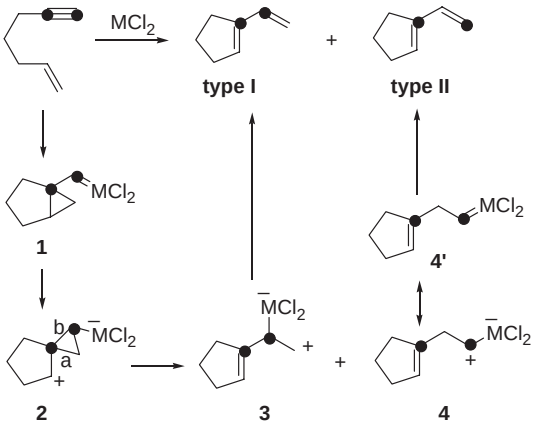
^{2}H- and ^{13}C-Labelling Studies on Skeletal Reorganization of 1,6-Enynes

Hiromi Nakai and Naoto Chatani*
Department of Applied Chemistry, Faculty of Engineering, Osaka University, Suita, Osaka 565-0871

(Received October 9, 2007; CL-071103; E-mail: chatani@chem.eng.osaka-u.ac.jp)

^{2}H- and ^{13}C-labelling studies on skeletal reorganization of 1,6-enynes having a terminal alkyne moiety have been performed with various catalysts. The products are 1-vinylcyclopentenes, but two possible isomers, type **I** and **II** products, can be formed. The formation of type **I** involves the cleavage of the original C–C double bonds and migration of the terminal alkene carbon atom to the terminus of the alkyne. On the other hand, the formation of type **II** involves a double cleavage of the C–C double bond and the C–C triple bond, which is an anomalous bond connection. The product ratio is affected by the nature of the catalyst used. Type **II** is obtained as a major isomer in the case of late transition metal halides. On the other hand, the type **I** product forms exclusively in the presence of a typical element halide, such as $InCl_3$.

The skeletal reorganization of enynes leading to 1-vinylcycloalkenes has been the subject of intensive studies, since it provides a powerful method for the construction of a useful ring system by means of a simple operation and it is mechanistically interesting.[1] Two possible products, type **I** and **II**, can be formed (Scheme 1). Type **I** is the product in which the original C–C double bonds are cleaved. On the other hand, the formation of type **II** involves a double cleavage of the C–C double bond and the triple bond, the cleavage of the latter bond being difficult. In many cases, one of the two products will be obtained, and the selectivity is significantly dependent both on the structure of the substrates and on the catalysts used. The first report on the skeletal reorganization of enynes was published by Trost et al. in 1988.[2] Since we reported in 1994 that the simpler and more practical catalyst, $[RuCl_2(CO)_3]_2$, is highly active in the skeletal reorganization of enynes having a terminal alkyne moiety,[3] various electrophilic metal complexes, such as Pt^{II},[4] Pt^{IV},[5] Ru^{II},[6] Ir^{I},[7] Au^{I},[8] Ga^{III},[9] and In^{III},[10] subsequently were found to show catalytic activity for the skeletal reorganization of enynes. In all cases, the electrophilic interaction of the catalyst with an alkyne moiety is believed to initiate the catalysis. The reaction mechanism of the skeletal reorganization of enynes was proposed by Trost et al.[2] and Oi et al.,[4c] and DFT studies were performed by Echavarren et al.[8] Although the mechanism is still controversial,[11] the reaction course depends on the stability of zwitterionic intermediate **3** (via cleavage of bond a in **2**)[12] and on the intermediate **4** or **4′** (via cleavage of bond b in **2**).

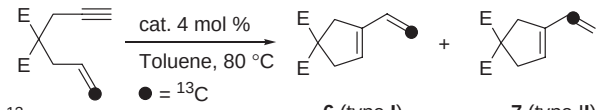


Scheme 1. Skeletal reorganization of 1,6-enynes

When either enynes having a substituent on a terminal alkyne carbon or a terminal alkene carbon are used, it is easy to recognize which type of products are formed. The presence of an alkyl or phenyl group at the terminal alkene carbon gives type **I** products selectively, irrespective of the nature of the catalysts. There are few catalytic systems where type **II** products are selectively obtained. When an ester group is attached at an alkyne carbon and $[RuCl_2(CO)_3]_2$ or $PtCl_2$ is used as the catalyst, type **II** is selectively obtained.[3,4a] In the case of enynes having a methyl group at a terminal alkyne, Pt^{II},[4c] Pt^{IV},[5] and Au^{I},[8c] type **II** are selectively formed. In the $InCl_3$-catalyzed reaction of enynes having an alkyl group longer than the ethyl group, products are not 1-vinylcyclopentenes but are 1-allylcyclopentenes, which have the same bond connection as when type **II** are obtained.[10] However, it is impossible to recognize which type of product is formed in the case of the simple enyne because two isomeric products are the same. It would be helpful to know the ratio of type **I** to **II** in order to consider the reaction mechanism of skeletal reorganization of enynes. While our group and others have conducted some of the labelling experiments, systematic studies have not yet been performed. Herein are reported systematic studies using ^{2}H- and ^{13}C-labeled simple 1,6-enynes.

