Catalytic Version of the Intramolecular Pauson–Khand Reaction

Nakcheol Jeong,* Sung Hee Hwang, and Youngshin Lee

Hanhyo Institutes of Technology, San 6
Daeyadong, Shiheungshi, Kyungkido 429-010, Korea

Young Keun Chung

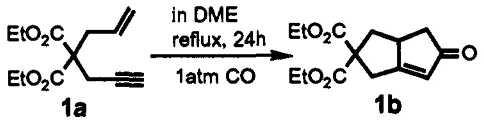
Department of Chemistry, Seoul National University
San 56, Shilimdong, Kwanakgu, Seoul 151-742, Korea

Received December 3, 1993

Cocyclization of alkynes with alkenes and carbon monoxide by cobalt leading to cyclopentenones (known as the Pauson–Khand reaction) has become one of the most powerful reactions in the synthesis of cyclopentenones.[1] The synthetic significance of this reaction has been greatly increased by the findings of various promoters, e.g., silica gel,[2] tertiary amine *N*-oxides,[3] and DMSO.[4] It has also been observed that the presence of a sulfur or oxygen atom in the right position of the substrates accelerated the rate of the thermal reaction.[5] Despite the progress and success in the stoichiometric reactions, a practical catalytic version of the Pauson–Khand reaction has not yet been identified.[6] Among several pioneering reports in the catalytic reaction, only the cocyclization of heptyne with ethylene and carbon monoxide is remarkable.[6e] Herein, we report our finding of a practical catalytic conversion of enynes into bicyclic cyclopentenones by employing phosphites as coligands.[7]

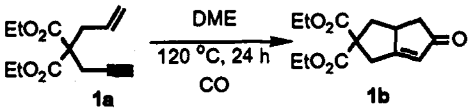
As reported in the literature[6a,b] and also demonstrated by us in Table 1 (entry 1), dicobalt octacarbonyl itself can afford a 1.5–3-fold excess amount of the bicyclic cyclopentenone product based on the amount of dicobalt octacarbonyl used in the thermal reaction under 1 atm of carbon monoxide. It was also observed that use of a catalytic amount of dicobalt octacarbonyl (10–20 mol %) in the presence of promoters such as tertiary amine *N*-oxides or DMSO produced only a trace amount of the bicyclic cyclopentenone instead of a 10–20% yield and led to the formation of dark purple precipitates, which were presumed to be oxidized metal clusters. The main obstacle to be overcome for the catalytic process is the formation of either metal clusters or inactive cobalt carbonyl species, such as tetracobalt dodecacarbonyl. Thus, we decided to add certain ligands which would stabilize the working intermediates throughout the reaction by intervening and preventing the above mentioned problems.[8,9]

Table 1. Examination of the Intramolecular Pauson–Khand Reaction with Coligands



entry	mol % of $Co_2(CO)_8$	coligand, mol %	yield %
1	20	none	47
2	10	PPh_3, 20	22
3	10	$P(NMe_2)_3$, 20	18
4	10	$P(OEt)_3$, 20	25
5	10	$P(OPh)_3$, 20	44

Table 2. Catalytic Reactions of the Intramolecular Pauson–Khand Reaction



entry	mol % of $Co_2(CO)_8$	coligand, mol %	CO pressure, atm	% yield
1	1	none	3	4
2	1	$P(OPh)_3$, 5	3	30
3	3	$P(OPh)_3$, 10	3	82
4	3	$P(OPh)_3$, 10	3	79[a]
5	3	PPh_3, 10	3	51[b]
6	3	$P(OPh)_3$, 10	10	14

[a] This reaction was carried out in heptane at 100 °C for 24 h. [b] This reaction was carried out for 48 h.

After much experimentation in the conversion of **1a** into **1b** in order to examine the effect of the external ligands with 10 mol % of dicobalt octacarbonyl under 1 atm of carbon monoxide in various solvents, it was observed that the catalytic turnover never exceeded 4, regardless of the presence of various external ligands. It was even detrimental when some of the external ligands were employed (entries 2–4 in Table 1). With triphenyl phosphite in DME, the turnover number was slightly improved up to 4 (entry 5).

The effects of the external ligands, however, became more distinctive and beneficial when the reactions were carried out under a relatively high pressure of CO (3 atm at ambient temperature).[10] As reported in Table 2, use of 1 mol % of dicobalt octacarbonyl without any external coligand produced only 4% of the bicyclic cyclopentenone after 48 h at 120 °C in DME. On the other hand, under the same reaction conditions, a successful catalytic process was realized by employing triphenyl phosphite (5 mol %) as a coligand to give the product **1b** in 30% yield along with the recovery of the starting material **1a** in 59% yield. The reaction was forced to completion by employing 3 mol % of dicobalt octacarbonyl with 10 mol % of triphenyl phosphite to produce the

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[1] (a) Khand, I. U.; Knox, G. R.; Pauson, P. L.; Watts, W. E.; Foreman, M. I. *J. Chem. Soc., Perkin Trans. 1* **1973**, 977. (b) Pauson, P. L. *Tetrahedron* **1985**, *41*, 5855. (c) Schore, N. E. *Chem. Rev.* **1988**, *88*, 1081. (d) Schore, N. E. *Org. React.* (*N.Y.*) **1991**, *41*, 1. (e) Schore, N. E. In *Comprehensive Organic Synthesis*; Trost, B. M., Ed.; Pergamon: Oxford, 1991; Vol. 5, p 1037.

