

Rh(I)-Catalyzed Carbonylative Carbocyclization of Tethered Ene— and Yne—cyclopropenes

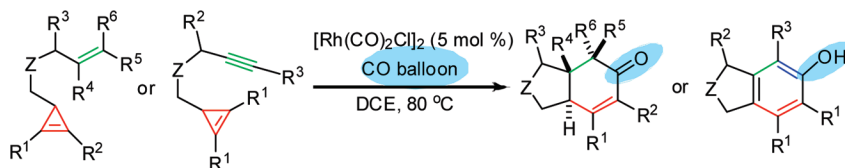
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ABSTRACT



Rh(I)-catalyzed carbonylative carbocyclization of ene— and yne—cyclopropene systems provides cyclohexenones and phenols with high efficiency, respectively.

Transition-metal-catalyzed carbocyclization of the polyunsaturated system has attracted significant attention.¹ In particular, carbonylative carbocyclization is a powerful tool to construct ring systems possessing carbonyl functional groups, as represented by carbonylative alkyne—alkene [2 + 2 + 1] carbocyclization (Pauson—Khand reaction), which has been widely used in the synthesis of cyclopentenones.² Pioneering work by Narasaka and Jeong demonstrated that rhodium complexes were efficient catalysts in the Pauson—Khand reaction.^{3,4} Wender and co-workers have expanded metal-catalyzed [2 + 2 + 1] carbocyclization into diene—yne, diene—ene, and diene—allene systems and observed a remarkable rate-accelerating

effect of the diene moiety.⁵ Furthermore, Wender and co-workers in 2002 reported the first Rh(I)-catalyzed intermolecular [5 + 2 + 1] carbocyclization, in which vinylcyclopropene provides the five-carbon component.⁶ Intramolecular Rh(I)-catalyzed [5 + 2 + 1] cycloaddition of the ene—vinylcyclopropane system has been developed recently by Yu and co-workers, which is an efficient method to construct bicyclooctenones.⁷

In contrast to these remarkable developments, the formation of a six-membered ring through [3 + 2 + 1] carbonylative carbocyclization has been much less developed, presumably due to the difficulty of introducing the required three-carbon component. An obvious source of a three-carbon component would be cyclopropane. Although cyclopropane has been utilized in metal-catalyzed carbocyclization reactions, the presence of a neighboring

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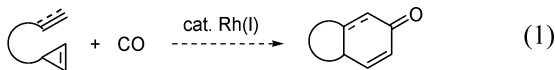
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double bond is necessary for metal coordination, which results in the participation of five-carbon component in the reaction in most cases.^{1,6–8} Koga and Narasaka have examined the Rh-catalyzed carbonylative carbocyclization of the tethered yne–cyclopropane system, in which the cyclopropane moiety does not bear a neighboring double bond.⁹ The cyclopropane did participate in the reaction as a three-carbon component, giving [3 + 2 + 1] carbocyclization products. However, the catalytic efficiency is not high, apparently due to the difficulty of ring-opening of an isolated cyclopropane moiety under the reaction conditions of Rh(I) catalysis.

We envisage that cyclopropene, which has a double bond in the three-membered ring for metal coordination and has much higher strain energy than cyclopropane or methylenecyclopropane, will show high reactivity in the carbocyclization reaction (eq 1).^{10–12} Indeed, it has been well documented that ring-opening and/or metallocyclobutene formation occurs easily when cyclopropene reacts with transition metals.^{13–16} In particular, Pd(II)- or Rh(I)-catalyzed intermolecular [3 + 2] carbocyclization reactions of cyclopropenone acetal or cyclopropenone with alkyne have been reported.¹⁶ We communicate herein the Rh(I)-catalyzed [3 + 2 + 1] carbonylative carbocyclization of ene– and yne–cyclopropene systems, which provides bicyclohexenones and phenols, respectively.



