EurJOC European Journal of Organic Chemistry

FULL PAPER

DOI: 10.1002/ejoc.201500726

Metal-Free Oxidative C–H Amidation of *N*,*N*′-Diarylureas with $PhI(OAc)_2$: Synthesis of Benzimidazol-2-one Derivatives

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Keywords: Synthetic methods / Nitrogen heterocycles / C–H activation / Iodine

Benzimidazol-2-ones have various biological functions and are usually prepared by reactions of substituted benzene-1,2-diamines with carbonyl-containing compounds or intramolecular *N*-arylations using substrates with carbon-halogen bonds. However, the starting materials of these protocols are often not readily available. Herein, a simple and practical metal-free oxidative C–H amidation of *N*,*N*′-diarylureas has been developed that takes place at room temperature. This protocol uses readily available *N*,*N*′-diarylureas as the starting materials and inexpensive $PhI(OAc)_2$ as the oxidant without the need of a catalyst, ligand, or the exclusion of air. The present method has a wide functional group tolerance and affords a new and practical strategy for the synthesis of N-heterocycles.

Introduction

Nitrogen-containing heterocycles are ubiquitous structures that exhibit a variety of biological activities[1] and have been assigned as privileged motifs in drug development.[2] The formation of C–N bonds is a key step in synthesis of N-heterocycles,[3] so it is of great value to develop new, efficient, and practical methods for their construction. Common approaches include the copper-catalyzed Ullmann-type coupling[4] and palladium-catalyzed Buchwald–Hartwig amination,[5] which occur between compounds that contain NH and aryl halides, and some N-heterocycles have been synthesized through coupling reactions by us[6] as well as other groups.[7] Recently, success has been achieved in the transition-metal-catalyzed formation of C–N bonds through direct C–H activation,[8] and various N-heterocycles have been constructed in this manner by us[9] and other groups.[10] Very recently, protocols for the formation of C–N bonds through C–H bond activation have been developed by using hypervalent iodine(III) reagents under metal-free conditions.[11] However, methods for the synthesis of N-heterocycles by using this strategy are limited.[12]

Benzimidazol-2-ones have various biological functions. For example, they are used as inhibitors of respiratory syncytial virus (RSV) fusion,[13] non-nucleoside reverse transcriptase (NNRT),[14] and farnesyltransferase (FTase)[15] as well as antagonists of the progesterone receptor.[16] Correspondingly, methods for the synthesis of these compounds have been developed. Common approaches include reactions between substituted benzene-1,2-diamines and phosgene,[17] triphosgene,[18] and carbonyldiimidazole (CDI).[19] However, substituted benzene-1,2-diamines are often not readily available. Recently, some alternative protocols have been developed for the transformation of carbon-halogen bonds into C–N bonds by transition-metal catalysis[20] or base promotion.[21] To the best of our knowledge, the aryl C–H amidation of *N*,*N*′-diarylureas has not been reported. Herein, we describe a metal-free oxidative C–H amidation reaction of readily available *N*,*N*′-diarylureas by using $PhI(OAc)_2$ at room temperature to prepare the corresponding benzimidazol-2-one derivatives.

Results and Discussion

We began by optimizing the reaction conditions for the oxidative C–H amidation of 1-methyl-1,3-diphenylurea (**1a**) with $PhI(OAc)_2$ to lead to 1-methyl-3-phenyl-1*H*-benzo[*d*]-imidazol-2(3*H*)-one (**2a**) and screened different solvents at room temperature without the exclusion of air (Table 1, Entries 1–10). The highest yield was obtained by carrying out the reaction in 1,1,1,3,3,3-hexafluoro-2-propanol (HFIP) for 12 h (Table 1, Entry 1). Other oxidants were then examined (Table 1, Entries 11–16), but they were inferior to $PhI(OAc)_2$. When the amount of $PhI(OAc)_2$ was reduced (Table 1, Entry 17), the yield of **2a** decreased. Finally, we

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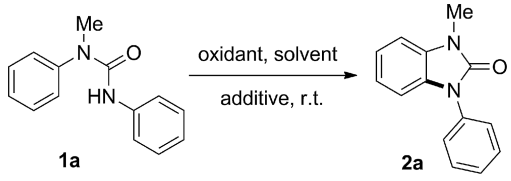
Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/ejoc.201500726.

employed several bases as additives (Table 1, Entries 18–20) and found that Cs_2CO_3 gave the best result (Table 1, Entry 18).

Table 1. Optimization of reaction conditions for intramolecular C–H oxidative amidation of 1-methyl-1,3-diphenylurea (**1a**).[a]



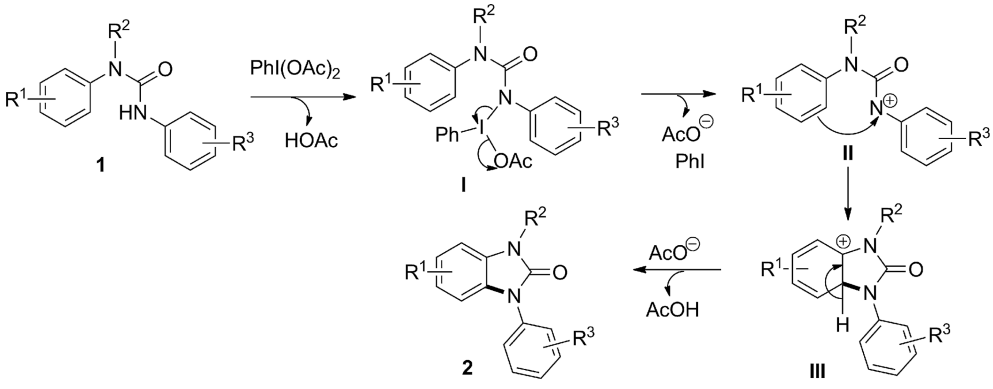
1a **2a**

Entry	Oxidant (equiv.)	Solvent	Additive	Time [h]	Yield [%][b]
1	$PhI(OAc)_2$ (1.5)	HFIP	–	12	63
2	$PhI(OAc)_2$ (1.5)	TFE[c]	–	12	50
3	$PhI(OAc)_2$ (1.5)	CF_3CO_2H	–	24	17
4	$PhI(OAc)_2$ (1.5)	CH_3CN	–	24	47
5	$PhI(OAc)_2$ (1.5)	THF[c]	–	24	0
6	$PhI(OAc)_2$ (1.5)	DMF[c]	–	24	trace
7	$PhI(OAc)_2$ (1.5)	DMSO[c]	–	24	trace
8	$PhI(OAc)_2$ (1.5)	*i*PrOH	–	24	0
9	$PhI(OAc)_2$ (1.5)	DCM[c]	–	24	39
10	$PhI(OAc)_2$ (1.5)	DCE[c]	–	24	23
11	PhI (0.2) + *m*-CPBA[c] (1.5)	HFIP	–	24	55
12	PhI (0.2) + TBHP[c] (1.5)	HFIP	–	24	0
13	$K_2S_2O_8$ (1.5)	HFIP	–	24	0
14	NIS[c] (1.5)	HFIP	–	24	0
15	NBS[c] (1.5)	HFIP	–	24	0
16	NCS[c] (1.5)	HFIP	–		0
17	$PhI(OAc)_2$ (1.1)	HFIP	–	24	51
18	$PhI(OAc)_2$ (1.5)	HFIP	Cs_2CO_3	12	71
19	$PhI(OAc)_2$ (1.5)	HFIP	K_2CO_3	12	57
20	$PhI(OAc)_2$ (1.5)	HFIP	Na_2CO_3	12	68

