-81.035 kcal mol^{-1} and the average energy necessary to break a C–H bond is 80.841 kcal mol^{-1}. The extent of covalent versus electrostatic contributions to hydrogen bonding have been the subject of numerous discussions in the chemical literature (see, for example, J. J. Dannenberg, L. Haskamp, A. Masunov, *J. Phys. Chem. A.* **1999**, *103*, 7083, and references therein) and depend on the particular system studied. Calculated Mulliken partial charges are $+0.077$ for H_a' and -0.13 for Se indicating an attractive interaction. The difference between an average bond order of C–H bonds (0.904; this value is less than the expected due to the destabilization of C–H bond by the oxazoline ring system) and of the C–H_a' bond (0.888) directly gives the destabilization by 0.016 bond orders and therefore the C–H_a' bond is destabilized by 1.293 kcal mol^{-1} (C–H = 80.841 kcal mol^{-1}).[6] The Se$\cdots H_a'$ interaction is equal to the total stabilization of the system (-0.194 kcal mol^{-1}) minus the destabilization of the C$\cdots H_a'$ bond (1.293 kcal mol^{-1}), that is, 1.487 kcal mol^{-1}.

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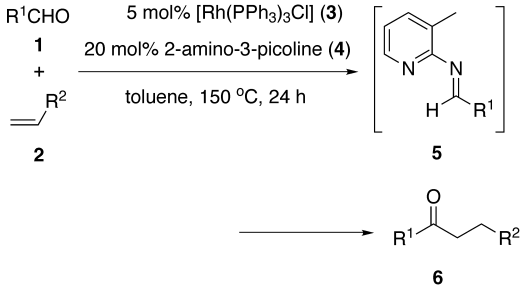
A Highly Active Catalyst System for Intermolecular Hydroacylation**

Chul-Ho Jun,* Dae-Yon Lee, Hyuk Lee, and Jun-Bae Hong

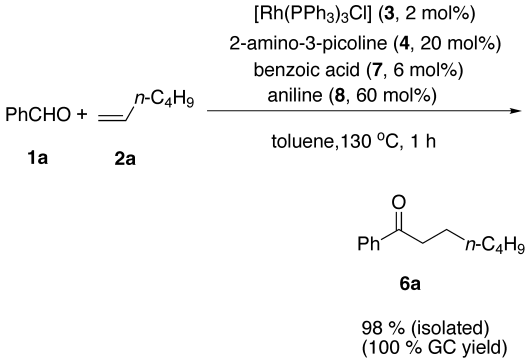
Hydroacylation[1–3] is a useful synthetic method for obtaining ketones from aldehydes and olefins by using C–H bond activation by transition metal complexes. Although the intramolecular hydroacylation of 4-pentenals has been extensively studied,[1] only a few successful intermolecular reactions have been reported.[2a–f] To effect intermolecular hydroacylation, ethylene,[2a,b] carbon monoxide,[2c] or vinylsilanes with a Co^{I} catalyst[2d,e] have been used to suppress the decarbonylation that results in catalytically inactive metal carbonyl species. We have developed a general intermolecular hydroacylation of 1-alkenes by using an Rh^{I} complex and 2-amino-3-picoline as cocatalyst, whereby aldimine **5** is assumed to be a key intermediate that suppresses decarbonylation and permits C–H bond activation [Eq. (1)].[3] Herein we report an efficient intermolecular hydroacylation for which a catalyst system was designed to ensure facile formation of the intermediate aldimine.



(1)

Recently, we found that the reactivity in the hydroacylation depicted in Equation (1) improved when benzaldehyde (**1a**) contaminated by benzoic acid (**7**)[4] was used as the substrate.[5] Benzoic acid was assumed to catalyze the condensation of aldehydes **1** with **4** to generate **5**; this may be the rate-determining step of the reaction (see below). This observation prompted us to search for a way to facilitate the formation of **5**, and we found a remarkable enhancement of the reactivity occurred when aniline (**8**), as well as **3**, **4**, and **7**, was used as an additive.

