Organic & Biomolecular Chemistry

COMMUNICATION

View Article Online
View Journal

Check for updates

Cite this: DOI: 10.1039/c7ob00818j

Received 1st April 2017,
Accepted 11th April 2017

DOI: 10.1039/c7ob00818j

rsc.li/obc

Published on 25 April 2017. Downloaded by Hacettepe Universitesi on 26/04/2017 00:45:51.

Ruthenium(II)-catalyzed *ortho*-C–H arylation of diverse N-heterocycles with aryl silanes by exploiting solvent-controlled N-coordination†

Pradeep Nareddy, Frank Jordan and Michal Szostak *

We report the first method for the direct, regioselective Ru(II)-catalyzed oxidative arylation of C–H bonds in diverse N-heterocycles with aryl silanes by exploiting solvent-controlled N-coordination. The reaction takes advantage of the attractive features of organosilanes as coupling partners, providing proof of concept for N-directed Ru(II)-catalyzed C–H arylation. This novel, operationally-simple and versatile protocol utilizes the Ru(II)/CuF_2 reagent system in which CuF_2 serves as a dual activator/oxidant in non-coordinating solvents to accommodate for ligand N-coordination. This first Ru(II)-catalyzed N-directed Hiyama C–H arylation offers broad implications to achieve numerous C–H bond functionalizations by versatile ruthenium(II) catalysis manifold.

The Hiyama cross-coupling reaction is widely-recognized as one of the most important methods for C–C bond formation due to major advantages of organosilicon coupling partners, including low toxicity, safe handling, accessibility and functional group compatibility.[1,2] The development of direct C–H functionalization strategies has exerted a profound impact on organic synthesis.[3] The use of organometallic reagents provides multiple sources of alternative carbon nucleophiles under mild, functional group tolerant, oxidative conditions with functional group tolerance and unique selectivity unattainable by other catalytic manifolds.[4]

Pioneering work demonstrated the utility of direct Hiyama C–H arylation based on Pd and Ni catalysis.[5a–c] More recently, synthetically useful methods have been reported.[5d–h] However, despite these advances, the use of organosilanes as viable cross-coupling partners in C–H functionalization remains severely underdeveloped due to (1) low nucleophilicity of organosilanes;[1a–d] (2) incompatibility of silane activation and metal re-oxidation steps within the C–H activation cycle.[3,4] This manuscript reports the first Ru-catalyzed C–H arylation with organosilanes by N-coordination. The reaction manifold is highly desirable for the following reasons:

(1) the manuscript describes the first Ru-catalyzed arylation with arylsilanes exploiting N-coordination. This includes Ru(II) and Ru(0) cycles,[6] and could lead to the development of a range of C–H arylation protocols by N-coordination in common substrates.

(2) the method shows much higher chemoselectivity than other methods for arylation of N-heterocycles using Ru-catalysis. Specifically, our method tolerates aryl halides, such as bromides which are beyond the scope of Ru(II)/(IV) cycle by N-coordination. In general, there are very few methods for direct C–H arylation of N-heterocycles in the presence of aryl bromides, and all of them limited to Pd and Rh catalysis.[3,4]

(3) we demonstrate that the reaction rate with organosilanes using Ru(II)-catalysis by N-coordination is much higher than by O-coordination,[7–10] which may lead to the development of a range of practical protocols for C–H arylation by this catalysis manifold.

(4) we demonstrate that Ru(II)-catalyzed C–H arylation of N-heterocycles using organosilanes proceeds with much higher efficiency than when using organoboranes,[7–10] which may lead to complementary selectivity in Ru(II)-catalyzed C–H arylation.

