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Ruthenium-Catalyzed Heteroatom-Directed Regioselective C−H Arylation of Indoles Using a Removable Tether

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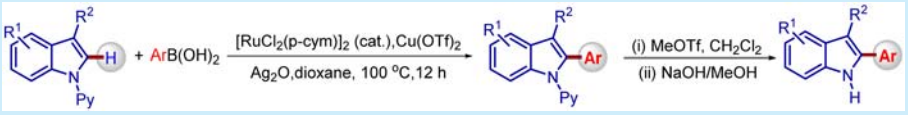
Supporting Information



ABSTRACT: A new approach to C-2 arylated indoles has been developed by utilizing a ruthenium-catalyzed, heteroatom-directed regioselective C−H arylation. The reaction is highly site-selective and results in very good yields. The highlight of the work is the use of a removable directing group and compatibility of the catalytic system with halogen functional groups in the substrates.

Over the past decade and a half, transition-metal-catalyzed C−H bond functionalization reactions have revolutionized transformations that were considered rather difficult without prefunctionalization.[1] Strategies adopted in C−H functionalization are usually atom- and step-economical and have therefore added a new dimension in organic transformations. These methods have been widely employed in the synthesis of biologically important and structurally complex natural products[2] and continue to undergo metamorphosis to evolve better catalyst systems for enhanced control on site-selectivities. Of the strategies adopted for the control of selectivity (chemo- and regio-), electronic factors and the use of Lewis-basic directing groups are the most widely employed methods.[3] The direct arylation reaction,[4] using transition-metal catalysis, forms a very important constituent of C−H functionalization, often proceeding via five- or six-membered cyclometalation. This also forms the basis of an efficient directing group system design where tighter transition states and compact metallacycles lead to high selectivities.[5]

The indole system has been one of the most studied heterocycles in terms of skeletal modification.[6] This is simply due to the high biological relevance of indoles being ubiquitous in nature and by virtue of it being part of several important natural products or pharmaceuticals including alkaloids. 2-Arylindoles are the constituent of several natural products and pharmaceutically important chemical entities (Figure 1).[7] The transition-metal-catalyzed C−H arylation of indoles has been quite well studied, with several research groups developing efficient catalyst systems to guide the regioselectivity to either C2 or C3 position of indoles. One of the strategies involving C−H arylation at the C2-position has utilized a postulated electrophilic metalation at C3, followed by a 1,2-shift of the metal, to achieve the desired transformation.[8] In other cases, directing groups on the indole nitrogen guide the site-selectivity.[9] In some of the pioneering works, arylations with high selectivities have been achieved even with NH-indoles.[10] Following an early report by

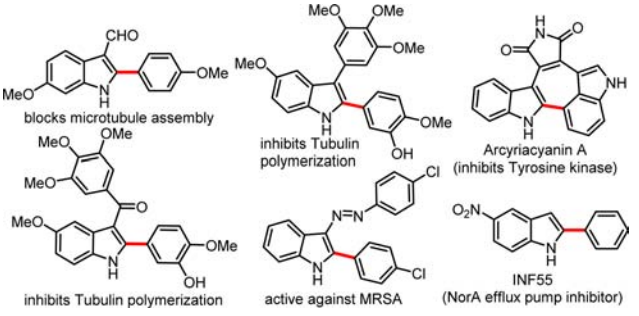


Figure 1. 2-Arylindole core in biologically active molecules.

Itahara,[9a] several other directing groups such as amides, carboxamides, carbamates, *N*-pyrimidyl, and *N*-pyridyl have been used for driving the arylation with C2 selectivity for indoles.

Of these, the synthetic utility of the method is greatly enhanced when removable directing groups are employed. Ackermann and co-workers showed the utility of *N*-pyrimidyl as well as *N*-pyridyl groups in the regioselective arylation of indoles when using a Ru(II)−Ru(IV) catalytic system with aryl halides.[9k,l] Recently, Loh and co-workers used *N*-pyrimidyl as a directing group and arylsilanes as the coupling partner in a Rh(III)−Rh(I) catalytic system.[9q] We report herein the use of a removable *N*-pyridyl directing group in regioselective C2 direct arylation of indoles with arylboronic acids using a Ru(II)−Ru(0) catalytic system. The reaction works extremely well with a very broad substrate scope and very good yields. The highlight of the work is the use of bromo-substituted arylboronic acids as well as substituted bromoindoles for the coupling, which cannot be used with most of the methods used in the literature, thereby providing a handle for further functionalization.

