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Ruthenium-Catalyzed [2 + 2] Cycloaddition of Allenynes Leading to a Bicyclo[4.2.0]octa-1(8),5-diene Skeleton

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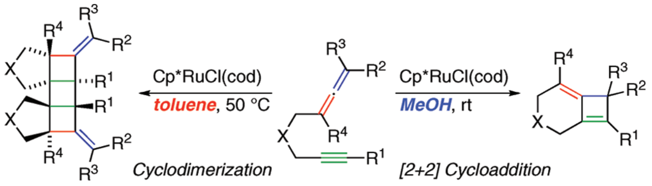
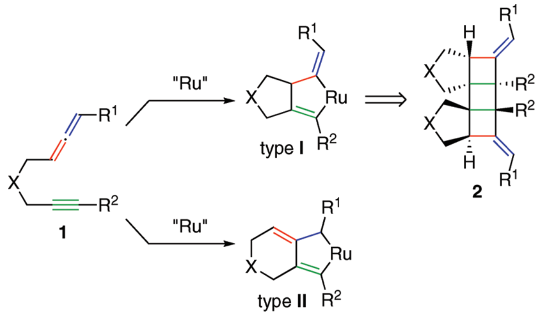
ABSTRACT



The reaction pathway of Cp*RuCl(cod)-catalyzed cyclization of allenynes was dramatically changed depending on the type of solvent employed. That is, while a cyclodimerization of allenyne proceeded to give a pentacyclic compound in toluene, a bicyclo[4.2.0]octa-1(8),5-diene derivative was exclusively produced by [2 + 2] cycloaddition of allenyne in methanol. It was also demonstrated that the [2 + 2] cycloaddition was catalyzed by a cationic ruthenium complex generated from Cp*RuCl(cod) and methanol in situ.

A cyclization of enynes via a ruthenacyclopentene generated by oxidative cycloaddition of alkyne and alkene to a low-valent ruthenium complex has been recognized as a powerful and efficient methodology for the construction of various carbo- and heterocycles in recent organic synthesis, and a variety of useful reactions have been reported to date.[1−3] In contrast to the extensive studies on ruthenium-catalyzed reactions of enynes, there are still only a few examples of reaction of allenyne with a ruthenium catalyst.[4] In the case of allenyne, two types of ruthenacycles can be formed from a substrate and a ruthenium complex, as shown in Scheme 1.

Scheme 1



Recently, we have reported a cyclodimerization of allenynes giving unique pentacyclic compounds **2**, which is the first example for the reaction via type **I** of ruthenacy-

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(1) For reviews, see: (a) Naota, T.; Takaya, H.; Murahashi, S.-i. *Chem. Rev.* **1998**, *98*, 2599. (b) Trost, B. M.; Toste, F. D.; Pinkerton, A. B. *Chem. Rev.* **2001**, *101*, 2067. (c) Trost, B. M.; Frederiksen, M. U.; Rudd, M. T. *Angew. Chem., Int. Ed.* **2005**, *44*, 6630. (d) *Ruthenium in Organic Synthesis*; Murahashi, S.-i., Ed.; Wiley-VCH, Inc.: New York, 2004. (e) *Top. Organomet. Chem. Vol. 11, Ruthenium Catalysts and Fine Chemistry*; Bruneau, C., Dixneuf, P. H., Eds.; Springer-Verlag: Berlin-Heidelberg, 2004.

(2) For representative examples of Ru-catalyzed enyne cyclizations, see: (a) Chatani, N.; Morimoto, T.; Muto, T.; Murai, S. *J. Am. Chem. Soc.* **1994**, *116*, 6049. (b) Morimoto, T.; Chatani, N.; Fukumoto, Y.; Murai, S. *J. Org. Chem.* **1997**, *62*, 3762. (c) Kondo, T.; Suzuki, N.; Okada, T.; Mitsudo, T. *J. Am. Chem. Soc.* **1997**, *119*, 6187. (d) Trost, B. M.; Toste, F. D. *J. Am. Chem. Soc.* **1999**, *121*, 9728. (e) Trost, B. M.; Toste, F. D. *J. Am. Chem. Soc.* **2000**, *122*, 714. (f) Trost, B. M.; Toste, F. D.; Shen, H. *J. Am. Chem. Soc.* **2000**, *122*, 2379. (g) Trost, B. M.; Doherty, G. A. *J. Am. Chem. Soc.* **2000**, *122*, 3801. (h) Ackermann, L.; Bruneau, C.; Dixneuf, P. H. *Synlett* **2001**, 397.

