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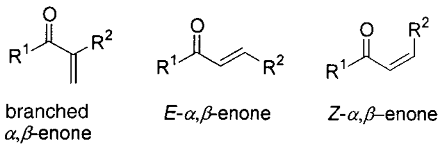
[25] Data for **10**: $[\alpha]_D^{20} = +44.0$ ($c = 0.04$, $CHCl_3$); IR (film): $\tilde{\nu}_{max} = 3440$, 1720, 1270, 1120, 720 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): $\delta = 8.08$ (m, 2H), 7.59 (m, 1H), 7.48 (m, 2H), 5.60 (q, $J = 6.9$ Hz, 1H), 4.09 (m, 1H), 3.52 (m, 2H), 3.36–3.24 (m, 2H), 2.28 (br s, 1H, OH), 1.89 (m, 1H), 1.67–1.60 (m, 3H), 1.55 (d, $J = 6.9$ Hz, 3H), 1.30–1.21 (m, 2H), 1.08 (d, $J = 7.0$ Hz, 3H), 0.87 (d, $J = 7.0$ Hz, 3H), 0.84 ppm (d, $J = 6.5$ Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 210.3$ (s), 165.8 (s), 133.3 (d), 129.8 (d, 2C), 129.6 (s), 128.5 (d, 2C), 78.8 (d), 74.7 (d), 73.2 (d), 66.6 (t), 43.9 (d), 35.6 (d), 30.3 (d), 26.4 (t), 24.8 (t), 17.9 (q), 16.1 (q), 13.9 (q), 10.4 ppm (q); MS (CI^+, CH_4): m/z (%): 363 (100) $[M+H^+]$, 241 (20), 207 (22), 157 (92), 139 (61); HRMS (CI^+, CH_4): calcd for $C_{21}H_{31}O_5$ $[M+H^+]$: 363.2172, found: 363.2169. The relative configuration of compound **10** was confirmed by NMR spectroscopy, by differential NOE experiments performed on **11**.

[26] Data for **14**: $[\alpha]_D^{20} = +65.6$ ($c = 1.16$, $CHCl_3$); IR (film): $\tilde{\nu}_{max} = 3460$, 1740, 1720, 1460, 1435, 1380, 1275, 1255, 1170, 1040, 1020 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): $\delta = 3.92$ (ddd, $J = 11.0$, 5.5, and 1.5 Hz, 1H), 3.73 (s, 3H), 3.52 (dd, $J = 9.6$ and 2.6 Hz, 1H), 3.46 (m, 2H), 3.15 (dq, $J = 11.0$ and 7.0 Hz, 1H), 3.02 (br s, 1H, OH), 1.84 (m, 1H), 1.76–1.49 (m, 4H), 1.25 (m, 1H), 1.06 (d, $J = 6.6$ Hz, 3H), 0.82 (d, $J = 7.0$ Hz, 3H), 0.81 ppm (d, $J = 6.3$ Hz, 3H), ^{13}C NMR (75 MHz, $CDCl_3$): $\delta =$ 176.3 (s), 76.7 (d), 75.1 (d), 65.7 (t), 51.9 (q), 40.0 (d), 35.7 (d), 31.8 (d), 27.2 (t), 25.1 (t), 17.4 (q), 14.2 (q), 8.8 ppm (q); MS (EI): m/z (%): 244 (3) $[M^+]$, 185 (100), 157 (38), 153 (93), 139 (26), 126 (34), 125 (43), 121 (28), 99 (28), 97 (44), 95 (41), 88 (49), 82 (28), 81 (34), 69 (43), 59 (42), 55 (65); HRMS (CI^+, CH_4): calcd for $C_{13}H_{25}O_4$ $[M+H^+]$: 245.1753, found: 245.1750.

Efficient and Selective Hydroacylation of 1-Alkynes with Aldehydes by a Chelation-Assisted Catalytic System[**]

Chul-Ho Jun,* Hyuk Lee, Jun-Bae Hong, and Bong-Il Kwon

Intermolecular hydroacylation is one of the most efficient methods for preparing ketones from olefins and aldehydes.[1] Recently, we developed an efficient catalytic system for the intermolecular hydroacylation of 1-alkenes by using 2-aminopyridine derivatives as a chelating auxiliary.[2] Hydroacylation of alkynes with aldehydes is also very interesting in terms of regio- and stereoselective synthesis since three possible isomers of α,β-enones can be generated from this reaction: branched as well as linear *E*- and *Z*-α,β-enones (Scheme 1).

