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Asymmetric Pauson−Khand-type Reaction Mediated by Rh(I) Catalyst at Ambient Temperature

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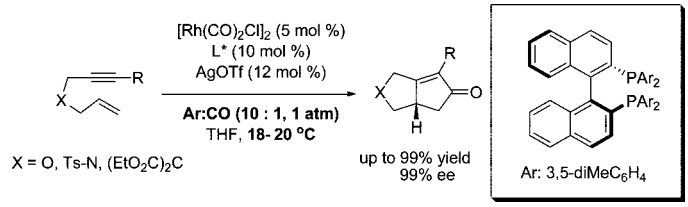

An efficient asymmetric PKR mediated by Rh(I) catalyst at ambient temperature was developed. The reaction utilizing a Rh(I) catalyst bearing a (*R*)-3,5-diMeC$_4$H$_4$-BINAP ligand at 18−20 °C under a reduced partial pressure of CO (0.1 atm) provided PKR products in high chemical yield as well as high enantioselectivity.

Introduction

In recent years, a great deal of research has been devoted to the asymmetric catalytic Pauson−Khand reaction (denoted as the APKR hereafter).[1,2] Various versions of the enantioselective PK-type reaction using cobalt,[3] titanium,[4] rhodium,[5] and iridium[6] together with chiral ligands have been published.

Many years ago, we described the first rhodium-catalyzed enantioselective PKR under a CO atmosphere in the presence of the atropisomeric BINAP ligand (Scheme 1).[5a,b] These early results were promising in terms of the enantioselectivity, but some limitations were encountered with certain classes of substrates. Systematic efforts to perfect this protocol in terms of the chemical yield and enantioselectivity have since been made by us[7] and others.

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(1) (a) Khand, I. U.; Knox, G. R.; Pauson, P. L.; Watts, W. E. *Chem. Commun.* **1971**, 36. (b) Khand, I. U.; Knox, G. R.; Pauson, P. L.; Watts, W. E.; Foreman, M. I. *J. Chem. Soc., Perkin Trans. 1* **1973**, 977.

(2) (a) Jeong, N. In *Comprehensive Organometallic Chemistry III*; Crabtree, R. H., Mingos, M. P., Eds. Elsevier: Oxford, 2006; Vol. 11, pp 335−366. (b) Gibson, S. E.; Mainolfi, N. *Angew. Chem., Int. Ed.* **2005**, *44*, 3022. (c) Park, K. H.; Chung, Y. K. *Synlett* **2005**, 545. (d) Boñaga, L. V. R.; Krafft, M. E. *Tetrahedron* **2004**, *60*, 9795. (e) Blanco-Urgoiti, J.; Anõrbe, L.; Pérez-Serrano, L.; Domínguez, G.; Pérez-Castells, J. *Chem. Soc. Rev.* **2004**, *33*, 32. (f) Gibson, S. E.; Stevenazzi, A. *Angew. Chem., Int. Ed.* **2003**, *42*, 1800. (g) Rivero, M. R.; Adrio, J.; Carretero, J. C. *Eur. J. Org. Chem.* **2002**, 2881. (h) Fletcher, A. J.; Christie, S. D. R. *J. Chem. Soc., Perkin Trans. 1* **2000**, 1657. (i) Brummond, K. M.; Kent, J. L. *Tetrahedron* **2000**, *56*, 3263. (j) Buchwald, S. L.; Hicks, F. A. In *Comprehensive Asymmetric Catalysis*; Jacobsen, E. N., Pfaltz, A., Yamamoto, H., Eds.; Springer: Berlin, Heidelberg, 1999; Vol. II, pp 491−510. (k) Ingate, S. T.; Marco-Contelle, J. *Org. Prep. Proced. Int.* **1998**, *30*, 121. (l) Chung, Y. K. *Coord. Chem. Rev.* **1999**, *188*, 297. (m) Jeong, N. In *Transition Metals in Organic Synthesis: Building Blocks and Fine Chemicals*; Beller, M., Bolm, C., Eds.; Wiley-VCH: Weinheim, 1998; Vol. 1, pp 560−577.