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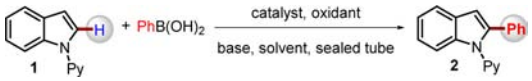
Our group has been interested in C−H functionalization of heterocycles,[11] especially the direct arylation reactions of heteroarenes and their application in natural product synthesis. In one of the natural product syntheses, we were required to introduce on a substituted indole, an aryl group, which carried two bromide substituents for further functionalization. In this regard, we decided to develop a new catalytic system with a removable directing group for the direct C2 arylation of indoles. Our initial efforts started with scanning of several catalyst systems along-with an appropriate directing group for the indole system. For this, the acetyl, arylsulfonyl, pyrimidyl, pyridyl groups were among the ones scanned. The best results were obtained with *N*-2-pyridyl as the directing group and $[RuCl_2(p\text{-cym})]_2/Ag_2O/Cu(OTf)_2$/dioxane with arylboronic acids as the coupling partner (Table 1).

Under these conditions, use of *N*-phenyl, *N*-Ts, or *N*-phenylsulfonyl groups resulted only in the homocoupling of arylboronic acids, and the starting material mostly remained unreacted. The use of *N*-Me resulted only into decomposition of the starting material. With free −NH indole, the reaction was very sluggish, and it probably deactivated the catalyst. Although K_3PO_4 worked well as a base, better results were obtained with Ag_2O. DMA as a solvent also yielded good results; however, dioxane was the solvent of choice since better yields for the desired conversions were obtained in it. Reactions in acidic conditions did not work. Use of palladium catalysts resulted in sluggish reactions, and selectivity between C2 and C3 was often compromised. Both the ruthenium catalyst and $Cu(OTf)_2$ were necessary for the transformation. Without either of them, the reaction did not work. Use of catalytic quantities of $Cu(OTf)_2$ resulted in low conversions. Therefore, the use of oxidant was necessary in this transformation. Depicted in Scheme 1 is the substrate scope for the standardized reaction conditions. The reaction worked very well for almost all of the arylboronic acids tried, and the site-selectivity was exclusive. Electronic effects on the indole were also well tolerated. The reaction worked with electron-donating as well as electron-withdrawing substituents at the C5 position of the indole. Better yields were obtained with electron-withdrawing substituents at C5. This could be attributed to enhanced acidity of C2 C−H and low nucleophilic character at C3 of the indole when substituents such as $-NO_2$ were present at C5. The reaction worked beautifully well even with a methyl substitutent at C3. Electronic effects were well tolerated on the arylboronic acid, too. Good results were obtained even with a free hydroxyl substituent (Scheme 1, entry **2ah**). In the case of the 2-nitrophenylboronic acid, only the protodeboronation product was observed. Sterically encumbered arylboronic acids also worked out quite well (Scheme 1, entry **2an**−**ao**). As desired, the reaction worked extremely well with bromide substituents on both the coupling partners. With 4-bromo-*N*-pyridylindole, small amounts of the cross-coupling product of the bromide with the boronic acid were observed, resulting in a C2,C4-diaryl product (~5%) along with the C2-monoaryl product (**2cc**).

A plausible mechanism is depicted in Scheme 2. The first step is probably the coordination of the ruthenium catalyst to the *N*-pyridyl group. This is followed by C−H activation at C2 to result in the ruthenacycle. Transmetalation with the arylboronic acid, followed by reductive elimination, results in the C2-aryl indole. The Ru(0) is then oxidized to Ru(II) by Cu(II). Silver oxide not only acts as a base, it facilitates the transmetalation and also assists the reoxidation step. Since, with this catalyst system, the reaction did not work with *N*-phenyl or *N*-Me groups on the indole, the role of the directing group seems to be necessary. Therefore, it seems rather unlikely that the reaction would be proceeding by an electrophilic metalation mechanism. An

