

Rhodium(I)-Catalyzed Intramolecular Pauson–Khand Reaction[†]

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Summary: Cocyclization of alkynes, alkenes, and carbon monoxide by rhodium(I) catalysts was realized for the first time. Contrary to the previously employed late transition metals, these catalysts possess tunable ligands that make this reaction more versatile.

Cocyclization of alkynes, alkenes, and carbon monoxide by transition metals (known as the Pauson–Khand reaction when dicobalt octacarbonyl complexes are used) has been accepted as one of the most powerful tools in the synthesis of cyclopentenones.^{1,2} This transformation offers a simple, efficient, and highly selective method to cyclopentenones from readily available starting materials. Recent advances in this class of reaction are quite impressive. These include the discovery of promoters,³ such as amine *N*-oxides and sulfoxides, for the reaction with a dicobalt hexacarbonyl–alkyne complex at ambient temperature and a catalytic version employing cobalt carbonyls,⁴ titanium(II),⁵ and ruthenium carbonyl.⁶ Successful catalytic reaction using dicobalt octacarbonyl in the super critical fluids of

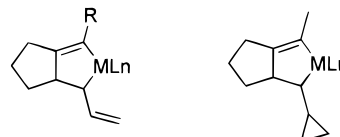


Figure 1. Proposed metallocycle intermediates for the six- and seven-membered ring formation.

carbon dioxide⁷ will constitute a major step forward toward the potential industrial application of this class of reactions.

Despite such significant progress in the development of the catalytic reaction, we were still in need of a new catalyst. Since the reacting species in the reactions employing late transition metals such as cobalt and ruthenium possess only nontunable ligands, e.g., carbon monoxide, there are serious limitations to expand the scope of the reaction further. Only early transition metal titanium catalysts have been able to extend its use to the enantioselective catalytic reaction so far.⁸ However, susceptibility of this catalyst to air and moisture required special care during the operation of the reaction. Thus, we hope to have a new stable catalyst bearing tunable ligands that will allow further elaboration to provide versatility of the reactions.²

Rhodium(I) has been used for the cycloaddition to give six- and seven-membered rings from acetylene–butadiene and acetylene–vinylcyclopropane, respectively.⁹ Metallacyclopentenones, depicted in Figure 1, were presumed as transient intermediates in these transformations. We envision that if carbon monoxide is inserted into these intermediates, a new catalytic version of the Pauson–Khand-like reaction can be achieved. Herein, we report our preliminary results dealing with the remarkably facile carbon monoxide incorporation in the reaction with rhodium(I) catalysts.

After many trial experimentations with the various rhodium catalysts given in Table 1, we were able to

[†] This paper is dedicated to Prof. E. J. Corey on the occasion of his 70th birthday.

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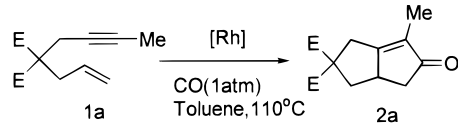
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Table 1. Rhodium(I)-Catalyzed Cocyclization of Enyne and CO^a


entry	catalyst (mol %)	additive (mol %)	reaction time (h)	conversion (%)	yield (%)
1	3a (5)	none	12	0	0
2	3a (5)	AgOH (10)	18	100	89
3	3b (5)	none	12	0	0
4	3b (5)	AgOH (10)	18	100	90
5	3c (5)	none	18	60	58
6	3c (5)	AgOH (10)	24	90	82
7	3d (2.5)	none	24	100	96

^a **3a**, RhCl(PPh₃)₃; **3b**, *trans*-RhCl(CO)(PPh₃)₂; **3c**, RhCl(CO)(dppe); **3d**, *trans*-[RhCl(CO)(dppp)]₂.

figure out the trend in the carbonylation reaction. In the early stages of this work, we often encountered erratic results, which were mainly attributed to the inconsistency of CO incorporation. We soon noticed that the purity of CO was critical to the success of the reaction. Thus, we ran all reactions in Table 1 under a CO atmosphere whose purity was greater than 99.9%.

