DOI: 10.1002/chem.200902646

Iridium-Catalyzed Coupling Reaction of Primary Alcohols with 2-Alkynes Leading to Hydroacylation Products

Shintaro Hatanaka, Yasushi Obora,* and Yasutaka Ishii*[a]

Abstract: A novel iridium-catalyzed intermolecular coupling reaction of primary alcohols or aldehydes with 2-alkynes was successfully achieved with high regioselectivity to give hydroacylation products such as α,β-unsaturated ketones in good yields. The mechanistic investigation of the reaction strongly indicated that the coupling proceeds through the initial formation of homoallylic alcohols followed by dehydrogenation to β,γ-unsatutated ketones and then isomerisation, which leads to the hydroacylation products.

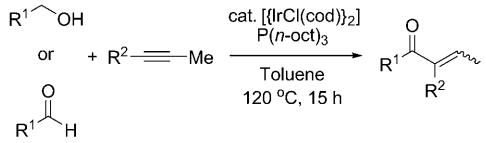
Keywords: alcohols · aldehydes · alkynes · hydroacylation · iridium

Introduction

Transition-metal-catalyzed hydroacylation of alkynes with aldehydes is a useful methodology for introducing carbonyl functionalities into unsaturated compounds.[1] To date, the hydroacylation of alkynes has been mainly limited to intramolecular reactions[2] in contrast with intermolecular alkyne hydroacylation, which is mostly found in the reactions with substrates that have directing groups that accelerate the hydroacylation process.[3] However, the intermolecular hydroacylation of alkynes with simple aldehydes without directing groups has been far less explored.[4]

It is well known that Ir complexes serve as efficient hydrogen-transfer catalysts from alcohols to aldehydes, which can be utilized in the α-alkylation of ketones and activated methylene compounds with alcohols, as well as the β-alkylation of alcohols (the Guerbet reaction).[5,6]

Recently, we reported an Ir-catalyzed coupling reaction of 1-aryl-1-propynes with primary alcohols leading to secondary homoallylic alcohols through the formation of hydrido-(π-allyl)iridium as a possible key intermediate.[7] During the course of this study, we found a novel Ir-catalyzed transformation of 2-alkynes with primary alcohols to afford hydroacylation products such as α,β-unsaturated ketones. In addition, we found that the hydroacylation products were also obtained from aldehydes and 2-butyne.[8] Quite recently, Krische and co-workers reported the relevant Ru-catalyzed hydroacylation reaction of alcohols or aldehydes with alkynes.[9] This work prompted us to report our independent findings on an Ir-catalyzed reaction of primary alcohols or aldehydes with 2-alkynes (Scheme 1).



Scheme 1. Ir-catalyzed hydroacylation of 2-alkynes with primary alcohols or aldehydes.

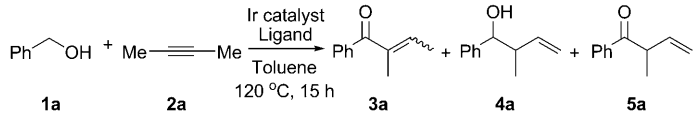
Results and Discussion

The reaction of benzyl alcohol (**1a**) with 2-butyne (**2a**) was chosen as a model reaction and was carried out under various conditions (Table 1). For instance, **1a** (0.5 mmol) was allowed to react with **2a** (1 mmol) in the presence of [{IrCl-(cod)}$_2$] (cod = 1,5-cyclooctadiene, 0.025 mmol, 5 mol %) combined with tri(*n*-octyl)phosphine (P(*n*-oct)$_3$; 0.1 mmol, 20 mol %) in toluene (1 mL) at 120 °C for 15 h to give 2-methyl-1-phenyl-2-buten-1-one (**3a**) in 92 % isolated yield (Table 1, entry 1). The highest yield of **3a** was obtained when 2 equivalents of **2a** was reacted with **1a**, whereas the equimolar reaction of **1a** and **2a** resulted in a considerable

[a] S. Hatanaka, Dr. Y. Obora, Prof. Dr. Y. Ishii
Department of Chemistry and Material Engineering
Faculty of Chemistry, Materials and Bioengineering
High Technology Research Center, and ORDIST
Kansai University, Suita, Osaka 564-8680 (Japan)
Fax: (+81) 6-6339-4026
E-mail: obora@kansai-u.ac.jp
ishii@ipcku.kansai-u.ac.jp

Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/chem.200902646.

Table 1. Ir-catalyzed coupling of **1a** with **2a** under various reaction conditions.[a]



1a **2a** **3a** **4a** **5a**

Entry	Ir-catalyst (mol%)	Ligand (mol%)	Yield [%][b] **3a** (*E*:*Z*)	**4a**	**5a**
1	$[\{IrCl(cod)\}_2]$ (5)	$P(n\text{-oct})_3$ (20)	94 [92] (66:34)	–	trace
2[c]	$[\{IrCl(cod)\}_2]$ (5)	$P(n\text{-oct})_3$ (20)	32 (91:9)	trace	–
3[d]	$[\{IrCl(cod)\}_2]$ (5)	$P(n\text{-oct})_3$ (20)	7 (63:37)	40	11
4	$[\{IrCl(cod)\}_2]$ (5)	$P(n\text{Bu})_3$ (20)	49 (57:43)	21	9
5	$[\{IrCl(cod)\}_2]$ (5)	PPh_3 (20)	6 (51:49)	15	trace
6	$[\{IrCl(cod)\}_2]$ (5)	PCy_3 (20)	trace	trace	–
7	$[\{IrCl(cod)\}_2]$ (5)	dppp (10)	26 (51:49)	–	9
8	$[\{IrCl(cod)\}_2]$ (5)	none	–	–	–
9	$[\{IrCl(coe)_2\}_2]$ (5)	$P(n\text{-oct})_3$ (20)	90 (63:35)	–	7
10	$[\{Ir(cod)(OH)\}_2]$ (5)	$P(n\text{-oct})_3$ (20)	–	10	30
11	$[\{IrCl_2Cp^*\}_2]$ (5)	$P(n\text{-oct})_3$ (20)	–	–	–