Table 1. Optimization Studies



entry	reaction conditions	yield (%)
1	$[RuCl_2(p\text{-cym})]_2/Cu(OTf)_2/Ag_2O/CHCl_3$/ 70 °C/12 h	trace
2	$[RuCl_2(p\text{-cym})]_2/Cu(OTf)_2/Ag_2O/ClCH_2CH_2Cl$/70 °C/12 h	trace
3	$[RuCl_2(p\text{-cym})]_2/Cu(OTf)_2/Ag_2O$/DMF/100 °C/12 h	55[a]
4	$[RuCl_2(p\text{-cym})]_2/Cu(OTf)_2/Ag_2O$/DMSO/100 °C/12 h	trace
5	$[RuCl_2(p\text{-cym})]_2/Cu(OTf)_2/Ag_2O$/THF/50 °C/12 h	47[a]
6	$[RuCl_2(p\text{-cym})]_2/Cu(OTf)_2/Ag_2O$/xylene/100 °C/12 h	5[b]
7	$[RuCl_2(p\text{-cym})]_2/Cu(OAc)_2/Ag_2O$/dioxane/100 °C/12 h	trace
8	$[RuCl_2(p\text{-cym})]_2$/BQ/Ag_2O/dioxane/100 °C/ 12 h	NR
9	$[RuCl_2(p\text{-cym})]_2$/DDQ/Ag_2O/dioxane/100 °C/ 12 h	NR
10	$[RuCl_2(p\text{-cym})]_2/K_2CO_3$ (2 equiv)/dioxane/100 °C/12 h	trace
11	$[RuCl_2(p\text{-cym})]_2/Ag_2O$ (2 equiv)/dioxane/100 °C/12 h	trace
12	$[RuCl_2(p\text{-cym})]_2/Cu(OTf)_2$ (2 equiv)/dioxane/ 100 °C/12 h	30[a]
13	$[RuCl_2(p\text{-cym})]_2/Cu(OTf)_2/Ag_2O$/DMA/100 °C/12 h	86[a]
14	**$[RuCl_2(p\text{-cym})]_2/Cu(OTf)_2/Ag_2O$/dioxane/ 100 °C/12 h**	**90[a]**
15	$[RuCl_2(p\text{-cym})]_2/Cu(OTf)_2/K_3PO_4$/dioxane/ 100 °C/12 h	81[a]
16	$[RuCl_2(p\text{-cym})]_2/Cu(OTf)_2$/CsOPiv/dioxane/ 100 °C/12 h	51[a]
17	$[RuCl_2(p\text{-cym})]_2/Cu(OTf)_2/Cs_2CO_3$/dioxane/ 100 °C/12 h	65[a]
18	$[RuCl_2(p\text{-cym})]_2/Cu(OTf)_2/CF_3CO_2Na$/ dioxane/100 °C/12 h	10[a]
19	$[RuCl_2(p\text{-cym})]_2/Cu(OTf)_2/Ag_2CO_3$/dioxane/ 100 °C/12 h	58[a]
20	$[RuCl_2(p\text{-cym})]_2/Cu(OTf)_2$/CsOAc/dioxane/ 100 °C/12 h	59[a]
21	$[RuCl_2(p\text{-cym})]_2/Cu(OTf)_2$/AcONa/dioxane/ 100 °C/12 h	60[a]
22	$[RuCl_2(p\text{-cym})]_2/Ag_2O$ (2 equiv)/dioxane/100 °C/12 h	0
23	$[RuCl_2(p\text{-cym})]_2/Ag_2O$ (2 equiv)/TFA/70 °C/ 12 h	0
24	$[RuCl_2(p\text{-cym})]_2$/(1-Ad)CO_2H/K_2CO_3/xylene/ 120 °C/30 h	trace
25	$Cu(OTf)_2/Ag_2O$/dioxane/100 °C/16 h	0
26	$Pd(OAc)_2/Cu(OTf)_2/Ag_2O$/dioxane/ 100 °C/12 h	12[b]
27	$Pd(OAc)_2/Cu(OTf)_2/Ag_2O$/TFA/70 °C/12 h	25[b], 1:3 C2:C3[c]
28	$Pd(TFA)_2/Cu(OTf)_2/Ag_2O$/dioxane/ 100 °C/12 h	9[b], 1:7.5 C2:C3[c]
29	$Pd(TFA)_2/Cu(OTf)_2/Ag_2O$/TFA/70 °C/12 h	25[b]
30	$Pd(OPiv)_2/Cu(OTf)_2/Ag_2O$/dioxane/ 100 °C/12 h	5[b]
31	$[RuCl_2(p\text{-cym})]_2/Cu(OTf)_2$ (30 mol %), Ag_2O (2 equiv)/dioxane/O_2 balloon/100 °C/12 h	25[a]
32	$Pd(OAc)_2$, PPh_3, $Na_2S_2O_8$, AcOH, rt, 5 h	NR

[a]Isolated yields. [b]GC yields. [c]Determined by NMR; NR = no reaction.

