HETEROCYCLES, Vol. 86, No. 1, 2012, pp. 267 - 280. © 2012 The Japan Institute of Heterocyclic Chemistry
Received, 21st March, 2012, Accepted, 16th April, 2012, Published online, 19th April, 2012
DOI: 10.3987/COM-12-S(N)7

REISSERT-LIKE ALKENYLATION OF AZAAROMATIC COMPOUNDS WITH ALKENYLZIRCONOCENE CHLORIDE COMPLEXES

Akio Saito,[¶]* Kohei Sudo, Koichi Iimura, Miki Hayashi, and Yuji Hanzawa*

Laboratory of Organic Reaction Chemistry, Showa Pharmaceutical University, 3-3165 Higashi-tamagawagakuen, Machida, Tokyo 194-8543, Japan; hanzaway@ac.shoyaku.ac.jp.

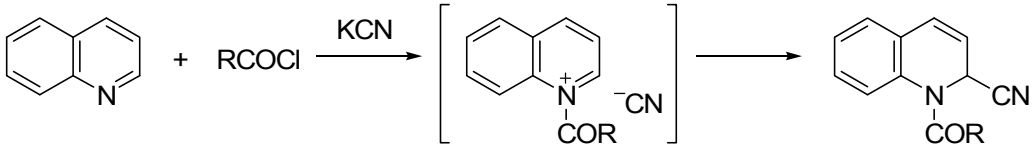
Abstract –Reissert-like alkenylation of azaaromatic compounds by the use of alkenylzirconocene chloride as a nucleophile was carried out in the presence of a stoichiometric amount of $ClCO_2Et$. The regioselectivity of the nucleophilic attack depends on reacting heterocycles, solvent, and the presence of copper catalyst. Thus, the reaction of quinoline derivatives with alkenylzirconocene chloride in $MeNO_2$ proceeded in a preferential 1,2-addition manner to give *N*-ethoxycarbonyl-2-alkenyl-1,2-dihydroquinolines, and the reaction of pyridine in CH_2Cl_2 under Cu(I)-catalyzed conditions proceeded in a 1,4-addition manner to give *N*-ethoxycarbonyl-4-alkenyl-1,4-dihydropyridine. The alkenylation of 3,4-dihydroisoquinoline with alkenylzirconocene chloride was also carried out in an enantioselective manner under Cu(I)/chiral Box-catalyzed conditions to give alkenylated tetrahydroisoquinoline compound (75%ee).

INTRODUCTION

Nucleophilic additions of carbon nucleophiles to *N*-acyliminium ions provide us with efficient procedures for the preparation of amine derivatives, and the procedure has been applied to the synthesis of alkaloids and medicinally significant molecules.[1] One of the typical reactions applied to azaaromatics, known as the Reissert reaction, employs a cyanide nucleophile in the presence of *N*-acylating agents affording *N*-acyl-2-cyano-1,2-dihydroheterocycles (Scheme 1).[2] On the other hand, Reissert-like reactions of the azaaromatic compounds using organometallics (Mg,[3] Cu,[4] Sn,[5] and their allyl[6] or alkynyl species[7]) or metal enolates[8] instead of the cyanide nucleophile have been extensively studied to enhance the chemical value of the Reissert reaction. Recently, it was shown that alkenyl boronic acid (Petasis-type reaction)[9] or

[¶] Present address: Division of Applied Chemistry, Institute of Engineering, Tokyo University of Agriculture and Technology, 2-24-16 Nakamachi, Koganei 184-8588, Japan

of the aluminum[10] was another choice of organometallics for the Reissert-like alkenylation process.



Scheme 1. Reissert reaction

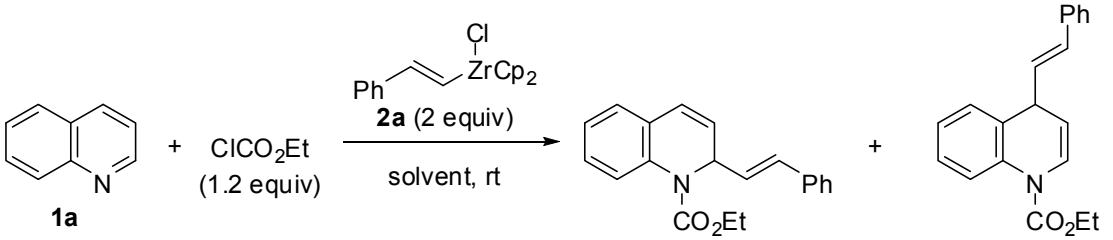
In our continuous study about the carbon-carbon bond formation using organozirconocene chloride complexes as a synthetic reagent,[11,12] we are tempted to examine the use of organozirconocene chloride complexes for the Reissert-like alkenylation. Although the alkenylzirconocene chlorides are readily accessible through the hydrozirconation of alkyne compounds with Schwartz reagent [$Cp_2Zr(H)Cl$][13] or by the treatment of alkenyl halide with Negishi reagent [Cp_2Zr-*n*Bu_2],[14] the poor reactivity of the complexes toward the electrophiles, such as aldehydes, ketones and imines, often hampered their use for organic synthesis. Thus, the search for catalysts and/or activating agents is necessitated to achieve the objective carbon-carbon bond forming reactions. Our recent work revealed that the reaction of alkenylzirconocene chloride complexes and 3,4-dihydroisoquinoline in the presence of acylating agent brought about the enantioselective formation of 1-alkenyl-2-acyltetrahydroisoquinoline under the Cu(I)/chiral Box-catalyzed conditions.[15] It was also found that Reissert-like alkenylation of quinoline with alkenylzirconocene chloride was promoted by the activation through acylating agent without the use of Cu(I)-catalyst, albeit the poor regioselectivity (1,2- vs 1,4-addition).[15] In this paper, we describe the influence upon the regioselectivity of the Reissert-like alkenylation of azaaromatic compounds with alkenylzirconocene chlorides.

RESULTS AND DISCUSSION

At the outset, we focused on the improvement of the regioselectivity in the reaction of quinoline (**1a**) and (*E*)-styrylzirconocene chloride (**2a**, 2 equiv) in the presence of ethyl chloroformate ($ClCO_2Et$, 1.2 equiv) (Table 1). In CH_2Cl_2 solvent, treatment of **1a** with $ClCO_2Et$ at 0 °C for 30 min followed by the addition of **2a** to the reaction mixture proceeded the Reissert-like alkenylation at ambient temperature within 2 h (by TLC) to afford a mixture of 1,2-adduct **3a** (70%) and 1,4-adduct **4a** (25%) (**3a**/**4a** = 2.8/1) (entry 1). The use of nitromethane ($MeNO_2$) solvent, however, suppressed the formation of 1,4-adduct **4a** (3-7%, entries 5-7), and the yield of 1,2-adduct **3a** was improved up to 82% in the presence of 2.4 equiv of $ClCO_2Et$ (**3a**/**4a** = 27/1) (entry 7). Thus, the solvent choice is important for the regioselective formation of 1-acyl-2-alkenylation product **3a**, albeit other examined solvents (toluene, THF and CH_3CN) are unattractive (entries 2-4). Based on the results, the Reissert-like reactions of quinoline derivatives **1** with

2a and $ClCO_2Et$ were examined in either CH_2Cl_2 or $MeNO_2$ solvent (Table 2). The reactions of quinoline derivatives **1a-d** in CH_2Cl_2 completed at ambient temperature within 2 h (by TLC), except for the nitro-substituted **1e** (24 h). In all cases examined, however, a considerable amount of 1,4-adducts **4a-e** (10-36%) were formed along with 1,2-adducts **3a-e** (63-83%) (left column, Table 2). The use of $MeNO_2$ as a solvent brought about the improved 1,2-regioselectivities for the additions (**3a-e**: 52-93%, **4a-e**: 3-9%) (right column).