(3) For our previous studies on Ru-catalyzed enyne cyclizations, see: (a) Mori, M.; Saito, N.; Tanaka, D.; Takimoto, M.; Sato, Y. *J. Am. Chem. Soc.* **2003**, *125*, 5606. (b) Mori, M.; Tanaka, D.; Saito, N.; Sato, Y. *Organometallics* **2008**, *27*, 6313. (c) Tanaka, D.; Sato, Y.; Mori, M. *Organometallics* **2006**, *25*, 799. (d) Tanaka, D.; Sato, Y.; Mori, M. *J. Am. Chem. Soc.* **2007**, *129*, 7730.

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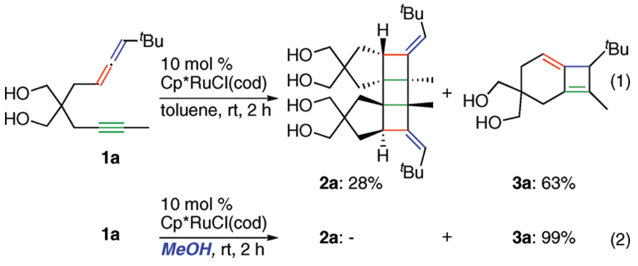
clopentene derived from allenynes.[5] For the reactions via type **II** of ruthenacyclopentene, only intramolecular [2 + 2] cycloaddition[4a] and intermolecular coupling using cyclonona-1,2-diene have been reported so far.[4b] During the course of further studies on the cyclodimerization via type **I** ruthenacyclopentene, we encountered an unexpected cyclization via type **II** ruthenacyclopentene. That is, when an allenyne **1a** was reacted with Cp*RuCl(cod) in toluene under the previous optimal conditions, the desired cyclodimerization product **2a** was obtained in only 28% yield, and an unidentified compound **3a** was produced in 63% yield (Scheme 2, eq 1).

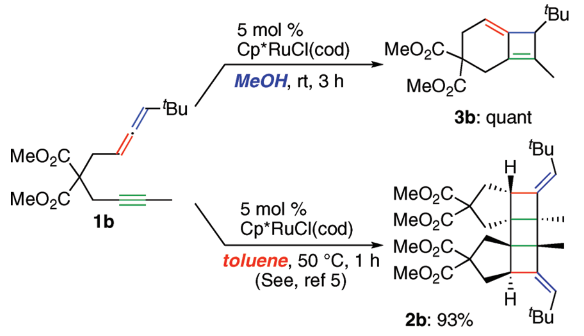
Scheme 2



Detailed analyses of various spectral data, including 2D-NMR (COSY, NOESY, HMBC, HSQC, and INADEQUATE, see Supporting Information), revealed the structure of **3a**, which has a bicyclo[4.2.0]octa-1(8),5-diene skeleton. It was speculated that the product **3a** is formed by [2 + 2] cycloaddition via formation of type **II** ruthenacycle followed by reductive elimination[6−8] and that the existence of the hydroxy group(s) in **1a** affects the reaction pathway. To examine the influence of hydroxy functional groups on this reaction, the reaction of **1a** with Cp*RuCl(cod) catalyst was carried out in methanol instead of toluene (Scheme 2, eq 2). We were surprised to find that the reaction was completed within 2 h, and only the [2 + 2] cycloaddition product **3a** was exclusively produced in quantitative yield.

Furthermore, the reaction of **1b** with Cp*RuCl(cod) catalyst in methanol again produced only [2 + 2] cycloaddition product **3b** in quantitative yield, while the use of toluene as a solvent in the same reaction exclusively produced cyclodimerization product **2b** in an excellent yield, as was previously reported (Scheme 3).[5] *These results indicate that the reaction pathway of ruthenium-catalyzed cyclization of allenynes was dramatically changed depending on the type of solvent employed and that the formation of two quite different types of products from the identical allenyne could be controlled by only changing the solvent.*[9]

Scheme 3



Thus, the [2 + 2] cycloaddition of various allenynes in methanol was investigated, and the results are summarized in Table 1. The cyclization of **1c** in methanol proceeded smoothly to afford the bicyclic compound **3c** in 94% yield (run 1). The reactions of **1d−g** having an aromatic group or a siloxymethyl group on the alkyne afforded **3d−g** in high yields (runs 2−5). When the allenyne with a cyclic acetal part **1h** was used as a substrate, the spiro compound **3h** was produced in 98% yield (run 6). Furthermore, fused-nitrogen heterocyclic compound **3i** was also synthesized by [2 + 2] cycloaddition of **1i** (run 7). It is noteworthy that the reaction of these substrates in toluene under the previously optimized conditions had exclusively proceeded via type **I** ruthenacyclopentene, affording the corresponding cyclodimerization products in high yields.