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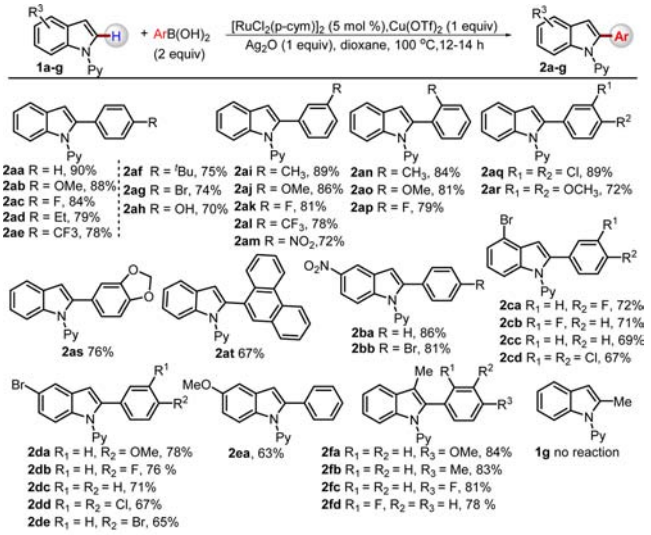
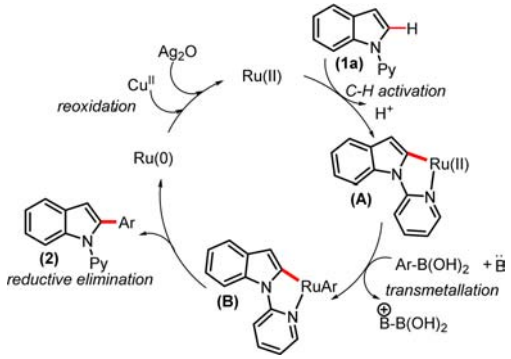
Scheme 1. Substrate Scope[a]



X-ray structure of **2aq**[12] X-ray structure of **2am**[12]

[a]All yields are isolated yields

Scheme 2. Plausible Mechanism for the Direct Arylation

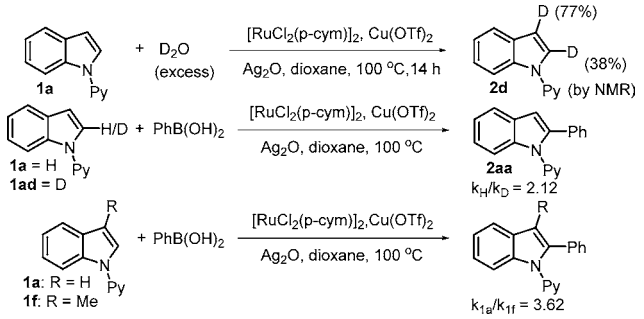


attempt to study deuteration with this system expectedly resulted in a mixture of C3 and C2 deuterated products (77:38, C3:C2). It is, however, difficult to draw conclusions with this observation. A study of the kinetic isotope effect at C2 gave a value of 2.12 for initial rates (Scheme 3). This moderate value probably indicated that the C−H activation via a concerted metalation deprotonation[13] may not be the rate-limiting step or may be a reversible process.[14]

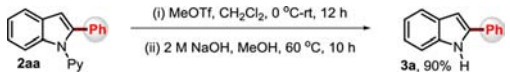
An attempt to compare rates of reaction for *N*-pyridylindole with 3-methyl-*N*-pyridylindole resulted in a value of 3.62 for relative rates. This probably could be attributed to steric reasons arising out of the C3 substituent.

Finally, we successfully removed the directing group from the arylated product in very high yields by simply treating it with MeOTf and subsequent base treatment to result in the free NH-indole (Scheme 4).[15] The use of MeI, unfortunately, did not provide the desired product.