[a] Reagents and conditions: 1-methyl-1,3-diphenylurea (**1a**) (0.2 mmol), $PhI(OAc)_2$ (0.3 mmol), additive (0.24 mmol), and solvent (2.0 mL) at r.t. (approximately 25 °C) for 12 or 24 h in a sealed Schlenk tube without the exclusion of air. [b] Isolated yield. [c] TFE = 2,2,2-trifluoroethanol, THF = tetrahydrofuran, DMF = *N*,*N*-dimethylformamide, DMSO = dimethyl sulfoxide, DCM = 1,2-dichloromethane, DCE = 1,2-dichloroethane, *m*-CPBA = *meta*-chloroperoxybenzoic acid, TBHP = *tert*-butyl hydroperoxide, NIS = *N*-iodosuccinimide, NBS = *N*-bromosuccinimide, NCS = *N*-chlorosuccinimide.

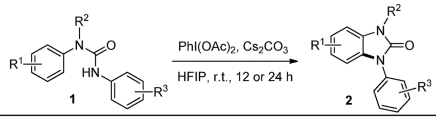
After the optimized reaction conditions were determined, the scope for oxidative C–H amidation of *N*,*N*′-diarylureas **1** with $PhI(OAc)_2$ was investigated. The substrates that were examined provided moderate to good yields (Table 2). The *N*,*N*′-diarylureas **1** with a neutral or electron-donating group for R^1 provided higher yields than those with electron-withdrawing substituents. With the exception of ethyl 4-(1-methyl-3-phenylureido)benzoate (**1y**), the other substrates afforded moderate to good yields at room temperature. However, the reaction of **1y**, which contained an ester group, did not work under the reaction conditions, and a higher temperature (80 °C) was required, which afforded only 40% yield. The *N*,*N*′-diarylureas **1** with an alphatic substituent for R^2 afforded lower yields as the substrate became more sterically hindered. 1-Benzyl-1,3-diphenylurea (**1h**) yielded two products **2h** and **2h**′. 1-Allyl-1,3-diphenylurea (**1g**) afforded a low yield of **2g** along with some unknown products (Table 2, Entry 7). Compound **1z**, in which R^2 = Ph, afforded a high yield of 88% (Table 2, Entry 26). The reaction of 1-methyl-3-phenyl-1-*m*-tolylurea (**1t**) gave major product **2t**. Because of steric hindrance, only a trace amount of **2t**′ was observed (Table 2, Entry 20). The *N*,*N*′-diarylureas **1** that contain electron-donating groups for R^3 showed higher reactivity than those with electron-withdrawing groups. The oxidative C–H amidation of *N*,*N*′-diarylureas **1**, which led to benzimidazol-2-one derivatives **2**, could tolerate various functional groups including a C–F bond (Table 2, Entries 12 and 22), a C–Cl bond (Table 2, Entries 13–15 and 23), a C–Br bond (Table 2, Entries 16 and 24), a CF_3 group (Table 2, Entry 17), and an ester group (Table 2, Entries 18 and 25).

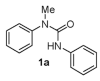
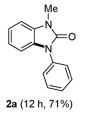
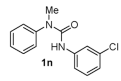
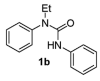
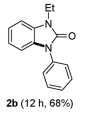
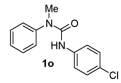
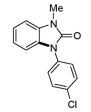
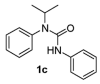
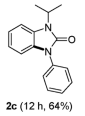
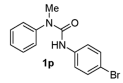
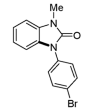
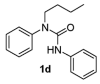
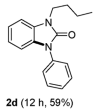
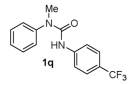
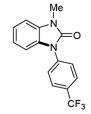
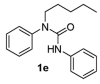
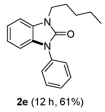
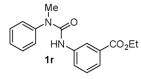
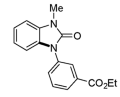
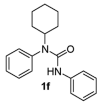
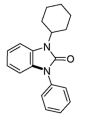
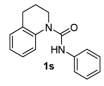
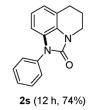
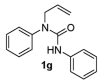
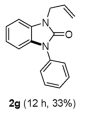
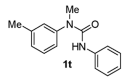
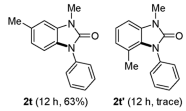
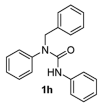
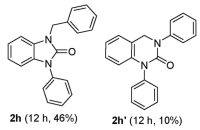
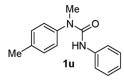
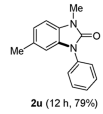
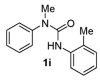
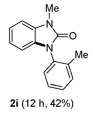
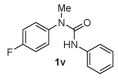
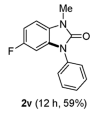
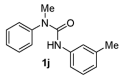
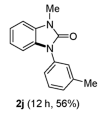
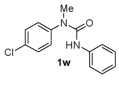
A possible mechanism for the oxidative C–H amidation of *N*,*N*′-diarylureas, which is in agreement with the results above and previous references,[12] is presented in Scheme 1. The treatment of **1** with $PhI(OAc)_2$ gives **I**, and heterolysis of the N–I bond of **I** results in the leaving of PhI and AcO^- to provide cation **II**. An intramolecular electrophilic addition of **II** leads to **III**, and the deprotonation of **III** in the presence of AcO^- affords target product **2**.



Scheme 1. Possible mechanism for the oxidative C–H amidation of *N*,*N*′-diarylureas.

Table 2. Oxidative C–H amidation of *N*,*N*′-diarylureas (**1**) to lead to benzimidazol-2-one derivatives (**2**).[a]



Entry	1	2 (time, yield[b])	Entry	1	2 (time, yield[b])
1		 **2a** (12 h, 71%)	14		 **2n** (12 h, 82%)
2		 **2b** (12 h, 68%)	15		 **2o** (12 h, 87%)
3		 **2c** (12 h, 64%)	16		 **2p** (12 h, 66%)
4		 **2d** (12 h, 59%)	17		 **2q** (12 h, 52%)
5		 **2e** (12 h, 61%)	18		 **2r** (12 h, 35%)
6		 **2f** (12 h, 55%)	19		 **2s** (12 h, 74%)
7		 **2g** (12 h, 33%)	20		 **2t** (12 h, 63%) **2t′** (12 h, trace)
8		 **2h** (12 h, 46%) **2h′** (12 h, 10%)	21		 **2u** (12 h, 79%)
9		 **2i** (12 h, 42%)	22		 **2v** (12 h, 59%)
10		 **2j** (12 h, 56%)	23		**2w** (12 h, 63%)
11		**2k** (12 h, 67%)	24		**2x** (12 h, 74%)
12		**2l** (12 h, 48%)	25		**2y** (24 h, 40%)[c]
13		**2m** (12 h, 55%)	26		**2z** (24 h, 88%)

[a] Reagents and conditions: *N*,*N*′-diarylureas **1** (0.2 mmol), $PhI(OAc)_2$ (0.3 mmol), Cs_2CO_3 (0.24 mmol), HFIP (2.0 mL), at r.t. (approximately 25 °C) for 12 or 24 h in a sealed Schlenk tube without the exclusion of air. [b] Isolated yield. [c] The reaction was performed at 80 °C.