Over the past decade, there have been remarkable advances in ruthenium(II)-catalyzed C–H functionalizations owing to (1) economic advantages of ruthenium; (2) operationally-simple reaction protocols; (3) high functional group tolerance.[6] The groups of Jeganmohan[7] and Pilarski[8] have designed new catalytic systems for C–H arylation with boronic acids (Fig. 1A). We have reported direct arylation of *N*,*N*-dialkyl benzamides by weak O-coordination.[9] More recently, we have achieved the first Ru(II)-catalyzed C–H arylation with organosilanes in *N*,*N*-dialkyl benzamide substrates exploiting weak O-coordination.[10] This is the only successful example of Ru(II)-catalyzed direct Hiyama C–H functionalization with organosilanes accomplished to date.[11]

Herein, we report the first method for the direct, regioselective Ru(II)-catalyzed oxidative Hiyama arylation of C–H

Department of Chemistry, Rutgers University, 73 Warren Street, Newark, NJ 07102, USA. E-mail: michal.szostak@rutgers.edu; Fax: (+1)-973-353-1264; Tel: (+1)-973-353-532

† Electronic supplementary information (ESI) available: Experimental details and characterization data. See DOI: 10.1039/c7ob00818j

Published on 25 April 2017. Downloaded by Hacettepe Universitesi on 26/04/2017 00:45:51.

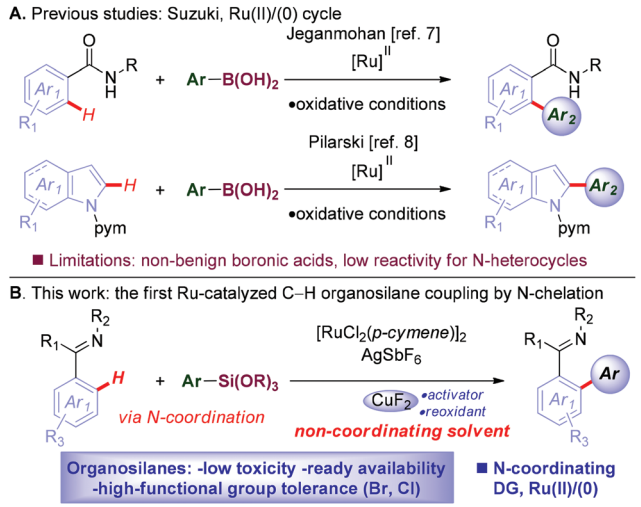
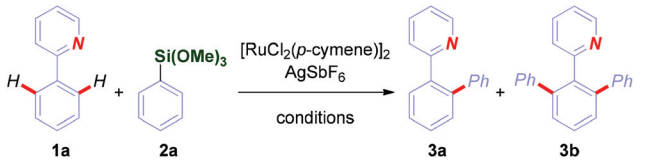


Fig. 1 (a) Ruthenium-catalyzed arylation using boronic acids (previous studies), and (b) ruthenium(II)-catalyzed C–H arylation using organosilanes by N-coordination (this study).

Table 1 Optimization of Ru(II)-catalyzed C–H arylation of **1a** with phenyltrimethoxysilane[a]



Entry	Additive	Oxidant	Solvent	**3a** : **3b**[b] (%)	Yield[b,c] (%)
1	CuF_2	—	DCE	6 : 94	>95 (83)[d]
2	CuF_2	—	$PhCH_3$	69 : 31	>95
3	CuF_2	—	THF	75 : 25	>95
4	CuF_2	—	*i*-PrOH	74 : 26	>95
5	CuF_2	—	DMF	86 : 14	70
6	CuF_2	—	CH_3CN	—	<5
7	CuF_2	—	$CHCl_3$	—	<2
8	CuF_2	—	NMP	—	<2
9	CuF_2	AgF	DCE	—	<2
10	AgF	Ag_2O	DCE	>95 : 5	40
11	AgF	$Cu(OTf)_2$	DCE	—	<2
12	AgF	$Cu(OAc)_2$	DCE	—	<2
13	AgF	$Cu(OAc)_2H_2O$	DCE	—	<2
14	KF	$Cu(OTf)_2$	DCE	—	<2
15	CsF	$Cu(OTf)_2$	DCE	—	<2
16	CuF_2	$Cu(OTf)_2$	DCE	—	<2

[a] 2-Phenylpyridine (1.0 equiv.), $[RuCl_2(p\text{-cymene})]_2$ (5 mol%), $AgSbF_6$ (20 mol%), $PhSi(OMe)_3$ (3.0 equiv.), additive (3.5 equiv.), oxidant (2.0 equiv.), solvent (0.20 M), 140 °C, 20 h. [b] Determined by ^1H NMR and GC. [c] Yield of **3a** and **3b**. [d] Isolated yield of **3b**. See ESI for details.

