# Ruthenium-Catalyzed Processes: Dual [2+2] Cycloaddition versus Cyclopropanation of Bicyclic Alkenes with Propargylic Alcohols

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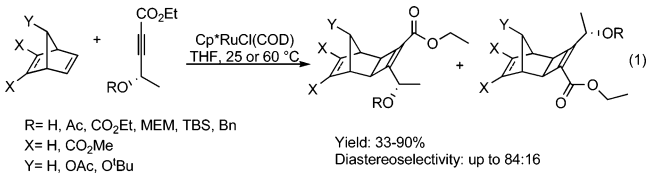
Propargylic alcohols have been found to exhibit dual reactivity with bicyclic alkenes in the presence of Cp*Ru(cod)X (X =Cl, Br, I; Cp* = pentamethylcyclopentadienyl, cod = 1,4-cyclooctadiene). Cyclopropane and cyclobutene products can be obtained in a highly stereoselective fashion, but their formation is dependent on a variety of factors including the functional groups attached to the alkyne or alkene moieties and the nature of the ruthenium catalyst. To the best of our knowledge, this cyclopropanation proceeding through a $\beta$-hydride elimination or a [1,2]-hydride shift is an unprecedented catalytic pathway for ruthenium complexes.

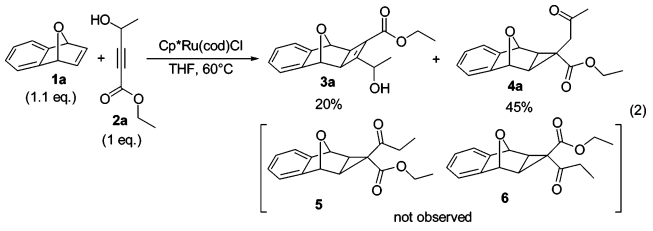
## Introduction

The development of ruthenium-catalyzed processes has become an emerging field over the past decade.[1] With their wide range of oxidation states (from −2 to +8) and several coordination geometries, ruthenium catalysts can form a variety of intermediates such as $\pi$-allylruthenium, ruthenium-carbene, and ruthenacycle species. Among various ruthenium complexes, Cp′Ru(cod)Cl (Cp′ = substituted cyclopentadienyl) have been found to be the catalysts of choice in many processes such as [2+2+2] cycloadditions,[2] conjugate additions,[3] bis-Diels−Alder cycloadditions,[4] Alder-ene reactions,[5] cross-benzannulations,[6] and many other reactions.[1] We[7] and other groups[8] have been greatly involved in the preparation of cyclobutene rings via ruthenium-catalyzed [2+2] cycloadditions.

During the course of investigating diastereoselective ruthenium-catalyzed [2+2] cycloaddition between propargylic alcohols and bicyclic alkenes, we were interested in studying the scope and limitation of the method (eq 1).[7d] We showed that different bicyclic alkenes bearing a carbon-containing group at the bridgehead position would undergo the [2+2] cycloaddition in modest to moderate diastereoselectivities with propargylic alcohol **2a** (R = H, eq 1).




However, when expanding the scope of this reaction to oxabicyclic alkenes using the same methodology, the unexpected cyclopropane **4a** was isolated as the major product (eq 2). The formation of this product was shown to be highly stereoselective, giving only one stereoisomer.




A similar structure was observed by Takahashi et al.[9] where the cyclopropane **7** was formed when norbornene and a terminal propargylic alcohol were reacted in the presence of a [Cp′Ru-$(CH_3CN)_3$]$PF_6$ catalyst (Scheme 1, Cp′ = $\eta^5$-ethoxycarbonyl-2,4-dimethylcyclopentadienyl). A mechanism involving the formation of a ruthenacyclopentene followed by a $\beta$-hydroxy elimination was proposed. However, the reaction presented herein involves a different mechanism since cyclopropanes **5** and **6** were not observed. In addition, cyclopropane **7** was not formed when reacting norbornene with propargyl alcohol in the presence of Cp*Ru(cod)Cl. We wish to report details about the formation of *meso* cyclopropane **4** through an unprecedented

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(1) For a review on ruthenium-catalyzed reactions, see: (a) Trost, B. M.; Toste, F. D.; Pinkerton, A. B. *Chem. Rev.* **2001**, *101*, 2067. (b) Naota, T.; Takaya, H.; Murahashi, S.-I. *Chem. Rev.* **1998**, *98*, 2599. (c) *Topics in Organometallic Chemistry*, Vol. 11; Bruneau, C., Dixneuf, P. H., Eds.; Springer-Verlag GmbH: Berlin, 2004. (d) *Ruthenium in Organic Synthesis*; Murahashi, S.-I., Ed.; Wiley-VCH: Weinheim, 2004.

