

Catalytic Carbon–Carbon Bond Activation of Unstrained Ketone by Soluble Transition-Metal Complex

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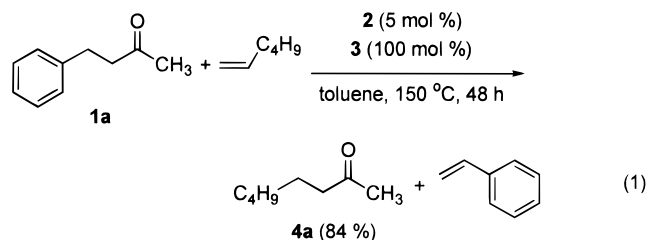
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The activation of carbon–carbon bonds by soluble transition-metal complexes has been one of the most prominent challenges in recent years.¹ Although C–C single bonds are generally inert to transition metals under homogeneous conditions, some possible ways to cleave C–C bonds have been devised: relieving ring energy,² inducing aromatic stabilization,³ forming stable metal-lacyclic complexes (cyclometalation),⁴ etc.⁵ These methods all involve stoichiometric reactions, not catalytic ones. Only a few examples of homogeneous catalytic activation of C–C bonds have been known,^{6–8} and these are limited to strained molecules,⁶ or to model compounds.⁷ In this report, we describe the unprecedented catalytic C–C bond activation of unstrained ketone compounds. This catalytic C–C bond activation can be achieved by using 2-amino-3-picoline, which solves the problem of the accessibility of metal complexes to C–C bonds. We suggest that

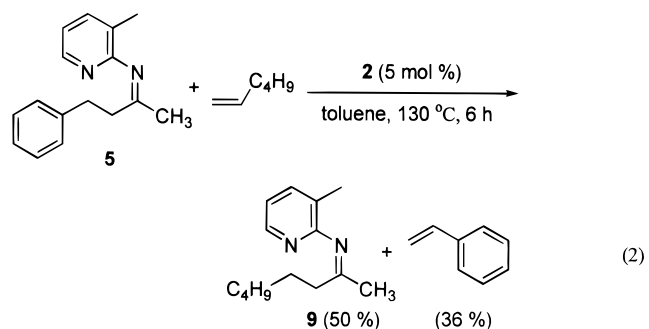
this reaction could be applied to the general exchange reaction of an alkyl group to other alkyl groups in ketones through C–C bond activation.

Our experiment was conducted under the following reaction conditions: Benzylacetone (**1a**) reacted with 1-hexene at 150 °C for 48 h in a mixture of [chlorotris(triphenylphosphine)rhodium(I)] (**2**, 5 mol % based upon **1**) and 2-amino-3-picoline (**3**, 100 mol %) to give 2-octanone (**4a**) in 84% yield along with a trace amount of styrene (eq 1).⁹



A possible mechanism for the transformation of ketone **1a** to ketone **4a** is illustrated in Scheme 1. The ketimine **5** must be formed in situ by condensation of ketone **1a** and **3**. A C–C bond in **5** might be cleaved by rhodium(I) in **2** to give an (iminoacyl)rhodium(III) phenethyl **6**. A β -hydrogen elimination of phenethyl group in **6** provides (iminoacyl)rhodium(III) hydride **7** and styrene. A hydride insertion of **7** into 1-hexene leads to an (iminoacyl)rhodium(III) hexyl **8**, and reductive elimination in **8** produces ketimine **9** with regeneration of catalyst **2**. Hydrolysis of **9** with H₂O, previously formed from condensation of **3** and ketone **1a**, affords ketone **4a**. In this reaction, **3** as well as metal complex **2** acts as a catalyst. When the reaction was carried out under identical conditions in the absence of **3** to clarify its effect, no reaction occurred, and the starting ketone **1a** was completely recovered. This implies that the C–C bond α to carbonyl group in **1a** is not directly cleaved by complex **2**. Recently, this type of chelation-assisted carbon–hydrogen bond activation has been applied to the direct synthesis of ketone from aldehyde and 1-alkene, or primary alcohol and 1-alkene.¹⁰

To identify the involvement of C–C bond cleavage of ketimine **5**, **5** was allowed to react with 1-hexene at 130 °C for 6 h under catalyst **2** (5 mol %), which resulted in a mixture of ketimine **9** and styrene in 50 and 36% yield (based upon **5**) (eq 2).



Formation of styrene and ketimine **9** confirms that the carbon–carbon bond of **5** is clearly cleaved and that 1-hexene is exchanged with the phenethyl group in **5**. Since β -hydrogen elimination is a necessary step preceding catalytic C–C bond cleavage, the starting ketone should have a β -hydrogen.