bonds in diverse N-heterocycles with aryl silanes by exploiting solvent-controlled N-coordination (Fig. 1B). Notable features of our study include: (1) the first N-directed Hiyama cross-coupling using cost-effective, versatile Ru(II) catalysis; (2) the use of benign, functional group tolerant organosilanes, including tolerance for aryl halides; (3) Ru(II)/CuF_2 reagent system in which CuF_2 serves as a dual activator/oxidant in non-coordinating solvents to accommodate for ligand N-chelation;[12] (4) synthesis of biaryl N-heterocyclic motifs that are prevalent in natural products, pharmaceuticals and advanced organic materials;[13,14] (5) key mechanistic studies that support reversible cycloruthenation. Notably, we demonstrate that (i) the present Ru(II)-catalyzed Hiyama cross-coupling shows higher reactivity than the Ru(II)-catalyzed direct C–H arylation with boronic acids; (ii) N-coordination leads to significantly improved reactivity than O-coordination[10] under oxidative Ru(II)-Hiyama conditions. This first Ru(II)-catalyzed N-directed Hiyama C–H arylation offers broad implications to achieve numerous C–H bond functionalizations by versatile ruthenium(II) catalysis manifold that is beyond the scope of classic Ru(0)/(II) arylations.[11j]

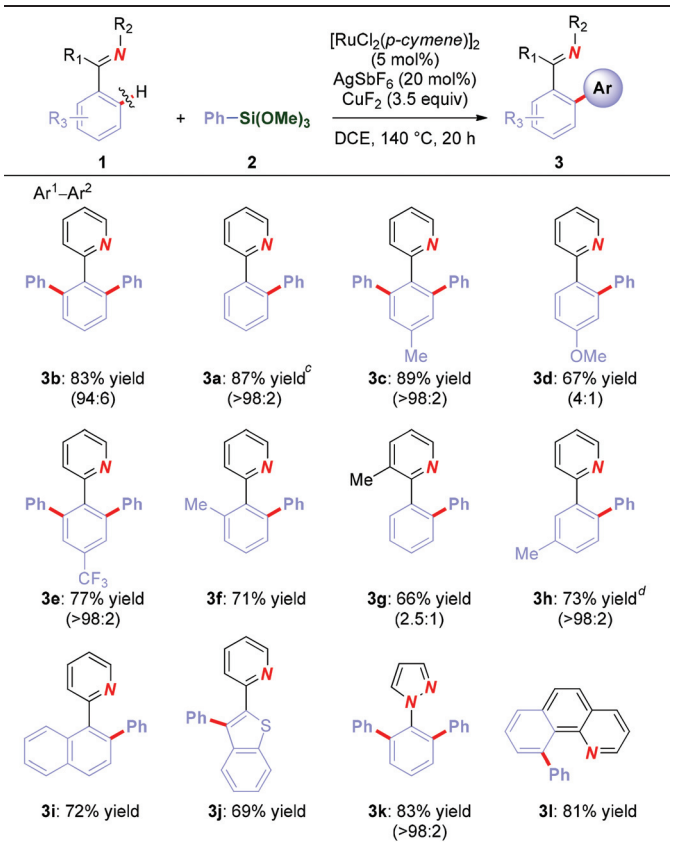
We initiated our investigations by studying arylation of **1a** with trimethoxyphenylsilane (Table 1). At the outset, we hypothesized that by fine-tuning the coordinating properties of the solvent to accommodate for N-chelation may enable the first direct Ru(II)-catalyzed C–H arylation of N-heterocycles with aryl silanes. After extensive optimization, we were delighted to find that the use of cationic Ru(II) catalyst, $[RuCl_2(p\text{-cymene})]_2$ (5 mol%), $AgSbF_6$ (20 mol%), trimethoxyphenylsilane (3 equiv.), and CuF_2 (3.5 equiv.) in DCE (1,2-dichlorethane) cleanly delivered the desired diarylation product in 83% isolated yield (Table 1, entry 1). It is worth noting that the reaction is efficiently promoted by a single and cheap additive, CuF_2, which serves as a dual silane activator and Ru(0)-re-oxidant.[15] Key optimization results are shown in Table 1. Other solvents are inferior to DCE due to less efficient arylation and decomposition (entries 2–8). Modest monoselectivity using $PhCH_3$, THF, *i*-PrOH and DMF was observed. As anticipated, the efficiency of the reaction is strongly dependent of the nature of the catalytic system used (entries 9–16). In agreement with our hypothesis, the combined use of other well-established Ru(0)-re-oxidants (Ag_2O, $Cu(OTf)_2$, $Cu(OAc)_2$)[7–9,11] and silane activators (AgF, KF, CsF) gave inferior results (entries 9–16).[5] Notably, the attempted C–H arylation of **1a** with phenylboronic acid under various Ru(II) conditions gave the desired product with low conversions (*vide infra*, see ESI†), suggesting the high potential of the Ru(II)-catalyzed Hiyama cross-coupling in C–H functionalization of N-coordinating substrates.

