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Catalytic Transformation of Aldimine to Ketimine by Wilkinson's Complex through Transimination

Chul-Ho Jun* and Jun-Bae Hong

Department of Chemistry, Yonsei University, Seoul 120-749, Korea

junch@alchemy.yonsei.ac.kr

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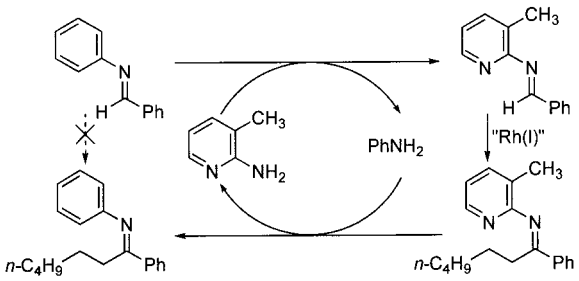
ABSTRACT



The C–H bond activation in homogeneous catalysis is important for carbon skeleton construction through C–C bond formation. In this report, a new direct synthesis of ketimine from aldimine bearing no coordination site is demonstrated with high catalytic efficiency. Transimination is the major role for this catalytic reaction.

The C−C bond formation by transition metal catalyzed reaction involving C−H bond activation is one of the most active and challenging areas in organometallic research.[1] Up to now, the addition of an sp^2 C−H bond to an unsaturated C−C bond has been extensively studied and applied to new C−C bond formation in organic synthesis.[2] The sp^2 C−H bond of aldimine is added to an unsaturated C−C bond to give ketimine, which is an important synthetic intermediate since it performs a significant role as a precursor to amine by the asymmetric catalytic hydrogenation.[3] Especially, the ketimine, produced through alkylation of aldimine, is a precursor for ketone through a convenient hydrolysis process. But the C−H bond of aldimine is inert to transition metal catalysts, except to a model compound bearing a heteroatom for cyclometalation, which solves the problem of accessibility between the catalyst and the carbon−hydrogen bond.[4] Below, we report a new type of catalytic system for the direct conversion of a common aldimine into a ketimine which is not confined within a specially designed aldimine. This reaction is a remarkably efficient catalytic system in comparison with other catalytic C−H/ olefin coupling reactions.

In our experiment, *N*-phenyl-*N*-(1-phenylmethylidene)-amine (**1a**) reacted with 1-hexene (**2a**) in toluene at 130 °C for 24 h under a mixture of 0.5 mol % of chlorotris-

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(4) For C−H bond activation, see: (a) Suggs, J. W. *J. Am. Chem. Soc.* **1979**, *101*, 489. (b) Jun, C.-H.; Kang, J.-B.; Kim, J.-Y. *J. Organomet. Chem.* **1993,** *458*, 193−198. (c) Jun, C.-H.; Han, J.-S.; Kang, J.-B.; Kim, S.-I. *J. Organomet. Chem.* **1994,** *474*, 183−189. For C−C bond activation, see: (d) Jun, C.-H.; Lee, H. *J. Am. Chem. Soc.* **1999**, *121*, 880−881.

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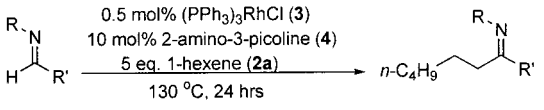
(triphenylphosphine)rhodium(I) (**3**) and 10 mol % of 2-amino-3-picoline (**4**) as a cocatalyst system based upon **1a** (Scheme 1). Following the reaction, *N*-phenyl-*N*-(1-phenylheptylidene)amine (**5a)** was isolated in 90% yield by column chromatography.[5]

