HETEROCYCLES, Vol. 92, No. 9, 2016, pp. 1674 - 1686. © 2016 The Japan Institute of Heterocyclic Chemistry
Received, 11th May, 2016, Accepted, 29th June, 2016, Published online, 7th July, 2016
DOI: 10.3987/COM-16-13501

SYNTHESIS OF ISOQUINOLINIUM VIA RHODIUM(III)-CATALYZED OXIDATIVE ANNULATION BETWEEN ALDIMINES AND ALKYNES

Cheng-Qi Wang, Wei Zhang, Hui Lin, Fu Su,* and Lin Dong*

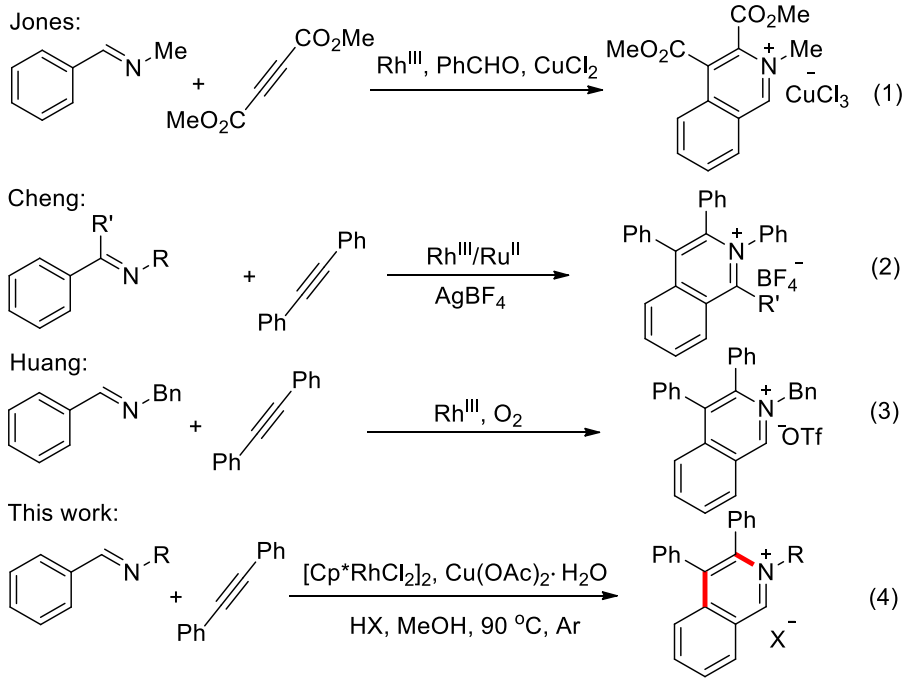
Key Laboratory of Drug-Targeting and Drug Delivery System of the Education Ministry, West China School of Pharmacy, Sichuan University, Chengdu 610041, China; E-mail: dongl@scu.edu.cn, sufu@scu.edu.cn

Abstract – Various isoquinolinium salts have been efficiently synthesized from aldehyde imines and alkynes via Rh^{III}-catalyzed C–H activation and annulation reaction. A broad substrate scope has also been studied to provide various isoquinolinium triflate salts.

Isoquinolinium salts represent an attractive class of intermediates for the construction of various bioactive compounds.[1] In this respect, various synthetic methods for the synthesis of these scaffolds have been developed over the past few years.[2] The common methods of metal-catalyzed cyclization of *o*-halobenzaldimine with alkynes usually suffer from limited substrate scope and halide waste formation.[3] Recently, transition-metal-catalyzed C–H bonds functionalization has become an increasingly important strategy for the synthesis of various complex compounds.[4] Heck developed an important approach to access isoquinolinium salts starting from cyclopalladated benzaldimines tetrafluoroborates and alkynes, while metal-catalyzed functionalization was not the key step.[5] In 2008, Jones has reported Rh^{III}-catalyzed C–H functionalization/annulation between *N*-benzylidenemethylamine and dimethyl acetylenedicarboxylate to synthesize isoquinolinium $CuCl_3$ salts, however, which cannot be isolated and required further transformed to BF_4 salts (eq 1).[6] Cheng has revealed that isoquinolinium BF_4 salts can be directly produced through Rh- and Ru-catalyzed C–H activation (eq 2).[7] Huang developed a novel Rh/O_2 reaction providing isoquinolinium triflate salts (eq 3).[8]

Despite such progress, the isolated anions of isoquinolinium salts are generally limited to BF_4 anion and triflate anion by using C–H activation process, although some analogues might have potent biological activities and different physical properties. Therefore, the development of convenient approaches to broadly functionalized isoquinolinium salts is still highly desirable. Herein, we report an efficient

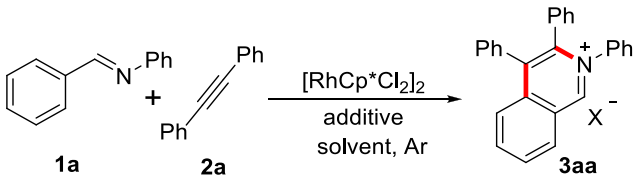
protocol to access isolation isoquinolinium salts with a wide range of anions via Rh^{III}-catalyzed oxidative annulation of benzaldimine with alkynes in moderate to excellent yields (eq 4). A broad substrate scope has also been studied to provide various isoquinolinium triflate salts.



Scheme 1. Transition-metal-catalyzed synthesis of isoquinolinium salts from imines and alkynes via C–H bonds functionalization

Classical reaction conditions were introduced for this reaction system between benzaldimine **1a** with diphenylactetylene **2a** (**Table 1**).

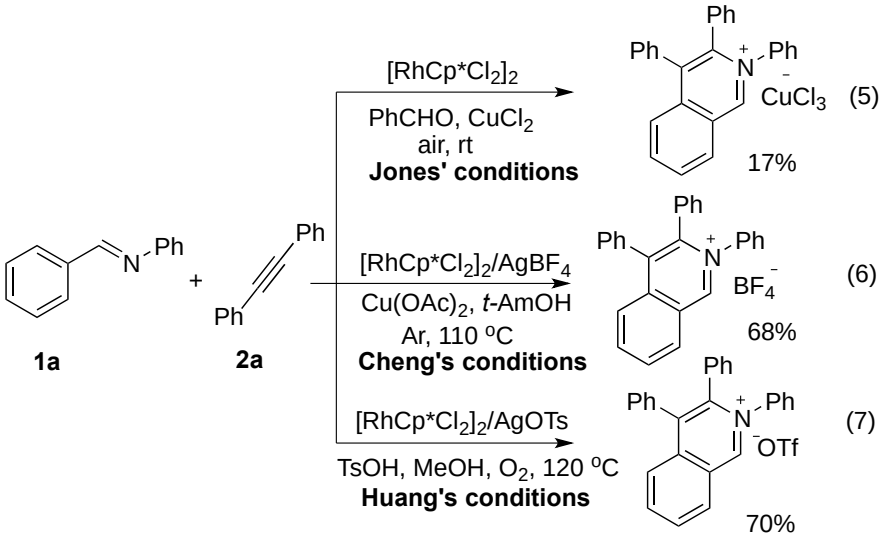
Table 1. Optimization of the reaction conditions[a]