With the optimized conditions in hand, the scope of this new Ru(II)-catalyzed Hiyama C–H arylation of N-heterocycles was surveyed (Table 2). We were delighted to find that the developed Ru(II)/CuF_2 catalyst system is effective for arylation of a wide range of N-heterocycles with high arylation selectivity, including medicinally-relevant pyridines, pyrazoles and quinolines.[16] The example with substoichiometric amount of 2-phenylpyridine (entry 2, **3a**) illustrates that monoarylation is possible with high selectivity, a process difficult to achieve with aryl halides.[11] The arylation proceeds in high yields for electron-donating and withdrawing substrates (entries 3–5, **3c–3e**). In

 This journal is © The Royal Society of Chemistry 2017

Published on 25 April 2017. Downloaded by Hacettepe Universitesi on 26/04/2017 00:45:51.

Table 2 Ruthenium(II)-catalyzed C–H arylation of N-heterocycles with phenyltrimethoxysilane[a,b]



[a] N-heterocycle (1.0 equiv.), $[RuCl_2(p\text{-cymene})]_2$ (5 mol%), $AgSbF_6$ (20 mol%), $PhSi(OMe)_3$ (3.0 equiv.), CuF_2 (3.5 equiv.), DCE (0.20 M), 140 °C, 20 h. [b] Isolated yields. [c] $PhSi(OMe)_3$ (0.50 equiv.). [d] $PhSi(OMe)_3$ (1.0 equiv.). Selectivity is indicated in brackets. See ESI for full details.

these examples, significant electronic effects favoring arylation of electron-deficient arenes (**3e** *vs.* **3d**) are observed (*vide infra*). The sterically-demanding *ortho*-methyl substrate underwent arylation in good yield (entry 6, **3f**). Moreover, monoarylation is selectively achieved with (1) substrates bearing *ortho*-substituents on the pyridine ring (entry 7, **3g**); (2) substrates featuring *meta*-substitution on the arene[17] (entry 8, **3h**), representing another strategy to achieve selective mono-arylation. Furthermore, substrates bearing other heterocycles such as sterically-demanding naphthalene (entry 9, **3i**), electronically-biased benzothiophene (entry 10, **3j**), as well as directing groups such as pyrazole (entry 11, **3k**), and quinoline (entry 12, **3l**) were successfully arylated to deliver the C–H arylation products in high yields. Of note, our results provide the first example of a direct arylation of 2-pyrimidyl-benzothiophene (**3j**), providing a modular access to benzothiophenes that are prevalent in functional material applications.[18] Taken together, these results clearly demonstrate that this Ru(II)-catalyzed N-directed Hiyama protocol might set the stage for the development of numerous C–H arylation methods with versatile Ru(II) catalysts.

