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Molybdenum-Catalyzed Ring-Closing Metathesis of Allenynes

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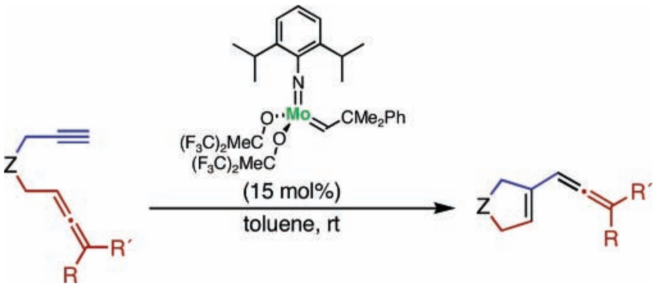
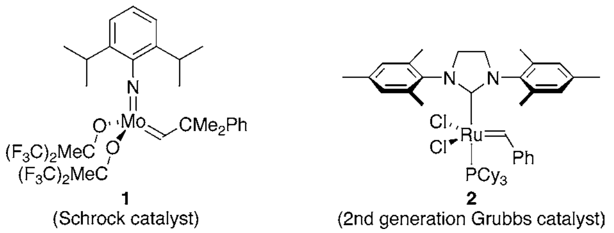
ABSTRACT



A ring-closing metathesis reaction of allenynes occurred at room temperature in the presence of a molybdenum alkylidene complex to give ring-closed vinylallenes. The vinylallene skeletons were constructed by a metathesis-type reaction between the alkyne moiety and the proximal carbon–carbon double bond of the allene moiety.

Ring-closing metathesis (RCM) reactions have rapidly become one of the most versatile and efficient methods for constructing carbo- and heterocyclic compounds.[1,2] They have been widely employed as a key step in a number of natural product syntheses to install cyclic structure. The molybdenum imido alkylidene complex **1** (Schrock catalyst)[3] and the ruthenium benzylidene complex **2** (second-generation Grubbs catalyst)[4] are the most commonly used catalysts beacuse of their high catalytic activities and their tolerance of a range of functional groups (Figure 1).



1
(Schrock catalyst)

2
(2nd generation Grubbs catalyst)

Figure 1.

While a variety of cross-metathesis reactions between alkenes and alkynes (enyne metathesis) have been reported,[1,5] there has been only one example of metathesis that involves allenes; 1,3-disubstituted allenes are formed by a ruthenium-catalyzed metathesis of monosubstituted allenes.[6] Herein, we report a molybdenum-catalyzed RCM reaction of allenynes[7] producing allenyl-substituted cyclic alkenes.

Allenyne **3a** was treated with complex **1** (15 mol %) in

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[1] Grubbs, R. H., Ed. *Handbook of Metathesis*; Wiley-VCH: Weinheim, 2003.

[2] (a) Katz, T. J.; Sivavec, T. M. *J. Am. Chem. Soc.* **1985**, *107*, 737. (b) Maifeld, S. V.; Miller, R. L.; Lee, D. *J. Am. Chem. Soc.* **2004**, *126*, 12228. For reviews, see: (c) Nakamura, I.; Yamamoto, Y. *Chem. Rev.* **2004**, *104*, 2127. (d) Deiters, A.; Martin, S. F. *Chem. Rev.* **2004**, *104*, 2199. (e) McReynolds, M. D.; Dougherty, J. M.; Hanson, P. R. *Chem. Rev.* **2004**, *104*, 2239. (f) Wallace, D. J. *Angew. Chem., Int. Ed.* **2005**, *44*, 1912.

[3] (a) Schrock, R. R.; Hoveyda, A. H. *Angew. Chem., Int. Ed.* **2003**, *42*, 4592. (b) Schrock, R. R. *J. Mol. Catal. A* **2004**, *213*, 21.