(3) (a) Gibson, S. E.; Kaufmann, K. A. C.; Loch, J. A.; Steed, J. W.; White, A. J. P. *Chem. Eur. J.* **2005**, *11*, 2566. (b) Verdaguer, X.; Lledó, A.; López-Mosquera, C.; Maestro, M. A.; Pericàs, M. A.; Riera, A. *J. Org. Chem.* **2004**, *69*, 8053. (c) Konya, D.; Robert, F.; Gimbert, Y.; Greene, A. E. *Tetrahedron Lett.* **2004**, *45*, 6975. (d) Gibson, S. E.; Lewis, S. E.; Loch, J. A.; Steed, J. W.; Tozer, M. J. *Organometallics* **2003**, *22*, 5382. (e) Verdaguer, X.; Pericàs, M. A.; Riera, A.; Maestro, M. A.; Mahía, J. *Organometallics* **2003**, *22*, 1868. (f) Sturla, S. J.; Buchwald, S. L. *J. Org. Chem.* **2002**, *67*, 3398. (g) Hiroi, K.; Watanabe, T.; Kawagishi, R.; Abe, I. *Tetrahedron Lett.* **2000**, *41*, 891. (h) Hiroi, K.; Watanabe, T.; Kawagishi, R.; Abe, I. *Tetrahedron: Asymmetry* **2000**, *11*, 797. (i) Sturla, S. J.; Buchwald, S. L. *J. Org. Chem.* **1999**, *64*, 5547.

(4) (a) Mandal, S. K.; Amin, S. R.; Crowe, W. E. *J. Am. Chem. Soc.* **2001**, *123*, 6457. (b) Hicks, F. A.; Buchwald, S. L. *J. Am. Chem. Soc.* **1999**, *121*, 7026. (c) Hicks, F. A.; Buchwald, S. L. *J. Am. Chem. Soc.* **1996**, *118*, 11688.

(5) (a) Jeong, N.; Sung, B. K.; Choi, Y. K. *J. Am. Chem. Soc.* **2000**, *122*, 6771. (b) Jeong, N.; Sung, B. K.; Kim, J. S.; Park, S. B.; Seo, S. D.; Shin, J. Y.; In, K. Y.; Choi, Y. K. *Pure Appl. Chem.* **2002**, *74*, 85. (c) Jeong, N.; Kim, D. H.; Choi, J. H. *Chem. Commun.* **2004**, 1134. (d) Jeong, N. In *Modern Rhodium-Catalyzed Organic Reactions*; Evans, P. A., Ed.; Wiley-VCH: Weinheim, 2005; Chapter 11, pp 215−240.

(6) (a) Shibata, T.; Takagi, K. *J. Am. Chem. Soc.* **2000**, *122*, 9852. (b) Kwong, F. Y.; Lee, H. W.; Lam, W. H.; Qiu, L.; Chan, A. S. C. *Tetrahedron: Asymmetry* **2006**, *17*, 1238.

(7) (a) Kim, D. E.; Choi, C.; Kim, I. S.; Jeulin, S.; Ratovelomanana-Vidal, V.; Genêt, J.-P.; Jeong, N. *Synthesis* **2006**, *23*, 4053. (b) Kim, D. E.; Choi, C.; Kim, I. S.; Jeulin, S.; Ratovelomanana-Vidal, V.; Genêt, J.-P.; Jeong, N. *Adv. Synth. Catal.* **2007**, *349*, 1999.

(8) (a) Kobayashi, T.; Koga, Y.; Narasaka, K. *J. Organomet. Chem.* **2001**, *62*, 73. (b) Schmid, T. M.; Consiglio, G. *Chem. Commun.* **2004**, 2318.

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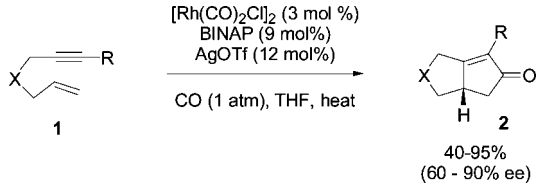
SCHEME 1. Enantioselective Catalytic Pauson−Khand Reaction



In an earlier optimization effort for the reaction *under atmospheric pressure of CO*, our attention was directed to two key steps in the reaction: a complexation of enyne to metal (step **a** in Scheme 2) and an oxidative metalla-cyclopentene formation (step **b**).

