Rhodium(I)-Catalyzed Asymmetric Intramolecular Pauson−Khand-Type Reaction

Nakcheol Jeong,* Byung Kee Sung, and Yoon Kyung Choi

Department of Chemistry and Division of Chemistry and Molecular Engineering Korea University, 1-5 ka, Anam-dong, Sungbuk-ku Seoul, 136-701, Korea

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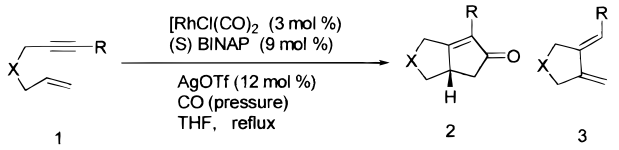
Despite impressive recent advances in the catalytic Pauson−Khand-type reaction (PKR hereafter),[1−3] the development of the enantioselective version is far behind the expectation. A titanium catalyst, (*S*,*S*)(EBTHI)Ti(CO)$_2$, has been used for this end successfully.[4a,b] Although a number of late transition metal catalysts, which might be more useful because of their stability toward moisture and air and well-defined structure, have been successfully employed for PKR variations meantime, only cobalt with BINAP has been used for the catalytic enantioselective transformation with limited success recently.[4c,d] This is attributed to the fact that most of the late transition metal catalysts required carbon monoxide, a strong π-acceptor and a nontunable ligand, as a ligand because of their intrinsic high electron density of metal center. Since the modification of catalyst by introduction of other ligands, e.g. phosphine ligand, made it much less effective, it has been difficult to introduce the chiral environment on the catalyst.

We have recently shown that rhodium(I) catalysts bearing bisdentate phosphine ligands were also effective for this cyclization and opened the possibility for the development of new catalytic asymmetric reaction by tuning of phosphine ligands.[3q] Herein, we would like to report our preliminary results in this endeavor.

In a control experiment we confirmed that the reaction with a catalyst bearing a phosphine ligand, e.g. RhCl(CO)(dppe),[3q] was significantly decelerated compared to the reaction with [RhCl(CO)$_2$]$_2$.[3p] It might be attributed to the diminished Lewis acidity of the phosphine-bound catalyst and this was also true for Co catalyst.[4d] It implied that catalysts with strongly bound phosphine ligand were desirable to suppress the unwanted competition arising from the phosphine-free catalyst, which might be in equilibrium with the phosphine-bound catalyst at high temperature under CO atmosphere.

Scheme 1. Rh(I)-Catalyzed Enantioselective Pauson−Khand-Type Reaction



After extensive study to identify the optimum reaction conditions, we were able to figure out the following features in this transformation: (1) The catalysts prepared in situ by mixing of a slight excess of chiral bisphosphine ligands and [RhCl(CO)$_2$]$_2$ based on the protocol of Sanger[5] were effective for this cyclization. (2) Choice of solvent is important. Although the reaction proceeded more efficiently in toluene than in a coordinating solvent such as THF, it must be run in THF for high enantioselectivity. (3) Silver salt, e.g. AgOTf, is required for the proper initiation of the reaction in THF. (4) Among a number of ligands we have screened, (*S*)-BINAP turned out to be the best.[6] (5) Balancing of CO pressure from case to case is quite critical for the high enantioslectivity as well as the chemical yield because there is a tradeoff between the chemical yield and enantioselectivity of PKR product. More PKR products tend to occur under higher CO pressure, but better enantioselectivities might be obtained under lower CO pressure because the unfavorable equilibrium between potential catalysts is suppressed.

On the basis of these preliminary results, we set up the experimental protocol for further studies as follow: the reaction was carried out with 1 equiv of enynes (**1**) in the presence of 3 mol % [RhCl(CO)$_2$]$_2$, 9 mol % (*S*)-BINAP, and 12 mol % AgOTf under 1 atm of CO in THF at appropriate reaction temperatures (Scheme 1).

A variety of 1,6-enynes (**1**) were converted to bicyclic cyclopentenones (**2**) and the results are summarized in Table 1. In most cases, this transformation proceeded nicely to furnish the PKR products with good to excellent enantioselectivity in reasonable reaction time (4−6 h) under 1 atm of CO.

Substrates with oxygen and nitrogen tethers (**1-h** to **1-l**) proceeded smoothly to give the corresponding products (**2-h** to **2-l**) with high chemical *yields* (greater than 80%) and enantioselectivities (74−86% ee) (entry 11, 13, 15, and 17 in Table 1). Under forcing conditions, there are significant improvements in chemical yield at the cost of enantioselectivity (entries 11 and 12; 85% yield of **2-h** with 86% ee at 3 atm of CO pressure vs 40% yield of **2-h** with 96% ee under 1 atm).

