

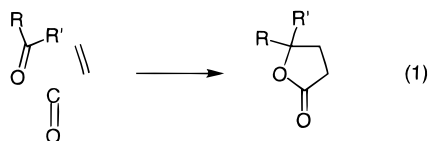
Ruthenium Carbonyl-Catalyzed [2 + 2 + 1]-Cycloaddition of Ketones, Olefins, and Carbon Monoxide, Leading to Functionalized γ -Butyrolactones

Naoto Chatani, Mamoru Tobisu, Taku Asaumi, Yoshiya Fukumoto, and Shinji Murai*

Department of Applied Chemistry, Faculty of Engineering
Osaka University, Suita, Osaka 565-0871, Japan

Received April 19, 1999

Transition-metal-catalyzed cycloaddition reactions using carbon monoxide as a one-carbon unit represent a useful method for the synthesis of carbocyclic and heterocyclic carbonyl compounds from acyclic building blocks.^{1,2} A three component [2 + 2 + 1]cycloaddition, which incorporates the ketone or the aldehyde π -bond, the alkene π -bond, and the carbon atom of CO into the five-membered ring represents an attractive route to γ -butyrolactones (reaction 1).³ However, as of 1996, such an approach had not been reported. Crowe reported that the exposure of titanium metallacycles, obtained by the reaction of a stoichiometric amount of $\text{Cp}_2\text{Ti}(\text{PMe}_3)_2$ with olefinic aldehydes (e.g., 5-hexenal), with CO followed by an oxidatively induced reductive elimination gives γ -lactones.⁴ Buchwald independently reported a similar transformation in which γ -lactones are formed when the reaction of $\text{Cp}_2\text{Ti}(\text{PMe}_3)_2$ with tethered olefinic ketones is carried out in an atmosphere of CO at 70 °C, and found that the transformation can be catalytic, for the case of *o*-allylacetophenone as a substrate.⁵ We wish to report the use of $\text{Ru}_3(\text{CO})_{12}$ as a catalyst for the cyclocoupling of ketones (or aldehydes), olefins, and CO leading to functionalized γ -butyrolactones. The system described here represents the first example of the *catalytic intermolecular* [2 + 2 + 1] cyclocoupling of ketones (or aldehydes), olefins, and CO (reaction 1).



In the past, we examined the reactivities of a wide variety of aldehydes and ketones in the hope of carrying out the cyclocoupling reaction shown in reaction 1, but our experiments were unsuccessful. Finally, we explored the use of α -dicarbonyl

(1) For reviews on transition-metal-catalyzed cycloaddition reactions, see: Schore, N. E. *Chem. Rev.* **1988**, *88*, 1081. Lautens, M.; Klute, W.; Tam, W. *Chem. Rev.* **1996**, *96*, 49. Ojima, I.; Tzamaridouaki, M.; Li, Z.; Donovan, R. *J. Chem. Rev.* **1996**, *96*, 635.

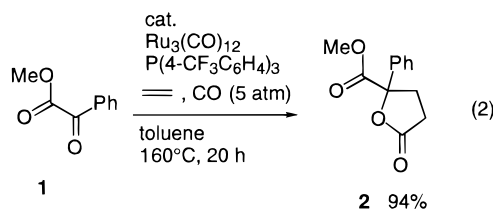
(2) For recent papers on [2 + 2 + 1] cycloaddition reactions using CO, see: Chatani, N.; Morimoto, T.; Fukumoto, Y.; Murai, S. *J. Am. Chem. Soc.* **1998**, *120*, 5335. Koga, Y.; Kobayashi, T.; Narasaka, K. *Chem. Lett.* **1998**, 249. Jeong, N.; Lee, S.; Sung, B. K. *Organometallics* **1998**, *17*, 3642. Kim, J. W.; Chung, Y. K. *Synthesis* **1998**, 142. Sugihara, T.; Yamaguchi, M. *J. Am. Chem. Soc.* **1998**, *120*, 10782. For a recent paper on [4 + 1] cycloaddition reactions using CO, see: Morimoto, T.; Chatani, N.; Murai, S. *J. Am. Chem. Soc.* **1999**, *121*, 1758. Murakami, M.; Itami, K.; Ito, Y. *J. Am. Chem. Soc.* **1999**, *121*, 4130. For a recent paper on [4 + 4 + 1] cycloaddition reactions using CO, see: Murakami, M.; Itami, K.; Ito, Y. *Angew. Chem., Int. Ed.* **1998**, *37*, 3418.

