ORGANIC
LETTERS

2001
Vol. 3, No. 8
1217−1219

Iridium Complex Catalyzed Carbonylative Alkyne–Alkyne Coupling for the Synthesis of Cyclopentadienones

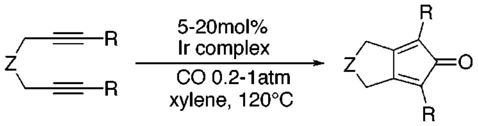
Takanori Shibata,* Koji Yamashita, Hiroyuki Ishida, and Kentaro Takagi

Department of Chemistry, Faculty of Science, Okayama University, Tsushima,
Okayama 700-8530, Japan

tshibata@cc.okayama-u.ac.jp

Received February 14, 2001

ABSTRACT



Catalytic carbonylative alkyne–alkyne coupling proceeds using iridium–phosphine complexes under carbon monoxide at atmospheric pressure or a partial pressure of 0.2 atm. This reaction provides various cyclopentadienones in high isolated yields.

Cyclopentadienones are potent synthetic intermediates[1] and are used to construct polycyclic compounds[2] and polymers.[3] Transition metal-mediated alkyne−alkyne−CO coupling[4] is a direct and effective synthesis of cyclopentadienones. But all reported procedures are stepwise processes.[5−7] CpCo($(PPh_3)_2$)[5a] and $RhCl(PPh_3)_3$[5b] mediate alkyne−alkyne couplings to give metallacyclopentadienes, which were derived into cyclopentadienones by insertion of carbon monoxide and elimination of metals. $CpCo(CO)_2$[6] and $Fe(CO)_5$[7] have been shown to mediate the carbonylative coupling, but cyclopentadienones are obtained as η^4-metal complexes and the following oxidative demetalations are necessary to obtain uncomplexed cyclopentadienones. There is no practical example of catalytic carbonylative alkyne−alkyne coupling for the preparation of cyclopentadienones.[8,9]

We report here the iridium complex-catalyzed carbonylative alkyne−alkyne coupling, which provides cyclopentadienones in high isolated yields. We recently reported carbonylative alkyne−alkyne coupling using a stoichiometric

---

[1] Review: Ogliaruso, M.; Romanelli, M. G.; Becker, E. I. *Chem. Rev.* **1965**, *65*, 261.

[2] (a) Yamashita, Y.; Masumura, M. *Tetrahedron Lett*. **1979**, 1765. (b) Yamashita, Y.; Miyauchi, Y.; Masumura, M. *Chem. Lett*. **1983**, 489. (c) Baraldi, P. G.; Barco, A.; Benetti, S.; Pollini, G. P.; Polo, E.; Simoni, D. *J. Chem. Soc., Chem. Commun*. **1984**, 1049. (d) Gamba, A.; Gandolfi, R.; Oberti, R.; Sardone, N. *Tetrahedron* **1993**, *49*, 6331. (e) Jikyo, T.; Eto, M.; Harano, K. *J. Chem. Soc., Perkin Trans. 1* **1998**, 3463. (f) Jikyo, T.; Eto, M.; Harano, K. *Tetrahedron* **1999**, *55*, 6051. (g) Rainier, J. D.; Imbriglio, J. E. *Org. Lett*. **1999**, *1*, 2037.

[3] Kumar, U.; Neenan, T. X. *Macromolecules* **1995**, *28*, 124.

[4] Reviews of transition metal catalyzed cycloadditions: (a) Ojima, I.; Tzamarioudaki, M.; Li, Z.; Donovan, R. J. *Chem. Rev.* **1996**, *96*, 635. (b) Frühauf, H.-W. *Chem. Rev.* **1997**, *97*, 523.

[5] (a) Yamazaki, H.; Hagihara, N. *J. Organomet. Chem.* **1967**, *7*, 21. (b) Comprehensive work of alkyne−alkyne coupling using Rh(I) complexes: Müller, E. *Synthesis* **1974**, 761. (c) Synthesis of iminocyclopentadienes, which are readily hydrolyzed into cyclopentadienones, by Ni(0)-promoted alkyne−alkyne coupling with isocyanide: Tamao, K.; Kobayashi, K.; Ito, Y. *J. Org. Chem*. **1989**, *54*, 3517.

[6] (a) Gesing, E. R. F.; Tane, J.-P.; Vollhardt, K. P. C. *Angew. Chem., Int. Ed. Engl.* **1980**, *19*, 1023. (b) Halterman, R. L.; Vollhardt, K. P. C. *Organometallics* **1988**, *7*, 883.