(2) (a) Yamamoto, Y.; Takagishi, H.; Itoh, K. *Org. Lett.* **2001**, *3*, 2117. (b) Yamamoto, Y.; Takagishi, H.; Itoh, K. *J. Am. Chem. Soc.* **2002**, *124*, 28. (c) Yamamoto, Y.; Takagishi, H.; Itoh, K. J. C *J. Am. Chem. Soc.* **2002**, *124*, 6844.

(3) Trost, B. M.; Krause, L.; Portnoy, M. *J. Am. Chem. Soc.* **1997**, *119*, 11319.

(4) Huang, X.; Lin, Z. *Organometallics* **2003**, *22*, 5478.

(5) (a) Trost, B. M.; Müller, T. J. J. *J. Am. Chem. Soc.* **1994**, *116*, 4985. (b) Trost, B. M.; Müller, T. J. J.; Martinez, J. *J. Am. Chem. Soc.* **1995**, *117*, 1888.

(6) Kondo, T.; Kaneko, Y.; Tsunawaki, F.; Okada, T.; Shiotsuki, M.; Morisaki, Y.; Mitsudo, T. *Organometallics* **2002**, *21*, 4564.

(7) (a) Jordan, R. W.; Tam, W. *Org. Lett.* **2000**, *2*, 3031. (b) Jordan, R. W.; Tam, W. *Org. Lett.* **2001**, *3*, 2367. (c) Jordan, R. W.; Tam, W. *Tetrahedron Lett.* **2002**, *43*, 6051. (d) Villeneuve, K.; Jordan, R. W.; Tam, W. *Synlett* **2003**, 2123. (e) Villeneuve, K.; Tam, K. *Angew. Chem., Int. Ed.* **2004**, *43*, 610. (f) Villeneuve, K.; Riddell, N. G.; Jordan, R. W.; Tsui, G.; Tam, W. *Org. Lett.* **2004**, *6*, 4543. (g) Jordan, R. W.; Khoury, P. R.; Goddard, J. D.; Tam, W. *J. Org. Chem.* **2004**, *69*, 8467. (h) Riddell, N.; Villeneuve, K.; Tam, W. *Org. Lett.* **2005**, *7*, 3681.

(8) (a) Mitsudo, T.; Naruse, H.; Kondo, T.; Ozaki, Y.; Watanabe, Y. *Angew. Chem.* **1994**, *106*, 595. (b) Tenaglia, A.; Giordano, L. *Synlett* **2003**, 2333.

(9) Matsushima, Y.; Kikuchi, H.; Uno, M.; Takahashi, S. *Bull. Chem. Soc. Jpn.* **1999**, *72*, 2475.

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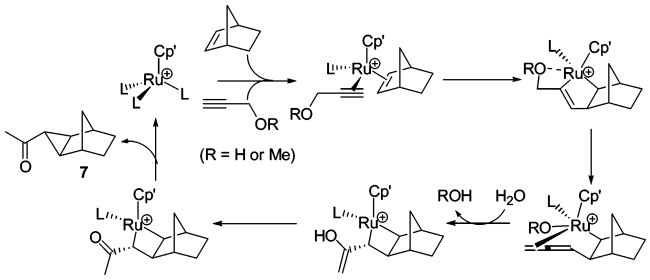
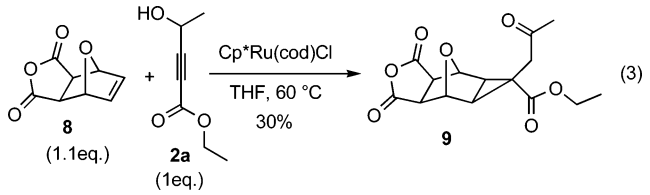
**Scheme 1. Proposed Mechanism by Takahashi and Co-workers for the Formation of 7**




catalytic pathway of Cp*Ru(cod)Cl. The scope of this reaction will also be discussed.