The replacement of one carbon monoxide on **3**, a presumed active species, under 1 atm of CO by an olefin (step **a**) requires a substantial amount of energy.[7] This step should be significantly influenced by the bond strength between rhodium and carbon monoxide. For example, with a better electron-donating ancillary ligand, the π back-bonding between the metal and carbon monoxide becomes stronger, and thus more energy is required to make the reaction proceed. On the other hand, the oxidative formation of the metalla-cyclopentene **7** (step **b**) is presumed to be accelerated by the presence of the better electron donor secondary ligands. Thus, the electronic requirement in the ligands for the rate acceleration of step **b** is opposed to that of step **a**.

To obtain insight, we extensively examined the effects of various atropisomeric ligands (Figure 1) on the chemical yield and enantioselectivity of the Rh(I)-catalyzed PKR under thermal condition. It was found that the overall reaction is influenced not only by the electronic character of the ligand but also by the dihedral angle of the ligands, when they are bound to the metal center.[7] Ligands either with the electron-rich phosphorus or with small dihedral angles, when they are bound to the metal,[7b] accelerated the reaction substantially, indicating that step **b** is more likely a rate-determining step for most cases. However, this rate acceleration is associated with complications because step **d** became competitive under such circumstances.

As a result, ligands having the electron-deficient phosphorus, such as **L4** and **L8**, slowed the reaction down significantly but provided significantly improved chemical yield with a better enantioselectivity.

Meanwhile, Narasaka and co-workers showed that even thermal Rh(I)-mediated PKR reaction proceeded faster under a reduced pressure of CO.[8a] In a subsequent study, Consiglio and Schmidt performed the first highly enantioselective reaction with substrate **1c-1** at ambient temperature by a slow release of CO (96% ee for the PKR product).[8b] These results can be explained

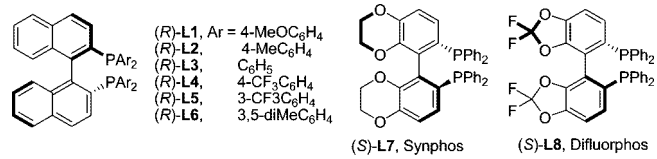
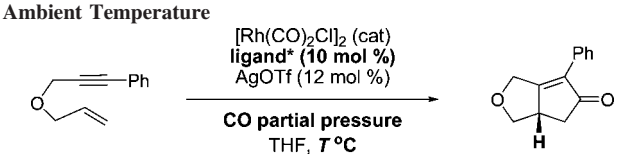


FIGURE 1. Ligands previously examined to optimize the asymmetric PKR.

TABLE 1. Effect of CO Pressure on Asymmetric PKR by Rh(I) at Ambient Temperature



	entry			
condition	1	2	3	4
cat (mol %)	3	3	5	5
CO (atm)	1	0.1	0.1	0.05
temp (°C)	80	18−20	18−20	18−20
ligands	yield/ee(%)			
(*R*)-**L3**	72/85	70/91	**77/93**	70/93
(*R*)-**L6**	77/75	86/90	**95/94**	90/91

by the proposition of a different pathway (**a′** and **b′**) in which intermediate **5** played a role. In addition, they were able to provide evidence for a new reaction pathway involving [Rh(bisphosphane ligand)(solvent)$_n$]$^+$ as an active catalytic species instead of [Rh(bisphosphane ligand)(CO)$_n$]$^+$, a presumed active species under 1 atm of CO. However, this beneficial effect on stereoselectivity was obtained at the cost of PKR product (58% even after the complete consumption of **1c-1**) because of the insufficient CO concentration. Thus, it is desirable to identify the reaction condition providing an excellent enantioselectivity for a wide range of substrates without the sacrifice of the PKR product.