Conclusions

We have developed a simple, efficient, and practical metal-free oxidative C–H amidation of *N*,*N*′-diarylureas. The corresponding benzimidazol-2-one derivatives were prepared in moderate to good yields. This protocol uses readily available *N*,*N*′-diarylureas as the starting materials and inexpensive $PhI(OAc)_2$ as the oxidant without the need for a catalyst, ligand, or the exclusion of air. The reactions performed well with wide tolerance for various functional groups. Therefore, the present method provides a new strategy for the synthesis of N-heterocycles.

Experimental Section

General Methods: All reactions were carried out under air. The ^1H and ^{13}C NMR spectroscopic data were recorded in $CDCl_3$ with tetramethylsilane as the internal standard (for ^1H NMR: TMS at δ = 0.00 ppm and $CHCl_3$ at δ = 7.26 ppm; for ^{13}C NMR: $CDCl_3$ at δ = 77.26 ppm). Compounds **1a**–**1z** were prepared according to previously reported procedures.[22]

General Procedure for Synthesis of Compounds 2a–2z: A 25 mL Schlenk tube was charged with a magnetic stirrer, *N*,*N*′-diarylurea **1** (0.2 mmol), $PhI(OAc)_2$ (0.3 mmol), Cs_2CO_3 (0.24 mmol), and 1,1,1,3,3,3-hexafluoro-2-propanol (2.0 mL). The tube was sealed, and the mixture was stirred at room temperature (approximately 25 °C; 80 °C for substrate **1y**, see Table 2) until the reaction reached completion (monitored by TLC). The mixture was concentrated by rotary evaporation, and the residue was purified by column chromatography on silica gel (petroleum ether/ethyl acetate) to give the desired target product **2**.

1-Methyl-3-phenyl-1*H*-benzo[*d*]imidazol-2(3*H*)-one (2a): Purification of the crude product by flash chromatography on silica gel (petroleum ether/ethyl acetate, 5:1) afforded **2a** (71% isolated yield) as a light yellow solid, m.p. 126–127 °C; ref.[21a] m.p. 127–129 °C. ^1H NMR (400 MHz, $CDCl_3$): δ = 7.54–7.49 (m, 4 H), 7.40–7.36 (m, 1 H), 7.17–7.13 (m, 1 H), 7.08–7.02 (m, 3 H), 3.49 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 153.6, 134.9, 130.3, 129.6, 129.5, 127.7, 126.1, 122.1, 121.5, 108.7, 107.7, 27.3 ppm. MS (ESI): *m*/*z* = 225.3 $[M + H]^+$.

1-Ethyl-3-phenyl-1*H*-benzo[*d*]imidazol-2(3*H*)-one (2b): Purification of the crude product by flash chromatography on silica gel (petroleum ether/ethyl acetate, 5:1) afforded **2b** (68% isolated yield) as a light yellow gum. ^1H NMR (300 MHz, $CDCl_3$): δ = 7.60–7.49 (m, 4 H), 7.42–7.37 (m, 1 H), 7.18–7.03 (m, 4 H), 4.03 (q, *J* = 7.2 Hz, 2 H), 1.41 (t, *J* = 7.2 Hz, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 153.1, 134.8, 129.6, 129.3, 127.6, 126.1, 122.0, 121.3, 108.9, 107.8, 36.1, 13.7 ppm. MS (ESI): *m*/*z* = 238.3 $[M + H]^+$.

1-Isopropyl-3-phenyl-1*H*-benzo[*d*]imidazol-2(3*H*)-one (2c): Purification of the crude product by flash chromatography on silica gel (petroleum ether/ethyl acetate, 5:1) afforded **2c** (64% isolated yield) as a light yellow solid; m.p. 105–106 °C. ^1H NMR (400 MHz, $CDCl_3$): δ = 7.54–7.49 (m, 4 H), 7.42–7.36 (m, 1 H), 7.21 (d, *J* = 7.8 Hz, 1 H), 7.13–7.01 (m, 3 H), 4.81 (m, 1 H), 1.60 (d, *J* = 7.0 Hz, 6 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 152.8, 134.8, 129.7, 129.5, 128.5, 127.6, 126.3, 121.7, 121.0, 109.2, 108.8, 45.3, 20.3 ppm. MS (ESI): *m*/*z* = 252.2 $[M + H]^+$.

1-Butyl-3-phenyl-1*H*-benzo[*d*]imidazol-2(3*H*)-one (2d): Purification of the crude product by flash chromatography on silica gel (petroleum ether/ethyl acetate, 5:1) afforded **2d** (59% isolated yield) as a light yellow gum. ^1H NMR (400 MHz, $CDCl_3$): δ = 7.56–7.49 (m, 4 H), 7.38 (t, *J* = 6.9 Hz, 1 H), 7.15–7.03 (m, 4 H), 3.95 (t, *J* = 7.2 Hz, 2 H), 1.84–1.76 (m, 2 H), 1.50–1.40 (m, 2 H), 0.98 (t, *J* = 7.3 Hz, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 153.4, 134.9, 129.7, 129.5, 127.6, 126.0, 121.9, 121.3, 108.8, 107.9, 41.1, 30.5, 20.2, 13.9 ppm. MS (ESI): *m*/*z* = 267.5 $[M + H]^+$.

1-Pentyl-3-phenyl-1*H*-benzo[*d*]imidazol-2(3*H*)-one (2e): Purification of the crude product by flash chromatography on silica gel (petroleum ether/ethyl acetate, 5:1) afforded **2e** (61% isolated yield) as a light yellow gum. ^1H NMR (400 MHz, $CDCl_3$): δ = 7.56–7.49 (m, 4 H), 7.40–7.36 (m, 1 H), 7.15–7.02 (m, 4 H), 3.94 (t, *J* = 7.3 Hz, 2 H), 1.85–1.78 (m, 2 H), 1.44–1.36 (m, 4 H), 0.91 (t, *J* = 7.0 Hz, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 153.4, 134.9, 129.7, 129.5, 127.6, 126.0, 121.9, 121.3, 108.8, 107.9, 41.1, 29.1, 28.1, 22.5, 14.1 ppm. MS (ESI): *m*/*z* = 281.1 $[M + H]^+$.