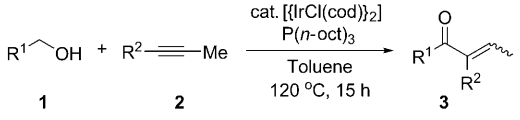
[a] Conditions: Alcohol **1a** (0.5 mmol) was allowed to react with **2a** (1 mmol) in the presence of the Ir-catalyst (5 mol%) combined with the phosphine ligand (20 mol%) in toluene (1 mL) at 120 °C for 15 h. [b] GC yields based on **1a** were used. The numbers in parentheses show the *E*/*Z* ratio estimated by GC. The number in square brackets shows the isolated yield. [c] Alkyne **2a** (0.5 mmol) was used. [d] The reaction was performed at 100 °C.

decrease of the yield of **3a** (Table 1, entry 1 vs. entry 2). As for the reaction temperature, the best result was obtained at 120 °C, but the reaction at 100 °C led to homoallylic alcohol **4a** as a major product (40%) along with a small amount of **3a** (7%) and β,γ-unsaturated ketone **5a** (11%; Table 1, entry 3). Among the phosphine ligands examined, the best performance of $[\{IrCl(cod)\}_2]$ was accomplished by a combination of tri(*n*-octyl)phosphine as a ligand. Other selected phosphine ligands such as $P(n\text{Bu})_3$, PPh_3, PCy_3, and dppp (1,3-bis(diphenylphosphino)propane) were found to be less efficient (Table 1, entries 4–7). No reaction was induced in the absence of a phosphine ligand (Table 1, entry 8). As for the selection of an iridium complex, $[\{IrCl(coe)_2\}_2]$ (coe = cyclooctene) also realized high catalytic activity and produced **3a** in 90% yield along with a small amount of **4a** (7%; Table 1, entry 9). However, other iridium complexes such as $[\{Ir(cod)(OH)\}_2]$ and $[\{IrCl_2Cp^*\}_2]$ (Cp* = 1,2,3,4,5-pentamethylcyclopentadiene), which are efficient catalysts for the hydrogen-transfer process,[5,6] showed low or no catalytic activity in the present reaction (Table 1, entries 10–11).

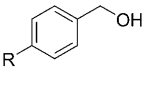
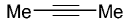
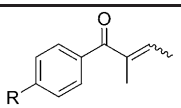
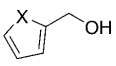
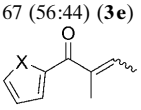
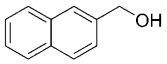
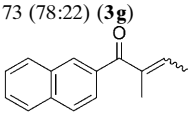
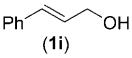
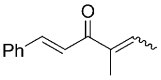
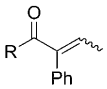
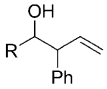
Under the optimized conditions shown in Table 1, entry 1, the reaction of various primary alcohols **1** with 2-alkynes **2** was examined (Table 2). The reaction of **2a** with benzylic alcohols that had electron-donating or -withdrawing groups on the benzene ring (**1b–1e**) afforded the corresponding hydroacylation products **3b–e** in 67–85% isolated yields (Table 2, entries 1–4). Other primary alcohols such as furfuryl alcohol (**1f**), 2-thiophen methanol (**1g**), 2-naphthyl methanol (**1h**), and cinnamyl alcohol (**1i**) also reacted with **2a** to produce **3f–3i** in good yield (Table 2, entries 5–8).

The reaction of 1-phenyl-1-propyne (**2b**) with **1a** gave **3j** in 70% yield (Table 2, entry 9). Aliphatic alcohols such as

Table 2. Ir-catalyzed coupling of primary alcohols **1** with 2-alkynes **2** leading to hydroacylation products.[a]



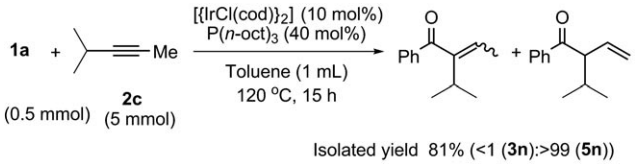
1 **2** **3**

Entry	Alcohol **1**	Alkyne **2**	Yield [%][b]
			
1[c]	R = Me (**1b**)	**2a**	83 (50:50) (**3b**)
2[c]	R = MeO (**1c**)	**2a**	76 (54:46) (**3c**)
3	R = Cl (**1d**)	**2a**	85 (60:40) (**3d**)
4	R = CF_3 (**1e**)	**2a**	67 (56:44) (**3e**)
			
5[d]	X = O (**1f**)	**2a**	71 (81:19) (**3f**)
6[d]	X = S (**1g**)	**2a**	73 (78:22) (**3g**)
7[c]	 (**1h**)	**2a**	 89 (57:43) (**3h**)
8[d,e]	 (**1i**)	**2a**	 63 (79:21) (**3i**)
			 
9[d,e]	R = Ph (**1a**)	**2b**	70 (16:84) (**3j**) –
10[f,g]	R = Me (**1j**)	**2b**	34 (98:2) (**3k**) 12 (**4k**)
11[f,g]	R = n-C_3H_7 (**1k**)	**2b**	43 (86:14) (**3l**) 22 (**4l**)
12[f,g]	R = n-C_7H_{15} (**1l**)	**2b**	45 (82:18) (**3m**) 10 (**4m**)

[a] Conditions: Alcohol **1a** (0.5 mmol) was allowed to react with **2a** (1 mmol) in the presence of $[\{IrCl(cod)\}_2]$ (0.025 mmol) combined with $P(n\text{-oct})_3$ (0.1 mmol) in toluene (1 mL) at 120 °C for 15 h. [b] Isolated yields. The numbers in parentheses show the *E*/*Z* ratio estimated by ^1H NMR spectroscopy. [c] Alkyne (2 mmol) was used. [d] $[\{IrCl(cod)\}_2]$ (0.05 mmol) and $P(n\text{-oct})_3$ (0.2 mmol) were used. [e] Alkyne (5 mmol) was used. [f] Alkyne (2.5 mmol) was used. [g] $[\{Ir(cod)(OH)\}_2]$ (0.05 mmol) and $P(n\text{-oct})_3$ (0.3 mmol) were used.