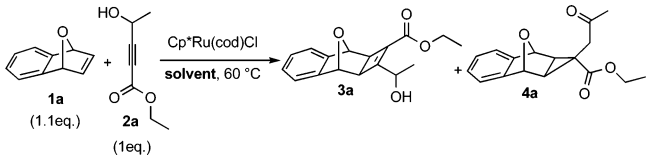
## Results and Discussion

**Elucidation of the Structure and influence of Reaction Conditions on Product Formation.** Nuclear magnetic resonance experiments ($^1$H, JMOD, COSY, HMBC) in addition to infrared and high- and low-resolution mass spectrometry were sufficient to establish the structure of *meso* compound **4a**. However, the relative stereochemistry at the quaternary center on the cyclopropane was fully elucidated by X-ray diffraction of the crystalline product **9** formed in 30% yield from alkene **8** and alkyne **2a**.[10]




Interestingly, the formation of cyclopropanes similar to **4a** was not observed when reacting **2a** with carbobicyclic alkenes such as norbornene and norbornadiene.[7d] To better understand the formation of **4a**, the influence of reaction conditions was first studied. As depicted in Table 1, solvent had a modest effect on the reaction. The ratio **3a**:**4a** could be slightly altered by changing from a less to a more polar solvent, favoring **4a** with the more polar solvent. Also as previously observed by our group, DMF was found to deactivate the catalyst and no reaction was detected.[7a] Performing the reaction in polar aprotic solvent such as sulfolane (entry 6) also gave a ratio of products similar to what we observed in THF, although lower yields were obtained. The main change in the outcome of the reaction was found to occur in trifluoroethanol (entry 7). In this case, cyclobutene **3a** was formed as the major product in 43% yield. It is noteworthy that polar solvents such as methanol promote halide ionization to form cationic ruthenium species.[11] Therefore, the distinct selectivity observed in the case of trifluoroethanol is probably due to the presence of a radically different ruthenium complex in solution.

**Table 1. Solvent Optimization**

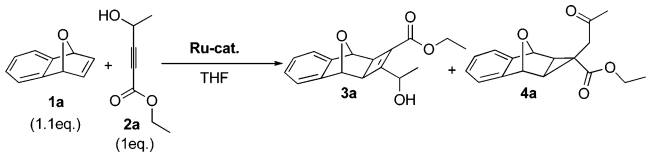



| entry | solvent[a] | time (h) | ratio[b] **3a**:**4a** | yield[c] (%) **3a** | **4a** |
|---|---|---|---|---|---|
| 1 | toluene | 2 | 42:58 | 21 | 29 |
| 2 | 1,2-DCE | 1 | 38:62 | 21 | 35 |
| 3 | THF | 1 | 31:69 | 25 | 56 |
| 4 | acetone | 2.5 | 28:72 | 11 | 39 |
| 5 | DMF | 3 | N/A | 0 | 0 |
| 6 | sulfolane | 5 | 32:68 | 15 | 32 |
| 7 | TFEOH[d] | 1 | 94:6 | 43 | <5 |

[a] DCE = dichloroethane, THF = tetrahydrofuran, DMF = dimethylformamide, TFEOH = trifluoroethanol. [b] Determined by analysis of the crude $^1$H NMR. [c] Yields were based on the crude $^1$H NMR with dimethoxyethane as internal standard. [d] Another unidentified product was also present.

Another factor that can play an important role in product ratio is the temperature at which the reaction is carried out. In our case no significant change was observed in the product ratio; however, the yield was found to vary significantly (Table 2). At 25 °C (entry 1), 41% of the starting alkyne was still present after 68 h, but when raised to 60 °C (entry 2), the reaction was complete in 1 h. Further increases in temperature (85 °C, entry 3) led to a decrease in the overall yield (**3a** + **4a** = 81% at 60 °C versus 53% at 85 °C) and the ratio of **3a**:**4a** remained the same.

