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A Hydroacylation-Triggered Carbon−Carbon Triple Bond Cleavage in Alkynes via Retro-Mannich Type Fragmentation

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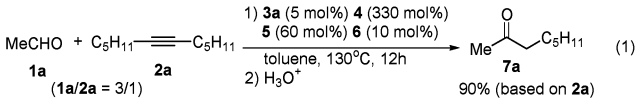
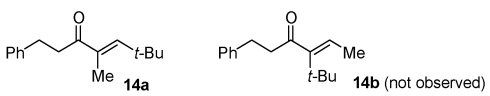
The carbon−carbon bond activation is one of the most challenging areas in organometallic chemistry.[1] Despite the significant developments in this field during the past decade, the cleavage of an alkyne triple bond has remained only as a few examples including alkyne-ligand scission on transition metal complexes,[2] oxidative cleavage,[3] alkyne metathesis,[4] and so on.[5] In the course of our studies on the chelation-assisted activation of C−H and C−C bonds in organic molecules,[6,7] we found that the reaction of alkynes and allylamines resulted in the cleavage of the C−C triple bond through an α,β-unsaturated ketimine intermediate.[8] However, an allylamine as a substrate caused a limitation to its versatile use. Herein, we describe a new protocol for the cleavage of the carbon−carbon triple bond in alkyne, which is triggered by a chelation-assisted hydroacylation.

In our reaction, acetaldehyde (**1a**) reacted with 6-dodecyne (**2a**) in the presence of $(PPh_3)_3RhCl$ (**3a**, 5 mol % based on **2a**), cyclohexylamine (**4**), 2-amino-3-picoline (**5**), and aluminum chloride (**6**) to afford 2-octanone (**7a**) after hydrolysis (eq 1).



A plausible mechanism for the reaction is depicted in Scheme 1. The first step might be condensation of aldehyde **1a** and **5** to give aldimine **8**, which reacts with alkyne **2a** to give α,β-unsaturated ketimine **9a**. A conjugate addition of cyclohexylamine **4** into **9a** and subsequent retro-Mannich type fragmentation of the resulting β-aminoketimine **10** afford aldimine **11** and enamine **12**.[8,9] Enamine **12** then isomerizes into ketimine **13a**, which is hydrolyzed to yield ketone **7a**.

The reaction of various aromatic and aliphatic aldehydes with alkynes gave corresponding ketones in good to moderate yields (Table 1). When an internal alkyne bearing different substituents such as 4,4-dimethyl-2-pentyne (**2e**) was used for the reaction with hydrocinnamaldehyde (**1b**), only 1-phenyl-pentan-3-one (**7b**) was obtained in a 33% yield along with α,β-unsaturated ketone **14a** (47%), a hydrolysis product of intermediate ketimine (entry 4). This result implies that the reactivity and regioselectivity of this reaction largely depend on the bulkiness of substituents in alkynes. While two regioisomers of the initial hydroacylation product, that is, **14a** and **14b**, are possible from the reaction of **1b** and **2e**, a bulky *tert*-butyl group suppresses the formation of **14b**. Furthermore, subsequent fragmentation of α,β-unsaturated ketone **14a** was inhibited due to the steric hindrance of the *tert*-butyl group, which gives rise to a low yield of **7b** as compared to the case of 2-butyne (**2b**, entry 1).



Scheme 1. A Plausible Mechanism for C−C Bond Cleavage of Alkyne

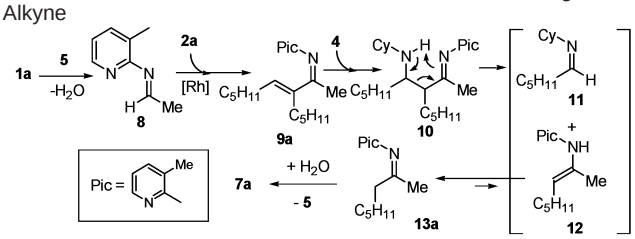
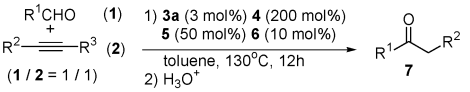


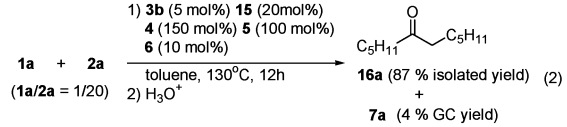
Table 1. The Reaction of Various Aldehydes (**1**) and Alkynes (**2**)



entry	R^1 (**1**)	R^2, R^3 (**2**)	isolated yield of product (**7**, **7'**)
1	$PhCH_2CH_2$ (**1b**)	$R^2 = R^3 =$ Me (**2b**)	90% (**7b**)
2		$R^2 = R^3 =$ Et (**2c**)	91% (**7c**)
3		$R^2 = R^3 =$ Pr (**2d**)	94% (**7d**)
4[a]		$R^2 =$ Me, $R^3 =$ *t*-Bu (**2e**)	33% (**7b**)
5	C_5H_{11} (**1c**)	(**2d**)	91% (**7e**)
6	$PhCH_2$ (**1d**)	(**2b**)	82% (**7f**)
7[b]	*p*-$MeOC_6H_4$ (**1e**)	(**2b**)	54% (**7g**)

[a] A parent α,β-unsaturated ketone **14a** remained unreacted (47% yield). [b] The unreacted starting material was detected in 35% GC yield. 100 mol % of **5** was used.

