent solvent dichloromethane/diethyl ether, 40:3.

First Diastereoisomer (*M*). Yield: 70%. $^{31}P\{^1H\}$ NMR: δ 18.9. ^1H NMR: δ 0.84 (m, 2H), 1.07 (m, 4H), 2.33 (s, 6H), 2.88 (m, 2H), 3.24 (m, 2H), 3.59 (bs, 4H), 4.20 (m, 2H), 6.53−6.64 (m, 10H), 6.75 (m, 4H), 7.05 (m, 4H), 7.17 (d, J = 8 Hz, 4H), 7.62 (m, 4H), 7.72 (d, J = 8 Hz, 4H). $^{13}C\{^1H\}$ NMR: δ 21.4, 24.3, 29.7, 49.0, 63.1, 109.4 (d, J = 22.6 Hz), 115.0 (m), 124.4−143.3 (aromatic signals), 161.9 (d, J = 253.1 Hz), 163.26 (d, J = 247.5 Hz), 163.85 (d, J = 253.1 Hz), 168.94 (m), 182.2. $^{19}F\{^1H\}$: δ −112.60 (m), −112.05 (m), −111.75 (m). $[\alpha]^{20}_D$ −275 (*c* 0.012, $CHCl_3$).

Second Diastereoisomer (*P*). Yield: 65%. $^{31}P\{^1H\}$ NMR: δ 18.4. ^1H NMR: δ 1.00−1.48 (m, 8H), 2.36 (s, 6H), 2.90−3.15 (m, 4H), 3.48 (bs, 4H), 4.14 (m, 2H), 6.46−6.80 (m, 14H), 7.03 (m, 4H), 7.23 (d, J = 10.8 Hz, 4H), 7.55 (m, 4H), 7.73 (d, J = 11.2 Hz, 4H). $^{13}C\{^1H\}$ NMR: δ 21.7, 24.6, 30.2, 49.3, 63.1, 109.4 (d, J = 9.9 Hz), 109.7 (d, J = 9.9 Hz), 115.2−143.5 (aromatic signals), 161.2 (d, J = 254.19 Hz), 161.97 (d, J = 41.84 Hz), 168.65 (m), 182.3. $^{19}F\{^1H\}$: δ −111.20 (m), −110.75 (m), −111.30 (m). $[\alpha]^{20}_D$ −125 (*c* 0.012, $CHCl_3$).

Rh_2(protos)$_2$[(C_6H_4)P(CH_3)$_2$]$_2$·(H_2O)$_2$. Diastereoisomers were separated by chromatography using a mixture of eluent solvent hexane/acetone, 10:2, but only the first one of the two diastereoisomers was recovered with significant yield.

First Diastereoisomer (*M*). Yield: 30%. $^{31}P\{^1H\}$ NMR: δ −3.14. ^1H NMR: δ 0.97 (s, 3H), 1.00 (s, 3H), 1.39(m, 2H), 1.64 (s, 3H), 1.68 (s, 3H), 1.98 (m, 4H), 2.36 (s, 6H), 3.11 (m, 2H), 3.42−3.57 (m, 4H), 4.37 (m, 2H), 6.90 (m, 6H), 7.20−7.32 (m, 6H), 7.68 (d, J = 7.91 Hz, 4H). $^{13}C\{^1H\}$ NMR: δ 15.4, 15.9, 16.1, 16.5, 21.4, 24.6, 31.2, 49.0, 63.0, 122.0−149.4 (aromatic signals), 160.7, 181.4, 181.5. $[\alpha]^{20}_D$ +141 (*c* 0.012, $CHCl_3$). Anal. Calcd for $C_{40}H_{52}N_2O_{10}P_2Rh_2S_2$: C, 45.63; H, 4.99; N, 2.66. Found: C, 45.25; H, 5.25; N, 2.56.