1-Cyclohexyl-3-phenyl-1*H*-benzo[*d*]imidazol-2(3*H*)-one (2f): Purification of the crude product by flash chromatography on silica gel (petroleum ether/ethyl acetate, 5:1) afforded **2f** (55% isolated yield) as a light yellow solid; m.p. 94–95 °C. ^1H NMR (400 MHz, $CDCl_3$): δ = 7.54–7.49 (m, 4 H), 7.41–7.36 (m, 1 H), 7.24 (d, *J* = 7.7 Hz, 1 H), 7.12–7.00 (m, 3 H), 4.40–4.32 (m, 1 H), 2.26–2.17 (m, 2 H), 1.94 (d, *J* = 10.9 Hz, 4 H), 1.77 (d, *J* = 12.9 Hz, 1 H), 1.52–1.42 (m, 2 H), 1.34–1.25 (m, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 152.9, 134.8, 129.7, 129.5, 128.8, 127.6, 126.3, 121.6, 120.9, 109.5, 108.8, 53.3, 30.2, 26.1, 25.5 ppm. MS (ESI): *m*/*z* = 293.1 $[M + H]^+$.

1-Allyl-3-phenyl-1*H*-benzo[*d*]imidazol-2(3*H*)-one (2g): Purification of the crude product by flash chromatography on silica gel (petroleum ether/ethyl acetate, 5:1) afforded **2g** (33% isolated yield) as a light yellow gum. ^1H NMR (600 MHz, $CDCl_3$): δ = 7.55–7.51 (m, 4 H), 7.39 (t, *J* = 6.8 Hz, 1 H), 7.13–7.08 (m, 2 H), 7.05 (t, *J* = 7.9 Hz, 2 H), 5.99–5.93 (m, 1 H), 5.32–5.26 (m, 2 H), 4.58 (dd, *J* = 5.5 Hz, *J* = 1.0 Hz, 2 H) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = 153.2, 134.8, 132.0, 129.6, 129.3, 127.7, 126.1, 125.9, 122.0, 121.5, 117.9, 108.8, 108.5, 43.8 ppm. MS (ESI): *m*/*z* = 251.2 $[M + H]^+$.

1-Benzyl-3-phenyl-1*H*-benzo[*d*]imidazol-2(3*H*)-one (2h): Purification of the crude product by flash chromatography on silica gel (petroleum ether/ethyl acetate, 5:1) afforded **2h** (46% isolated yield) as a light yellow solid, m.p. 99–100 °C; ref.[21b] m.p. 99.8–100.7 °C. ^1H NMR (400 MHz, $CDCl_3$): δ = 7.59–7.51 (m, 4 H), 7.41–7.38 (m, 3 H), 7.34 (t, *J* = 7.9 Hz, 2 H), 7.28 (d, *J* = 7.3 Hz, 1 H), 7.11–7.07 (m, 1 H), 7.06–7.03 (m, 2 H), 6.96–6.94 (m, 1 H), 5.14 (s, 2 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 153.6, 136.3, 134.8, 129.6, 129.4, 128.9, 127.9, 127.8, 127.7, 126.0, 122.1, 121.6, 108.9, 108.6, 45.1 ppm. MS (ESI): *m*/*z* = 301.3 $[M + H]^+$.

1-Benzyl-3-phenyl-1*H*-benzo[*d*]imidazol-2(3*H*)-one (2h′): Purification of the crude product by flash chromatography on silica gel (petroleum ether/ethyl acetate, 5:1) afforded **2h′** (10% isolated yield) as a light yellow gum. ^1H NMR (400 MHz, $CDCl_3$): δ = 7.58–7.47 (m, 4 H), 7.42–7.28 (m, 6 H), 7.09–7.05 (m, 3 H), 6.98–6.95 (m, 1 H), 5.14 (s, 2 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 153.4, 136.1, 133.4, 133.3, 129.8, 129.4, 129.2, 128.9, 127.9, 127.8, 127.2, 122.4, 121.8, 108.7, 45.2 ppm. MS (ESI): *m*/*z* = 301.2 $[M + H]^+$.

1-Methyl-3-(*o*-tolyl)-1*H*-benzo[*d*]imidazol-2(3*H*)-one (2i): Purification of the crude product by flash chromatography on silica gel (petroleum ether/ethyl acetate, 5:1) afforded **2i** (42% isolated yield) as a light yellow solid; m.p. 89–91 °C. ^1H NMR (300 MHz, $CDCl_3$): δ = 7.41–7.27 (m, 4 H), 7.14 (t, *J* = 7.6 Hz, 1 H), 7.06–7.01 (m, 2 H), 6.69 (d, *J* = 7.6 Hz, 1 H), 3.51 (s, 3 H), 2.18 (s, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 153.6, 137.0, 133.2,

131.6, 130.4, 130.2, 129.2, 128.7, 127.2, 121.8, 121.5, 108.7, 107.6, 27.4, 17.9 ppm. MS (ESI): *m*/*z* = 239.2 [M + H]$^+$.

1-Methyl-3-(*m*-tolyl)-1*H*-benzo[*d*]imidazol-2(3*H*)-one (2j): Purification of the crude product by flash chromatography on silica gel (petroleum ether/ethyl acetate, 5:1) afforded **2j** (56% isolated yield) as a light yellow solid; m.p. 77–76 °C. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.40 (t, *J* = 7.7 Hz, 1 H), 7.34 (s, 1 H), 7.31 (d, *J* = 7.9 Hz, 1 H), 7.20 (d, *J* = 7.6 Hz, 1 H), 7.15–7.12 (m, 1 H), 7.06–7.02 (m, 3 H), 3.48 (s, 3 H), 2.42 (s, 3 H) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = 153.7, 139.6, 134.7, 130.2, 129.6, 129.3, 128.5, 126.8, 123.1, 121.9, 121.5, 108.8, 107.6, 27.3, 21.5 ppm. MS (ESI): *m*/*z* = 239.2 [M + H]$^+$.

Methyl-3-(*p*-tolyl)-1*H*-benzo[*d*]imidazol-2(3*H*)-one (2k): Purification of the crude product by flash chromatography on silica gel (petroleum ether/ethyl acetate, 5:1) afforded **2k** (67% isolated yield) as a light yellow solid; m.p. 107–108 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.40 (d, *J* = 8.4 Hz, 2 H), 7.32 (d, *J* = 8.2 Hz, 2 H), 7.17–7.12 (m, 1 H), 7.06–7.02 (m, 3 H), 3.49 (s, 3 H), 2.42 (s, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 153.8, 137.6, 132.2, 130.2, 129.7, 126.0, 121.9, 121.5, 108.7, 107.6, 27.3, 21.3 ppm. MS (ESI): *m*/*z* = 239.1 [M + H]$^+$.

1-(4-Fluorophenyl)-3-methyl-1*H*-benzo[*d*]imidazol-2(3*H*)-one (2l): Purification of the crude product by flash chromatography on silica gel (petroleum ether/ethyl acetate, 5:1) afforded **2l** (48% isolated yield) as a light yellow solid; m.p. 132–133 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.51–7.47 (m, 2 H), 7.22–7.13 (m, 3 H), 7.09–7.00 (m, 3 H), 3.48 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 161.7 (d, *J* = 247.6 Hz), 153.6, 130.7 (d, *J* = 0.7 Hz), 130.2, 129.5, 127.9 (d, *J* = 8.6 Hz), 122.2, 121.6, 116.5 (d, *J* = 22.9 Hz), 108.5, 107.8, 27.4 ppm. MS (ESI): *m*/*z* = 243.2 [M + H]$^+$.

