Communications to the Editor

First Ruthenium-Catalyzed Intramolecular Pauson−Khand Reaction

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Metal-mediated cocyclization of alkynes, alkenes, and carbon monoxide (the Pauson−Khand reaction) is becoming increasingly popular as a tool for selective organic synthesis.[1−8] This method provides an easy way to prepare a cyclopentenone skeleton from simple starting materials through a formal [2 + 2 + 1] process and has been used successfully as the key step in the synthesis of several natural products.[9] In addition, cocyclization of enynes with carbon monoxide (intramolecular Pauson−Khand reaction) also offers a simple, efficient, and highly selective route to bicyclic cyclopentenones. Recently, considerable attention has been focused on a catalytic version of the Pauson−Khand reaction. However, the catalytic systems reported so far are strictly limited to Co[10] and Ti[11] catalysts. We previously reported the [2 + 2] cycloaddition of norbornenes with alkynes catalyzed by ruthenium complexes,[12] in which ruthenacyclopentene is a key intermediate.[12c] If carbon monoxide is inserted into this ruthenacyclopentene, a catalytic version of the Pauson−Khand reaction can be achieved. After many trials, we finally found the first example of a ruthenium-catalyzed Pauson−Khand reaction of enynes with carbon monoxide.[13] We report here the development of this new catalyst system for the intramolecular Pauson−Khand reaction.

Treatment of dimethyl 8-nonen-3-yne-6,6-dicarboxylate (**1a**) with 2 mol % $Ru_3(CO)_{12}$ in DMAc (*N*,*N*-dimethylacetamide) under 15 atm of carbon monoxide gave the corresponding bicyclic cyclopentenone **2a** in high yield with high selectivity (eq 1). The effects of the catalyst and the solvent as well as the reaction temperature were examined with **1a**, and the results are listed in Table 1. An appropriate catalyst and solvent were both critically important for a successful catalytic Pauson−Khand reaction. For example, Cp*RuCl(cod) [Cp* = pentamethylcyclopentadienyl, cod = cycloocta-1,5-diene], which is an efficient catalyst for [2 + 2] cycloaddition of norbornenes with alkynes,[12c] is totally ineffective in the present reaction. When $[RuCl_2(CO)_3]_2$ was used as a catalyst, **2a** was obtained in 53% yield together with the byproduct **3a** which is generated by β-hydride elimination and subsequent reductive elimination/isomerization from a ruthenacyclopentene intermediate. Interestingly, Ru(cod)(cot) [cot = cycloocta-1,3,5-triene] gave a mixture of **2a** and **4a**. At elevated temperature (160 °C) using Ru(cod)(cot) catalyst, **4a** was obtained in 64% yield (eq 2).

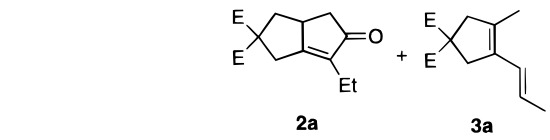
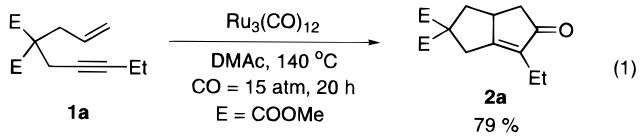
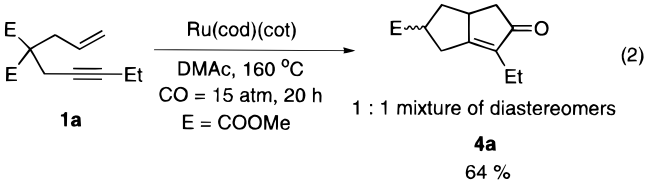


Table 1. Ruthenium-Catalyzed Pauson−Khand Reaction of Dimethyl 8-Nonen-3-yne-6,6-dicarboxylate (**1a**)[a]

catalyst	solvent	conv. of **1a**[b] (%)	yield[b] (%) **2a**	yield[b] (%) **3a**
$Ru_3(CO)_{12}$	DMAc	100	79 (75)	trace
$Ru_3(CO)_{12}$	DMF	100	74	trace
$Ru_3(CO)_{12}$	THF	100	71	3
$Ru_3(CO)_{12}$	toluene	100	67	15
$Ru_3(CO)_{12}$[c]	DMAc	100	71	trace
$[RuCl_2(CO)_3]_2$	DMAc	100	53	9
Cp*RuCl(cod)	DMAc	0	0	0
Ru(cod)(cot)[d]	DMAc	100	22	trace

[a] Ru complex (0.150 mmol as metal atom) solvent (2.0 mL), **1a** (2.5 mmol), CO (15 atm), 140 °C, 20 h. [b] Determined by GLC. Figure in parentheses is an isolated yield. [c] $Ru_3(CO)_{12}$ (0.025 mmol). [d] Methyl 2-ethyl-3-oxobicyclo[3.3.0]oct-1-ene-7-carboxylate (**4a**) was obtained in 38% yield.