Scheme 3. Kinetic Isotope Effect and Relative Rate Studies



Scheme 4. Removal of the Directing Group



In summary, we have developed a new ruthenium(II)-catalyzed method for the regioselective C−H arylation of indoles incorporating a removable directing group. The method provides access to 2-arylindoles bearing halogen substituents with scope for further functionalization, thereby opening new avenues for natural product synthesis. The method is simple, high yielding, and very selective with very good substrate scope and is expected to have good synthetic utility.

■ ASSOCIATED CONTENT

Supporting Information

Experimental procedures and full spectroscopic data for all new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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■ REFERENCES

(1) For some selected reviews, see: (a) Shilov, A. E.; Shul'pin, G. B. *Chem. Rev.* **1997**, *97*, 2879−2932. (b) Stahl, S. S.; Labinger, J. A.; Bercaw, J. E. *Angew. Chem., Int. Ed.* **1998**, *37*, 2180−2192. (c) Labinger, J. A.; Bercaw, J. E. *Nature* **2002**, *417*, 507−514. (d) Ritleng, V.; Sirlin, C.; Pfeffer, M. *Chem. Rev.* **2002**, *102*, 1731−1769. (e) Bergman, R. G. *Nature* **2007**, *446*, 391−393. (f) Kakiuchi, F.; Kochi, T. *Synthesis* **2008**, 3013−3039. (g) Chen, X.; Engle, K. M.; Wang, D.-H.; Yu, J.-Q. *Angew. Chem., Int. Ed.* **2009**, *48*, 5094−5115. (h) Wencel-Delord, J.; Dröge, T.; Liu, F.; Glorius, F. *Chem. Soc. Rev.* **2011**, *40*, 4740−4761. (i) Wencel-Delord, J.; Glorius, F. *Nat. Chem.* **2013**, *5*, 369−375.

(2) (a) Godula, K.; Sames, D. *Science* **2006**, *312*, 67−72. (b) McMurray, L.; O'Hara, F.; Gaunt, M. J. *Chem. Soc. Rev.* **2011**, *40*, 1885−1898. (c) Gutekunst, W. R.; Baran, P. S. *Chem. Soc. Rev.* **2011**, *40*, 1976−1991. (d) Yamaguchi, J.; Yamaguchi, A. D.; Itami, K. *Angew. Chem., Int. Ed.*

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Org. Lett. 2015, 17, 1766−1769