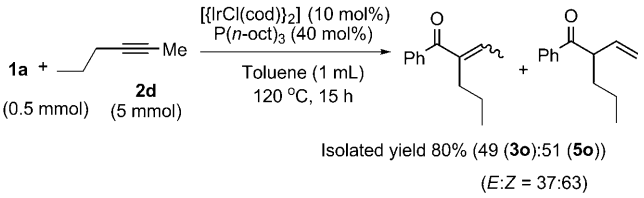
ethanol (**1j**), *n*-butanol (**1k**) and *n*-octanol (**1l**) were tolerated as substrates in this reaction to produce the corresponding hydroacylation products **3k–3m** in moderate to good yields together with the corresponding homoallylic alcohols (**4k**, **4l**, and **4m**, respectively), which were formed as by-products in 10–22% yield (Table 2, entries 10–12). This is believed to be due to the difficulty of dehydrogenation of initially formed aliphatic homoallylic alcohols compared with that of benzylic homoallylic alcohols.

In contrast to the hydroacylation of **2a** and **2b** in which the reaction smoothly proceeded with various alcohols, when 4-methyl-2-pentyne (**2c**) was employed as the alkyne substrate, the desired hydroacylation product (**3n**) was not formed at all, but β,γ-unsaturated ketones **5n** was exclusively obtained in 81% isolated yield (Scheme 2). On the other



Scheme 2. Reaction of **1a** with **2c**.

hand, the reaction of 2-hexyne (**2d**), which has a less bulky substituent, with **1a** gave rise to a mixture of **3o** and **5o** in a ratio of 49:51 (Scheme 3). The above-mentioned results



Scheme 3. Reaction of **1a** with **2d**.

strongly suggest that the resulting hydroacylation products **3** could be formed through the β,γ-unsaturated ketones **5** from homoallylic alcohols **4** as intermediates, which lead to hydroacylation products **3** (see below for further experimental elucidations). For the reaction of **2c** with **1a**, however, the isomerization of β,γ-unsaturated ketone **5n**, which has an anchoring bulky isopropyl group, to the α,β-unsaturated ketone **3n** may be difficult (Scheme 2).

To reveal the reaction pathway that involves the initial formation of homoallylic alcohols as intermediates, the reaction of aromatic aldehydes **6** with **2a** under these reaction conditions was examined (Table 3).

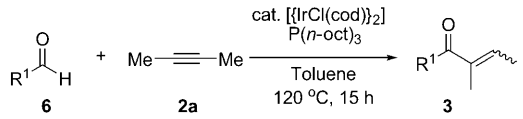
As expected, various aromatic aldehydes **6a–6i** reacted with **2a** to produce the corresponding hydroacylation products **3** in good yields (Table 3, entries 1–9). Note that this reaction did not require the addition of 2-propanol, in contrast with the Ru-catalyzed reaction of aldehydes with 2-butyne reported by Krische and co-workers in which the reaction requires the presence of 2-propanol.[9]

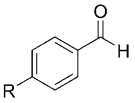
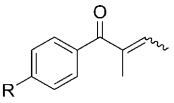
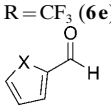
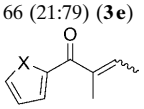
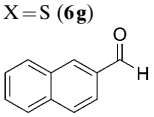
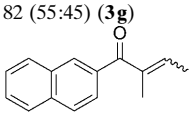
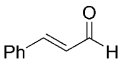
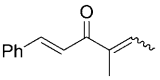
To obtain further insight about the reaction mechanism, time-course monitoring of the reaction of **1a** with **2a** under the conditions in Table 1, entry 1 was investigated. It was found that **4a** and **5a** are observed as principal products at the early stage of the reaction (<10 h). As the reaction proceeded, **4a** and **5a** disappeared and were converted to **3a** almost completely as the final product (Figure 1).

Thus, we suppose that this reaction proceeds through dehydrogenation of **4a** to give **5a**, which is followed by isomerization to **3a** as the final product. In fact, the reaction of **4a** with **2a** under the same conditions as showed in Table 1, entry 1 resulted in the formation of **3a** in 74% yield (Scheme 4).

Although a detailed reaction mechanism of the present coupling reaction has not been fully confirmed at this stage,

Table 3. Ir-catalyzed coupling of aromatic aldehydes **6** with **2a** leading to hydroacylation products.[a]



Entry	Aldehyde **6**	Yield [%][b]
		
1	R = H (**6a**)	84 (9:91)[c] (**3a**)
2[d]	R = Me (**6b**)	81 (64:36) (**3b**)
3[d]	R = MeO (**6c**)	80 (57:43) (**3c**)
4	R = Cl (**6d**)	82 (14:86) (**3d**)
5	R = CF_3 (**6e**)	66 (21:79) (**3e**)
		
6[e]	X = O (**6f**)	70 (70:30) (**3f**)
7[e]	X = S (**6g**)	82 (55:45) (**3g**)
8	 (**6h**)	 81 (43:57) (**3h**)
9[d,f]	 (**6i**)	 72 (84:16) (**3i**)

[a] Conditions: Aldehyde **6** (0.5 mmol) was allowed to react with **2a** (2 mmol) in the presence of [{IrCl(cod)}2] (0.025 mmol) combined with P(*n*-oct)3 (0.1 mmol) in toluene (1 mL) at 120 °C for 15 h. [b] Isolated yields. The numbers in parentheses show the *E*/*Z* ratio estimated by ^{1}H NMR spectroscopy. [c] **5a** was formed in 6% yield as a by-product. [d] [{IrCl(cod)}2] (0.05 mmol) and P(*n*-oct)3 (0.2 mmol) were used. [e] Alkyne (4 mmol) was used. [f] Alkyne (5 mmol) was used.