[4] (a) Trnka, T. M.; Morgan, J. P.; Sanford, M. S.; Wilhelm, T. E.; Scholl, M.; Choi, T.-L.; Ding, S.; Day, M. W.; Grubbs, R. H. *J. Am. Chem. Soc.* **2003**, *125*, 2546. (b) Grubbs, R. H. *Tetrahedron* **2004**, *60*, 7117.

[5] (a) Hansen, E. C.; Lee, D. *J. Am. Chem. Soc.* **2004**, *126*, 15074. (b) Castarlenas, R.; Eckert, M.; Dixneuf, P. H. *Angew. Chem., Int. Ed.* **2005**, *44*, 2576. (c) Galan, B. R.; Giessert, A. J.; Keister, J. B.; Diver, S. T. *J. Am. Chem. Soc.* **2005**, *127*, 5762. (d) Kim, M.; Lee, D. *Org. Lett.* **2005**, *7*, 1865. For reviews, see: (e) Poulsen, C. S.; Maden, R. *Synthesis* **2003**, 1. (f) Mori, M. *J. Mol. Catal. A* **2004**, *213*, 73. (g) Diver, S. T.; Giessert, A. J. *Chem. Rev.* **2004**, *104*, 1317.

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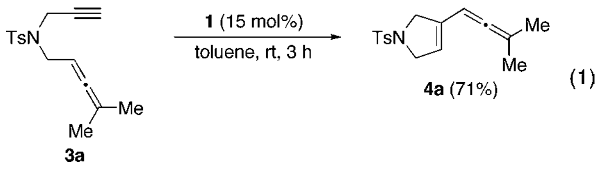
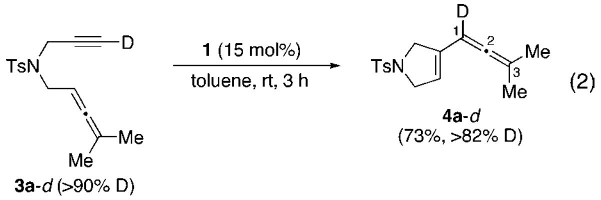
toluene[8] at room temperature for 3 h. Metathesis between the alkyne and the proximal carbon−carbon double bond of the allene moiety took place to afford five-membered ring product **4a** with an allene side chain in 71% yield (eq 1).[9] Surprisingly, only the Schrock catalyst **1** successfully mediated the reaction of **3**. Grubbs catalyst **2**, which has been most often employed in enyne metathesis reactions,[5] gave a complex mixture of products.[10]

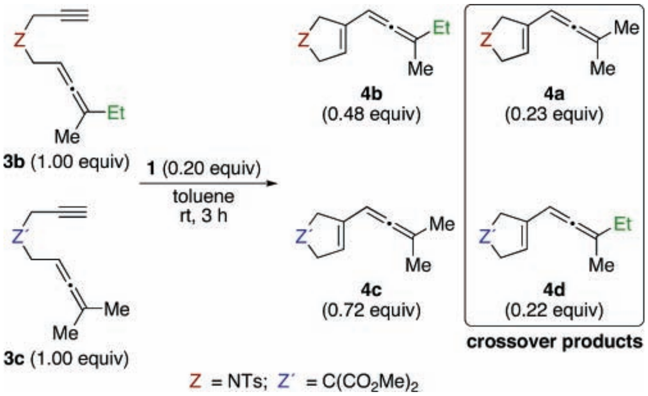


When allenyne **3a**-*d* with the alkyne terminus deuterated (>90% D) was used, the deuterium was labeled at the 1-position of the produced allene (>82% D) (eq 2).