It is known that a chloro ligand on the Ru(II) complex having a Cp ligand dissociates in alcoholic solvents, giving a cationic ruthenium species.[10] Therefore, the reaction of **1b** with the cationic ruthenium complex prepared from Cp*RuCl(cod) and AgOTf in situ in THF was examined, and it was found

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(4) For reaction of allenynes via ruthenacyclopentene, see: (a) Oh, C. H.; Gupta, A. K.; Park, D. I.; Kim, N. *Chem. Commun.* **2005**, 5670. (b) Bai, T.; Xue, P.; Zhang, L.; Ma, S.; Jia, G. *Chem. Commun.* **2008**, 2929. For Ru-catalyzed reaction of allene and other multiple bonds, see: (c) Yamaguchi, M.; Kido, Y.; Omata, K.; Hirama, M. *Synlett* **1995**, 1181. (d) Trost, B. M.; Pinkerton, A. B. *J. Am. Chem. Soc.* **1999**, *121*, 4068. (e) Kang, S.-K.; Kim, K.-J.; Hong, Y.-T. *Angew. Chem., Int. Ed.* **2002**, *41*, 1584. (f) Bustelo, E.; Guérot, C.; Hercouet, A.; Carboni, B.; Toupet, L.; Dixneuf, P. H. *J. Am. Chem. Soc.* **2005**, *127*, 11582. (g) Ngai, M.-Y.; Skucas, E.; Krische, M. J. *Org. Lett.* **2008**, *10*, 2705. (h) Vovard-Le Bray, C.; Dérien, S.; Dixneuf, P. H.; Murakami, M. *Synlett* **2008**, 193.

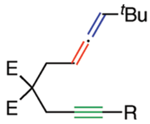
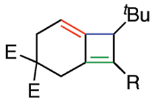
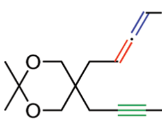
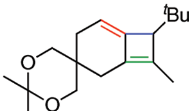
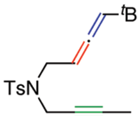
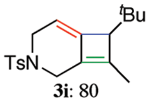
(5) Saito, N.; Tanaka, Y.; Sato, Y. *Organometallics* **2009**, *28*, 669.

(6) For transition-metal-catalyzed [2 + 2] cycloaddition of allenynes, see: (a) Shen, Q.; Hammond, G. B. *J. Am. Chem. Soc.* **2002**, *124*, 6534. (b) Oh, C. H.; Park, D. I.; Jung, S. H.; Reddy, V. R.; Gupta, A. K.; Kim, Y. M. *Synlett* **2005**, 2092. See also: ref 4a.

(7) For recent examples of thermal [2 + 2] cycloaddition of allenynes, see: (a) Cao, H.; Van Ornum, S. G.; Deschamps, J.; Flippen-Anderson, J.; Laib, F.; Cook, J. M. *J. Am. Chem. Soc.* **2005**, *127*, 933. (b) Brummond, K. M.; Chen, D. *Org. Lett.* **2005**, *7*, 3473. (c) Mukai, C.; Hara, Y.; Miyashita, Y.; Inagaki, F. *J. Org. Chem.* **2007**, *72*, 4454. (d) Jiang, X.; Ma, S. *Tetrahedron* **2007**, *63*, 7589. (e) Ohno, H.; Mizutani, T.; Kadoh, Y.; Aso, A.; Miyamura, K.; Fujii, N.; Tanaka, T. *J. Org. Chem.* **2007**, *72*, 4378. (f) Buisine, O.; Gandon, V.; Fensterbank, L.; Aubert, C.; Malacria, M. *Synlett* **2008**, 751. See also: ref 4a.