In general, aryl-substituted acetylenes provided better chemical yields of PKR products but lower ee than alkyl-substituted acetylenes, some of which required mildly forcing conditions (2−3 atm of CO) for the clean reaction (entry 1, 2, 3, 7, and 10 vs 4, 5, 6, 8 and 11).

Substrates (**1-a** to **1-g**) with the malonate tether are inferior to the previous substrates in terms of chemical yields and enantioselectivities. Steric factors played a critical role. Changing

(1) (a) Pauson, P. L.; Khand, I. U. *Ann. N.Y. Acad. Sci.* **1977**, *295*, 2. (b) Pauson, P. L. *Tetrahedron* **1985**, *41*, 5855. (c) Schore, N. E. *Chem. Rev.* **1988**, *88*, 1081. (d) Schore, N. E. *Org. React.* **1991**, *40*. (e) Schore, N. E. In *Comprehensive Organic Synthesis*; Trost, B. M., Ed.; Pergamon: Oxford, U.K., 1991; Vol. 5, pp 1037−1064. (f) Schore, N. E. In *Comprehensive Organometallic Chemistry II*; Abel, E. W., Stone, F. G. A., Wilkinson, G., Eds.; Pergamon: Oxford, U.K., 1995; Vol. 12, pp 703−739. (g) Geis, O.; Schmalz, H. G. *Angew. Chem., Int. Ed. Engl.* **1998**, *37*, 911. (h) Chung, Y. K. *Coord. Chem. Res.* **1999**, *188*, 297.

(2) For the references using other metals see: (a) Aumann, R.; Weidenhauft, J. *Chem. Ber*. **1987**, *120*, 23. (b) Tamao, K.; Kobayashi, K.; Ito, Y. *J. Am. Chem. Soc.* **1988**, *110*, 1286. Tamao, K.; Kobayashi, K.; Ito, Y. *Synlett* **1992**, 539. (c) Grossman, R. B.; Buchwald, S. L. *J. Org. Chem*. **1992**, *57*, 5803. (d) Jeong, N.; Lee, S. J.; Lee, B. Y.; Chung, Y. K. *Tetrahedron Lett*. **1993**, *34*, 4027. (e) Hoye, T. R.; Suriano, J. A. *J. Am. Chem. Soc*. **1993**, *115*, 1154. (f) Pearson, A. J.; Dubbert, R. A. *J. Chem. Soc., Chem. Commun*. **1991**, 202. Pearson, A. J.; Dubbert, R. A. *Organometallics* **1994**, *13*, 1656. (g) Negishi, E.-i.; Takahashi, T. *Acc. Chem. Res.* **1994**, *27*, 124

(3) For Co see: (a) Rautenstrauch, V.; Megard, P.; Conesa, J.; Kuster, W. *Angew. Chem., Int. Ed. Engl.* **1990**, *29*, 1413. (b) Jeong, N.; Hwang, S. H.; Lee, Y.; Chung, Y. K. *J. Am. Chem. Soc.* **1994**, *116*, 3159. (c) Lee, B. Y.; Chung, Y. K.; Jeong, N.; Lee, Y.; Hwang, S. H. *J. Am. Chem. Soc.* **1994**, *116*, 8793. (d) Pagenkopf, B. L.; Livinghouse, T. *J. Am. Chem. Soc.* **1996**, *118*, 2285. (e) Lee, N. Y.; Chung, Y. K. *Tetrahedron Lett.* **1996**, *37*, 3145. (f) Jeong, N.; Hwang, S. H.; Lee, Y. W.; Lim, J. S. *J. Am. Chem. Soc*. **1997**, *119*, 10549. (g) Sugihara, T.; Yamaguchi, M. *J. Am. Chem. Soc*. **1998**, *120*, 10782. (h) Hayashi, M.; Hashimoto, M.; Yamamoto, Y.; Usuki, J.; Saigo, K. *Angew. Chem., Int. Ed. Engl.* **2000**, *39*, 631. (i) Jeong, N.; Hwang, S. H. *Angew. Chem., Int., Ed. Engl*. **2000**, *39*, 636. For Ti see: (j) Berk, S. C.; Grossman, R. B.; Buchwald, S. L. *J. Am. Chem. Soc.* **1993**, *115*, 4912. (k) Berk, S. C.; Grossman, R. B.; Buchwald, S. L. *J. Am. Chem. Soc.* **1994**, *116*, 8593. (l) Hicks, F. A.; Berk, S. C.; Buchwald, S. L. *J. Org. Chem.* **1996**, *61*, 2713. (m) Hick, F. A.; Kablaoui, N. M.; Buchwald, S. L. *J. Am. Chem. Soc.* **1996**, *118*, 9450. For Ru see: (n) Kondo, T.; Suzuki, N.; Okada, T.; Mitsudo, T. *J. Am. Chem. Soc.* **1997**, *119*, 6187. (o) Morimoto, T.; Chatani, N.; Fukumoto, Y.; Murai, S. *J. Org. Chem.* **1997**, *62*, 3762. For Rh see: (p) Koga, Y.; Kobayashi, T.; Narasaka, K. *Chem. Lett.* **1998**, 249. (q) Jeong, N.; Lee, S.; Sung, B. K. *Organometallics* **1998**, *17*, 3642.