[7] (a) Pearson, A. J.; Dubbert, R. A. *J. Chem. Soc., Chem. Commun.* **1991**, 202. (b) Pearson, A. J.; Shively, R. J., Jr.; Dubbert, R. A. *Organometallics* **1992**, *11*, 4096. (c) Pearson, A. J.; Shively, R. J., Jr. *Organometallics* **1994**, *13*, 578. (d) Pearson, A. J.; Perosa, A. *Organometallics* **1995**, *14*, 5178. (e) Pearson, A. J.; Yao, X. *Synlett* **1997**, 1281. (f) Knölker, H.-J.; Heber, J.; Mahler, C. H. *Synlett* **1992**, 1002. (g) Knölker, H.-J.; Heber, J. *Synlett* **1993**, 924. (h) Knölker, H.-J.; Baum, E.; Heber, J. *Tetrahedron Lett*. **1995**, *42*, 7647.

[8] The only example of catalytic carbonylative coupling of *tert*-butyl-substituted alkynes for the synthesis of cyclopentadienones but in low yields: Kelley, E. A.; Wright, G. A.; Maitlis, P. M. *J. Chem. Soc., Dalton Trans.* **1979**, 178.

[9] Pd(II) catalyzes such couplings to give cyclopentadienones, but they are isolated as nucleophilic adducts of alcohols or Diels−Alder products with dienophiles: (a) Chiusoli, G. P.; Costa, M.; Gerbella, M.; Salerno, G. *Gazz. Chim. Ital.* **1985**, *115*, 697. (b) Chiusoli, G. P.; Costa, M.; Gerbella, M.; Reverberi, S.; Salerno, G.; Terenghi, M. G. *Gazz. Chim. Ital.* **1987**, *117*, 695.

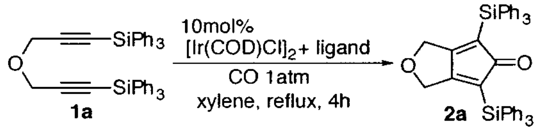
[10] (a) Shibata, T.; Ohta, T.; Soai, K. *Tetrahedron Lett.* **1998**, *39*, 5785. (b) Shibata, T.; Yamashita, K.; Takagi, K.; Ohta, T.; Soai, K. *Tetrahedron* **2000**, *56*, 9259.

10.1021/ol015708c CCC: $20.00

amount of cobalt carbonyl complex.[10,11] The iridium−phosphine complexes realize catalytic coupling under carbon monoxide at atmospheric pressure or less.

We chose dipropargyl ether **1a** as a model diyne and examined the coupling reaction using a catalytic amount of iridium complex under carbon monoxide at atmospheric pressure. $[Ir(COD)Cl]_2$ promoted this coupling, and cyclopentadienone **2a** was obtained in 18% yield along with recovered diyne **1a** and unidentified products. After various phosphines and a phosphite were screened as the ligand, triphenylphosphine and dppp (bis(1,3-diphenylphosphino)propane) were found to give the best results (Table 1).

Table 1. Screening of Phosphine Ligands for the Iridium Complex-Catalyzed Carbonylative Coupling of **1a**



ligand[a]	yield (%)	ligand[a]	yield (%)
none	18	2dppe	37
$4PPh_3$	49	2dppp	52
$4P(p\text{-}F\text{-}C_6H_4)_3$	42	2dppb	0
$4P(OPh)_3$	10	2dppf	14

[a] Coefficients at the beginning of the ligand designation are molar ratio against $[Ir(COD)Cl]_2$.

Iridium−dppp complex was prepared in hot toluene and isolated by crystallization. Its structure was ascertained by X-ray measurement to be IrCl(COD)(dppp) (Figure 1).[12] IrCl(COD)(dppp) and $IrCl(CO)(PPh_3)_2$ (Vaska's complex) were used in the carbonylative coupling (eq 1). The coupling of diyne **1b** was catalyzed by only small amounts of these iridium complexes at a lower reaction temperature and multicyclic product **2b** was obtained in high yield (eq 2).

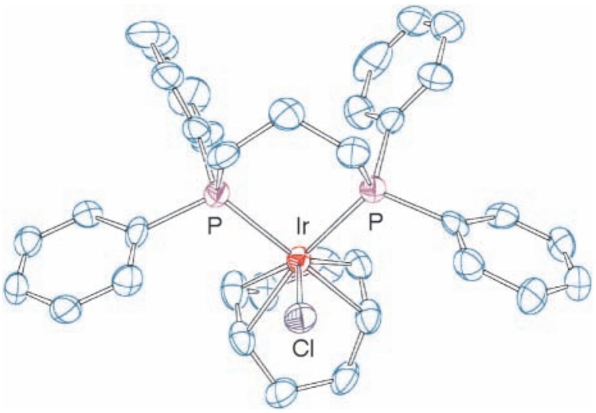
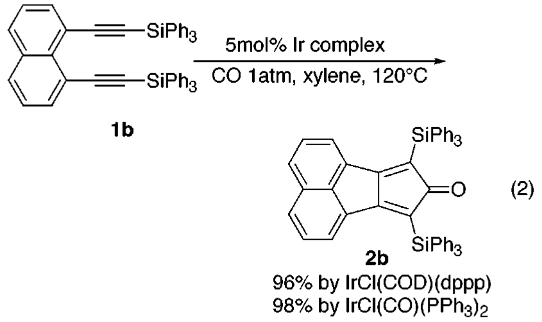


Figure 1. Crystal structure of $IrCl(COD)(dppp)\cdot CHCl_3$. $CHCl_3$ is omitted.

