

Ruthenium-Catalyzed Carbonylative Cycloaddition of α -Keto Lactones with Alkenes or Alkynes: The Participation of an Ester-Carbonyl Group in Cycloaddition Reactions as the Two-Atom Assembling Unit

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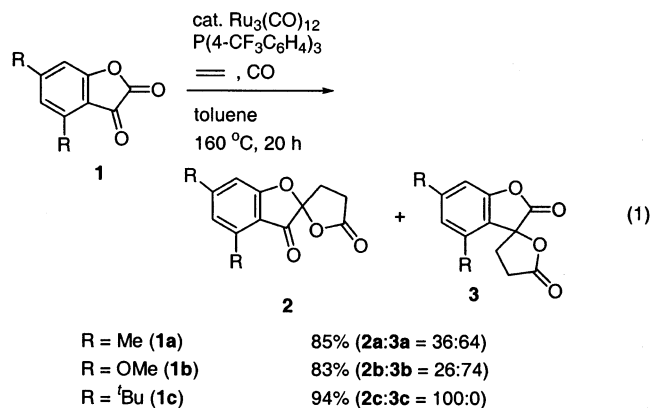
Abstract: The reaction of benzofuran-2,3-dione derivatives **1** with CO and alkenes (or alkynes) results in a carbonylative [2+2+1] cycloaddition in which the ester-carbonyl group is incorporated into a two-atom assembling unit to give spiro-lactone derivatives **2**. This reaction provides the first example of an ester-carbonyl group participating in a carbonylative cycloaddition reaction.

The cycloaddition reaction represents a useful, reliable, and powerful method for the construction of ring systems from simple acyclic building blocks.¹ Unsaturated hydrocarbons, such as olefins, acetylenes, allenes, and 1,3-dienes, have been used extensively as two- or four-atom assembling units. Carbonyl functionalities, such as aldehydes, ketones, and imines, are also useful coupling partners because the heteroatoms may be incorporated into a newly formed ring system,² e.g., a hetero-Diels–Alder reaction.³ On the other hand, the use of an ester carbonyl function as a two-atom assembling unit is rare,⁴ because of its reduced reactivity compared with aldehydes and ketones. In 1975, Russian chemists reported on the intramolecular [4+2] cycloaddition of a furan ring and an ester-carbonyl group, leading to tricyclic compounds under thermal conditions.⁵ To the best of our knowledge, this is the only reported example where an ester carbonyl group was used in cycloaddition chemistry under thermal conditions. The scope of this reaction, however, remains unclear, since they reported only one example in their study and the identification of the reaction product has not been described in detail. Cycloaddition reactions utilizing carbon monoxide as the one-carbon unit (carbonylative cycloaddition) of aldehydes, ketones, and imines have also been interested because of their great potential for the preparation of

heterocyclic carbonyl compounds from acyclic substrates.^{6–10} On the other hand, no example of a carbonylative cycloaddition reaction in which the ester carbonyl group is incorporated as the two-carbon unit exists. Our interest involved the development of a new type of carbonylative cycloaddition reaction, in which the ester carbonyl group is incorporated as the two-carbon unit, which has not been reported.

On the basis of our success in accomplishing carbonylative cycloaddition of ketones,^{7f} we chose $\text{Ru}_3(\text{CO})_{12}$ as the catalyst, 2-pyridinecarboxylates or α -diesters as the substrates, and ethylene as a coupling partner in a model reaction system. Although the reactions were undertaken under a wide range of reaction conditions, we were not able to achieve the carbonylative cycloaddition reaction of esters. Next we chose lactones as a substrate because of their higher reactivity compared with esters.¹¹ In the screening of a number of lactones, the use of benzofuran-2,3-diones **1** resulted in successful cycloaddition, in which the ester-carbonyl group was incorporated. We wish to report on the first example of carbonylative cycloaddition of the ester carbonyl functionality.