Next, the substrate scope with respect to the aryl silane component was evaluated (Table 3). The scope with respect to the aryl silane component is also broad. We were pleased to find that trimethoxyphenylsilane was similarly effective as trimethoxyphenylsilane without modification of the reaction conditions (entry 1 *vs.* entry 2).[5c] Electron-rich (entries 3 and 4) and electron-deficient silanes (entry 5) are suitable cross-coupling partners, affording the desired mono-arylation product with high arylation selectivity. Especially noteworthy is the finding that fluoro (entry 6), chloro (entry 7) and bromo (entry 8) substituents on the silane component can be employed, providing valuable handles for further manipulation. Of note, these results provide the first example of an aryl bromide tolerated in C(sp^2)–H direct Hiyama cross-coupling using N-coordinating groups.[5] Selectivity for halides (entries 7 and 8) is complementary to Ru(II)/carboxylate systems,[6,11] paving the way for sequential techniques to construct polyarenes.

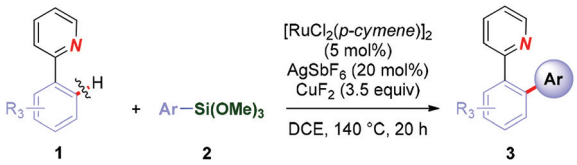
Preliminary mechanistic studies were conducted (Schemes 1–3). (1) In agreement with silane activation, intermolecular competition studies with different arylsilanes revealed that electron deficient silanes react preferentially (Scheme 1A). (2) Electron-withdrawing groups on the arene facilitate C–H arylation (Scheme 1B). Selectivity trends observed in the arylation of electronically-differentiated substrates (Table 1) provide additional insights into the arylation selectivity. (3) Deuterium incorporation studies revealed reversibility of the cycloruthenation step (Scheme 2).[6] Most notably, competition experiments reveal that N-coordination leads to significantly improved reactivity than O-coordination[10] under oxidative Ru(II)-Hiyama conditions (Scheme 3). Moreover, the utility of this new Hiyama direct coupling is highlighted by the fact that the attempted Ru(II)-catalyzed arylation of N-heterocycles with boronic acids proceeds with low efficiency (Scheme 4, see ESI† for details). Further studies to elucidate the mechanism are ongoing.

In summary, we have developed the first direct ruthenium(II)-catalyzed oxidative C–H Hiyama cross-coupling method for regioselective arylation of diverse N-heterocycles with aryl silanes by N-coordination. This strategy is characterized by low toxicity of arylsilanes, the functional group tolerance for aryl halides, and broad substrate scope with respect to both components. The protocol provides an operationally-simple method to produce a wide range of valuable heterocyclic biaryls that are particularly common in natural products and pharmaceuticals under mild oxidative conditions with user-friendly Ru(II). This reaction employs CuF_2 as a dual silane activator/Ru re-oxidant, and no added ligand or additive is necessary. We anticipate that this study will set the stage for the discovery of numerous valuable C–H bond functionalization reactions with versatile ruthenium(II) catalysts.

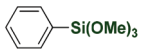
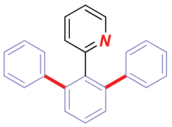
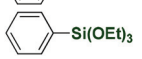
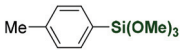
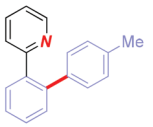
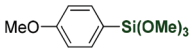
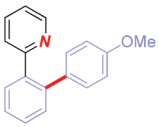
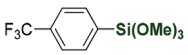
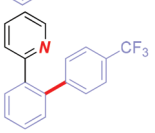
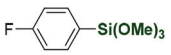
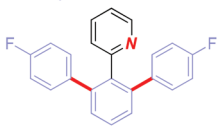
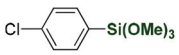
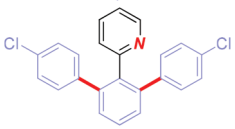
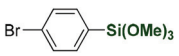
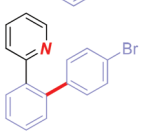
Financial support was provided by Rutgers University. The Bruker 500 MHz spectrometer used in this study was supported by the NSF-MRI grant (CHE-1229030). We thank SEED Grant (Rutgers University) to the Center for Sustainable Synthesis for partial support of this project.

Published on 25 April 2017. Downloaded by Hacettepe Universitesi on 26/04/2017 00:45:51.