2012, *51*, 8960−9009. (e) Chen, D. Y.-K.; Youn, S. W. *Chem. −Eur. J.* **2012**, *18*, 9452−9474.
(3) (a) Colby, D. A.; Bergman, R. G.; Ellman, J. A. *Chem. Rev.* **2010**, *110*, 624−655. (b) Lyons, T. W.; Sanford, M. S. *Chem. Rev.* **2010**, *110*, 1147−1169. (c) Engle, K. M.; Mei, T.-S.; Wasa, M.; Yu, J.-Q. *Acc. Chem. Res.* **2012**, *45*, 788−802.
(4) (a) Alberico, D.; Scott, M. E.; Lautens, M. *Chem. Rev.* **2007**, *107*, 174−238. (b) Ackermann, L.; Vicente, R.; Kapdi, A. R. *Angew. Chem., Int. Ed.* **2009**, *48*, 9792−9826.
(5) For a review on cyclometallation using *d*-block transition metals, see: Albrecht, M. *Chem. Rev.* **2010**, *110*, 576−623.
(6) For some reviews on indoles and their syntheses, see: (a) Gribble, G. W. *J. Chem. Soc., Perkin Trans. 1* **2000**, 1045−1075. (b) Humphrey, G. R.; Kuethe, J. T. *Chem. Rev.* **2006**, *106*, 2875−2911. (c) Cacchi, S.; Fabrizi, G. *Chem. Rev.* **2011**, *111*, PR215−PR283. (d) Taber, D. F.; Tirunahari, P. K. *Tetrahedron* **2011**, *67*, 7195−7210. (e) Platon, M.; Amardeil, R.; Djakovitch, L.; Hierso, J.-C. *Chem. Soc. Rev.* **2012**, *41*, 3929−3968. (f) Inman, M.; Moody, C. J. *Chem. Sci.* **2013**, *4*, 29−41.
(7) (a) Murase, M.; Watanabe, K.; Kurihara, T.; Tobinaga, S. *Chem. Pharm. Bull.* **1998**, *46*, 889−892. (b) Kaushik, N. K.; Kaushik, N.; Attri, P.; Kumar, N.; Kim, C. H.; Verma, A. K.; Choi, E. H. *Molecules* **2013**, *18*, 6620−6662. (c) Daly, S.; Hayden, K.; Malik, I.; Porch, N.; Tang, H.; Rogelj, S.; Frolova, L. V.; Lepthien, K.; Kornienko, A.; Magedov, I. V. *Bioorg. Med. Chem. Lett.* **2011**, *21*, 4720−4723. (d) Ambrus, J. I.; Kelso, M. J.; Bremner, J. B.; Ball, A. R.; Casadei, G.; Lewis, K. *Bioorg. Med. Chem. Lett.* **2008**, *18*, 4294−4297. (e) Potavathri, S.; Kantak, A.; DeBoef, B. *Chem. Commun.* **2011**, *47*, 4679−4681.
(8) (a) Lane, B. S.; Sames, D. *Org. Lett.* **2004**, *6*, 2897−2900. (b) Lane, B. S.; Brown, M. A.; Sames, D. *J. Am. Chem. Soc.* **2005**, *127*, 8050−8057. (c) Yanagisawa, S.; Sudo, T.; Noyori, R.; Itami, K. *J. Am. Chem. Soc.* **2006**, *128*, 11748−11749. (d) Deprez, N. R.; Kalyani, D.; Krause, A.; Sanford, M. S. *J. Am. Chem. Soc.* **2006**, *128*, 4972−4973. (e) Touré, B. B.; Lane, B. S.; Sames, D. *Org. Lett.* **2006**, *8*, 1979−1982. (f) Nandurkar, N. S.; Bhanushali, M. J.; Bhor, M. D.; Bhanage, B. M. *Tetrahedron Lett.* **2008**, *49*, 1045−1048. (g) Lebrasseur, N.; Larrosa, I. *J. Am. Chem. Soc.* **2008**, *130*, 2926−2927. (h) Ban, I.; Sudo, T.; Taniguchi, T.; Itami, K. *Org. Lett.* **2008**, *10*, 3607−3609. (i) Roger, J.; Doucet, H. *Adv. Synth. Catal.* **2009**, *351*, 1977−1990. (j) Kirchberg, S.; Fröhlich, R.; Studer, A. *Angew. Chem., Int. Ed.* **2009**, *48*, 4235−4238. (k) Jafarpour, F.; Hazrati, H. *Adv. Synth. Catal.* **2010**, *352*, 363−367. (l) Shibahara, F.; Yamaguchi, E.; Murai, T. *Chem. Commun.* **2010**, *46*, 2471−2473. (m) For an indication that the metalation at C2 may be via a CMD process, see: Potavathri, S.; Pereira, K. C.; Gorelsky, S. I.; Pike, A.; LeBris, A. P.; DeBoef, B. *J. Am. Chem. Soc.* **2010**, *132*, 14676−14681. (n) Liégault, B.; Petrov, I.; Gorelsky, S. I.; Fagnou, K. *J. Org. Chem.