Rhodium Complex-Catalyzed Pauson−Khand-Type Reaction with Aldehydes as a CO Source

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With aldehydes as a CO source under solvent-free conditions, rhodium complex efficiently catalyzed an intramolecular carbonylative alkene−alkyne coupling (Pauson−Khand-type reaction) and various bicyclic enones were obtained in high yield. Experiments under argon flow and a ^{13}C-labeling experiment suggested that almost no free carbon monoxide was generated in this reaction. When noncationic rhodium complex with chiral phosphine was used as a chiral catalyst, the reaction proceeded enantioselectively to give various chiral cyclopentenones in up to 90% ee under solvent-free conditions.

Introduction

The transition metal-catalyzed carbonylative reaction is one of the major procedures for preparing carbonyl compounds. Carbonylative alkene−alkyne coupling (Pauson−Khand-type reaction) has drawn particular attention[1] and various transition metal complexes (Co,[1c,2] Ti,[3] Ru,[4] Rh[5] complexes) have been reported as efficient catalysts. Since the first reaction with a chiral Ti complex,[6] several highly enantioselective Pauson−Khand(-type) reactions have been reported with chiral Ir,[7] Rh,[8] and Co[9] complexes. On the other hand, transition metal-mediated and -catalyzed decarbonylation from carbonyl compounds is a fundamental process and has been closely studied since the 1960s, in the early stage of organometallic chemistry.[10] Rh complexes are effective catalysts[11] and catalytic decarbonylation under mild reaction conditions is still an intriguing topic.[12] While the use of a decarbonylative step in synthetic procedures, including total syntheses, has already been reported,[13] the synthetic utilization of the generated carbon monoxide has been largely ignored.[14] In this study, we noted that decarbonylation and Pauson−Khand-type reactions can be catalyzed by the same transition metal (Rh) complex, and that if two catalytic cycles of decarbonylation and carbonylation occur in concert, the carbon monoxide generated by the decarbonylation of aldehyde can be efficiently used as a CO source for Pauson−Khand-type reactions (Figure 1).

We report here rhodium complex-catalyzed carbonylation using aldehydes as a CO source under an argon atmosphere.[15,16] A mechanistic study of CO transfer and an enantioselective reaction with chiral Rh complex are also described.

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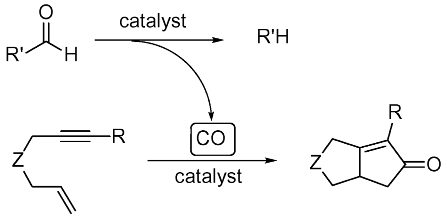
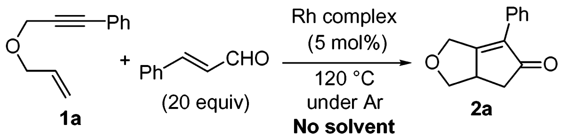


FIGURE 1. Carbonylative coupling with CO generated by decarbonylation.

TABLE 1. Screening of Various Rh Complexes



entry	catalyst[a]	time, h	yield, %
1	$^1/_2$ $[RhCl(CO)_2]_2$	4	13
2	$^1/_2$ *trans*-$[RhCl(CO)dppp]_2$	4	67
3	$^1/_2$ $[Rh(cod)Cl]_2$+dppp	6	75
4	$Rh(dppe)_2Cl$	12	37
5	$Rh(dppp)_2Cl$	2	98
6	$Rh(dppb)_2Cl$	20	43

[a] dppp = 1,3-bis(diphenylphosphino)propane, dppe = 1,2-bis(diphenylphosphino)ethane, dppb = 1,4-bis(diphenylphosphino)butane.

Results and Discussion

We first examined intramolecular alkene−alkyne coupling using $[Rh(CO)_2Cl]_2$[5a] in the presence of cinnamaldehyde as a CO source without a solvent at 120 °C under an atmospheric pressure of argon. Enyne **1a** was consumed to give a complex mixture, but cyclopentenone **2a** was obtained in poor yield (Table 1, entry 1). This result implies that the carbonyl moiety of aldehyde is incorporated into cyclopentenone, as expected. Under the same reaction conditions, a carbonyl complex with a dppp ligand[5b] gave a much better result (entry 2). Entry 3 shows that dppp complex prepared in situ without CO ligand also has high catalytic activity. Among the isolated rhodium complexes with bidentate phosphine ligands, dppp was the best choice to give the product in very high yield (entries 4−6).