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At the outset, nitrogen-tethered ene–cyclopropene substrate **1a** was used to examine the Rh(I)-catalyzed cycloaddition with CO (Table 1). The Wilkinson catalyst

Table 1. Optimization for Rh(I)-Catalyzed Carbonylative Cycloaddition^a

entry	catalyst (5 mol %)	solvent	temp (°C)	yield ^b (%)
1	Rh(PPh ₃) ₃ Cl	DCE	80	<5 ^c
2	Rh(PPh ₃) ₃ Cl+AgSbF ₆	DCE	80	<5 ^c
3	[Rh(COD)Cl] ₂	DCE	80	74
4	[Rh(COD)Cl] ₂ +AgSbF ₆	DCE	80	42
5	[Rh(CO) ₂ Cl] ₂	DCE	80	89
6	[Rh(CO) ₂ Cl] ₂ +AgSbF ₆	DCE	80	57
7	[Rh(CO) ₂ Cl] ₂	toluene	100	58
8	[Rh(CO) ₂ Cl] ₂	<i>p</i> -xylene	130	71

^a Reaction conditions: **1a** (50 mg, 0.12 mmol) in 5 mL of solvent.

^b Isolated yield. ^c **1a** was recovered.

alone or its combination with AgSbF₆ at 80 °C in DCE afforded only a trace amount of the desired bicyclohexenone **2a**, with most of the starting material recovered (entries 1 and 2). To our delight, [Rh(COD)Cl]₂ under the same conditions gave much higher yield (entry 3). Compound **2a** was obtained in 89% yield with [Rh(CO)₂Cl]₂ (entry 5). Addition of Ag(I) salt had negative effects (entries 4 and 6), presumably due to the side reaction catalyzed by AgSbF₆. Reaction in toluene and *p*-xylene at high temperature with [Rh(CO)₂Cl]₂ gave only moderate yields with recovery of starting materials (entries 7 and 8). The structure of **2a** was confirmed by X-ray crystallographic analysis (Figure 1). It is noteworthy that **2a** has a *trans* configuration for the fused rings.

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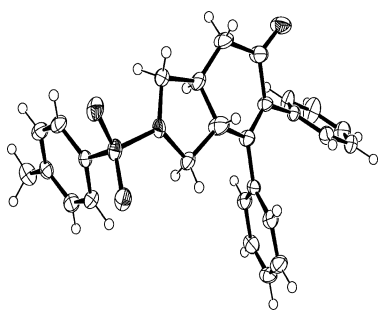
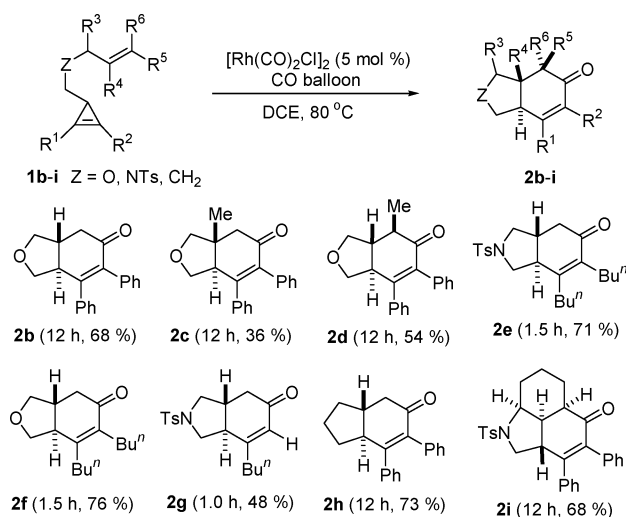


Figure 1. X-ray structure of **2a**.