Entry	Oxidant	HX	Solvent	T [°C]	Yield[b] [%]
1[c]	$Cu(OAc)_2·H_2O$	–	EtOH	110	19
2[d]	$Cu(OAc)_2·H_2O$	–	EtOH	110	11
3[e]	$Cu(OAc)_2·H_2O$	–	EtOH	110	25
4	$Cu(OAc)_2·H_2O$	–	EtOH	110	27
5	$Cu(OAc)_2·H_2O$	AcOH	EtOH	110	42

6	$CuCl_2$	HCl	EtOH	110	Trace
7	CF_3CO_2Ag	CF_3CO_2H	EtOH	110	30
8[f]	AgOTf	TfOH	EtOH	110	30
9[f]	CuO	TsOH	EtOH	110	55
10[f]	CuO	$PhSO_2OH$	EtOH	110	33
11[g]	$Cu(OAc)_2·H_2O$	TsOH	EtOH	110	29+43
12[h]	$Cu(OAc)_2·H_2O$	MsOH	EtOH	110	45+36
13	$Cu(OAc)_2·H_2O$	TfOH	MeOH	110	84
14[i]	$Cu(OAc)_2·H_2O$	TfOH	MeOH	110	63
15[j]	$Cu(OAc)_2·H_2O$	TfOH	MeOH	110	57
16[k]	$Cu(OAc)_2·H_2O$	TfOH	MeOH	110	58
17[l]	$Cu(OAc)_2·H_2O$	TfOH	MeOH	110	37
18	$Cu(OAc)_2·H_2O$	TfOH	DMF	110	42
19	$Cu(OAc)_2·H_2O$	TfOH	*t*-AmOH	110	61
20	$Cu(OAc)_2·H_2O$	TfOH	HFIP	110	83
21	$Cu(OAc)_2·H_2O$	TfOH	dioxane	110	46
22	**$Cu(OAc)_2·H_2O$**	**TfOH**	**MeOH**	**90**	**82**
23	$Cu(OAc)_2·H_2O$	TfOH	MeOH	70	73

[a] Reaction conditions unless otherwise specified: 0.05 mmol of **1a**, 0.075 mmol of **2a**, 5 mol% of $[RhCp^*Cl_2]_2$, 1 equiv of additive, 1 equiv of acid, 0.5 mL of solvent, 1 h, Ar atmosphere. [b] Isolated yield. [c] 5 mol% of $RhCp^*(MeCN)_3(SbF_6)_2$. [d] 5 mol% of $[Ru(p\text{-cymene})_2]_2Cl_2$. [e] 5 mol% of $RuCl_2(PPh_3)_3$. [f] Yields were determined by ^1H NMR spectroscopy. [g] 29% yield of acetate salt, 43% yield of tosylate salt. [h] 45% yield of acetate salt, 36% yield of mesylate salt. [i] 1.3 equiv of acid. [j] 1.6 equiv of acid. [k] 3 mol% of $[RhCp^*Cl_2]_2$. [l] 1 mol% of $[RhCp^*Cl_2]_2$. TfOH = trifluoromethanesulfonic acid. TsOH = 4-methylbenzenesulfonic acid. MsOH = methanesulfonic acid. HFIP= 1,1,1,3,3,3-hexafluoro-2-propanol.



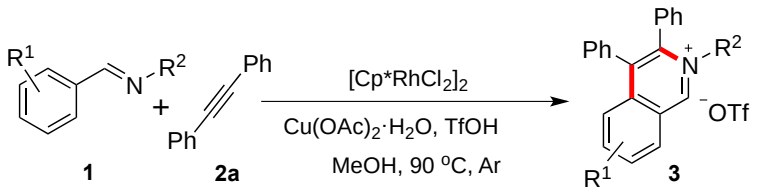
Scheme 2. Control experiments under the reported conditions

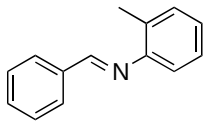
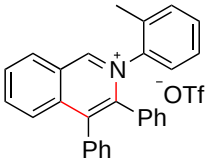
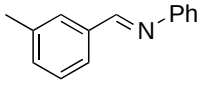
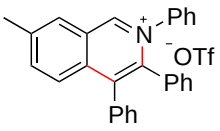
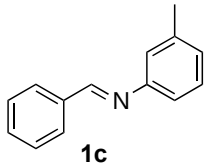
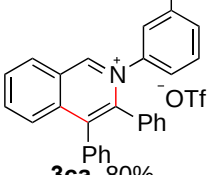
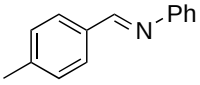
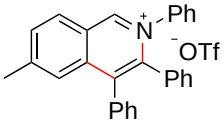
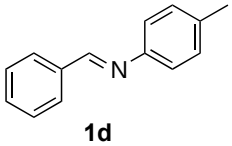
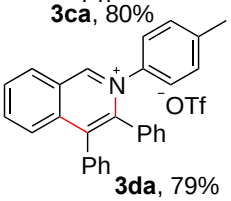
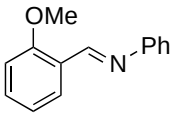
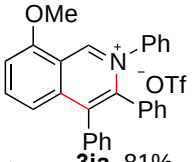
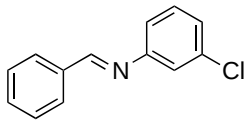
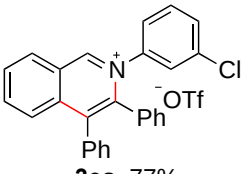
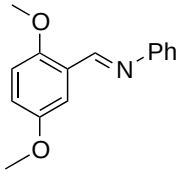
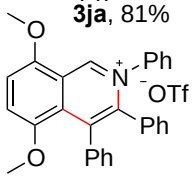
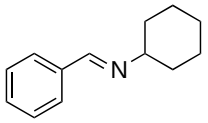
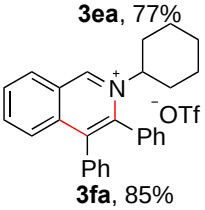
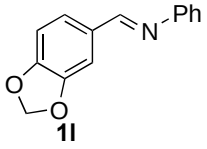
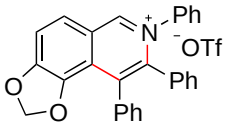
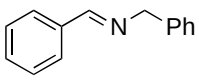
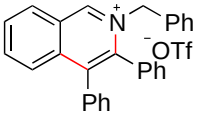
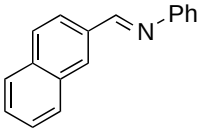
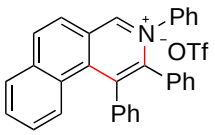
Various catalysts were initially tested in the presence of $Cu(OAc)_2 \cdot H_2O$ acting as an additive, and the $[Cp^*RhCl_2]_2$ exhibited better catalytic activity to form isoquinolinium (entries 1-4). To our delight, isoquinolinium cation and diverse anions could be isloated when different additives and acids were used in this system (entries 5-10). However, ^1H NMR analysis confirmed that the products contain two different anions when $Cu(OAc)_2 \cdot H_2O$ was used as an additive and TsOH or MsOH as an acid (entries 11 and 12). Fortunately, single triflate anion product was obtained in 84% yield by using stoichiometric TfOH as an acid, probably owing to triflate anion possessing strong capability of coordination with isoquinolinium cation (entry 13).