**Table 2. Catalyst and Temperature Effects**




| entry | catalyst | temp (°C) | time (h) | ratio[a] **3a**:**4a** | yield[b] (%) **3a** | **4a** |
|---|---|---|---|---|---|---|
| 1 | Cp*Ru(cod)Cl | 25 | 68 | N/A | N/A | 13[c] |
| 2 | Cp*Ru(cod)Cl | 60 | 1 | 31:69 | 25 | 56 |
| 3 | Cp*Ru(cod)Cl | 85 | 1 | 32:68 | 17 | 36 |
| 4 | Cp*Ru(cod)Br | 60 | 1 | 49:51 | 28 | 29 |
| 5 | Cp*Ru(cod)I | 60 | 3 | 87:13 | 55 | 8 |
| 6 | $[CpRu(AN)_3]PF_6$[d] | 60 | 3 | N/A | 0 | 0 |
| 7 | CpRu(cod)Cl | 60 | 24 | N/A | 0 | 0 |

[a] Determined by analysis of the crude $^1$H NMR. [b] Yields were based on the crude $^1$H NMR with dimethoxyethane as internal standard. [c] 41% of starting alkynol was still present. [d] AN = acetonitrile.

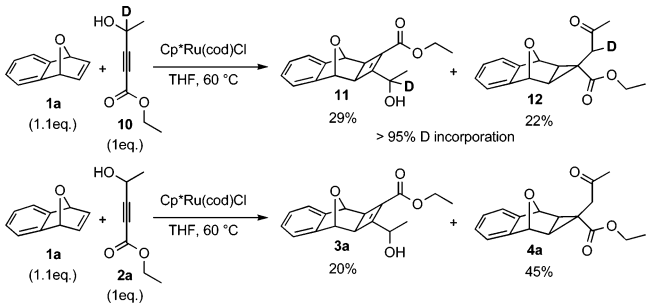
In contrast, significantly different product ratios were found upon slightly modifying the catalyst (Table 2, entries 2, 4−7). Literature precedents have shown that varying the halide on certain transition-metal catalysts can modulate their activity and/or selectivity.[12] This applies to our system, as we observed a complete reversal of the selectivity when the halide X on the catalyst Cp*Ru(cod)X was varied (Table 2, entries 2, 4, 5). Descending the periodic table, the cyclopropane product was favored with X = Cl (**3a**:**4a** = 31:69, entry 2), an equal mixture of cyclopropane/cyclobutene was obtained when X = Br (**3a**:**4a** = 49:51, entry 4), and the cyclobutene product was mainly observed in the case of X = I (**3a**:**4a** = 87:13, entry 5). A possible explanation for this trend is the increase in steric bulk on the catalyst when moving from Cl to I, which favors the reductive elimination process that affords cyclobutene **3a**, once the ruthenacyclopentene intermediate is formed (vide supra, Scheme 3). On the other hand, no reaction was observed when $[CpRu(CH_3CN)_3]PF_6$ or an electron-poor catalyst such as CpRu(cod)Cl was employed. It is also worth mentioning that treating

(10) Lough, A. J.; Villeneuve, K.; Tam, W. *Acta Crystallogr.* **2004**, *E60*, o1659.

(11) Davies, S. G.; McNally, J. P.; Smalllridge, A. J. *Adv. Organomet. Chem.* **1990**, *30*, 1.

(12) Fagnou, K.; Lautens, M. *Angew. Chem., Int. Ed.* **2002**, *41*, 26.

**Scheme 2. Deuterium-Labeling Studies**




**1a** and **2a** with a variety of Lewis acids ($ZnCl_2$, $AlCl_3$, $ZrCl_4$, $BF_3{\cdot}OEt_2$) did not afford any reaction.

**Scope of the Reaction.** Table 3 shows different alkynes that were tested. As found with entries 1−3, substitution at the propargylic position played an important role in the product formation. Secondary propargylic alcohol **2a** led to a 2.2:1.0 mixture of cyclopropane **4a**:cyclobutene **3a**, whereas primary propargylic alcohol **2b** and the tertiary alcohol **2c** (bearing no hydrogen at the propargylic position) both provided only the cyclobutene products **3b** and **3c**, respectively. Varying the position of the alcohol also changed the product ratio; only the cyclobutene product **3d** was observed with the homopropargylic alcohol **2d**. The electronics of the alkynol were then investigated, and as for our usual ruthenium-catalyzed [2+2] cycloaddition, increasing the electron-withdrawing ability of the acetylenic group enhanced the rate and the yield of the reaction. When a phenyl group was used (Table 3, entry 5), the reaction was found to be very slow and starting material decomposition as well as unidentified side products formation was observed. On the other hand, when substituting the ethyl ester group for the better electron-withdrawing methyl ketone group (entry 6), much cleaner reaction and higher yield (67%) were obtained. In addition, the cyclopropane product **4f** was exclusively produced, showcasing the importance of the alkynyl substituent in the formation of the cyclopropane product. It was then expected that utilizing alkyne **2g** bearing an electron-withdrawing group on the ester portion would provide a product distribution somewhere between **2a** and **2f**. Although cyclopropane **4g** was formed preferentially, the product ratio **3g**:**4g** in the crude mixture was 41:59, which is less predominant than that observed for **3a**:**4a** (31:69).