We next examined the effect of aldehydes and the amount of aldehyde as a CO source using $Rh(dppp)_2Cl$ as a catalyst (Table 2). When cinnamaldehyde was used, 5 equiv of aldehyde was sufficient for high yield (entry 2). Even with almost an equivalent amount of the CO source, the reaction proceeded smoothly to give **2a** in good yield (entry 3). Carbonylative coupling at a larger scale proceeded within the same reaction time and simple distillation gave the pure product **2a** in almost the same yield (entry 4). This means that all of these procedures can be performed in a completely solvent-free system. It is noteworthy that this reaction, which includes both catalytic decarbonylation and Pauson−Khand-type coupling, proceeds with a moderate yield at as low as 60 °C (entry 5). In the case of benzaldehyde, excess amounts are necessary for a high yield and the use of almost an equivalent amount of aldehyde and a lower reaction temperature gave poor results (entries 6−8). When 2-hexenal was compared with hexanal, α,β-unsaturated aldehyde was the better CO donor (entries 9 and 10). These results imply that cinnamaldehyde is the best CO source among these four aldehydes, and that a phenyl group and carbon−carbon double bond are important components of the CO donor. On the basis of the results of decarbonylation in an NMR tube with $Rh(dppp)_2Cl$ (5 mol %) at 120 °C for 24 h in toluene-d_8, cinnamaldehyde is mostly consumed to give styrene, but only about 5% of benzaldehyde is consumed.

TABLE 2. Carbonylative Coupling of 1a with Various CO Sources[a]

$$\mathbf{1a} + \text{CO source} \xrightarrow[\substack{120\ ^\circ\text{C} \\ \textbf{No solvent}}]{\substack{Rh(dppp)_2Cl \\ (5\ \text{mol\%})}} \mathbf{2a}$$

entry	CO source (equiv)	time, h	yield, %
1	cinnamaldehyde (20)	2	98
2	cinnamaldehyde (5)	3	93
3	cinnamaldehyde (1.2)	3	83
4[b]	cinnamaldehyde (1.2)	3	80
5[c]	cinnamaldehyde (20)	24	54
6	benzaldehyde (20)	3	87
7	benzaldehyde (1.2)	4	12
8[c]	benzaldehyde (20)	24	18
9	2-hexenal (20)	2	68
10	hexanal (20)	2	30
11	CO gas	24	31
12[d]	CO gas	5	85

[a] The reaction was carried out by using the 0.3 mmol scale and **2a** was purified by preparative TLC, except entry 4. [b] The reaction was carried out by using the 2.1 mmol scale and **2a** was purified by bulb-to-bulb distillation. [c] The reaction was carried out at 60°C. [d] Xylene was used as solvent.

When the present reaction was examined under an atmospheric pressure of CO without solvent, a much longer reaction time was needed and enone **2a** was obtained in low yield from a complex mixture (entry 11). Even under typical reaction conditions for a Pauson−Khand-type reaction (under an atmospheric pressure of CO in xylene), the results (reaction time and yield) were inferior to those with cinnamaldehyde as a CO source (entry 12). These results show the advantage of a solvent-free Pauson−Khand-type reaction using cinnamaldehyde as a CO source.

Various enynes were examined by using an excess amount (20 equiv: method A) and almost an equivalent amount (1.2 equiv: method B) of cinnamaldehyde as a CO source in the presence of $Rh(dppp)_2Cl$ (Table 3). Enynes **1b**,**c** bridged by heteroatoms such as oxygen and nitrogen gave good results with a short reaction time (2 h) to give the corresponding enones **2b**,**c** (entries 1 and 2). The yield by method B is good, but is lower than that by method A. Enyne **1d** with an alkyl substituent on alkyne was also an appropriate substrate for providing **2d** in high yield (entry 3). The carbonylative coupling of enynes **1e**,**f** bridged by a carbon chain took a longer reaction time than that of enynes bridged by heteroatoms, but enones **2e**,**f** were obtained in acceptable yields (entries 4 and 5) and methods A and B gave almost the same results. Enyne **1g** with a 1,1-disubstituted olefin

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(16) Independently, Pauson−Khand-type reaction with pentafluorobenzaldehyde as a CO source in xylene was reported, see: Morimoto, T.; Fuji, K.; Tsutsumi, K.; Kakiuchi, K. *J. Am. Chem. Soc.* **2002**, *124*, 3806−3807.