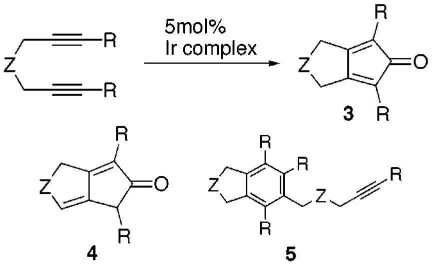
$$\mathbf{1a} \xrightarrow[\text{CO 1atm, xylene, reflux}]{\text{10mol\% Ir complex}} \mathbf{2a} \qquad (1)$$

76% by IrCl(COD)(dppp)
78% by $IrCl(CO)(PPh_3)_2$



In place of silyl group-substituted diynes, aryl group-substituted ones were examined next (Table 2). In the presence of $IrCl(CO)(PPh_3)_2$ or IrCl(COD)(dppp) (5 mol %), dipropargylmalonate with phenyl groups on the terminal positions of the diyne was placed under carbon monoxide at atmospheric pressure (entries 1 and 2).[13] While both iridium catalysts are active for carbonylative coupling, the

Table 2. Iridium Complex-Catalyzed Carbonylative Coupling of Various Diynes



entry[a]	R	Z	catalyst[b]	yield (%)
1	Ph	$C(CO_2Bn)_2$	A	86 (**3a**)
2	Ph	$C(CO_2Bn)_2$	B	70[c] (**3a**)
3[d]	Ph	$C(CO_2Bn)_2$	A	85 (**3a**)
4	Ph	$C(CO_2Et)_2$	A	99 (**3b**)
5	Ph	$C(CO_2t\text{-}Bu)_2$	A	92 (**3c**)
6	4-MeO-Ph	$C(CO_2Bn)_2$	A	94 (**3d**)
7	4-Cl-Ph	$C(CO_2Bn)_2$	A	79[e] (**3e**)
8	$4\text{-}MeO_2C\text{-}Ph$	$C(CO_2Bn)_2$	A	89[f] (**4f**)
9	Ph	CH_2	A	79 (**3g**)
10	Ph	O	A	65 (**3h**)

[a] Reaction conditions: CO 1 atm, xylene 120 °C, 2−7 h, unless otherwise noted. [b] A, $IrCl(CO)(PPh_3)_2$; B, IrCl(COD)(dppp). [c] **4a** (5%) and **5a** (6%) are also obtained. [d] The reaction was examined under a mixture of CO (0.2 atm) and Ar (0.8 atm). [e] **4e** (20%) is also obtained. [f] A mixture of **3f** and **4f** (1:2) was obtained. **3f** was isomerized into **4f**, which was isolated and characterized.

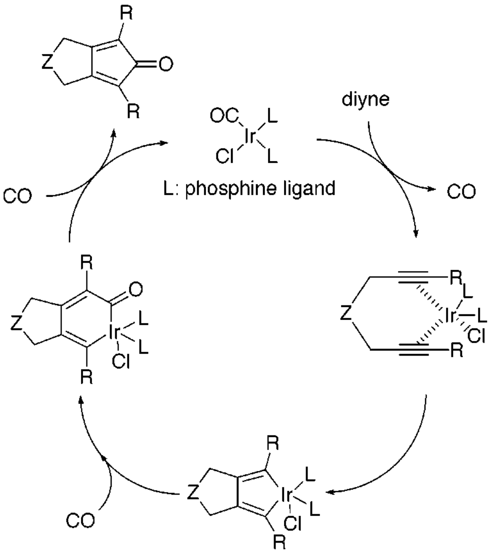
---

(11) After our publication (ref 10a), $Co_2(CO)_8$-catalyzed carbonylative alkyne−alkyne coupling under carbon monoxide at high pressure was used in tandem cycloaddition reactions. They provide multicyclic products via cyclopentadienones, which are not isolated: (a) Hong, S. H.; Kim, J. W.; Choi, D. S.; Chung, Y. K.; Lee, S.-G. *Chem. Commun.* **1999**, 2099. (b) Son, S. U.; Chung, Y. K.; Lee, S.-G. *J. Org. Chem.* **2000**, *65*, 6142. (c) Son, S. U.; Choi, D. S.; Chung, Y. K.; Lee, S.-G. *Org. Lett.* **2000**, *2*, 2097.