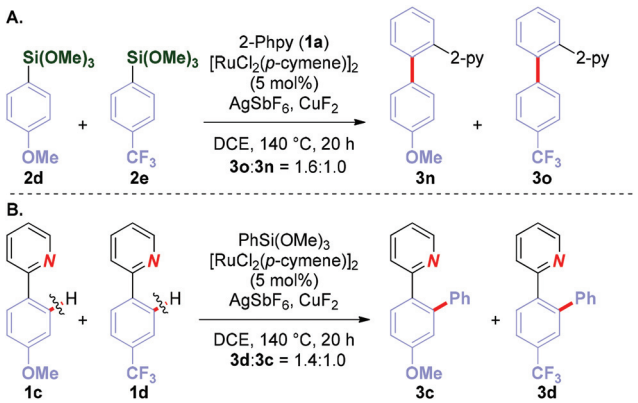
Table 3 Ruthenium(II)-catalyzed C–H arylation of N-heterocycles with various organosilanes[a]



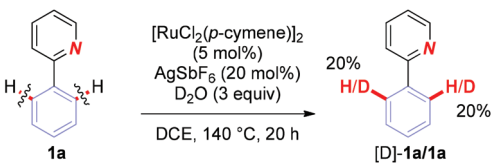
1 2 3

Entry	Organosilane	2	Product	3	Yield[a] (%)
1		2a		3a	83
2		2b		3a	79
3		2c		3m	67
4		2d		3n	59
5		2e		3o	67
6		2f		3p	75
7		2g		3q	70
8		2h		3r	57

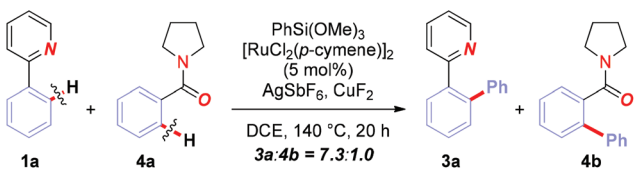
[a] See Table 2. Selectivity: **3m** (4 : 1), **3o** (2.5 : 1), all other examples >98 : 2. See ESI for full details.



Scheme 1 Mechanistic studies.



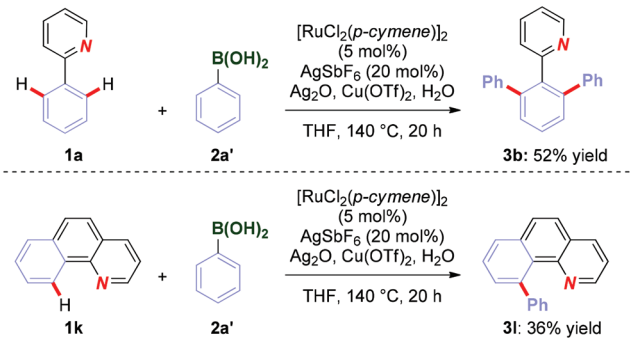
Scheme 2 Deuterium incorporation studies.



Scheme 3 Selectivity studies: N- *vs.* O-coordination.

 This journal is © The Royal Society of Chemistry 2017

Published on 25 April 2017. Downloaded by Hacettepe Universitesi on 26/04/2017 00:45:51.



Scheme 4 Ru(II)-catalyzed arylation of N-heterocycles using organoboranes. Representative examples are shown (see ESI†).

Notes and references

1 Reviews: (*a*) S. E. Denmark and C. S. Regens, *Acc. Chem. Res.*, 2008, **41**, 1486; (*b*) S. E. Denmark and J. H. C. Liu, *Angew. Chem., Int. Ed.*, 2010, **49**, 2978; (*c*) Y. Nakao and T. Hiyama, *Chem. Soc. Rev.*, 2011, **40**, 4893; (*d*) S. E. Denmark and A. Ambrosi, *Org. Process Res. Dev.*, 2015, **19**, 982. Select examples: (*e*) L. Zhang and J. Wu, *J. Am. Chem. Soc.*, 2008, **130**, 12250; (*f*) S. K. Gurung, S. Thapa, A. S. Vangala and R. Giri, *Org. Lett.*, 2013, **15**, 5378.

