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Hydroacylation of 1-Alkene with Heteroaromatic Aldehyde by Rh(I) and Additives

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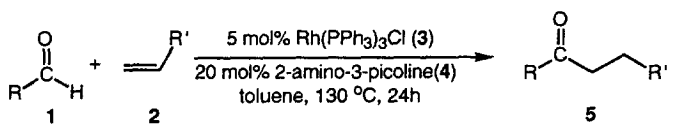
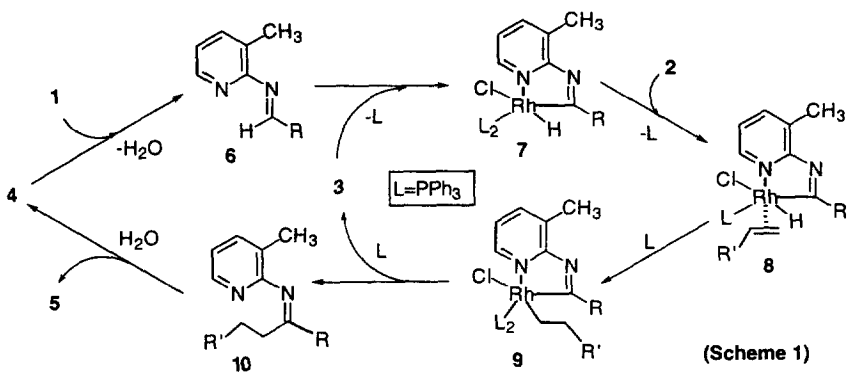
Abstract: Hydroacylation of 1-alkene with a heteroaromatic aldehyde such as pyridinecarboxaldehyde, thiophenecarboxaldehyde and furfural derivatives under cocatalyst of Wilkinson's complex and 2-amino-3-picoline gave poor yield of hydroacylated product. The addition of a catalytic amount of bis-(cyclopentadienyl)zirconium dichloride or bis(cyclopentadienyl)titanium dichloride as an additive dramatically increased the yield of the hydroacylated ketone product. © 1997 Elsevier Science Ltd.

There have been many efforts to develop a system that transforms aldehyde into ketone (i.e. hydroacylation).[1-3] Although intramolecular hydroacylation with 4-pentenal derivatives has been studied in detail,[1] intermolecular reaction is not well-documented due to its limitations.[2] Recently we have reported the new development of a direct chelation-assisted intermolecular hydroacylation of 1-alkene (**2**) with aldehyde (**1**) under cocatalysts of $Rh(PPh_3)_3Cl$ (**3**) and 2-amino-3-picoline (**4**) (eq 1).[3]



1 2 5 (1)

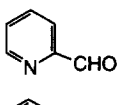
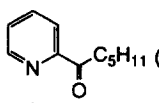
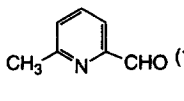
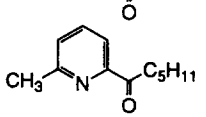
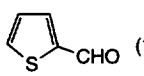
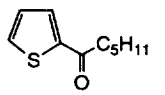
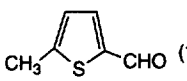
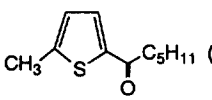
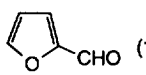
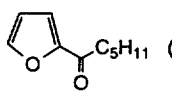
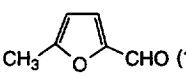
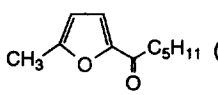
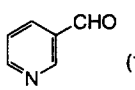
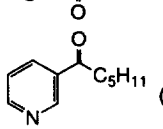
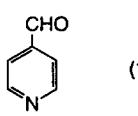
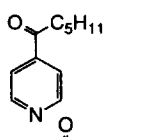
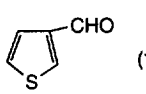
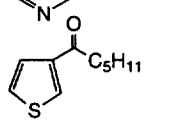
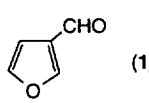
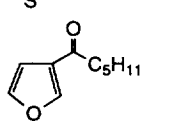
The mechanism is explained in Scheme 1. Aldimine **6** may form *in situ* from **4** and **1**. Subsequent hydroiminoacylation of **2** with **6** produces the ketimine **10** through C-H bond cleavage of **6** by **3**, hydride addition to 1-alkene in **8**, and reductive elimination in **9**. Then **10** is hydrolyzed by H_2O, to produce ketone **5**.



