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Ruthenium-Catalyzed Reconstructive Synthesis of Cyclopentenones by Unusual Coupling of Cyclobutenediones with Alkenes Involving Carbon−Carbon Bond Cleavage

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Cleavage of C−C bonds by transition metals under homogeneous conditions has recently received much scientific and technological interest and has opened the door to a new field of synthetic organic chemistry.[1] The next challenging subject is reconstruction of new carbon skeletons after C−C bond cleavage.[2] The C−C single bond between a carbonyl and the α-carbon is relatively weaker than other C−C single bonds. Moreover, it is likely that a carbonyl group kinetically facilitates insertion of a transition metal into the α-C−C bond.[1d,3] Cyclobutenediones have recently been recognized as versatile reagents for the construction of various multicyclic compounds[4] and are easily prepared from squaric acid.[5] Activation of C−C bonds in cyclobutenediones by transition-metal complexes follows the two pathways illustrated in Scheme 1. Most transition-metal complexes, including those of rhodium, cobalt, iron, and nickel gave (maleoyl)metal complexes as a thermodynamic product resulting from insertion of the metal between two carbonyl groups in cyclobutenediones (path a),[6] while treatment of cyclobutenediones with platinum[7] or rhodium[8] complexes gave unsymmetrical cleavage of the four-membered ring to give a kinetic product (path b).

The conversion of cyclobutenediones to quinones[9] and 5-alkylidene-2-cyclopentene-1,4-diones[10] using a stoichiometric amount of transition-metal complexes via (maleoyl)metal complexes (path a) has been studied in detail. However, neither transition-metal complex-catalyzed transformation of cyclobutenediones nor the synthetic reaction via metallacyclopentenedione or metallacyclobutenone complexes according to path b has been reported. On the basis of our investigation of ruthenium catalysis,[2c,g,h,11] we found a novel ruthenium-catalyzed reconstructive synthesis of cyclopentenones by an unusual coupling reaction of cyclobutenediones with alkenes involving C−C bond cleavage (path b). We report here that the development of this new ruthenium catalyst system enables the rapid synthesis of cyclopentenones without the use of alkynes.

Scheme 1

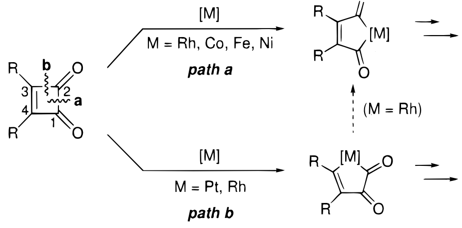
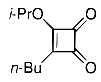
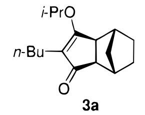
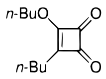
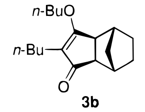
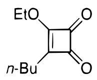
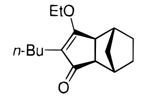
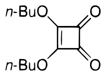
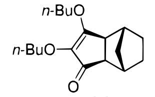


Table 1. Ru$_3$(CO)$_{12}$/PEt$_3$-Catalyzed Synthesis of Cyclopentenones from Cyclobutenediones (**1a**−**d**) and 2-Norbornene (**2a**)[a]

Run	Cyclobutenedione	Product	Isolated yield(%)
1	 **1a**	 **3a**	75
2	 **1b**	 **3b**	60
3	 **1c**	 **3c**	47
4[b]	 **1d**	 **3d**	46

[a] Cyclobutenedione (**1**) (1.0 mmol), 2-norbornene (**2a**) (3.0 mmol), Ru$_3$(CO)$_{12}$ (0.050 mmol), PEt$_3$ (0.15 mmol), and THF (1.0 mL) under CO (3 atm) at 160 °C for 20 h. [b] CO 15 atm.