General Procedure for the Synthesis of Enantiomerically Pure Rh(II) Catalysts. Each diastereoisomer (200 mg) was dissolved in 10 mL of dichloromethane. Three drops of trifluoroacetic acid was added, and the mixture was stirred for half an hour. The solution was concentrated, transferred to a column, and eluted with dichloromethane/hexane, 40:40, and 1% of trifluoroacetic acid to afford a complete exchange of the Protos.

$Rh_2(O_2CCF_3)_2$[(C_6H_4)P(C_6H_5)$_2$]$_2$·(HO_2CCF_3)$_2$. This compound was crystallized with a mixture of dichloromethane and hexane and one drop trifluoroacetic acid. Yield: 65%. $^{31}P\{^1H\}$ NMN: δ 16.2. ^1H NMR: δ 6.60−6.75 (m, 4H), 6.78−6.95 (m, 8H), 7.18, (m, 4H), 7.25−7.48 (m, 8H), 7.51 (m, 4H), 8.90 (bs, 2H). $^{13}C\{^1H\}$ NMR: δ 114.4 (q, J = 284.0 Hz), 114.7 (q, J = 290.3 Hz), 122.1−144.3 (aromatic signals), 160.2 (m), 163.8

(q, J = 42.9 Hz), 166.2 (q, J = 37.7 Hz). $^{19}F\{^1H\}$ NMR: δ −76.05 (s, 6F), −75.75 (s, 6F). *(M)*: $[\alpha]^{20}_D$ +83 (*c* 0.1, CH_3CN).

$Rh_2(O_2CCF_3)_2[(p\text{-}CH_3C_6H_3)P(p\text{-}CH_3C_6H_4)_2]_2\cdot(H_2O)_2$. Yield: 70%. $^{31}P\{^1H\}$ NMR: δ 15.6. ^1H NMR: δ 1.80 (s, 6H), 2.28 (s, 6H), 2.34 (s, 6H), 2.62 (bs, 4H), 6.25 (bs, 2H), 6.57 (m, 4H), 6.73 (dd, J = 10.4 and 8.4 Hz, 4H), 6.87 (dd, J = 7.9 and 1.6 Hz, 4H), 7.16 (dd, J = 8.0 and 1.6 Hz, 4H), 7.48 (t, J = 9.1 Hz, 4H). $^{13}C\{^1H\}$ NMR: δ 21.1 (d, J = 1.0 Hz), 21.2 (d, J = 1.1 Hz), 21.5, 115.0 (q, J = 288.2 Hz), 123.0−141.7 (aromatic signals), 161.3 (m), 165.9 (q, J = 37.7 Hz). $^{19}F\{^1H\}$ NMR δ −75.7. (*M*): $[\alpha]^{20}_D$ +97 (*c* 0.05, $CHCl_3$). Anal. Calcd for $C_{46}H_{44}F_6O_6P_2Rh_2$: C, 51.43; H, 4.13. Found: C, 51.11; H, 4.27.

$Rh_2(O_2CCF_3)_2[(m\text{-}CH_3C_6H_3)P(m\text{-}CH_3C_6H_4)_2]_2\cdot(H_2O)_2$. Yield: 80%. $^{31}P\{^1H\}$ NMR: δ 16.0. ^1H NMR: δ 1.98 (s, 6H), 2.09 (s, 6H), 2.22 (s, 6H), 2.34 (s, 4H), 6.25 (d, J = 11.3 Hz, 2H), 6.30 (m, 6H), 7.04 (m, 6H), 7.28 (m, 6H), 7.41 (d, J = 9.1 Hz, 2H). $^{13}C\{^1H\}$ NMR: δ 20.5, 21.2, 21.5, 115.0 (q, J = 289.2 Hz), 127.3−144.8 (aromatic signals), 156.7 (m), 165.7 (q, J = 39.2 Hz). $^{19}F\{^1H\}$ NMR: δ −75.32. (*M*): $[\alpha]^{20}_D$ +583 (*c* 0.012, $CHCl_3$). Anal. Calcd for $C_{46}H_{44}O_6P_2Rh_2F_6$: C, 51.39; H, 4.13. Found: C, 51.61; H, 4.48.