With the electron-poor alkynol **2f** giving exclusively the cyclopropane product when reacted with **1a** under our optimized conditions, we decided to utilize this alkyne and study the scope with respect to the alkene component. As shown in Table 4, formation of the cyclopropane product was also discovered to be dependent on the alkene used. Unlike alkynol **2a**, **2f** underwent cyclopropanation exclusively with norbornene **1b** (24%, entry 2) and alkene **1c**, which bears a tertiary carbamate at the bridgehead position (72%, entry 3).[13] However, an interesting limitation was observed with **1d**, where cycloadduct **3j** was found to be the major product in 46% yield (entry 4). Again, we believe that this occurred due to increased steric hindrance on the ruthenacyclopentene intermediate, which would favor the reductive elimination process leading to **3j**. The formation of this product was found to be highly regioselective, giving **3j** (methyl group next to the allylic alcohol) as a single regioisomer.[14] To the best of our knowledge, this is the first example of a regioselective ruthenium-catalyzed [2+2] cycloaddition reaction directed by a group at the $C_1$ position of the bicyclic alkene.

**Mechanistic Considerations.** The outlined cyclopropanation reaction showed a different pattern of reactivity with respect to other reactions previously reported using a ruthenium catalyst and propargylic alcohols. Unlike the Alder-ene reaction developed by Trost[5] or the cyclopropanation reaction by Takahashi,[9] the actual catalyst does not involve a cationic ruthenium species. Treating Cp*Ru(cod)Cl with silver triflate in tetrahydrofuran to form the cationic $[Cp^*Ru]^+$ species resulted in decreased activity (10% isolated yield of **4a**). This strongly suggests that the active species is a neutral [Cp*RuCl] species, which is consistent with what Mitsudo and co-workers[15] proposed for the ruthenium-catalyzed [2+2] cycloaddition. Using aprotic solvent to perform the reaction also possibly plays an important role in the formation of the cyclopropane products **4**, since the