To this end, it is still necessary to keep the CO concentration as low as possible throughout the reaction to discourage the regeneration of **3** after each catalytic cycle. In addition, it is envisioned that the use of the electron-deficient ancillary ligands could provide a distinctive improvement. Those ligands are expected to make the π back-bonding between the metal and carbon monoxide weaker and make the ratio between **3** and **5** favor **5**; the reaction temperature can be lowered considerably. Furthermore, these ligands would make the potential rate-determining step **b** slower and thus may exaggerate the energy difference between two competing diastereomeric intermediates.

SCHEME 2. Proposed Mechanism of Enantioselective Catalytic Pauson−Khand Reaction

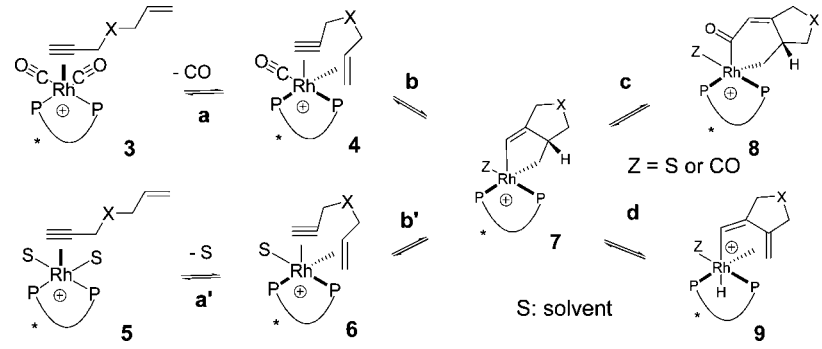
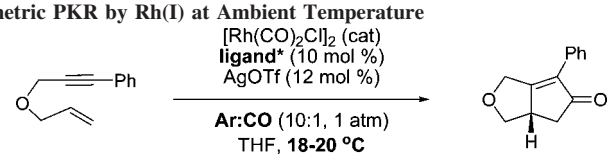


TABLE 2. Ligand Effects on Asymmetric PKR by Rh(I) at Ambient Temperature



1a-7 **2a-7**

	ligand	dihedral angle of ligand (L) in [RhCl(CO)(L)] (deg) [a]	δ of ^{31}P (ppm) [b]	**2a-7**, yield/ee (%)
1	(*R*)-4-MeOC$_6$H$_4$-BINAP (**L1**)	78.3	−16.9	52/87
2	(*R*)-4-MeC$_6$H$_4$-BINAP (**L2**)	*c*	−15.8	80/94
3	(*R*)-BINAP (**L3**)	78.3	−14.4	77/93
4	(*S*)-Synphos (**L7**)	73.0	−14.3	70/−91[e]
5	(*R*)-4-CF$_3$C$_6$H$_4$-BINAP (**L4**)	78.0	−13.8	72/87[d]
6	(*R*)-3-CF$_3$C$_6$H$_4$-BINAP (**L5**)	*c*	−13.7	71/89[d]
7	(*R*)-3,5-diMeC$_6$H$_4$-BINAP (**L6**)	*c*	−13.6	**95/94**
8	(*S*)-Difluorphos (**L8**)	72.2	−12.3	66/−93[e]

[a] Structures minimized by Molecular Mechanics calculations (CAChe MM2 program).[7b,9] [b] We correlated the electron density on phosphorus through the ^{31}P NMR spectra of the free ligands.[7b,10] [c] This number has not been calculated but is assumed to be similar to that of **L3**. [d] The reaction was carried out at 40 °C. [e] The negative sign means that the major enantiomer is the antipode.

In addition, it is expected to suppress step **d** and to afford a higher PKR product yield.

Results and Discussion

We first wished to determine the lower limit of the CO partial pressure with the reaction temperature variation. Two typical examples are given in Table 1. Unsurprisingly, the reaction with ligand **L3** or **L6** did not proceed at all at ambient temperature when CO pressure was 1 atm. This was mainly because most rhodium species of the reaction were present as **3**, in which the replacement of CO by olefin (**3** to **4**) might require the high energy. Upon reducing the partial pressure of CO to 0.1 atm, the reaction started smoothly at ambient temperature and was completed in several hours. The yield reached a maximum plateau without any loss of stereoselectivity under these conditions when the reaction was carried out with 5 mol % of catalyst under 0.1 atm of CO at ambient temperature (entries 3 and 4 in Table 1).