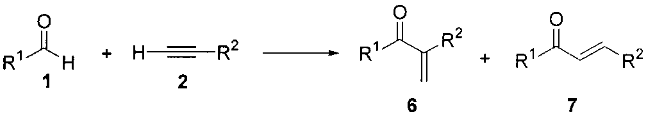


Scheme 1. Possible isomers of α,β-enones that can be generated from the hydroacylation of alkynes with aldehydes.

Although the intramolecular hydroacylation of alkynals was developed recently,[3] intermolecular hydroacylation of alkynes still remains little explored, and only a few nonselective examples have been reported with limited applications to internal alkynes[4] or benzaldehydes that bear a coordination site such as a hydroxy group at the *ortho* position.[5] Herein, we report a highly regio- and stereoselective intermolecular hydroacylation of terminal alkynes **2** with aldehydes **1** in the presence of a chelation-assisted catalytic system: $[Rh(PPh_3)_3Cl]$ (**3**), 2-amino-3-picoline (**4**), and benzoic acid (**5**). This is the most efficient catalytic system to date for the synthesis of branched or linear α,β-enones from 1-alkynes and aldehydes.

The reaction of benzaldehyde (**1a**) and 1-hexyne (**2a**) in the presence of the cocatalyst system consisting of **3** (5 mol%), **4** (40 mol%), and **5** (20 mol%) was performed in toluene at 80°C for 12 h to afford the branched α,β-enone **6a** in 92% yield after chromatographic isolation (Table 1, entry 1). No direct selective synthetic methods for the preparation of branched α,β-enones have been reported previously, although syntheses of branched (1,1-disubstituted) vinyl compounds by hydrosilylation,[6] hydrophosphorylation,[7] and dimerization of 1-alkynes[8] have been reported. It was found that most aromatic aldehydes tested underwent smooth hydroacylation with primary alkyl alkynes to produce branched α,β-enones **6** exclusively in good to excellent yields (Table 1, entries 2–9).[9]

Table 1. Rh^I-catalyzed hydroacylation of various aldehydes and 1-alkynes.[a]



Entry	**1** (R^1)	**2** (R^2)[b]	**6**/**7**	Yield [%][c]
1	**a** (Ph)	**a** (n-C_4H_9)	100:0 (**6a**/**7a**)	92 (100)
2		**b** (n-C_6H_{13})	100:0 (**6b**/**7b**)	93 (98)
3		**c** ($PhCH_2$)	100:0 (**6c**/**7c**)	66 (71)
4	**b** (p-$CF_3C_6H_4$)	**a**	100:0 (**6d**/**7d**)	95 (100)
5	**c** (p-$MeOC_6H_4$)		100:0 (**6e**/**7e**)	76(85)
6	**d** (naphthyl)		100:0 (**6f**/**7f**)	83 (88)
7	**e** (3-thiophenyl)		100:0 (**6g**/**7g**)	96 (100)
8	**f** (4-pyridyl)		100:0 (**6h**/**7h**)	78 (100)
9	**g** (3-pyridyl)		100:0 (**6i**/**7i**)	79 (100)
10	**h** (2-pyridyl)			0
11	**i** (n-C_5H_{11})	**a**	78:22 (**6j**/**7j**)	85
12		**d** (t-C_4H_9)	0:100 (**6k**/**7k**)	74
13	**j** (cyclohexyl)	**a**	81:19 (**6l**/**7l**)	98 (100)[d]
14		**d**	0:100 (**6m**/**7m**)	63

[a] Reagents and conditions: $[Rh(PPh_3)_3Cl]$ (**3**; 5 mol%), 2-amino-3-picoline (**4**; 40 mol%), benzoic acid (**5**; 20 mol%), toluene, 80°C, 12 h. [b] Two equivalents of **2** (based on the aldehyde) were used. [c] GC yields are given in parentheses, and <1% yields of side products were ignored. [d] Reaction time: 2 h.