In our experiment **1a** was treated with 1-hexene (**2a**) at 130 °C for 1 h in the presence of 2 mol % of [Rh(PPh$_3$)$_3$Cl](**3**), 20 mol % of **4**, 6 mol % of **7**, and 60 mol % of **8** as cocatalysts to give heptanophenone (**6a**) in 98 % yield after chromatographic separation [Eq. (2)]. A significant decrease in reactivity was observed when the reaction was performed under



(2)

the same conditions but without **7** and **8** (Figure 1). For example, while the reaction was complete (100 % GC yield) after 1 h when both **7** and **8** were added, only a 9 % yield of **6a** was obtained when the reaction was performed without additives. The yield increased to 28 % with the addition of **7**.

The postulated mechanism is depicted in Scheme 1. Cycle A represents the mechanism for the catalyst system consisting of **3** and **4**. The first step is believed to be the formation of aldimine **9** from **1a** and **4**. Aldimine **9** reacts with **2a** to yield ketimine **10** by hydroiminoacylation.[6] The resulting ketimine **10** is hydrolyzed by H_2O, generated from

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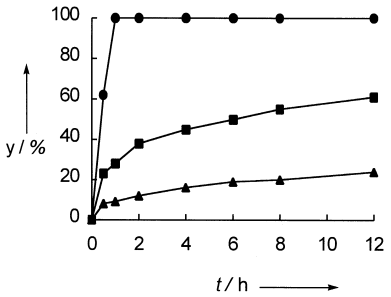
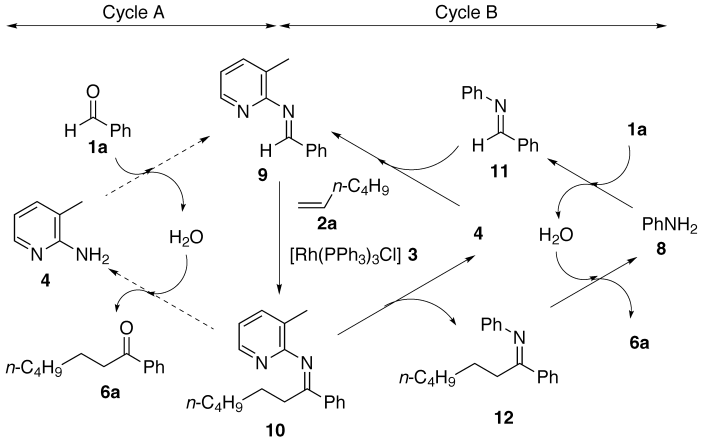


Figure 1. Conversion (yield of **6a**) versus time plot for the hydroacylation of **2a** with **1a** in the of presence 2 mol% of **3**, and 20 mol% of **4** in toluene at 130 °C. Results for the reaction with **7** and **8** (●), the reaction with **7** (■), and the reaction without any additives (▲) are shown (y = yield of **6a** determined by GC).

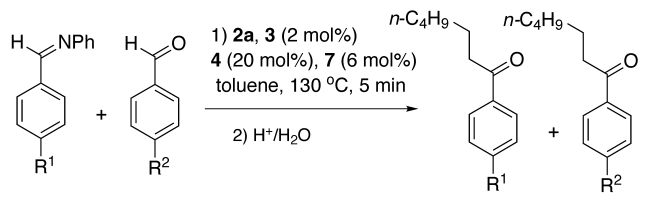


Scheme 1. The postulated mechanism for the hydroacylation of **2a** with **1a**.

the reaction of **1a** and **4**, to produce **6a** with the regeneration of **4**. The role of benzoic acid might be to catalyze the condensation of **4** and **1a** to generate intermediate **9**, which resulted in an increased reactivity.[7]

Cycle B depicts the reaction mechanism with a cocatalyst system consisting of **8**, **3**, **4**, and **7**, in which imine **11** may also be involved.[8] The initial formation of **11** from **1a** and **8** is followed by transimination[9] of **11** with **4** to give **9**. A similar type of semicarbazone formation from carbonyl compounds catalyzed by aniline in an acidic medium was previously reported.[10a] This process, known as nucleophilic catalysis,[10] consists of the initial formation of the imine compound and consecutive transimination with semicarbazide to form semicarbazone. We also demonstrated the conversion of **11** into ketimine **12** by transition metal catalyzed alkylation through transimination with **4**.[11] To confirm this mechanism, the following experiments were carried out.