The effects of the ligands on the reaction rate and enantioselectivity were then examined. These effects are also evident and follow faithfully the trend reported for the thermal condition that we reported previously (Table 2).[7] Under a reduced pressure of CO, the reaction, with a few exceptions, proceeded smoothly at ambient temperature regardless of the electronic and steric characters of ligands. Ligands possessing the more electron-rich phosphorus (**L1**−**L3** and **L7**) accelerated the reaction considerably. In addition, the ligands (**L7** and **L8**) having narrower dihedral angles in the metal-bound Rh(I) complex accelerated the reaction. However, irrespective of the factor of acceleration, the acceleration of the reaction rate was associated with a loss of chemical yield of the desired PKR product as we have seen in the thermal reaction.

On the other hand, when the reaction was performed using catalysts having the electron-deficient phosphorus atom, the characteristics of the reaction varied according to the ligands employed. Binap-based ligands (**L4** and **L5**) behaved inconsistently at the inception. The reaction did not start reliably and was markedly slow. For consistent initiation, a somewhat elevated reaction temperature (40 °C) is required. Again, even this mildly forcing condition resulted in the loss of chemical yield, especially under a reduced pressure of CO (entries 5 and 6 in Table 2). Another interesting electron-deficient ligand **L8**, contrary to **L4**, with a narrower dihedral angle made the reaction proceed at ambient temperature smoothly, but the acceleration again is tainted by the significant loss of PKR product because of the competition of a side reaction.

Finally, we found that (*R*)-3,5-diMeC$_4$H$_4$-BINAP (**L6**), which has the electron-deficient phosphorus atom and the relatively wider dihedral angle, turned out to be the ligand of choice and provided a high chemical yield (95%) and excellent enantiomeric excess (94%) (entry 7 in Table 2).[15] From the fact that **L6** is superior to **L5**, which is similar to **L6** except for the substitutions on the phenyl ring, in overall aspects of the reaction, we could assume that the extra steric factor is playing an additional important role in the transition state.

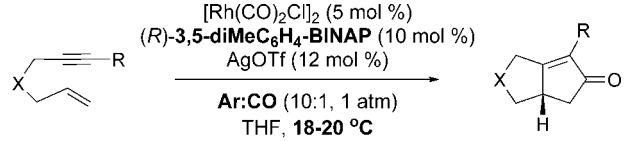
Thus, we examined the scope of this reaction with a variety of substrates based on this catalyst (Table 3).[15] A wide variety of oxygen-tethered substrates (**1a**) provided the desired products (**2a**) in excellent chemical yield and enantioselectivity (entries 2−11 in Table 3). The enantioselectivities are impressive for all of the substrates giving ee's greater than 90%. Although **1a**-**2** bearing an alkyl substituent on the alkyne provided a somewhat lower chemical yield, those substrates having aryl substituents on the alkyne (**1a**-**3** through **1a**-**10**) provided nearly quantitative yields. The only exceptions are **1a**-**9** and **1a**-**11**, in which the alkynes have an electron-withdrawing substituent, which led to a slightly lower stereoselectivity.

Nevertheless, the effectiveness of this condition is well proved by comparison of the enantioselectivity with that obtained using the previously reported Rh(I)-catalyzed conditions, which clearly shows that the reaction at ambient temperature is superior to any of the previously reported protocols in terms of the chemical yield and enantioselectivity.

(9) All molecular geometries incorporating diphosphine ligands in Rh(CO)-Cl(L*) complexes were optimized with the same molecular mechanics program (CAChe Worksystem Pro 5.0). See ref 7b.