The reaction of 4,6-dimethylbenzofuran-2,3-dione (**1a**) with ethylene (initial pressure 3 atm at room temperature) and CO (initial pressure 5 atm) in toluene (3 mL) in the presence of a catalytic amount of $\text{Ru}_3(\text{CO})_{12}$ (0.025 mmol) and $\text{P}(4\text{-CF}_3\text{C}_6\text{H}_4)_3$ (0.075 mmol) at 160 °C gave the desired product **2a** as a minor product, along with **3a** in 85% total yield (36/64 ratio of **2a/3a**) (eq 1).¹²



Although intensive screening of the reaction conditions, for example, reaction temperatures, pressures of CO and

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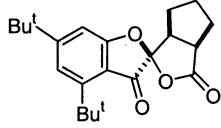

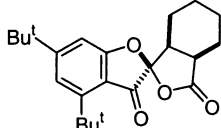
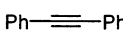
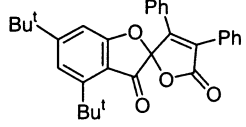
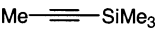
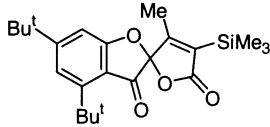
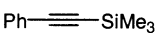
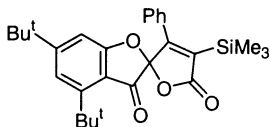
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TABLE 1. The Reaction of **1c** with CO and Alkenes or Alkynes^a

alkene or alkyne	product ^b
 10 mmol	 4 89% (88:12) ^c
 10 mmol	 5 41% (89:11) ^c 92% (91:9) ^d
 1.2 mmol	 6 83%
 5 mmol	 7 95%
 5 mmol	 8 95%

^a Reaction conditions: **1c** (1 mmol), Ru₃(CO)₁₂ (0.025 mmol), P(4-CF₃C₆H₄)₃ (0.075 mmol), alkene or alkyne, CO (initial pressure 5 atm at room temperature in a 50-mL stainless autoclave), toluene (3 mL) at 160 °C for 20 h. ^b Isolated yields based on **1c**. The numbers in parentheses are the ratios of stereoisomers, as determined by GC analysis. ^c For 90 h. ^d For 180 h.

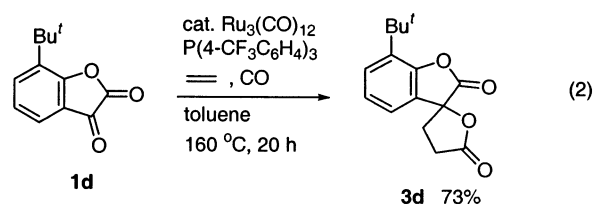
ethylene, additives, and solvents, was studied, an improvement in the ratios of **2a** to **3a** were not observed.

While the electronic nature of the substituent had a slight effect on the product distribution, as in **1b**, a bulky substituent, such as *t*-Bu, had a dramatic effect (eq 1). The reaction of **1c** with CO and ethylene took place at the lactone carbonyl selectively to give **2c** as a single product. Compared with the results of **1c** and **1d**, it was found that the steric bulkiness around the keto moiety retards the reactivity of the ketone portion of the molecule (eq 2).

