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Catalytic Activation of C–H and C–C Bonds of Allylamines via Olefin Isomerization by Transition Metal Complexes

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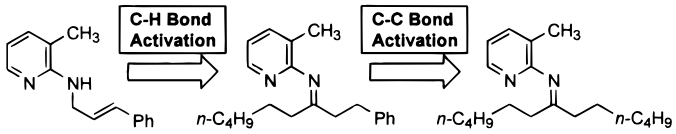
ABSTRACT



The metal-catalyzed reaction of olefins with allylamines bearing coordination sites (2-pyridyl groups) was studied. With $Ru_3(CO)_{12}$ as catalyst, activation of C–H bonds led to the formation of ketimines that were hydrolyzed to give asymmetric ketones. With $[(C_8H_{14})_2RhCl]_2$, both C–H and C–C bonds were activated and symmetric ketones were formed on hydrolysis. The reaction involves double bond migration of the allylamine to form an aldimine.

Catalytic activation of C−H[1,2] and C−C[3,4] bonds has a broad impact in organometallic chemistry because of its applications in organic synthesis. Aldehydic C−H bond activation[5] and chelation-assisted hydroacylation[6] were described earlier. In particular, the use of 2-amino-3-picoline avoids decarbonylation effectively.[7] Activation of the C−C bond in ketones bearing β-hydrogen using chelation assistance has also been documented.[8] Aldimines and ketimines are postulated intermediates for these C−H and C−C bond activations. Catalytic activation of aromatic aldehydes with 2-amino-3-picoline is more efficient than activation of aliphatic aldehydes.[7a,9] The formation of aminal side products during the reaction with aliphatic aldehydes reduces the yields. Double bond migration of allylamines in the presence of transition metal complexes provides a versatile approach to the preparation of aldimines of the aliphatic alkyl group.[10]

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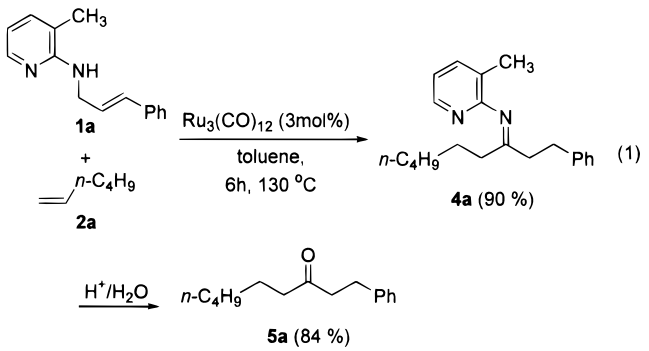
In this report, we describe synthesis of ketones from allylamines via catalytic activation of C−H and C−C bonds using organotransition metal complexes $Ru_3(CO)_{12}$ and $[(C_8H_{14})_2RhCl]_2$. The products of these reactions are hydrolyzed under acidic conditions to form asymmetric and/or symmetric ketones.

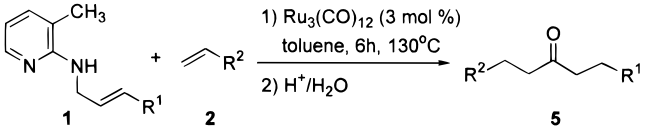
The reaction is exemplified by the synthesis of ketone **5a** (eq 1). *N*-(3-Methyl-2-pyridyl)-*N*-[(E)-3-phenyl-2-propenyl]-



amine (**1a**) was first converted to the corresponding ketimine **4a**. The reaction was performed in toluene at 130 °C with 3 equiv of 1-hexene (**2a**) and catalytic amount of $Ru_3(CO)_{12}$ (**3a**) and gave a 90% yield. Acid hydrolysis of this product afforded 1-phenyl-3-nonanone (**5a**) in an 84% yield based upon **1a**.

To establish the scope of this reaction, allylamines **1a** (R^1 = phenyl), **1b** (R^1 = methyl), and **1c** (R^1 = H) were allowed to react with various 1-alkenes under identical conditions. They gave the corresponding ketones, and Table 1 summarizes the products and yields from these substrates.

Table 1. Reaction of Allylamines **1** with 1-Alkene (**2**) in the Presence of $Ru_3(CO)_{12}$

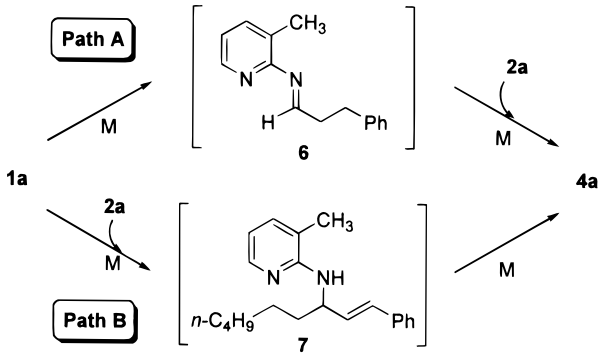


entry	allyl amine(**1**)	1-alkene (**2**)	ketone (**5**)	isolated yield [a]
1	**1a** (R^1=Ph)	**2a** (R^2=*n*-C_4H_9)	**5a**	84 %
2	**1a**	**2b** (R^2=*t*-C_4H_9)	**5b**	93 %
3	**1a**	**2c** (R^2=Cy)	**5c**	92 %
4	**1b** (R^1=CH_3)	**2a** (R^2=*n*-C_4H_9)	**5d**	93 %
5	**1b**	**2b** (R^2=*t*-C_4H_9)	**5e**	89 %
6	**1b**	**2c** (R^2=Cy)	**5f**	90 %
7	**1c** (R^1 = H)	**2d** (R^2=*n*-C_6H_{13})	**5g**	77 %