The generality of this reaction was then examined under the optimized conditions. As summarized in Scheme 1, the

Scheme 1. Rh(I)-Catalyzed Carbonylative Cycloaddition of **1a-i**



reaction with a series of ene-cyclopropene substrates **1b-i** provided the expected bicyclohexenone derivatives as single diastereomers in all cases. The reaction works well with the oxygen- (**1b-d,f**) and carbon-tethered substrates (**1h**). The substituent on the alkene moiety has an effect on the yield (**1c,d**). In the case of **1c**, the significant drop of yield may be attributed to the methyl substituent in the double bond, impeding the step of alkene insertion in the reaction mechanism. The stereochemistry of **2c** is confirmed by NOESY experiments, which demonstrates that the fused two rings also have a *trans* configuration. When the two substituents on cyclopropene were alkyl groups, the reaction was found to proceed much faster as compared to their phenyl-substituted counterparts (**1e-g**). In the case of **1g** (cyclopropene is unsymmetrically substituted), the Rh selectively inserts into the less substituted C-C bond of cyclopropene, affording **2g** as the only carbocyclization product. When the substrate bearing a cyclohexenyl moiety was subjected to the reaction, tricyclic cyclohexenone product **2i** was obtained

in 68% yield. The structure of **2i** was confirmed by X-ray crystallographic analysis (Figure 2).

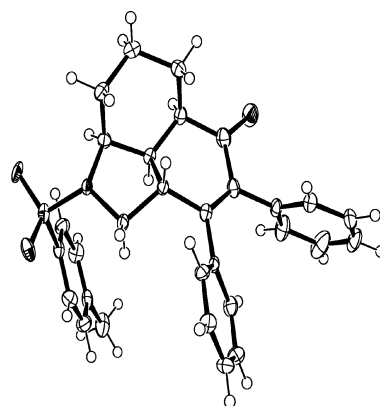
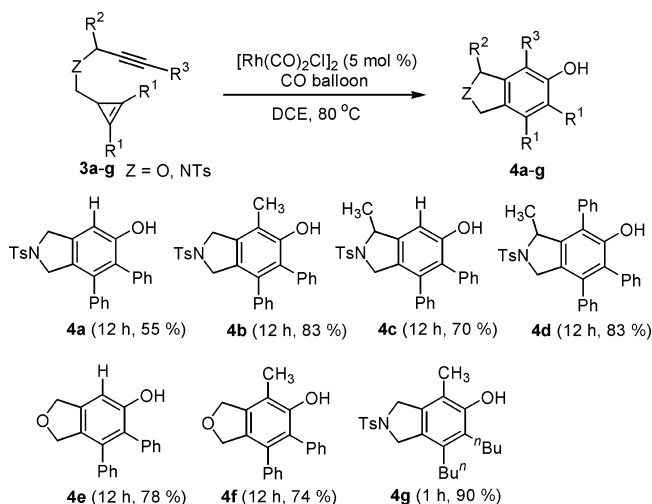


Figure 2. X-ray structure of **2i**.

Next, we examined the reactions of tethered yne-cyclopropene systems under the same reaction conditions. As shown in Scheme 2, the reaction provides bicyclic phenols

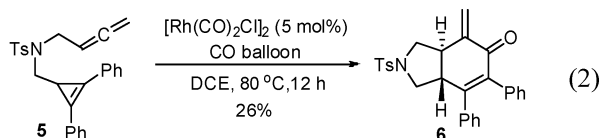
Scheme 2. Rh(I)-Catalyzed Carbonylative Cycloaddition of **3a-g**



in moderate to good yields. The reaction gave slightly higher yield when there was a substituent in the terminal carbon of alkyne (**3b,d,f,g**), while a substituent in the propargylic position (R^2) did not significantly affect the yields (**3c,d**). Similar to the reaction of ene-cyclopropenes, the reaction of the substrate **3g**, which bears an alkyl-substituted cyclopropenyl moiety, proceeded faster compared with its phenyl-substituted counterpart.

To further expand the scope of this reaction, we investigated the reaction of a tethered allene-cyclopropene system (eq 2). The allene moiety did participate in the reaction, and

the expected [3 + 2 + 1] carbocyclization product was obtained in 26% yield, with most of the starting material recovered.



To gain insight into the mechanism, the Rh(I)-catalyzed reaction of **1a** was carried out in the absence of CO. The [3 + 2] carbocyclization product **7** was isolated in 28% yield, together with **8** in 58% yield (eq 3). The structure of bicyclic product **7** was confirmed by X-ray crystallographic analysis (Figure 3). Interestingly, the fused bicyclic structure in product **7** has a *cis* configuration.