**Scheme 3. Proposed Mechanisms for the Formation of Cyclopropane 4a**

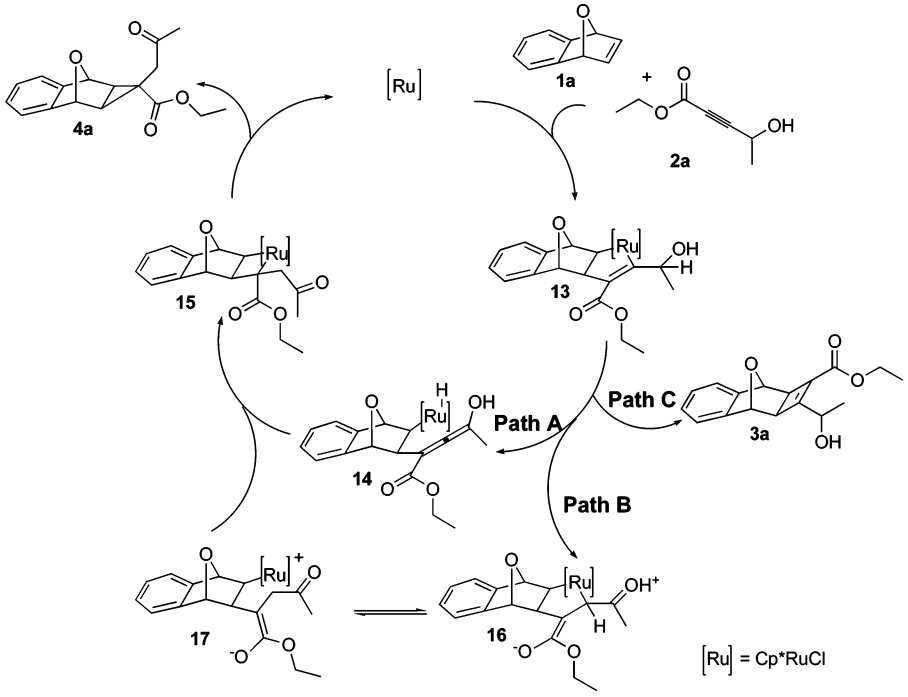
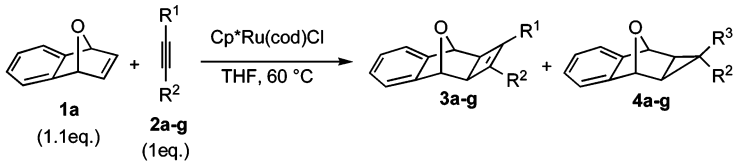
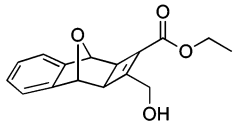
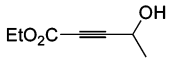
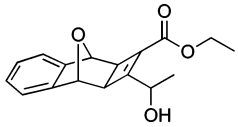
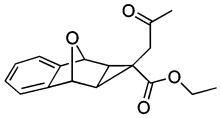
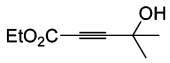
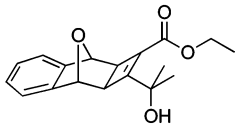
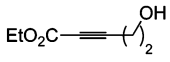
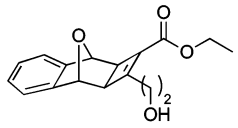
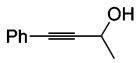
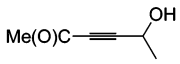
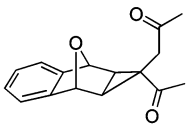
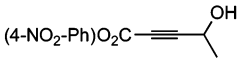
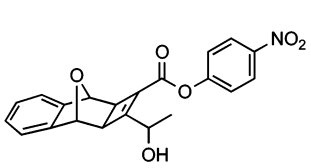
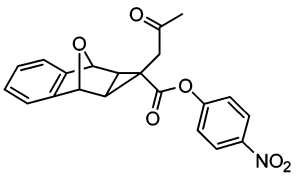


**Table 3. Substituent Effect on Alkyne**



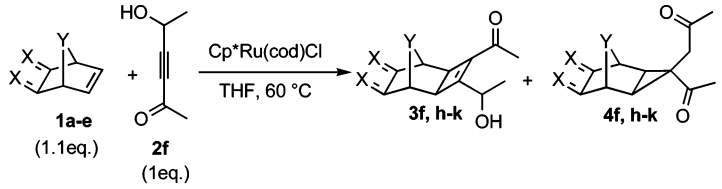

| entry | alkyne **2** | time (h) | products (yield[a]) cyclobutene **3** | cyclopropane **4** |
|---|---|---|---|---|
| 1 |  **2b** | 48 |  **3b** (59%) | - |
| 2 |  **2a** | 1 |  **3a** (20%) |  **4a** (45%) |
| 3 |  **2c** | 65 |  **3c** (81%) | - |
| 4 |  **2d** | 1.5 |  **3d** (81%) | - |
| 5 |  **2e** | 68 | N/A | N/A |
| 6 |  **2f** | 1 | - |  **4f** (67%) |
| 7 |  **2g** | 1 |  **3g** (23%) |  **4g** (30%) |

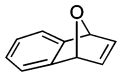
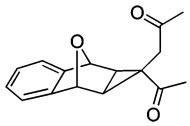
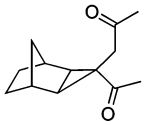
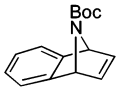
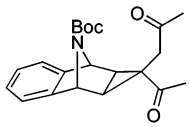
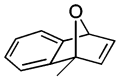
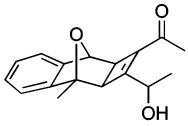
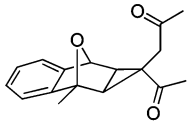
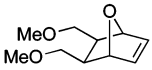
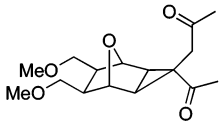
[a] Isolated yields.

cyclopropanation reaction reported by Takahashi uses methanol as a solvent to promote the rearrangement of the hydroxyl group.

