Chromium-Catalyzed Intramolecular Enyne Metathesis

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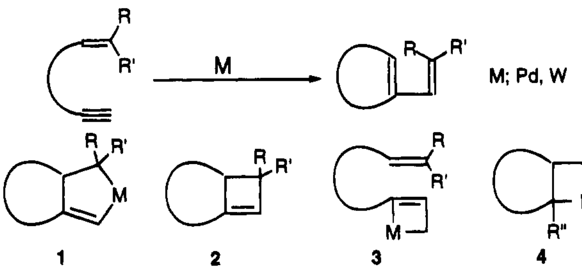
*Summary: The reaction of the enyne (E)-**5b**, which possesses the same substituents on the alkene as those on the carbene carbon, with 10 mol % of the Fischer chromium carbene complex in MeOH proceeded smoothly to give the metathesis product **12b** in 70% yield.*

Intramolecular enyne metathesis is quite interesting because the reaction involves formal [2 + 2] cycloaddition followed by ring opening of the resultant cyclobutene. As a result, one alkylidene group of the alkene migrates to the alkyne carbon.

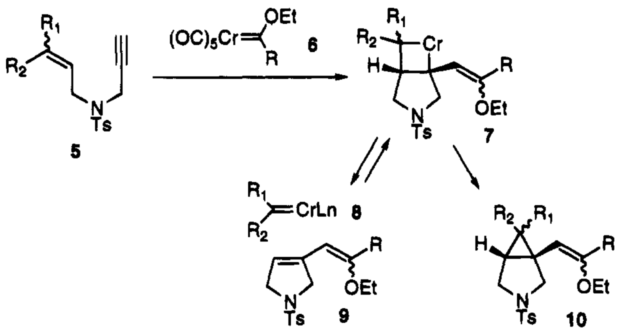
Until recently, two types of intramolecular enyne metathesis using transition metals have been known. One of them is the palladium-catalyzed [2 + 2] cycloaddition of the enyne reported by Trost,[1] and the other is the metal-catalyzed rearrangement of alkene to alkyne using the tungsten carbene complex reported by Katz.[2] In the former case, the highly strained cyclobutene **2** was formed from the five-membered metallacycles **1** by reductive elimination. Thus, the reaction seems to be like a formal [2 + 2] cycloaddition. On the other hand, in the latter case, the alkylidene carbene complex plays an important role. This process was successfully demonstrated by Katz using a molecule with restricted bond rotations and a catalytic amount of the tungsten carbene complex as an initiator. As a result, the tungsten alkylidene carbene complex, which is not stabilized by a heteroatom, is formed and it acts as a real catalyst. We now want to report the enyne metathesis catalyzed by the Fischer chromium carbene complex. In a previous paper,[3] we reported enyne methathesis using a chromium carbene complex and clarified the reaction course by substituent effects on the alkene. In this reaction, the important intermediate is chromacyclobutane **7**. If electron-donating groups are attached on the alkene, the metathesis reaction is accelerated because the generated chromium alkylidene carbene complex **8** is stabilized by the substituents R_1 and R_2.

In order to make the metathesis reaction proceed using a catalytic amount of the Fischer chromium carbene complex, the same substituents on the alkene and on the carbene carbon are required. Our plan for the chromium-catalyzed intramolecular metathesis reaction is shown in Scheme 3. For that purpose, we prepared the enyne **5a**[4] because the electron-donating phenyl and ethoxy groups on the alkene would accelerate the metathesis reaction.

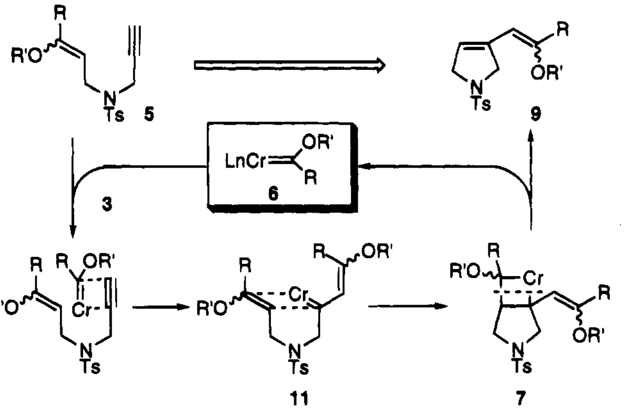
Scheme 1



Scheme 2



Scheme 3



When a THF solution of enyne **5a** and chromium carbene complex **6a** (30 mol %) was refluxed for 17 h followed by treatment with $[FeCl_4][Fe(DMF)_3Cl_2]$,[5] the pyrrolidine derivatives **12a** and **9a** were obtained in 22% and 9% yields, respectively, along with the indanone **13**[6] in 22% yield. The yield of the metathesis products **12a** and **9a** was increased to 35% when EtOH was used as a solvent. However, the formation of **13** could not be suppressed. In order to confirm the regeneration of the carbene complex **6a**, the carbene complex **6b** was used for this reaction. In this case, the pyrrolidine derivatives **12b**, **12a**, and **9a** were obtained in 18%, 11%, and