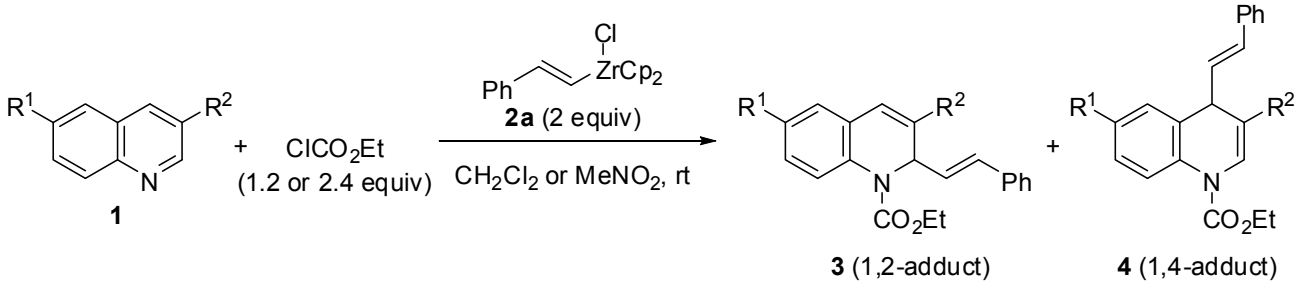
Table 1. Optimization for the regioselective Reissert-like alkenylation of quinoline (**1a**) with **2a**



Entry	Solvent	Time (h)	Yield		Recovery of **1a** (%)[a]
			3a (%)[a]	**4a** (%)[a]	
1	CH_2Cl_2	2	70[b]	25[b]	-
2	toluene	2	38	23	11
3	THF	2	36	35	17
4	MeCN	2	26	6	43
5	$MeNO_2$	2	33	4	40
6	$MeNO_2$	14	49	7	7
7[c]	$MeNO_2$	14	82[b]	3[b]	-
8[d]	CH_2Cl_2	2	46	35	-

[a] The yield was determined by ^{1}H-NMR analysis. [b] Isolated yield. [c] $ClCO_2Et$: 2.4equiv.
[d] Additive: 10 mol% CuBr.

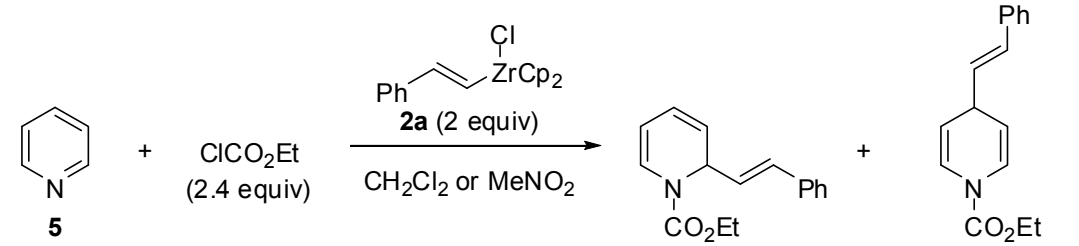
Table 2. Reissert-like alkenylation of quinoline derivatives **1** with **2a**



1	R^1	R^2	Reaction in CH_2Cl_2[a]			Reaction in $MeNO_2$[b]		
			Time (h)	**3** (%)[c]	**4** (%)[c]	Time (h)	**3** (%)[c]	**4** (%)[c]
1a	H	H	2	70	25	14	82	3
1b	H	Me	2	70	22	14	82	5
1c	Me	H	2	83	10	14	93	4
1d	MeO	H	2	63	36	14	74	5
1e	NO_2	H	24	66	23	22	52	9

[a] $ClCO_2Et$: 1.2 equiv. [b] $ClCO_2Et$: 2.4equiv. [c] Isolated yield.

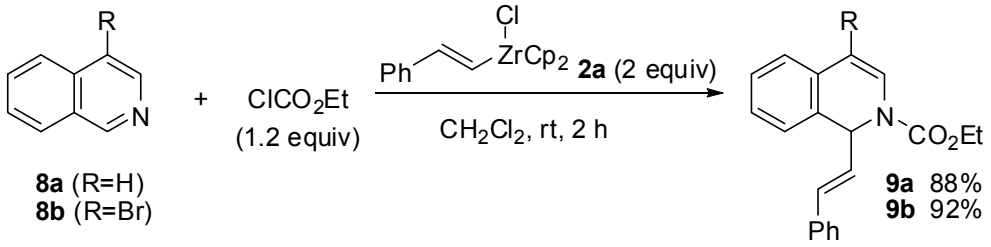
In the reaction of pyridine (**5**) and **2a** in the presence of $ClCO_2Et$, however, the use of $MeNO_2$ afforded a mixture of regioisomers **6** and **7** (53%) with a poor 1,2-regioselectivity (**6**/**7** = 3.8/1) (Scheme 2). It should be noted that the alkenylation in CH_2Cl_2 brought about the nonselective formation of products (67%, **6**/**7** = 1/1.4). The 1,4-regioselectivity was remarkably enhanced by the addition of catalytic CuBr (10 mol%) to the reaction mixture at -78 °C to give a mixture of products in high yield (95%, **6**/**7** = 1/18). Contrary to the reaction of pyridine, CuBr-catalyzed reaction of quinoline (**1a**) did not give an improved selectivity of regioisomers (81%, **3a**/**4a** = 1.3/1) (Table 1, entry 8) under otherwise identical conditions with pyridine. The presence of $ClCO_2Et$ is essential to bring about the reaction in every examined case. Thus, it is necessary to activate the azaaromatic compounds as shown in Scheme 1. Although details about the solvent effect and the role of the Cu(I)-catalyst for the regioselectivity remain uncertain at present,[16] it has been reported that the addition of Cu(I)-catalysts to Grignard reagents[3a] or the use of organocoppers[4] led to the preferred formation of the Reissert-like 1,4-addition product.