Compound **4a** is the dealkoxycarbonylated product of **2a**. However, the simple treatment of **2a** in the presence of Ru(cod)(cot) at 160 °C for 20 h under 15 atm of CO gave **4a** in only 8% yield. The selective conversion of **2a** into **4a** was

(1) For reviews on the Pauson−Khand reaction, see: (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*, 1. (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.

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

(3) For recent examples of Co-promoted reactions, see: (a) Park, H. J.; Lee, B. Y.; Kang, Y. K.; Chung, Y. K. *Organometallics* **1995**, *14*, 3104. (b) Hay, A. M.; Kerr, W. J.; Kirk, G. G.; Middlemiss, D. *Ibid.* **1995**, *14*, 4986. (c) Gordon, A. R.; Johnstone, C.; Kerr, W. J. *Synlett* **1995**, 1083. (d) Kerr, W. J.; Kirk, G. G.; Middlemiss, D. *Ibid.* **1995**, 1085. (e) Ahmar, M.; Antras, F.; Cazes, B. *Tetrahedron Lett.* **1995**, *36*, 4417. (f) Fonquerna, S.; Moyano, A.; Pericas, M. A.; Riera, A. *Tetrahedron* **1995**, *51*, 4239. (g) Castro, J.; Moyano, A.; Pericas, M. A.; Riera, A. *Ibid.* **1995**, *51*, 6541.

(4) For Zr-promoted reactions, see: (a) Negishi, E.; Holmes, S. J.; Tour, J. M.; Miller, J. A. *J. Am. Chem. Soc.* **1985**, *107*, 2568. (b) Negishi, E.; Holmes, S. J.; Tour, J. M.; Miller, J. A.; Cederbaum, F. E.; Swanson, D. R.; Takahashi, T. *Ibid.* **1989**, *111*, 3336.

(5) For Mo-promoted reactions, see: (a) Mukai, C.; Uchiyama, M.; Hanaoka, M. *J. Chem. Soc., Chem. Commun.* **1992**, 1014. (b) Jeong, N.; Lee, S. J.; Lee, B. Y.; Chung, Y. K. *Tetrahedron Lett.* **1993**, *34*, 4027. (c) Kent, J. L.; Wan, H.; Brummond, K. M. *Ibid.* **1995**, *36*, 2407.

(6) For a W-promoted reaction, see: Hoye, T. R.; Suriano, J. A. *J. Am. Chem. Soc.* **1993**, *115*, 1154.

(7) For Fe-promoted reactions, see: (a) Aumann, R.; Weidenhaupt, H.-J. *Chem. Ber.* **1987**, *120*, 23. (b) Pearson, A. J.; Dubbert, R. A. *Organometallics* **1994**, *13*, 1656.

(8) For a Ni-promoted reaction, see: Pages, L.; Llebaria, A.; Camps, F.; Molins, E.; Miravitlles, C.; Moretó, J. M. *J. Am. Chem. Soc.* **1992**, *114*, 10449.

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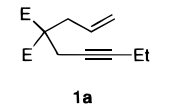
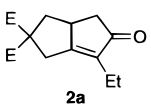
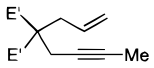
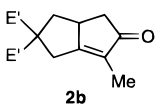
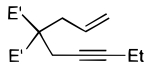
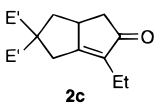
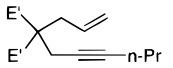
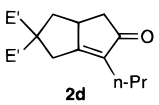
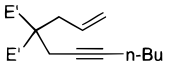
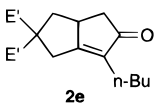
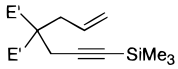
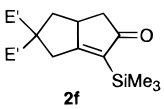
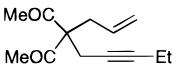
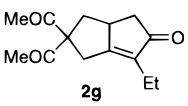
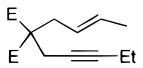
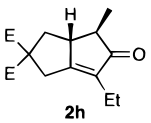
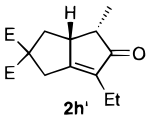
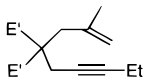
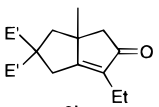
S0002-7863(97)00793-2 CCC: $14.00

Table 2. $Ru_3(CO)_{12}$-Catalyzed Intramolecular Pauson−Khand Reaction[a]