(3) γ -Butyrolactones are important precursors for the preparation of α -methylene- γ -butyrolactones or butenolides which are found in the skeleton of various natural products. For reviews, see: Hoffmann, H. M. R.; Rabe, J. *Angew. Chem., Int. Ed. Engl.* **1985**, *24*, 94. Petragani, N.; Ferraz, H. M. C.; Silva, G. V. J. *Synthesis* **1986**, 157. Ito, M. *Pure Appl. Chem.* **1991**, *63*, 13.

(4) Crowe, W. E.; Vu, A. T. *J. Am. Chem. Soc.* **1996**, *118*, 1557.

(5) Kablaoui, N. M.; Hicks, F. A.; Buchwald, S. L. *J. Am. Chem. Soc.* **1996**, *118*, 5818. Kablaoui, N. M.; Hicks, F. A.; Buchwald, S. L. *J. Am. Chem. Soc.* **1997**, *119*, 4424.

compounds as substrates, since these would be expected to be more reactive than simple carbonyl compounds. As a result, we found that reaction 1 can be realized by the use of α -keto esters as a substrate and $\text{Ru}_3(\text{CO})_{12}$ as the catalyst. The reaction of methyl benzoylformate (**1**) (2 mmol) with ethylene (initial pressure 3 atm at 25 °C in a 50-mL stainless steel autoclave) at 5 atm of CO (initial pressure at 25 °C) at 160 °C in toluene (6 mL) in the presence of $\text{Ru}_3(\text{CO})_{12}$ (0.05 mmol) for 20 h gave tetrahydro-5-oxo-2-phenyl-2-furancarboxylic acid methyl ester (**2**)⁶ in 23% isolated yield, based on **1**, along with 75% of **1** being recovered. A variety of transition-metal complexes were examined for their ability to catalyze the coupling reaction, and none of these catalysts, which included $\text{Fe}_3(\text{CO})_{12}$, $\text{Co}_2(\text{CO})_8$, $\text{Rh}_4(\text{CO})_{12}$, $\text{Ir}_4(\text{CO})_{12}$, $\text{Os}_3(\text{CO})_{12}$, $[\text{RuCl}_2(\text{CO})_3]_2$, $\text{RuCl}_2(\text{PPh}_3)_3$, and $\text{CpRuCl}(\text{PPh}_3)_2$, were found to be active. The use of PPh_3 (0.15 mmol) as an additive in the $\text{Ru}_3(\text{CO})_{12}$ -catalyzed reaction of **1** increased the yield to 61%. We then examined a variety of phosphines as additives and found that the yields are relatively parallel to the $\text{p}K_a$ values. Thus, the lower the $\text{p}K_a$, the higher the yield; (PBu_3 , 25%), ($\text{P}(4\text{-MeOC}_6\text{H}_4)_3$, 59%), (PPh_3 , 61%), ($\text{P}(4\text{-FC}_6\text{H}_4)_3$, 64%), ($\text{P}(4\text{-ClC}_6\text{H}_4)_3$, 72%), ($\text{P}(4\text{-CF}_3\text{C}_6\text{H}_4)_3$, 94%). Finally, we found that $\text{P}(4\text{-CF}_3\text{C}_6\text{H}_4)_3$ is the additive of choice (reaction 2).




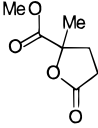

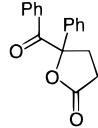

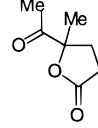
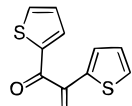
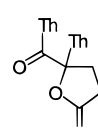
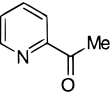
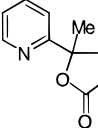
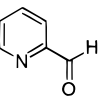
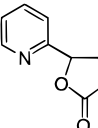
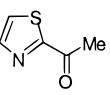
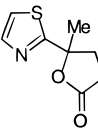
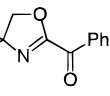
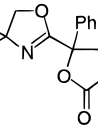
A variety of ketones containing a carbonyl group at the α -position were examined in the reaction with CO and ethylene, as shown in Table 1. In all cases, the reactions were clean, and no byproducts were detected by GC and TLC, even in the crude reaction mixture. It was found that α -diketones, such as **5**, **7**, and **9**, undergo a cyclocoupling reaction to afford the corresponding lactones, **6**, **8**, and **10**, respectively. Similar to the case of α -keto esters, the addition of $\text{P}(4\text{-CF}_3\text{C}_6\text{H}_4)_3$ gave higher yields than were obtained in the absence of the phosphine for the reaction of α -diketones.