Treatment of 4-butyl-3-isopropoxycyclobut-3-ene-1,2-dione (**1a**) with 2-norbornene (**2a**) in the presence of 5 mol % Ru$_3$(CO)$_{12}$ and 15 mol % PEt$_3$ in THF under 3 atm of carbon monoxide at 160 °C for 20 h gave the corresponding cyclopentenone **3a** in 75% yield with high stereoselectivity (*exo* 100%) (Table 1, run 1).

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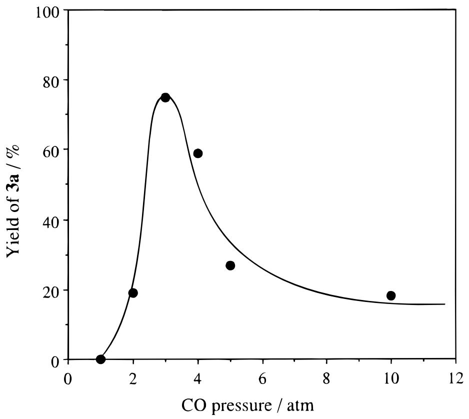


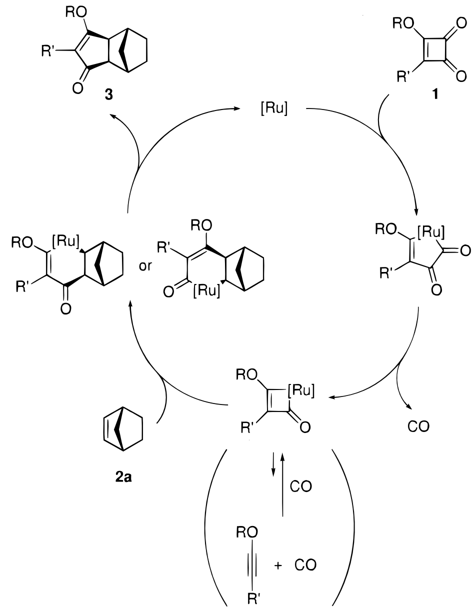
Figure 1. Effect of CO pressure on $Ru_3(CO)_{12}/PEt_3$-catalyzed synthesis of **3a** from **1a** and **2a**. Reaction conditions: **1a** (1.0 mmol), **2a** (3.0 mmol), $Ru_3(CO)_{12}$ (0.050 mmol), PEt_3 (0.15 mmol), THF (1.0 mL) at 160 °C for 20 h.

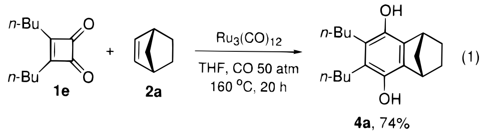
The effects of the catalysts, ligands, and reaction conditions were examined in the synthesis of **3a** from the reaction of **1a** with **2a**. An appropriate catalyst combined with a phosphorus ligand was critical for the success of the reaction. For example, the catalytic activity of $Ru_3(CO)_{12}$ *itself* is quite low (**3a**, 17%), but the concomitant use of PEt_3 ligand dramatically increased the catalytic activity to give **3a** in the best yield of 75%. Catalyst systems combined with other phosphorus ligands, such as PBu_3, PCy_3, PPh_3, and $P(OBu)_3$, showed moderate catalytic activity, while bidentate phosphorus ligands, such as dppe and depe, were almost ineffective. Other ruthenium catalyst systems, such as $RuH_2(PPh)_4$, $RuHCl(CO)(PPh_3)_3$, $RuH_2(CO)(PPh_3)_3$, $RuCl_2(PPh_3)_3$, $[Ru(CO)_3Cl_2]_2/PEt_3$, $[(\eta^6\text{-}C_6H_6)RuCl_2]_2/PEt_3$, and $CpRuCl(PPh_3)_2$, only promoted the polymerization or decomposition of cyclobutenediones. No cyclopentenone was obtained with $CoCl(PPh_3)_3$ nor $RhCl(PPh_3)_3$ catalysts, which are known to react with cyclobutenediones to give the corresponding (maleoyl)metal complexes.[6] This result strongly suggests that the present reaction does not involve a (maleoyl)ruthenium intermediate. Among the solvents examined (benzene, 43%; 1,4-dioxane, 32%; acetonitrile, 21%; DMF, 0%; *N*-methylpiperidine, 0%), THF gave the best result (yield of **3a**, 75%).