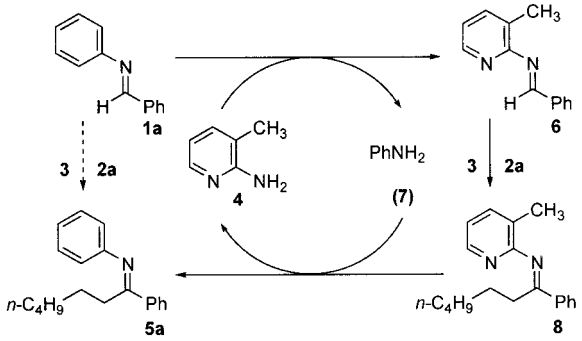
Scheme 1. Alkylation of Aldimine through C−H Bond Activation



1a:	R=Ph-	R'= Ph-	**5a**: 90 %
1b:	Ph-	4-$CF_3C_6H_4$-	**5b**: 84 %
1c:	Ph-	4-$Me_2NC_6H_4$-	**5c**: 41 %
1d:	*o*-$CH_3C_6H_4$-	Ph-	**5d**: 87 %
1e:	Cy-	Ph-	**5e**: 90 %
1f:	PhNH-	Ph-	**6f**: trace
1g:	HO-	Ph-	no reaction

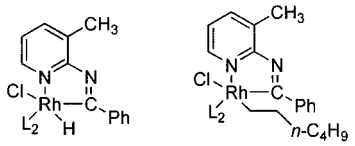
However, when the reaction was carried out without **4**, the starting aldimine **1a** was completely recovered, implying no direct conversion of **1a** to **5a**. The proposed mechanism is shown in Scheme 2. The first step must be the formation

Scheme 2. Transimination and Alkylation Process



of aldimine **6** through transimination of **1a** with **4**, liberating aniline (**7**). There are some reports about transimination for the synthesis of the desired imine from primary imine and amine.[6] The resulting aldimine **6** reacts with olefin to give ketimine **8** on the rhodium(I) catalyst by hydroiminoacylation, previously studied: the C−H bond activation of **6** by **3** to give **9**, a hydride insertion of **9** into **2a** to form **10**, and reductive elimination in **10** to generate **8**.[4a] Then the second transimination of **8** with **7** produces **5a** with regeneration of **4**.

To identify the involvement of the transimination of **1a** with **4** in the reaction pathway, **1a** was allowed to react with **3** (10 mol %) and **4** (20 mol %) in C_6D_6 at 130 °C for 2 h without olefin **2a**, and it was observed by ^{1}H NMR spectra that 50% of **4** was transformed into complex **9**, which should be formed from **6**.[7]



Various imines, **1b**−**1e**, reacted with **2a** to give corresponding ketimines, **5b**−**5e**, in fairly high yield except **1c** under identical reaction conditions. The reason for the low yield of **5c** from **1c** is that the electron-donating substituent in aldimine may inhibit facile transimination due to reduced electrophilicity of the imine−carbon center. Among imines, hydrazone **1f** and oxime **1g** did not undergo alkylation with **2a**.[8] This result can be explained by the fact that **1f** and **1g** are too stable to undergo transimination with **4** since the thermodynamic stability of C═N bond in imine increases in the order of imine of NH_3 < aliphatic amine < aromatic amine < amine with an adjacent electronegative atom.[9]

When the concentration of **4**, one of the catalysts, was changed from 0 to 100 mol % based upon **1a**, the best results (94−98% yield of **5a**) were obtained with 10−20 mol % of **4** as shown in Figure 1. As the concentration of **4** was

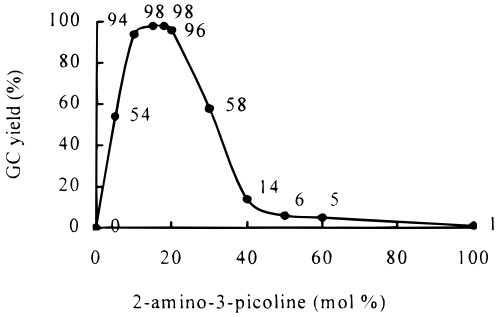


Figure 1. Effect of 2-amino-3-picoline: **1a** (0.65 mmol) reacted with **2a** (3.2 mmol) under 0.5 mol % of **3** (0.0032 mmol) and 0−100 mol % of **4** at 130 °C for 12 h, and the yield of product **5a** is determined by GC.