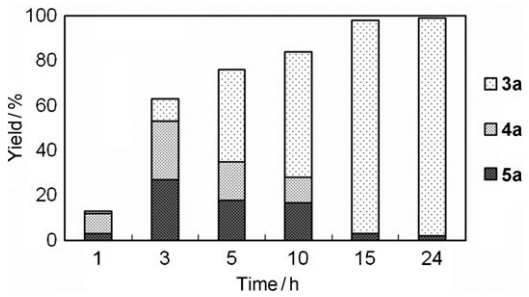
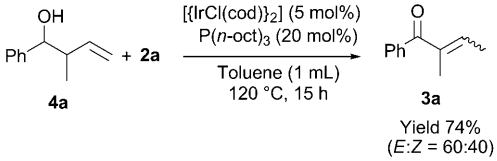
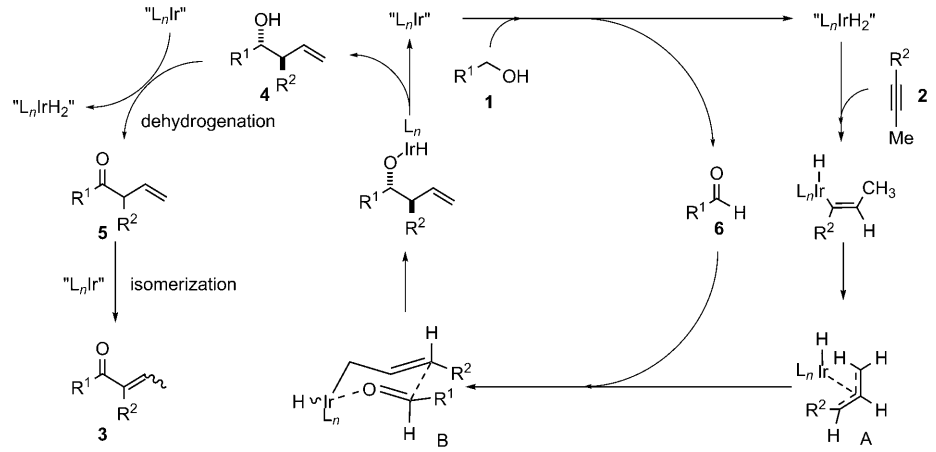


Figure 1. Time-course monitoring of the formation of **3a** in the reaction of **1a** with **2a** under the conditions in Table 1, entry 1.



Scheme 4. Reaction of **4a** with **2a**.



Scheme 5. A plausible reaction pathway for the formation of **3** via **4** and **5** as possible intermediates.

it is possible to explain the reaction rationally by the pathway shown in Scheme 5. First, the reaction initiates the hydrogen transfer from alcohols **1** to an iridium complex to produce aldehydes **6** and an iridium–hydride complex, which then reacts with alkynes **2** to form the hydrido(π-allyl)iridium (**A**) as previously reported.[7] Thereafter, the formed **A** reacts with aldehydes through a six-membered intermediate **B** to form homoallylic alcohols **4**.[7] Subsequently, dehydrogenation of the resulting **4** followed by isomerization would lead to the desired hydroacylation products **3**.[10]

Conclusion

In conclusion, we have reported a novel Ir-catalyzed coupling reaction of primary alcohols with 2-alkynes leading to hydroacylation products such as α,β-unsaturated ketones in good to excellent yields. The experimental mechanistic investigations revealed that the reaction would proceed through the initial formation of homoallylic alcohols, followed by dehydrogenation and isomerization to lead to hydroacylation products. Further investigation with regard to the detailed reaction mechanism is currently in progress.

Experimental Section

GC analysis was performed with a flame ionization detector using a 0.22 mm × 25 m capillary column (BP-5). ^{1}H and ^{13}C NMR spectra were measured at 400 and 100 MHz, respectively, in $CDCl_3$ with Me_4Si as the internal standard. The products were characterized by ^{1}H NMR, ^{13}C NMR, NOESY, DEPT, HMQC spectroscopy and by GC–MS. The yields of the products were estimated from the peak areas based on the internal standard technique by using GC. All starting materials were commercially available and were used without any purification. Compounds **3a** (*E* isomer,[11] *Z* isomer),[12] **3b** (*E* isomer),[11] **3d** (*E* isomer,[13] *Z* isomer),[14] **3f** (*E* isomer, *Z* isomer),[15] **3g** (*E* isomer),[11] **3i** (*E*,*E* isomer),[16] **3j** (*E* isomer,[17] *Z* isomer),[18] **3k** (*E* isomer,[19] *Z* isomer),[20] **3l** (*E* isomer),[19] **3o** (*E* isomer, *Z* isomer),[21] **4a**,[22] **4k**,[7] **4l**[7] **4m**,[7] and **5a**[23] have been previously reported.

Typical reaction conditions for the Ir-catalyzed coupling of 1a with 2a (Table 1, entry 1): A mixture of [{IrCl(cod)}$_2$] (16 mg, 0.025 mmol), P(*n*-oct)$_3$ (37 mg, 0.1 mmol), **1a** (54 mg, 0.5 mmol), and **2a** (54 mg, 1 mmol) in toluene (1 mL) was stirred at 120 °C for 15 h under Ar in a pressure tube. The conversions and yields of the products were estimated from peak areas based on an internal standard by using GC, and the product **3a** was obtained (yield = 94 %) along with a trace amount of **5a**. A mixture of the product **3a** (*E*,*Z* mixture) and **5a** was separated by column chromatography (230–400 mesh silica gel, *n*-hexane/ethyl acetate = 20/1) and was distilled by Kugelrohr distillation to give **3a** (yield = 74 mg, 92 %).

Typical reaction conditions for the Ir-catalyzed coupling of 6 with 2a (Table 3, entry 1): A mixture of [{IrCl(cod)}$_2$] (16 mg, 0.025 mmol), P(*n*-oct)$_3$ (37 mg, 0.1 mmol), **6a** (53 mg, 0.5 mmol), and **2a** (108 mg, 2 mmol) in toluene (1 mL) was stirred at 120 °C for 15 h under Ar in a pressure tube. The conversions and yields of the products were estimated from peak areas based on an internal standard by using GC, and the product **3a** was obtained (yield = 91 %). The product **3a** (*E*,*Z* mixture) was isolated by column chromatography (230–400 mesh silica gel, *n*-hexane/ethyl acetate = 20/1) and was distilled by Kugelrohr distillation to give **3a** (yield = 67 mg, 84 %).

Reaction of 4a with 2a (Scheme 4): A mixture of [{IrCl(cod)}$_2$] (16 mg, 0.025 mmol), P(*n*-oct)$_3$ (37 mg, 0.1 mmol), **4a** (81 mg, 0.5 mmol), and **2a** (54 mg, 1 mmol) in toluene (1 mL) was stirred at 120 °C for 15 h under Ar in pressure tube. The conversions and yields of the products were estimated from peak areas based on an internal standard by using GC, and the product **3a** was obtained (74 % yield).