1-(2-Chlorophenyl)-3-methyl-1*H*-benzo[*d*]imidazol-2(3*H*)-one (2m): Purification of the crude product by flash chromatography on silica gel (petroleum ether/ethyl acetate, 5:1) afforded **2m** (55% isolated yield) as a light yellow solid; m.p. 124–126 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.61–7.57 (m, 1 H), 7.46–7.41 (m, 3 H), 7.15 (dt, *J* = 7.7 Hz, *J* = 1.0 Hz, 1 H), 7.06–7.02 (m, 2 H), 6.70 (d, *J* = 7.3 Hz, 1 H), 3.50 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 153.3, 133.4, 132.2, 130.9, 130.6, 130.4, 130.3, 129.6, 128.1, 122.1, 121.6, 108.9, 107.8, 27.4 ppm. MS (ESI): *m*/*z* = 259.3 [M + H]$^+$, 261.3.

1-(3-Chlorophenyl)-3-methyl-1*H*-benzo[*d*]imidazol-2(3*H*)-one (2n): Purification of the crude product by flash chromatography on silica gel (petroleum ether/ethyl acetate, 5:1) afforded **2n** (82% isolated yield) as a light yellow solid; m.p. 141–143 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.56 (s, 1 H), 7.48–7.42 (m, 2 H), 7.38–7.32 (m, 1 H), 7.18–7.14 (m, 1 H), 7.10–7.03 (m, 3 H), 3.48 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 153.3, 136.1, 135.1, 130.5, 130.3, 128.9, 127.8, 126.1, 124.1, 122.4, 121.7, 108.7, 107.9, 27.4 ppm. MS (ESI): *m*/*z* = 259.3 [M + H]$^+$, 261.3.

1-(4-Chlorophenyl)-3-methyl-1*H*-benzo[*d*]imidazol-2(3*H*)-one (2o): Purification of the crude product by flash chromatography on silica gel (petroleum ether/ethyl acetate, 5:1) afforded **2o** (87% isolated yield) as a light yellow solid; m.p. 159–160 °C. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.48 (s, 4 H), 7.16 (dt, *J* = 7.7 Hz, *J* = 1.2 Hz, 1 H), 7.08–7.03 (m, 3 H), 3.48 (s, 3 H) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = 153.4, 133.4, 133.2, 130.3, 129.8, 129.1, 127.2, 122.3, 121.7, 108.6, 107.9, 27.4 ppm. MS (ESI): *m*/*z* = 259.4 [M + H]$^+$, 261.4.

1-(4-Bromophenyl)-3-methyl-1*H*-benzo[*d*]imidazol-2(3*H*)-one (2p): Purification of the crude product by flash chromatography on silica gel (petroleum ether/ethyl acetate, 5:1) afforded **2p** (66% isolated yield) as a light yellow solid; m.p. 160–162 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.64 (d, *J* = 8.7 Hz, 2 H), 7.43 (d, *J* = 8.7 Hz, 2 H), 7.20–7.13 (m, 1 H), 7.11–7.03 (m, 3 H), 3.48 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 153.4, 134.0, 132.7, 130.3, 129.0, 127.5, 122.4, 121.7, 121.1, 108.9, 107.9, 27.4 ppm. MS (ESI): *m*/*z* = 303.1 [M + H]$^+$, 305.1.

1-Methyl-3-[4-(trifluoromethyl)phenyl]-1*H*-benzo[*d*]imidazol-2(3*H*)-one (2q): Purification of the crude product by flash chromatography on silica gel (petroleum ether/ethyl acetate, 5:1) afforded **2q** (52% isolated yield) as a light yellow solid; m.p. 146–148 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.79 (d, *J* = 8.5 Hz, 2 H), 7.71 (d, *J* = 8.5 Hz, 2 H), 7.19 (dt, *J* = 7.5 Hz, *J* = 1.4 Hz, 1 H), 7.11 (dq, *J* = 7.7 Hz, *J* = 1.1 Hz, 2 H), 7.06 (d, *J* = 8.1 Hz, 1 H), 3.49 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 152.1, 137.1, 129.3, 128.2 (d, *J* = 33.0 Hz), 125.6 (d, *J* = 3.6 Hz), 124.7, 122.4 (q, *J* = 272.0 Hz), 121.6, 120.7, 107.6, 106.9, 26.3 ppm. MS (ESI): *m*/*z* = 293.5 [M + H]$^+$.

Ethyl 3-(3-Methyl-2-oxo-2,3-dihydro-1*H*-benzo[*d*]imidazol-1-yl)-benzoate (2r): Purification of the crude product by flash chromatography on silica gel (petroleum ether/ethyl acetate, 5:1) afforded **2r** (35% isolated yield) as a light yellow solid; m.p. 90–92 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.22 (d, *J* = 1.8 Hz, 1 H), 8.08 (dt, *J* = 7.8 Hz, *J* = 1.3 Hz, 1 H), 7.78–7.74 (m, 1 H), 7.61 (t, *J* = 7.9 Hz, 1 H), 7.21–7.15 (m, 1 H), 7.09–7.04 (m, 3 H), 4.40 (q, *J* = 7.1 Hz, 2 H), 3.50 (s, 3 H), 1.39 (t, *J* = 7.1 Hz, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 165.8, 153.5, 135.1, 132.1, 130.4, 130.3, 129.7, 129.1, 128.7, 126.9, 122.4, 121.7, 108.7, 107.9, 61.4, 27.4, 14.4 ppm. MS (ESI): *m*/*z* = 297.5 [M + H]$^+$.

1-Phenyl-5,6-dihydro-1*H*-imidazo[4,5,1-*ij*]quinolin-2(4*H*)-one (2s): Purification of the crude product by flash chromatography on silica gel (petroleum ether/ethyl acetate, 5:1) afforded **2s** (74% isolated yield) as a light yellow gum. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.59–7.48 (m, 4 H), 7.38–7.34 (m, 1 H), 7.00–6.90 (m, 3 H), 3.94 (t, *J* = 5.8 Hz, 2 H), 2.91 (t, *J* = 6.0 Hz, 2 H), 2.22–2.14 (m 2 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 152.6, 135.4, 129.5, 127.8, 127.2, 126.8, 125.4, 121.0, 120.2, 119.8, 106.6, 39.3, 24.1, 21.9 ppm. MS (ESI): *m*/*z* = 251.1 [M + H]$^+$.

3,5-Dimethyl-1-phenyl-1*H*-benzo[*d*]imidazol-2(3*H*)-one (2t): Purification of the crude product by flash chromatography on silica gel (petroleum ether/ethyl acetate, 5:1) afforded **2t** (63% isolated yield) as a light yellow solid; m.p. 127–128 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.53–7.49 (m, 4 H), 7.39–7.34 (m, 1 H), 6.96 (d, *J* = 8.5 Hz, 1 H), 6.86 (d, *J* = 7.5 Hz, 2 H), 3.46 (s, 3 H), 2.42 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 153.7, 135.1, 131.9, 130.4, 129.5, 127.4, 127.3, 125.9, 121.9, 108.5, 108.4, 27.3, 21.6 ppm. MS (ESI): *m*/*z* = 239.2 [M + H]$^+$.