	$MeNO_2$,	rt, 24 h	42%	11%
	CH_2Cl_2,	rt, 3 h	27%	40%
Additive: 10mol% CuBr	CH_2Cl_2,	-78 °C, 3 h	5%	90%

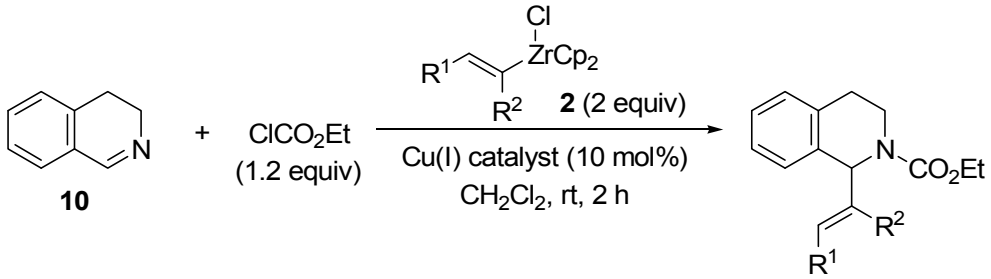
Scheme 2. Reissert-like alkenylation of pyridine (**5**) with **2a**

The alkenylation of isoquinoline derivative **8a** or **8b** with **2a** in the presence of $ClCO_2Et$ proceeded smoothly in CH_2Cl_2 at ambient temperature giving rise to the corresponding product **9a** or **9b** as a sole product in high yield (Scheme 3). Extension of the alkenylation using **2a** to 3,4-dihydroisoquinoline (**10**) reveals that Cu(I) catalyst in the coexisitence of *N*-acylating agent is required to bring about the efficient formation of alkenylated tetrahydroisoquinoline **11a** (Table 3). Among the examined Cu(I) catalysts,[17] Cu(OTf) (Entry 3) or $[Cu(MeCN)_4]PF_6$ (Entries 4-7) showed high efficiency for the formation of **11**, and alkyl-substituted alkenylzirconocene chlorides (**2b**, **2c** and **2d**) were also efficient nucleophiles in the reaction.



Scheme 3. Alkenylation of isoquinolines **8** with **2a**

Table 3. Reissert-like alkenylation of 3,4-dihydroisoquinoline (**10**) with **2a**

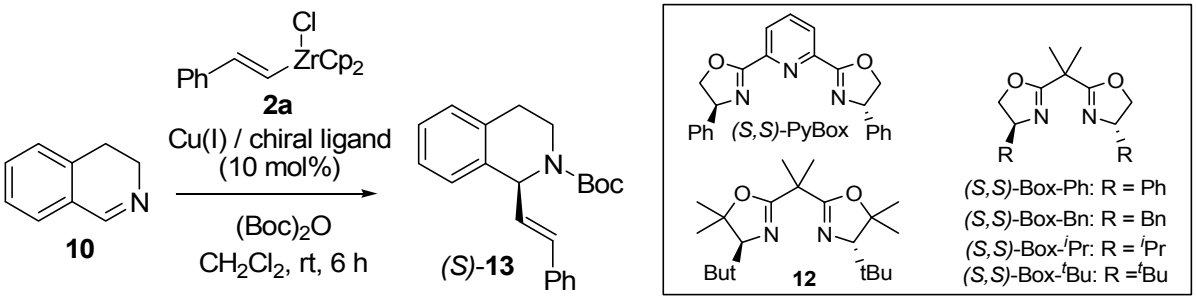


Entry	**2**	R^1	R^2	Cu(I)	**11**	Yield (%)[a]
1[b]	**2a**	Ph	H	-	**11a**	36
2				CuBr		68
3				CuOTf		81
4				$[Cu(MeCN)_4]PF_6$		87
5	**2b**	*n*Bu	H	$[Cu(MeCN)_4]PF_6$	**11b**	78
6	**2c**	*t*Bu	H	$[Cu(MeCN)_4]PF_6$	**11c**	72
7	**2d**	Et	Et	$[Cu(MeCN)_4]PF_6$	**11d**	80

[a] Isolated yield. [b] Reaction time: 16 h.

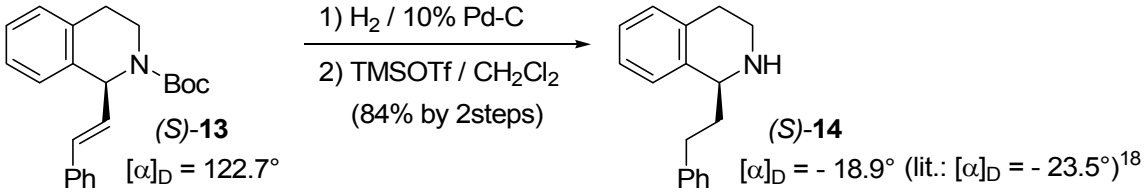
An attempt to carried out the enantioselective addition of **2a** to **10** using Cu(I)/chiral ligand catalytic systems indicated that chiral Box ligands to Cu(I) catalyst turned out to be fairly efficient in a sense of chiral induction (Table 4). Thus, by using a $[Cu(MeCN)_4]PF_6$ and *(S,S)*-Box ligand **12**,[18] the reaction of **10** with **2a** and di-*t*-butyl dicarbonate [$(Boc)_2O$] as an *N*-acylating agent at 0 °C for 24 h afforded *(S)*-**13** (75%ee) in 65% yield (Entry 12). The absolute configuration of *(S)*-**13** was determined by the conversion to compound **14**[19] whose absolute configuration has been established (Scheme 4).

Table 4. Enantioselective reactions of **2a** and **10**



Entry	Cu(I)	ligand	Yield (%)[a]	ee (%)[b]
1	CuOTf	*(S,S)*-PyBox-Ph	67	22
2		*(S,S)*-Box-Ph	87	30
3		*(S,S)*-Box-Bn	89	32
4		*(S,S)*-Box-^{i}Pr	84	40
5		*(S,S)*-Box-^{t}Bu	74	44
6	$[Cu(MeCN)_4]PF_6$	*(S,S)*-Box-^{t}Bu	90	50
7[c]		*(S,S)*-Box-^{t}Bu	63	68
8[c]		**12**	65	75

[a] Isolated yield. [b] Ee was determined by HPLC analysis (Chiralpak AD). [c] 0 °C, 24 h.



Scheme 4. Determination of the absolute configuration of (*S*)-**13**

CONCLUSIONS

The alkenylzirconocene chloride complex was found to be an efficient nucleophile for the Reissert-type alkenylation of azaaromatic compounds in the presence of a stoichiometric amount of $ClCO_2Et$. In the reaction, solvent effect ($MeNO_2$ or CH_2Cl_2) and/or the presence of Cu-catalyst are important for the regioselectivity of the alkenylation of quinolines and pyridines. The enantioselective addition of the alkenylzirconocene chloride to 3,4-dihydroisoquinoline was also achieved by the Cu(I)/chiral Box ligand catalytic system to give the biologically attractive tetrahydroisoquinoline compound in an optically active form.[20] We believe that the reactivity of alkenylzirconocene chloride described in the present paper indicates a new possibility for the use of organozirconocene complexes in organic synthesis.

EXPERIMENTAL

All melting points were taken on a Yanaco SP-M1 melting point apparatus (Yanagimoto Co.) and were uncorrected. IR spectra were taken on a HORIBA FT-710 FT-IR spectrometer. ^{1}H and ^{13}C NMR spectra were measured in $CDCl_3$ with a Bruker AV300M FT NMR spectrometer at 300 and 75 MHz, and the chemical shifts are given in ppm using $CHCl_3$ (7.26 ppm) for ^{1}H NMR and $CDCl_3$ (77.0 ppm) for ^{13}C NMR as an internal standard, respectively. Mass spectra and HRMS were recorded by FAB method on a

JMS-HX110 Mass spectrometer. Elemental analysis were measured on a Perkin-Elmer 240B or Elemental Vavio EL. For the TLC analysis, Merck precoated TLC plates (silica gel 60 F_{254}) were used. Column chromatography was performed on Silica gel 60N (63-200 μm, Kanto Kagaku Co., Ltd.). All of the organic solvents were dried over appropriate drying agents. Unless otherwise stated, all reactions were conducted under an argon atmosphere.

