Novel Synthesis of Disubstituted Alkyne Using Molybdenum Catalyzed Cross-Alkyne Metathesis

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A novel disubstituted alkyne synthesis was developed using molybdenum catalyzed cross-alkyne metathesis by Mortreux's catalyst [$Mo(CO)_6$-*p*-ClC_6H_4OH]. The reaction was carried out using $Mo(CO)_6$ (5 mol% for total amounts of alkynes) and *p*-ClC_6H_4OH (1 equiv.) in the presence of an excess amount of another alkyne (3~11 equiv.) in refluxing toluene.

The synthesis of disubstituted alkyne is very important in synthetic organic chemistry. In general, disubstituted alkynes are prepared by dehydrohalogenation of vinyl halide, alkylation of terminal alkynes in the presence of a base, or arylation of terminal alkyne by palladium catalyst reported by Sonogashira.[1] Alkyne metathesis has attracted much attention recently as a new process of alkyne reformation. Mortrex reported that a catalytic amount of $Mo(CO)_6$-PhOH was quite effective for alkyne metathesis, but the reaction mechanism is still not clear.[2, 3] We have recently reported the reaction of alkyne having a hydroxyphenyl group on the alkyne carbon with $Mo(CO)_6$.[4] Here, we report a novel disubstituted alkyne synthesis using molybdenum catalyzed cross-alkyne metathesis.

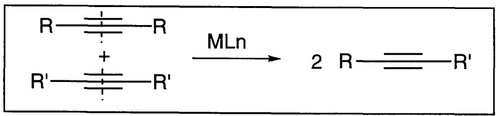
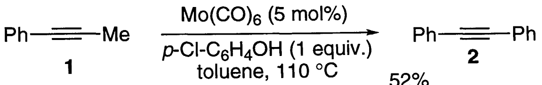


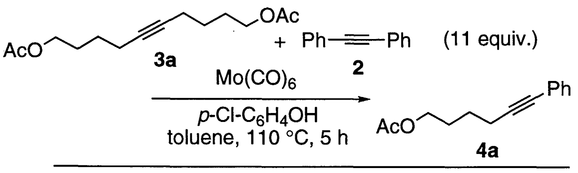
Figure 1. A mode of alkyne metathesis.

In order to use alkyne metathesis for disubstituted alkyne synthesis, it is important to shift the equilibrium to the direction of the desired product because in the metathesis reaction, two alkynes are in a state of equilibrium in the presence of the molybdenum catalyst. At first, we attempted to obtain the desired symmetrical disubstituted alkyne in a high yield by removing the alkyne having a low boiling point (for example, dimethylacetylene, bp 27 °C) from the reaction system.[5] A toluene solution of phenylpropyne, $Mo(CO)_6$ (5 mol %) and *p*-ClC_6H_4OH (1 equiv.) was refluxed for 1 h, but diphenylacetylene (**2**) was obtained in only 52% yield.



Scheme 1.

Although it is not clear why diphenylacetylene could not be obtained in a high yield in spite of the removal of the low boiling point alkyne from the reaction system, it seems likely that the catalytic activity of molybdenum decreased under the reaction conditions. The next attempt was to shift the equilibrium to the direction of the desired alkyne by use of an excess amount of another alkyne. For the synthesis of **4a** from **3a** and **2**, an excess amount of **2** (11 equiv.) was used. A toluene solution of **3a** (1 equiv.) and **2** (11 equiv.) was refluxed in the presence of 10 mol % of $Mo(CO)_6$ and *p*-ClC_6H_4OH (1 equiv. based on **3a**) for 5 h. However, **4a** was obtained in only 19% yield.[6] It was thought that the reaction system could not be attained at equilibrium under these reaction conditions because the use of 5 mol % of $Mo(CO)_6$ for the substrate **3a** in this reaction corresponded to that of 0.8 mol % for total amounts of the alkynes **3a** and **2**. Surprisingly, the yield of **3a** increased to 74% when 5 mol% of $Mo(CO)_6$ for total amounts of alkynes, **3a** and **2**, was used for this reaction. The molar ratio of diphenylacetylene (**2**) to substrates **3a** was examined and the results are shown in Figure 2. In any case, the conversion yield was high and use of only 3 equiv. of diphenylacetylene (**2**) gave **4a** in a good yield (65% yield, 97% conversion yield).



run	conditions (molar ratio)	yield
1	**3a**+**2**/$Mo(CO)_6$/*p*-Cl-C_6H_4OH=1/0.0083/0.16	19%
2	**3a**+**2**/$Mo(CO)_6$/*p*-Cl-C_6H_4OH=1/0.05/1	74%

Scheme 2.