(Scheme 1)

This hydroacylation could be applied only to nonheteroaromatic aldehyde. The acylation of heteroaromatic

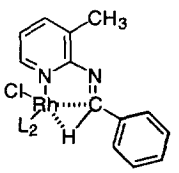
Table 1. Hydroacylation of 1-Pentene with Heteroaromatic Aldehyde under Wilkinson's Complex with or without Additive[a]

Entry	Aldehyde	product (ketone)[b]	Isolated Yield of Ketone(%)		
			No Additive	Cp_2ZrCl_2(**14**)[c]	Cp_2TiCl_2(**15**)[c]
1	 (**1a**)	 (**5a**)	<1	50	32
2	 (**1b**)	 (**5b**)	2	75	47
3	 (**1c**)	 (**5c**)	11	66	79
4	 (**1d**)	 (**5d**)	15	74	82
5	 (**1e**)	 (**5e**)	6	77	69
6	 (**1f**)	 (**5f**)	18	83	74
7	 (**1g**)	 (**5g**)	24	76	56
8	 (**1h**)	 (**5h**)	<1	32	19
9	 (**1i**)	 (**5i**)	77	92	84
10	 (**1j**)	 (**5j**)	<1	61	60

[a]A mixture of heteroaromatic aldehyde(100 mol%) and 1-pentene(500 mol%) was heated at 100 °C for 40 h under catalysts of $(Ph_3P)_3RhCl$(10 mol%) and 2-amino-3-picoline(100 mol%) with or without additive. [b]C_5H_{11} is the normal pentyl group. [c]10 mol% of additive (based upon aldehyde) was used.

compound is not common despite its usefulness in organic synthesis.[2f,4] In this report, we try to explain the development of the effective catalytic system for hydroacylation of 1-alkene with heteroaromatic aldehyde.

In our experiment 1-pentene (**2a**) reacted with 2-pyridinecarboxaldehyde (**1a**) in THF at 100 °C for 40 h under 10 mol% of **3** and 100 mol% of **4** based upon **1a** (Table 1, entry 1), 1-(2-pyridyl)-1-hexanone (**5a**) was obtained in a trace of yield (<1 %). For comparison, when benzaldehyde, nonheteroaromatic aldehyde, instead of **1a**, was applied under identical condition, a 72 % yield of hexanophenone was isolated.



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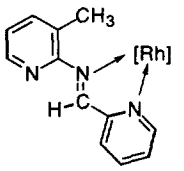

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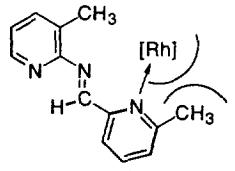
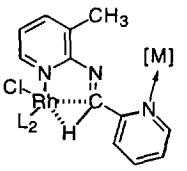


13



16

The reason for the poor yield of **5a** is not clear. Our speculation for the inefficient catalytic activity for **1a** is as follows. To cleave the C-H bond of **6** by **3** in Scheme 1, Rh(I) catalyst should have precoordinated to the nitrogen atom in picolinyl group as in **11**. But in case of **1a**, Rh(I) catalyst may coordinate to the nitrogen atom in the pyridyl group of aldimine generated *in situ* from **1a** and **4** as in **12**. As expected, hydroacylation of **2a** with other heteroaromatic aldehydes such as 2-thiophenecarboxaldehyde(**1c**) and 2-furfural(**1e**) under identical condition produced the corresponding ketones, **5c** and **5e**, in very poor yields; 11 % and 6 %, respectively (entry 3 and 5). Rh(I) catalyst may preferentially coordinate to the nitrogen atom in pyridyl group, oxygen, and sulfur atom in the heteroaromatic compounds with assistance of the nitrogen atom in imino group which may form the chelate complex as **12**. The coordination of Rh(I) catalyst as in **12** may be partially confirmed by using the sterically hindered aldehyde. When **1b**, **1d** and **1f** were applied, slightly better yields of the corresponding ketones were obtained as 2 % for **5b**, 15 % for **5d**, and 18 % for **5f**, respectively (entry 2, 4 and 6). The Rh(I) catalyst may have a better chance to cleave the C-H bond of aldimine since the methyl group nearby heteroatom in aldimine retards the coordination of Rh(I) catalyst due to the steric hindrance as in **13** for **1b**.