Characterization data

3b (Z isomer): ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.88–7.19 (m, 4H), 5.75 (qq, ^3J(H,H) = 7, 2 Hz, 1H), 2.39 (s, 3H), 1.98–1.94 (m, 3H), 1.51 ppm (dq, ^3J(H,H) = 7, 2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 200.4 (*C*=O), 144.1 (C), 136.6 (C), 134.0 (C), 129.4 (CH), 128.7 (CH), 126.1 (C=*C*H), 21.5 (Ph*C*H$_3$), 21.2 (*C*H$_3$), 15.4 ppm (*C*H$_3$); IR (neat): $\tilde{\nu}$ = 3028, 2976, 2916, 1646, 1602, 1450, 1274, 1167, 975, 823, 739 cm^{-1}; MS (EI, 70 eV): *m*/*z* (%): 174 [*M*$^+$] (14), 160 (10), 159 (86), 131 (16), 119 (100), 91 (64), 65 (27), 55 (12); HRMS: (EI, 70 eV): *m*/*z* calcd for $C_{12}H_{14}O$ [*M*$^+$]: 174.1045; found: 174.1050.

3c (E,Z mixture): ^{1}H NMR (400 MHz, $CDCl_3$) for the *E* isomer: δ = 7.94–6.82 (m, 4H), 6.32 (q, ^3J(H,H) = 7 Hz, 1H), 3.85 (s, 3H), 1.97–1.94 (m, 3H), 1.87 ppm (d, ^3J(H,H) = 7 Hz, 3H); ^{1}H NMR (400 MHz, $CDCl_3$) for the *Z* isomer: δ = 7.94–6.82 (m, 4H), 5.72 (q, ^3J(H,H) = 7 Hz, 1H), 3.87 (s, 3H), 1.97–1.94 (s, 3H), 1.51 ppm (d, ^3J(H,H) = 7 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) for the *E*,*Z* mixture: δ = 199.4, 197.8 (2*C*=O, *E*- and *Z*-isomer), 163.7, 162.4 (2C, *E*- and *Z*-isomers), 138.9 (C=*C*H, *E*-isomer), 137.5, 136.6 131.0, 129.4 (4C, *E*- and *Z*-isomers) 131.6, 113.9, 113.3 (4CH, *E*- and *Z*-isomer), 125.5 (C=*C*H, *Z*-isomer), 55.4, 55.4 (2*C*H$_3$O, *E*- and *Z*-isomers), 21.2, 12.6 (2CH$_3$, *E*- and *Z*-isomers), 15.3 (CH$_3$, *Z*-isomer), 14.5 ppm (CH$_3$, *E*-isomer); IR (neat): $\tilde{\nu}$ = 2992, 2941, 1653, 1596, 1507, 1247, 1150, 978, 841, 749, 600 cm^{-1}; MS (EI, 70 eV) for the *E* isomer: *m*/*z* (%): 190 [*M*$^+$] (22), 175 (11), 159 (13), 135 (100), 107 (13), 92 (12), 77 (20); HRMS (EI, 70 eV): *m*/*z* calcd for $C_{12}H_{14}O_2$ [*M*]$^+$: 190.0994; found: 190.0986; MS (EI) for the *Z* isomer: *m*/*z* (%): 190 [*M*$^+$] (17), 175 (25), 173 (11), 159 (24), 135 (100), 107 (16), 92 (16), 77 (26); HRMS (EI, 70 eV): *m*/*z* calcd for $C_{12}H_{14}O_2$ [*M*$^+$]: 190.0994; found: 190.0996.

3e (E,Z mixture): ^{1}H NMR (400 MHz, $CDCl_3$) for the *E* isomer: δ = 8.02–7.65 (m, 4H), 6.41 (q, ^3J(H,H) = 7 Hz, 1H), 1.99–1.97 (m, 3H), 1.91 ppm (d, ^3J(H,H) = 7 Hz, 3H); ^{1}H NMR (400 MHz, $CDCl_3$) for the *Z*

isomer: $\delta = 8.02$–7.65 (m, 4H), 5.89 (qq, $^3J(H,H) = 7$, 2 Hz, 1H), 1.99–1.97 (m, 3H), 1.52 ppm (dq, $^3J(H,H) = 7$, 2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) for the *E* isomer: $\delta = 197.4$ (*C*=O), 143.3 (C=*C*H), 142.2 (C), 137.7 (C), 132.8 (C), 132.4 (CH), 129.2 (CH), (125.07, 125.04, 125.00, 124.96) (CF_3), 14.9 (CH_3), 11.8 ppm (CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) for the *Z* isomer: $\delta = 199.4$ (*C*=O), 139.5 (C), 135.7 (C), 134.4 (q, J(C,F) = 33 Hz, C), 129.4 (CH), 128.5 (C=*C*H), 126.8 (q, J(C,F) = 4 Hz, CH), 20.9 (CH_3), 15.6 ppm (CH_3); ^{19}F NMR (376 MHz, $CDCl_3$) for the *E* isomer: $\delta = 62.9$ ppm; ^{19}F NMR (376 MHz, $CDCl_3$) for the *Z* isomer: $\delta = 63.1$ ppm; IR (neat) for the *E*,*Z* mixture: $\tilde{\nu} = 3044$, 2975, 2929, 2801, 1642, 1402, 1321, 1270, 841, 755 cm^{-1}; MS (EI, 70 eV) for the *E* isomer: *m*/*z* (%): 228 [M^+] (32), 213 (29), 200 (13), 173 (100), 159 (83), 145 (88), 95 (16), 83 (38), 75 (9), 55 (58); HRMS: (EI, 70 eV): *m*/*z* calcd for $C_{12}H_{11}OF_3$ [M]$^+$: 228.0762; found: 228.0770; MS (EI, 70 eV) for the *Z* isomer: *m*/*z* (%): 228 [M^+] (21), 227(13), 213 (25), 173 (78), 159 (100), 145 (87), 131 (15), 95 (15), 83 (18), 75 (9), 55 (49); HRMS (EI, 70 eV): *m*/*z* calcd for $C_{12}H_{11}OF_3$ [M^+]: 228.0762; found: 228.0758.