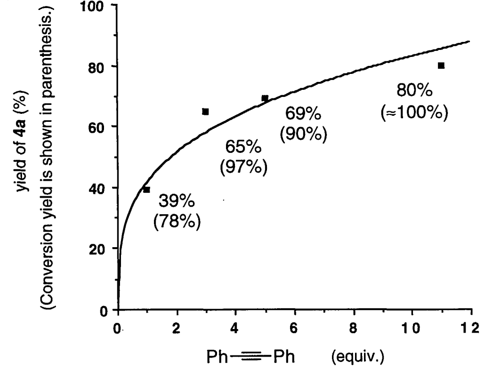
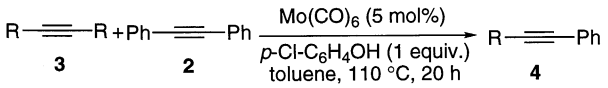


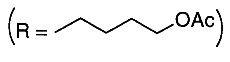
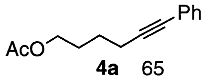
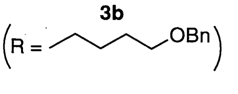
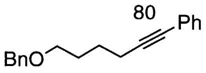
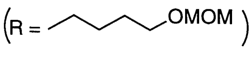
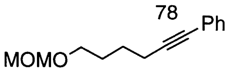
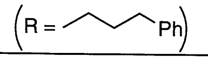
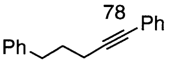
Figure 2. Change of the molar ratio of **3a** to **2**.
All reactions were carried out in the presence of 5 mol% of $Mo(CO)_6$ for total amounts of alkynes and *p*-Cl-C_6H_4OH (1equiv. based on **3a**) in refluxing toluene for 20 h.

This procedure is widely applicable for various alkyne syntheses, and the results are shown in Table 1. In these cases, 5 mol% of $Mo(CO)_6$ was used for total amounts of alkynes. The reaction of **1** having ester or ether as the functional group in a chain with an excess amount of diphenylacetylene (**2**) (11 equiv.) smoothly proceeded to give the desired alkynes **4** in high yields. Even the use of 3 equiv. of diphenylacetylene (**2**) gave the desired product **4** in good yields and high conversion yields. These results indicate that the metathesis reaction can be used for alkyne synthesis.



Scheme 3.

Table 1. Reaction of symmetrical alkyne **3** with diphenylacetylene[a]

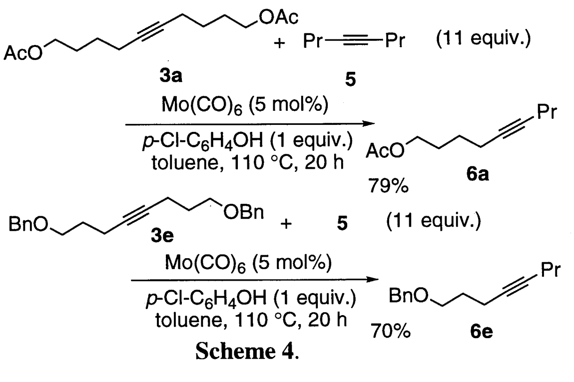
Symmetrical Alkyne **3**	Ph—≡—Ph (equiv.)	Product **4** (yield/%)
3a 	3	 **4a** 65
	11	80
3b 	3	 **4b** 69
	11	78
3c 	3	 **4c** 63
	11	78
3d 	3	 **4d** 72
	11	75

[a] All reactions were carried out using 5 mol % of $Mo(CO)_6$ for the total alkynes and p-Cl-C_6H_4OH (1 equiv. based on **3**) for 20 h upon heating.