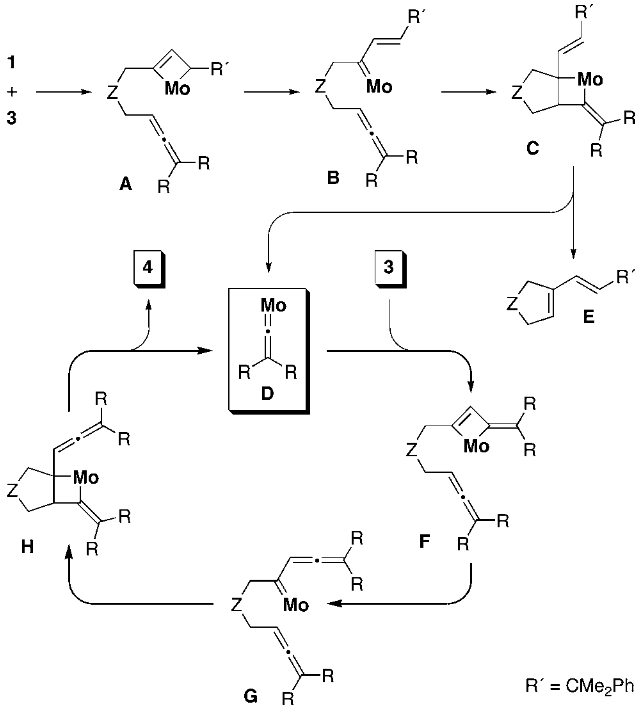
Next, a crossover reaction using a mixture of **3b** (1.00 equiv) and **3c** (1.00 equiv) was carried out in the presence of complex **1** (0.20 equiv) (Scheme 1). Crossover products **4a** (0.23 equiv) and **4d** (0.22 equiv) were obtained together with products **4b** (0.48 equiv) and **4c** (0.72 equiv).

Scheme 1. Crossover Experiment with **3b** and **3c** in the Presence of Molybdenum Complex **1**



There are two mechanisms, A and B, conceivable for the formation of **4** from **3**. In mechanism A (Scheme 2), molybdenum vinylidene species **D**[11,12] is initially generated from the alkylidene complex **1** and allenyne **3**; a molybdacyclobutene **A** is formed by [2 + 2] cycloaddition of **1** with the alkyne moiety of **3**.[13] Electrocyclic ring-opening affords vinylcarbene species **B**, which undergoes intramolecular [2 + 2] cycloaddition with the proximal allenic carbon−carbon double bond. A resulting methylenemolybdacyclobutane **C** splits into the molybdenum vinylidene species **D** and a 1,3-diene **E** by retro [2 + 2] cycloaddition. The species **D** thus formed turns over the catalytic cycle by following a sequence analogous to that through **A**, **B**, and **C**, i.e., via [2 + 2] cycloaddition forming **F**, electrocyclic ring-opening giving **G**, intramolecular [2 + 2] cycloaddition forming **H**, and finally retro [2 + 2] cycloaddition affording the product **4** and **D**.

Scheme 2. Mechanism A



Alternatively, mechanism B, which does not involve molybdenum vinylidene species **D**, also explains the forma-

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(6) Ahmed, M.; Arnauld, T.; Barrett, A. G. M.; Braddock, D. C.; Flack, K.; Procopiou, P. A. *Org. Lett.* **2000**, *2*, 551.

(7) For cycloisomerization and cyclization of allenynes, see: (a) Hashmi, A. S. K. In *Modern Allene Chemistry*; Krause, N., Hashmi, A. S. K., Eds.; Wiley-VCH: Weinheim, 2004; Vol. 2, p 877. (b) Mandai, T. In *Modern Allene Chemistry*; Krause, N., Hashmi, A. S. K., Eds.; Wiley-VCH: Weinheim, 2004; Vol. 2, p 925.

(8) Unsatisfactory results were obtained with other solvents such as 1,2-dimethoxyethane (no reaction) and CH_2Cl_2 (12% yield).

(9) Intermolecular cross-metathesis of terminal alkynes with allenes has so far failed with the catalysis of **1**; the alkynes were completely consumed, whereas the allenes remained unchanged.