3g *(Z isomer)*: ^{1}H NMR (400 MHz, $CDCl_3$) : $\delta = 7.64$ (dd, $^3J(H,H) = 5$, 1 Hz, 1H), 7.55 (dd, $^3J(H,H) = 4$, 1 Hz, 1H), 7.09 (dd, $^3J(H,H) = 5$, 4 Hz, 1H), 5.73 (qq, $^3J(H,H) = 7$, 2 Hz, 1H), 2.00–1.98 (m, 3H), 1.60 ppm (dq, $^3J(H,H) = 7$, 2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 190.1$ (*C*=O), 147.2 (C), 134.6 (CH), 134.1 (CH), 128.2 (CH), 136.6 (C), 126.2 (C=*C*H), 21.1 (CH_3), 15.6 ppm (CH_3); IR (neat): $\tilde{\nu} = 3100$, 2968, 2849, 1658, 1506, 1350, 1270, 1150, 1047, 959, 831, 727 cm^{-1}; MS (EI, 70 eV): *m*/*z* (%): 166 [M^+] (18), 151 (34), 133 (53), 111 (100), 105 (16), 83 (14), 55 (16); HRMS: (EI, 70 eV): *m*/*z* calcd for $C_9H_{10}OS$ [M^+]: 166.0452; found: 166.0451.

3h *(E,Z mixture)*: ^{1}H NMR (400 MHz, $CDCl_3$) for the *E* isomer: $\delta =$ 8.42–7.48 (m, 7H), 6.46 (q, $^3J(H,H) = 7$ Hz, 1H), 2.05–2.01 (m, 3H), 1.90 ppm (d, $^3J(H,H) = 7$ Hz, 3H); ^{1}H NMR (400 MHz, $CDCl_3$) for the *Z* isomer: $\delta = 8.42$–7.48 (m, 7H), 5.86 (q, $^3J(H,H) = 7$ Hz, 1H), 2.05–2.01 (m, 3H), 1.55 ppm (d, $^3J(H,H) = 7$ Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) for the *E*,*Z* mixture: $\delta = 200.7$, 198.9 (2*C*=O, *E* and *Z* isomers), 141.3 (C=*C*H, *E*-isomer), 137.8, 136.5, 136.0, 135.7, 134.7, 133.8, 132.7, 132.2 (8C, *E*- and *Z*-isomers), 131.6, 130.1, 129.6, 129.0, 128.6, 128.5, 127.9, 127.8, 127.7, 127.6, 126.7, 126.5, 125.7, 124.3 (14CH, *E*- and *Z*-isomers) 126.8 (C=*C*H, *Z*-isomer), 21.28, 21.29 (2CH_3, *E*- and *Z*-isomers), 15.5 (CH_3, *Z*-isomer), 14.8 ppm (CH_3, *E*-isomer); IR (neat): $\tilde{\nu} = 3055$, 2974, 2917, 1640, 1466, 1356, 1281, 1160, 1120, 821, 757, 717 cm^{-1}; MS (EI, 70 eV) for the *E* isomer: *m*/*z* (%): 210 [M^+] (29), 195 (50), 167 (29), 155 (93), 127 (100), 77 (13), 55 (13); HRMS: (EI, 70 eV): *m*/*z* calcd for $C_{15}H_{14}O$ [M^+]: 210.1045; found: 210.1046; MS (EI, 70 eV) for the *Z* isomer: *m*/*z* (%): 210 [M^+] (47), 195 (66), 167 (23), 155 (71), 127 (100), 77 (13), 55 (13); HRMS: (EI, 70 eV): *m*/*z* calcd for $C_{15}H_{14}O$ [M^+]: 210.1045; found: 210.1038.

3i *(E,Z isomer)*: ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 7.62$–7.26 (m, 7H), 5.81 (qq, $^3J(H,H) = 7{,}2$ Hz, 1H), 1.97–1.95 (m, 3H), 1.75 ppm (dq, $^3J(H,H) = 7$, 2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 198.6$ (*C*=O), 144.8 (CH), 130.5 (CH), 128.7 (CH), 128.3 (CH), 126.1 (CH), 136.8, 134.7 (C), 128.9 (C=*C*H), 20.8 (CH_3), 15.6 ppm (CH_3); IR (neat): $\tilde{\nu} = 3066$, 3014, 2921, 1652, 1600, 1449, 1073, 980, 750, 690 cm^{-1}; MS (EI, 70 eV): *m*/*z* (%): 186 [M^+] (10), 159 (10), 131 (100), 103 (53), 77 (27), 43 (22); HRMS: (EI, 70 eV): *m*/*z* calcd for $C_{13}H_{14}O$ [M^+]: 186.1045; found: 186.1043.

3l *(Z isomer)*: ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 7.39$–7.08 (m, 5H), 5.99 (q, $^3J(H,H) = 7$ Hz, 1H), 2.43 (t, $^3J(H,H) = 7$ Hz, 2H), 1.90 (d, $^3J(H,H) =$ 7 Hz, 3H), 1.64–1.58 (m, 2H), 0.88 ppm (t, $^3J(H,H) = 7$ Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 206.9$ (C=O), 144.3 (C), 138.0 (C), 129.5 (C=*C*H), 128.6 (CH), 127.5 (CH), 126.9 (CH), 44.9 (CH_2), 17.2 (CH_2), 15.4 (CH_3), 13.7 ppm (CH_3); IR (neat): $\tilde{\nu} = 3053$, 2963, 2934, 1673, 1591, 1494, 1379, 1141, 760, 702 cm^{-1}; MS (EI, 70 eV): *m*/*z* (%): 188 [M^+] (25), 173 (5), 145 (17), 118 (11), 117 (100), 91 (15), 43 (12); HRMS: (EI): *m*/*z* calcd for $C_{13}H_{16}O$ [M^+]: 188.1201; found: 188.1195.