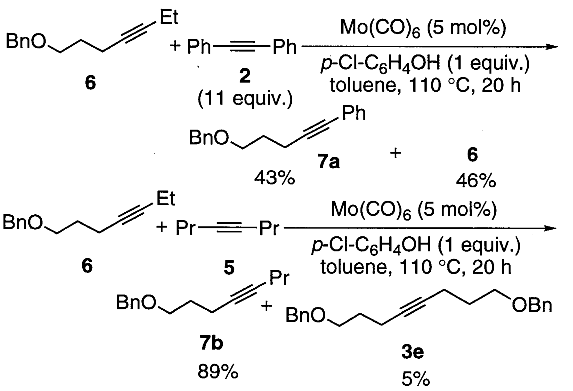
Subsequently, we examine the synthesis of disubstituted alkynes using 4-octyne (**5**) as the partner alkyne instead of diphenylacetylene **2**. The reaction of **3a** with **5** or of **3e** with **5** smoothly proceeded in a similar manner to give the desired alkyne **6a** or **6e** in 79% or 70% yield, respectively.

The reaction was further extended for the synthesis of disubstituted alkyne from unsymmetrical alkyne **6** for the starting alkyne. The reaction of **6** with diphenylacetylene (**2**) or 4-octyne (**5**) gave the desired alkyne **7a** or **7b** in a similar manner in 43% (conversion yield, 80%) or 89% yield, respectively.

For alkyne metathesis, two possible reaction courses can be considered; carbyne mechanism[2e,3] and metalacycle mechanism.[7] However, the mechanism for this molybdenum catalyzed cross-alkyne metathesis is still not clear.



Scheme 4.



Scheme 5.

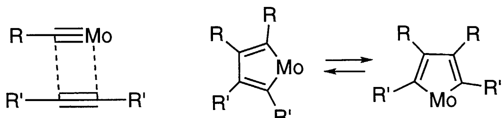


Figure 3.

The remarkable characteristics in the synthetic procedure of disubstituted alkyne are as follows. The reaction contains a new process of alkyne reformation, i.e., two triple bonds of two alkynes were cleaved, and new triple bonds are formed. The reaction procedure is very simple. It can be applied to the synthesis of disubstituted alkyne having various functional groups. Various disubstituted alkynes can be synthesized from two alkynes.

Further studies for alkyne synthesis are in progress.

References and Notes

1 a) K. Sonogashira, Y. Tohda, and N. Hagihara, *Tetrahedron Lett.*, **1975**, 4467; b) S. Takahashi, Y. Kuroyama, K. Sonogashira, and N. Hagihara, *Synthesis*, **1980**, 627.

2 a) A. Mortreux and M. Blanchard, *J. Chem. Soc., Chem. Commun.*, **1974**, 786; b) A. Mortreux, N. Dy, and M. Blanchard, *J. Mol. Catal.*, **1**, 101 (1975/76); c) A. Mortreux, J. C. Delgrange, M. Blanchard, and B. Lubochinsky, *J. Mol. Catal.*, **2**, 73 (1977); d) A. Mortreux, F. Petit, and M. Blanchard, *Tetrahedron Lett.*, **1978**, 4967; e) A. Bencheick, M. Petit, A. Mortreux, and F. Petit, *J. Mol. Catal.*, **15**, 93 (1982); f) D. Villemin and P. Cadiot, *Tetrahedron Lett.*, **23**, 5139 (1982); g) J. A. K. Du Plessis and H. C. M. Vosloo, *J. Mol. Catal.*, **65**, 51 (1991).

3 Schrock and co-workers reported that the active catalyst in alkyne metathesis using $Mo(CO)_6$-PhOH[2] was molybdenum carbyne complex. L. G. McCullough and R. R. Schrock, *J. Am. Chem. Soc.*, **106**, 4067 (1984).

4 N. Kaneta, T. Hirai, and M. Mori, *Chem. Lett.*, **1995**, 627.

5 In the cross-metathesis of terminal alkenes, ethylene was removed. a) W. E. Crowe and Z. J. Zhang, *J. Am. Chem. Soc.*, **115**, 10998 (1993); b) W. E. Crowe and D. R. Goldberg, *J. Am. Chem. Soc.*, **117**, 5162 (1995).

6 When the reaction of **3a** (1 equiv.) with **2** (1 equiv.) in the presence of 5 mol% of $Mo(CO)_6$ and p-ClC_6H_4OH (1 equiv. based on **3a**) was carried out in refluxing toluene for 20 h, the desired product **4a** was obtained in 39% yield.

7 A tungstenacyclopentatriene complex derived from W(II) complex and two moles of alkynes was reported. J. L. Kerschner, P. E. Fanwick, and I. P. Rothwell, *J. Am. Chem. Soc.*, **110**, 8235 (1988).