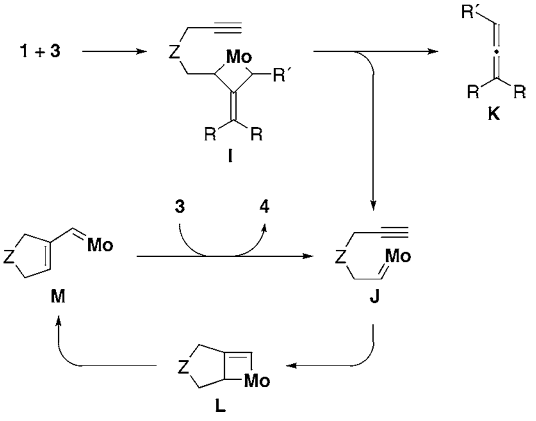
(10) No RCM occurred at room temperature when other Ru complexes such as $(PCy_3)_2Cl_2Ru{=}CHPh$ and $(PCy_3)_2Cl_2Ru{=}C{=}CHPh$ were used as the catalyst.

(11) Mo(VI) vinylidene complexes have not been reported. For a theoretical study, see: Stegmann, R.; Neuhaus, A.; Frenking, G. *J. Am. Chem. Soc.* **1993**, *115*, 11930.

(12) For vinylidene complexes of Mo in lower oxidation states, see: (a) Bruce, M. I. *Chem. Rev.* **1991**, *91*, 197. (b) McDonald, F. E.; Schultz, C. C. *J. Am. Chem. Soc.* **1994**, *116*, 9363. (c) Lin, Y.-C. *J. Organomet. Chem.* **2001**, *617*−*618*, 141. (d) Ipaktschi, J.; Mohsseni-Ala, J.; Uhlig, S. *Eur. J. Inorg. Chem.* **2003**, 4313.

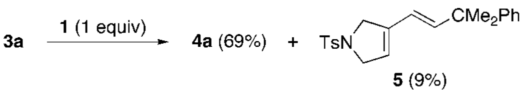
(13) For a theoretical study on [2 + 2] cycloaddition of Mo alkylidene with alkyne and ring-opening of molybdacyclobutene, see: Sheng, Y.; Wu, Y.-D.; Leszczynski, J. *Organometallics* **2004**, *23*, 3189.

Scheme 3. Mechanism B



tion of **4** (Scheme 3). The initial [2 + 2] cycloaddition of the molybdenum alkylidene complex **1** with the proximal allenic carbon−carbon double bond of **3** forms molybdenum alkylidene species **J** and an allene **K**. Then, intramolecular [2 + 2] cycloaddition with the alkyne moiety and ring-opening follow to give a new Mo alkylidene species **M**, which reacts with another allenyne **3** to afford **4**.

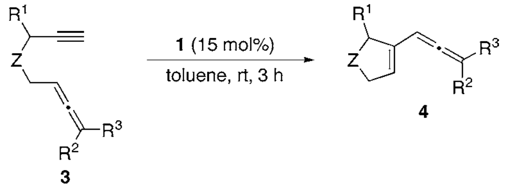
We carried out a stoichiometric reaction of **3** with **1** in order to get further mechanistic insights. Diene **5** was isolated (9%) in addition to **4a** (69%) (eq 3). The formation of the diene **5**, albeit the yield is low, is explained by assuming mechanism A rather than mechanism B. These product yields of **5** and **4a** suggest that the reaction of vinylidene complex **D** with **3** occurs much faster than the reaction of alkylidene complex **1** with **3**. A considerable amount of the catalyst precursor **1** remained unchanged.[14] Thus, we at this stage with these results favor mechanism A although further experimental studies are desired for discussion in more detail.



(3)

Other examples of the allenyne RCM are listed in Table 1. Allenynes **3a**,**b**,**e**−**h** having tosylamine in a tether were successfully transformed into the corresponding vinylallenes in a range of 68−84% yields (entries 1−6). *N*-Benzyl derivative **3i** also afforded the product **4i** in 73% yield (entry 7). Malonate derivatives **3c** and **3j** were excellent substrates for this reaction and led to nearly quantitative yield (entries 8 and 9). The product **4c** was isolated in 88% yield even with a lower catalyst loading (7.5 mol %), although it required a longer reaction time. Allenyne **3k** with the allenic terminus monosubstituted also participated in the RCM but with less efficiency, giving a mixture of vinylallene **4k** (26%) and diene **5** (13%) (entry 10).