3m *(E,Z mixture)*: ^{1}H NMR (400 MHz, $CDCl_3$) for the *E* isomer: $\delta =$ 7.39–7.08 (m, 5H), 6.96 (q, $^3J(H,H) = 7$ Hz, 1H), 2.52 (t, $^3J(H,H) = 7$ Hz, 2H), 1.71 (d, $^3J(H,H) = 7$ Hz, 3H), 1.61–1.54 (m, 2H), 1.30–1.20 (m, 8H), 0.86 ppm (t, $^3J(H,H) = 7$ Hz, 3H); ^{1}H NMR (400 MHz, $CDCl_3$) for the *Z* isomer: $\delta = 7.39$–7.08 (m, 5H), 5.99 (q, $^3J(H,H) = 7$ Hz, 1H), 2.44 (t, ^3J-(H,H) = 7 Hz, 2H), 1.90 (d, $^3J(H,H) = 7$ Hz, 3H), 1.61–1.54 (m, 2H), 1.30–1.20 (m, 8H), 0.86 ppm (t, $^3J(H,H) = 7$ Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) for the *E* isomer: $\delta = 201.1$ (C=O), 143.9 (C), 136.1 (C), 137.5 (C=*C*H), 129.6 (CH), 128.2 (CH), 127.3 (CH), 39.5 (CH_2), 31.6 (CH_2), 29.5 (CH_2), 29.2 (CH_2), 29.1 (CH_2), 22.6 (CH_2), 15.5 (CH_3), 14.0 ppm (CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) for the *Z* isomer: $\delta = 207.1$ (C=O), 144.3 (C), 138.1 (C), 129.5 (C=*C*H), 128.6 (CH), 127.5 (CH), 126.9 (CH), 43.0 (CH_2), 31.6 (CH_2), 29.3 (CH_2), 29.0 (CH_2), 23.8 (CH_2), 23.7 (CH_2), 15.4 (CH_3), 14.0 ppm (CH_3); IR (neat): $\tilde{\nu} = 2920$, 2855, 1692, 1625, 1494, 1132, 1069, 760, 702 cm^{-1}; MS (EI, 70 eV) for the *E* isomer: *m*/*z* (%): 244 [M^+] (14), 229 (16), 160 (59), 145 (33), 117 (100), 115 (42), 91 (19), 57 (17); HRMS: (EI, 70 eV): *m*/*z* calcd for $C_{17}H_{24}O$ [M^+]: 244.1827; found: 244.1836; MS (EI, 70 eV) for the *Z* isomer: *m*/*z* (%): 244 [M^+] (14), 160 (24), 145 (22), 117 (100), 115 (28), 91 (14), 57 (12); HRMS: (EI, 70 eV): *m*/*z* calcd for $C_{17}H_{24}O$ [M^+]: 244.1827; found 244.1833.

5n: ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 7.98$–7.40 (m, 5H), 5.89 (dt, ^3J-(H,H) = 19, 9 Hz, 1H), 5.18–5.14 (m, 2H), 3.78 (t, $^3J(H,H) = 9$ Hz, 1H), 2.30–2.16 (m, 1H), 0.93 ppm (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta =$ 201.6 (C=O), 137.3 (CH), 136.2 (C), 132.9 (CH), 128.5 (CH), 128.3 (CH), 118.3 (CH_2), 59.3 (CH), 30.6 (CH), 21.3 (CH_3), 19.7 ppm (CH_3); IR (neat): $\tilde{\nu} = 3066$, 2956, 1682, 1594, 1442, 1202, 999, 919, 839, 759, 707 cm^{-1}; MS (EI, 70 eV): *m*/*z* (%): 188 [M^+] (1), 170 (2), 145 (2), 115 (2), 105 (100), 77 (34), 55 (3), 51 (7); HRMS: (EI, 70 eV): *m*/*z* calcd for $C_{13}H_{16}O$ [M^+]: 188.1201; found: 188.1205.

5o: ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 8.00$–7.37 (m, 5H), 5.91 (ddd, ^3J-(H,H) = 18, 10, 7 Hz, 1H), 5.19–5.13 (m, 2H), 4.06 (dd, $^3J(H,H) = 15$, 7 Hz, 1H), 1.65–1.55 (m, 2H), 1.50–1.30 (m, 2H), 0.92 ppm (t, $^3J(H,H) =$ 7 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 201.2$ (C=O), 137.2 (CH), 136.8 (C), 132.9 (CH), 128.6 (CH), 128.4 (CH), 117.3 (CH_2), 51.5 (CH), 34.3 (CH_2), 20.4 (CH_2), 14.0 ppm (CH_3); IR (neat): $\tilde{\nu} = 3050$, 2960, 1682, 1446, 1230, 991, 915, 703 cm^{-1}; MS (EI, 70 eV): *m*/*z* (%): 188 [M^+] (3), 145 (1), 120 (1), 106 (11), 105 (100), 77 (40), 51 (8); HRMS: (EI, 70 eV): *m*/*z* calcd for $C_{13}H_{16}O$ [M^+]: 188.1201; found: 188.1208.

Acknowledgements

This work was supported by a Grant-in-Aid for Scientific Research from the Ministry of Education, Culture, Sports, Science and Technology, Japan, "High-Tech Research Center" Project for Private Universities: matching fund subsidy from the Ministry of Education, Culture, Sports, Science and Technology, 2005–2009.

[1] a) G. C. Fu, *Modern Rhodium-Catalyzed Organic Reactions* (Ed.: P. A- Evans), Wiley-VCH, Weinheim, **2005**, Chapter 7, pp. 79–91; b) C.-H. Jun, E. A. Jo, J.-W. Park, *Eur. J. Org. Chem.* **2007**, 1869; c) K. Tanaka, *J. Synth. Org. Chem. Jpn.* **2005**, *63*, 351.

[2] For examples of intramolecular alkyne hydroacylations, see: a) G. C. Fu, K. Tanaka, *J. Am. Chem. Soc.* **2001**, *123*, 1434; b) G. C. Fu, K. Tanaka, *Angew. Chem.* **2002**, *114*, 1004; *Angew. Chem. Int. Ed.* **2002**, *41*, 962; c) G. C. Fu, K. Tanaka, *J. Am. Chem. Soc.* **2002**, *124*, 10296; d) G. C. Fu, K. Tanaka, *J. Am. Chem. Soc.* **2003**, *125*, 8078; e) K. Takeishi, K. Sugishima, K. Sasaki, K. Tanaka, *Chem. Eur. J.* **2004**, *10*, 5681; f) K. Tanaka, K. Sasaki, K. Takeishi, M. Hirano, *Eur. J. Org. Chem.* **2007**, 5675.