[a] The isolated yield is based upon **1**.

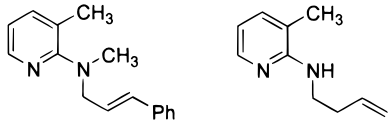
Two plausible mechanisms for the conversion of **1a** to **4a** are illustrated in Scheme 1. Path A represents a well-known

Scheme 1



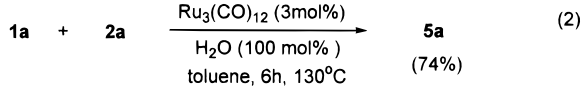
organotransition metal catalyzed double bond migration[10] of **1a** to form aldimine **6** followed by hydroiminoacylation of **2a**.

Path B involves allylic alkylation of **1a** by 1-hexene (**2a**) and subsequent double bond migration of **7**. In a very recent paper, we reported a similar type of alkylation of benzylamine with 1-alkenes through benzylic C−H bond activation catalyzed by Ru(0).[2a] To distinguish between the two mechanisms, we tested both tertiary amine **8** and homoallylamine **9** under the reaction conditions. When treated with



2a in the presence of **3a**, tertiary amine **8** did not undergo alkylation. However, exposure of **9** to **2a** followed by hydrolysis generated **5d** in 85% yield.[11] This suggested path A, double bond migration followed by hydroiminoacylation, as the likely mechanism.

When water was present in the reaction of **1a** and **2a**, in situ hydrolysis of **4a** occurred and ketone **5a** was obtained in 74% yield (eq 2). This suggests that the intermediate



aldimine undergoes hydroiminoacylation much faster than

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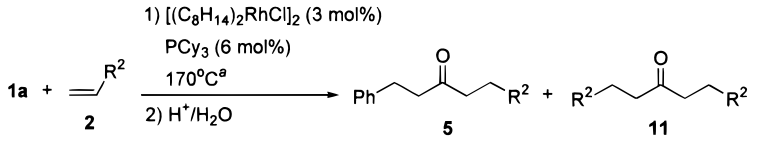
Table 2. Reactions of **1a** with Various 1-Alkenes (**2**) in the Presence of $[(C_8H_{14})_2RhCl]_2$

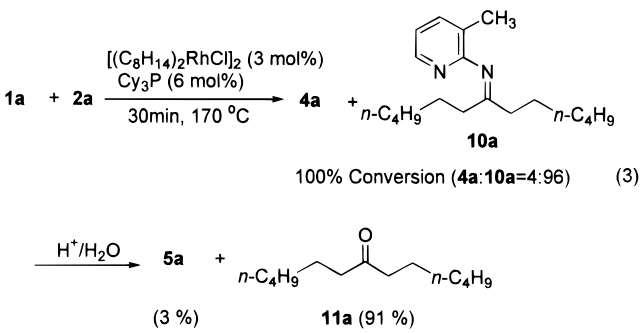


entry	1-alkene (**2**)	time	conversion rate[b]	products (ratio)[c] **5** : **11**	isolated yield of **5**&**11**
1	**2b** (R^2=*t*-C_4H_9)	5 min	82%	**5b**:**11b** (15:85)	78%
2	**2b** (R^2=*t*-C_4H_9)	10 min	97%	**5b**:**11b** (14:86)	94%
3	**2b** (R^2=*t*-C_4H_9)	15 min	100%	**5b**:**11b** (12:88)	97%
4	**2b** (R^2=*t*-C_4H_9)	30 min	100%	**5b**:**11b** (9:91)	98%
5	**2b** (R^2=*t*-C_4H_9)	1 h	100%	**5b**:**11b** (5:95)	97%
6	**2c** (R^2=Cy)	1 h	100%	**5c**:**11c** (10:90)	97%
7[d]	**2d** (R^2=*n*-C_6H_{13})	30 min	100%	**5h**:**11d** (9:91)	93%
8[d]	**2e** (R^2=*n*-C_8H_{17})	30 min	100%	**5i**:**11e** (10:90)	95%

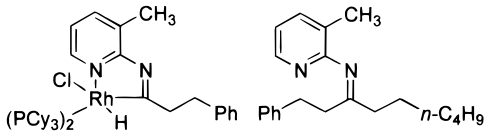
[a] bath temp. [b] the conversion rate of **1a** to ketones **5** and **11** was determined by G.C. [c] the ratio of **5**/**11** was determined by G.C. from isolated products. [d] the reaction was performed without solvent.

hydrolysis and that H_2O participates only in the hydrolysis of ketimine **4a**.