Starting Materials. 3,4-dihydroisoquinoline (**10**) was prepared by previously reported procedure.[21] All other compounds were commercially available.

General procedure for the preparation of alkenylzirconocene chlorides 2 in CH_2Cl_2. To a suspension of $Cp_2Zr(H)Cl$ (258 mg, 1.0 mmol) in CH_2Cl_2 (2.0 mL) was added an alkyne compound (1.2 mmol) at an ambient temperature. After the reaction mixture was stirred for 30 min at the same temperature, the CH_2Cl_2 solutions were used in the following experiments without any changes.

Preparation of (*E*)-styrylzirconocene chloride (2a) in $MeNO_2$. According to the above manner, the solution of **2a** in CH_2Cl_2 (2.0 mL) was prepared from $Cp_2Zr(H)Cl$ (258 mg, 1.0 mmol) and phenylalkyne (132 μL, 1.2 mmol). After the CH_2Cl_2 was removed in vacuo, $MeNO_2$ (2.0 mL) was added to the residue.

General procedure for the Reissert-like alkenylation of 2 with azaaromatic compounds. A premixed solution (30 min at 0 °C) of an azaaromatic compound (0.5 mmol) and $ClCO_2Et$ (0.6 or 1.2 mmol) in CH_2Cl_2 or $MeNO_2$ (3.0 mL) was added to a solution of **2** (1.0 mmol) in CH_2Cl_2 or $MeNO_2$ (2.0 mL) at an ambient temperature. After the consumption of the starting material (by TLC analysis), the reaction mixture was diluted with ether and filtered through a short alumina column. After concentration of the filtrate to dryness, the subsequent purification gave the corresponding acyl-alkenylated compound **3**, **4**, **6**, **7**, and/or **9**.

Ethyl 2-[(*E*)-styryl]quinoline-1(2*H*)-carboxylate (3a). IR (neat) ν 1716 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$) δ 1.33 (t, 3H, *J* = 7.1 Hz), 4.21-4.35 (m, 2H), 5.66-5.70 (m, 1H), 6.00-6.08 (m, 2H), 6.47-6.56 (m, 1H), 7.00-7.09 (m, 2H), 7.14-7.28 (m, 6H), 7.61 (br.d, 1H, *J* = 7.9 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.5, 54.3, 62.2, 124.1, 124.3, 125.6, 126.4, 126.7, 126.9, 127.1, 127.6, 127.7, 128.5, 131.5, 134.7, 136.5, 154.3; FAB-LM *m/z* 305.3 ($M+H^+$); FAB-HM Calcd for $C_{20}H_{20}NO_2$ 306.1494, Found 306.1481. Anal. Calcd for $C_{20}H_{19}NO_2$: C, 78.66; H, 6.27; N, 4.59. Found: C, 78.59; H, 6.36; N, 4.57.

Ethyl 4-[(*E*)-styryl]quinoline-1(4*H*)-carboxylate (4a). IR (neat) ν 1716 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$) δ 1.36 (t, 3H, *J* = 7.1 Hz), 4.16 (dd, 1H, *J* = 8.0, 5.0 Hz), 4.32 (q, 2H, *J* = 7.1 Hz), 5,28 (dd, 1H, *J* = 7.8, 5.0 Hz), 6.16 (dd, 1H, *J* = 15.7, 8.0 Hz), 6.41 (d, 1H, *J* = 15.7 Hz), 7.06-7.34 (m, 9H), 8.04 (d, 1H, *J* = 7.5 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.5, 41.5, 62.5, 111.1, 121.4, 125.0, 126.2, 126.3, 127.4, 128.5, 128.7, 129.4, 131.6, 135.8, 137.0, 152.6; FAB-LM *m/z* 304.2 ($M+H^+$); FAB-HM Calcd for $C_{20}H_{20}NO_2$ 306.1494, Found 306.1483.

Ethyl 3-methyl-2-[(*E*)-styryl]qunoline-1(2*H*)-carboxylate (3b). IR (neat) ν 1712 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$) δ 1.34 (t, 3H, *J* = 7.1 Hz), 1.97 (s, 3H), 4.19-4.39 (m, 2H), 5.44 (d, 1H, *J* = 7.3 Hz), 6.00 (dd, 1H, *J* = 15.7, 7.3 Hz), 6.30 (s, 1H), 6.35 (d, 1H, *J* = 15.7 Hz), 7.00-7.06 (m, 2H), 7.11-7.31 (m, 6H), 7.59 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.6, 20.7, 58.9, 62.2, 121.4, 124.0, 124.1, 124.4, 125.7, 126.6, 126.7, 127.7, 128.4, 131.8, 133.4, 136.5, 136.7, 154.2; FAB-LM *m/z* 319.2 ($M+H^+$); FAB-HM Calcd for $C_{21}H_{22}NO_2$ 320.1651. Found 320.1658.

Ethyl 3-methyl-4-[(*E*)-styryl]qunoline-1(4*H*)-carboxylate (4b). IR (neat) ν 1719 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$) δ 1.36 (t, 3H, *J* = 7.1 Hz), 1.83 (s, 3H), 3.91 (d, 1H, *J* = 8.3 Hz), 4.32 (q, 2H, *J* = 7.1 Hz), 6.08 (dd, 1H, *J* = 15.5, 8.3 Hz), 6.41 (d, 1H, *J* = 15.5 Hz), 6.83-6.84 (m, 1H), 7.09-7.37 (m, 8H), 8.01 (d, 1H, *J* = 8.3 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.5, 18.5, 47.6, 62.4, 119.7, 121.3, 121.5, 124.8, 126.4, 126.6, 127.3, 128.5, 128.6, 129.3, 130.3, 131.6, 135.8, 137.0, 152.6; FAB-LM *m/z* 319.2 ($M+H^+$); FAB-HM Calcd for $C_{21}H_{22}NO_2$ 320.1651. Found 320.1642.

Ethyl 6-methyl-2-[(*E*)-styryl]qunoline-1(2*H*)-carboxylate (3c). IR (neat) ν 1722 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$) δ 1.33 (t, 3H, *J* = 7.1 Hz), 2.29 (s, 3H), 4.20-4.38 (m, 2H), 5.65-5.70 (mt, 1H), 5.99-6.09 (m, 2H), 6.47-6.53 (m, 2H), 6.90 (d, 1H, *J* = 1.7 Hz), 7.00 (dd, 1H, *J* = 8.3, 1.7 Hz), 7.15-7.29 (m, 5H), 7.48-7.50 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.5, 20.8, 54.3, 62.1, 124.1, 125.7, 126.6, 126.7, 126.9, 127.7, 128.3, 128.4, 131.4, 132.2, 133.6, 136.6, 154.4; FAB-LM *m/z* 319.3 ($M+H^+$); FAB-HM Calcd for $C_{21}H_{22}NO_2$ 320.1651. Found 320.1659. Anal. Calcd for $C_{21}H_{21}NO_2$: C, 78.97; H, 6.63; N, 4.39. Found: C, 78.81; H, 6.72; N, 4.29.