[3] For examples of directing-group assisted alkyne hydroacylation, see: a) K. Kokubo, K. Matsumasa, M. Miura, M. Nomura, *J. Org. Chem.* **1997**, *62*, 4564; b) C.-H. Jun, H. Lee, J.-B. Hong, B.-I. Kwon, *Angew. Chem.* **2002**, *114*, 2250; *Angew. Chem. Int. Ed.* **2002**, *41*, 2146; c) M. C. Willis, H. E. Randell-Sly, S. Brayshaw, G. S. Currie, *Org. Lett.* **2005**, *7*, 2249; d) G. L. Moxham, H. E. Randell-Sly, S. K. Brayshaw, R. L. Woodward, A. S. Weller, M. C. Willis, *Angew. Chem.* **2006**, *118*, 7780; *Angew. Chem. Int. Ed.* **2006**, *45*, 7618; e) M. C. Willis, H. E. Randell-Sly, R. L. Woodward, S. McNally, G. S. Currie, *J. Org. Chem.* **2006**, *71*, 5291; f) X. Y. Rueda, S. Castillon, *J. Organomet. Chem.* **2007**, *692*, 1628; g) G. L. Moxham, H. E. Randell-Sly,

S. K. Brayshaw, A. S. Weller, M. C. Willis, *Chem. Eur. J.* **2008**, *14*, 8383, and references therein.
[4] T. Tsuda, T. Kiyoi, T. Saegusa, *J. Org. Chem.* **1990**, *55*, 2554.
[5] For reviews, see: a) *Iridium Complexes in Organic Synthesis* (Eds.: L. A. Oro, C. Claver), Wiley, New York, **2009**; b) G. Guillena, D. J. Rámon, M. Yus, *Angew. Chem.* **2007**, *119*, 2410; *Angew. Chem. Int. Ed.* **2007**, *46*, 2358; c) Y. Ishii, S. Sakaguchi, *Bull. Chem. Soc. Jpn.* **2004**, *77*, 909; d) R. Takeuchi, S. Kezuka, *Synthesis* **2006**, 3349; e) K. Fujita, R. Yamaguchi, *Synlett* **2005**, 560, and references therein.
[6] a) K. Taguchi, H. Nakagawa, T. Hirabayashi, S. Sakaguchi, Y. Ishii, *J. Am. Chem. Soc.* **2004**, *126*, 72; b) K. Maeda, Y. Obora, S. Sakaguchi, Y. Ishii, *Bull. Chem. Soc. Jpn.* **2008**, *81*, 689; c) M. Morita, Y. Obora, Y. Ishii, *Chem. Commun.* **2007**, 2850; d) T. Matsu-ura, S. Sakaguchi, Y. Obora, Y. Ishii, *J. Org. Chem.* **2006**, *71*, 8306; e) H. Koda, T. Matsu-ura, Y. Obora, Y. Ishii, *Chem. Lett.* **2009**, *38*, 838.
[7] Y. Obora, S. Hatanaka, Y. Ishii, *Org. Lett.* **2009**, *11*, 3510.
[8] Communicated in part in the following: a) S. Hatanaka, Y. Obora, Y. Ishii, Abstract of Papers, 89th Annual Meeting of Chemical Society of Japan, Chemical Society of Japan, Tokyo, **2009**; b) S. Hatanaka, Y. Obora, Y. Ishii, 56th Symposium on Organometallic Chemistry Kyoto, Japan, The Kinki Chemical Society, Osaka, **2009**.
[9] V. M. Williams, J. C. Leung, R. L. Patman, M. J. Krische, *Tetrahedron* **2009**, *65*, 5024.
[10] We also performed time-course monitoring experiments of the reaction of **6a** with **2a** under the reaction conditions in Table 3, entry 1. In contrast to the result shown in Figure 1, negligible amounts of the formation of **4a** were observed during the reaction course (see Figure S1 in the Supporting Information). Therefore, another possible reaction pathway that initiates the oxidative addition of aldehydes to the iridium catalyst followed by alkyne insertion can not be ruled out. An alternative reaction path is shown in the Supporting Information (Figure S2).
[11] Y. Urawa, K. Nishiura, S. Souda, K. Ogura, *Synthesis* **2003**, 2882.
[12] a) M. Steiniger, H. J. Schaefer, *Bull. Chem. Soc. Jpn.* **1988**, *61*, 125; b) J. W. Labadie, J. K. Stille, *J. Am. Chem. Soc.* **1983**, *105*, 6129.
[13] T. E. Goodwin, D. G. Ratcliff, C. M. Crowder, N. K. Seitzinger, *J. Org. Chem.* **1982**, *47*, 815.
[14] G. Dana, S. Le Thi Thuan; J. Gharbi-Benarous, *Bull. Soc. Chim. Fr.* **1974**, 2089.
[15] Y. L. Pascal, *Ann. Chim.* **1968**, 245.
[16] J. D. Sieber, S. Liu, J. P. Morken, *J. Am. Chem. Soc.* **2007**, *129*, 2214.
[17] a) V. V. Diev, O. N. Stetsenko, T. Q. Tung, J. Kopf, R. R. Kostikov, A. P. Molchanov, *J. Org. Chem.* **2008**, *73*, 2396; b) M. Ochiai, A. Yoshimura, T. Mori, Y. Nishi, M. Hirobe, *J. Am. Chem. Soc.* **2008**, *130*, 3742.
[18] A. Aaziz, S. Oudeyer, E. Leonel, J. P. Paugam, J.-Y. Nedelec, *Synth. Commun.* **2007**, *37*, 1147.
[19] T. Takahashi, C. Xi, Z. Xi, M. Kageyama, R. Fischer, K. Nakajima, E. Negishi, *J. Org. Chem.* **1998**, *63*, 6802.
[20] G. Combaut, L. Giral, *Bull. Soc. Chim. Fr.* **1969**, *9*, 3258.
[21] A. T. Nielsen, C. Gibbons, C. A. Zimmerman, *J. Am. Chem. Soc.* **1951**, *73*, 4696.
[22] K.-T. Tan, S.-S. Chng, H.-S. Cheng, T.-P. Loh, *J. Am. Chem. Soc.* **2003**, *125*, 2958.
[23] M. Gohain, B. J. Gogoi, D. Prajapati, J. S. Sandhu, *New J. Chem.* **2003**, *27*, 1038.

Received: September 25, 2009
Published online: December 22, 2009