2 Reports on mutagenicity of boronic acids: (*a*) M. M. Hansen, R. A. Jolly and R. J. Linder, *Org. Process Res. Dev.*, 2015, **19**, 1507; (*b*) M. R. O'Donovan, C. D. Mee, S. Fenner, A. Teasdale and D. H. Phillips, *Mutat. Res., Genet. Toxicol. Environ. Mutagen.*, 2011, **724**, 1.

3 Select reviews: (*a*) J. Q. Yu, *Science of Synthesis: Catalytic Transformations via C–H Activation*, Thieme, Stuttgart, 2015; (*b*) R. Rossi, F. Bellina, M. Lessi and C. Manzini, *Adv. Synth. Catal.*, 2014, **356**, 17; (*c*) J. Wencel-Delord and F. Glorius, *Nat. Chem.*, 2013, **5**, 369; (*d*) G. Rouquet and N. Chatani, *Angew. Chem., Int. Ed.*, 2013, **52**, 11726; (*e*) C. S. Yeung and V. M. Dong, *Chem. Rev.*, 2011, **111**, 1215; (*f*) T. Lyons and M. Sanford, *Chem. Rev.*, 2010, **110**, 1147.

4 Review on C–H arylation with organometallics: R. Giri, S. Thapa and A. Kafle, *Adv. Synth. Catal.*, 2014, **356**, 1395.

5 (*a*) S. Yang, B. Li, X. Wan and Z. J. Shi, *J. Am. Chem. Soc.*, 2007, **129**, 6066; (*b*) H. Zhou, Y. H. Xu, W. J. Chung and T. P. Loh, *Angew. Chem., Int. Ed.*, 2009, **48**, 5355; (*c*) H. Hachiya, K. Hirano, T. Satoh and M. Miura, *Angew. Chem., Int. Ed.*, 2010, **49**, 2202; (*d*) W. Li, Z. Yin, X. Jiang and P. Sun, *J. Org. Chem.*, 2011, **76**, 8543; (*e*) N. Senthilkumar, K. Parthasarathy, P. Gandeepan and C. H. Cheng, *Chem. – Asian J.*, 2013, **8**, 2175; (*f*) M. Z. Lu, P. Lu, Y. H. Xu and T. P. Loh, *Org. Lett.*, 2014, **16**, 2614; (*g*) J. He, R. Takise, H. Fu and J. Q. Yu, *J. Am. Chem. Soc.*, 2015, **137**, 4618; (*h*) S. Zhao, B. Liu, B. B. Zhan, W. D. Zhang and B. F. Shi, *Org. Lett.*, 2016, **18**, 4586.

6 (*a*) P. B. Arockiam, C. Bruneau and P. H. Dixneuf, *Chem. Rev.*, 2012, **112**, 5879; (*b*) S. De Sarkar, W. Liu, S. L. Kozushkov and L. Ackermann, *Adv. Synth. Catal.*, 2014, **356**, 1461. In March 2017, the average prices of Rh, Ir, Pd and Ru were 875, 690, 769, and 42 US$/oz. https://tax-freegold.co.uk (3/3/2017).