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[1] (a) Trost, B. M.; Yanai, M.; Hoogsteen, K. *J. Am. Chem. Soc.* **1993**, *115*, 5294. (b) Trost, B. M.; Hashmi, S. K. *Angew. Chem., Int. Ed. Engl.* **1993**, *32*, 1085. (c) For a review, see: Trost, B. M. *Acc. Chem. Res.* **1990**, *23*, 34. Trost, B. M.; Matsubara, S.; Caringi, J. J. *J. Am. Chem. Soc.* **1989**, *111*, 8745. Trost, B. M.; Chan, C.; Ruhter, G. *J. Am. Chem. Soc.* **1987**, *109*, 3486.

[2] (a) Katz, T. J.; Sivavec, T. M. *J. Am. Chem. Soc.* **1985**, *107*, 737. (b) Sivavec, T. M.; Katz, T. J. *Organometallics* **1989**, *8*, 1620.

[3] (a) Mori, M.; Watanuki, S. *J. Chem. Soc., Chem. Commun.* **1992**, 1082. (b) Watanuki, S.; Mori, M. *Heterocycles* **1993**, *35*, 679.

[4] The enyne **5a** was prepared from the acetal of the corresponding ketone by treatment with TMSI.

[5] Tobinaga, S.; Kotani, E. *J. Am. Chem. Soc.* **1972**, *94*, 309.

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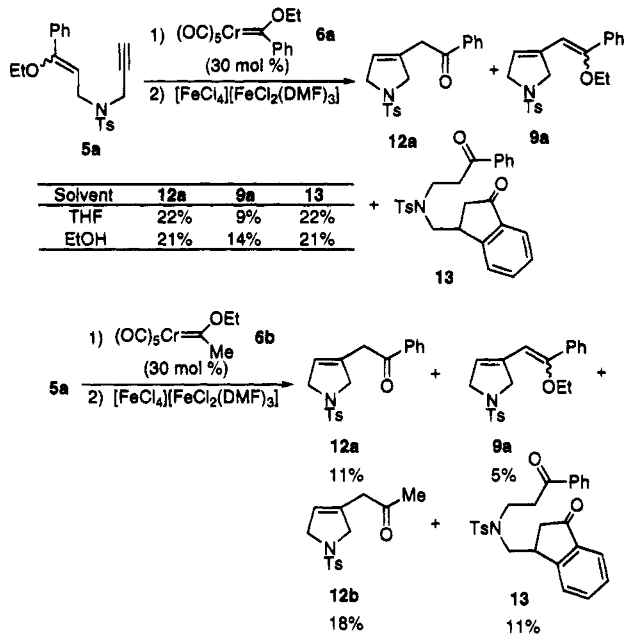
Scheme 4

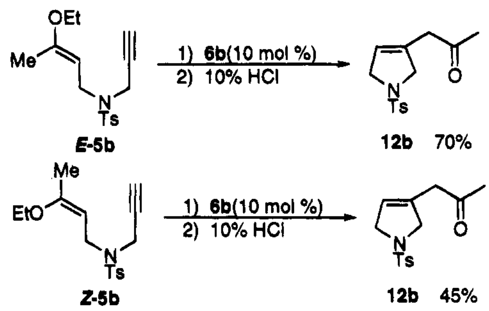


Solvent	12a	9a	13
THF	22%	9%	22%
EtOH	21%	14%	21%

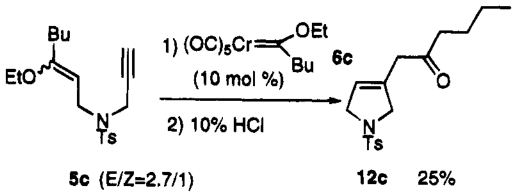
5% yields, respectively. Formation of **12a** and **9a** indicates that the carbene complex **6a** is generated in the reaction system.