When the coupling reaction of **1a** and **2a** (10 equiv of **1a**) was carried out at 170 °C in the presence of 3 mol % of $[(C_8H_{14})_2RhCl]_2$ (**3b**) and 6 mol % of tricyclohexylphosphine (Cy_3P) without solvent,[12] ketimines **10a** was obtained along with a small amount of **4a** (**10a**:**4a** = 96:4). After acid hydrolysis, **11a** and **5a** were isolated in 91% and 3% yields, respectively (eq 3).



The sequence of the events in this reaction appears to be as follows: Double bond migration of **1a** generates aldimine **6** which reacts with $[(C_8H_{14})_2RhCl]_2$ and Cy_3P to form iminoacylrhodium(III) hydride **12**.[13] The hydroiminoacylation



of 1-hexene (**2a**) with **12** gives ketimine **4a**. Probably, *anti*−*syn* isomerization of the imine[14] that occurs easily under the reaction conditions may lead to the formation of ketimine **13**. The C−C bond activation of **13** followed by hydroiminoacylation of **2a** generates ketimine **10a**. Among the various catalytic systems examined, the $[(C_8H_{14})_2RhCl]_2$ and Cy_3P system has proven to be most effective.[15]

The rate of alkylation of **1a** with various 1-alkenes was also measured. Table 2 summarizes the products and yields. With sterically hindered olefin such as 3,3-dimethyl-1-butene (**2b**), the reaction was completed within 15 min (Table 2, entry 3). Activations of C−C bond using other catalytic systems require much longer exposure times (9−48 h).[4] After **1a** disappeared completely, prolonged reaction times increase the **11b** to **5b** ratio from 85/15 to 95/5 (entries 3−5). Alkenes **2c**−**e** reacted with **1a** and yielded the corresponding symmetric (**11**) and asymmetric (**5**) ketones upon hydrolysis (Table 2, entries 6−8).

(11) Double bond migration of homoallylamine is not common for the metal catalyzed reaction. However, the coordination by 2-pyridyl group in **9** might provide a directing effect for this isomerization.

(12) When the reaction was carried out in toluene, a mixture of **4a** and **10a** was obtained in a 20:80 ratio.

In conclusion, allylamines bearing coordination sites such as the 2-pyridyl group can react with olefins in the presence of Ru(0) to give asymmetric ketones. However, Rh(I) catalysis of these coupling reactions provided the corresponding symmetric ketones as well. These results indicate that Ru(0) complexes activate the C−H bond selectively and Rh(I) complexes activate both C−H and C−C bonds.

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Supporting Information Available: Experimental procedures for the preparation of allylamine derivatives **1a**−**c**, **8**, and **9**, catalytic C−H bond activation of **1a** with 1-hexene by $Ru_3(CO)_{12}$ and the same reaction adding H_2O, and catalytic C−H bond and C−C bond activation of **1a** with 1-hexene by $[(C_8H_{14})_2RhCl]_2$ and Cy_3P, including the characterization data for **1a**−**c**, **4a**, **5b**, **5e**, **8**, **9**, and **10a**. This material is available free of charge via the Internet at http://pubs.acs.org.

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(13) This intermediate was formed and isolated in a control reaction in which **1a** reacted with **3b** and Cy_3P in the absence of **2a** at 100 °C for 2 h. **12**: ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm) 9.11 (d, J = 4.5 Hz, 1H, 6-**H** in picoline group), 7.48 (d, J = 7.5 Hz, 4-**H** in picoline group), 7.30−7.16 (m, 5Hs, 2,3,4,5,6-**H**s in phenyl group), 6.89 (t, J = 6.3 Hz, 1H, 5-**H** in picoline group), 3.28 (t, J = 7.1 Hz, 2Hs, α-C**H**$_2$ to C═N), 3.21 (t, J = 7.0 Hz, 2Hs, β-*C***H**$_2$ to C═N), 2.50 (s, 3Hs, C**H**$_3$- in picoline group), −13.54 (overlapping d of t, J = 14.5 Hz, J = 14.5 Hz, 1H, **H**-Rh); ^{13}C NMR (125 MHz, $CDCl_3$) δ (ppm) 232.11 (d, J = 124 Hz, **C**═N); IR spectrum (KBr) 3024, 2921, 2850, 2659, 2129, 2025, 1591, 1447, 1406, 1270, 1001, 847, 734 cm^{-1}; HRMSFAB calcd for $C_{51}H_{82}ClN_2P_2Rh$ (M^+) 922.4664, found 922.4694.

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(15) Other ligands such as triphenylphosphine, tri(*p*-toly)phosphine, tri(*p*-methoxyphenyl)phosphine, tributylphosphine, and dicyclohexylphenylphosphine were tested in this reaction with **3b** but were not as efficient as Cy_3P.