The reaction of a 10% ^{13}C-enriched enyne, ^{13}C-**5**,[4c] was performed with a catalytic amount of catalysts, which are known to be active in the skeletal reorganization of simple enyne **5**, under the reported reaction conditions. In all cases where late transition metal halides, such as $[RuCl_2(CO)_3]_2$, $PtCl_2$, and $PtCl_4$ were used as the catalyst, **7** (type **II**) was obtained as a major isomer. We expected that type **II** would exclusively form in the case of Au^{I} and Rh^{II}, because these metals are known to stabilize intermediate **4** or **4′**.[13] However, the ratio of type **II** was lower than expected. On the other hand, **6** (type **I**) was exclusively formed in the case of $InCl_3$, as expected.

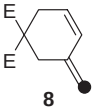
Next, we examined the product ratio using enyne **9**, in which a methyl group is attached at the internal alkene carbon. The skeletal reorganization product, type **I** and type **II**, also could not be differentiated. The enyne d^2-**9** was easily prepared in a single step by a Wittig-type reaction with the corresponding ketone.[14] Similar to results shown in Scheme 2, type **II** **11** was a major isomer in the late transition metal halides, except Rh^{II} catalyst, which gave type **I** as a major product (Scheme 3).[15,16] The product ratios shown in Scheme 3 compare favorably the ratios shown in Scheme 2, indicating that the presence of a methyl group at the internal alkene carbon did not significantly affect



^{13}C-**5** (0.1 mmol) **6** (type **I**) **7** (type **II**)

$[RuCl_2(CO)_3]_2$	12 h	81% (7:93)[1]
$PtCl_2$	2 h	53% (6:94)
$PtCl_4$	20 h	57% (7:93)
$[IrCl(CO)_3]_n$	20 h	83% (21:79)
$[Rh(OOCCF_3)_2]_2$	3 h	81% (39:61)[2]
$AuCl_3$	12 h	42% (40:60)[3]
$AuCl(PPh_3)/AgSbF_6$	0.5 h	nd (60:40)[2,4]
$InCl_3$	1 h	68% (>99:1)[5,6]

[1]The reaction was run under CO (1 atm). [2]2 mol % of catalyst. [3]10 mol % of $AuCl_3$. [4]nd = yield not determined. A major product was a six-membered product **8**. The reactiion was run in CH_2Cl_2 at 0 °C. [5]10 mol % of $InCl_3$. A six-memberd product **8** was obtained in 13% yield. [6]98%^{13}C-enriched **5** was used.



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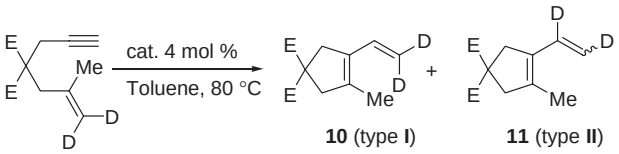
Scheme 2. ^{13}C-Labelling experiments using enyne ^{13}C-**5**.

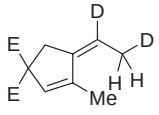


10 (type **I**) **11** (type **II**)

d^2-**9** (0.1 mmol)

$[RuCl_2(CO)_3]_2$	2 h	59% (2:98)[1,2]
$PtCl_2$	2 h	61% (1:99)
$PtCl_4$	1 h	56% (1:>99)[2]
$[IrCl(CO)_3]_n$	2 h	55% (2:98)
$[Rh(OOCCF_3)_2]_2$	4 h	55% (76:24)[3]
$AuCl_3$	1 h	66% (4:96)[2,4]

[1]The reaction was run under CO (1 atm). [2]Double bond isomerization product **12** was also formed. The ratio of **12** is included in **11**. [3]2 mol % of $[Rh(OOCCF_3)_2]_2$. [4]10 mol % of $AuCl_3$.



12 (type **II**)

Scheme 3. ^{2}H-Labelling experiments using enyne ^{2}H-**9**.

on the reaction course.

In summary, we performed ^{2}H- and ^{13}C-labelling studies on the skeletal reorganization of 1,6-enynes. While the reaction course had already been found to be significantly affected by nature of catalysts used and the substituent pattern of enynes having a substituent on a terminal alkyne carbon or a terminal alkene carbon, we also found that the product ratios of type **I** and **II** were significantly affected by the nature of catalysts even in the case of simple enynes. Type **II** products were exclusively obtained in the presence of $[RuCl_2(CO)_3]_2$, $PtCl_2$, and $PtCl_4$ as catalysts. The $[Rh(OOCCF_3)_2]_2$- and $AuCl_3$-catalyzed reactions gave a mixture of type **I** and type **II**, slightly in favor of type **II**. On the other hand, the use of typical elemental metal halides, such as $InCl_3$ as the catalyst led to the exclusive formation of type **I**. These remarkable contrasts indicate a complexity of the mechanism in skeletal reorganization of enynes.

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11 Echavarren proposed that **3** or **4** is formed directly from **1** and not through a spiro intermediate **2** on the basis of DFT studies. See also Ref. 8.

12 A direct formation of an alkene metal complex of type **I** from a spiro intermediate **2** is possible.

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15 Because the use of $InCl_3$ as the catalyst gave a complex mixture, the result is not shown in Scheme 3.

16 Isomerization of **11** to **12** occurred easily, compared with non-labeled product.

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