Ethyl 6-methyl-4-[(*E*)-styryl]qunoline-1(4*H*)-carboxylate (4c). Mp 50 °C; IR (KBr) ν 1729 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$) δ 1.34 (t, 3H, *J* = 7.1 Hz), 2.29 (s, 3H), 4.12 (dd, 1H, *J* = 8.0, 5.0 Hz), 4.32 (q, 2H, *J* = 7.1 Hz), 5.26 (dd, 1H, *J* = 8.0, 5.0 Hz), 6.16 (dd, 1H, *J* = 15.7, 8.0 Hz), 6.42 (d, 1H, *J* = 15.7 Hz), 6.95-7.08 (m, 3H), 7.19-7.38 (m, 5H), 7.94 (d, 1H, *J* = 8.5 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.5, 20.7, 41.6, 62.4, 110.9, 121.2, 126.2, 126.4, 127.4, 127.5, 128.5, 129.1, 129.2, 131.8, 133.3, 134.5, 137.1, 152.6; FAB-LM *m/z* 319.2 ($M+H^+$); FAB-HM Calcd for $C_{21}H_{22}NO_2$ 320.1651, Found 320.1641.

Ethyl 6-methoxy-2-[(*E*)-styryl]qunoline-1(2*H*)-carboxylate (3d). IR (neat) ν 1716 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$) δ 1.28 (t, 3H, *J* = 7.1 Hz), 3.79 (s, 3H), 4.16-4.33 (m, 2H), 5.65-5.69 (m, 1H), 5.99-6.07 (m, 2H), 6.45-6.52 (m, 2H), 6.62 (d, 1H, *J* = 2.9 Hz), 6.74 (dd, 1H, *J* = 8.9, 2.9 Hz), 7.13-7.28 (m, 5H), 7.50-7.52 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.6, 54.2, 55.5, 62.1, 111.2, 113.1, 125.5, 125.6, 126.6, 127.7, 128.0, 128.4, 131.5, 136.5, 154.4, 156.1; FAB-LM *m/z* 335.2 ($M+H^+$); FAB-HM Calcd for $C_{21}H_{22}NO_3$ 336.1600. Found 336.1602.

Ethyl 6-methoxy-4-[(*E*)-styryl]qunoline-1(4*H*)-carboxylate (4d). IR (neat) ν 1716 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$) δ 1.35 (t, 3H, *J* = 7.1 Hz), 3.96 (s, 3H), 4.12 (dd, 1H, *J* = 8.0, 4.9 Hz), 4.31 (q, 2H, *J* = 7.1

Hz), 5,24 (dd, 1H, *J* = 7.8, 4.9 Hz), 6.14 (dd, 1H, *J* = 15.7, 8.0 Hz), 6.32 (d, 1H, *J* = 15.7 Hz), 6.68 (d, 1H, *J* = 3.0 Hz), 6.78 (dd, 1H, *J* = 9.2, 3.0 Hz), 7.04-7.07 (m, 1H), 7.16-7.43 (m, 4H), 7.99 (d, 1H, *J* = 9.2 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.5, 41.8, 55.5, 62.4, 110.5, 112.2, 113.4, 122.5, 126.1, 126.4, 127.4, 128.5, 129.5, 130.1, 130.8, 131.5, 152.6, 156.6; FAB-LM *m/z* 335.2 ($M+H^+$); FAB-HM Calcd for $C_{21}H_{22}NO_3$ 336.1600. Found 336.1598.

Ethyl 6-nitro-2-[(*E*)-styryl]qunoline-1(2*H*)-carboxylate (3e). Mp 125 °C; IR (KBr) ν 1720 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$) δ 1.38 (t, 3H, *J* = 7.1 Hz), 4.31-4.38 (m, 2H), 5.71-5.75 (m, 1H), 6.03 (dd, 1H, *J* = 15.8, 6.6 Hz), 6.10-6.24 (m, 1H), 6.47-6.52 (m, 1H), 6.61-6.65 (m, 1H), 7.19-7.30 (m, 5H), 7.81-7.90 (m, 1H), 7.97-8.12 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.4, 45.1, 54.8, 63.1, 121.8, 122.9, 124.1, 124.5, 126.6, 127.2, 128.2, 131.8, 132.5, 135.9, 140.2, 143.5, 153.7; FAB-LM *m/z* 351.3 ($M+H^+$); FAB-HM Calcd for $C_{20}H_{19}N_2O_4$ 351.1345. Found 351.1344. Anal. Calcd for $C_{20}H_{18}N_2O_4$: C, 68.56; H, 5.18; N, 8.00. Found: C, 68.85; H, 5.26; N, 7.74.

Ethyl 6-nitro-4-[(*E*)-styryl]qunoline-1(4*H*)-carboxylate (4e). Mp 71 °C; IR (KBr) ν 1735 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$) δ 1.40 (t, 3H, *J* = 7.1 Hz), 4.26 (dd, 1H, *J* = 8.1, 5.0 Hz), 4.37 (q, 2H, *J* = 7.1 Hz), 5,34 (dd, 1H, *J* = 7.8, 5.0 Hz), 6.15 (dd, 1H, *J* = 15.7, 8.1 Hz), 6.47 (d, 1H, *J* = 15.7 Hz), 7.10 (d, 1H, *J* = 7.8 Hz), 7.22-7.41 (m, 5H), 8.06-8.29 (m, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.4, 41.3, 63.4, 110.7, 115.6, 121.8, 121.9, 122.3, 124.4, 125.7, 126.5, 127.8, 128.6, 130.1, 130.3, 130.7, 136.4, 144.3; FAB-LM *m/z* 351.3 ($M+H^+$); FAB-HM Calcd for $C_{20}H_{19}N_2O_4$ 351.1345. Found 351.1351.

Ethyl 2-[(*E*)-styryl]pyridine-1(2*H*)-carboxylate (6). Mp 52 °C; IR (KBr) ν 1716 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$) δ 1.34 (t, 3H, *J* = 7.1 Hz), 4.20-4.30 (m, 2H), 5.26-5.59 (m, 3H), 5.99-6.04 (m, 1H), 6.18-6.25 (m, 1H), 6.44-6.58 (m, 1H), 6.70-6.84 (m, 1H), 7.21-7.41 (m, 5H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.5, 53.3, 62.3, 105.3, 120.5, 122.0, 124.9, 125.6, 127.7, 128.5, 131.2, 136.7, 155.7; FAB-LM *m/z* 255.2 ($M+H^+$); FAB-HM Calcd for $C_{16}H_{18}NO_2$ 256.1338. Found 256.1336.

