C-C Double Bond Cleavage of Linear α,β-Unsaturated Ketones†

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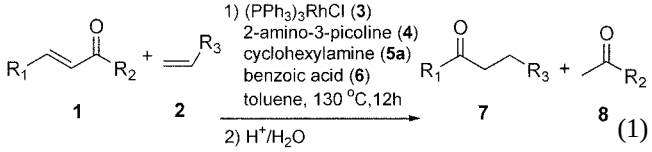
The activation of C-H bonds by transition-metal complexes is one of the most efficient methods to form C-C bonds in organic synthesis.[1] We have successfully developed a Rh(I)-catalyzed C-H bond activation series using 2-amino-pyridine derivatives[2] or benzylamine[3] as a chelation auxiliary to induce cyclometalation.[4] In the course of our studies on chelation-assisted C-H bond activation, we reported a Rh(I)-catalyzed hydroiminoacylation of alkynes with allylamine derivatives[5] or aldehydes,[6] which was further applied to the retro-Mannich-type fragmentation of the resulting α,β-unsaturated ketimine by primary amines. Encouraged by these results, we also developed a Rh(I)-catalyzed C-H bond activation of the ring opening in 2-cycloalkenones[7] and a chelation-assisted β-alkylation of α,β-unsaturated ketone using Rh(I) catalyst and various amines.[8]

Herein, we wish to report on the amine-assisted C-C double bond cleavage of α,β-unsaturated ketone *via* retro-Mannich-type fragmentation followed by Rh(I)-catalyzed C-H bond activation.

In our experiment, α,β-unsaturated ketone **1** reacts with 1-alkene **2** under a cocatalyst system of $(PPh_3)_3RhCl$ (**3**), 2-amino-3-picoline (**4**), cyclohexylamine (**5a**), and benzoic acid (**6**) to give a mixture of ketones **7** and **8** in high yields after hydrolysis (eq. 1).



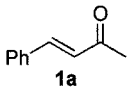
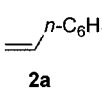
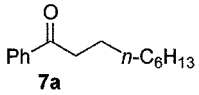
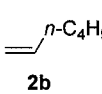
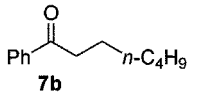
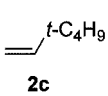
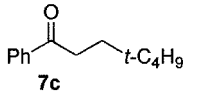
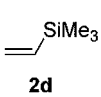
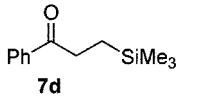
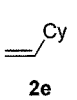
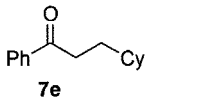
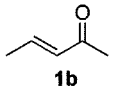
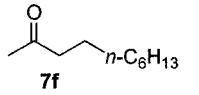
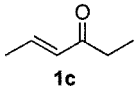
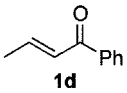
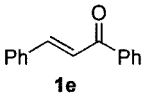
(1)

For example, when the reaction of 4-phenyl-but-3-en-2-one (**1a**) and 1-octene (**2a**) was carried out at 130 °C for 12 h in the presence of **3** (5 mol%), **4** (20 mol%), **5a** (200 mol%), and **6** (5 mol%), 1-phenyl-nonan-1-one (**7a**) was isolated in a 94% yield (Table 1, Entry 1).[9] Other olefins (**2b-e**) were also applied in this reaction to give fairly good yields of corresponding ketones (**7b-e**) (Entries 2-5). Various α,β-unsaturated ketones (**1b-e**) reacted with **2a** to give the corresponding decan-2-one (**7f**) and **7a** in fairly good yields (Entries 6-9).

A plausible mechanism of the reaction is depicted in Scheme 1. Cyclohexylamine **5a** undergoes conjugate addition into intermediate α,β-unsaturated ketimine **9**, derived from the condensation of α,β-unsaturated ketone **1** with **5a** in the presence of benzoic acid (**6**) and the subsequent retro-Mannich-type fragmentation of **10** to form a mixture of aldimine **11** and ketimine **14** through intermediate enamine **12**.[6,10] The generated aldimine **11** is hydroiminoacylated with 1-alkene **2** under the cocatalyst system of **3** and **4** to afford ketimine **13**. This transimination/hydroiminoacylation protocol was already utilized in the efficient conversion of aldimines to ketimines.[2] The hydrolysis of ketimines **13** and **14** produces the corresponding ketones **7** and **8**.

To support our proposed mechanism, α,β-unsaturated ketimine (**9a**, 1.0 equiv)[11] was allowed to react with 1-

Table 1. C-C Double Bond Cleavage of α,β-Unsaturated Ketone (**1**)[a]

Entry	α,β-Unsaturated-ketone (**1**)	1-Alkene (**2**)	Product (**7**)	Isolated yield (%)
1	 **1a**	 **2a**	 **7a**	94
2		 **2b**	 **7b**	93
3		 **2c**	 **7c**	92
4		 **2d**	 **7d**	81
5		 **2e**	 **7e**	78
6	 **1b**	**2a**	 **7f**	98
7	 **1c**		**7f**	98
8	 **1d**		**7f**	91
9	 **1e**		**7a**	79

[a]Reagents and conditions: α,β-Unsaturated Ketone (**1**; 0.216 mmol), 1-alkene (**2**; 0.648 mmol), $(PPh_3)_3RhCl$ (**3**; 0.0108 mmol), 2-amino-3-picoline (**4**; 0.0432 mmol), cyclohexyl-amine (**5a**; 0.432 mmol), benzoic acid (**6**; 0.0108 mmol), toluene (100 mg), 130 °C, 12 h.

