Tetrahedron 69 (2013) 2565–2571

Contents lists available at SciVerse ScienceDirect

Tetrahedron

journal homepage: www.elsevier.com/locate/tet

Palladium-catalyzed and copper-mediated cross-coupling reaction of aryl- or alkenylboronic acids with acid chlorides under neutral conditions: efficient synthetic methods for diaryl ketones and chalcones at room temperature

Daisuke Ogawa, Keita Hyodo, Masato Suetsugu, Jing Li, Yoshiaki Inoue, Mamoru Fujisawa, Masayuki Iwasaki, Kentaro Takagi, Yasushi Nishihara *

Division of Earth, Life, and Molecular Sciences, Graduate School of Natural Science and Technology, Okayama University, 3-1-1 Tsushimanaka, Kita-ku, Okayama 700-8530, Japan

ARTICLE INFO

Article history:
Received 28 December 2012
Received in revised form 16 January 2013
Accepted 21 January 2013
Available online 1 February 2013

Keywords:
Palladium
Copper
Cross-coupling
Ketones
Chalcones

ABSTRACT

Palladium-catalyzed cross-coupling reaction of aryl- or alkenylboronic acids with acid chlorides in the presence of copper(I) thiophene-2-carboxylate (CuTC) as an activator in diethyl ether at room temperature under strictly non-basic conditions affords the diaryl ketones or chalcones in moderate to excellent yields. A wide range of substrates bearing an electron-donating or an electron-withdrawing substituent on the aromatic ring are compatible.

1. Introduction

Unsymmetrical diaryl ketone and chalcone motifs are important building blocks to construct natural products and pharmaceuticals.[1] For example, as shown in Fig. 1, sulisobenzone is an important class of unsymmetrical diaryl ketones used as UV absorbers in some sunscreens that protects the skin from UV lights.[1a] Optically active (*S*)-ketoprofen is a nonsteroidal anti-inflammatory drug with approximately 160 times the anti-inflammatory potency of aspirin.[1b] On the other hand, sofalcone is one of the chalcone derivatives, which is used as an anti-ulcer with mucosa protective effect and isolated from the root of the Chinese medicinal plant *Sophora subprostrata*.[1c] Rottlerin (ROT) is widely used as an inhibitor toward protein kinase *C*-delta.[1d]

Since Haddach and McCarthy have reported the palladium-catalyzed cross-coupling reaction of acid chlorides with arylboronic acids under basic conditions for the synthesis of diaryl ketones,[2] the analogous reactions have been developed for a construction of diaryl ketone[3] and chalcone[4,5] derivatives. These coupling reactions involve several advantageous features relative to Friedel–Crafts acylation[6] or carbonylative Suzuki–Miyaura[7] and Mizoroki–Heck type reactions[8,9] of aryl halides in the presence of carbon monoxide: mild reaction conditions, high regioselectivity, and compatibility with various functional groups. In addition, organoboronic acids are non-toxic and stable toward heat, air, and

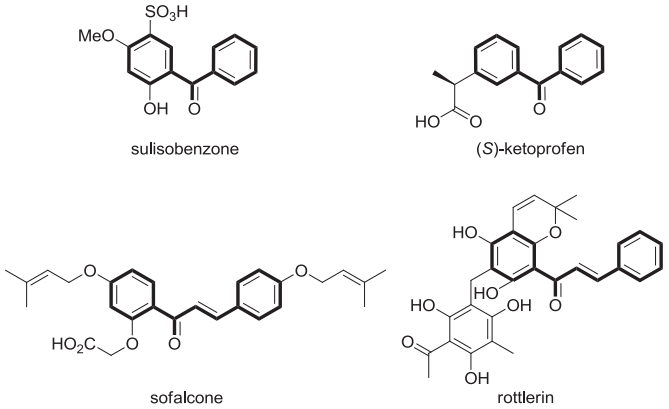


Fig. 1. Examples of representative diaryl ketones and chalcones.

* Corresponding author. Tel./fax: +81 86 251 7855; e-mail address: ynishiha@okayama-u.ac.jp (Y. Nishihara).

0040-4020/$ – see front matter © 2013 Elsevier Ltd. All rights reserved.
http://dx.doi.org/10.1016/j.tet.2013.01.058

moisture. Although numerous reports described the coupling of organoboron compounds with carboxylic acid derivatives under basic conditions,[10,11] to the best of our knowledge, there are no reports describing the synthesis of diaryl ketones or chalcones by cross-coupling reaction of organoboronic acids with acid chlorides under neutral conditions. We herein report the Pd-catalyzed cross-coupling reaction of aryl- or alkenylboronic acids with acid chlorides, which proceeds with an assistance of copper(I) thiophene-2-carboxylate (CuTC) under non-basic and mild reaction conditions (room temperature), leading to various diaryl ketones and chalcones.[12]

2. Results and discussion

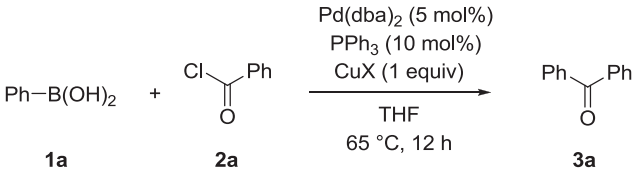
2.1. Cross-coupling reaction of arylboronic acids 1 with acid chlorides 2

Our initial investigation started with a cross-coupling reaction of phenylboronic acid (**1a**) with benzoyl chloride (**2a**) as model substrates in the presence of 5 mol % of $Pd(dba)_2$ plus 10 mol % of PPh_3 as the catalyst and 1 equiv of various copper compounds in THF at 65 °C for 12 h.[13] The results obtained are shown in Table 1. Benzophenone (**3a**) was obtained in the presence of various copper halides in 39–52% yields (Table 1, entries 1–3). Both $Cu(OAc)_2$ and CuOAc were found to be inferior (Table 1, entries 4 and 5). To our delight, when we used copper(I) thiophene-2-carboxylate (CuTC), the desired product **3a** was formed in 57% yield (Table 1, entry 6). The similar copper compounds, such as CuFC and CuPC showed low activity. In all cases, the reaction gave rise to the formation of a little amount of 4-chlorobutyl benzoate and biphenyl, presumably derived from homocoupling of **1a**. Formation of 4-chlorobutyl benzoate was attributed to Pd-mediated reaction of **2a** with THF as the reactant.[14] The similar boiling point and polarity of 4-chlorobutyl benzoate would be a drawback for an isolation of the desired **3a**.

Therefore, we screened other solvents for the reaction of **1a** with **2a** by using CuTC as an additive, as shown in Table 2. Reactions proceeded in ethereal solvents, such as 1,2-dimethoxyethane (DME) and Bu_2O in moderate yields (Table 2, entries 2 and 3). Reactions in higher temperature increased the yield (Table 2, entries 4 and 5). Surprisingly, diethyl ether as the solvent significantly suppressed the side reactions and the reaction preceded at room temperature in 78% yield (Table 2, entry 6). However, the yield of the reaction in less polar toluene decreased to 37% (Table 2, entry 7). Unfortunately, reactions in DMF or DMSO did not afford **3a** at all (Table 2, entries 8 and 9). When methanol was used as the solvent, methyl benzoate was formed in 59% yield (Table 2, entry 10). Diethyl ether seems to play an important role as the low concentration of CuTC and boronic acid **1a** in the reaction system is favorable to avoid excess amounts of activated organoboron species leading to homocoupling during the reaction, thereby giving rise to biphenyl as a byproduct. Further examination revealed that the reaction was completed within 3 h and **1a**/**2a**=2:1 ratio gave superior yield (97%).