$Rh_2(O_2CCF_3)_2[(C_6H_4)P(m\text{-xylyl})_2]_2\cdot(H_2O)_2$. Yield: 92%. $^{31}P\{^1H\}$ NMR: δ 16.0. ^1H NMR: ($CDCl_3$) δ 2.04 (s, 12H), 2.24 (s, 12H), 2.53 (s, 4H), 6.43 (d, J = 11.0 Hz, 4H), 6.59 (m, 4H), 6.79 (m, 6H), 7.00 (s, 2H), 7.12 (d, J = 10.7 Hz, 4H). $^{13}C\{^1H\}$ NMR: δ 21.2, 21.3, 115.1 (q, J = 289.8 Hz), 121.4−145.9 (aromatic signals), 162.7 (m), 165.6 (q, J = 37.1 Hz). $^{19}F\{^1H\}$ NMR: δ −75.6. (*M*): $[\alpha]^{20}_D$ +92 (*c* 0.05, $CHCl_3$).

$Rh_2(O_2CCF_3)_2[(p\text{-}^tBuC_6H_3)P(p\text{-}^tBuC_6H_4)_2]_2\cdot(H_2O)_2$. Yield: 92%. $^{31}P\{^1H\}$ NMR: δ 14.9. ^1H NMR: δ 1.21 (s, 18H), 1.22 (s, 18H), 1.25 (s, 18H), 2.40 (s, 4H), 6.41 (t, J = 8.8 Hz, 2H), 6.81 (m, 8H), 7.06 (dd, J = 8.2 and 1.7 Hz, 4H), 7.29 (m, 4H), 7.42 (t, J = 9.2 Hz, 4H). $^{13}C\{^1H\}$ NMR: δ 30.8, 31.0, 33.7, 34.3, 34.6, 115.0 (q, J = 288.4 Hz), 119.7−152.45 (aromatic signals), 161.5 (m); 165.3 (q, J = 38.7 Hz). $^{19}F\{^1H\}$ NMR: δ −75.2. *(M)*: $[\alpha]^{20}_D$ +94 (*c* 0.05, $CHCl_3$).

$Rh_2(O_2CCF_3)_2[(p\text{-}FC_6H_3)P(p\text{-}FC_6H_4)_2]_2\cdot(H_2O)_2$. Yield: 60%. $^{31}P\{^1H\}$ NMR: δ 17.9. ^1H NMR: δ 6.28 (bs, 2H), 6.61 (m, 4H), 6.74 (m, 4H), 6.83 (m, 4H), 6.87 (m, 4H), 7.08 (m, 4H), 7.53 (m, 4H). $^{13}C\{^1H\}$ NMR: δ 110.2 (d, J = 9.8 Hz), 110.5 (d, J = 10.26 Hz), 114.7 (q, J = 286.7 Hz), 115.2−140.1 (aromatic signals), 161.9 (d, J = 257.1 Hz), 162.2 (d, J = 34.2 Hz), 165.1 (m), 165.5 (d, J = 34.2 Hz), 166.5 (d, J = 37.2 Hz). $^{19}F\{^1H\}$ NMR: δ −109.48, −109.19, −108.01, −75.80. *(M)*: $[\alpha]^{20}_D$ +47 (*c* 0.012, $CHCl_3$).

$Rh_2(O_2CCF_3)_2[(C_6H_4)P(CH_3)_2]_2\cdot(H_2O)_2$. Yield: 50%. $^{31}P\{^1H\}$ NMR: δ −1.06. ^1H NMR: δ 1.02 (s, 3H), 1.06 (s, 3H), 1.52 (s, 3H), 1.56 (s, 3H), 2.62 (s, 4H), 6.89−6.99 (m, 6H), 7.36−7.38 (m, 2H). $^{13}C\{^1H\}$ NMR: δ 14.8, 15.3, 16.0, 16.5, 115.5 (q, J = 289.4 Hz), 122.8−149.4 (aromatic signals), 157.8 (m), 167.3 (q, J = 38.0 Hz). $^{19}F\{^1H\}$ NMR: δ −75.03 (s, 6F). *(M)*: $[\alpha]^{20}_D$ +183 (*c* 0.012, $CHCl_3$).