1,5-Dimethyl-3-phenyl-1*H*-benzo[*d*]imidazol-2(3*H*)-one (2u): Purification of the crude product by flash chromatography on silica gel (petroleum ether/ethyl acetate, 5:1) afforded **2u** (79% isolated yield) as a light yellow solid; m.p. 78–80 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.58–7.47 (m, 4 H), 7.44–7.36 (m, 1 H), 6.98–6.89 (m, 3 H), 3.47 (s, 3 H), 2.36 (s, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 153.8, 135.0, 131.4, 129.6, 128.1, 127.6, 126.2, 122.6, 109.3, 107.4, 27.4, 21.6 ppm. MS (ESI): *m*/*z* = 239.3[M + H]$^+$.

5-Fluoro-1-methyl-3-phenyl-1*H*-benzo[*d*]imidazol-2(3*H*)-one (2v): Purification of the crude product by flash chromatography on silica gel (petroleum ether/ethyl acetate, 5:1) afforded **2v** (59% isolated yield) as a light yellow solid; m.p. 145–147 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.54–7.49 (m, 4 H), 7.39 (t, *J* = 6.8 Hz, 1 H), 6.94–6.90 (m, 1 H), 6.87–6.80 (m, 2 H), 3.47 (s, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 160.5, 155.6 (d, *J* = 258.0 Hz), 134.5, 130.0 (d, *J* = 12.4 Hz), 129.7, 127.9, 126.0, 125.9, 108.3 (d, *J* = 24.3 Hz),

107.8 (d, J = 9.4 Hz), 97.2 (d, J = 29.2 Hz), 27.5 ppm. MS (ESI): m/z = 243.2 $[M + H]^+$.

5-Chloro-1-methyl-3-phenyl-1*H*-benzo[*d*]imidazol-2(3*H*)-one (2w): Purification of the crude product by flash chromatography on silica gel (petroleum ether/ethyl acetate, 5:1) afforded **2w** (63% isolated yield) as a light yellow solid; m.p. 150–152 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.55–7.47 (m, 4 H), 7.40 (t, J = 7.0 Hz, 1 H), 7.11 (dd, J = 8.3 Hz, J = 1.5 Hz, 1 H), 7.04 (d, J = 1.6 Hz, 1 H), 6.93 (d, J = 8.3 Hz, 1 H), 3.46 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 153.5, 134.3, 130.3, 129.8, 128.8, 128.1, 127.1, 126.0, 121.9, 109.1, 108.4, 27.5 ppm. MS (ESI): m/z = 259.3 $[M + H]^+$, 261.3.

5-Bromo-1-methyl-3-phenyl-1*H*-benzo[*d*]imidazol-2(3*H*)-one (2x): Purification of the crude product by flash chromatography on silica gel (petroleum ether/ethyl acetate, 5:1) afforded **2x** (74% isolated yield) as a light yellow solid, m.p. 175–176 °C; ref.[23] m.p. 175–177 °C. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.53 (t, J = 8.2 Hz, 2 H), 7.48 (d, J = 7.3 Hz, 2 H), 7.41 (t, J = 7.3 Hz, 1 H), 7.26–7.24 (m, 1 H), 7.17 (d, J = 1.3 Hz, 1 H), 6.89 (d, J = 8.3 Hz, 1 H), 3.46 (s, 3 H) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = 153.4, 134.3, 130.6, 129.8, 129.3, 128.1, 126.0, 124.8, 114.2, 111.8, 108.9, 27.5 ppm. MS (ESI): m/z = 303.3 $[M + H]^+$, 305.3.

Ethyl 2,3-Dihydro-1-methyl-2-oxo-3-phenyl-1*H*-benzo[*d*]imidazole-5-carboxylate (2y): Purification of the crude product by flash chromatography on silica gel (petroleum ether/ethyl acetate, 5:1) afforded **2y** (40% isolated yield) as a light yellow solid; m.p. 127–128 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.93 (dd, J = 8.2 Hz, J = 1.6 Hz, 1 H), 7.74 (d, J = 1.5 Hz, 1 H), 7.58–7.51 (m, 4 H), 7.47–7.41 (m, 1 H), 7.06 (d, J = 8.2 Hz, 1 H), 4.35 (q, J = 7.1 Hz, 2 H), 3.53 (s, 3 H), 1.37 (t, J = 7.1 Hz, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 166.6, 153.8, 134.3, 133.9, 129.8, 129.3, 128.1, 126.1, 124.6, 124.1, 109.9, 107.1, 61.1, 27.6, 14.5 ppm. MS (ESI): m/z = 297.3 $[M + H]^+$.

1,3-Diphenyl-1*H*-benzo[*d*]imidazol-2(3*H*)-one (2z): Purification of the crude product by flash chromatography on silica gel (petroleum ether/ethyl acetate, 5:1) afforded **2z** (88% isolated yield) as a light yellow solid; m.p. 100–101 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.63–7.60 (m, 4 H), 7.59–7.53 (m, 4 H), 7.44–7.40 (m, 2 H), 7.16–7.10 (m, 4 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 152.5, 134.6, 129.6, 127.9, 126.2, 122.2, 109.19 ppm. MS (ESI): m/z = 287.1 $[M + H]^+$.

Supporting Information (see footnote on the first page of this article): Copies of ^{1}H and ^{13}C NMR spectra of compounds **2a**–**2z**.

Acknowledgments

The authors wish to thank the National Natural Science Foundation of China (NSFC) (grant numbers 21172128, 21372139, and 21221062) and the Ministry of Science and Technology of China (grant number 2012CB722605) for financial support.

[1] R. W. DeSimone, K. S. Currie, S. A. Mitchell, J. W. Darrow, D. A. Pippin, *Comb. Chem. High Throughput Screening* **2004**, *7*, 473.

[2] P. D. Leeson, B. Springthorpe, *Nat. Rev. Drug Discov.* **2007**, *6*, 881.

[3] a) D. S. Surry, S. L. Buchwald, *Angew. Chem. Int. Ed.* **2008**, *47*, 6338; *Angew. Chem.* **2008**, *120*, 6438; b) J. F. Hartwig, *Acc. Chem. Res.* **2008**, *41*, 1534; c) D. N. Zalatan, J. Du Bois, *Top. Curr. Chem.* **2010**, *292*, 347; d) M. Carril, R. SanMartin, E. Dominguez, *Chem. Soc. Rev.* **2008**, *37*, 639.