All catalysts, RhCl(PPh₃)₃ (**3a**), *trans*-RhCl(CO)(PPh₃)₂ (**3b**), RhCl(CO)(dppe) (**3c**), and *trans*-[RhCl(CO)(dppp)]₂ (**3d**), tested for this transformation with **1a** turned out to be effective under 1 atm of CO in toluene. Catalysts **3a** and **3b** behaved similarly and required an additive, e.g., AgOTf, for the initial activation. Otherwise, they were totally inert in the absence of an additive (entries 1 and 3 in Table 1). Treatment of **1a** with Wilkinson's catalyst (**3a**) and catalyst **3b** with AgOTf in toluene at reflux for 18 h with a CO balloon provided **2a** in 89% and 90% yield after chromatographic isolation, respectively (entry 2 and 4 in Table 1).

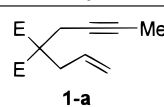
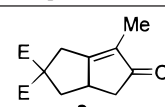
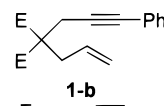
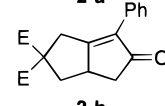
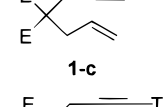
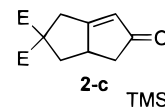
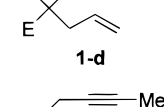
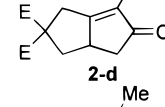
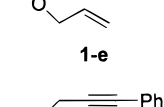
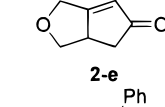
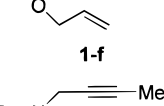
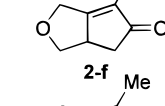
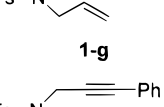
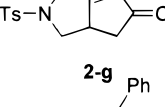
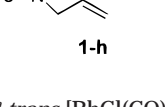
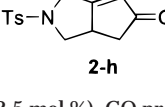
A mononuclear catalyst (**3c**)¹⁰ with a bidentate ligand, e.g., dppe, reacted in a similar manner with one distinction: The presence of silver triflate still accelerated the reaction but was not essential. The reaction rate was substantially slowed without it. The reaction of **1a** employing **3c** together with AgOTf proceeded to near completion in 24 h to give **2a** in 82% yield with recovery of starting material (10%). On the other hand, the reaction with **3c** alone only went halfway to completion after 18 h (entry 5 and 6 in Table 1).

The best reaction condition was using a dinuclear rhodium catalyst, *trans*-[RhCl(CO)(dppp)]₂ (**3d**).¹¹ Treatment of **1a** with 2.5 mol % of **3d** in toluene at reflux for 24 h under 1 atm of CO provided **2a** cleanly in 96% yield. No additive was required.

On the basis of these preliminary results, we first set up the experimental protocol with **3d** because of the stability of the catalyst and the operational simplicity of the reaction. All reactions, with a few exceptions, were carried out in the presence of a catalytic amount (2.5 mol %) of rhodium catalyst **3d** in toluene at 110 °C under 1 atm of carbon monoxide.

Various substrates tested under the standard protocol of the reaction conditions gave high chemical yields. The results are summarized in Table 2.

Table 2. *trans*-[RhCl(CO)(dppp)]₂ Catalyzed Intramolecular Cocyclization of Enyne and CO

enyne	product	yield (%)
		96
		99
		55
		0 (20) ^b
		60
		82
		94
		97

^a *trans*-[RhCl(CO)(dppp)]₂ (2.5 mol %), CO pressure (1 atm), 110 °C, 24 h, toluene. ^b RhCl(PPh₃)₃ (5 mol %), AgOTf (10 mol %), CO pressure (1 atm), 110 °C, 18 h, toluene.