The issue of whether the carbonyl group, adjacent to the ketone, could be replaced with another electron-withdrawing group is of interest. However, the reaction of benzoylcyanide and pentafluoroacetophenone did not proceed. In addition, the reaction of benzophenone, acetophenone, 3-acetylpyridine, 2-pyridylacetone, 2-acetylpyrrole, 2-acetylfuran, and 2-acetylthiophene did not take place. Interestingly and importantly, however, a $\text{C}=\text{N}$ unit adjacent to the ketone worked well. The reaction of 2-acetylpyridine (**11**) with ethylene at 5 atm of CO at 140 °C in toluene in the presence of $\text{Ru}_3(\text{CO})_{12}$ for 20 h gave 4-methyl-4-(2-pyridyl)- γ -butyrolactone (**12**) in 92% isolated yield. Curiously, the addition of phosphine is not required in the reaction of **11**. In contrast, the addition of PPh_3 had a dramatic effect on the reaction of pyridinecarbaldehyde (**13**). A heteroaromatic ketone containing a thiazole ring, as in **15**, gave the corresponding lactone **16** in nearly quantitative yield. The reaction is not limited to heteroaromatic ketones. An oxazoline system, such as **17** also serves as a good substrate. The acceleration effect of the heterocyclic moiety on this catalytic reaction can be attributed to its coordinating ability.

Although the mechanism for this reaction is not clear, the coordination of 1-aza-4-oxo-1-diene ($\text{N}=\text{C}-\text{C}=\text{O}$) in *N*-hetero-

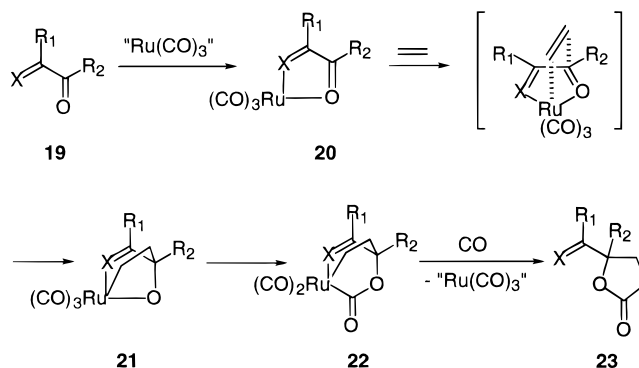
(6) All new compounds were characterized by NMR, IR, mass spectral data, and by elemental analyses or high-resolution mass spectra. See Supporting Information.

Table 1. Ru₃(CO)₁₂-Catalyzed [2 + 2 + 1] Cyclocoupling of Ketones, Ethylene, and CO^a

| ketone | additive ^b | product ^c | |
|--|-----------------------|--|------------------|
|  3 | + |  4 | 28% ^d |
| | - | | 0% |
|  5 | + |  6 | 98% |
| | - | | 73% |
|  7 | + |  8 | 70% |
| | - | | 37% |
|  9 | + |  10 | 58% |
| | - | | 52% |
|  11 | + |  12 | 92% ^e |
| | - | | 92% ^e |
|  13 | + ^f |  14 | 85% |
| | - | | 37% |
|  15 | - |  16 | 97% ^e |
| | | | |
|  17 | - |  18 | 78% ^e |
| | | | |

^a Reaction conditions: ketone (2 mmol), ethylene (initial pressure 3 atm at 25 °C), CO (initial pressure 5 atm at 25 °C), Ru₃(CO)₁₂ (0.05 mmol) in toluene (6 mL) at 160 °C for 20 h in a 50-mL stainless autoclave, unless otherwise noted. ^b +: P(4-CF₃C₆H₄)₃ (0.15 mmol) was added. -: No phosphine was added. ^c Isolated yields based on the starting ketones. ^d The reaction was run at 180 °C. ^e The reaction was run at 140 °C. ^f PPh₃ (0.15 mmol) was added in place of P(4-CF₃C₆H₄)₃.