[4] For recent reviews of copper-catalyzed cross-coupling reactions, see: a) D. S. Surry, S. L. Buchwald, *Chem. Sci.* **2010**, *1*, 13; b) K. Kunz, U. Scholz, D. Ganzer, *Synlett* **2003**, 2428; c) S. V. Ley, A. W. Thomas, *Angew. Chem. Int. Ed.* **2003**, *42*, 5400; *Angew. Chem.* **2003**, *115*, 5558; d) D. Ma, Q. Cai, *Acc. Chem. Res.* **2008**, *41*, 1450; e) I. P. Beletskaya, A. V. Cheprakov, *Coord. Chem. Rev.* **2004**, *248*, 2337; f) G. Evano, N. Blanchard, M. Toumi, *Chem. Rev.* **2008**, *108*, 3054; g) F. Monnier, M. Taillefer, *Angew. Chem. Int. Ed.* **2009**, *48*, 6954; *Angew. Chem.* **2009**, *121*, 7088; h) H. Rao, H. Fu, *Synlett* **2011**, 745, and references cited therein.

[5] a) A. S. Guram, S. L. Buchwald, *J. Am. Chem. Soc.* **1994**, *116*, 7901; b) F. Paul, J. Patt, J. F. Hartwig, *J. Am. Chem. Soc.* **1994**, *116*, 5969.

[6] a) X. Liu, H. Fu, Y. Jiang, Y. Zhao, *Angew. Chem. Int. Ed.* **2009**, *48*, 348; *Angew. Chem.* **2009**, *121*, 354; b) X. Yang, H. Fu, R. Qiao, Y. Jiang, Y. Zhao, *Adv. Synth. Catal.* **2010**, *352*, 1033; c) D. Yang, H. Liu, H. Yang, H. Fu, L. Hu, Y. Jiang, Y. Zhao, *Adv. Synth. Catal.* **2009**, *351*, 1999; d) J. Lu, X. Gong, H. Yang, H. Fu, *Chem. Commun.* **2010**, *46*, 4172; e) C. Huang, Y. Fu, H. Fu, Y. Jiang, Y. Zhao, *Chem. Commun.* **2008**, 6333; f) H. Zhao, H. Fu, R. Qiao, *J. Org. Chem.* **2010**, *75*, 3311; g) D. Yang, H. Fu, L. Hu, Y. Jiang, Y. Zhao, *J. Org. Chem.* **2008**, *73*, 7841; h) F. Wang, H. Liu, H. Fu, Y. Jiang, Y. Zhao, *Org. Lett.* **2009**, *11*, 2469; i) X. Gong, H. Yang, H. Liu, Y. Jiang, Y. Zhao, H. Fu, *Org. Lett.* **2010**, *12*, 3128.

[7] a) R. Martín, M. Rodríguez Rivero, S. L. Buchwald, *Angew. Chem. Int. Ed.* **2006**, *45*, 7079; *Angew. Chem.* **2006**, *118*, 7237; b) B. Zou, Q. Yuan, D. Ma, *Angew. Chem. Int. Ed.* **2007**, *46*, 2598; *Angew. Chem.* **2007**, *119*, 2652; c) X. Yuan, X. Xu, X. Zhou, J. Yuan, L. Mai, Y. Li, *J. Org. Chem.* **2007**, *72*, 1510; d) G. Evindar, R. A. Batey, *J. Org. Chem.* **2006**, *71*, 1802; e) F. Bonnaterre, M. Bois-Choussy, J. Zhu, *Org. Lett.* **2006**, *8*, 4351; f) G. Altenhoff, F. Glorius, *Adv. Synth. Catal.* **2004**, *346*, 1661.

[8] For selected papers, see: a) J. A. Jordan-Hore, C. C. C. Johansson, M. Gulias, E. M. Beck, M. J. Gaunt, *J. Am. Chem. Soc.* **2008**, *130*, 16184; b) W. C. P. Tsang, N. Zheng, S. L. Buchwald, *J. Am. Chem. Soc.* **2005**, *127*, 14560; c) J. J. Neumann, S. Rakshit, T. Dröge, F. Glorius, *Angew. Chem. Int. Ed.* **2009**, *48*, 6892; *Angew. Chem.* **2009**, *121*, 7024; d) B. H. Li, S. L. Tian, Z. Fang, Z. H. Shi, *Angew. Chem. Int. Ed.* **2008**, *47*, 1115; *Angew. Chem.* **2008**, *120*, 1131.

[9] a) J. Yu, Y. Jin, H. Zhang, X. Yang, H. Fu, *Chem. Eur. J.* **2013**, *19*, 16804; b) J. Yu, H. Yang, Y. Jiang, H. Fu, *Chem. Eur. J.* **2013**, *19*, 4271; c) H. Xu, H. Fu, *Chem. Eur. J.* **2012**, *18*, 1180; d) C. Wang, S. Li, H. Liu, Y. Jiang, H. Fu, *J. Org. Chem.* **2010**, *75*, 7936; e) J. Lu, Y. Jin, H. Liu, Y. Jiang, H. Fu, *Org. Lett.* **2011**, *13*, 3694; f) W. Xu, H. Fu, *J. Org. Chem.* **2011**, *76*, 3846; g) X. Wang, Y. Jin, Y. Zhao, L. Zhu, H. Fu, *Org. Lett.* **2012**, *14*, 452; h) W. Xu, Y. Jin, H. Liu, Y. Jiang, H. Fu, *Org. Lett.* **2011**, *13*, 1274.

[10] For selected papers, see: a) G. Brasche, S. L. Buchwald, *Angew. Chem. Int. Ed.* **2008**, *47*, 1932; *Angew. Chem.* **2008**, *120*, 1958; b) S. Ueda, H. Nagasawa, *Angew. Chem. Int. Ed.* **2008**, *47*, 6411; *Angew. Chem.* **2008**, *120*, 6511; c) H. Wang, Y. Wang, D. Liang, L. Liu, J. Zhang, Q. Zhu, *Angew. Chem. Int. Ed.* **2011**, *50*, 5678; *Angew. Chem.* **2011**, *123*, 5796; d) S. Ueda, H. Nagasawa, *J. Am. Chem. Soc.* **2009**, *131*, 15080; e) Y.-F. Wang, H. Chen, X. Zhu, S. Chiba, *J. Am. Chem. Soc.* **2012**, *134*, 11980; for a review, see: f) T. Liu, H. Fu, *Synthesis* **2012**, *44*, 2805.

[11] For recent examples of C–N bond formation using hypervalent iodine(III) reagents, see: a) U. Farid, T. Wirth, *Angew. Chem. Int. Ed.* **2012**, *51*, 3462; *Angew. Chem.* **2012**, *124*, 3518; b) J. A. Souto, C. Martínez, I. Velilla, K. Muñiz, *Angew. Chem. Int. Ed.* **2013**, *52*, 1324; *Angew. Chem.* **2013**, *125*, 1363; c) C. Röben, J. A. Souto, Y. González, A. Lishchynskyi, K. Muñiz, *Angew. Chem. Int. Ed.* **2011**, *50*, 9478; *Angew. Chem.* **2011**, *123*, 9650; d) A. Lishchynskyi, K. Muñiz, *Chem. Eur. J.* **2012**, *18*, 2212; e) R. D. Richardson, M. Desaize, T. Wirth, *Chem. Eur. J.* **2007**, *13*, 6745; f) A. Yoshimura, V. N. Nemykin, V. V. Zhdankin, *Chem. Eur. J.* **2011**, *17*, 10538; g) A. A. Kantak, S. Potavathri, R. A. Barham, K. M. Romano, B. Deboef, *J. Am. Chem. Soc.*