In the following experiments, the increasing loading of acid did not enhance the yield of desired product (entries 14 and 15). Meanwhile, the lower catalyst loading gave worse reactivity (entries 16 and 17). In addition, distinctive solvents were further examined but providing inferior yields (entries 18-21). Finally, the paralleled yield was obtained even when we reduced the temperature from 110 °C to 90 °C (entries 22 and 23). From the results that obtained above, we drew the conclusion that TfOH is identified as the most compatible acid which can efficiently give isoquinolinium triflate salts, although other anions can also be isolated in the catalytic system. The control experiments between **1a** and **2a**, which were conducted under respective optimized condition as shown in eqs (1)-(3), gave 17%,[6] 68%[7a] and 70%[8] isolated yields, respectively, probably owing to the strong electron-withdrawing groups maladjusted with our reaction system (**Scheme 2**). Form above experiments, it seems that our reaction system exhibits higher efficiency.

With the optimized conditions in hand, we investigated a variety of aldehyde imines which contained different electron-donating, -withdrawing and bulky groups to examine the standard conditions (**Table 2**). *N*-(*o*-, *m*-, and *p*-tolyl)benzaldimine proceeded smoothly to give isoquinoline salts **3ba-3da** in good yields. In addition, *N*-(*m*-chlorophenyl)benzaldimine **1e** was also suitable for this reaction. Moreover, *N*-alkyl substituted benzaldimines **1f** and **1g** showed good reactivity and the corresponding products were obtained in 85% and 52% yields, respectively, which indicated that the presenting reaction has good functional tolerance. Meta-methyl-substituted benzaldimine **1h** furnished single product **3ha** in 78% yield, probably due to the steric effect. In addition, benzaldimines fused with an array of diversely substituted benzene ring prepared **3ia-3ka** under the standard conditions in good to excellent yields. Interestingly, **1l** showed different position selectivity albeit with perfect regioselectivity, probably because of the strong electronic effect. Likewise, naphthaldimine **1m** could be successfully employed, affording the product **3ma** in good yield with single steric selectivity.

Table 2. Rh^{III}-Catalyzed oxidative annulation of aldehyde imines with diphenylactetylene[a]



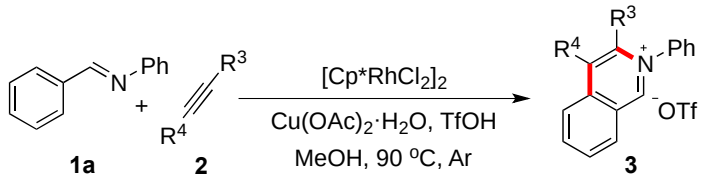
Entry	Imine **1**	Yield [%]	Entry	Imine **1**	Yield [%]
1	 **1b**	 **3ba**, 85%	7	 **1h**	 **3ha**, 78%
2	 **1c**	 **3ca**, 80%	8	 **1g**	 **3ga**, 52%
3	 **1d**	 **3da**, 79%	9	 **1j**	 **3ja**, 81%
4	 **1e**	 **3ea**, 77%	10	 **1k**	 **3ka**, 75%
5	 **1f**	 **3fa**, 85%	11	 **1l**	 **3la**, 74% (10:1)[b]
6	 **1g**	 **3ga**, 52%	12	 **1m**	 **3ma**, 80%

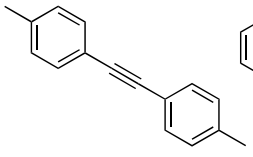
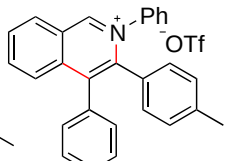
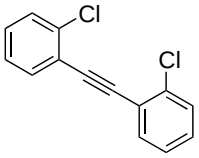
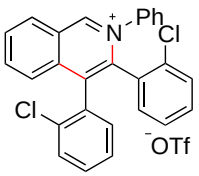
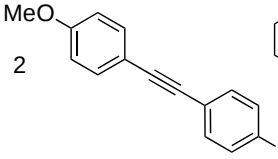
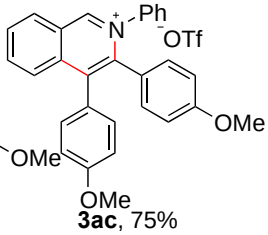
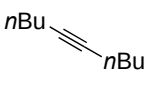
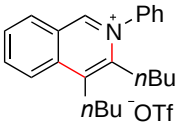
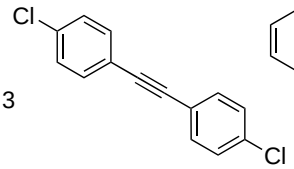
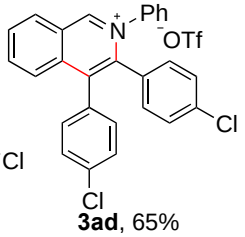
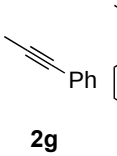
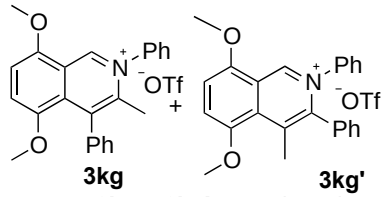
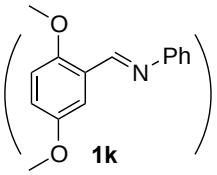
[a] Reaction conditions unless otherwise specified: **1** (0.1 mmol), **2a** (0.15 mmol), $[Cp^*RhCl_2]_2$ (5 mol%), $Cu(OAc)_2·H_2O$ (1.0 equiv), TfOH (1.0 equiv), MeOH (1 mL), 90 °C, 1 h, Ar atmosphere. Yields are reported for the isolated products. Ratios of regioisomers are given within parentheses and were determined by ^1H NMR analysis. [b] Major isomers are shown.