[2] (a) Smit, W. A.; Simonyan, S. O.; Tarasov, G. S.; Mikaelian, G. S.; Gybin, A. S.; Ibragimov, I. I.; Caple, R.; Froen, O.; Kraeger, A. *Synthesis* **1989**, 472 and leading references therein.

[3] (a) Shambayati, S.; Crowe, W. E.; Schreiber, S. L. *Tetrahedron Lett.* **1990**, *31*, 5289. (b) Jeong, N.; Chung, Y. K.; Lee, B. Y.; Lee, S. H.; Yoo, S.-e. *Synlett* **1991**, 204.

[4] Chung, Y. K.; Lee, B. Y.; Jeong, N.; Hudecek, M.; Pauson, P. L. *Organometallics* **1993**, *12*, 220.

[5] Krafft, M. E.; Scott, I. L.; Romero, R. H.; Feibelmann, S.; Van Pelt, C. E. *J. Am. Chem. Soc.* **1993**, *115*, 7199.

[6] For examples of the use of a catalytic amount of $Co_2(CO)_8$, see: (a) Billington, D. C. *Tetrahedron Lett.* **1983**, *24*, 2905. (b) Magnus, P.; Principe, L. M.; Slater, M. J. *J. Org. Chem.* **1987**, *52*, 1483. (c) Billington, D. C.; Kerr, W. J.; Pauson, P. L.; Farnochi, C. F. *J. Organomet. Chem.* **1988**, *356*, 213. (d) MacWhorter, S. E.; Sampath, V.; Olmstead, M. M.; Schore, N. E. *J. Org. Chem.* **1988**, *53*, 203. (e) Rautenstrauch, V.; Megrard, P.; Conesa, J.; Kuster, W. *Angew. Chem., Int. Ed. Engl.* **1990**, *29*, 1413. (f) A batch-catalytic protocol with $W(CO)_5THF$ is described by Hoye and Suriano: Hoye, T. R.; Suriano, J. A. *J. Am. Chem. Soc.* **1993**, *115*, 1154.

[7] More recently, the catalytic conversion of enynes into bicyclic cyclopentenones by employing an early transition metal, $Cp_2Ti(PMe_3)_2$, had been reported. This reaction constitutes the only example of a catalytic version in this class of reactions. Berk, S. C.; Grossman, R. B.; Buchwald, S. L. *J. Am. Chem. Soc.* **1993**, *115*, 4912.

[8] It was reported in ref 5c that either phosphine- or phosphite-substituted dicobalt carbonyl complexes slowed down the reaction rate in the intermolecular reaction under atmospheric pressure. We reexamined these issues with the intramolecular version. Our results at atmospheric pressure are parallel to those in ref 5c. Generally it is known that the presence of phosphine or phosphite ligands in the alkyne-cobalt complexes makes the reaction much slower. It is mainly attributed to the retardation of the initial decarbonylation by strong backbonding between the metal and carbon monoxide.

[9] Similar results employing a catalytic amount of dicobalt octacarbonyl (10 mol %) and triphenyl phosphite (20 mol %) in the rearrangement of 1-alkynylcyclopropanols to 2-cyclopentenones were reported. Iwasawa, N.; Matsuo, T.; Iwamoto, M.; Ikeno, T. *Abstracts in OMCOS 7*; Seventh IUPAC Symposium on Organo-Metallic Chemistry directed towards Organic Synthesis, Kobe, Japan, Sept 19–23, 1993; S-10.

[10] The carbon monoxide pressure of the reaction vessel was set to 3 atm at the inception of the reaction and usually increased to 4–5 atm during the reaction at 120 °C.