Finally, we explored various catalyst systems and the results are summarized in Table 3. When we employed $Pd(PPh_3)_4$, **3a** was obtained in lower yield (60%, Table 3, entry 2) presumably due to suppression of catalytic reaction rate by the presence of excess PPh_3 ligands. Although $P(OPh)_3$ and P(2-furyl)$_3$ in combination with $Pd(dba)_2$ gave satisfactory yields (Table 3, entries 3 and 4), P(*t*-Bu)$_3$ and PMe_3 as the ligand and $Pd(dba)_2$ alone gave poor results (Table 3, entries 5–7). As the other palladium catalyst precursor, $Pd(OAc)_2$ with PPh_3 afforded **3a** in 71% yield, albeit along with 8% yield of biphenyl as the byproduct (Table 3, entry 8). Palladium catalyst containing bidentate phosphine ligand, such as $PdCl_2$(dppf) gave

Table 1
Effect of Cu compounds for cross-coupling reaction of **1a** with **2a**[a]

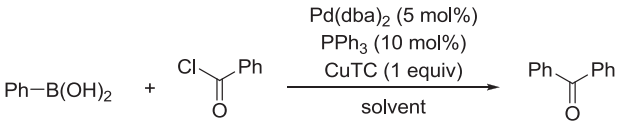


1a **2a** **3a**

Entry	Copper compound	Yield[b] (%)
1	CuCl	52
2	CuBr	39
3	CuI	45
4	$Cu(OAc)_2$	34
5	CuOAc	42
6	CuTC	57
7	CuFC[c]	39
8	CuPC[d]	41

[a] Reaction conditions: **1a** (0.1 mmol), **2a** (0.15 mmol), $Pd(dba)_2$ (5 mol %), PPh_3 (10 mol %), and copper compound (0.1 mmol) in THF at 65 °C for 12 h.
[b] GC yields.
[c] CuFC=copper(I) furan-2-carboxylate.
[d] CuPC=copper(I) pyridine-2-carboxylate.

Table 2
Solvent effect on cross-coupling reaction of **1a** with **2a**[a]

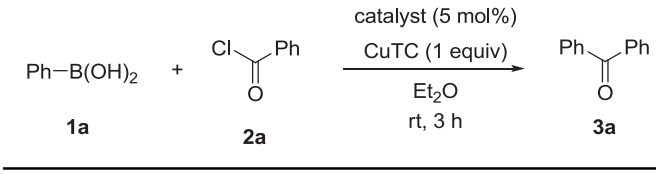


1a **2a** **3a**

Entry	Solvent	Temp (°C)	Yield[b] (%)
1	THF	65	57
2	DME	65	59
3	Bu_2O	65	51
4	THP	80	72
5	1,4-dioxane	100	72
6	Et_2O	25	78 (97)[c]
7	toluene	65	37
8	DMF	65	0
9	DMSO	65	0
10	methanol	25	0[d]

[a] Reaction conditions: **1a** (0.1 mmol), **2a** (0.15 mmol), $Pd(dba)_2$ (5 mol %), PPh_3 (10 mol %), and CuTC (0.1 mmol) for 12 h.
[b] GC yields.
[c] A GC yield is shown in parenthesis under the following conditions: ratio of **1a**/**2a**=2:1, reaction time; 3 h.
[d] Methyl benzoate was formed in 59% yield.

Table 3
Cross-coupling reaction of **1a** with **2a** using various catalyst systems[a]



1a **2a** **3a**

Entry	Catalyst	Yield[b] (%)
1	**$Pd(dba)_2$/2 PPh_3**	**97**
2	$Pd(PPh_3)_4$	60
3	$Pd(dba)_2$/2 $P(OPh)_3$	92
4	$Pd(dba)_2$/2 P(2-furyl)$_3$	72
5	$Pd(dba)_2$/2 P(*t*-Bu)$_3$	14
6	$Pd(dba)_2$/2 PMe_3	0
7	$Pd(dba)_2$	6
8	$Pd(OAc)_2$/2 PPh_3	71
9	$PdCl_2$(dppf)[c]	15
10	$Ni(cod)_2$	<1

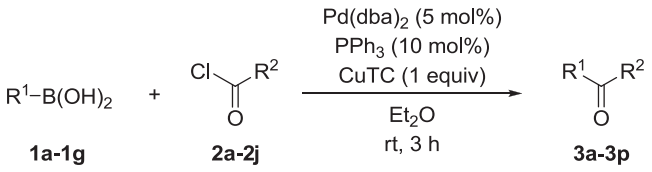
[a] Reaction conditions: **1a** (0.2 mmol), **2a** (0.1 mmol), catalyst (5 mol %) and CuTC (0.1 mmol) in Et_2O (3 mL) at room temperature for 3 h.
[b] GC yields.
[c] dppf=1,1′-bis(diphenylphosphino)ferrocene.

poor results, along with 6% yield of biphenyl (Table 3, entry 9). $Ni(cod)_2$ was completely ineffective as the catalyst (Table 3, entry 10). Deletion of $Pd(dba)_2$ yielded no product, confirming the requirement for a palladium catalyst for this cross-coupling reaction.

The use of catalytic (10 mol %) and substoichiometric (50 mol %) amounts of CuTC for the reaction of **1a** with **2a** afforded **3a** in 7% and 44% yields, respectively, whereas the use of excess (200 mol %) amounts of CuTC did not disturb the reaction progress. Thus, we employed a stoichiometric amount (100 mol %) of CuTC as the optimal conditions.

A series of cross-coupling reactions of arylboronic acids **1a**–**g** with acid chlorides **2a**–**j** were conducted and the results are summarized in Table 4. The reactions of **1a** with acid chlorides bearing electron-donating (Table 4, entries 2 and 3) and electron-withdrawing groups proceeded in good to excellent yields (Table 4, entries 4–6). Acid chlorides **2g** and **2h**, having heteroatomatics, such as 2-furyl and 2-thienyl groups, afforded the corresponding cross-coupled products **3g** and **3h** in 73% and 82% yields, respectively (Table 4, entries 7 and 8). Alkyl- and alkenyl-substituted acid chlorides **2i** and **2j** underwent the reactions to give **3i** and **3j** in moderate yields (Table 4, entries 9 and 10). On the other hand, the reaction of **2a** with arylboronic acids **1b**–**g** bearing various functional groups similarly underwent the cross-coupling reactions in up to 96% yield (Table 4, entries 11–16). However, a sterically hindered arylboronic acid, 2,6-dimethylphenylboronic acid, completely retarded the reaction of **2a** and gave no desired product.