Subsequently, a range of alkynes were studied with benzaldimine **1a** (**Table 3**). With *para*-substituted diarylacetylene, the corresponding isoquinolinium salts **3ab-3ad** were prepared in good yields. In contrast, the diarylacetylene with chlorine on the *ortho*-position of the benzene ring was also well tolerated, and the

desired product **3ae** was isolated in similar yield. In addition, the *ortho*-chlorinated diphenylacetylene **1f** reacted smoothly to gain annulated product **3af** in slightly low yield. Unfortunately, asymmetric disubstituted alkynes as coupling partners can be employed in the reaction but giving the two isomers which were very hard to separate and confirm the structure.[9] Only the structure of **3kg** and **3kg'** can be confirmed in 82% yield but albeit with poor regioselectivity.

Table 3. Substrate scope of alkynes[a]



Entry	Alkyne **2**	Yield [%]	Entry	Alkyne **2**	Yield [%]
1	 **2b**	 **3ab**, 72%	4	 **2e**	 **3ae**, 64%
2	 **2c**	 **3ac**, 75%	5	 **2f**	 **3af**, 49%
3	 **2d**	 **3ad**, 65%	6	 **2g**	 **3kg** + **3kg'**, 82% (1.8:1)
				 **1k**	

[a] Reaction conditions unless otherwise specified: **1a** (0.1 mmol), **2** (0.15 mmol), $[Cp^*RhCl_2]_2$ (5 mol%), $Cu(OAc)_2·H_2O$ (1.0 equiv), TfOH (1.0 equiv), MeOH (1 mL), 90 °C, 1 h, Ar atmosphere. Yields are reported for the isolated products.

In conclusion, we have successfully developed a new Rh^{III}-catalyzed protocol for the synthesis of various isoquinolinium salts directly from aldehyde imines and alkynes via C–H functionalization/annulation. Isoquinolinium salts with a wide range of anions have been isolated in the reaction, such as tosylate,

triflate, mesylate, and acetate anions. In addition, we also broaden the substrate scope to form various isoquinolinium triflate salts. Further applications of the method to biologically active compounds are currently underway in our laboratory.

EXPERIMENTAL

General remarks

NMR data were obtained for ^{1}H at 400 MHz or 600 MHz, and for ^{13}C at 100 MHz or 151 MHz. Chemical shifts were reported in ppm from tetramethylsilane with the solvent resonance as the internal standard in $CDCl_3$ solution. ESI HRMS was recorded on a Waters SYNAPT G2 and Water XEVO G2 Q-ToF. UV detection was monitored at 220 nm. TLC was performed on glass-backed silica plates. Column chromatography was performed on silica gel (200-300 mesh), eluting with ethyl acetate and petroleum ether. *N*-phenylacetamide, benzamide and alkynes were commercially available.

General procedure for synthesis of isoquinoliniums derived fused compounds and characterization data

(*E*)-*N*-Benzylideneaniline **1a** (19.7 mg, 0.10 mmol), diphenylacetylene **2a** (26.7 mg, 0.15 mmol), $[Cp^*RhCl_2]_2$ (3.1 mg, 5 mol%), $Cu(OAc)_2{\cdot}H_2O$ (20 mg, 1 equiv) and trifluoromethanesulfonic acid (15 mg, 1 equiv) were stirred in MeOH (1 mL) at 90 °C for 1 h. After completion, the reaction mixture was purified by flash chromatography eluting with CH_2Cl_2 and MeOH (10:1) to give the desired product **3aa** as a grey solid (42.6 mg, 82%).

2,3,4-Triphenylisoquinolinium trifluoromethanesulfonate (3aa-CF_3SO_3). 82% yield; IR (KBr) 3565, 3499, 3062, 1625 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.93 (s, 1H), 8.68 (d, *J* = 8.0 Hz, 1H), 8.08 (t, *J* = 8.0 Hz, 1H), 7.98 (t, *J* = 8.0 Hz, 1H), 7.75 (d, *J* = 8.0 Hz, 1H), 7.55-7.53 (m, 2H), 7.37-7.32 (m, 6H), 7.28-7.27 (m, 2H), 7.08-7.03 (m, 5H). ^{13}C NMR (151 MHz, $CDCl_3$): δ 150.5, 142.1, 139.3, 138.8, 137.8, 133.1, 131.9, 131.3, 131.2, 131.0, 130.4, 130.3, 129.5, 129.1, 128.7, 128.4, 127.9, 126.9, 126.8, 126.5, 120.6, 119.4, 112.4. ESI HRMS: calcd. for $C27H20N^+$ 358.1590, found 358.1586.

2,3,4-Triphenylisoquinolinium acetate (3aa-OAc). IR (KBr) 3453, 2960, 2926, 1713, 1625 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 11.09 (s, 1H), 9.29 (d, *J* = 8.0 Hz, 1H), 8.08 (t, *J* = 8.0 Hz, 1H), 8.01 (t, *J* = 8.0 Hz, 1H), 7.75 (t, *J* = 8.0 Hz, 1H), 7.66-7.65 (m, 2H), 7.39-7.34 (m, 5H), 7.27-7.26 (m, 3H), 7.09-7.04 (m, 5H), 2.04 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$): δ 152.6, 138.8, 138.4, 137.8, 133.5, 133.2, 131.2, 131.2, 131.2, 130.3, 129.5, 128.7, 128.5, 128.0, 127.2, 126.9, 126.1.

2,3,4-Triphenylisoquinolinium iodide (3aa-I). IR (KBr) 3422, 3062, 1622 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 10.09 (s, 1H), 8.74 (d, *J* = 8.0 Hz, 1H), 8.05 (t, *J* = 8.0 Hz, 1H), 7.94 (t, *J* = 8.0 Hz, 1H), 7.72 (d, *J* = 8.0 Hz, 1H), 7.66-7.64 (m, 2H), 7.33-7.29 (m, 8H), 7.13 (d, *J* = 8.0 Hz, 1H), 7.04-6.93 (m, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 149.3, 143.3, 141.1, 138.4, 137.9, 136.8, 132.2, 130.9, 130.3, 130.3, 130.1, 129.4, 128.4, 128.2, 127.7, 127.4, 126.9, 126.0, 125.9, 125.6.