former is more effective for preparing cyclopentadienone **3a**. Isomerized product **4a** and hexasubstituted benzene **5a** were also formed by the latter iridium catalyst. Reducing the partial pressure of carbon monoxide had almost no effect on the yield of cyclopentadienone **3a**, and even under carbon monoxide at a partial pressure of ca. 0.2 atm, carbonylative coupling proceeded efficiently (entry 3). Diethyl or di-*tert*-butyl malonates are also appropriate substrates, and the coupling of diethyl malonate proceeded almost quantitatively to give **3b** (entries 4 and 5).[14] Both electron-donating and -withdrawing substituents on the aryl moieties are acceptable for this coupling (entries 6−8). However, electron-withdrawing substituents destabilized the cyclopentadienones, and isomerization of the double bond occurred during purification for **3e** and during the coupling reaction for **3f** (entries 7 and 8). 1,6-Diyne and propargyl ether are also substrates, and the corresponding cyclopentadienones **3g** and **3h** are obtained in acceptable yields (entries 9 and 10).[15,16]

The precise mechanism of this carbonylative coupling remains unclear; however, a plausible mechanism is depicted in Scheme 1. From the π-complex between diyne and Ir(I), a metallacyclopentadiene is formed. The insertion of carbon monoxide following reductive elimination of iridium gives cyclopentadienone and regenerates Ir(I) catalyst. The main path for formation of the benzene derivative **5** is probably alkyne insertion to a metallacyclopentadiene prior to carbonyl insertion, because **5** can be obtained as a major product by the iridium-catalyzed reaction of diyne under argon, but not carbon monoxide, and cannot be obtained by thermal reaction of cyclopentadienone **3a** and diyne. However, the possibility of a prompt Diels−Alder reaction between the formed cyclopentadienone and diyne along with aromatization cannot be fully excluded.

Scheme 1



In summary, we have developed the first practical example of catalytic carbonylative alkyne−alkyne coupling for the synthesis of cyclopentadienones using iridium−phosphine complexes. These results imply further utilization of iridium complexes as efficient catalysts for carbonylative coupling.[17,18] Compared with carbonylations under carbon monoxide at high pressure using $Co_2(CO)_8$,[11] it is notable that a low partial pressure of carbon monoxide is sufficient in iridium complex-catalyzed carbonylative alkyne−alkyne coupling.

Acknowledgment. Financial support by Sumitomo Foundation and by a Grant-in-Aid for Scientific Research from the Ministry of Education, Culture, Sports, Science and Technology is gratefully acknowledged.

Supporting Information Available: X-ray structure report for IrCl(COD)(dppp)·$CHCl_3$ and listing of spectral data for cyclopentadienones. This material is available free of charge via the Internet at http://pubs.acs.org.

OL015708C

---

(12) A single crystal of IrCl(COD)(dppp) was prepared by crystallization in a toluene−chloroform solution. Crystallographic data of IrCl(COD)(dppp)·$CHCl_3$ have been deposited at the Cambridge Crystallographic Data Centre (CCDC) as supplementary publication No. CCDC 157001 and can be obtained free of charge on application to the CCDC, 12 Union Road, Cambridge CB2 1EZ, UK.

(13) **Typical experimental procedure** (Table 2, entry 1): IrCl(CO)$(PPh_3)_2$ (4.2 mg, 0.005 mmol) was placed in a flask and then flushed by carbon monoxide. A degassed xylene solution (5 mL) of dipropargylmalonate (56.5 mg, 0.11 mmol) was added and then the resulting mixture was stirred at 120 °C (bath temperature) for 5 h. After excluding the solvent, the crude products were purified by column chromatography using neutral silica gel to give cyclopentadienone **3a** (51.0 mg, 0.094 mmol, 86%).

(14) Diethyl malonate gave the best yield, but cyclopentadienone **3b** is less stable than **3a** and readily isomerized to **4b**. We chose dibenzyl malonate as a suitable substrate for further investigation.

(15) Rh(I) complexes also catalyze the carbonylative coupling but are less effective than Ir(I) complexes under the same reaction conditions (**3g** was obtained in 29% yield by $[Rh(COD)Cl]_2$ and in 9% yield by $[Rh(COD)Cl]_2 + 4PPh_3$ and 1,6-diyne was recovered).

(16) An alkyl-substituted diyne, dibenzyl di-2-butynylmalonate, was examined under the same reaction conditions but hexasubstituted benzene **5** (R = Me) was a major product and a carbonylated product could not be detected.

(17) Shibata, T.; Takagi, K. *J. Am. Chem. Soc.* **2000**, *122*, 9852.

(18) Murakami, M.; Itami, K.; Ubukata, M.; Tsuji, I.; Ito, Y. *J. Org. Chem.* **1998**, *63*, 4.