Ethyl 4-[(*E*)-styryl]pyridine-1(4*H*)-carboxylate (7). IR (neat) ν 1718 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$) δ 1.32 (t, 3H, *J* = 7.1 Hz), 3.74-3.77 (m, 1H), 4.26 (q, 2H, *J* = 7.1 Hz), 4.86-4.93 (m, 2H), 6.15 (dd, 1H, *J* = 15.8, 7.4 Hz), 6.36 (d, 1H, *J* = 15.8 Hz), 6.77-6.92 (m, 2H), 7.20-7.42 (m, 5H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.5, 36.2, 62.5, 108.5, 120.8, 122.8, 126.3, 127.0, 128.5, 132.9, 137.2, 150.2; FAB-LM *m/z* 254.2 ($M+H^+$); FAB-HM Calcd for $C_{16}H_{18}NO_2$ 256.1338. Found 256.1332.

Ethyl 1-[(*E*)-styryl]isoqunoline-2(1*H*)-carboxylate (9a). IR (neat) ν 1712 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$) δ 1.36 (t, 3H, *J* = 7.1 Hz), 4.26-4.39 (m, 2H), 5.87 (d, 1H, *J* = 7.8 Hz), 6.01 (br.s, 1H), 6.29 (dd, 1H, *J* = 15.8, 6.0 Hz), 6.38 (d, 1H, *J* = 15.8 Hz), 6.96 (br.s, 1H), 7.07-7.34 (m, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.4, 57.3, 62.2, 108.0, 124.7, 124.9, 126.6, 126.7, 127.0, 127.6, 127.8, 128.3, 130.9, 136.5, 153.1; FAB-LM *m/z* 305.2 ($M+H^+$); FAB-HM Calcd for $C_{20}H_{20}NO_2$ 306.1494. Found 306.1489.

Ethyl 4-bromo-1-[(*E*)-styryl]isoqunoline-2(1*H*)-carboxylate (9b). IR (neat) ν 1733 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$) δ 1.34 (t, 3H, *J* = 7.1 Hz), 4.25-4.32 (m, 2H), 5.80-6.03 (m, 1H), 6.20-6.27 (m, 1H), 6.35 (d, 1H, *J* = 15.7 Hz), 6.89-7.35 (m, 9H), 7.48-7.51 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.5, 57.2, 62.9, 103.3, 124.9, 125.6, 128.3, 128.5, 131.0, 136.1,153.5; FAB-LM *m/z* 383.1 ($M+H^+$); FAB-HM Calcd for $C_{20}H_{19}NO_2Br$ 384.0599. Found 383.0526. Anal. Calcd for $C_{20}H_{18}NO_2Br$: C, 62.51; H, 4.72; N, 3.65. Found: C, 62.65; H, 5.11; N, 3.57.

Cu(I)-catalyzed acyl-alkenylation of 2a with pyridine (5). A premixed solution (30 min at 0 °C) of pyridine (40 mL, 0.5 mmol) and $ClCO_2Et$ (114 mL, 1.2 mmol) in CH_2Cl_2 (3.0 mL) was added to solution of **2a** (1.0 mmol) with CuBr (7.2 mg, 50 mmol) in CH_2Cl_2 (2.0 mL) at -78 °C. After being stirred at -78 °C for 3 h, the yields of **6** and **7** was determined by ^{1}H-NMR analysis using toluene as a internal standard.

Cu(I)-catalyzed acyl-alkenylation of 2 with 3,4-dihydroisoquinoline (10). A premixed solution (30 min at 0 °C) of pyridine (40 mL, 0.5 mmol) and $ClCO_2Et$ (114 mL, 1.2 mmol) in CH_2Cl_2 (3.0 mL) was added to solution of **2a** (1.0 mmol) with $[Cu(MeCN)_4]PF_6$ (18.6 mg, 50 μmol) in CH_2Cl_2 (2.0 mL) at an ambient temperature. After the consumption of the starting material (by TLC analysis), workup and purification as above described yielded **11**.

Ethyl 3,4-dihydro-1-[(E)-styryl]isoquinoline-2(*1H*)-carboxylate (11a). IR (neat) ν 1704 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$) δ 1.29 (t, 3H, *J* = 7.1 Hz), 2.73-2.81 (m, 1H), 2.90-3.01 (m, 1H), 3.29-3.33 (m, 1H), 4.12-4.25 (m, 2H), 5.78-5.81 (m, 1H), 6.32 (dd, 1H, *J* = 15.8, 5.6 Hz), 6.41 (d, 1H, *J* = 15.8 Hz), 7.13-7.37 (m, 10H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.8, 28.7, 38.5, 56.3, 61.5, 126.2, 126.5, 126.8, 127.7, 128.1, 129.0, 129.1, 131.4, 134.7, 136.6, 155.6; FAB-LM *m/z* 307.4 ($M+H^+$); FAB-HM Calcd for $C_{20}H_{22}NO_2$ 308.1651. Found 308.1644. Anal. Calcd for $C_{20}H_{21}NO_2$: C, 78.15; H, 6.89; N, 4.56. Found: C, 77.98; H, 7.09; N, 4.52.

Ethyl 1-[*(E)*-hex-1-enyl]-3,4-dihydroisoquinoline-2(*1H*)-carboxylate (11b). IR (neat) ν 1714 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$) δ 0.88 (t, 3H, *J* = 7.1 Hz), 1.24-1.38 (m, 4H), 1.29 (t, 3H, *J* = 7.1 Hz), 2.02 (dt, 2H, *J* = 6.8, 6.8 Hz), 2.73 (dt, 1H, *J* = 16.0, 3.7 Hz), 2.86-2.99 (m, 1H), 3.19-3.33 (m, 1H), 4.03-4.32 (m, 3H), 5.49 (dt, 1H, *J* = 14.9, 6.8 Hz), 5.50-5.66 (m, 2H), 7.08-7.23 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 13.8, 14.7, 22.1, 28.6, 31.2, 31.8, 38.1, 56.1, 61.2, 125.9, 126.5, 127.9, 128.7, 129.3, 132.9, 134.4, 135.6, 155.4; FAB-LM *m/z* 288.3 ($M+H^+$); FAB-HM Calcd for $C_{18}H_{26}NO_2$ 288.1964. Found 288.1956. Anal. Calcd for $C_{18}H_{25}NO_2$: C, 75.22; H, 8.77; N, 4.87. Found: C, 75.01; H, 8.76; N, 4.74.

Ethyl 3,4-dihydro-1-[*(E)*-3,3-dimethylbut-1-enyl]isoquinoline-2(*1H*)-carboxylate (11c). IR (neat) ν 1716 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$) δ 0.99 (s, 9H), 1.28 (t, 3H, *J* = 7.1 Hz), 2.73 (dt, 1H, *J* = 16.0, 3.7 Hz), 2.86-3.00 (m, 1H), 3.18-3.30 (m, 1H), 4.12-4.31 (m, 3H), 5.46 (dd, 1H, *J* = 15.4, 5.5 Hz),

5.51-5.67 (m, 2H), 7.07-7.25 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.7, 28.7, 29.4, 32.9, 38.1, 56.3, 61.2, 123.9, 126.0, 126.5, 127.9, 128.8, 134.5, 135.8, 143.7, 155.5; FAB-LM *m/z* 288.3 ($M+H^+$); FAB-HM Calcd for $C_{18}H_{26}NO_2$ 288.1964. Found 288.1971.