(10) Andersen, N. G.; Parvez, M.; Keay, B. A. *Org. Lett.* **2000**, *2*, 2817.
(11) (a) Kwong, F. Y.; Lee, H. W.; Qiu, L.; Lam, W. H.; Li, Y. M.; Kwong, H. L.; Chan, A. S. C. *Adv. Synth. Catal.* **2005**, *347*, 1750. (b) Kwong, F. Y.; Li, Y. M.; Lam, W. H.; Qiu, L.; Yeung, C. H.; Chan, K. S.; Chan. A. S. C., *Chem. Eur. J.* **2005**, *11*, 3872.
(12) Fuji, K.; Morimoto, T.; Tsutsumi, K.; Kakiuchi, K. *Tetrahedron Lett.* **2004**, *45*, 9163.
(13) Shibata, T.; Toshida, N.; Takagi, K. *J. Org. Chem.* **2002**, *67*, 7446.
(14) Fan, B. M.; Li, S.; Xie, J.; Wang, L.; Tu, Y.; Zhou, Q. L. *Science in China, Ser. B: Chem.* **2006**, *49*, 81.
(15) Please refer to Supporting Information.

TABLE 3. Asymmetric PKR by Rh(I) at Ambient Temperature

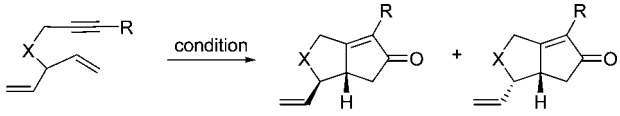


1 2

X	substrate	R	t (h)	yield/ee (%) this study	yield/ee (%) previous record[a]
O (**1a**)	**1**	H	0.5	18/99	
	2	Me	0.5	45/99	85/86[5a]
	3	4-MeOC$_6$H$_4$	3	82/92	93/93[11b]
	4	2-MeOC$_6$H$_4$	3	99/88	
	5	4-MeC$_6$H$_4$	3	95/90	83/69[14]
	6	3,5-diMeC$_6$H$_3$	5	99/92	61/93[12]
	7	C$_6$H$_5$	3	99/92	92/88[11b]
	8	4-ClC$_6$H$_4$	2	95/90	82/79[13]
	9	2-ClC$_6$H$_4$	2	99/77	
	10	4-CF$_3$C$_6$H$_4$	6	99/84	80/90;[7] 42/96[6b]
	11	3,5-diCF$_3$C$_6$H$_3$	12[b]	40/71	99/74[14]
			6[c]	99/63	
Ts-N (**1b**)	**1**	H	0.5	27/99	
	2	Me	1	96/98	98/88[11a]
	3	4-MeOC$_6$H$_4$	4[d]	99/75	74/89[7]
	4	C$_6$H$_5$	12	31/60	58/91[12]
			5[d]	99/72	
	5	4-CF$_3$C$_6$H$_4$	6[d]	99/70	90/71[7]
(EtO$_2$C)$_2$C (**1c**)	**1**	H	0.5	60/99	58/98[8b]
	2	Me	1	50/96	47/91[12]
	3	4-MeOC$_6$H$_4$[e]	12	NR	89/92[4b,e]
			6[f]	98/74	
	4	C$_6$H$_5$	12[g]	40/68	83/81[12]
			12[f]	96/67	
	5	4-CF$_3$C$_6$H$_4$[e]	12[f]	NR	88/93[4b]
			12[f]	96/63	

[a] The best results previously reported in terms of the enantioselectivity for the corresponding substrates were picked from the literature. [b] 70% conversion. [c] Reactions were carried out at 40 °C. [d] [Rh(CO)$_2$Cl]$_2$ (10 mol %), (*R*)-3,5-diMeC$_4$H$_4$-BINAP (20 mol %), AgOTf (24 mol %) in THF at 40 °C under Ar:CO (10:1, 1 atm). [e] The comparison is made with the result obtained by Ti(II) catalyst. [f] [Rh(CO)$_2$Cl]$_2$ (10 mol %), (*R*)-3,5-diMeC$_4$H$_4$-BINAP (20 mol %), AgOTf (24 mol %) in THF at 60 °C under Ar:CO (10:1, 1 atm). [g] 90% conversion.