2,3,4-Triphenylisoquinolinium 4-methylbenzenesulfonate (3aa-TsO&OAc). ^{1}H NMR (400 MHz, $CDCl_3$): δ 10.50 (s, 1H), 8.93 (d, *J* = 8.0 Hz, 1H), 7.95 (t, *J* = 8.0 Hz, 1H), 7.54 (t, *J* = 6.8 Hz, 1H), 7.48 (d, *J* = 8.0 Hz, 2H), 7.26-7.19 (m, 6H), 7.15-7.13 (m, 2H), 7.00-6.93 (m, 7H), 2.23 (s, 3H), 1.90 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 153.1, 144.1, 143.9, 142.1, 138.8, 138.5, 138.4, 137.6, 133.3, 133.2, 131.3, 131.3, 130.4, 130.2, 129.4, 129.1, 128.7, 128.5, 128.3, 127.9, 127.2, 127.1, 127.0, 126.1, 125.9, 21.3.

2,3,4-Triphenylisoquinolinium benzenesulfonate (3aa-PhSO$_3$). IR (KBr) 3427, 3054, 1627 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 10.48 (s, 1H), 8.94 (d, *J* = 8.0 Hz, 1H), 8.02 (t, *J* = 8.4 Hz, 1H), 7.92 (t, *J* = 6.8 Hz, 1H), 7.70 (d, *J* = 8.4 Hz, 1H), 7.64 (d, *J* = 7.2 Hz, 2H) 7.59 (d, *J* = 7.2 Hz, 2H), 7.31-7.27 (m, 6H), 7.22-7.18 (m, 5H), 7.06-7.00 (m, 5H).

2,3,4-Triphenylisoquinolinium methanesulfonate (3aa-MeSO$_3$). IR (KBr) 3493, 3434, 3057, 1626 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 10.58 (s, 1H), 9.07 (s, 1H), 8.10-8.03 (m, 2H), 7.76 (t, *J* = 8.0 Hz, 1H), 7.62 (m, 2H), 7.38-7.34 (m, 6H), 7.28-7.25 (m, 2H), 7.05 (m, 5H), 2.53 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 152.7, 143.9, 142.1, 138.9, 138.6, 137.8, 133.3, 133.2, 131.3, 131.2, 130.4, 129.5, 129.2, 128.8, 128.6, 128.0, 127.2, 127.0, 126.3, 39.4.

3,4-Diphenyl-2-*o*-tolylisoquinolinium trifluoromethanesulfonate (3ba). 85% yield; IR (KBr) 3436, 3057, 1627 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.93 (s, 1H), 8.69 (d, *J* = 8.0 Hz, 1H), 8.06 (t, *J* = 8.0 Hz, 1H), 7.97 (t, *J* = 8.0 Hz, 1H), 7.76 (d, *J* = 8.4 Hz, 1H), 7.37-7.32 (m, 4H), 7.26-7.17 (m, 5H), 7.05 (m, 5H), 2.29 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 150.0, 149.9, 143.4, 141.0, 139.2, 138.3, 137.7, 136.8, 132.2, 131.0, 131.0, 130.3, 130.2, 129.3, 128.2, 128.1, 127.7, 127.5, 126.9, 126.3, 126.0, 125.5, 122.7, 119.6 (q, *J* = 319 Hz), 21.2. ESI HRMS: calcd. for $C_{28}H_{22}N^+$ 372.1747, found 372.1747.

3,4-Diphenyl-2-*m*-tolylisoquinolinium trifluoromethanesulfonate (3ca). 80% yield; IR (KBr) 3440, 3069, 1622 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.93 (s,1H), 8.78 (d, *J* = 8.0 Hz, 1H), 8.11 (t, *J* = 8.0 Hz, 1H), 8.02 (t, *J* = 8.0 Hz, 1H), 7.81 (d, *J* = 8.4 Hz, 1H), 7.66 (d, *J* =7.6 Hz, 1H), 7.37-7.23 (m, 8H), 7.18-7.16 (m, 1H), 7.08-7.07 (m, 2H), 7.01-7.00 (m, 1H), 6.93-6.91 (m, 1H), 2.09 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$): δ 151.2, 144.5, 141.1, 139.6, 138.8, 138.0, 133.0, 132.3, 132.0, 131.4, 131.2, 130.9, 130.6, 130.5, 129.4, 129.3, 128.9, 128.8, 128.2, 127.9, 127.6, 127.3, 127.2, 126.5, 120.5 (q, *J* = 319 Hz), 17.6. ESI HRMS: calcd. for $C_{28}H_{22}N^+$ 372.1747, found 372.1748.

3,4-Diphenyl-2-*p*-tolylisoquinolinium trifluoromethanesulfonate (3da). 79% yield; IR (KBr) 3482, 3060, 1626 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.93 (s, 1H), 8.69 (d, *J* = 8.0 Hz, 1H), 8.06 (t, *J* = 8.0 Hz, 1H), 7.97 (t, *J* = 8.0 Hz, 1H), 7.76 (d, *J* = 8.0 Hz, 1H), 7.37-7.26 (m, 4H), 7.26-7.17 (m, 5H), 7.05 (m,

5H), 2.30 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 151.1, 144.5, 140.8, 139.8, 139.3, 138.7, 137.8, 133.2, 132.0, 131.3, 131.2, 130.3, 130.1, 129.2, 128.7, 128.5, 128.0, 127.0, 126.5, 126.5, 120.6 (q, *J* = 319 Hz), 21.2. ESI HRMS: calcd. for $C_{28}H_{22}N^+$ 372.1747, found 372.1752.

2-(3-Chlorophenyl)-3,4-diphenylisoquinolinium trifluoromethanesulfonate (3ea). 77% yield; IR (KBr) 3468, 3240, 1624 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.88 (s, 1H), 8.62 (d, *J* = 8.0 Hz, 1H), 8.07 (t, *J* = 8.0 Hz, 1H), 7.95 (t, *J* = 7.2 Hz, 1H), 7.76 (d, *J* = 8.8 Hz, 1H), 7.58 (d, *J* = 7.2 Hz, 1H), 7.52 (s, 1H), 7.32-7.31 (m, 5H), 7.28-7.26 (m, 2H), 7.11-7.08 (m, 5H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 150.9, 144.3, 142.7, 139.5, 139.0, 138.1, 135.0, 133.1, 132.0, 131.4, 131.2, 130.9, 130.8, 130.7, 130.3, 129.4, 128.8, 128.5, 128.1, 127.1, 127.0, 125.6, 120.4 (q, *J* = 319 Hz). ESI HRMS: calcd. for $C_{27}H_{19}ClN^+$ 392.1201, found 392.1119, 394.1229.