Ethyl 1-[*(E)*-hex-3-en-3-yl]-3,4-dihydroisoquinoline-2(*1H*)-carboxylate (11d). IR (neat) ν 1704 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$) δ 0.87 (t, 3H, *J* = 7.5 Hz), 1.05 (t, 3H, *J* = 7.5 Hz), 1.27 (t, 3H, *J* = 7.1 Hz), 1.94-2.09 (m, 3H), 2.13-2.28 (m, 1H), 2.71 (dt, 1H, *J* = 16.0, 3.8 Hz), 2.84-3.01 (m, 1H), 3.19-3.37 (m, 1H), 3.92-4.35 (m, 3H), 4.80 (t, 1H, *J* = 7.2 Hz), 5.59-5.85 (m, 1H), 6.98-7.05 (m, 1H), 7.08-7.20 (m, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 13.6, 14.3, 14.7, 20.8, 21.6, 28.1, 37.5, 58.3, 61.2, 125.4, 126.5, 128.6, 131.8, 135.2, 135.4, 141.0, 155.7; FAB-LM *m/z* 288.3 ($M+H^+$); FAB-HM Calcd for $C_{18}H_{26}NO_2$ 288.1964. Found 288.1965. Anal. Calcd for $C_{18}H_{25}NO_2$: C, 75.22; H, 8.77; N, 4.87. Found: C, 74.95; H, 8.84; N, 4.66.

Enantioselective acyl-alkenylation of 2a with 3,4-dihydroisoquinoline (10). A premixed solution (30 min at 0 °C) of **10** (65.6 mg, 0.5 mmol) and $(Boc)_2O$ (131 mg, 1.2 mmol) in CH_2Cl_2 (3.0 mL) was added at 0 °C to solution of **2a** (1.0 mmol) in CH_2Cl_2 (2.0 mL), which was pretreated with a premixed solution (5 min at a ambient temperature) of $[Cu(MeCN)_4]PF_6$ (18.6 mg, 50 μmol) and Box ligand **12** (11.8 mg, 50 μmol) in CH_2Cl_2 (1.0 mL). After being stirred at 0 °C for 24 h, the workup and purification as above described yielded **13** (115.7 mg, 69%, 75% ee, $[\alpha]_D$ = 122.7).

***tert*-Butyl 3,4-dihydro-1-[*(E)*-styryl]isoquinoline-2(*1H*)-carboxylate (13)**. IR (neat) ν 1698 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$) δ 1.52 (s, 9H), 2.71-2.79 (m, 1H), 2.88-2.99 (m, 1H), 3.23-3.29 (m, 1H), 4.07-4.13 (m, 1H), 5.69-5.71 (m, 1H), 6.29 (dd, 1H, *J* = 15.8, 5.8 Hz), 6.40 (d, 1H, *J* = 15.8 Hz), 7.12-7.34 (m, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 28.5, 28.8, 79.9, 126.2, 126.3, 126.5, 126.8, 127.6, 128.1, 128.5, 128.9, 129.3, 131.1, 134.9, 134.9, 136.7, 154.7; FAB-LM *m/z* 336.4 ($M+H^+$); FAB-HM Calcd for $C_{22}H_{26}NO_2$ 336.1964. Found 336.1962. Anal. Calcd for $C_{22}H_{25}NO_2$: C, 78.77; H, 7.51; N, 4.18. Found: C, 78.84; H, 7.63; N, 4.18.

Conversion of 13 to *(R)*-1,2,3,4-tetrahydro-1-phenethylisoquinoline (14). Under hydrogen atmosphere, a solution of **13** (124.4 mg, 0.37 mmol, 75% ee) and 10% Pd-C (150 mg) was stirred at an ambient temperature for 12 h. After concentration of the obtained filtrate by the removal of Pd-C, a solution of the residue in CH_2Cl_2 (5.0 mL) was treated with TMSOTf (130 μL, 0.72 mmol) at an ambient temperature for 10 min. The reaction mixture was quenched with sat. $NaHCO_3$ and extrated with AcOEt. The combined organic extracts was dried over anhydrous $MgSO_4$ and concentrated on vacuo. The residue was purified on silica gel column chromatography to give **14** (73.5 mg, 84%, $[\alpha]_D$ = -18.9). **14** was identified by ^{1}H-NMR spectrum reported in the literature.[19]

ACKNOWLEDGEMENTS

This work was supported by Grant-in-Aid for Scientific Research (C), Japan Society for the Promotion of Science (No 22590016).

REFERENCES AND NOTES

1. (a) W. N. Speckamp and M. J. Moolenaar, *Tetrahedron*, 2000, **56**, 3817; (b) A. Yazici and S. G. Pyne, *Synthesis*, 2009, 339; (c) A. Yazici and S. G. Pyne, *Synthesis*, 2009, 513; (d) W. Sliwa, *Heterocycles*, 1986, **24**, 181; (e) M. Ahamed and M. H. Todd, *Eur. J. Org. Chem.*, 2010, 5935; (f) N. Kielland and R. Lavilla, *Top. Heterocycl. Chem.*, 2010, **25**, 127.
2. (a) A. Reissert, *Ber. Dtsch. Chem. Ges.* 1905, **38**, 1603; (b) F. D. Popp and A. Soto, *J. Chem. Soc.*, 1963, 1760; (c) R. H. Reuss, N. G. Smith, and L. J. Winters, *J. Org. Chem.*, 1974, **39**, 2027. Recent examples; (d) M. Takamura, K. Funabashi, M. Kanai, and M. Shibasaki, *J. Am. Chem. Soc.*, 2001, **123**, 6801; (e) M. Pauvert, S. C. Collet, M.-J. Bertrand, A. Y. Guingant, and M. Evain, *Tetrahedron Lett.*, 2005, **46**, 2983; (f) J. S. Yadav, B. V. S. Reddy, M. Srinivas, and K. Sathaiah, *Tetrahedron Lett.*, 2005, **46**, 3489.
3. (a) D. L. Comins and A. H. Abdullah, *J. Org. Chem.*, 1982, **47**, 4315; (b) R. Yamaguchi, Y. Nakazono, T. Matsuki, E. Hata, and M. Kawanishi, *Bull. Chem. Soc. Jpn.*, 1987, **60**, 215; (c) S. Wendeborn, T. Winkler, and I. Foisy, *Tetrahedron Lett.*, 2000, **41**, 6387; (d) A. B. Charette, M. Grenon, A. Lemire, M. Pourashraf, and J. Martel, *J. Am. Chem. Soc.*, 2001, **123**, 11829.
4. (a) E. Piers and M. Soucy, *Can. J. Chem*., 1974, **52**, 3563; (b) K. Akiba, Y. Iseki, and M. Wada, *Bull. Chem. Soc. Jpn*., 1984, **57**, 1994; (c) P. Mangeney, R. Gosmini, S. Raussou, M. Commerçon, and A. Alexakis, *J. Org. Chem*., 1994, **59**, 1877; (d) M. J. Shiao, K. H. Liu, and L. G. Lin, *Synlett*, 1992, 655.
5. (a) R. Yamaguchi, M. Moriyasu, M. Yoshioka, and M. Kawanishi, *J. Org. Chem.*, 1985, **50**, 287; (b) R. Yamaguchi, M. Moriyasu, and M. Kawanishi, *Tetrahedron Lett.*, 1986, **27**, 211; (c) R. Yamaguchi, E. Hata, and K. Utimoto, *Tetrahedron Lett.*, 1988, **29**, 1785; (d) R. Yamaguchi, A. Otsuji, and K. Utimoto, *J. Am. Chem. Soc.*, 1988, 110, 2186; (e) R. Yamaguchi, E. Hata, and K. Utimoto, *J. Org. Chem.*, 1988, **53**, 3507.
6. (a) R. Yamaguchi, M. Tanaka, T. Matsuda, T. Okano, T. Nagura, and K. Fujita, *Tetrahedron Lett.*, 2002, **43**, 8871; (b) S.-H. Lee, Y.-S. Park, M.-H. Nam, and C.-M. Yoon, *Org. Biomol. Chem.*, 2004, **2**, 2170; (c) S. Yamada and M. Inoue, *Org. Lett.,* 2007, **9**, 1477.
7. (a) R. Yamaguchi, Y. Omoto, M. Miyake, and K. Fujita, *Chem. Lett.*, 1998, **17**, 547; (b) G. Guanti, S. Perrozzi, and R. Riva, *Tetrahedron: Asymmetry*, 1998, **9**, 3923; (c) Y. Yamazaki, K. Fujita, and R. Yamaguchi, *Chem. Lett.*, 2004, **33**, 1316; (d) J. S. Yadav, B. V. S. Reddy, M. Sreenivas, and K.