TABLE 4. Asymmetric Desymmetrization of Dienynes by Enantioselective PKR at Ambient Temperature



1b-6, X = Ts-N; R = Me
1a-12, X = O, R = Ph
2b-6-a
2a-12-a
2b-6-b
2b-12-b

sub	condition[a]	ligand	t (h)	product **2**, yield/ee (%) *ds*-**a**	*ds*-**b**
1b-6	*a*[5c]	(*R*)-**L2**	0.5	11/52	61/80
	b	(*R*)-**L6**	1	22/56	75/71
	b	(*S*)-**L8**	1	19/42	**79/86**
1a-12	*a*[5c]	(*R*)-**L2**	2.5	60/86	
	a	(*R*)-**L6**	2	88/84	
	c	(*S*)-**L8**	2	**91/95**	

[a] Conditions: (*a*) [Rh(CO)$_2$Cl]$_2$ (3 mol %), (*R*)-4-*tol*-BINAP (9 mol %), AgOTf (12 mol %) in THF at 90 °C under CO (1 atm). (*b*) [Rh(CO)$_2$Cl]$_2$ (10 mol %), ligand (20 mol %), AgOTf (24 mol %) in THF at 10 °C under Ar:CO (10:1, 1 atm). (*c*) [Rh(CO)$_2$Cl]$_2$ (5 mol %), ligand (10 mol %), AgOTf (12 mol %) in THF at 18−20 °C under Ar:CO (10:1, 1 atm).

These conditions worked for other classes of substrates as well but exhibited a certain limitation in some cases. For example, **1b-2**, whose alkyne has an alkyl substituent, afforded **2b-2** in excellent enantioselectivity (98%) as well as high chemical yield (96%). However, when the alkyl group on the alkyne was replaced by aryl groups, the enantioselectivity decreased substantially (70−74%).

A similar trend is observed for the malonate-tethered substrates (**1c**). Substrate **1c-1** was transformed into the corresponding PKR product (**2c-1**) in 60% chemical yield with 99% ee. These numbers are as good as or slightly better than those reported by Consiglio.[8b] Further extension of these conditions to substrate (**1c-2**) having a methyl on the alkyne gave excellent enantioselectivity (96% ee). However, the reaction suffers from a substantial loss of chemical yield (50%). Disappointingly, this condition did not work for the enynes (**1c-3** through **1c-5**) having an aryl substituent, unless relatively forcing conditions were applied. Moreover, these conditions still need to be optimized for substrates bearing an acidic proton on the terminal alkyne, such as **1a-1** and **1b-1**.

The desymmetrization of the dienynes was also reexamined with this protocol, and significantly improved results were obtained.[5c] First, the existence of an extra vinyl group in **1b-6** accelerated the reaction drastically, but the reaction was tainted by serious side product formation at 20 °C. This problem was solved by lowering the reaction temperature further to 10 °C, and in this way, a nearly quantitative yield of a combined diastereomeric mixture of PKR products **2b-6** was obtained. In addition, the chemical yield and enantioselectivity of the major diastereomer **2b-6-b** were significantly improved when (*S*)-Difluorphos (**L8**) was used in these specific cases. The beneficial effect is more evident with an oxygen-tethered substrate **1a-12**. A nearly quantitative yield (91%) of a single diastereomer and almost perfect stereoselection (95% ee) are realized.

However, a couple of limitations need to be mentioned. For example, the preparation of [4.3.0] bicyclic skeleton from 1,7-heptaenyne failed, and substrates having olefins other than terminal are reluctant to react under the condition.

Conclusion

We have described a successful asymmetric Pauson-Khand-type reaction mediated by Rh(I) at ambient temperature by identifying the proper ligand, (*R*)-3,5-diMeC$_4$H$_4$-BINAP (**L6**) and providing reaction conditions with a low carbon monoxide concentration. The scope and limitations of this protocol were thoroughly determined. While substrates (**1a**) having an oxygen tether responded to this condition very well, *N*-tosyl (**1b**) and malonate tethered substrates (**1c**) remained a challenge. Further optimization and the application of this protocol to the synthesis of complex molecules will be reported in due course.