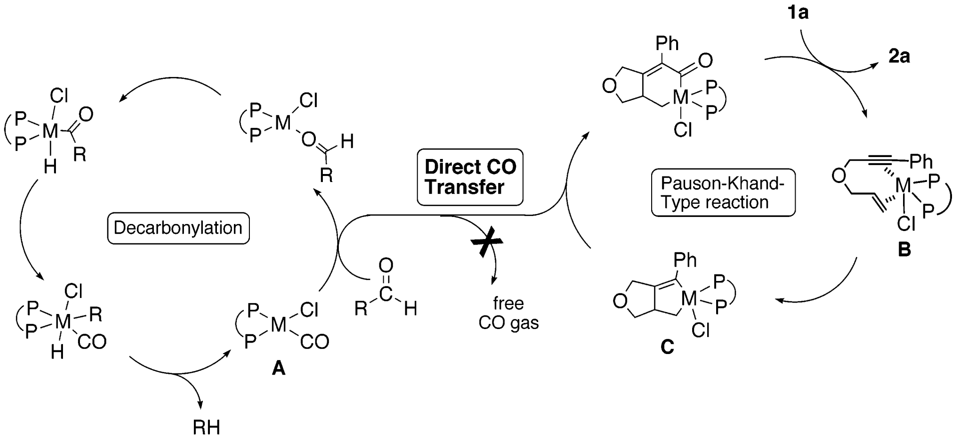
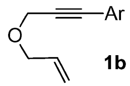
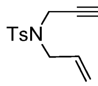
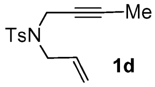
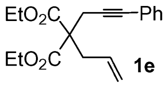
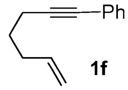
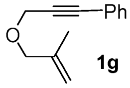


FIGURE 2. Proposed mechanism by direct CO transfer.

TABLE 3. Carbonylative Coupling of Various Enynes with Cinnamaldehyde as a CO Source

entry	enyne	method A[a]		method B[b]	
		time/h	yield/%	time/h	yield/%
1	 **1b** Ar: p-MeO-C_6H_4	2	88	3	71
2	 **1c**	2	98	3	85
3	 **1d**	2	90	3	72
4	 **1e**	5	56	6	58
5	 **1f**	5	65	7	68
6	 **1g**	24	75	24	78

[a] Rh(dppp)$_2$Cl:enyne:cinnamaldehyde = 0.05:1.0:20. [b] Rh(dppp)$_2$Cl:enyne:cinnamaldehyde = 0.05:1.0:1.2.

is a rather inactive substrate in the Pauson–Khand-type reaction, but coupling proceeded to give **2g** in good yield by both methods A and B.

Figure 2 shows the reaction mechanism with **1a** as a representative enyne. The catalytic cycle on the left is the established mechanism of decarbonylation from an aldehyde[10] and carbon monoxide is introduced into metallacyclopentene **C**. As a result, the carbonyl moiety of aldehyde is incorporated into cyclopentenone.[17] Moreover, we propose a novel direct CO transfer from a decarbonylative cycle to a Pauson–Khand-type reaction. Thus, almost no free CO was generated and CO for carbonylative coupling was mainly provided by metal carbonyl complex **A**, rather than by free CO. The following results (Table 4 and Figure 3) support this hypothesis.

Carbonylative coupling with cinnamaldehyde as a CO source was examined under argon flow conditions (Table 4). We investigated different flow rates, but the results were almost the same (entries 1 and 2). Even when argon was bubbled into the reaction mixture, the yield was not significantly changed (entry 3). If free CO exists in the liquid phase or gas phase of the reaction vessel, different flow rates of argon and bubbling of argon should signifi-

TABLE 4. Carbonylative Coupling under Ar Flow and Ar Bubbling Conditions

$$\mathbf{1a}\ \xrightarrow[\text{cinnamaldehyde (1.2 equiv)}\ 120\ ^\circ\text{C, 8 h}]{\text{Rh(dppp)}_2\text{Cl (5 mol\%)}}\ \mathbf{2a}$$

entry	condition of Ar	flow rate, mL/min	yield, %
1	flow	150	63
2	flow	750	66
3	bubbling	150	64

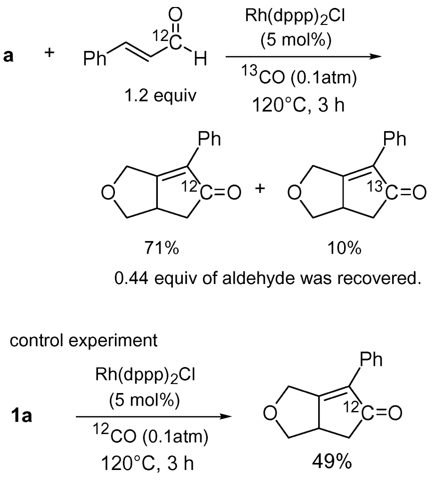


FIGURE 3. Label experiment with use of ^{13}CO.