When **2a** was treated with aldimine **11** and anisaldehyde **1b** at 130 °C for 5 min in the presence of a catalyst system consisting of **3**, **4**, and **7**, a mixture of **6a** and **13** was isolated in 21 and 5% yield, respectively, after hydrolysis (Scheme 2). In contrast, the reaction of aldimine **14** and benzaldehyde **1a** with **2a** produced a mixture of **6a** and **13** in 5 and 26% yield, respectively. Regardless of the substituents, aldimines that undergo hydroacylation by transimination (cycle B of Scheme 1) are more reactive than aldehydes that follow the

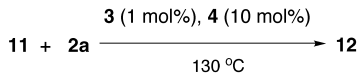


Reactants		Products (yield)	
11 (R^1 = H),	**1b** (R^2 = OMe)	**6a** (R^1 = H, 21 %)	**13** (R^2 = OMe, 5 %)
14 (R^1 = OMe),	**1a** (R^2 = H)	**13** (R^1 = OMe, 26 %)	**6a** (R^2 = H, 5 %)

Scheme 2. The reactions of **2a** with aldimines **11** and **14** and aldehydes **1a** and **1b** in the presence of **3**, **4**, and **7**.

mechanism of cycle A in Scheme 1.[12] These results imply that the transimination of **11** with **4** is more facile than the direct condensation of **1a** and **4** as a route to **9**.

To examine the effect of carboxylic acid on transimination an alkylation of **11** with **2a** was carried out in the presence of a cocatalyst system comprising **3** and **4** [Eq. (3)]; the results are



(3)

shown in Figure 2. With the addition of **7**, the reactivity increased and the reaction was complete in 3 h, while it took more than 18 h to obtain a 90% yield of **12** in the absence of **7**. This result strongly suggests that transimination is catalyzed by carboxylic acid.

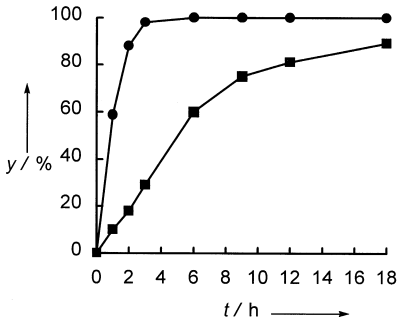


Figure 2. The effect of **7** on the alkylation of imine **11** with **2a** in the presence of 2 mol% of **3**, amd 20 mol% of **4** [Eq. (3)]. Results for the reaction with **7** (●) and the reaction without **7** (■) are shown (y = yield of **12** determined by GC).

The reactions of various aldehydes and olefins are summarized in Table 1. All terminal olefins were hydroacylated in fairly good yields within 1 h. However, trimethylvinylsilane (**2e**) was so reactive that the reaction went to completion with only 1.1 equivalents of **2e** (entry 5). The reactions of pentafluorostyrene (**2f**) and allyl phenyl ether (**2g**) were complete after 40 min (entries 6 and 7). However, internal olefins such as cyclohexene and 2-pentene failed to undergo hydroacylation. The reaction with aldehydes bearing various substituents gave moderate yields of the corresponding ketones (entries 8–11). Even aliphatic aldehyde underwent hydroacylation to give ketones in moderate yield (entry 12).

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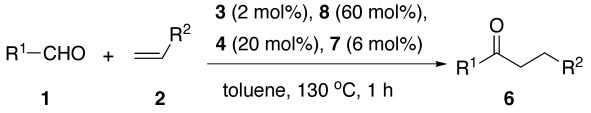
Table 1. The reaction of various aldehydes and olefins.