Catalytic Studies. All the catalytic reactions were performed dissolving the appropriate diazocompound (30 mg) in dried CH_2Cl_2 (30 mL) under an argon atmosphere. The catalyst (1.5 mg, [substrate]/[Rh(II)-complex] = 100) was added to the solution and the mixture immersed in a water bath at 45 °C. The reaction was controlled by TLC until complete transformation of the diazocompound. The solvent was evaporated and the crude product filtered in a short chromatography column to eliminate the catalyst. The yield of the reaction was calculated by proton NMR, the cyclization product was purified by HPLC, and the enantiomeric excesses were calculated by gas chromatography.

Synthesis of Diazocompounds. 1-Diazo-5-*p*-methoxyphenyl-2-pentanone: oil. ^1H NMR: δ 1.89 (m, 2H), 2.29 (t, J = 6.9 Hz, 2H), 2.57 (t, J = 7.4 Hz, 2H), 3.76 (s, 3H), 5.19 (bs, 1H), 6.80 (d, J = 8.6 Hz, 2H); 7.06 (d, J = 8.6 Hz, 2H). $^{13}C\{^1H\}$ NMR: δ 26.7, 34.0, 39.9, 54.2, 55.0, 113.6, 129.2, 133.2, 157.7, 194.8. Anal. Calcd for $C_{12}H_{14}N_2O$: C, 65.73; H, 6.90. Found: C, 65.91; H, 6.74.

1-Diazo-5-*p*-chlorophenyl-2-pentanone: oil. ^1H NMR: δ 1.89 (m, 2H), 2.28 (t, J = 6.3 Hz, 2H), 2.58 (t, J = 7.8 Hz, 2H), 5.20 (bs, 1H), 7.07 (d, J = 8.4 Hz, 2H), 7.21 (d, J = 8.4 Hz, 2H). $^{13}C\{^1H\}$ NMR: δ 26.3, 34.3, 39.8, 54.4, 128.4, 129.8, 131.6, 139.9, 194.4. Anal. Calcd for $C_{11}H_{11}N_2ClO$: C, 59.33; H, 4.98. Found: C, 59.00; H, 5.33.

1-Diazo-5-*p*-fluorophenyl-2-pentanone: oil. ^1H NMR: δ 1.88 (m, 2H), 2.27 (t, J = 7.6 Hz, 2H), 2.57 (t, J = 7.4 Hz, 2H), 5.19 (bs, 1H), 6.88−6.95 (m, 2H), 7.05−7.11 (m, 2H). $^{13}C\{^1H\}$ NMR: δ 26.6, 34.1, 39.8, 54.4, 115.0 (d, J = 21 Hz), 129.7 (d, J = 7.8 Hz), 129.7 (d, J = 7.8 Hz), 136.9, 163.1, 194.6. $^{19}F\{^1H\}$ NMR: δ −117.74 (m, 1F). Anal. Calcd for $C_{11}H_{11}N_2O$: C, 64.07; H, 5.38. Found: C, 64.02; H, 5.69.

1-Diazo-5-cyclohexyl-2-pentanone: oil. ^1H NMR: 0.88 (m, 2H), 1.15 (m, 6H), 1.58 (m, 7H), 2.25 (t, J = 7 Hz, 2H), 5.21 (bs, 1H). $^{13}C\{^1H\}$ NMR: δ 22.6, 26.2, 26.6, 33.2, 36.9, 37.4, 41.4, 54.2, 195.4. Anal. Calcd for $C_{11}H_{18}N_2$: C, 68.01; H, 9.34. Found: C, 67.94; H, 9.58.

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