Table 4
Cross-coupling reactions of arylboronic acids **1** with acid chlorides **2**[a]



1a-1g **2a-2j** **3a-3p**

Entry	Boronic acid (R^1)	Acid chloride (R^2)	Product	Yield[b] (%)
1[c]	Ph (**1a**)	Ph (**2a**)	**3a**	78
2[c]		3-MeC_6H_4 (**2b**)	**3b**	78
3		4-*n*-BuC_6H_4 (**2c**)	**3c**	87
4		4-$O_2NC_6H_4$ (**2d**)	**3d**	76
5[c]		4-ClC_6H_4 (**2e**)	**3e**	93
6[c]		4-NCC_6H_4 (**2f**)	**3f**	75
7		2-Furyl (**2g**)	**3g**	73
8		2-Thienyl (**2h**)	**3h**	82
9		*n*-C_7H_{15} (**2i**)	**3i**	47
10		(*E*)-PhCH=CH (**2j**)	**3j**	52
11	4-MeC_6H_4 (**1b**)	Ph (**2a**)	**3k**	87
12	4-$MeOC_6H_4$ (**1c**)		**3l**	71
13	2-$MeOC_6H_4$ (**1d**)		**3m**	76
14	4-$CF_3C_6H_4$ (**1e**)		**3n**	82
15	4-BrC_6H_4 (**1f**)		**3o**	80
16	4-$MeCOC_6H_4$ (**1g**)		**3p**	96

[a] Reaction conditions: arylboronic acid **1** (2 mmol), acid chloride **2** (1 mmol), $Pd(dba)_2$ (5 mol %), PPh_3 (10 mol %), and CuTC (1 mmol) in Et_2O (30 mL).
[b] Isolated yields.
[c] Reaction time is 1 h.

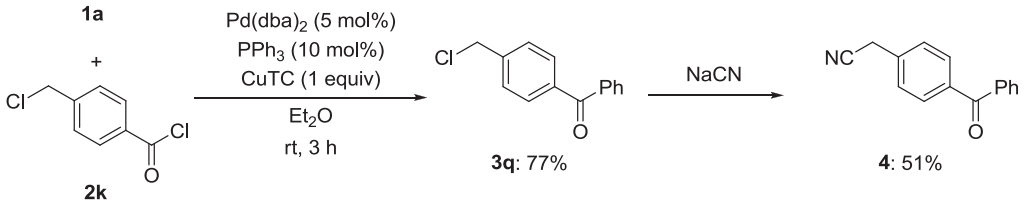
In order to demonstrate an advantageous feature of the present cross-coupling reaction under neutral conditions, the reaction of **1a** with 4-(chloromethyl)benzoyl chloride was subjected to compare with the result of the reported basic conditions,[3b] as shown in Scheme 1. In the presence of a stoichiometric amount of CuTC at room temperature in Et_2O, chemoselective cross-coupling occurred to generate 4-chloromethylbenzophenone (**3q**) as a sole product in 77% isolated yield (81% GC yield). In a sharp contrast, under basic conditions with K_3PO_4 gave the formation of **3q** in 43% yield, with other multiple products including 4-benzylbenzophenone (7%), indicating that phenylation toward a chloromethyl group also proceeded under basic conditions. α-Aryl nitriles are versatile intermediates for the synthesis of carboxylic acids, amides, primary amines, aldehydes, and heterocycles. They can also have biological activity as exemplified by medicinal compounds, such as anastrozole.[15] A chemoselective reaction allowed us to perform the subsequent cyanation of **3q** with NaCN to generate **4** in 51% yield.

2.2. Cross-coupling reaction of alkenylboronic acids 5 with acid chlorides 2

We next progressed to employ alkenylboronic acids as coupling partners to give chalcones. The cross-coupling reactions of various alkenylboronic acids **5** with acid chlorides **2** were investigated under the optimized conditions. The results obtained are shown in Table 5. The reaction of (*E*)-styrylboronic acid (**5a**) with various acid chlorides **2** bearing electron-neutral and -withdrawing groups afforded the chalcone derivatives **3j** and **6a**–**c** in moderate yields (Table 5, entries 1–4). Acid chlorides **2g** and **2h** having heteroaromatic rings, such as 2-furyl and 2-thienyl groups afforded the corresponding products **6d** and **6e** in 70% and 85% yields, respectively (Table 5, entries 5 and 6). Although the reaction of **5a** with 4-methoxybenzoyl chloride (**2k**) gave low yield of **6f** even in prolonged reaction time (45%, Table 5, entry 7), the reaction of **5a** with 4-methylbenzoyl chloride (**2l**) yielded 82% yield of **6g** (Table 5, entry 8). Alkenylboronic acid **5b** bearing a methoxy group in the para-position underwent the cross-coupling reaction with acid chlorides **2a** and **2e** to give **6h** and **6i**, respectively, in good yields (Table 5, entries 9 and 10). In addition, the reaction of alkenylboronic acid bearing an electron-withdrawing trifluoromethyl group with acid chlorides **2a**, **2k**, and **2l** proceeded and gave the corresponding cross-coupled products **6j**, **6k**, and **6l** in moderate to good yields (Table 5, entries 11–13). The reactions of an alkyl-substituted alkenylboronic acid **5d** with aroyl and heteroaromatic acid chlorides underwent the cross-coupling reactions in good yields (Table 5, entries 14 and 15). Unfortunately, the reaction of an acid chloride **2i** bearing an alkyl group gave a poor result (24%, Table 5, entry 16). It seems that the low isolated yields of products **6** contain a certain amount of technical loss due to the difficulty to isolate the desired products from the dibenzylideneacetone (DBA) ligand.

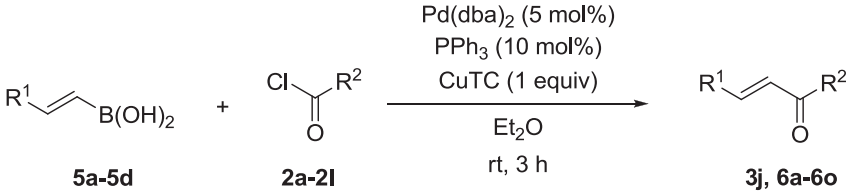
2.3. Reaction mechanism

We propose a reaction mechanism shown in Scheme 2. Oxidative addition of acid chlorides **2** to the $Pd(dba)_2/PPh_3$ catalyst



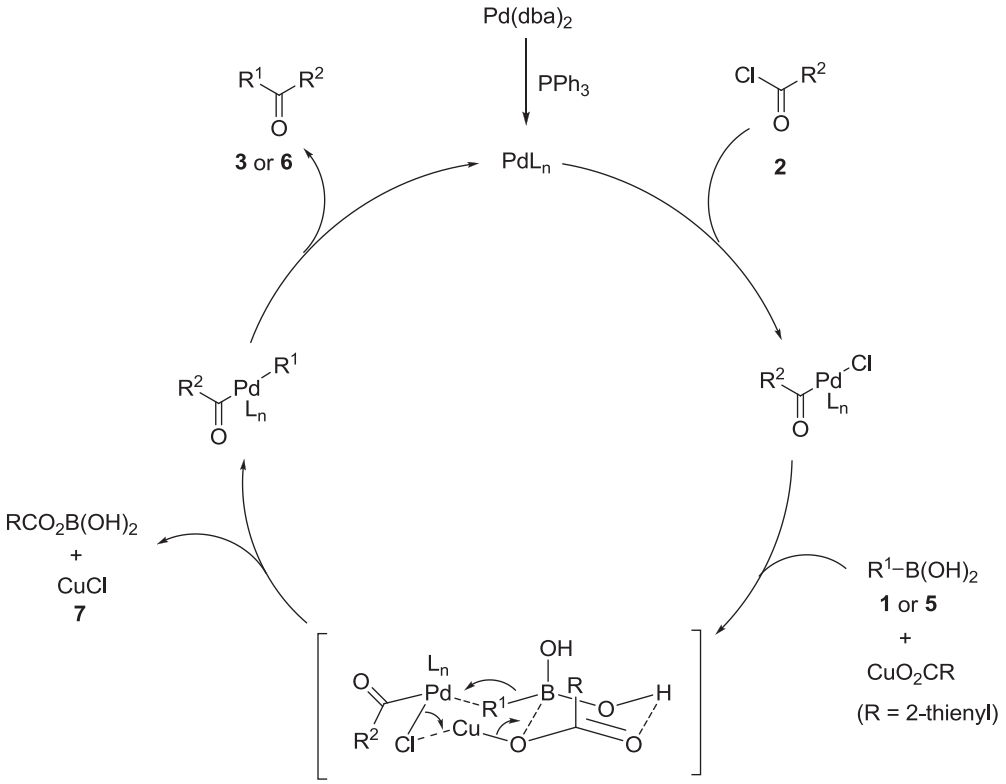
Scheme 1.