increased above 30 mol %, the yield of **5a** was dramatically decreased. The phosphine ligand in this catalytic reaction is very important because it may enforce the facile reductive elimination in intermediate **10**. However, excess use of **4** may inhibit the phosphine ligand-promoted reductive elimi-

(5) In a typical experiment, a mixture of imine **1a** (117.4 mg, 0.649 mmol) and 1-hexene (**2a**) (272 mg, 3.24 mmol) in a screw-capped pressure vial (1 mL) was heated at 130 °C for 24 h with [chlorotris(triphenylphosphine)rhodium(I)] (**3**) (3 mg, 0.00324 mmol) and 2-amino-3-picoline (**4**) (7.0 mg, 0.0649 mmol). The reaction mixture was cooled to room temperature and purified by column chromatography (*n*-hexane:ethyl acetate = 5:2) to give 144.5 mg (84%) of *N*-(1-phenylheptylidene)aniline (**5a**) and 7.4 mg (6%) of heptanophenone (**11a**). **5a**:^{1}H NMR (250 MHz, $CDCl_3$) δ (ppm) 7.9 (m, 2H), 7.4−6.8 (m, 8H), 2.6 (t, J = 7.9 Hz, 2H, α-CH_2 to C═N), 1.4−1.1 (m, 8H), 0.8 (t, J = 6.8 Hz, 3H, $-CH_3$); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ (ppm) 169.7 (C═N), 150−120 (C_s in phenyl group), 31.4 (α-CH_2 to C═N), 30.1 (δ-CH_2 to C═N), 29.1 (γ-CH_2 to C═N), 27.8 (ϵ-CH_2 to C═N), 22.3 (β-CH_2 to C═N), 13.8 (CH_3 in hexyl group); MS *m*/*z* (%) 265 (9) [M^+], 208 (42), 193 (30), 173 (34), 129 (35), 117 (100), 115 (70), 93 (31), 77 (42); IR (neat) 3054, 3027, 2952, 2924, 2854, 1685, 1625, 1588, 1485, 1443, 1313, 1206, 1024, 768, 689 cm^{-1}; HRMS calcd for $C_{19}H_{23}N_1$ (M^+) 265.183 050, found 265.183 044.

nation by occupying the coordination site of **10** with **4**. Therefore the reaction scarcely proceed in excess use of **4**. This postulate was confirmed by the fact that when an identical reaction was carried out under 0.5 mol % of chlorobis(cyclooctene)rhodium(I) dimer that has no phosphine ligand, no alkylation product was obtained. When the reaction was carried out in increasing order of the additional triphenylphosphine (30−40 mol %) under 40 mol % of **4**, the catalytic activity of complex **3** was completely restored as shown in Figure 2.

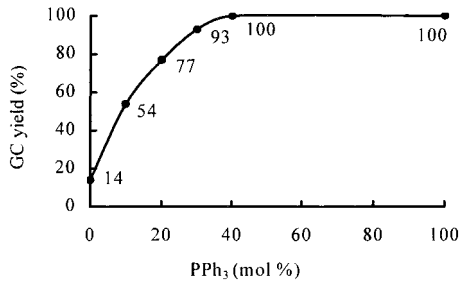
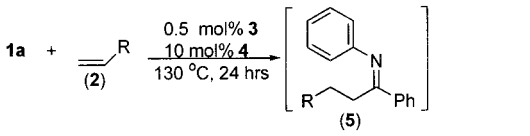


Figure 2. Effect of PPh_3: **1a** (0.65 mmol) reacted with **2a** (3.2 mmol) under 0.5 mol % of **3** (0.0032 mmol), 40 mol % of **4** (0.26 mmol), and 0−100 mol % of PPh_3 at 130 °C for 12 h, and the yield of product **5a** is determined by GC.