†Dedicated to Professor Yong Hae Kim for his distinguished achievements in organic chemistry.

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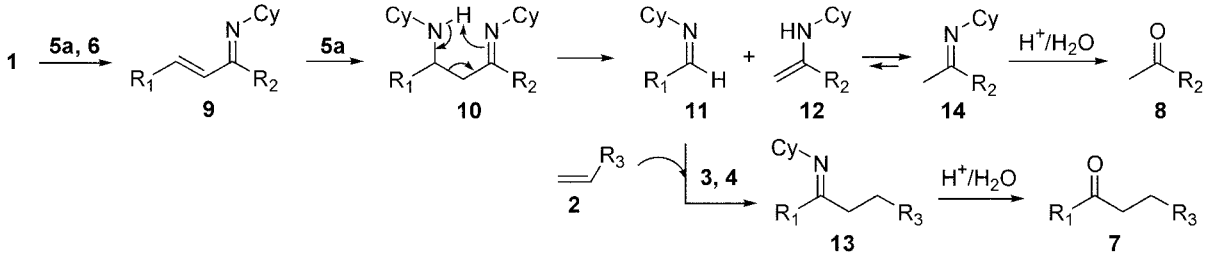
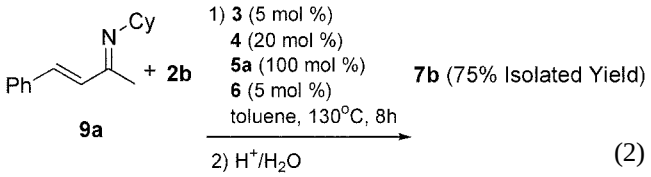


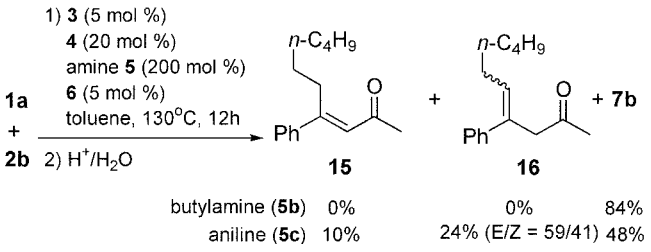
Scheme 1

hexene (**2b**, 3.0 equiv) under the given reaction conditions to furnish 1-phenyl-1-heptan-1-one (**7b**) in a 75% isolated yield (eq. 2). This result confirms the above mechanism.



(2)

To compare the activity of cyclohexylamine with those of other primary amines, the C-C double bond cleavage of α,β-unsaturated ketone **1a** was investigated with *n*-butylamine (**5b**) or aniline (**5c**) under the conditions as shown in Table 1 (eq. 3). *n*-Butylamine (**5b**) gave **7b** in a 84% isolated yield. In the case of aniline (**5c**), the β-alkylated products[8] of **1a**, (*E*)-4-phenyl-3-decen-2-one (**15**) and (*E/Z*)-4-phenyl-4-decen-2-one (**16**, E/Z=59/41), were obtained in 10% and 24% isolated yields along with a 48% yield of **7b**. This result informs that aniline is not good enough to undergo retro-Mannich fragmentation compared with aliphatic amine such as cyclohexylamine or *n*-butylamine, and it partly acts as a directing group for β-alkylation.



(3)

In conclusion, we have demonstrated the C-C double bond cleavage of α,β-unsaturated ketone under a catalytic system consisting of Rh(I) complex, 2-amino-3-picoline, cyclohexylamine, and benzoic acid. This reaction undergoes a retro-Mannich-type fragmentation of α,β-unsaturated ketone through the conjugate addition of cyclohexylamine followed by Rh(I)-catalyzed C-H bond activation.

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9. A typical procedure (Table 1): A screw-capped pressure vial (1 mL) was charged with 0.216 mmol of α,β-unsaturated ketone **1**, 0.648 mmol of 1-alkene **2**, 10 mg (0.011 mmol) of $(PPh_3)_3RhCl$ (**3**), 4.7 mg (0.043 mmol) of 2-amino-3-picoline (**4**), 43.0 mg (0.216 mmol) of cyclohexylamine (**5a**), 1.3 mg (0.011 mmol) of benzoic acid (**6**), and 0.1 mL of toluene. The reaction mixture was stirred at 130 °C for 12 h. After the reaction, the mixture was hydrolyzed by 1 N HCl and extracted with diethyl ether. The organic layer was dried over $MgSO_4$, and the ratio of **7** and **8** was determined by integration in gas chromatography (GC). The reaction mixture was purified by column chromatography (*n*-hexane : ethyl acetate = 5 : 1) to give **7** and **8**.
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11. Preparation of intermediate α,β-unsaturated ketimine **9a**: the reaction mixture of **1a** (2.00 g, 13.7 mmol) and **5a** (1.36 g, 13.7 mmol) was stirred in the presence of molecular sieves at room temperature for 15 h. After the reaction, the mixture was filtered on a sinter glass to remove molecular sieves. The filtrate was concentrated under reduced pressure and the resulting crude product was purified by kugelrohr distillation to afford 1.25 g (40%) of α,β-unsaturated ketimine **9a**.