It should be noted that an aldehyde, which was generated through the fragmentation of α,β-unsaturated ketone (Scheme 1), could react with the remaining alkyne. Therefore, we envisaged a serial cleavage of alkyne induced by a small amount of external aldehyde, a hydroacylation-triggered C−C bond cleavage of alkyne. For example, when **2a** was subject to react with a small amount of **1a** (5 mol % based on **2a**) in the presence of $[(C_8H_{14})_2RhCl]_2$ (**3b**), 4-diphenylphosphinobenzoic acid (**15**) as an external ligand, **4**, **5**, and **6**, 6-dodecanone (**16a**), as well as 2-octanone (**7a**, 4% GC yield) were obtained in an 87% yield after hydrolysis (eq 2).[10]



A possible mechanism of this reaction is depicted in Scheme 2. The initial step might be chelation-assisted hydroacylation of **2a** with **1a** to give α,β-unsaturated ketimine **9a**, which undergoes fragmentation to afford aldimine **11** and ketone **7a**. The reaction of the resulting aldimine **11** and remaining alkyne **2a** gives another α,β-unsaturated ketimine **9b**, and then ketone **16a** through the subsequent fragmentation of **9b** and hydrolysis. A newly generated aldimine **11** could react with **2a** along the catalytic cycle.

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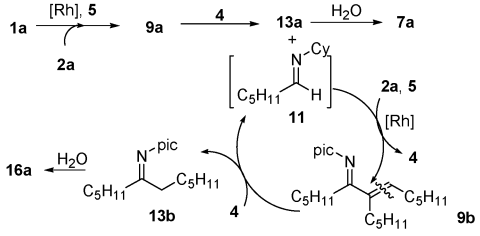
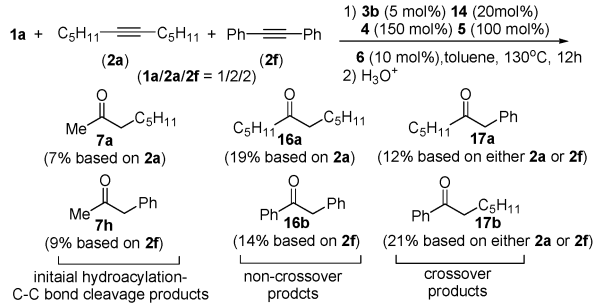
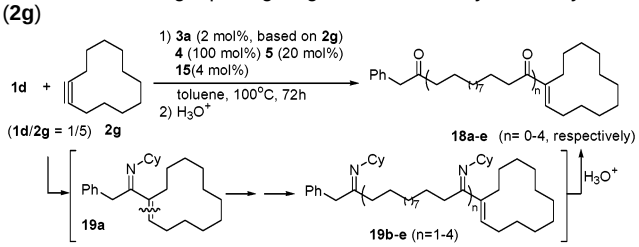
Scheme 2. A Proposed Mechanism for the Hydroacylation-Triggered C−C Bond Cleavage of Alkyne



Scheme 3. A Crossover Experiment



Scheme 4. A Ring-Opening Oligomerization of Cyclododecyne (**2g**)



A direct hydroamination of **2a** is also a possible mechanism for the formation of **16a**.[11] Therefore, the crossover experiment was performed using two different alkynes, **2a** and diphenylacetylene (**2f**) as shown in Scheme 3. In this reaction, crossover products, **17a** and **17b**, were obtained as well as noncrossover products, **16a** and **16b**, in a ratio of 50/50 (33% for **16a** and **16b**, 33% for **17a** and **17b**, determined by GC analysis). This result indicates that the mechanism for the formation of **16** is a chelation-assisted hydroacylation-triggered mechanism rather than the direct hydroamination of alkyne where crossover products could not be formed.[12]

Encouraged by the results, we attempted to apply the protocol of alkyne cleavage to the ring opening of strain-free cycloalkyne, where consecutive hydroacylation and fragmentation would result in the ring-opening oligomerization of cycloalkyne to yield polyketone. For example, cyclododecyne (**2g**) was reacted in the presence of 20 mol % of **1d** under the catalyst system of **3a**, **4**, **5**, and **15** at 100 °C for 72 h to give polyketones **18** in a 30% isolated yield (based on total amount of all starting materials, Scheme 4). In this reaction, α,β-unsaturated ketimine **19a** is an imine of the initial hydroacylation product, which is identified as **18a** after hydrolysis. Successive retro-Mannich fragmentation and hydroacylation gave polyketones **18** after hydrolysis. The degree of oligomerization was determined by ESI-MS, which showed that polyketones **18b**−**e** (n = 1−4) as well as **18a** were formed in this one-pot reaction, and among them polyketone **18c** (n = 2) was a major component (Figure 1).

In conclusion, we demonstrated the cleavage of the C−C triple bond in alkyne, utilizing a chelation-assisted hydroacylation followed by retro-Mannich type fragmentation of the resulting α,β-unsaturated ketone under the catalyst system of Rh(I) complex, 2-amino-3-picoline, cyclohexylamine, and Lewis acid. This one-pot protocol was also applied to the ring-opening oligomerization of cycloalkyne.

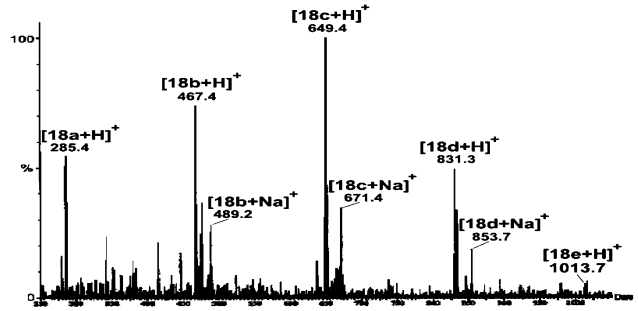


Figure 1. ESI-MS spectrum of polyketones **18**.

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

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(12) Furthermore, when the reaction of **2a** (eq 2) was performed without **1a**, only a small amount of **16a** (3% isolated yield) was obtained.

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