2011, *133*, 19960; h) J. A. Souto, D. Zian, K. Muñiz, *J. Am. Chem. Soc.* **2012**, *134*, 7242; i) J. A. Souto, P. Becker, A. Iglesias, K. Muñiz, *J. Am. Chem. Soc.* **2012**, *134*, 15505; j) Y. Du, R. Liu, G. Linn, K. Zhao, *Org. Lett.* **2006**, *8*, 5919; k) R. Samanta, J. O. Bauer, C. Strohmann, A. P. Antonchick, *Org. Lett.* **2012**, *14*, 5518; l) H. J. Kim, S. H. Cho, S. Chang, *Org. Lett.* **2012**, *14*, 1424; m) Y. Kikugawa, A. Nagashima, T. Sakamoto, E. Miyazawa, M. Shiiya, *J. Org. Chem.* **2003**, *68*, 6739; n) X. Ban, Y. Pan, Y. Lin, S. Wang, Y. Du, K. Zhao, *Org. Biomol. Chem.* **2012**, *10*, 3606; o) J. Huang, Y. He, Y. Wang, Q. Zhu, *Chem. Eur. J.* **2012**, *18*, 13964.

[12] a) A. P. Antonchick, R. Samanta, K. Kulikov, J. Lategahn, *Angew. Chem. Int. Ed.* **2011**, *50*, 8605; *Angew. Chem.* **2011**, *123*, 8764; b) J. Huang, Y. He, Y. Wang, Q. Zhu, *Chem. Eur. J.* **2012**, *18*, 13964; c) J. Zhu, H. Xie, Z. Chen, S. Li, Y. Wu, *Synlett* **2009**, *20*, 3299; d) Y. He, J. Huang, D. Liang, L. Liu, Q. Zhu, *Chem. Commun.* **2013**, *49*, 7352; e) S. K. Alla, R. K. Kumar, P. Sadhu, T. Punniyamurthy, *Org. Lett.* **2013**, *15*, 1334; f) J.-P. Lin, F.-H. Zhang, Y.-Q. Long, *Org. Lett.* **2014**, *16*, 2822; g) Y. Chi, W.-X. Zhang, Z. Xi, *Org. Lett.* **2014**, *16*, 6274.

[13] K.-L. Yu, N. Sin, R. L. Civiello, X. A. Wang, K. D. Combrink, H. B. Gulgeze, B. L. Venables, J. J. K. Wright, R. A. Dalterio, L. Zadjura, A. Marino, S. Dando, C. D'Arienzo, K. F. Kadow, C. W. Cianci, Z. Li, J. Clarke, E. V. Genovesi, I. Medina, L. Lamb, R. J. Colonno, Z. Yang, M. Krystal, N. A. Meanwell, *Bioorg. Med. Chem. Lett.* **2007**, *17*, 895.

[14] M. L. Barreca, A. Rao, L. De Luca, N. Iraci, A.-M. Monforte, G. Maga, E. De Clercq, C. Pannecouque, J. Balzarini, A. Chimirri, *Bioorg. Med. Chem. Lett.* **2007**, *17*, 1956.

[15] Q. Li, T. Li, K. W. Woods, W.-Z. Gu, J. Cohen, V. S. Stoll, T. Galicia, C. Hutchins, D. Frost, S. H. Rosenberg, H. L. Sham, *Bioorg. Med. Chem. Lett.* **2005**, *15*, 2918.

[16] E. A. Terefenko, J. Kern, A. Fensome, J. Wrobel, Y. Zhu, J. Cohen, R. Winneker, Z. Zhang, P. Zhang, *Bioorg. Med. Chem. Lett.* **2005**, *15*, 3600.

[17] For selected examples, see: a) P. H. Elsinga, A. van Waarde, K. A. Jaeggi, G. Schreiber, M. Heldoorn, W. Vaalburg, *J. Med. Chem.* **1997**, *40*, 3829; b) R. Henning, R. Lattrell, H. J. Gerhards, M. Leven, *J. Med. Chem.* **1987**, *30*, 814.

[18] For selected examples, see: a) D. J. Gustin, C. A. Sehon, J. Wei, H. Cai, S. P. Meduna, H. Khatuya, S. Sun, Y. Gu, W. Jiang, R. L. Thurmond, L. Karlsson, J. P. Edwards, *Bioorg. Med. Chem. Lett.* **2005**, *15*, 1687; b) R. Poulain, D. Horvath, B. Bonnet, C. Eckhoff, B. Chapelain, M.-C. Bodinier, B. Déprez, *J. Med. Chem.* **2001**, *44*, 3378.

[19] For selected examples, see: a) I. Tapia, L. Alonso-Cires, P. L. López-Tudanca, R. Mosquera, L. Labeaga, A. Innératy, A. Orjales, *J. Med. Chem.* **1999**, *42*, 2870; b) H. Kawamoto, H. Nakashima, T. Kato, S. Arai, K. Kamata, Y. Iwasawa, *Tetrahedron* **2001**, *57*, 981.

[20] For palladium-catalyzed reactions, see: a) C. Benedí, F. Bravo, P. Uriz, E. Fernández, C. Claver, S. Castillón, *Tetrahedron Lett.* **2003**, *44*, 6073; b) X.-J. Xu, Y.-X. Zong, *Tetrahedron Lett.* **2007**, *48*, 129; for copper-catalyzed reactions, see: c) X. Diao, Y. Wang, Y. Jiang, D. Ma, *J. Org. Chem.* **2009**, *74*, 7974; d) Z. Li, H. Sun, H. Jiang, H. Liu, *Org. Lett.* **2008**, *10*, 3263.

[21] a) Y. Yuan, I. Thomé, S. H. Kim, D. Chen, A. Beyer, J. Bonnamour, E. Zuidema, S. Chang, C. Bolm, *Adv. Synth. Catal.* **2010**, *352*, 2892; b) A. Beyer, C. M. M. Reucher, C. Bolm, *Org. Lett.* **2011**, *13*, 2876; c) R. Cano, D. J. Ramón, M. Yus, *J. Org. Chem.* **2011**, *76*, 654; d) B. A. Trofimov, *Sulfur Rep.* **1992**, *74*, 207.

[22] a) D. Liu, T. Zhen, Z. Yan, L. Wu, Y. Ma, Q. Wang, W. Liu, H. Zhou, C. Yang, *Bioorg. Med. Chem.* **2013**, *21*, 2960; b) N. Busschaert, I. L. Kirby, S. Young, S. J. Coles, P. N. Horton, *Angew. Chem. Int. Ed.* **2012**, *51*, 4426; *Angew. Chem.* **2012**, *124*, 4502; c) A. Chicu, C. Csunderlik, R. Bacaloglu, *Buletinul Stiintific si Tehnic al Institutului Politehnic Traian Vuia Timisoara, Ser. Chim.* **1981**, *26*, 107.

[23] M. Bianchi, A. Butti, S. Rossi, F. Barzaghi, V. Marcaria, *Eur. J. Med. Chem.* **1981**, *16*, 321.

Received: June 3, 2015
Published Online: July 31, 2015