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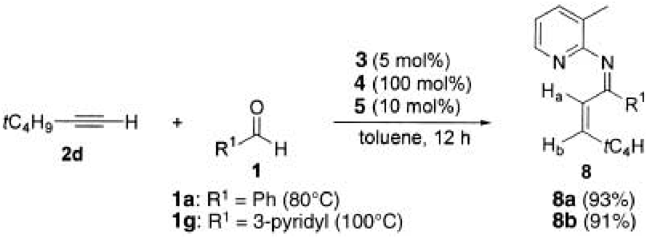
Supporting information for this article is available on the WWW under http://www.angewandte.org or from the author.

No other regio- and stereoisomeric products were detected by GC and NMR spectroscopic analysis.

An electron-withdrawing substituent, for example, the trifluoromethyl group in **1b**, shows better reactivity than the electron-donating substituent in **1c** (Table 1, entries 4 and 5) owing to the facile condensation of **1b** with **4**. Interesting results were also obtained with pyridinecarboxaldehydes (Table 1, entries 8–10), since 3- and 4-pyridinecarboxaldehydes (**1g**,**f**) showed good reactivities, whereas 2-pyridinecarboxaldehyde (**1h**) did not react at all.[2c]

When the reaction was carried out with aliphatic aldehydes, a small amount of the *E* isomer as well as the branched adduct was obtained. For example, hexanal (**1i**) reacted with **2a** under the previous reaction conditions to give a 78:22 mixture of branched α,β-enone **6j** and *E*-α,β-enone **7j** in 85% yield (Table 1, entry 11). When the reaction was performed with an alkyne substituted with a sterically demanding group, *tert*-butylacetylene (**2d**), *E*-α,β-enone **7k** was isolated exclusively in 74% yield without any branched adduct **6k**. Similar results were also obtained in the reaction of cyclohexanecarboxaldehyde (**1j**) (Table 1, entries 13 and 14). These results imply that the ratio of **6**/**7** seems to be controlled by the alkyl substituent of the 1-alkyne.

When hydroacylation of **2d** with benzaldehyde **1a** was performed at 80°C, compound **8a** ($J_{\mathrm{Ha,Hb}} = 6.0$ Hz),[10] the ketimine of the *Z*-α,β-enone, was isolated in 93% yield without any branched or *E*-α,β-enone (Scheme 2). Since the product was obtained as the ketimine, an equimolar amount of 2-amino-3-picoline (**4**) must be added to complete the reaction. Attempts to hydrolyze the ketimine **8a** failed.[11] The heteroaromatic aldehyde **1g** was also used in this reaction and yielded the corresponding ketimine **8b**. At the present time, it is not clear why the *Z* isomer of the α,β-unsaturated ketimine was obtained only with aromatic aldehydes.



Scheme 2. Hydroacylation of **2d** with aromatic aldehydes to give ketimines **8**.

In summary, when the hydroacylation of 1-alkynes with aldehydes was carried out in the presence of a chelation-assisted catalytic system, branched α,β-enones were isolated in high yields and with high regioselectivity. In the reaction of the sterically demanding *tert*-butylacetylene, aliphatic aldehydes gave *E*-α,β-enones exclusively, whereas aromatic aldehydes gave *Z*-α,β-unsaturated ketimines.

Experimental Section

General procedure: A mixture of **1a** (22.9 mg, 0.216 mmol) and **2a** (35.5 mg, 0.432 mmol) in a 1-mL screw-capped pressure vial was heated at 80°C for 12 h with **3** (10 mg, 0.0108 mmol), **4** (9.4 mg, 0.0870 mmol), **5** (5.4 mg, 0.0443 mmol), and toluene (0.2 g). The resulting reaction mixture was purified by column chromatography (hexane/Et_2O 15:1) to give **6a** (37.4 mg, 92%).

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[9] A plausible mechanism for this reaction is as follows: Formation of an aldimine from the condensation of the aldehyde **1** with **4** followed by a C–H bond activation by **3** leads to an iminoacylrhodium(III) hydride species. Hydrometalation or carbometalation of 1-alkynes with the iminoacylrhodium(III) hydride complex and reductive elimination of the resulting complex furnishes a branched α,β-unsaturaed ketimine, which is hydrolyzed by H_2O generated during the initial condensation step to give branched α,β-enone.

[10] Ketimine **8** is very stable and was characterized by COSY($^1H/^{13}C$), DEPT, and HMBC NMR spectroscopic analysis; see Supporting Information.

[11] Heating the ketimine **8** with HCl (aqueous, 1N, 100 mol%) at 130°C for 12 h in a 1-mL screw-capped vial did not give any hydrolyzed ketone compound.