Other mechanistic information was obtained using the deuterium-labeled alkynol **10** (Scheme 2). Deuterated products **11** and **12** were produced in a yield of 29 and 22%, respectively, with over 95% of deuterium incorporation, which suggests the migration of the propargylic hydrogen/deuterium in the formation of **12**. A qualitative isotopic effect was observed since the

**Table 4. Scope of the Reaction with 2f and Various Alkenes**




| entry | Alkene **1** | time (h) | product (yield[a]) cyclobutene **3** | cyclopropane **4** |
|---|---|---|---|---|
| 1 |  **1a** | 1 | - |  **4f** (67%) |
| 2 |  **1b** | 72 | - |  **4h** (24%) |
| 3 |  **1c** | 2 | - |  **4i** (72%) |
| 4 |  **1d** | 15 |  **3j** [b] (46%) |  **4j** (17%) |
| 5 |  **1e** | 150 | - |  **4k** (23%) |

[a] Isolated yields. [b] Regiochemistry determined by GOESY NMR experiments.

amount of cyclopropane formed substantially decreased upon deuteration, whereas the quantity of cyclobutene did not significantly change. If **12** arises from the same ruthenacyclopentene intermediate as for **11**, the ease of H abstraction/shift would determine the product mixture composition. The presence of the hydroxyl group also appears to be crucial in the formation the cyclopropane product. When using propargylic ether (e.g., 2-methoxyethoxymethyl (MEM)), no cyclopropane product was formed and only the [2+2] cycloadduct was observed in the crude reaction mixture.

From these data, two pathways are possible after the oxidative cyclization step where the contraelectronic ruthenacyclopentene[16] species **13** is formed (Scheme 3). One route would involve a mechanism similar to that proposed by Takahashi, where a $\beta$-hydride elimination to form the allene **14** followed by a hydrometalation and a reductive elimination would give **4a** (Path A, Scheme 3). The second pathway would occur via a [1,2]-hydride shift forming the zwitterion **16**, which can rearrange to give the intermediate **15** via the intermediate **17** and finally reductively eliminate to produce **4a** (Path B, Scheme 3). If the cyclopropanation occurs through this path, performing the reaction in a polar solvent should therefore favor the formation

(13) Decomposition was observed when alkene **1c** was reacted with **2a**. On the other hand, norbornene **1b** reacted smoothly with **2a** to give only the [2+2] cycloaddition product.

(14) Based on crude $^1$H NMR.

(15) Mitsudo, T.; Naruse, H.; Kondo, T.; Ozaki, Y.; Watanabe, Y. *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 580.

(16) A contraelectronic ruthenacyclopentene intermediate has been previously proposed to explain the very good regioselectivity obtained in ruthenium-catalyzed Alder-ene reaction using propargylic alcohols; see ref 3.

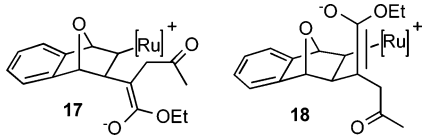



**Figure 1.** Other possible conformer of intermediate **17**.

of **4a**. Since very little solvent effect was observed in the product distribution, Path A tends to be plausible. However, based on results presented above in Tables 3 and 4, Path B cannot be completely discarded since (i) no cyclopropane product was observed with a homopropargylic alcohol, which suggests anchimeric assistance from the propargylic hydroxyl group, (ii) utilizing the better electron-withdrawing methyl ketone group versus esters at the acetylenic position enhances the rate of formation of the cyclopropane product by favoring the [1,2]-hydride shift, and (iii) the presence of a heteroatom at the bridgehead position of the alkene facilitates the cyclopropanation pathway by complexing to the ruthenium and thereby stabilizing the cationic ruthenium intermediate **15**. In this case, the stereoselection at the quaternary center may occur during the formation of intermediate **17** (Scheme 3). After Ru−C bond cleavage then tautomerization, a rotation of the enolate is needed in order to afford the proper orbital overlap for the nucleophilic attack on the cationic ruthenium. One preliminary hypothesis is that intermediate **17** would be favored over **18** because of an electronic repulsion of the negative charge of the enolate with the lone pair of the oxygen at the bridgehead position of the latter (Figure 1).