7 R. K. Chinnagolla and M. Jeganmohan, *Org. Lett.*, 2012, **14**, 5246.

8 C. Sollert, K. Devaraj, A. Orthaber, P. J. Gates and L. T. Pilarski, *Chem. – Eur. J.*, 2015, **21**, 5380.

9 P. Nareddy, F. Jordan, S. E. Brenner-Moyer and M. Szostak, *ACS Catal.*, 2016, **6**, 4755.

10 P. Nareddy, F. Jordan and M. Szostak, *Chem. Sci.*, 2017, **8**, 3204.

11 Select examples of Ru-catalyzed functionalization: (*a*) S. Oi, S. Fukita, N. Hirata, N. Watanuki, S. Miyano and Y. Inoue, *Org. Lett.*, 2001, **3**, 2579; (*b*) L. Ackermann, *Org. Lett.*, 2005, **7**, 3123; (*c*) L. Ackermann, A. Althammer and R. Born, *Angew. Chem., Int. Ed.*, 2006, **45**, 2619; (*d*) I. Özdemir, S. Demir, B. Cetinkaya, C. Gourlaouen, F. Maseras, C. Bruneau and P. H. Dixneuf, *J. Am. Chem. Soc.*, 2008, **130**, 1156; (*e*) R. K. Chinnagolla and M. Jeganmohan, *Chem. Commun.*, 2014, **50**, 2442; (*f*) R. K. Chinnagolla, A. Vijeta and M. Jeganmohan, *Chem. Commun.*, 2015, **51**, 12992; (*g*) K. Padala and M. Jeganmohan, *Org. Lett.*, 2011, **13**, 6144; (*h*) H. Li, W. Wei, Y. Xu, C. Zhang and X. Wan, *Chem. Commun.*, 2011, **47**, 1497; (*i*) K. Devaraj, C. Sollert, C. Juds, P. J. Gates and L. J. Pilarski, *Chem. Commun.*, 2016, **52**, 5868; (*j*) F. Kakiuchi, Y. Matsuura, S. Kan and N. Chatani, *J. Am. Chem. Soc.*, 2005, **127**, 5936; (*k*) F. Hu and M. Szostak, *Org. Lett.*, 2016, **18**, 4186; (*l*) F. Hu and M. Szostak, *Chem. Commun.*, 2016, **52**, 9715; (*m*) M. K. Lakshman, A. C. Deb, R. R. Chamala, P. Pradhan and R. Pratap, *Angew. Chem., Int. Ed.*, 2011, **50**, 11400; (*n*) M. Simonetti, G. J. P. Perry, X. C. Cambeiro, F. Julia-Hernandez, J. N. Arokianathar and I. Larrosa, *J. Am. Chem. Soc.*, 2016, **138**, 3596; (*o*) L. Huang and D. J. Weix, *Org. Lett.*, 2016, **18**, 5432; (*p*) A. Biafora, T. Krause, D. Hackenberger, F. Belitz and L. J. Gooßen, *Angew. Chem., Int. Ed.*, 2016, **55**, 14752; (*q*) R. Mei, C. Zhu and L. Ackermann, *Chem. Commun.*, 2016, **52**, 13171; (*r*) M. Simonetti, D. M. Cannas, A. Panigrahi, S. Kujawa, M. Kryjewski, P. Xie and I. Larrosa, *Chem. – Eur. J.*, 2017, **23**, 549.

12 (*a*) K. M. Engle, T. S. Mei, M. Wasa and J. Q. Yu, *Acc. Chem. Res.*, 2012, **45**, 788; (*b*) J. F. Hartwig, *Organotransition Metal Chemisty: From Bonding to Catalysis*, University Science Books, 2010.

13 (*a*) J. Hassan, M. Sevignon, C. Gozzi, E. Schulz and M. Lemaire, *Chem. Rev.*, 2002, **102**, 1359; (*b*) A. J. Burke and C. S. Marques, *Modern Arylation Methods*, Wiley-VCH, Weinheim, 2015; (*c*) J. A. Garcia-Lopez and M. F. Greaney, *Chem. Soc. Rev.*, 2016, **45**, 6766; (*d*) Y. Chen and R. C. Larock, in *Modern Arylation Methods*, ed. L. Ackermann, Wiley-VCH, New York, 2009, pp. 401–473.

14 J. A. Joule and K. Mills, *Heterocyclic Chemistry*, Wiley, 2010.

15 K. M. Engle, T. S. Mei, X. Wang and J. Q. Yu, *Angew. Chem., Int. Ed.*, 2011, **50**, 1478.

16 R. D. Taylor, M. Maccoss and A. D. G. Lawson, *J. Med. Chem.*, 2014, **57**, 5845.
17 Seminal example of Ru(II)-catalyzed meta-functionalization: O. Saidi, J. Marafie, A. E. W. Ledger, P. M. Liu, M. F. Mahon, G. Kociok-Köhn, M. K. Whittlesey and C. G. Frost, *J. Am. Chem. Soc.*, 2011, **133**, 19298.
18 Y. Li, *Organic Optoelectronic Materials*, Springer, 2015.

Published on 25 April 2017. Downloaded by Hacettepe Universitesi on 26/04/2017 00:45:51.

This journal is © The Royal Society of Chemistry 2017