When the reaction was carried out with catalytic amount (10 mol%) of bis(cyclopentadienyl)zirconium dichloride (**14**) or bis(cyclopentadienyl)titanium dichloride (**15**) as an additive, the yield of hydroacylated product was dramatically increased.[5] For **1a**, addition of 10 mol% of **14** increased the yield of **5a** from <1 % up to 50 %. This kind of yield-improvement of the hydroacylated product was observed only in hydroacylation of heteroaromatic aldehyde, not in that of nonheteroaromatic aldehyde. The reason for improving the yield of hydroacylated product must be that **14** or **15** may bind to the nitrogen atom as in **16** to allow Rh(I) catalyst to cleave the C-H bond. It is also possible that **14** or **15** may enhance the rate of formation of aldimine due to the increasing susceptibility to the nucleophilic attack of heteroaromatic aldehyde with coordination of additive. However, with or without additive **14** (10 mol%), the rates of formation of aldimine from **1a** and **4** under 10 mol% of **3** were almost identical, monitored by GC, informing no such effect. Hydroacylated products from heteroaromatic aldehydes with **14** were obtained in fairly good yield (50-83 % isolated yield; entry 1-6). When other heteroaromatic aldehydes in which the position of aldehyde in heteroaromatic aldehyde is different were applied, similar results were obtained (entry 7-10).[6-8]

In conclusion, chelation-assisted intermolecular hydroacylation of 1-pentene with heteroaromatic aldehyde could be dramatically improved by the addition of the catalytic amount (10 mol%) of **14** or **15**. The metal complex additive probably binds to the heteroatom in heteroaromatic aldehyde to render the Rh to act as catalyst. Detailed mechanistic studies are under investigation.