Enyne	Product	Yield[b] (%)
 **1a**	 **2a**	75[c]
 **1b**	 **2b**	78
 **1c**	 **2c**	89
 **1d**	 **2d**	84
 **1e**	 **2e**	84
 **1f**	 **2f**	85[d]
 **1g**	 **2g**	74
 **1h**	 **2h**  **2h'**	41[e] (**2h : 2h'** = 5.6 : 1)
 **1i**	 **2i**	73

[a] $Ru_3(CO)_{12}$ (0.050 mmol), *N*,*N*-dimethylacetamide (2.0 mL), **1** (2.5 mmol), CO (15 atm), 140 °C, 8 h, E = COOMe, E′ = COOEt. [b] Isolated yield. [c] 20 h. [d] THF in place of *N*,*N*-dimethylacetamide was used. [e] 24 h.

attained by concomitant use of a catalytic amount of **1a** with Ru(cod)(cot) to give **4a** in 79% yield, which suggests that the active catalyst species for dealkoxycarbonylation of **2a** should be formed by complexation of Ru(cod)(cot) with **1a**. This reaction may offer a novel and general method for catalytic demonoalkoxycarbonylation of *gem*-diesters. As for the solvent, a considerable amount of **3a** was obtained in either THF or toluene. However, $Ru_3(CO)_{12}$ in an amide solvent showed the highest catalytic activity for selective production of the desired bicyclic cyclopentenone **2a**.

The results obtained for a series of enynes (**1a**−**i**) are summarized in Table 2.[14] In all cases, the starting enynes were completely consumed to give the corresponding bicyclic cyclopentenones (**2a**−**i**) in good to high yields. No byproducts, such as **3a** or **4a**, could be detected by GLC. The reaction of enynes with an alkyl group at either the internal or external carbon of the olefinic moiety also proceeded smoothly to give the corresponding bicyclic cyclopentenones exclusively (**2h**, **h′**, and **i**). Note that the trimethylsilyl-substituted enyne **1f**, which gave the desilylated product in the titanocene-catalyzed reaction of enynes with silylcyanide,[15] also gave the corresponding silylated product **2f** in 85% isolated yield.

While the reaction mechanism is not yet clear, we now believe that the ruthenacyclopentene, which is generated by oxidative cyclization of enynes to ruthenium, is a key intermediate in the present reaction. The formation of the byproduct **3a** can be explained by assuming this intermediate (*vide supra*).

In summary, we have developed the first and practical ruthenium-catalyzed intramolecular Pauson−Khand reaction. Since the Pauson−Khand reaction is a very powerful reaction, this catalytic process could become a valuable tool in the field of organic synthesis. The development of an enantioselective and intermolecular version of this reaction as well as its mechanistic aspects are the subjects of current investigation.

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Supporting Information Available: Complete experimental procedures and lists of spectral data and elemental analyses for all of the new compounds (6 pages). See any current masthead page for ordering and Internet access instructions.

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(10) For Co catalyst, 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. *Ibid.* **1994**, *116*, 8793. (d) Lee, N. Y.; Chung, Y. K. *Tetrahedron Lett.* **1996**, *37*, 3145. (e) Pagenkopf, B. L.; Livinghouse, T. *J. Am. Chem. Soc.* **1996**, *118*, 2285.

(11) For titanocene catalyst, see: (a) Hicks, F. A.; Kablaoi, N. M.; Buchwald, S. L. *J. Am. Chem. Soc.* **1996**, *118*, 9450. (b) Hicks, F. A.; Buchwald, S. L. *Ibid.* **1996**, *118*, 11688.

(12) (a) Mitsudo, T.; Kokuryo, K.; Takegami, Y. *J. Chem. Soc., Chem. Commun.* **1976**, 722. (b) Mitsudo, T.; Kokuryo, K.; Shinsugi, T.; Nakagawa, Y.; Watanabe, Y.; Takegami, Y. *J. Org. Chem.* **1979**, *44*, 4492. (c) Mitsudo, T.; Naruse, H.; Kondo, T.; Ozaki, Y.; Watanabe, Y. *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 580.

(13) Selective skeletal reorganization of enynes to 1-vinylcycloalkanes catalyzed by ruthenium has been reported, see: Chatani, N.; Morimoto, T.; Muto, T.; Murai, S. *J. Am. Chem. Soc.* **1994**, *116*, 6049.

(14) Typical procedure: Enyne (**1**) (2.5 mmol), $Ru_3(CO)_{12}$ (0.032 g, 0.050 mmol), and *N*,*N*-dimethylacetamide (2.0 mL) were placed in a 50 mL stainless autoclave. Carbon monoxide was then pressurized to 15 atm at room temperature, and the mixture was magnetically stirred at 140 °C for 8−24 h. After the reaction mixture was cooled, the products were isolated by Kugelrohr distillation.

(15) Berk, S. C.; Grossman, R. B.; Buchwald, S. L. *J. Am. Chem. Soc.* **1994**, *116*, 8593.