Experimental Section

Catalytic Enantioselective Pauson−Khand Reaction at Ambient Temperature. General Procedure. [Rh(CO)$_2$Cl]$_2$ (3.4 mg, 0.009 mmol, 5 mol %) and (*R*)-3,5-diMeC$_4$H$_4$-BINAP (**L6**) (12.8 mg, 0.017 mmol, 10 mol %) were placed in THF (2 mL), and the mixture was stirred for 30 min at 20 °C under atmospheric pressure of argon. A solution of AgOTf (4.5 mg, 0.017 mmol, 10 mol %) in THF (1 mL) was added, and the resultant reaction mixture was stirred for another 30 min at 20 °C. The argon atmosphere was replaced with CO in argon (1:10, 1 atm), and then a solution of **1a-6** (30 mg, 0.174 mmol) in THF (1 mL) was introduced. The reaction mixture was stirred at 20 °C. After completion of the reaction, a gaseous mixture was released in the hood. The crude reaction mixture was concentrated in vacuo, and then the residue

was purified by column chromatography on silica gel using *n*-hexane/ethyl acetate mixture as an eluent to afford PKR product. The enantiomeric excess of the product was determined by chiral HPLC analysis using Daicel columns.

3a,4-Dihydro-6-(2-methoxyphenyl)-1*H*-cyclopenta[*c*]furan-5-one (2a-4). Yield 99%, colorless oil. $[\alpha]^{25}_{D} = -138.5$ (*c* 0.6, CH_2Cl_2). IR (KBr): 1701 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 2.32 (dd, $J = 17.7$, 3.3 Hz, 1 H), 2.82 (dd, $J = 17.7$, 5.9 Hz, 1 H), 3.32 (dd, $J = 15.0$, 6.0 Hz, 1 H), 3.37 (m, 1 H), 3.81 (s, 3 H), 4.37 (dd, $J = 15.0$, 6.0 Hz, 1 H), 4.39 (d, $J = 18.0$ Hz, 1 H), 4.64 (d, $J = 18.0$ Hz, 1 H), 6.93 (d, $J = 8.2$ Hz, 1 H), 7.02 (t, $J = 7.4$ Hz, 1 H), 7.34 (t, $J = 7.4$ Hz, 1 H), 7.51 (d, $J = 8.2$ Hz, 1 H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 40.2, 43.5, 55.5, 67.6, 72.5, 111.0, 119.3, 120.8, 130.2, 130.6, 131.1, 156.9, 179.6, 207.6. HRMS (FAB+): *m*/*z* $[M + H]^+$ calcd for $C_{14}H_{15}O_3$ 231.1021, found 231.1028. The ee value was determined as 87% by HPLC analysis using a chiral column (DAICEL CHIRALPAK AD-H, *n*-Hex/IPA = 4/1, flow 0.8 mL/min, detection at 254 nm); retention times 10.11 min (major) and 12.26 min (minor).

3a,4-Dihydro-6-(2-chloro phenyl)-1*H*-cyclopenta[*c*]furan-5-one (2a-9). Yield 99%, colorless oil. $[\alpha]^{25}_{D} = -58.5$ (*c* 0.65, CH_2Cl_2). IR (KBr): 1710 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 2.36 (dd, $J = 17.9$, 3.2 Hz, 1 H), 2.87 (dd, $J = 17.9$, 6.0 Hz, 1 H), 3.36 (dd, $J = 12.0$, 6.0 Hz, 1 H), 3.42 (m, 1 H), 4.40 (d, dd, $J = 12.0$, 6.0 Hz, 1 H), 4.42 (d, $J = 15.0$ Hz, 1 H), 4.74 (d, $J = 15.0$ Hz, 1 H), 7.29−7.45 (m, 4 H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 39.9, 43.8, 67.0, 72.3, 126.9, 129.7, 130.1, 130.2, 131.3, 133.4, 134.1, 180.6, 206.5. HRMS (FAB+): *m*/*z* $[M + H]^+$ calcd for $C_{13}H_{12}ClO_2$ 235.0526, found 235.0528. The ee value was determined as 77% by HPLC analysis using a chiral column (DAICEL CHIRALPAK AD-H, *n*-Hex/IPA = 4/1, flow 0.8 mL/min, detection at 254 nm); retention times 9.03 min (major) and 9.77 min (minor).

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Supporting Information Available: Experimental procedures and full spectroscopic data for all new compounds and HPLC data for all enantiomers including the previously reported compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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