Refluxing a mixture of enyne (*E*)-**5b**,[7] prepared from the acetal by treatment with TMSI and $(TMS)_2NH$,[8] and 10 mol % chromium carbene complex **6b** in MeOH for 2 h followed by treatment with 10% HCl gave the metathesis product **12b** in 70% yield. Even with the use of 5 mol % chromium catalyst, the desired product **12b** was obtained in 39% yield (starting material was recovered in 44% yield). THF (43%), toluene (50%), benzene (39%), EtOH (39%), and dichloroethane (31%) can be used as solvents for this reaction, but use of CH_3CN (4%) or HMPA (0%) did not give good results. Treatment of (*Z*)-**5b** with **6b** (10 mol %) in MeOH in a similar manner afforded the same metathesis product **12b** in 45% yield.[9]

Scheme 5



Scheme 6



Moreover, compound **5c** (*E*/*Z* = 2.7/1) was treated with chromium carbene complex **6c** in MeOH followed by treatment with 10% HCl to give metathesis product **12c** in 25% yield (starting material was recovered in 56% yield).[10,11] The important characteristics of this reaction are as follows. The reaction proceeds with a catalytic amount of the Fischer chromium carbene complex. It is accelerated by the alkoxy group on the alkene. The alkoxyalkylidene group of the alkene formally migrates to the alkyne. Further studies concerning enyne metathesis using the chromium carbene complex are now in progress.

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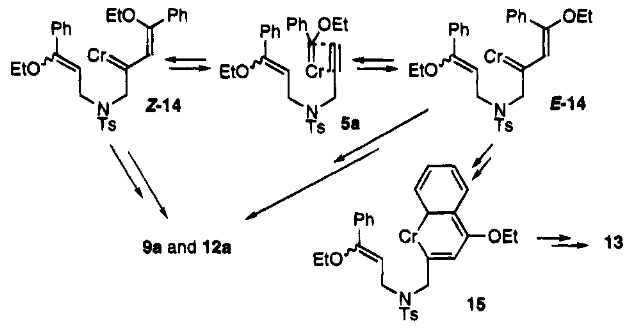
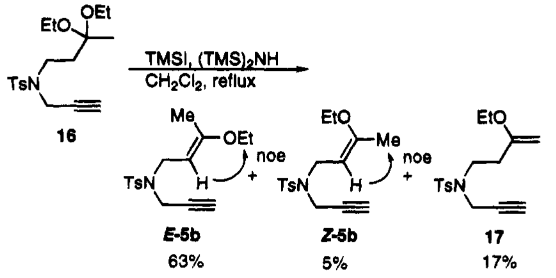
(6) The structure of **13** was determined by the spectral data (IR, ^1H NMR, COSY, and mass spectra). Indanone **13** is derived from the carbene complex (*E*)-**14** generated from **5a** and **2a**, and the metathesis products **9a** and **12a** are formed from (*Z*)-**14** and (*E*)-**14**. The chromium-catalyzed enyne metathesis is intercepted by formation of indanone **13** because a stoichiometric amount of the chromium carbene complex is consumed to produce the indanone **13**. See: Yamashita, A. *Tetrahedron Lett.* **1986**, *27*, 5915.

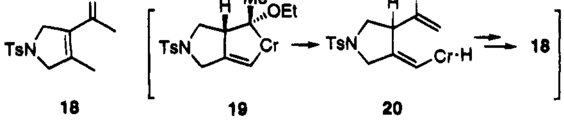


(7) The enol ether **5b** was prepared as shown below. These enol ethers were separated by silica gel column chromatography (1:5 ethyl acetate–hexane). The stereochemistries of compounds (*E*)-**5b** and (*Z*)-**5b** were determined by NOE experiments.



(8) Miller, R. D.; McKean, D. R. *Tetrahedron Lett.* **1982**, *23*, 323.

(9) In this reaction, a fair amount of **18** (22%) was obtained. Presumably, **18** would be formed by a reductive cyclization. That is, the reaction of (*Z*)-**5b** and **2b** afforded chromacyclopentene **19**, which was converted into **20** by β-elimination from the methyl group of **19**. The reason why **18** was obtained from only (*Z*)-**5b** is not yet clear.



(10) Use of 30 mol % **2c** for this reaction afforded the desired product **12c** in 48% yield.

(11) The starting material was recovered in 56% yield, and the chromium-promoted reductive cyclization product was not produced in this case, though the starting material was a mixture of *E* and *Z* isomers (*E*:*Z* = 2.7:1). Presumably, β-elimination from the methylene group did not occur.