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[17] A reaction mechanism with one catalytic cycle is also possible, where metal carbonyl complex **A** itself acts as a catalyst for carbonylative coupling. But this mechanism conflicts with highly enantioselective induction by chiral diphosphine (Table 6), since the dissociation of phosphine ligand from the metal center is needed for coordination of an enyne, which is an enantiomerically differentiated step.

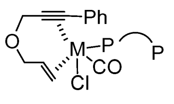


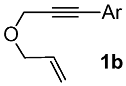
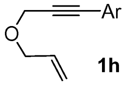
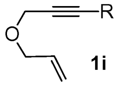
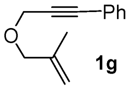
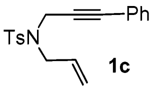
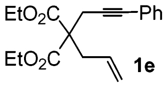
TABLE 5. Advantage of Enantioselective Coupling with Aldehyde under Solvent-Free Conditions

$$\mathbf{1a} \xrightarrow[\text{CO source, } 120\ ^\circ\text{C}]{[\mathrm{Rh(cod)Cl}]_2+2(S)\text{-tolBINAP (5 mol\%)}} \mathbf{2a}$$

entry	CO source	solvent	time, h	yield, %	ee, %
1	cinnamaldehyde	none	4	89	82
2[a]	CO gas	none	4	23	60
3	cinnamaldehyde	xylene	36	54	8
4	CO gas	xylene	36	51	10

[a] Chiral catalyst was prepared in xylene and enyne **1a** was added after removing xylene.

TABLE 6. Enantioselective Coupling of Various Enynes with Cinnamaldehyde as a CO Source[a]

entry	enyne	time/h	yield/%	ee/%
1	 **1b** Ar: p-MeO-C_6H_4	6	86	81
2	 **1h** Ar: p-Cl-C_6H_4	9	82	79
3	 **1i** R: $Ph(CH_2)_3$	2	72	90
4	 **1g**	18	41	82
5[b]	↑	36	59	81
6	 **1c**	4	99	56
7[b]	↑	12	82	69
8	 **1e**	4	79	45

[a] $[Rh(cod)Cl]_2$:tolBINAP:enyne:cinnamaldehyde = 0.05: 0.10: 1.0:20. The reaction was carried out at 120 °C. [b] Benzaldehyde was used as a CO source in place of cinnamaldehyde.

cantly affect carbonylative coupling. Therefore, these results imply that free CO is not generated in this reaction.

Next, carbonylative coupling was performed in the presence of cinnamaldehyde (1.2 equiv) under a partial pressure of ^{13}CO (Figure 3).[5c] Only 10% of the resulting cyclopentenone contained ^{13}CO. A control experiment showed that carbonylative coupling proceeded with CO gas as a CO source without aldehyde. A calculation based on the amount of recovered cinnamaldehyde (0.44 equiv) indicates that most of the consumed aldehyde (93%) was incorporated into cyclopentenone even under a CO atmosphere. These results also suggest that the carbonyl moiety of cyclopentenone is mainly supplied by the metal carbonyl complex rather than by free CO.

We further studied an enantioselective reaction using cinnamaldehyde as a CO source (Table 5). A chiral catalyst was prepared in situ from $[Rh(cod)Cl]_2$ and tolBINAP (2,2′-bis(di-*p*-tolylphosphino)-1,1′-binaphthyl) and was used in the carbonylative reaction under solvent-free conditions.[18] The coupling of enyne **1a** proceeded smoothly to give **2a** in good yield and ee (Table 5, entry 1).[19] When CO gas was used as a CO source under the same reaction conditions, both yield and ee significantly decreased (entry 2). When asymmetric carbonylative coupling was examined in xylene, the yield was moderate even with a longer reaction time but the ee was very poor both in the presence of cinnamaldehyde and under an atmospheric pressure of CO (entries 3 and 4). Rhodium cationic complex, which is prepared in situ from $[RhCl(CO)_2]_2$, chiral phosphine, and AgOTf, has been reported to be an efficient chiral catalyst.[8] Therefore, these results imply that the solvent-free conditions with aldehyde as a CO source have an advantage for a high yield and ee in enantioselective coupling catalyzed by a noncationic Rh complex.