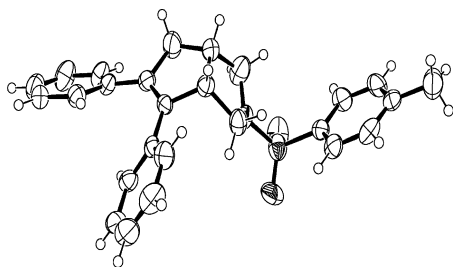
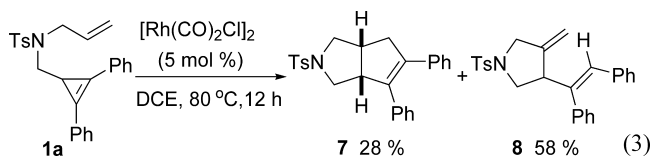
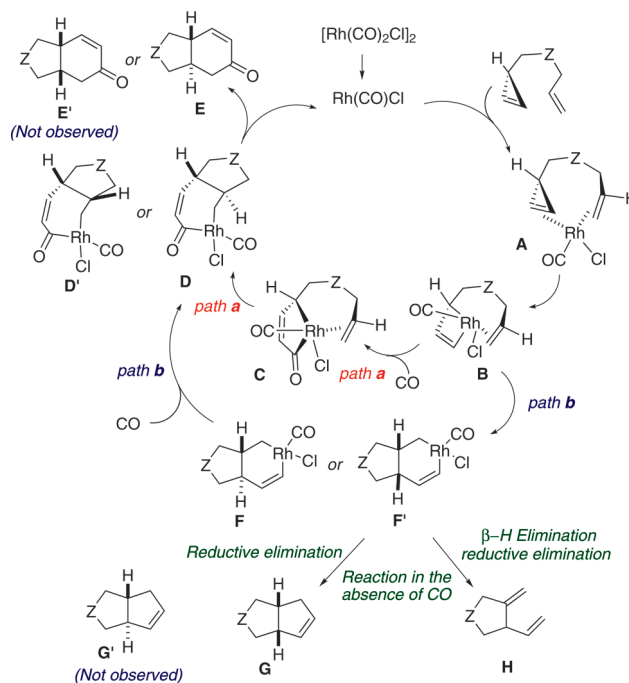


Figure 3. X-ray structure of **7**.

A mechanistic rationale is proposed in Scheme 3.¹⁷ Complexation of the dissociated Rh(I) catalyst with substrate forms intermediate **A**. Direct oxidative addition of the Rh(I) to the σ -bond of the cyclopropene moiety generates rhodacyclobutene intermediate **B**.¹³ From intermediate **B**, there are two possible pathways: path a and path b. In path a, CO insertion occurs first to give **C**, from which insertion of alkene leads to intermediate **D**, which undergoes reductive elimination to provide the final product **E**. In path b, alkene insertion occurs first to generate **F** or **F'**, followed by CO insertion and reductive elimination to give final product **E**

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Scheme 3. Proposed Reaction Mechanism



or **E'**. In the absence of CO as shown in eq 3, **G** and **H** are obtained from **F'** through reductive elimination or β -hydride elimination/reductive elimination. Since the possible *cis*-fused cycloadduct **E'** was not observed in the carbonylative reaction and the reaction in the absence of CO only afforded *cis*-fused cycloadduct **G**, it can be deduced that the carbonylative carbocyclization follows path a rather than path b. However, more rigorous study is needed to confirm the mechanism.

In conclusion, we have developed the first Rh(I)-catalyzed [3 + 2 + 1] carbonylative carbocyclization reactions of ene- and yne-cyclopropene systems. The results demonstrate that the highly strained cyclopropene structure can be used as an excellent three-carbon component in a transition-metal-catalyzed carbocyclization reaction of polyunsaturated systems.

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Supporting Information Available: Experimental procedures, characterization data, ¹H and ¹³C NMR spectra for all new compounds, and X-ray crystallography data (CIF) for **2a**, **2i**, and **7**. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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