(4) (a) Hicks, F. A.; Buchwald, S. L. *J. Am. Chem. Soc*. **1996**, *118*, 11688. (b) Hicks, F. A.; Buchwald, S. L. *J. Am. Chem. Soc.* **1999**, *121*, 7026. (c) Hiroi, K.; Watanabe, T.; Kawagishi, R.; Abe, I. *Tetrahedron Lett.* **2000**, *41*, 891. (d) Derdau, V.; Laschat, S.; Dix, I.; Jones, P. G. *Organometallics* **1999**, *18*, 3859.

(5) Sanger, A. R. *J. Chem. Soc., Dalton Trans.* **1977**, 120.

(6) Chemical yields and enantioselectivities from the reaction of **1-l** with various ligands under the typical condition described in the text are given as follow. The data are given in the following order. Ligand (chemical yield (%), ee (%)); (*S*) BINAP (94; 74), (−) DIOP (95; 25), (−) Chiraphos (86; 0), (*R*,*R*) Norphos (84; 14), (−) Me-DuPhos (86; 0), (−) Binaphos (85; 27).

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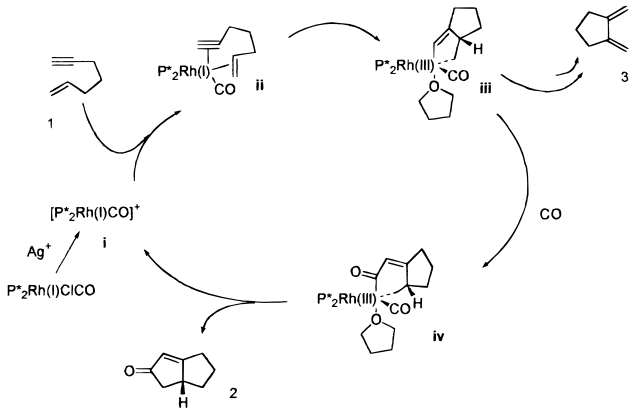
Table 1. Rh(I)-Catalyzed Asymmetric Pauson−Khand-Type Cyclization[a]

entry	substrate	X	R	CO (atm)[f]	temp (°C)	time (h)	yield[b,d] (%)	ee (%)[c]	$[\alpha]_D^{25}$ (*c* in $CHCl_3$)[g]	absolute config[g]
1	**1-a**	$(MeO_2C)_2C$	Me	2	130	20	91	62	−55 (1.00)	
2	**1-b**	$(EtO_2C)_2C$	Me	3	130	20	93	71	−91.8 (1.70)	*S*
3	**1-b**	$(EtO_2C)_2C$	Me	2	130	20	95	67		
4	**1-b**	$(EtO_2C)_2C$	Me	1	130	20	70	70		
5	**1-c**	$(^iPrO_2C)_2C$	Me	1	90	4	40	90	+10.8 (0.17)	
6	**1-d**	$(MeO_2C)_2C$	Ph	1	90	5	78	42	−13.9 (1.60)	
7	**1-e**	$(EtO_2C)_2C$	Ph	3	130	20	96	22		
8	**1-e**	$(EtO_2C)_2C$	Ph	1	90	6	67[e]	61	−24.6 (1.30)	*S*
9	**1-f**	$(^iPrO_2C)_2C$	Ph	1	90	3	80	58	+12.2 (0.20)	
10	**1-g**	CH_2	Ph	1	90	5	61	51	+27.5 (0.20)	*S*
11	**1-h**	O	Me	2	130	20	85	86		
12	**1-h**	O	Me	1	90	5	40	96	−140 (0.40)	
13	**1-i**	O	Ph	1	90	5	88	81	+8.3 (1.50)	*R*
14	**1-j**	O	C_4H_9	1	90	3	60	65		
15	**1-k**	$N\text{-}SO_2C_7H_7$	Me	1	90	3	80	84	−84.7 (0.60)	
16	**1-l**	$N\text{-}SO_2C_7H_7$	Ph	3	130	20	96	46		
17	**1-l**	$N\text{-}SO_2C_7H_7$	Ph	1	90	3	93	74	65.8 (1.30)	
18	**1-l**	$N\text{-}SO_2C_7H_7$	Ph	0.5[j]	90	5	99	71		

[a] $[RhCl(CO)_2]_2$ (3 mol %)/(*S*)-BINAP (6 mol %) and AgOTf (12 mol %) were employed in THF. [b] Isolated yield by Silica gel column chromatography. [c] Determined by HPLC analysis with chiral stationary columns. Refer to the Supporting Information. [d] All starting material was consumed completely. Full characterizations of side products will be reported. [e] Diene (**3a**) product was obtained as a byproduct. [f] The CO pressure given in this column is the value at ambient temperature. The reactions under CO pressure higher than 1 atm were carried out in a stainless steel bomb. [g] See ref 7. [i] See ref 4. [j] Ar:CO = 1:1 (1 atm).