Table 5
Cross-coupling reactions of alkenylboronic acids **5** with acid chlorides **2**[a]



Entry	Alkenylboronic acid (R^1)	Acid chloride (R^2)	Product	Yield[b] (%)
1	Ph (**5a**)	Ph (**2a**)	**3j**	75
2		4-$O_2NC_6H_4$ (**2d**)	**6a**	62
3		4-ClC_6H_4 (**2e**)	**6b**	60
4		4-NCC_6H_4 (**2f**)	**6c**	64
5		2-Furyl (**2g**)	**6d**	70
6		2-Thienyl (**2h**)	**6e**	85
7[c]		4-$MeOC_6H_4$ (**2k**)	**6f**	45
8		4-MeC_6H_4 (**2l**)	**6g**	82
9	4-$MeOC_6H_4$ (**5b**)	Ph (**2a**)	**6h**	65
10		4-ClC_6H_4 (**2e**)	**6i**	74
11	4-$F_3CC_6H_4$ (**5c**)	Ph (**2a**)	**6j**	73
12		4-$MeOC_6H_4$ (**2k**)	**6k**	71
13		4-MeC_6H_4 (**2l**)	**6l**	66
14	*n*-C_6H_{13} (**5d**)[d]	Ph (**2a**)	**6m**	89
15		2-Furyl (**2g**)	**6n**	81
16		*n*-C_7H_{15} (**2i**)	**6o**	24

[a] Reaction conditions: boronic acid (1 mmol), acid chloride (0.5 mmol), $Pd(dba)_2$ (5 mol %), PPh_3 (10 mol %), and CuTC (0.5 mmol) in Et_2O (15 mL).
[b] Isolated yield.
[c] Reaction time was 6 h.
[d] $Pd(dba)_2$ (10 mol %), PPh_3 (20 mol %), reaction time was 7 h.



Scheme 2. A plausible mechanism for Pd-catalyzed and Cu-mediated cross-coupling reaction of organoboronic acids with acid chlorides.

generates an acylpalladium(II) chloride complex. Subsequent transmetalation of the organic group on aryl- or alkenylboronic acid (**1** or **5**) to palladium takes place at the Pd–Cl bond. CuTC seems to play dual important roles as an activator: the soft Cu(I) ion accelerates the polarization of the palladium–chlorine bond, while the hard carboxylate counterion activates the C–B bond of the organoboronic acids via a six-membered ring. Although the reaction with other copper salts, such as CuCl, CuBr, CuI, CuOAc, and

$Cu(OAc)_2$ have been examined, inefficient reaction occurred, because they cannot construct such a six-membered ring. Compared to the analogous copper compounds like CuFC and CuPC showed the lower activity, implying that the thiophene moiety would also play a role to activate the organoboronic acid by a coordination to boron.

The measurement of X-ray diffraction (XRD) pattern analysis of the copper residue, after completion of the reaction of phenylboronic acid (**1a**) with 2-furoyl chloride (**2g**) in the presence of 100 mol % of CuTC, indicated that a part of new peaks was found identical with those of CuCl (**7**). As a result, we found that both CuTC and organoboronic acids are critical to the smooth transmetalation, presumably due to the presence of a hydrogen bond between the carbonyl oxygen in CuTC and a hydroxy group of the organoboronic acids.

Attempt to demonstrate the reactions by using relatively labile phenylboronates $PhB(OR)_2$ [$(OR)_2$=$-OCH_2CH_2O-$, $-OCH_2CMe_2CH_2O-$, and $-OCHMeCH_2CHMeO-$] with **2a** was failed even after 48 h at room temperature.

3. Conclusion

In conclusion, we have successfully developed a preparative synthetic method for the generation of ketones and chalcones from the cross-coupling reactions of acid chlorides with arylboronic acids or alkenylboronic acids in the presence of $Pd(dba)_2$ and a stoichiometric amount of CuTC as a neutral activator. These reactions proceed under neutral conditions at room temperature within 3 h. It is remarkable that diethyl ether as the solvent effects the transformation of boronic acids into ketones, forming a carbon–carbon bond through the cross-coupling by the activation with CuTC. These reactions are synthetically useful methods for syntheses of ketones and chalcones from a viewpoint of non-toxic, tolerant of many functional groups, and mild conditions. Further application of this method to the synthesis of natural products and pharmaceuticals is in progress.

4. Experimental section

4.1. General

All the reactions were carried out under an Ar atmosphere using standard Schlenk techniques. Glassware was dried in an oven (130 °C) and heated under reduced pressure before use. For thin layer chromatography (TLC) analyses throughout this work, Merck precoated TLC plates (silica gel 60 GF_{254}, 0.25 mm) were used. Silica gel column chromatography was carried out using Silica gel 60 N (spherical, neutral, 40–100 μm) from Kanto Chemicals Co., Ltd. NMR spectra (^1H, $^{13}C\{^1H\}$, and $^{19}F\{^1H\}$) were recorded on Varian INOVA-600 (600 MHz) or Mercury-300 (300 MHz) spectrometers. $CHCl_3$: 7.26 ppm for ^1H NMR and $CDCl_3$: 77.0 ppm for $^{13}C\{^1H\}$ NMR were used as internal standards. GC analyses were performed on a Shimadzu GC-14A equipped with a flame ionization detector using Shimadzu Capillary Column (CBP1-M25-025) and Shimadzu C-R6A-Chromatopac integrator. The GC yields were determined using suitable hydrocarbon internal standards. GC/MS analyses were carried out on a SHIMADZU GC-17A equipped with a SHIMADZU QP-5050 GC–MS system. XRD patterns were measured with Rigaku X-RAY DIFFRACTIOMETER RAD-1C.

Boronic acids **1a**, **1d**, and **1g** and **1b**, **1c**, **1e**, and **1f** were purchased from Aldrich Chemical Co. and Tokyo Chemical Industry Co., respectively, and used as received. Dehydrated diethyl ether was purchased from Kanto Chemicals Co., Ltd. Copper(I) thiophene-2-carboxylate (CuTC)[16] and $Pd(dba)_2$[17] were synthesized according to the literature procedures.