cyclic ketones or 1,4-dioxo-1,3-diene (O=C-C=O) in α -dicarbonyl compounds to ruthenium leading to σ -X, σ -O chelate ruthenium carbonyl complexes (X = N or O)⁷ or the related metallacycles would be a key step for the present cyclocoupling

Scheme 1

reaction to proceed. One possible mechanism is shown in Scheme 1.⁸⁻¹⁰ The coordination of a substrate **19** to "Ru(CO)₃" forms a σ , σ -chelate ruthenium complex **20**. The complex **20** reacts with ethylene to form metallacycle **21**, with the coordination of X to ruthenium remaining intact. The insertion of CO into a Ru-O bond in **21** followed by reductive elimination gives the final product **23**. The influence of the phosphine derivative on the yields is dramatic in the reaction of α -dicarbonyl compounds but is not so for the case of *N*-heterocyclic ketones. The exact role of the phosphine is not clear at the present time.¹¹ Further experiments will be required to rationalize the reaction mechanism.

In summary, the first example of the *catalytic intermolecular* [2 + 2 + 1] cyclocoupling of ketones (or aldehydes), ethylene, and CO has been demonstrated. This reaction is potentially useful in the synthesis of γ -butyrolactones which bear a functional group at the γ -position and would be amenable to further elaboration. The mechanism, especially the effects of phosphine and the role of a C = X (O or N) moiety adjacent to ketones, will be addressed in future studies.

Acknowledgment. This work was supported in part by grants from Monbusho, Japan. Thanks are also given to the Instrumental Analysis Center, Faculty of Engineering, Osaka University, for assistance in obtaining MS, HRMS, and elemental analyses.

Supporting Information Available: Lists of spectral data and elemental analyses for the products (PDF). This material is available free of charge via the Internet at <http://pubs.acs.org>.

JA991223W

(7) Beers, O. C. P.; Bouman, M. M.; Elsevier, C. J.; Smeets, W. J. J.; Spek, A. L. *Inorg. Chem.* **1993**, *32*, 3015.

(8) The mechanism shown in Scheme 1 is drawn with the basis on the results on stoichiometric reactions using (X=C-C=X)Fe(CO)₃ or (X=C-C=X)Ru(CO)₃ (X = O or N), which underwent the coupling reaction with acetylenes (or olefins) and CO. See also refs 9 and 10.

(9) Frühauf reported that a stoichiometric reaction of σ -N, σ -O chelate complex (Bu-N=CH-C(R)=O)Fe(CO)₃ with dimethyl acetylenedicarboxylate leading to Fe(CO)₃(butenolide) complexes. A similar reaction route to **20** \rightarrow **23** was proposed: van Wijnkoop, M.; Siebenlist, R.; de Lange, P. P. M.; Frühauf, H.-W.; Vieze, K.; Smeets, W. J. J.; Spek, A. L. *Organometallics* **1993**, *12*, 4172; van Wijnkoop, M.; Siebenlist, R.; de Lange, P. P. M.; Frühauf, H.-W.; Horn, E.; Spek, A. L. *J. Organomet. Chem.* **1994**, *482*, 99.

(10) Frühauf reported that a stoichiometric reaction of σ -N, σ -N chelate complex (Bu-N=CH-CH=CH-Bu)Ru(CO)₃ with dimethyl maleate or dimethyl fumarate leading to a ruthenium complex similar to **22**: van Wijnkoop, M.; de Lange, P. P. M.; Frühauf, H.-W.; Vieze, K.; Smeets, W. J. J.; Spek, A. L. *Organometallics* **1995**, *14*, 4781.

(11) Frühauf found that (Pr-N=CH-CH=NPr)FeL₃ (L = isonitrile) show much higher activity than (Pr-N=CH-CH=NPr)Fe(CO)₃ in the coupling reaction with olefins: de Lange, P. P. M.; de Boer, R. P.; van Wijnkoop, M.; Ernsting, J. M.; Frühauf, H.-W.; Vieze, K.; Smeets, W. J. J.; Spek, A. L.; Goubitz, K. *Organometallics* **1993**, *12*, 440.