Scheme 2. A Proposed Mechanism of Rh(I)-Catalyzed Enantioselective Pauson−Khand-Type Reaction



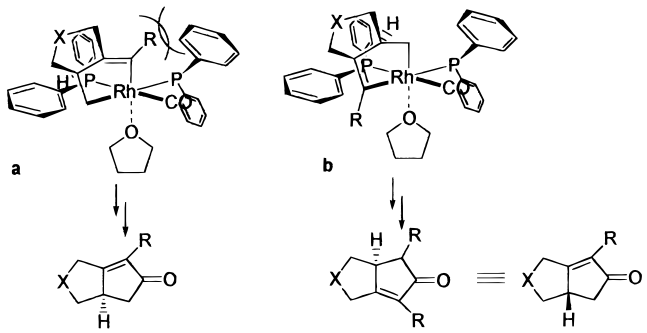
substrate from **1-a** and **1-d** to **1-b** and **1-e** (entries 1 and 2 and 6 and 8, respectively) made significant improvements in enantioselectivities without loss of chemical yields. However, introduction of a bulkier group such as the isopropyl group (**1-c**) changed the reaction pathway to give PKR product (**2-c)** in only 40% yield but in higher enantioselectivity (90% ee; entry 5).

As we anticipated and mentioned earlier, the balancing of CO pressure is critical for the high enantioselectivity and has to be tuned from case to case. For example, substrate **1-e** (entries 7 and 8 in Table 1) produced more PKR product under higher CO pressure (67% of **2-e** and 30% of **3-e** under 1 atm of CO vs 96% of **2-e** under 3 atm of CO). But the ee values of PKR product (**2-e**) substantially dropped from 61% to 22% as CO pressure increased. The efficiency of the reaction with substrate **1-l** to **2-l** is independent of CO pressure (96% at 3 atm vs 93% at 1 atm of CO), but the ee is very much dependent on pressure again (46% under 3 atm vs 74% under 1 atm) (entries 16 and 17).

A proposed reaction pathway based on the previous results is given in Scheme 2. The cationic catalytic species [Rh(CO)(*S*)-BINAP]$^+$ binds to 1,6-enyne first. This intermediate (**ii**) is converted to octahedral Rh(III) metallacyclopentene intermediate (**iii**) by the aid of THF. Subsequent migratory insertion of CO to give **iv** and reductive elimination would eventually yield the PKR product.

Either low effective concentration of CO in the reaction mixture or strain energy on intermediate III due to bulkiness of the substituents would facilitate the formation of CO missing products such as dienes (**3**).

Absolute configurations of some products were assigned by comparison of optical rotation with the previously reported value by Buchwald.[4b,7] Substrate **1-a** produced (*S*) **2-a** as depicted in Scheme 1 when (*S*)-BINAP was employed as a chiral ligand. From this stereochemical outcome we proposed the cyclometalated intermediate (III) for the origin of enantioselectivity:



Because of the highly skewed structure known for transition metal complexes coordinated with a (*S*)-BINAP, only the left-upper part is available for 1,6-enynes. Of the two possible structures **b** is more stable than **a** because it can avoid the steric congestion between one of the phenyl groups of (*S*)-BINAP and the substituent on acetylene.

In conclusion, we have developed an efficient catalytic asymmetric Pauson−Khand-type cyclization with Rh(I). A variety of 1,6-enynes are converted to the corresponding bicyclic cyclopentenones with good to excellent enantioselectivities. Further optimization and mechanistic study will be reported in due course.

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Supporting Information Available: Experimental details, spectroscopic data (^1H, ^{13}C, $[\alpha]_D^{25}$ (in $CHCl_3$)), and HPLC determination of ee of each compound in the table (PDF). This material is available free of charge via the Internet at http://pubs.acs.org.

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(7) The optical rotation values reported here are uniformly higher than those previously reported.[4b] The following data are given for comparison. ($[\alpha]_D^{25}$ (in $CHCl_3$), % ee (obtained by HPLC) of this study; from ref 4b); **1-b** (−81.8, 71% ee (*S*); +86.4, 87% ee (*R*)), **1-e** (−24.6, 61% ee (*S*); +20.4, 94% ee (*R*)), **1-i** (+8.3, 81% ee (*R*); −7.69, 96% ee (*S*)), **1-g** (+27.5, 51% ee (*S*); −19.6, 87% ee (*R*)).