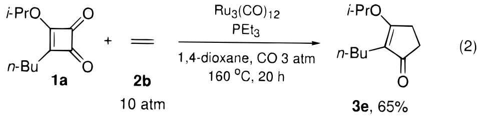
The carbon monoxide pressure also had a dramatic effect (Figure 1). The best result was obtained under 3 atm of carbon monoxide, and either an increase or decrease in the carbon monoxide pressure caused a rapid decrease in the yield of **3a**. Use of ^{13}CO gave the ^{13}C-labeled cyclopentenone (70% scrambling), which indicates that the external carbon monoxide is needed to suppress complete decarbonylation of cyclobutenediones to the corresponding alkynes and carbon monoxide.

The results obtained from the reactions of several cyclobutenediones (**1a**−**d**) with 2-norbornene (**2a**) under optimum conditions are listed in Table 1. In all cases, the starting cyclobutenediones were completely consumed, and the products detected by GLC were only the corresponding cyclopentenones, **3a**−**d**. As for **1d**, the carbon monoxide pressure had to be increased to 15 atm because of the high reactivity of **1d** toward complete decarbonylation. On the other hand, 3,4-di*alkyl*cyclobutenedione, such as 3,4-dibutylcyclobut-3-ene-1,2-dione (**1e**), gave the corresponding hydroquinone **4a** instead of the cyclopentenone, probably via a (maleoyl)ruthenium intermediate (eq 1).[11b] Accordingly, the ring-opening of cyclobutenediones by ruthenium catalysts depends on the substituents of the cyclobutenediones. The reaction of ethylene (**2b**) with **1a** in 1,4-dioxane also gave the corresponding cyclopentenone **3e** in 65% yield (eq 2).

Scheme 2







While the reaction mechanism is not yet clear, the present reaction involves regioselective C−C bond cleavage (Scheme 2). First, oxidative addition of cyclobutenedione **1** to an active ruthenium center would occur at the C2−C3 bond selectively under the direction of an alkoxy substituent to give a ruthenacyclopentenedione intermediate.[12] Appropriate carbon monoxide pressure (3 atm) is needed to control selective *mono*-decarbonylation of a ruthenacyclopentenedione to a ruthenacyclobutenone intermediate, as well as to suppress complete decarbonylation to an (alkoxy)alkyne and CO. Subsequent stereoselective *cis*-carboruthenation of 2-norbornene (**2a**) and reductive elimination with a retention of stereochemistry gives the corresponding cyclopentenone **3** exclusively in *exo* form.[11c,d]

In conclusion, we have developed a novel method for preparing cyclopentenones by the ruthenium-catalyzed unusual coupling of cyclobutenediones with alkenes involving C−C bond cleavage. The present reaction offers a novel ruthenium-catalyzed construction of cyclopentenones without the use of alkyne substrates, which may be the complement of the *catalytic intermolecular* Pauson−Khand reaction.[13]

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Supporting Information Available: Experimental details and characterization of all new compounds are provided (PDF). This material is available free of charge via the Internet at http://pubs.acs.org.

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[13] The Pauson−Khand reaction mediated or catalyzed by transition-metal complexes has been accepted as a powerful and convergent method for the construction of cyclopentenones; however, the use of *alkyne* substrates is essential for the reaction. For reviews, see: (a) 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. (b) Hicks, F. A.; Buchwald, S. L. *J. Am. Chem. Soc.* **1999**, *121*, 7026 and references therein.