## Conclusion

In summary, we have reported an atypical cyclopropanation of bicyclic alkenes by propargylic alcohols catalyzed by Cp*Ru(cod)Cl. This unprecedented catalytic pathway of Cp*Ru(cod)Cl is characterized by the highly stereoselective formation of a single *exo* cyclopropane adduct. Mechanistic considerations suggest that this reaction proceeds through neutral ruthenacycle species, where the cyclopropane product is formed through a $\beta$-hydride elimination or a [1,2]-hydride shift. Substituting the chloride group on the catalyst for a bromide or iodide strongly altered its reactivity by favoring the [2+2] cycloadduct over the cyclopropane product. Finally, modulating the electron-withdrawing ability of the acetylenic group (ketone versus ester) modified the outcome of the reaction.

## Experimental Section

Only a representative procedure and characterization of the products is described here. Full details can be found in the Supporting Information.

**General Procedure for the Preparation of Cyclobutene and Cyclopropane Products. Cyclobutene 3a and Cyclopropane 4a.** A mixture of oxabicyclic alkene **1a** (47.1 mg, 0.327 mmol), acetylene **2a** (42.8 mg, 0.296 mmol), and THF (0.4 mL) in an oven-dried vial was added via a cannula to an oven-dried screw-cap vial containing Cp*Ru(cod)Cl (weighed out from a drybox, 4.3 mg, 0.011 mmol) under nitrogen. The oven-dried vial was rinsed with THF (0.1 mL) and added by cannula to the reaction mixture. The reaction mixture was stirred at 60 °C for 1 h. The crude product was purified by column chromatography (gradient elution, EtOAc/hexanes = 1:9 to 3:7) to give cycloadducts **3a** (17.0 mg, 0.0592 mmol, 20%) and **4a** (38.1 mg, 0.133 mmol, 45%).

**3a:** $R_f$ 0.43 (EtOAc/hexanes = 3:2); IR (neat) 3425 (br m), 3054 (w), 2979 (s), 2936 (w), 1715 (vs), 1251 (s) $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 400 MHz) $\delta$ 7.28−7.34 (m, 2H), 7.17−7.22 (m, 2H), 5.11 (s, 1H), 5.02 (s, 1H), 4.72−4.83 (m, 2H), 4.29 (q, 2H, $J$ = 7.1 Hz), 2.81 (br dd, 1H, $J$ = 3.4, 1.0 Hz), 2.71 (br d, 1H, $J$ = 3.4 Hz), 1.41 (d, 3H, $J$ = 7.3 Hz), 1.37 (t, 3H, $J$ = 7.1 Hz); $^{13}C$ NMR (APT, $CDCl_3$, 75 MHz) $\delta$ 166.7, 163.3, 144.1, 143.8, 129.5, 126.9, 126.8, 119.9, 119.7, 75.9, 75.3, 65.4, 61.1, 45.5, 44.4, 21.2, 14.2. Anal. Calcd for $C_{17}H_{18}O_4$: C, 71.31; H, 6.34. Found: C,71.10; H, 6.48. HRMS (CI) for $C_{17}H_{18}O_4$ ($(M + H)^+$): calcd 287.1283; found 287.1280.

**4a:** $R_f$ 0.26 (EtOAc/hexanes = 3:7); IR (neat) 3073 (m), 3054 (m), 2989 (s), 2940 (s), 1726 (vs), 1713 (vs) $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 400 MHz) $\delta$ 7.31 (dd, 2H, $J$ = 5.2, 3.0 Hz), 7.14 (dd, 2H, $J$ = 5.2, 3.0 Hz), 5.23 (s, 2H), 4.03 (q, 2H, $J$ = 7.1 Hz), 3.42 (s, 2H), 2.20 (s, 3H), 1.98 (s, 2H), 1.16 (t, 3H, $J$ = 7.1 Hz); $^{13}C$ NMR (APT, $CDCl_3$, 75 MHz) $\delta$ 207.1, 171.8, 147.3, 126.2, 119.7, 78.2, 61.2, 39.7, 39.4, 33.2, 30.1,14.0. HRMS (CI) for $C_{17}H_{18}O_4$ ($(M + H)^+$): calcd 287.1283; found 287.1274.

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**Supporting Information Available:** Detailed procedures and full characterization of new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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