Sathaiah, *Tetrahedron Lett.*, 2005, **46**, 8905; (e) D. A. Black, R. E. Beveridge, and B. A. Arndtsen, *J. Org. Chem.*, 2008, **73**, 1906.

8. (a) K. Akiba, M. Nakatani, M. Wada, and Y. Yamamoto, *J. Org. Chem.*, 1985, **50**, 63; (b) S. Yamada and C. Morita, *Chem. Lett.*, 2001, **30**, 1034; (c) Y.-M. Chang, Y.-S. Park, S.-H. Lee, and C. M. Yoon, *Tetrahedron Lett.*, 2004, **45**, 9049; (d) H. Rudler, B. Denise, Y. Xu, A. Parlier, and J. Vaissermann, *Eur. J. Org. Chem.*, 2005, 3724; (e) J. S. Yadav, B. V. S. Reddy, M. K. Gupta, U. Dash, D. C. Bhunia, and S. S. Hossain, *Synlett*, 2007, 2801; (f) H. Huang and W. Hu, *Tetrahedron*, 2007, **63**, 11850.
9. (a) Y.-M. Chang, S.-H. Lee, M.-H. Nam, M.-Y. Cho, Y.-S. Park, and C.-M. Yoon, *Tetrahedron Lett.*, 2005, **46**, 3053; (b) Y. Yamaoka, H. Miyabe, and Y. Takemoto, *J. Am. Chem. Soc.*, 2007, **129**, 6686; (c) T. Kodama, P. N. Moquist, and S. E. Schaus, *Org. Lett.*, 2011, **13**, 6316.
10. G. Signore, C. Malanga, and R. Menicagli, *Tetrahedron*, 2008, **64**, 197.
11. Y. Hanzawa, 'Titanium and Zirconium in Organic Chemistry,' ed. by I. Marek, Wiley-VHC, Weinheim, Germany, 2002; pp 149–179; Y. Hanzawa and T. Taguchi, *J. Synth. Org. Chem., Jpn.*, 2004, **62**, 314.
12. Recent examples; (a) A. Kakuuchi, T. Taguchi, and Y. Hanzawa, *Tetrahedron Lett.*, 2003, **44**, 923; (b) A. Kakuuchi, T. Taguchi, and Y. Hanzawa, *Tetrahedron*, 2004, **60**, 1293; (c) Y. Ikeuchi, T. Taguchi, and Y. Hanzawa, *Tetrahedron Lett.*, 2004, **45**, 4495; (d) Y. Ikeuchi, T. Taguchi, and Y. Hanzawa, *J. Org. Chem.*, 2005, **70**, 756; (e) Y. Ikeuchi, T. Taguchi, and Y. Hanzawa, *J. Org. Chem.*, 2005, **70**, 4354; (f) A. Saito, Y. Oka, Y. Nozawa, and Y. Hanzawa, *Tetrahedron Lett.*, 2006, **47**, 2201; (g) Y. Ikeuchi, T. Saitoh, T. Taguchi, and Y. Hanzawa, *Tetrahedron Lett.*, 2007, **48**, 2477; (h) Y. Hanzawa, Y. Takebe, A. Saito, A. Kakuuchi, and H. Fukaya, *Tetrahedron Lett.*, 2007, **48**, 6471; (i) Y. Hanzawa, Y. Oka, and M. Yabe, *J. Organometal. Chem.*, 2007, **692**, 4528.
13. J. Schwartz and J. A. Labinger, *Angew. Chem., Int. Ed. Engl.*, 1976, **15**, 333.
14. T. Takahashi, M. Kotora, R. Fischer, Y. Nishihara, and K. Nakajima, *J. Am. Chem. Soc.,* 1995, **117**, 11039.
15. A. Saito, K. Iimura, M. Hayashi, and Y. Hanzawa, *Tetrahedron Lett.*, 2009, **50**, 587.
16. It might be possible that the generation of alkenyl copper species through transmetalation takes part in the present alkenylations. Recently, however, in the copper(I)-catalyzed conjugate addition of alkenylzirconocene chloride to α,β-enone, Wipf *et al.* proposed a simultaneous three-component mechanism engaged by a π-base complexation of the Zr-alkene to Cu(I). See; (a) A. El-Batta, T. R. Hage, S. Plotkin, and M. Bergdahl, *Org. Lett.*, 2004, **6**, 107; (b) P. Wipf, W. Xu, J. H. Smitrovich, R. Lehmann, and L. M. Venanzi, *Tetrahedron*, 1994, **50**, 1935.
17. Other Cu(I)-catlysts (CuCl, CuI, CuCN), $[RhCl(cod)_2]_2$, and Et_2Zn brought about inferior results to

the cationic Cu(I)-catalysts.

18. M. Itagaki and Y. Yamamoto, *Tetrahedron Lett.*, 2006, **47**, 523.
19. A. I. Meyers, D. A. Dickman, and M. Boes, *Tetrahedron*, 1987, **43**, 5095.
20. Recent examples: a) K.-X. Chen, H.-Y. Xie, Z.-G. Li, and J.-R. Gao, *Bioorg. Med. Chem. Lett.*, 2008, **18**, 5381; (b) A.-J. Deng, and H.-L. Qin, *Phytochemistry*, 2010, **71**, 816; (c) Y.-J. Oh, J.-H. Youn, H.-J. Min, D.-H. Kim, S.-S. Lee, I.-H. Choi, and J.-S. Shin, *Int. Immunopharmacol*., 2011, **11**, 1160.
21. J. C. Pelletier and M. P. Cava, *J. Org. Chem.*, 1987, **52**, 616.