(8) For examples of four-membered ring formation by ruthenium-catalyzed [2 + 2] cycloaddition of multiple bonds, see: (a) Mitsudo, T.; Kokuryo, K.; Takegami, Y. *J. Chem. Soc., Chem. Commun.* **1976**, 722. (b) Mitsudo, T.; Kokuryo, K.; Shinsugi, T.; Nakagawa, Y.; Watanabe, Y.; Takegami, Y. *J. Org. Chem.* **1979**, *44*, 4492. (c) Mitsudo, T.; Naruse, H.; Kondo, T.; Ozaki, Y.; Watanabe, Y. *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 580. (d) Yi, C. S.; Lee, D. W.; Chen, Y. *Organometallics* **1999**, *18*, 2043. (e) Yamamoto, Y.; Kitahara, H.; Ogawa, R.; Kawaguchi, H.; Tatsumi, K.; Itoh, K. *J. Am. Chem. Soc.* **2000**, *122*, 4310. (f) Jordan, R. W.; Tam, W. *Org. Lett.* **2000**, *2*, 3031. (g) Le Paih, J.; Dérien, S.; Bruneau, C.; Demerseman, B.; Toupet, L.; Dixneuf, P. H. *Angew. Chem., Int. Ed.* **2001**, *40*, 2912. (h) Alvarez, P.; Gimeno, J.; Lastra, E.; García-Granda, S.; Van der Maelen, J. F.; Bassetti, M. *Organometallics* **2001**, *20*, 3762. (i) Tenaglia, A.; Giordano, L. *Synlett* **2003**, 2333. (j) Le Paih, J.; Dérien, S.; Demerseman, B.; Bruneau, C.; Dixneuf, P. H.; Toupet, L.; Dazinger, G.; Kirchner, K. *Chem.−Eur. J.* **2005**, *11*, 1312. See also: ref 4f.

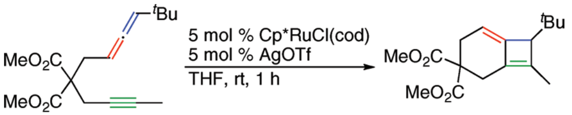
Table 1. [2 + 2] Cycloaddition of Various Allenynes[a]

run	allenyne **1**	time (h)	yield (%)
			
1	**1c** (E = CH_2OBz-*p*-NO_2, R = Me)	2	**3c**: 94
2	**1d** (E = CO_2Me, R = C_6H_5)	2	**3d**: 95
3	**1e** (E = CO_2Me, R = 4-$MeOC_6H_4$)	3	**3e**: 94
4	**1f** (E = CO_2Me, R = 4-$MeO_2CC_6H_4$)	2	**3f**: 98
5	**1g** (E = CO_2Me, R = CH_2OTBS)	4	**3g**: 97
6	 **1h**	2	 **3h**: 98
7	 **1i**	3	 **3i**: 80

[a] Reaction conditions: Cp*RuCl(cod) (5 mol %), MeOH, room temperature.

that the reaction resulted in production of the bicyclic product **3b** in quantitative yield (Scheme 4). This result strongly supports our speculation that the cationic ruthenium complex generated from Cp*RuCl(cod) in methanol is the real active species and that it promotes the [2 + 2] cycloaddition.

Scheme 4



1b

3b: quant

In summary, we have succeeded in developing a Ru-catalyzed [2 + 2] cycloaddition of allenynes that provides various bicyclo[4.2.0]octa-1(8),5-diene derivatives in high yields. The remarkable points of this study are as follows: (1) the [2 + 2] cycloaddition via type **II** ruthenacyclopentene formed from allenynes and ruthenium complex has been established as a rare example and (2) it has been revealed that the reaction pathway of ruthenium-catalyzed cyclization of allenynes was dramatically changed depending on the nature of the solvent employed. We also demonstrated that the real active species of the [2 + 2] cyclization would be a cationic ruthenium complex generated from Cp*RuCl(cod) and methanol in situ. Although the reason why the [2 + 2] cycloaddition proceeded via type **II** ruthenacycle by using cationic species while the neutral ruthenium complex gave a cyclodimerization product via type **I** intermediate is not clear yet,[11] it is notable that two quite different types of cyclic compounds can be synthesized from the identical allenyne by a simple operation, exchange of solvents. Further studies are in progress.

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Supporting Information Available: Experimental procedure and spectral data. This material is available free of charge via the Internet at http://pubs.acs.org.

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(9) The [2 + 2] cycloaddition of **1b** in MeOH at 50 °C is completed within 1 h, giving **3b** in 98% yield.

(10) For examples, see: (a) Albers, M. O.; Robinson, D. J.; Shaver, A.; Singleton, E. *Organometalllics* **1986**, *5*, 2199. (b) Davies, S. G.; McNally, J. P.; Smallridge, A. J. *Adv. Organomet. Chem.* **1990**, *30*, 1.

(11) It is known that the reaction pathways of transition-metal-catalyzed cyclization of allenynes are significantly different depending on the type of metal employed. For instance, when Rh(I) complex was used, oxidative cyclization proceeded between alkyne and the distal double bond of allene to give a type **I** metallacycle. On the other hand, a type **II** metallacycle was produced in the case of Mo(0) complex. In this context, theoretical studies on the metallacycle formation step from allenynes and Rh or Mo complex were conducted, see: Bayden, A. S.; Brummond, K. M.; Jordan, K. D. *Organometallics* **2006**, *25*, 5204.