2-Cyclohexyl-3,4-diphenylisoquinolinium trifluoromethanesulfonate (3fa). 85% yield; IR (KBr) 3440, 3065, 3019, 1625 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 10.40 (s, 1H), 8.95 (d, *J* = 7.2 Hz, 1H), 8.00 (t, *J* = 8.0 Hz, 1H), 7.97 (t, *J* = 7.6 Hz, 1H), 7.61 (d, *J* = 7.6 Hz, 1H), 7.39 (m, 3H), 7.29-7.27 (m, 3H), 7.23 (m, 2H), 7.12 (m, 2H), 4.34 (m, 1H), 2.39-2.36 (m, 2H), 2.13 (m, 2H), 1.93-1.90 (m, 2H), 1.58-1.48 (m, 2H), 1.07-1.04 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 148.2, 143.9, 139.4, 137.6, 137.4, 133.3, 132.1, 131.2, 131.0, 130.3, 129.8, 129.0, 128.7, 128.5, 128.0, 120.8 (q, *J* = 319 Hz), 68.5, 33.6, 25.8, 23.9. ESI HRMS: calcd. for $C_{27}H_{26}N^+$ 364.2060, found 364.2058.

2-Benzyl-3,4-diphenylisoquinolinium trifluoromethanesulfonate (3ga). 52% yield; IR (KBr) 3431, 3052, 1630 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 10.33 (s, 1H), 8.72 (d, *J* = 8.0 Hz, 1H), 8.02 (t, *J* = 8.0 Hz, 1H), 7.96 (t, *J* = 8.0 Hz, 1H), 7.65 (d, *J* = 8.4 Hz, 1H), 7.28-7.23 (m, 9H), 7.09-7.07 (m, 4H), 6.92 (d, *J* = 7.2 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 151.3, 144.3, 139.8, 138.1, 137.5, 133.1, 131.9, 131.2, 130.7, 130.6, 130.1, 130.0, 129.3, 129.2, 128.7, 128.6, 128.4, 128.3, 127.3, 63.3. ESI HRMS: calcd. for $C_{28}H_{22}N^+$ 372.1747, found 372.1755.

5-Methyl-2,3,4-triphenylisoquinolinium trifluoromethanesulfonate (3ha). 78% yield; IR (KBr) 3455, 3066, 1634 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.84 (s, 1H), 8.46 (s, 1H), 7.90 (t, *J* = 8.8 Hz, 1H), 7.67 (d, *J* = 8.4 Hz, 1H), 7.52-7.51 (m, 2H), 7.34-7.32 (m, 6H), 7.24 (m, 2H), 7.04 (m, 5H), 2.66 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 150.0, 143.7, 142.5, 142.2, 140.3, 139.1, 137.1, 133.3, 131.3, 131.2, 130.4, 130.3, 129.6, 129.2, 128.7, 128.5, 128.0, 127.3, 126.8, 126.3, 120.6 (q, *J* = 319 Hz), 21.8. ESI HRMS: calcd. for $C_{28}H_{22}N^+$ 372.1747, found 372.1746.

6-Methyl-2,3,4-triphenylisoquinolinium trifluoromethanesulfonate (3ia). 93% yield; IR (KBr) 3476, 3245, 3061, 1626 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.83 (s, 1H), 8.55 (d, *J* = 8.8 Hz, 1H), 7.79 (d, *J* = 8.0 Hz, 1H), 7.51-7.49 (m, 3H), 7.34-7.31 (m, 6H), 7.26-7.23 (m, 2H), 7.03-6.99 (m, 5H), 2.58 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 150.5, 150.1, 144.4, 142.1, 139.0, 138.3, 133.7, 133.3, 131.7, 131.2,

130.4, 130.3, 129.5, 129.1, 128.7, 128.5, 127.9, 126.9, 125.5, 125.4, 120.6 (q, *J* = 319 Hz), 23.3. ESI HRMS: calcd. for $C28H22N^+$ 372.1747, found 372.1748.

8-Methoxy-2,3,4-triphenylisoquinolinium trifluoromethanesulfonate (3ja). 81% yield. IR (KBr) 3488, 3245, 3060, 1622 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 9.74 (s, 1H), 8.00 (d, *J* = 8.0 Hz, 1H), 7.56 (t, *J* = 8.0 Hz, 1H), 7.37-7.35 (m, 3H), 7.29-7.26 (m, 7H), 7.14-7.13 (m, 2H), 7.04-7.00 (m, 3H), 4.15 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 157.7, 144.5, 144.0, 141.6, 138.8, 138.7, 137.8, 132.5, 130.2, 130.2, 129.4, 129.3, 128.5, 128.1, 127.6, 127.4, 126.8, 125.9, 119.6 (q, *J* = 319 Hz), 118.6, 117.4, 108.2, 55.9. ESI HRMS: calcd. for $C_{28}H_{22}NO^+$ 388.1696, found 389.1693.

5,8-Dimethoxy-2,3,4-triphenylisoquinolinium trifluoromethanesulfonate (3ka). 75% yield; IR (KBr) 3062, 2920, 1650 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 9.69 (s, 1H), 9.51-9.49 (s, 1H), 7.44 (d, *J* = 8.4 Hz, 1H), 7.34-7.33 (m, 3H), 7.27-7.25 (m, 1H), 7.17-7.16 (m, 2H), 7.17-7.16 (m, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 152.3, 149.9, 145.6, 145.1, 142.6, 137.7, 137.1, 131.5, 131.2, 130.3, 129.8, 129.5, 129.4, 128.8, 127.5, 127.1, 126.9, 126.8, 120.9, 120.7 (q, *J* = 319 Hz), 120.1, 110.3, 57.1, 56.8. ESI HRMS: calcd. for $C_{29}H_{24}NO_2^+$ 418.1802, found 418.1807.

6,7,8-Triphenyl-[1,3]dioxolo[4,5-*g*]isoquinolin-6-ium trifluoromethanesulfonate (3la). 67% yield; IR (KBr) 3470, 3062, 1630 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 9.74 (s, 1H), 8.43 (d, *J* = 8.0 Hz, 1H), 7.62 (d, *J* = 8.8 Hz, 1H), 7.45 (t, *J* = 8.0 Hz, 2H), 7.34 (m, 3H), 7.21 (m, 5H), 7.00 (m, 5H), 6.05 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 155.4, 151.4, 143.8, 142.1, 141.9, 131.3, 130.3, 130.1, 129.5, 129.1, 128.3, 127.8, 127.6, 126.8, 122.7, 122.6, 120.6 (q, *J* = 319 Hz), 116.0, 103.9. ESI HRMS: calcd. for $C_{28}H_{20}NO_2^+$ 402.1489, found 402.1493.