4.2. Reaction of phenylboronic acid (1a) with benzoyl chloride (2a) in the presence of a Pd catalyst and CuTC in THF (Table 1, entry 6)

Phenylboronic acid (**1a**) (12.2 mg, 0.1 mmol), CuTC (19.1 mg, 0.1 mmol), $Pd(dba)_2$ (2.9 mg, 0.005 mmol), and PPh_3 (2.6 mg, 0.01 mmol) were placed in 20 mL Schlenk tube. After a vacuum and argon cycle three times, dry THF (1 mL) and benzoyl chloride (**2a**) (17.3 μL, 0.15 mmol) were added at room temperature. The reaction mixture was heated at 65 °C for 12 h. Yields of a desired cross-coupled product **3a** (57%, based on **1a**), biphenyl (7%, based on **1a**), and 4-chlorobutyl benzoate (18%, based on **2a**) were detected by GC using *n*-dodecane (23 μL, 0.1 mmol) as an internal standard. The ^1H and $^{13}C\{^1H\}$ NMR data of 4-chlorobutyl benzoate were identical to a commercially available authentic sample. ^1H NMR (300 MHz, $CDCl_3$): δ 1.91–1.95 (m, 4H), 3.58–3.62 (m, 2H), 4.33–4.37 (m, 2H), 7.40–7.46 (m, 2H), 7.53–7.55 (m, 1H), 8.02–8.05 (m, 2H). $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$): δ 26.0, 29.1, 44.4, 64.0, 128.3, 129.4, 130.1, 132.9, 166.4.

4.3. General procedure for synthesis of unsymmetrical ketones by the cross-coupling reaction of arylboronic acids with acid chlorides

*4.3.1. Benzophenone (**3a**).*[18] To phenylboronic acid (**1a**, 244 mg, 2 mmol), CuTC (191 mg, 1 mmol), $Pd(dba)_2$ (29 mg, 0.05 mmol), and PPh_3 (26.2 mg, 0.1 mmol), were added dry Et_2O (30 mL) and benzoyl chloride (**2a**, 116 μL, 1 mmol) at rt and the reaction was monitored by GC and TLC. After completion of the reaction, the reaction mixture was passed briefly through a Celite pad. Further, the pad was washed with Et_2O (2×10 mL). The combined organics were concentrated with a rotary evaporator to give a viscous oil or solid. The residue was purified by flash column chromatography on silica gel (hexane/EtOAc=9:1, R_f=0.47), benzophenone (**3a**) (142 mg, 0.78 mmol, 78%) was obtained as a white solid. ^1H NMR (300 MHz, $CDCl_3$): δ 7.46–7.51 (m, 4H), 7.56–7.62 (m, 2H), 7.79–7.83 (m, 4H).

*4.3.2. 3-Methylbenzophenone (**3b**).*[19] ^1H NMR (300 MHz, $CDCl_3$): δ 2.43 (s, 3H), 7.34–7.43 (m, 2H), 7.45–7.51 (m, 2H), 7.56–7.59 (m, 2H), 7.61–7.64 (m, 1H), 7.79–7.83 (m, 2H).

*4.3.3. 4-n-Butylbenzophenone (**3c**).*[20] ^1H NMR (300 MHz, $CDCl_3$): δ 0.95 (t, *J*=7.2 Hz, 3H), 1.39 (m, 2H), 1.65 (m, 2H), 2.70 (t, *J*=7.5 Hz, 2H), 7.26–7.30 (m, 2H), 7.44–7.55 (m, 2H), 7.54–7.60 (m, 1H), 7.73–7.79 (m, 2H), 7.79–7.82 (m, 2H).

*4.3.4. 4-Nitrobenzophenone (**3d**).*[21] ^1H NMR (300 MHz, $CDCl_3$): δ 7.50–7.56 (m, 2H), 7.63–7.68 (m, 1H), 7.79–7.83 (m, 2H), 7.92–7.96 (m, 2H), 8.33–8.37 (m, 2H).

*4.3.5. 4-Chlorobenzophenone (**3e**).*[22] ^1H NMR (300 MHz, $CDCl_3$): δ 7.45–7.52 (m, 4H), 7.58–7.63 (m, 1H), 7.75–7.80 (m, 4H).

*4.3.6. 4-Cyanobenzophenone (**3f**).*[23] ^1H NMR (300 MHz, $CDCl_3$): δ 7.49–7.54 (m, 2H), 7.61–7.67 (m, 1H), 7.77–7.81 (m, 4H), 7.86–7.89 (m, 2H).

*4.3.7. 2-Furyl phenyl ketone (**3g**).*[24] ^1H NMR (300 MHz, $CDCl_3$): δ 6.59 (dd, *J*=3.3, 1.5 Hz, 1H), 7.22–7.24 (m, 1H), 7.46–7.52 (m, 2H), 7.56–7.62 (m, 1H), 7.70–7.71 (m, 1H), 7.95–7.99 (m, 2H).

*4.3.8. Phenyl 2-thienyl ketone (**3h**).*[25] ^1H NMR (300 MHz, $CDCl_3$): δ 7.15 (dd, *J*=3.9, 1.2 Hz, 1H), 7.47–7.52 (m, 2H), 7.57–7.62 (m, 1H), 7.63 (dd, *J*=3.9, 1.2 Hz, 1H), 7.71 (dd, *J*=5.1, 1.2 Hz, 1H), 7.85–7.88 (m, 2H).

*4.3.9. 1-Phenyl-1-octanone (**3i**).*[26] ^1H NMR (300 MHz, $CDCl_3$): δ 0.88 (t, *J*=7.2 Hz, 3H), 1.29–1.40 (m, 8H), 1.73 (quint, *J*=7.2 Hz, 2H),

2.96 (t, J=7.2 Hz, 2H), 7.43–7.49 (m, 2H), 7.53–7.58 (m, 1H), 7.95–7.98 (m, 2H).

*4.3.10. (E)-1,3-Diphenyl-2-propen-1-one (**3j**).*[27] ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.40–7.45 (m, 3H), 7.48–7.67 (m, 6H), 7.83 (d, J=15.7 Hz, 1H), 8.01–8.06 (m, 2H).

*4.3.11. 4-Methylbeonzophenone (**3k**).*[28] ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.44 (s, 3H), 7.27–7.29 (m, 2H), 7.44–7.50 (m, 2H), 7.55–7.60 (m, 1H), 7.71–7.74 (m, 2H), 7.77–7.80 (m, 2H).

*4.3.12. 4-Methoxybenzophenone (**3l**).*[28] ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.87 (s, 3H), 6.93–6.98 (m, 2H), 7.46–7.49 (m, 2H), 7.53–7.58 (m, 1H), 7.73–7.77 (m, 2H), 7.80–7.85 (m, 2H).

*4.3.13. 2-Methoxybenzophenone (**3m**).*[28] ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.73 (s, 3H), 7.00 (d, J=8.3 Hz, 1H), 7.04 (dt, J=7.5, 0.9 Hz, 1H), 7.35–7.58 (m, 5H), 7.80–7.83 (m, 2H).

*4.3.14. 4-(Trifluoromethyl)benzophenone (**3n**).*[29] ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.48–7.54 (m, 2H), 7.61–7.66 (m, 1H), 7.74–7.77 (m, 2H), 7.79–7.83 (m, 2H), 7.88–7.91 (m, 2H). ^{19}F{^{1}H} NMR (282 MHz, $CDCl_3$): δ −63.5.

*4.3.15. 4-Bromobenzophenone (**3o**).*[30] ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.46–7.52 (m, 2H), 7.58–7.70 (m, 5H), 7.76–7.79 (m, 2H).

*4.3.16. 4-Acetylbenzophenone (**3p**).*[31] ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.66 (s, 3H), 7.47–7.52 (m, 2H), 7.59–7.65 (m, 1H), 7.78–7.81 (m, 2H), 7.84–7.87 (m, 2H), 8.04–8.07 (m, 2H).