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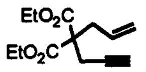
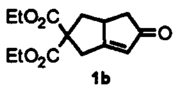
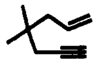
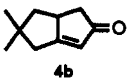
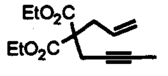
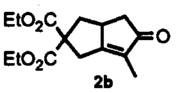
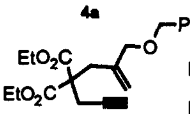
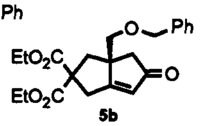
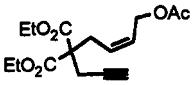
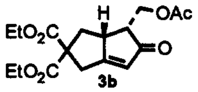
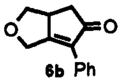
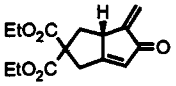
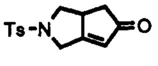
Table 3. Catalytic Pauson–Khand Reaction with Various Substrates under CO Pressure (3 atm)

substrates	products	yield[d]	substrates	products	yield[d]
 **1a**	 **1b**	82%[a]	 **4a**	 **4b**	77%[a]
 **2a**	 **2b**	90%[b]	 **5a**	 **5b**	81%[a,e]
 **3a**	 **3b**	58%[b]	 **6a**	 **6b**	51%[c]
	 **3c**	19%	 **7a**	 **7b**	94%[b]

[a] 3 mol % of $Co_2(CO)_8$ and 10 mol % of triphenyl phosphite were used. [b] 5 mol % of $Co_2(CO)_8$ and 20 mol % of triphenyl phosphite were used. [c] 10 mol % of $Co_2(CO)_8$, 30 mol % of triphenylphosphite, and 15 mol % of K_2CO_3 (powder) were used. [d] All yields given in this table are isolated yields. [e] This reaction was completed after 72 h.

bicyclic cyclopentenone **1b** in 82% yield. Replacement of the phosphite with triphenylphosphine slowed down the reaction to yield only 51% of the product **1b** even after 48 h.[11] The reaction seemed to be very sensitive to the pressure of carbon monoxide, too. Higher pressure of carbon monoxide (over 10 atm at ambient temperature) seemed to prevent the initial decarbonylation process to generate a vacancy for the incoming olefin (14% yield together with 58% of **1a** after 24 h). Switching solvent from DME to heptane made virtually no difference in the efficiency and yield (79% yield) of the reaction.

The scope of this catalytic process was examined with various substrates, and the results are summarized in Table 3.[12] The reactions proceeded quite efficiently to afford the corresponding products in yields comparable to those of tertiary amine *N*-oxide promoted reactions.[3] This catalytic reaction required only 3–5 mol % of dicobalt octacarbonyl in most cases (except for compound **6**). A couple of things regarding the substitution pattern of the substrates are worthwhile noting. This reaction was effective with terminal alkynes as well as disubstituted alkynes, which is in contrast to the catalytic titanium mediated reaction.[7] Variously substituted olefins (compounds **1**, **3**, **5**) were also found to be good substrates in this process. The reaction with compound **3a** was somewhat complicated by the elimination of acetic acid to give the side product **3c**.

As described for the stoichiometric reaction, the heteroatom tethered substrates were tested to generate the corresponding products in reasonable yield. In the case of propargyl allyl ether (compound **6**), the addition of K_2CO_3 to the reaction mixture turned out to be crucial for a reasonable yield because of the formation of traces of phenol during the reaction.[13]

The role of the triphenyl phosphite in this catalytic process remains unclear since no intermediate in the reaction has been isolated and characterized. The mechanistic aspects and the development of the enantioselective and intermolecular version[14] of this reaction are the subjects of current investigations.

In summary, we have developed a practical catalytic Pauson–Khand reaction by employing triphenyl phosphite as a coligand for the conversion of enynes into bicyclic cyclopentenones. Since the Pauson–Khand reaction is a very powerful reaction in terms of the scope of the substrate availability and practicality, this catalytic version will provide an additional asset in this field.

Acknowledgment. The authors are grateful to Mr. Bun Yeoul Lee for his contribution in the initial stage of this project.

Supplementary Material Available: A representative experimental procedure for the catalytic preparation of bicyclic cyclopentenones and the spectroscopic characterization of the products listed in Table 3 (4 pages). This material is contained in many libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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(11) This result is mainly attributed to the solubilities of the phosphine-ligand-substituted alkyne cobalt complexes or cobalt carbonyls. For example, phosphine-ligand-substituted cobalt carbonyls, e.g., $Co_2(CO)_6(PPh_3)_2$, are insoluble in organic solvents, while $Co_2(CO)_6[P(OPh)_3]_2$ is soluble. Manning, A. R. *J. Chem. Soc.* (*A*) **1968**, 1135.

(12) For reproducible results, it is recommended to prepare the alkyne-dicobalt hexacarbonyl complexes (3 mol %) by stirring for 10 min at room temperature before the addition of phosphite. Otherwise, the reactions were sometimes erratic, leading to incomplete reaction and inconsistent yield.

(13) The propargyl allyl ether–dicobalt carbonyl complex is sensitive to acids.

(14) In a preliminary experiment with phenylacetylene and norbornadiene (10 equiv) under identical condition to entry 3 in Table 2, a mixture of 1,3,5-triphenylbenzene and a cyclopentenone (1:1) was obtained in 20% yield after 24 h.