1,2,3-Triphenylbenzo[*f*]isoquinolinium trifluoromethanesulfonate (3ma). 80% yield; IR (KBr) 3463, 3062, 1613 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 10.12 (s, 1H), 8.85 (d, *J* = 7.6 Hz, 1H), 8.25 (t, *J* = 9.2 Hz, 1H), 8.03 (d, *J* = 7.6 Hz, 1H), 7.87 (t, *J* = 7.6 Hz, 1H), 7.82 (t, *J* = 7.6 Hz, 1H), 7.62-7.57 (m, 3H), 7.37-7.36 (m, 3H), 7.32 (m, 5H), 7.15-7.13 (m, 2H), 7.06-7.00 (m, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 147.3, 143.5, 142.6, 140.7, 139.7, 139.3, 133.5, 132.4, 131.1, 130.5, 129.7, 129.6, 129.3, 128.8, 128.6, 127.9, 127.1, 123.5, 122.8, 120.5 (q, *J* = 319 Hz). ESI HRMS: calcd. for $C_{31}H_{22}N^+$ 408.1747, found 408.1749.

2-Phenyl-3,4-di-*p*-tolylisoquinolinium trifluoromethanesulfonate (3ab). 72% yield; IR (KBr) 3564, 3492, 3066, 1625, 1491 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 9.96 (s, 1H), 8.70 (d, *J* = 8.0 Hz, 1H), 8.05 (t, *J* = 8.0 Hz, 1H), 7.97 (t, *J* = 8.0 Hz, 1H), 7.70 (d, *J* = 8.0 Hz, 1H), 7.50-7.48 (m, 2H), 7.37 (m, 3H), 7.15-7.09 (m, 4H), 6.91-6.89 (m, 2H), 6.84-6.82 (s, 2H), 2.34 (s, 3H), 2.15 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 150.9, 144.6, 142.3, 139.5, 139.3, 139.0, 138.6, 137.7, 132.0, 131.2, 131.0, 130.4, 130.2, 129.5, 129.3, 128.7, 128.2, 126.9, 126.8, 126.6, 120.6 (q, *J* = 319 Hz), 21.32, 21.27. ESI HRMS: calcd. for

$C_{29}H_{24}N^+$ 386.1903, found 386.1898.

3,4-Bis(4-methoxyphenyl)-2-phenylisoquinolinium trifluoromethanesulfonate (3ac). 75% yield; IR (KBr) 3561, 3500, 3066, 1611 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 9.83 (s, 1H), 8.61 (d, *J* = 8.0 Hz, 1H), 8.04 (t, *J* = 8.0 Hz, 1H), 7.93 (t, *J* = 7.6 Hz, 1H), 7.79 (d, *J* = 8.4 Hz, 1H), 7.50-7.48 (m, 2H), 7.37-7.35 (m, 3H), 7.15 (d, *J* = 8.4 Hz, 2H), 6.95 (d, *J* = 8.4 Hz, 2H), 6.85 (d, *J* = 8.4 Hz, 2H), 6.54 (d, *J* = 7.6 Hz, 2H), 3.79 (s, 3H), 3.64 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 159.7, 159.6, 150.6, 144.7, 142.4, 139.5, 139.2, 137.6, 132.7, 131.9, 131.7, 131.1, 130.4, 129.6, 126.9, 126.7, 126.6, 125.3, 123.3, 120.6 (q, *J* = 319 Hz), 114.1, 113.5, 55.3, 55.1. ESI HRMS: calcd. for $C_{29}H_{24}NO_2^+$ 418.1802, found 418.1798.

3,4-Bis(2-chlorophenyl)-2-phenylisoquinolinium trifluoromethanesulfonate (3ad). 64% yield; IR (KBr) 3564, 3242, 3064, 2924, 1626 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 9.80 (s, 1H), 8.58 (d, *J* = 8.4 Hz, 1H), 8.10 (t, *J* = 7.6 Hz, 1H), 7.96 (t, *J* = 7.6 Hz, 1H), 7.72 (d, *J* = 8.4 Hz, 1H), 7.57 (d, *J* = 7.6 Hz, 1H), 7.39-7.35 (m, 8H), 7.32-7.27 (m, 4H), 7.11-7.03 (m, 3H). ^{13}C NMR (151 MHz, $CDCl_3$): δ 151.3, 142.9, 141.8, 138.5, 138.1, 137.9, 134.7, 134.5, 133.9, 132.5, 131.9, 131.5, 130.7, 130.0, 129.6, 129.4, 129.2, 127.0, 126.8, 126.3, 120.4 (q, *J* = 319 Hz). ESI HRMS: calcd. for $C_{27}H_{18}Cl_2N^+$ 426.0811, found 426.0824, 426.0841, 430.0847.

3,4-Bis(4-chlorophenyl)-2-phenylisoquinolinium trifluoromethanesulfonate (3ae). 65% yield; IR (KBr) 3563, 3490, 3069, 1624 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 9.75 (s, 1H), 8.55 (d, *J* = 8.0 Hz, 1H), 8.09 (t, *J* = 8.0 Hz, 1H), 7.96 (t, *J* = 8.0 Hz, 1H), 7.72 (d, *J* = 8.0 Hz, 1H), 7.56-7.55 (m, 2H), 7.42-7.35 (m, 5H), 7.27-7.25 (m, 2H), 7.11-7.09 (m, 2H), 7.05-7.03 (m, 2H). ^{13}C NMR (151 MHz, $CDCl_3$): δ 150.9, 134.5, 141.9, 138.7, 138.4, 138.0, 135.7, 135.2, 132.6, 131.7, 131.7, 131.5, 131.5, 130.7, 129.7, 129.4, 129.0, 128.4, 127.0, 126.8, 126.4, 121.4, 120.4, 119.1 (q, *J* = 319 Hz). ESI HRMS: calcd. for $C_{27}H_{18}Cl_2N^+$ 426.0811, found 426.0815, 428.0798, 430.0801.