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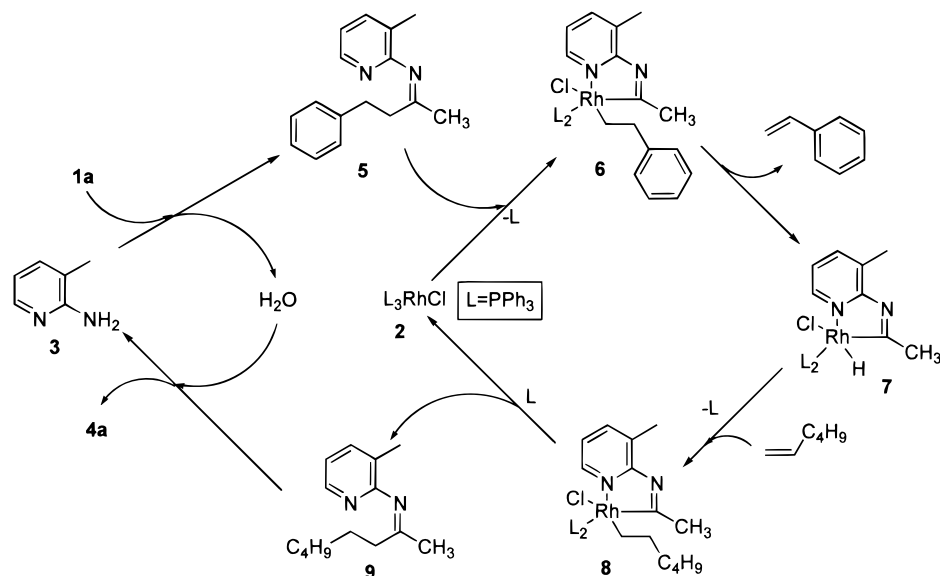
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Scheme 1. Presumed Catalytic Mechanism for Carbon–Carbon Bond Activation**Table 1.** Catalytic C–C Bond Cleavage of Unstrained Ketone with Alkene by **2**^a

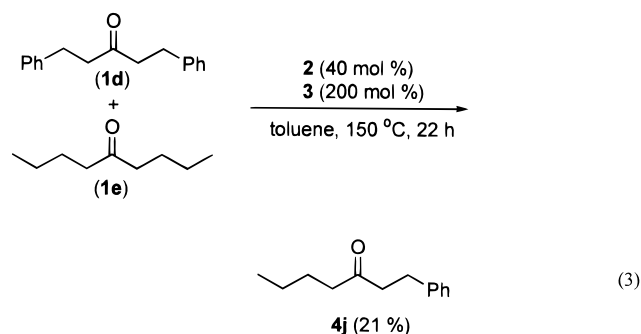
Entry	Ketone	Alkene	mol % of 3	Product	Yield (%) ^b
1			20		98 ^c
2			20		84 ^d
3			20		(73)
4			100		(90)
5			20		(42)
6			100		(55)
7			20		55
8			100		92
9			20		13
10			100		30
11			20		(77)
12			20		(61)
13			20		(55)
14			20	 	(19) + (32)

^a Reaction of ketone (**1**) and alkene (**1**/alkene = 1/10) was carried out at 150 °C for 48 h under 10 mol % of (PPh₃)₃RhCl (**2**) and 2-amino-3-picoline (**3**) except entry 2. ^b The yields of products were determined by gas chromatography detector (GCD), and isolated yields are shown in parentheses. ^c The ratio of **1a** and 1-hexene is 1/15. ^d Reaction of **1a** and 3,3-dimethyl-1-butene (**1a**/3,3-dimethyl-1-butene = 1/15) was carried out at 150 °C for 48 h under 5 mol % of **2** and 20 mol % of **3**.

yield (84%) under 5 mol % of **2** (entry 2). The yield of product **4** increased with the concentration of **3**: a 100 mol % concentration of **3** for ketones provided a higher yield of corresponding ketones than a 20 mol % of **3** (entry 3 and 4, 5 and 6, 7 and 8, 9 and 10). Even for internal olefins such as cyclohexene and cyclopentene, the reaction provided cyclohexyl ketone **4e** and cyclopentyl ketone **4f** in 92 and 30% yield with 100 mol %

concentration of **3** (entry 8 and 10). When 2-octanone (**4a**) and 2-butanone (**1b**) were allowed to react with 1-octene respectively, the corresponding 2-decanone (**4c**) were isolated in 77 and 61% yield (entry 11 & 12). The reaction of ketone having a α -phenyl substituent such as **1c** with 1-hexene showed lower catalytic activity (55% yield) for carbon–carbon bond activation than that of ketone having an α -methyl substituent like **1a** (entry 1 and 13). For 1,5-diphenyl-3-pentanone (**1d**), a mixture of the C–C bond-cleaved product **4h** and doubly C–C bond-cleaved product **4i** was isolated in 19 and 32% yields (entry 14).

Another interesting test for catalytic carbon–carbon bond activation is the crossover experiment. Without olefin, a mixture of 1,5-diphenyl-3-pentanone (**1d**) and 5-nonanone (**1e**) was heated at 150 °C for 22 h with **2** (40 mol % based upon **1e**) and **3** (200 mol % based upon **1e**) (eq 3).



After the reaction, the crossover product, 1-phenyl-3-heptanone (**4j**), was isolated in 21% yield (based upon **1e**). One of the butyl groups in **1e** was exchanged with one of the phenethyl groups in **1d**.

In conclusion, facile catalytic C–C bond activation of unstrained ketone has been successfully achieved through chelation assistance of 2-amino-3-picoline by a soluble rhodium(I) complex.

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Supporting Information Available: Experimental procedures for C–C bond activation of ketone by Rh(I), reaction of ketimine **5** with 1-hexene, and crossover reaction, including the characterization data for **5** and **9** (PDF). This material is available free of charge via the Internet at <http://pubs.acs.org>.