4.4. Synthesis of 4-chloromethylbenzophenone (3q)[32]

Following the general procedure, to phenylboronic acid (**1a**) (488 mg, 4 mmol), CuTC (382 mg, 2 mmol), Pd(dba)$_2$ (58 mg, 0.10 mmol), and PPh_3 (52.4 mg, 0.20 mmol), were added dry diethyl ether (60 mL) and a solution of 4-(chloromethyl)benzoyl chloride (378 mg, 2 mmol) in 5 mL of diethyl ether at room temperature. The suspension was stirred at room temperature for 3 h. After purification by column chromatography on silica gel (hexane/ethyl acetate=9:1, R_f=0.46), **3q** (358 mg, 1.55 mmol, 77%) was obtained as a pale yellow oil. Bp: 200–210 °C/4.1 Torr. ^{1}H NMR (300 MHz, $CDCl_3$): δ 4.60 (s, 2H), 7.42–7.48 (m, 4H), 7.53–7.59 (m, 1H), 7.56–7.78 (m, 4H). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$): δ 45.2, 128.1, 128.2, 129.8, 130.2, 132.4, 137.1, 137.2, 141.5, 195.7.

4.5. Synthesis of 2-(4-benzoylphenyl)acetonitrile (4)[33]

Diaryl ketone **3q** (115 mg, 0.5 mmol) and sodium cyanide (49 mg, 1.0 mmol) were dissolved in 1,4-dioxane/H_2O=7:3 (15 mL). The mixture was heated under reflux for 2 h, during which the organic product appeared as a separate layer. The cooled reaction mixture was extracted with EtOAc (2×10 mL). The combined organics were concentrated with a rotary evaporator to give yellow solid. After purification by column chromatography on silica gel (hexane/ethyl acetate=2:1, R_f=0.46) **4** (57 mg, 1.3 mmol, 51%) was obtained as pale yellow solid. ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.84 (s, 2H), 7.44–7.51 (m, 4H), 7.57–7.63 (m, 1H), 7.76–7.82 (m, 4H).

4.6. General procedure for synthesis of chalcones by the cross-coupling reaction of alkenylboronic acids with acid chlorides

*4.6.1. (E)-Chalcone (**3j**).*[4] To (*E*)-styrylboronic acid (**1a**, 148 mg, 1 mmol), CuTC (95 mg, 0.5 mmol), Pd(dba)$_2$ (14 mg, 0.0025 mmol), and PPh_3 (13 mg, 0.05 mmol), were added dry Et_2O (15 mL) and benzoyl chloride (**2a**, 58 μL, 0.5 mmol) at room temperature. The reaction was monitored by GC and TLC. After completion of the reaction, the reaction mixture was passed briefly through a Celite pad. Further, the pad was washed with Et_2O (2×10 mL). The combined organics were concentrated with a rotary evaporator to give viscous oil. The residue was purified by preparative TLC on silica gel (hexane/EtOAc=10:1, R_f=0.33) to give **3j** (78 mg, 0.38 mmol, 75%) as a white solid. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.40–7.45 (m, 3H), 7.48–7.67 (m, 6H), 7.83 (d, J=15.7 Hz, 1H), 8.01–8.06 (m, 2H).

*4.6.2. (E)-1-(4-Nitrophenyl)-3-phenyl-2-propen-1-one (**6a**).*[34] ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.43–7.51 (m, 4H), 7.65–7.68 (m, 2H), 7.85 (d, J=15.6 Hz, 1H), 8.13–8.17 (m, 2H), 8.34–8.38 (m, 2H).

*4.6.3. (E)-1-(4-Chlorophenyl)-3-phenyl-2-propen-1-one (**6b**).*[9] ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.42–7.52 (m, 6H), 7.63–7.67 (m, 2H), 7.83 (d, J=15.6 Hz, 1H), 7.95–7.99 (m, 2H).

*4.6.4. (E)-4-(3-Phenylacryloyl)benzonitrile (**6c**).*[4] ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.41–7.49 (m, 4H), 7.63–7.66 (m, 2H), 7.78–7.85 (m, 3H), 8.06–8.10 (m, 2H).

*4.6.5. (E)-1-(2-Furyl)-3-phenyl-2-propen-1-one (**6d**).*[35] ^{1}H NMR (300 MHz, $CDCl_3$): δ 6.58–6.60 (m, 1H), 7.33–7.48 (m, 5H), 7.63–7.66 (m, 3H), 7.88 (d, J=15.6 Hz, 1H).

*4.6.6. (E)-3-Phenyl-1-(2-thienyl)-2-propen-1-one (**6e**).*[36] ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.18–7.21 (m, 1H), 7.40–7.46 (m, 4H), 7.64–7.70 (m, 3H), 7.84–7.89 (m, 2H).

*4.6.7. (E)-1-(4-Methoxyphenyl)-3-phenyl-2-propen-1-one (**6f**).*[9] ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.88 (s, 3H), 6.98 (d, J=9.0 Hz, 2H), 7.40–7.42 (m, 3H), 7.55 (d, J=15.9 Hz, 1H), 7.63–7.66 (m, 2H), 7.81 (d, J=15.9 Hz, 1H), 8.03–8.06 (m, 2H).

*4.6.8. (E)-3-Phenyl-1-(4-methylphenyl)-2-propen-1-one (**6g**).*[4] ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.43 (s, 3H), 7.30 (d, J=7.8 Hz, 2H), 7.40–7.43 (m, 3H), 7.55 (d, J=15.6 Hz, 1H), 7.62–7.66 (m, 2H), 7.82 (d, J=15.6 Hz, 1H), 7.94–7.97 (m, 2H).

*4.6.9. (E)-3-(4-Methoxyphenyl)-1-phenyl-2-propen-1-one (**6h**).*[37] ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.85 (s, 3H), 6.93 (d, J=6.9 Hz, 2H), 7.42 (d, J=15.6 Hz, 1H), 7.47–7.62 (m, 5H), 7.79 (d, J=15.6 Hz, 1H), 8.01–8.03 (m, 2H).

*4.6.10. (E)-1-(4-Chlorophenyl)-3-(4-methoxyphenyl)-2-propen-1-one (**6i**).*[38] ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.85 (s, 3H), 6.93 (d, J=8.7 Hz, 2H), 7.35 (d, J=15.6 Hz, 1H), 7.45 (d, J=8.4 Hz, 2H), 7.59 (d, J=8.7 Hz, 2H), 7.78 (d, J=15.6 Hz, 1H), 7.95 (d, J=8.4 Hz, 2H).

*4.6.11. (E)-3-{(4-(Trifluoromethyl)phenyl)}-1-phenyl-2-propen-1-one (**6j**).*[39] ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.49–7.76 (m, 6H), 7.60 (d, J=15.6 Hz, 1H), 7.81 (d, J=8.4 Hz, 2H), 8.02–8.06 (m, 2H). ^{19}F{^{1}H} NMR (282 MHz, $CDCl_3$): δ −63.2.

*4.6.12. (E)-1-(4-Methoxyphenyl)-3-{4-(trifluoromethyl)phenyl}-2-propen-1-one (**6k**).*[40] ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.89 (s, 3H), 6.99 (d, J=8.7 Hz, 2H), 7.58–7.67 (m, 3H), 7.72–8.03 (m, 3H), 8.05 (d, J=8.7 Hz, 2H).