1 2 6

Entry	R^1 (**1**)	R^2 (**2**)[a]	Product	Yield [%][b]
1	Ph (**1a**)	*n*-C_4H_9 (**2a**)	**6a**	98 (100)
2	Ph (**1a**)	*n*-C_3H_7 (**2b**)	**6b**	83 (86)
3	Ph (**1a**)	*n*-C_6H_{13} (**2c**)	**6c**	99 (100)
4	Ph (**1a**)	*t*Bu (**2d**)	**6d**	84 (87)
5	Ph (**1a**)	Me_3Si (**2e**)	**6e**	95 (100)[c]
6	Ph (**1a**)	C_6F_5 (**2f**)	**6f**	98 (100)[d]
7	Ph (**1a**)	$PhOCH_2$ (**2g**)	**6g**	95 (100)[d]
8	*p*$MeOC_6H_4$ (**1b**)	*n*-C_4H_9 (**2a**)	**13**	79 (80)
9	*p*$CF_3C_6H_4$ (**1c**)	*n*-C_4H_9 (**2a**)	**6h**	71 (86)
10	*p*$Me_2NC_6H_4$ (**1d**)	*n*-C_4H_9 (**2a**)	**6i**	60 (64)
11	PhC_6H_4 (**1e**)	*n*-C_4H_9 (**2a**)	**6j**	95 (98)
12	$PhCH_2CH_2$ (**1f**)	*n*-C_4H_9 (**2a**)	**6k**	71[e]

[a] Five equivalents based on aldehyde were used. [b] Yield of product after isolation; GC yields are given in parenthesis. [c] 1.1 equivalents of **2e** was used. [d] Reaction time was 40 min. [e] 10% of the aldol condensation product of **1f** was obtained.

In summary, we have presented an efficient catalytic system for intermolecular hydroacylation. Further work is now directed toward understanding the mechanistic details of this reaction.

Experimental Section

Typical procedure for preparation of ketone **6a** (Table 1, entry 5): A screw-capped pressure vial (1 mL) was charged with freshly purified benzaldehyde (**1a**, 0.5 mmol), 2-amino-3-picoline (**4**, 0.1 mmol), benzoic acid (**7**, 0.03 mmol), aniline (**8**, 0.3 mmol), 1-hexene (**2a**, 2.5 mmol), and toluene (80 mg). After the mixture had been stirred at room temperature for several minutes, $[Rh(PPh_3)_3Cl]$ (**3**, 0.01 mmol) was added, and then it was stirred at 130 °C for 1 h. After cooling the reaction mixture to room temperature, it was purified by column chromatography (SiO_2, *n*-hexane/ethyl acetate 4/1) to yield pure **6a** (0.49 mmol, 98% yield).

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[5] To confirm the effect of carboxylic acid, the hydroacylation of 1-hexene with freshly purified benzaldehyde was performed with benzoic acid under the reaction conditions depicted in Equation (1). While it took 24 h to obtain a 72% yield without benzoic acid, the reaction time was shortened to 6 h with benzoic acid, and a 75% yield of heptanophenone **6a** was obtained.

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[7] The reactivity of **2a** with **9** towards hydroiminoacylation was not enhanced by the addition of **7**. This implies that carboxylic acid does not affect the hydroiminoacylation step. Therefore, we assume that the rate-determining step is the formation of **9**.

[8] It is also possible that **1a** condenses with **4** to form **9**. However, the condensation of **1a** with **8** is more facile than with **4**. When an equimolar mixture of **1a**, **4**, and **8** was heated at 130 °C for 10 min **1a** was completely consumed and the ratio of **9**:**11** was determined as 10:90 by GC.

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[12] It can be explained by the fact that the protonated aldimine is more electrophilic than the aldehyde. Since the aldimine is more basic than the aldehyde, it is the dominant reactant in the presence of acid.

Asymmetric Synthesis of a Chiral Secondary Grignard Reagent**

Reinhard W. Hoffmann,* Bettina Hölzer, Oliver Knopff, and Klaus Harms

Chiral organometallic reagents are of interest in stereoselective synthesis. This holds in particular for chiral α-heterosubstituted organolithium and Grignard reagents.[1] However, their reactions with electrophiles do not always take a stereochemically homogenous pathway. It is not clear

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