This reaction was good for both the terminal and the internal alkynes (**1a,c** in Table 2). But a terminal alkyne **1c** was not as effective as internal one **1a** in this reaction. The efficiency of the reaction could be increased by mildly forcing conditions (2–3 atm of CO). Nearly quantitative chemical yields were obtained with substrates **1a** and **1b**. However, because the decrease in the reaction time and the marginal improvement of the chemical yield at the cost of operational simplicity were not significant, we decided to carry out all of the reactions with CO balloon.

The steric factor of substituents on alkynes also played a critical role. While alkyl- and aryl-substituted alkynes **1a** and **1b** provided **2a** and **2b** in excellent chemical yield, the trimethylsilyl-substituted alkyne **1d** remained inert under this condition. Trials using Wilkinson's catalyst with AgOTf looked somewhat promising but was not satisfactory either. Allyl propargyl ethers **1e** and **1f**, which generated a modest yield in the previous case,^{4b} provided **2e** and **2f** in good to excellent chemical yields as well. The allyl propargyl sulfonamides, **1g** and **1h**, also yielded the products **2g** and **2h** quantitatively, as usual.

Although the working mechanism is not clear yet, it may be different for each catalyst as hinted by the results given in Table 1. Elucidation of the mechanistic details will be the subject of further study.

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In summary, we have developed the first practical rhodium(I) catalyzed cocyclization of alkynes, olefins, and carbon monoxide. This reaction is highly efficient and mild. Since the catalysts contain tunable ligands, further efforts will be focused on the development of the enantioselective catalytic reaction and the reaction in supercritical fluids by modification of the ligands.

A representative procedure for the intramolecular rhodium(I)-catalyzed Pauson–Khand reaction as follows. 6-Methyl-2-[(4-methylphenyl)sulfonyl]-1,2,3,3a,4,5-hexahydrocyclopenta [c]pyrrol-5-one (Table 2, **2g**) was prepared in a 50-ml round-bottom flask by mixing *trans*-[Rh(Cl)(CO)(dppp)]₂ (21.9 mg, 0.019 mmol), *N*¹-allyl-*N*¹-(2-butyryl)-4-methyl-1-benzenesulfonamide (200 mg, 0.759 mmol), and toluene (5 mL). The flask was evacuated and recharged 3 times with carbon monoxide under balloon pressure at 20 °C and then heated in an oil bath at 110 °C for 40 h. The flask was cooled, the solvent was removed *in vacuo*, and the resulting residue was subjected to column chromatography on silica gel with hexane/ethyl acetate (3/1) as the eluant to give the product **2g** (184 mg, 83%) as a white solid. Mp: 102.5–

123.0 MS calcd for C₁₅H₁₇NO₃S 292.1007; measured, 292.1002. ¹H NMR (300 MHz, CDCl₃): δ 7.70 (d, *J* = 8.3 Hz, 2H), 7.35 (d, *J* = 8.1 Hz, 2H), 4.21 (s, s, 1H) 4.30–3.95 (m, 2H), 3.10 (s(br), 1H), 2.64–2.54 (m, 2H), 2.44 (s, 3H) 1.68 (s, 3H) 2.03 (dd, *J* = 18.0 Hz, *J*_{AB} = 3.3 Hz, 1H). ¹³C NMR (75 MHz, CDCl₃): δ 207.86, 171.24, 144.28, 134.17, 130.22, 127.66, 52.87, 47.01, 41.90, 39.43, 31.82, 22.88, 21.80, 14.34, 9.03. IR (KBr): 1676.2, 1335.5, 1178.4 cm⁻¹.

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Notes Added in Proof. While this paper was in the review process, a similar work appeared in the literature (Koga, Y.; Kobayashi, T.; Narasaka, K. *Chem. Lett.* **1998**, 249). The authors used [RhCl(CO)₂]₂ as the catalyst.

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