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References and Notes

1. (a) Sakai, K.; Ide, J.; Oda, O.; Nakamura, N. *Tetrahedron Lett.* **1978**, *13*, 1287. (b) Miller, R. G.; Lochow, C. F. *J. Am. Chem. Soc.* **1976**, *98*, 1281. (c) Miller, R. G.; Campbell, R. E.; Lochow, C. F.; Vora, K. P. *J. Am. Chem. Soc.* **1980**, *102*, 5824. (d) Larock, R. C.; Potter, G. F.; Oertle, K. *J. Am. Chem. Soc.* **1980**, *102*, 190. (e) Fairlie, D. P.; Bosnich, B.; *Organometallics* **1988**, *7*, 946. (f) *ibid.* **1988**, *7*, 936. (g) Bosnich, B.; Whelan, J.; Bergens, S. H.; Noheda, P.; Wang, X.; Barnhart, R. W. *J. Am. Chem. Soc.* **1994**, *116*, 1821. (h) Bosnich, B.; Whelan, J.; Bergens, S. H.; Noheda, P.; Wang, X.; Barnhart, R. W. *Tetrahedron* **1994**, *50*, 4335. (i) Bosnich, B.; Wang, X. *Organometallics* **1994**, *13*, 4131. (j) Bosnich, B.; Barnhart, R. W. *Organometallics* **1995**, *14*, 4343.
2. (a) Schwartz, J.; Cannon, J. B. *J. Am. Chem. Soc.* **1974**, *96*, 4721. (b) Lenges, C. P.; Brookhart, M. *J. Am. Chem. Soc.* **1997**, *119*, 3165. (c) Miller, R. G.; Vora, K. P.; Lochow, C. F. *J. Organomet. Chem.* **1980**, *192*, 257. (d) Isnard, P.; Denise, B.; Sneeden, R. P. A. *J. Organomet. Chem.* **1982**, *240*, 285. (e) Marder, T. B.; Roe, D. C.; Milstein, D. *Organometallics* **1988**, *7*, 1451. (f) T. Kondo, T.; Akazome, M; Tsuji, Y.; Watanabe, Y. *J. Org. Chem.* **1990**, *55*, 1286. (g) Kondo, T.; Tsuji, Y.; Watanabe, Y. *Tetrahedron Lett.* **1987**, *28*, 6229.
3. Jun, C. -H.; Lee, H.; Hong, J. -B. *J. Org. Chem.* **1997**, *62*, 1200.
4. (a) Moore, E. J.; Pretzer, W. R.; O'Connell, T. J.; Harris, J.; LaBounty, L.; Chou, L.; Grimmer, S. S. *J. Am. Chem. Soc.* **1992**, *114*, 5888. (b) Chatani, N.; Fukuyama, T.; Kakiuchi, F.; Murai, S. *J. Am. Chem. Soc.* **1996**, 118, 493.
5. When the reaction was carried out with 100 mol% of LiCl as additive, the yield of hydroacylated product increased to 10 % for **1a**. A variety of other metal salts like NaCl, $MgCl_2$, $Mg(ClO_4)_2$, $HgCl_2$, $AgNO_3$, AgI, AgCl, $AgClO_4$, $AgBF_4$, CuI, $CuCl_2$, and ferrocene were examined, but they did not show any improvement in the catalytic activity for hydroacylation.
6. When catalytic amount(20 mol%) of **4** was used, the yields decreased; only 17 % yield of **5h** was obtained for **1h** with 10 mol% of **14**.
7. For **1h**, when the reaction was carried out without additive, white precipitate, hardly characterized, was formed, possibly indicating the formation of the intermolecular complexes.
8. **5b**: ^{1}H NMR (300 MHz, $CDCl_3$)δ(ppm) 7.8 (d, *J*=7.7 Hz, 1H), 7.7 (m, 2H), 3.2 (t, *J*=7.5 Hz, 2H) 2.6 (s, 3H), 1.7 (m, 2H), 1.4 (m, 4H), 0.9 (t, *J*=6.7Hz, 3H); ^{13}C NMR (72.5 MHz, $CDCl_3$)δ(ppm) 158.8-118.8 (Cs of pyridine group), 35.5 (α-Carbon to CO), 31.5 (γ-Carbon to CO), 24.5 (CH_3 in pyridine group), 23.7 (β-Carbon to CO), 22.5 (δ-Carbon to CO), 13.9 (terminal CH_3); IR spectrum (neat) 3057, 2962, 2929, 2868, 1698(CO), 1598, 1442, 1375, 1092, 1041 cm^{-1}, MS, m/e 191 (M^+, 6), 162 (10.4), 148 (53), 134 (19.3), 120 (33.2), 93 (100), 92 (73), HRMS calcd for $C_{12}H_{17}NO$ 191.131 014, found 191.130 199. **5d**: ^{1}H NMR (250 MHz, $CDCl_3$)δ(ppm) 7.5 (d, *J*=3.7 Hz, 1H), 6.8 (m, 1H), 2.8 (t, *J*=7.5 Hz, 2H) 2.5 (s, 3H), 1.7 (m, 2H), 1.4 (m, 4H), 0.9 (t, *J*=6.9Hz, 3H); ^{13}C NMR (62.9 MHz, $CDCl_3$)δ(ppm) 193.2 (CO), 149.2-126.6 (Cs of thiophene group), 38.8 (α-Carbon to CO), 31.4 (γ-Carbon to CO), 24.6 (β-Carbon to CO), 22.4 (δ-Carbon to CO), 15.9 (CH_3 in thiophene group), 13.8 (terminal CH_3); IR spectrum (neat) 3079, 2958, 2931, 2868, 1662 (CO), 1539, 1462, 1369, 1064, 808 cm^{-1}, MS, m/e 196 (M^+, 7), 153 (8.7), 140 (76.60, 125 (100), 97 (9.8), HRMS calcd for $C_{11}H_{16}OS$ 196.092 187, found 196.092 169. **5f**: ^{1}H NMR (250 MHz, $CDCl_3$)δ(ppm) 7.1 (d, *J*=3.3 Hz, 1H), 6.2 (d, *J*=3.3 Hz, 1H), 2.8 (t, *J*=7.5 Hz, 2H) 2.4 (s, 3H), 1.7 (m, 2H), 1.4 (m, 4H), 0.9 (t, *J*=6.7Hz, 3H); ^{13}C NMR (62.9 MHz, $CDCl_3$)δ(ppm) 188.9 (CO), 157.4-108.6 (Cs of furane group), 37.9 (α-Carbon to CO), 31.3 (γ-Carbon to CO), 24.2 (β-Carbon to CO), 22.3 (δ-Carbon to CO), 13.8 (terminal CH_3), 13.7 (CH_3 in furane group); IR spectrum (neat) 3124, 2956, 2932, 2869, 1672 (CO), 1588, 1517, 1457, 1373, 1267, 1207, 1026, 797 cm^{-1}. MS, m/e 180 (M^+, 2.5), 137 (13), 124 (100), 109 (84), 95 (7.7), 82 (11.6), HRMS calcd for $C_{11}H_{16}O_2$, 180.115 030, found 180.115 018. **5j**: ^{1}H NMR (250 MHz, $CDCl_3$)δ(ppm) 8.4 (m, 1H), 7.3 (m, 1H), 6.7 (m, 1H), 2.7 (t, *J*=7.4 Hz, 2H), 1.7 (m, 2H), 1.3 (m, 4H), 0.9 (t, *J*=6.4 Hz, 3H); ^{13}C NMR (62.9 MHz, $CDCl_3$)δ(ppm) 195.4 (CO), 147.0-108.6 (Cs of furane group), 40.4 (α-Carbon to CO), 31.5 (γ-Carbon to CO), 24.1 (β-Carbon to CO), 22.5 (δ-Carbon to CO), 13.9 (terminal CH_3), IR spectrum (neat) 3137, 2955, 2933, 2860, 1678 (CO), 1565, 1510, 1464, 1393, 1157, 1050, 874 cm^{-1}, MS, m/e 166(M^+, 9), 137 (3), 123 (5), 110 (62), 95 (100), 81 (4), 67 (4), HRMS calcd for $C_{11}H_{14}O_2$, 166.099 380, found 166.099 648.

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