3,4-Dibutyl-2-phenylisoquinolinium trifluoromethanesulfonate (3af). 49% yield; IR (KBr) 3446, 3066, 1631 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 9.73 (s, 1H), 8.59 (d, *J* = 8.0 Hz, 1H), 8.22-8.16 (m, 2H), 7.92 (t, *J* = 7.2 Hz, 1H), 7.69-7.68 (m, 3H), 7.63 (m, 2H), 3.20 (t, *J* = 8.0 Hz, 2H), 2.86 (t, *J* = 8.0 Hz, 2H), 1.75-1.71 (m, 2H), 1.65-1.59 (m, 2H), 1.48 (t, *J* = 8.0 Hz, 2H), 1.24-1.18 (m, 2H), 1.05 (t, *J* = 7.2 Hz, 3H), 0.73 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 149.2, 144.2, 140.1, 137.2, 136.7, 136.3, 131.6, 130.5, 129.6, 129.3, 125.1, 125.0, 122.6, 119.6 (q, *J* = 319 Hz), 31.7, 30.4, 28.6, 27.5, 22.2, 21.6, 12.7, 12.0. ESI HRMS: calcd. for $C_{23}H_{28}N^+$ 318.2216, found 318.2219.

ACKNOWLEDGEMENTS

We are grateful for the financial support from the NSFC (21572138).

REFERENCES

1. (a) R. B. Gupta, R. W. Franck, K. D. Onan, and C. E. Soll, *J. Org. Chem.*, 1989, **54**, 1097; (b) O. Tsuge, S. Kanemasa, K. Sakamoto, and S. Takenaka, *Bull. Chem. Soc. Jpn.*, 1988, **61**, 2513; (c) S. Su and J. A. Porco, Jr., *J. Am. Chem. Soc.*, 2007, **129**, 7744; (d) B. D. Krane, M. O. Fagbule, M. Shamma, and B. Gözler, *J. Nat. Prod.*, 1984, **47**, 1; (e) R. B. Gupta and R. W. Franck, *J. Am. Chem. Soc.*, 1987, **109**, 5393; (f) Z. S. Ye, R. N. Guo, X. F. Cai, M. W. Chen, L. Shi, and Y. G. Zhou, *Angew. Chem. Int. Ed.*, 2013, **43**, 3685; (g) X. Pan, C. Yang, J. L. Cleveland, and T. D. Bannister, *J. Org. Chem.*, 2016, **81**, 2194; (h) M. R. Sonawane, J. Vávra, D. Šaman, I. Císařová, and F. Teplý, *Synthesis*, 2015, **47**, 3479.
2. (a) G. Zhang, L. Yang, Y. Wang, Y. Xie, and H. Huang, *J. Am. Chem. Soc.*, 2013, **135**, 8850; (b) D. Ghorai and J. Choudhury, *ACS Catal.*, 2015, **5**, 2692; (c) Q. Huang, J. A. Hunter, and R. C. Larock, *Org. Lett.*, 2001, **3**, 2973; (d) N. Guimond and K. Fagnou, *J. Am. Chem. Soc.*, 2009, **131**, 12050; (e) S. Zhao, R. Yu, W. Chen, M. Liu, and H. Wu, *Org. Lett.*, 2015, **17**, 2828; (f) R. He, Z.-T. Huang, Q.-Y. Zheng, and C. Wang, *Tetrahedron Lett.*, 2014, **55**, 5705.
3. (a) W.-C. Shih, C.-C. Teng, K. Parthasarathy, and C.-H. Cheng, *Chem. Asian J.*, 2012, **7**, 306; (b) R. P. Korivi, Y.-C. Wu, and C.-H. Cheng, *Chem. Eur. J.*, 2009, **15**, 10727; (c) R. P. Korivi and C.-H. Cheng, *Org. Lett.*, 2005, **7**, 5179; (d) R. P. Korivi and C.-H. Cheng, *Chem. Eur. J.*, 2010, **16**, 282; (e) K. R. Roesch, H. Zhang, and R. C. Larock, *J. Org. Chem.*, 2001, **66**, 8042; (f) N. Asao, S. Yudha S., T. Nogami, and Y. Yamamoto, *Angew. Chem. Int. Ed.*, 2005, **44**, 5526; (g) K. Akiba, M. Nakatani, M. Wada, and Y. Yamamoto, *J. Org. Chem.*, 1985, **50**, 63.
4. For selected recent reviews, see: (a) D. A. Colby, R. G. Bergman, and J. A. Ellaman, *Chem. Rev.*, 2010, **110**, 624; (b) L. Ackermann, *Chem. Rev.*, 2011, **111**, 1315; (c) H. M. L. Davies, J. Du Bois, and J.-Q. Yu, *Chem. Soc. Rev.*, 2011, **40**, 1855; (d) O. Baudoin, *Chem. Soc. Rev.*, 2011, **40**, 4902; (e) S. H. Cho, J. Y. Kim, J. Kwak, and S. Chang, *Chem. Soc. Rev.*, 2011, **40**, 5068; (f) B.-J. Li and Z.-J. Shi, *Chem. Soc. Rev.*, 2012, **41**, 5588; (g) D. Zhao, J. You, and C. Hu, *Chem. Eur. J.*, 2011, **17**, 5466; (h) C. S. Yeung and V. M. Dong, *Chem. Rev.*, 2011, **111**, 1215; (i) C. Liu, H. Zhang, W. Shi, and A. Lei, *Chem. Rev.*, 2011, **111**, 1780; (j) J. Wencel-Delord and F. Glorius, *Nat. Chem.*, 2013, **5**, 369; (k) G. Song, F. Wang, and X. Li, *Chem. Soc. Rev.*, 2012, **41**, 3651; (l) T. Satoh and M. Miura, *Chem. Eur. J.*, 2010, **16**, 11212; (m) G. Song and X. Li, *Acc. Chem. Res.*, 2015, **48**, 1007.
5. (a) G. Wu, A. L. Rheingold, S. J. Geib, and R. F. Heck, *Organometallics*, 1987, **6**, 1941; (b) G. Wu, S. J. Geib, A. L. Rheingold, and R. F. Heck, *J. Org. Chem.*, 1988, **53**, 3238.
6. L. Li, W. W. Brennessel, and W. D. Jones, *J. Am. Chem. Soc.*, 2008, **130**, 12414.
7. (a) J. Jayakumar, K. Parthasarathy, and C.-H. Cheng, *Angew. Chem. Int. Ed.*, 2012, **51**, 197; (b) N. Senthilkumar, P. Gandeepan, J. Jayakumar, and C.-H. Cheng, *Chem. Commun.*, 2014, **50**, 3106; (c)

K. Parthasarathy, N. Senthilkumar, J. Jayakumar, and C.-H. Cheng, *Org. Lett.*, 2012, **14**, 3478; (d) C.-Z. Luo, P. Gandeepan, J. Jayakumar, K. Parthasarathy, Y.-W. Chang, and C.-H. Cheng, *Chem. Eur. J.*, 2013, **19**, 14181.

8. G. Zhang, L. Yang, Y. Wang, Y. Xie, and H. Huang, *J. Am. Chem. Soc.*, 2013, **135**, 8850.
9. For more details, see the Supporting Information.