*4.6.13. (E)-1-(4-Methylphenyl)-3-{(4-(trifluoromethyl)phenyl)}-2-propen-1-one (**6l**).*[39] ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.45 (s, 3H), 7.31 (d, J=8.1 Hz, 2H), 7.33–7.82 (m, 6H), 7.95 (d, J=8.1 Hz, 2H). ^{19}F{^{1}H} NMR (282 MHz, $CDCl_3$) δ −63.2.

*4.6.14. (E)-1-Phenyl-2-nonen-1-one (**6m**).*[41] ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.89 (t, J=6.9 Hz, 3H), 1.25–1.40 (m, 6H), 1.47–2.35 (m, 2H),

2.31 (qd, J=5.7, 1.2 Hz, 2H), 6.87 (dt, J=15.3, 1.2 Hz, 1H), 7.07 (dt, J=15.3, 6.9 Hz, 1H), 7.43–7.49 (m, 2H), 7.52–7.58 (m, 1H), 7.91–7.95 (m, 2H).

*4.6.15. (E)-1-(2-Furyl)-2-nonen-1-one (**6n**).* FTIR (KBr, cm^{-1}): 3443 (w), 2955 (m), 2928 (s), 2857 (m), 1667 (s), 1622 (s), 1566 (m), 1466 (s), 1395 (w), 764 (s). ^1H NMR (300 MHz, $CDCl_3$) δ 0.89 (t, J=6.6 Hz, 3H), 1.25–1.39 (m, 6H), 1.46–1.56 (m, 2H), 2.30 (qd, J=7.2, 1.8 Hz, 2H), 6.55 (dd, J=3.6, 1.8 Hz, 1H), 6.79 (dt, J=15.6, 1.5 Hz, 1H), 7.11–7.24 (m, 2H), 7.61 (d, J=1.5 Hz, 1H). $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$, rt): δ 14.0, 22.5, 28.1, 28.9, 31.6, 32.7, 112.3, 117.4, 124.8, 146.4, 149.4, 153.4, 178.2. MS (EI, m/z (relative intensity)): 206 (M^+, 5), 191 (1), 177 (5), 163 (4), 149 (25), 138 (9), 123 (38), 110 (90), 95 (100), 77 (16), 67 (10). Anal. Calcd for $C_{13}H_{18}O_2$: C, 75.69; H, 8.80%. Found: C, 75.75; H, 8.46%.

*4.6.16. (E)-9-Hexadecen-8-one (**6o**).*[42] ^1H NMR (300 MHz, $CDCl_3$): δ 0.87 (m, 6H), 1.25–1.41 (m, 14H), 1.43–1.48 (m, 2H), 1.55–1.64 (m, 2H), 2.16–2.24 (m, 2H), 2.52 (t, J=7.2 Hz, 2H), 6.08 (dt, J=15.9, 1.5 Hz, 1H), 6.82 (dt, J=15.9, 6.9 Hz, 1H).

4.7. XRD analysis of the residue from the reaction of 1a with 2g in the presence of 100 mol % of CuTC

Following the general procedure, to phenylboronic acid (**1a**) (244 mg, 2 mmol), CuTC (191 mg, 1 mmol), $Pd(dba)_2$ (29 mg, 0.05 mmol), and PPh_3 (26.2 mg, 0.1 mmol), were added dry diethyl ether (30 mL) and 2-furoyl chloride (**2g**) (99 μL, 1 mmol) at room temperature. The reddish brown suspension was stirred at room temperature for 5 h. The mixture involving a brown precipitate was filtered off and washed with diethyl ether. The resulting solid was dried under reduced pressure to give a brown powder (152 mg), which was subjected to the XRD analysis. Residue with 100 mol % of CuTC: 2θ (relative intensity) 28.54 (100), 36.42 (74), 42.28 (26), 47.45 (35), 56.27 (18), 61.38 (18), 73.53 (13). CuCl (measured): 2θ (relative intensity) 28.55 (100), 33.09 (3), 47.46 (21), 56.30 (10), 59.05 (2), 69.36 (3), 76.64 (4). CuCl:[43] 2θ (relative intensity) 28.59 (100), 33.03 (8), 47.43 (55), 56.29 (30), 69.34 (6), 76.58 (10), 88.34 (8), 95.30 (6), 107.13 (2), 114.58 (4), 128.16 (4).

Acknowledgements

The authors gratefully thank Ms. Megumi Kosaka and Mr. Motonari Kobayashi at the Department of Instrumental Analysis, Advanced Science Research Center, Okayama University for the measurements of elemental analyses and the SC-NMR Laboratory of Okayama University for the NMR spectral measurements. We are grateful to Professor Hideki Taguchi at Okayama University for the XRD measurements.

Supplementary data

Supplementary data associated with this article can be found in the online version, at http://dx.doi.org/10.1016/j.tet.2013.01.058. These data include MOL files and InChiKeys of the most important compounds described in this article.