Under the optimal reaction conditions, other allyl propargyl ethers were also transformed into chiral enones in high ee (Table 6, entries 1−5). In particular, enyne **1i** gave the best result of 90% ee (entry 3). In the case of enyne **1g**, benzaldehyde gave a better yield than cinnamaldehyde (entries 4 and 5). Although the reason for this result is unclear, benzaldehyde gave a significantly better ee than cinnamaldehyde only for allyl propargylamine **1c** (entries 6 and 7). The enantioselective coupling of allylpropargylmalonate **1e** also proceeded in good yield with moderate ee (entry 8).

Conclusions

We developed a rhodium complex-catalyzed Pauson−Khand-type reaction based on a new experimental protocol. In place of CO gas, which is very poisonous and must be handled with caution in an efficient fume hood, aldehyde was used as a CO source for carbonylation. The reaction proceeded efficiently even under solvent-free conditions to give various bicyclic enones in high yield. Argon flow and ^{13}C-labeling experiments indicated that almost no free CO exists in the reaction scheme and CO generated by the decarbonylation of aldehyde is directly incorporated into carbonylative coupling. Moreover, highly enantioselective coupling was also achieved by using chiral and noncationic Rh complex under solvent-free conditions.

Experimental Section

General. $[RhCl(CO)_2]_2$ and $[Rh(cod)Cl]_2$ were obtained commercially. *trans*-$[RhCl(CO)dppp]_2$[20] and RhL_2Cl (L = dppe, dppp, dppb) were prepared as reported in the literature.[21] Aldehydes were distilled from $CaCl_2$ prior to use.

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[18] A recent example of solvent-free enantioselective reaction with organometallic compounds: Sato, I.; Saito, T.; Soai, K. *Chem. Commun.* **2000**, 2471−2472.

[19] From the sign of optical rotation, the absolute configuration of obtained **2a** proved to be *S* (ref 3b). This means that the mechanism of asymmetric induction with aldehyde as a CO source by the Rh-tolBINAP system is the same as that with CO gas (refs 7 and 8).

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Experimental Procedure for the Pauson−Khand-Type Reaction with Cinnamaldehyde under Solvent-Free Conditions (Table 2, entry 4). Rh(dppp)$_2$Cl (101 mg, 0.105 mmol), enyne **1a** (362 mg, 2.10 mmol), and cinnamaldehyde (333 mg, 2.52 mmol) were placed in a flask under an atmosphere of argon and the mixture was stirred at 120 °C for 3 h. The flask was then attached to a bulb-to-bulb distillation apparatus. After removing styrene and a small amount of recovered cinnamaldehyde, the pure product **2a** was distilled (334 mg, 1.67 mmol, 80% yield).

General Procedure for the Enantioselective Pauson−Khand-Type Reaction with Cinnamaldehyde under Solvent-Free Conditions (Table 6). [Rh(cod)Cl]$_2$ (8.1 mg, 0.016 mmol), (*S*)-tolBINAP (22.4 mg, 0.033 mmol), enyne **1** (0.33 mmol), and cinnamaldehyde (872 mg, 6.60 mmol) were placed in a flask under an atmosphere of argon. The reaction mixture was then stirred at 120 °C for the number of hours shown in Table 6. After the exclusion of excess cinnamaldehyde, the crude product was purified by thin-layer chromatography (TLC) and pure bicyclic enone **2** was obtained. The ee was determined by HPLC analysis using a 4 mm × 250 mm chiral column (conditions: 254 nm UV detector, rt, flow rate of eluent = 1.0 mL/min).

2-Phenyl-7-oxabicyclo[3.3.0]oct-1-en-3-one (2a). Spectral data accorded with those in the literature.[5c,22] $[\alpha]^{28}_{D}$ 7.30 (*c* 1.25, CHCl$_3$). Ee was determined to be 82% by HPLC analysis, using Daicel Chiralpak AD (eluent = 10% 2-propanol in hexane; retention time = 12 min for minor isomer and 17 min for major isomer).

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Supporting Information Available: Listing of spectral data for new compounds and determination of ee by HPLC for all compounds (PDF). This material is available free of charge via the Internet at http://pubs.acs.org.

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