Table 1. Molybdenum-Catalyzed RCM of Allenynes **3**[a]



	allenyne					product	
entry	3	Z	R1	R2	R3	4	% yield[b]
1	**3a**	TsN	H	Me	Me	**4a**	71[c]
2	**3b**	TsN	H	Me	Et	**4b**	84
3	**3e**	TsN	H	$-(CH_2)_5-$		**4e**	81
4	**3f**	TsN	H	*i*-Pr	*i*-Pr	**4f**	76
5	**3g**	TsN	Me	Me	Me	**4g**	68
6	**3h**	TsN	H	Me	Ph	**4h**	84
7	**3i**	BnN	H	Me	Me	**4i**	73
8	**3c**	$(MeO_2C)_2C$	H	Me	Me	**4c**	96 (88[d])
9	**3j**	$(EtO_2C)_2C$	H	Me	Me	**4j**	95
10	**3k**	TsN	H	Me	H	**4k**	26[e]

[a] Allenyne **3** was stirred in toluene (0.02 M) in the presence of **1** (15 mol %) at room temperature for 3 h unless otherwise noted. [b] Isolated yield by preparative TLC. [c] Result with 20 mol % of **1** for 20 min. [d] Result with 7.5 mol % of **1** for 9 h. [e] Obtained as a mixture of **4k** (26%) and **5** (13%).

The reactions using substrates listed in Figure 2 were unsuccessful under the conditions described here, showing the limitations of the metathesis reaction. No reaction occurred with allenyne **3l** with the allenic terminus unsubstituted. Allenyne **3m** bearing an ether linkage failed to undergo the RCM, presumably because of coordination of the ether oxygen to the Mo center. Methyl-substituted allenyne **3n** gave a complex mixture that included the desired product in low yield (<40%), and the phenyl-substituted **3o** was unreactive. Attempts to form a six-membered ring by RCM of **3p** and **3q** were also unsuccessful.

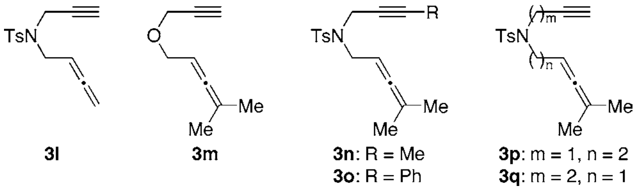
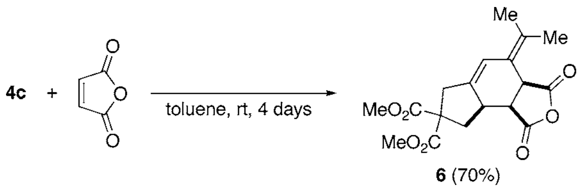


Figure 2.

Vinylallenes thus obtained can be used as a 1,3-diene in the Diels−Alder reaction.[15] The reaction of vinylallene **4c** with maleic anhydride in toluene at room temperature furnished cycloadduct **6** as a single diastereomer in 70% yield presumably via an *endo* transition state (eq 4).[16]



(4)

In conclusion, we have achieved the first RCM of allenynes producing vinylallenes by the use of molybdenum imido alkylidene complex **1**.

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

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(14) Such a phenomenon is often observed in Ru-catalyzed metathesis reaction. For a recent example, see ref 5b.

(15) Murakami, M.; Matsuda, T. In *Modern Allene Chemistry*; Krause, N., Hashmi, A. S. K., Eds.; Wiley-VCH: Weinheim, 2004; Vol. 2, p 727.

(16) The stereochemistry was assigned by analogy to a similar reaction. Regás, D.; Afonso, M. M.; Rodríguez, M. L.; Palenzuela, J. A. *J. Org. Chem.* **2003**, *68*, 7845.