Even with aldimine **6** as a starting material, previously studied,[4a] hydroiminoacylation of 1-hexene (**2a**) barely proceeds under 0.5 mol % of **3** (<1% yield of **8**). The reason might be that liberated triphenylphosphine cannot induce reductive elimination in **10**, probably due to the high concentration of **6** compared with that of **3**.[10]

The ketimine, produced through alkylation of aldimine, is a precursor for the ketone since it is easily hydrolyzed to give ketone. Heptanophenone (**11a**) was isolated in 88% yield from **1a** through acid hydrolysis of the resulting ketimine **5a** (Scheme 3).

Scheme 3. Ketone Synthesis through Transimination



		conversion to **5** (detected by GC)		isolated yield of **11**
2a	R = *n*-C_4H_9-	92	**11a**	88
2b	*n*-C_6H_{13}-	86	**11b**	84
2c	*n*-C_8H_{17}-	84	**11c**	80
2e	Cy-	82	**11e**	73[a]
2f	$(CH_3)_3C$-	100	**11f**	97[b]
2g	C_6F_5-	100	**11g**	96

[a] 1 mol% Rh(I) used. r.t.:18 h. [b] Yield involved 5 % of *o*-alkylation product.

This catalytic system is by far the most effective one in comparison with a previously reported ketone synthesis from aldehyde and olefin, namely intermolecular hydroacylation.[11,12] Various olefins were used in the alkylation of aldimine **1a** to give the corresponding ketimines at a fairly high conversion rate, which were isolated in the form of ketone through acid hydrolysis.

In summary, we have demonstrated that aldimines bearing no coordination site can be converted into ketimines by a rhodium(I) catalyst through transimination. This catalytic system showed excellent efficiency in catalytic turnover through the use of only 0.5 mol % of Rh complex.

Acknowledgment. This work was supported by the Korean Science and Engineering Foundation (Grant 97-05-01-05-01-3).

Supporting Information Available: General experimental procedures for alkylation and the characterization of compounds **5a**−**e**. This material is available free of charge via the Internet at http://pubs.acs.org.

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(7) **9**: ^1H NMR (250 MHz, C_6D_6) δ (ppm) 2.7 (s, 3H, $-CH_3$), −10.4 (overlapping d of t, J_{Rh-H} = 13.3 Hz, J_{P-H} = 12.4 Hz, 1H, Rh−H).

(8) The oxime **1g** was completely converted to phenylamide by a rhodium(I)-catalyzed Beckmann rearrangement: Gawley, R. E. In *Organic Synthesis*; Kende, A. S., Ed.; John Wiley & Sons: New York, 1988; Vol. 35, pp 14−43.

(9) Mäkelä, M. J.; Korpela, T. K. *Chem. Soc. Rev.* **1983**, *12*, 309−329.

(10) With increasing order of additional triphenylphosphine under identical reaction conditions, the GC yield of **8** was gradually increased (7% yield of **8** with 40 mol % of additional PPh_3; 21% yield with 100 mol % of PPh_3).

(11) While 5−10 mol % of Rh catalyst has been used in a previously reported reaction, this system requires only 0.5 mol % of Rh catalyst. The hydroacylation of 1-hexene (**2a**) with benzaldehyde in the presence of **4** produced only a 9% yield of **11a** under the reaction conditions of 0.5 mol % of Rh catalyst. The improvement of efficiency for this catalytic reaction is probably due to the adequate ratio of **6** to **3**: (a) Jun, C.-H.; Lee, H.; Hong, J.-B. *J. Org. Chem.* **1997**, *62*, 1200−1201. (b) Jun, C.-H.; Lee, D.-Y.; Hong, J.-B. *Tetrahedron Lett.* **1997**, *38*, 6673−6676. (c) Jun, C.-H.; Huh, C.-W.; Na, S.-J. *Angew. Chem. Int. Ed.* **1998**, *37*, 145−147.

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