References and notes

1. (a) Baughman, B. M.; Stennett, E.; Lipner, R. E.; Rudawsky, A. C.; Schidtke, S. J. *J. Phys. Chem. A* **2009**, *113*, 8011–8019; (b) Ong, A. L.; Kamaruddin, A. H.; Bhatia, S. *Process Biochem.* **2005**, *40*, 3526–3535; (c) Wen, A.; Wang, Z.; Hang, T.; Jia, Y.; Zhang, T.; Wu, Y.; Gao, X.; Yang, Z. *J. Chromatogr., B* **2007**, *856*, 348–352; (d) Furusawa, M.; Ido, Y.; Tanaka, T.; Ito, T.; Nakaya, K.; Ibrahim, I.; Ohyama, M.; Iinuma, M.; Shirataka, Y.; Takahashi, Y. *Helv. Chim. Acta* **2005**, *88*, 1048–1058.
2. Haddach, M.; McCarthy, J. R. *Tetrahedron Lett.* **1999**, *40*, 3109–3112.
3. (a) Urawa, Y.; Ogura, K. *Tetrahedron Lett.* **2003**, *44*, 271–273; (b) Urawa, Y.; Nishiura, K.; Souda, S.; Ogura, K. *Synthesis* **2003**, 2882–2885; (c) Korolev, D. N.; Bumagin, N. A. *Russ. Chem. Bull.* **2004**, *53*, 364–369; (d) Bandgar, B. P.; Patil, A. V. *Tetrahedron Lett.* **2005**, *46*, 7627–7630; (e) Xin, B.; Zhang, Y.; Cheng, K. *J. Org. Chem.* **2006**, *71*, 5725–5731; (f) Zhang, L.; Wu, J.; Shi, L.; Xia, C.; Li, F. *Tetrahedron Lett.* **2011**, *52*, 3897–3901; (g) Martins, D. L.; Aguiar, L. C. S.; Antunes, O. A. C. *J. Organomet. Chem.* **2011**, *696*, 2845–2849; (h) Yu, A.; Shen, L.; Cui, X.; Peng, D.; Wu, Y. *Tetrahedron* **2012**, *68*, 2283–2288.
4. Xin, B.; Zhang, Y.; Cheng, K. *Synthesis* **2007**, 1970–1978.
5. (a) Eddarir, S.; Cotelle, N.; Bakkour, Y.; Rolando, C. *Tetrahedron Lett.* **2003**, *44*, 5359–5363; (b) Poláčková, V.; Toma, Š.; Augustínová, I. *Tetrahedron* **2006**, *62*, 11675–11678; (c) Ekoue-Kovi, K.; Xu, H.; Wolf, C. *Tetrahedron Lett.* **2008**, *49*, 5773–5776; (d) Al-Masum, M.; Ng, E.; Wai, M. C. *Tetrahedron Lett.* **2011**, *52*, 1008–1010.
6. (a) Fürstner, A.; Voigtländer, D.; Schrader, W.; Giebel, D.; Reetz, M. T. *Org. Lett.* **2001**, *3*, 417–420; (b) Gmouh, S.; Yang, H.; Vaultier, M. *Org. Lett.* **2003**, *5*, 2219–2222; (c) Fillion, E.; Fishlock, D.; Wilsily, A.; Goll, J. M. *J. Org. Chem.* **2005**, *70*, 1316–1327.
7. (a) Ishiyama, T.; Kizaki, H.; Hayashi, T.; Suzuki, A.; Miyaura, N. *J. Org. Chem.* **1998**, *63*, 4726–4731; (b) Zheng, S.; Xu, L.; Xia, C. *Appl. Organomet. Chem.* **2007**, *21*, 772–776; (c) Neumann, A.; Brennführer, A.; Beller, M. *Adv. Synth. Catal.* **2008**, *350*, 2437–2442.
8. Wu, X.-F.; Neumann, H.; Beller, M. *Angew. Chem., Int. Ed.* **2010**, *49*, 5284–5288.
9. Wu, X.-F.; Neumann, H.; Spannenberg, A.; Schulz, T.; Jiao, H.; Beller, M. *J. Am. Chem. Soc.* **2010**, *132*, 14596–14602.
10. (a) Gooßen, L. J.; Ghosh, K. *Angew. Chem., Int. Ed.* **2001**, *40*, 3458–3460; (b) Gooßen, L. J.; Ghosh, K. *Chem. Commun.* **2001**, 2084–2085; (c) Gooßen, L. J.; Ghosh, K. *Eur. J. Org. Chem.* **2002**, 3254–3267; (d) Gooßen, J.; Winkel, L.; Döhring, A.; Ghosh, K.; Paetzold, J. *Synlett* **2002**, 1237–1240.
11. (a) Kakino, R.; Shimizu, I.; Yamamoto, A. *Bull. Chem. Soc. Jpn.* **2001**, *74*, 371–376; (b) Kakino, R.; Narahashi, H.; Shimizu, I.; Yamamoto, A. *Chem. Lett.* **2001**, 1242–1243; (c) Kakino, R.; Yasumi, S.; Shimizu, I.; Yamamoto, A. *Bull. Chem. Soc. Jpn.* **2002**, *75*, 137–148; (d) Kakino, R.; Narahashi, H.; Shimizu, I.; Yamamoto, A. *Bull. Chem. Soc. Jpn.* **2002**, *75*, 1333–1345.
12. Preliminary communication Nishihara, Y.; Inoue, Y.; Fujisawa, M.; Takagi, K. *Synlett* **2005**, 2309–2312.
13. Liebeskind, L. S.; Srogl, J. *J. Am. Chem. Soc.* **2000**, *122*, 11260–11261.
14. Yamashita, H.; Kobayashi, T.; Sakakura, T.; Tanaka, M. *J. Organomet. Chem.* **1988**, *356*, 125–131.
15. Friedrich, K.; Wallenfels, K. *The Chemistry of the Cyano Group*; Wiley-Interscience: New York, 1970.
16. Allred, G. D.; Liebeskind, L. S. *J. Am. Chem. Soc.* **1996**, *118*, 2748–2749.
17. (a) Djakovitch, L.; Wagner, M.; Hartung, C. G.; Beller, M.; Koehler, K. *J. Mol. Catal. A: Chem.* **2004**, *219*, 121–130; (b) Fairlamb, I. J. S.; Kapdi, A. R.; Lee, A. F. *Org. Lett.* **2004**, *6*, 4435–4438.
18. Smith, P. A. S.; Messing, C. R. *J. Org. Chem.* **1988**, *53*, 2959–2965.
19. Shevchuk, M. I.; Ganushchak, N. I.; Dombrovski, A. V. *Zh. Obshch. Khim.* **1964**, *34*, 2247–2250.
20. Xuong, N. D.; Buu-Hoi, N. P. *J. Chem. Soc. A* **1952**, 3741–3744.
21. Kulp, S. S.; McGee, M. J. *J. Org. Chem.* **1983**, *48*, 4097–4098.
22. Olah, G. A.; Mehrotra, A. K.; Narang, S. C. *Synthesis* **1982**, 151–152.
23. Partham, W. E.; Jones, L. D. *J. Org. Chem.* **1976**, *41*, 1187–1191.
24. Ramanathan, V.; Levine, R. *J. Org. Chem.* **1962**, *27*, 1216–1219.
25. Jeon, K. O.; Jun, J. H.; Yu, J. S.; Lee, C. K. *J. Heterocycl. Chem.* **2003**, *40*, 763–771.
26. Shakarashvili, T. S.; Bekauru, N. G. *Soobshch. Akad. Nauk Gruz. SSR* **1964**, *35*, 315–318.
27. Ueno, Y.; Yadav, L. D. S.; Okawara, M. *Chem. Lett.* **1983**, 831–834.
28. Scaiano, J. C.; Leigh, W.; Meador, M. A.; Wagner, P. J. *J. Am. Chem. Soc.* **1985**, *107*, 5806–5807.
29. Wagner, P. J.; Siebert, E. J. *J. Am. Chem. Soc.* **1981**, *103*, 7329–7335.
30. Morley, J. O. *Synthesis* **1977**, 54–55.
31. Suhana, H.; Srinivasan, P. C. *Synth. Commun.* **2003**, *33*, 3097–3102.
32. Kauer, J. C. US Patent, 1988, US 4762881.
33. Zderic, J. A.; Kubitschek, M. M. J.; Bonner, W. A. *J. Org. Chem.* **1961**, *26*, 1635–1637.
34. Fang, F.; Li, Y.; Tian, S.-K. *Eur. J. Org. Chem.* **2011**, 1084–1091.
35. Maji, T.; Karmakar, A.; Reiser, O. *J. Org. Chem.* **2011**, *76*, 736–739.
36. Thiot, C.; Mioskowski, C.; Wagner, A. *Eur. J. Org. Chem.* **2009**, 3219–3227.
37. Cabrera, M.; Simoens, M.; Falchi, G.; Lavaggi, M. L.; Piro, O. E.; Castellano, E. E.; Vidal, A.; Azqueta, A.; Monge, A.; Ceráin, A. L.; Sagrera, G.; Seoane, G.; Cerecetto, H.; González, M. *Bioorg. Med. Chem.* **2007**, *15*, 3356–3367.
38. Hayat, F.; Salahuddin, A.; Umar, S.; Azam, A. *Eur. J. Med. Chem.* **2010**, *45*, 4669–4675.
39. Al-Masum, M.; Ng, E.; Wai, M. C. *Tetrahedron Lett.* **2011**, *52*, 1008–1010.
40. Liu, M.; Wilairat, P.; Go, M.-L. *J. Med. Chem.* **2001**, *44*, 4443–4452.
41. Rueda, X. Y.; Castillón, S. *J. Organomet. Chem.* **2007**, *692*, 1628–1632.
42. Park, Y. J.; Kwon, B.-I.; Ahn, J.-A.; Lee, H.; Jun, C.-H. *J. Am. Chem. Soc.* **2004**, *126*, 13892–13893.
43. XRD pattern of CuCl is available from International Centre for Diffraction Data (ICDD).