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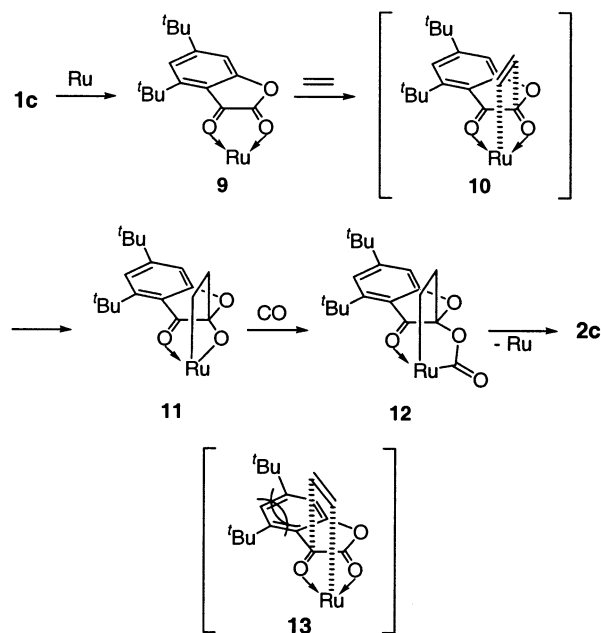
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(12) All new compounds were characterized by NMR, IR, mass spectral data, and elemental analyses or high-resolution mass spectra. See Supporting Information.



The reaction was not limited to ethylene, and other alkenes as well as alkynes were found to be applicable, as shown in Table 1. Reactions with cyclopentene or cyclohexene gave the corresponding spiro lactones **4** and **5** in a 9:1 mixture of stereoisomers in high yields. Diphenyl acetylene is also applicable to the reaction and the use of 1.2 equiv of the substrate is sufficient for obtaining a good yield. Reaction of trimethylsilyl acetylenes resulted in regioselective cycloaddition to give α,β -unsaturated lactones **7** and **8**, in which a trimethylsilyl group is bonded at the α -position to the resulting lactone carbonyl group.

The catalytic cycle starts with the formation of oxaruthenacyclopentane **11** from the oxidative cyclization of the chelation complex **9** with ethylene via **10**.^{7f,13} Insertion of CO followed by reductive elimination gives the final product **2c** and the ruthenium is regenerated.¹⁴ A transition state **10** is favored over **13** because steric repulsion between the *t*-Bu group and an approaching ethylene unstabilizes the transition state **13**.

SCHEME 1

(13) For related stoichiometric reactions, see: van Wijnkoop, M.; de Lange, P. P. M.; Frühauf, H.-W.; Vrieze, K.; Wang, Y.; Goubitz, K.; Stam, C. H. *Organometallics* **1992**, *11*, 3607. de Lange, P. P. M.; Frühauf, H.-W.; Kraakman, M. J. A.; van Wijnkoop, M.; Kranenburg, M.; Groot, A. H. J. P.; Vrieze, K.; Fraanje, J.; Wang, Y.; Neuman, M. *Organometallics* **1993**, *12*, 4172. van Wijnkoop, M.; Siebenlist, R.; Ernsting, J. M.; de Lange, P. P. M.; Frühauf, H.-W.; Horn, E.; Spek, A. L. *J. Organomet. Chem.* **1994**, *482*, 99. van Wijnkoop, M.; de Lange, P. P. M.; Frühauf, H.-W.; Vrieze, K.; Smeets, W. J. J.; Spek, A. L. *Organometallics* **1995**, *14*, 4781.

(14) The possibility that CO is inserted into a Ru-C bond in **11** cannot be excluded.

In summary, we demonstrate the first example of the participation of an ester-carbonyl group in a carbonylative cycloaddition reaction. Although the ester-carbonyl group is known to be generally less reactive than a ketone-carbonyl group, the ester-carbonyl group in α -keto lactones **1** is sufficiently reactive to compete with the ketone-carbonyl group.¹⁵ These results suggest that cycloaddition reactions with esters will be useful in organic chemistry and merit further investigation. Further studies on other related cycloaddition reactions of esters are currently under investigation.

(15) There are some examples on the Wittig reaction of α -keto lactones at the ester-carbonyl group. For reviews, see: Murphy, P. J.; Lee, S. E. *J. Chem. Soc., Perkin Trans. 1* **1999**, 3049. Osman, F. H.; El-Samahy, F. A. *Chem. Rev.* **2002**, *102*, 629.

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Supporting Information Available: Experimental procedures and characterization for all of the new compounds. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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