* **2010**, *75*, 1047−1060. (o) Liang, Z.; Yao, B.; Zhang, Y. *Org. Lett.* **2010**, *12*, 3185−3187. (p) For a transition-metal-free example, see: Vakuliuk, O.; Koszarna, B.; Gryko, D. T. *Adv. Synth. Catal.* **2011**, *353*, 925−930. (q) Wang, L.; Yi, W.-b.; Cai, C. *Chem. Commun.* **2011**, *47*, 806−808. (r) Huang, Y.; Lin, Z.; Cao, R. *Chem.—Eur. J.* **2011**, *17*, 12706−12712. (s) Lapointe, D.; Markiewicz, T.; Whipp, C. J.; Toderian, A.; Fagnou, K. *J. Org. Chem.* **2011**, *76*, 749−759. (t) Nadres, E. T.; Lazareva, A.; Daugulis, O. *J. Org. Chem.* **2011**, *76*, 471−483. (u) Wu, M.; Luo, J.; Xiao, F.; Zhang, S.; Deng, G.-J.; Luo, H.-A. *Adv. Synth. Catal.* **2012**, *354*, 335−340. (v) Nimje, R. Y.; Leskinen, M. V.; Pihko, P. M. *Angew. Chem., Int. Ed.* **2013**, *52*, 4818−4822. (w) Feng, J.; Lu, G.; Lv, M.; Cai, C. *J. Organomet. Chem.* **2014**, *761*, 28−31.
(9) (a) Itahara, T. *J. Chem. Soc., Chem. Commun.* **1981**, 254−255. (b) For a use of Catellani reaction to direct the arylation at C2, see: Bressy, C.; Alberico, D.; Lautens, M. *J. Am. Chem. Soc.* **2005**, *127*, 13148−13149. (c) Stuart, D. R.; Fagnou, K. *Science* **2007**, *316*, 1172−1175. (d) Stuart, D. R.; Villemure, E.; Fagnou, K. *J. Am. Chem. Soc.* **2007**, *129*, 12072−12073. (e) Pena, M. A.; Sestelo, J. P.; Sarandeses, L. A. *J. Org. Chem.* **2007**, *72*, 1271−1275. (f) Dwight, T. A.; Rue, N. R.; Charyk, D.; Josselyn, R.; DeBoef, B. *Org. Lett.* **2007**, *9*, 3137−3139. (g) Phipps, R. J.; Grimster, N. P.; Gaunt, M. J. *J. Am. Chem. Soc.* **2008**, *130*, 8172−8174. (h) Sagnes, C.; Fournet, G.; Joseph, B. *Synlett* **2009**, *3*, 433−436. (i) Zhou, J.; Hu, P.; Zhang, M.; Huang, S.; Wang, M.; Su, W. *Chem.—Eur. J.* **2010**, *16*, 5876−5881. (j) Campbell, A. N.; Meyer, E. B.; Stahl, S. S. *Chem. Commun.* **2011**, *47*, 10257−10259. (k) Ackermann, L.; Lygin, A. V. *Org. Lett.* **2011**, *13*, 3332−3335. (l) Song, W.; Ackermann, L. *Angew. Chem., Int. Ed.* **2012**, *51*, 8251−8254. (m) Biajoli, A. F. P.; Penha, E. T.; da Correia, C. R. D. *RSC Adv.* **2012**, *2*, 11930−11935. (n) Huang, Y.; Ma, T.; Huang, P.; Wu, D.; Lin, Z.; Cao, R. *ChemCatChem* **2013**, *5*, 1877−1883. (o) Islam, S.; Larrosa, I. *Chem.—Eur. J.* **2013**, *19*, 15093−15096. (p) Zheng, J.; Zhang, Y.; Cui, S. *Org. Lett.* **2014**, *16*, 3560−3563. (q) Lu, M.-Z.; Lu, P.; Xu, Y.-H.; Loh, T.-P. *Org. Lett.* **2014**, *16*, 2614−2617.
(10) See ref 9d and: (a) Wang, X.; Lane, B. S.; Sames, D. *J. Am. Chem. Soc.* **2005**, *127*, 4996−4997. (b) Bellina, F.; Cauteruccio, S.; Rossi, R. *Eur. J. Org. Chem.* **2006**, 1379−1382. (c) Wang, X.; Gribkow, D. V.; Sames, D. *J. Org. Chem.* **2007**, *72*, 1476−1479. (d) Yang, S.-D.; Sun, C.-L.; Fang, Z.; Li, B.-J.; Li, Y.-Z.; Shi, Z.-J. *Angew. Chem., Int. Ed.* **2008**, *47*, 1473−1476. (e) Zhao, J.; Zhang, Y.; Cheng, K. *J. Org. Chem.* **2008**, *73*, 7428−7431. (f) Ruiz-Rodriguez, J.; Albericio, F.; Lavilla, R. *Chem.—Eur. J.* **2010**, *16*, 1124−1127. (g) Joucla, L.; Batail, N.; Djakovitch, L. *Adv. Synth. Catal.* **2010**, *352*, 2929−2936. (h) Yang, L.; Luo, L.; Zhang, S.; Su, X.; Lan, J.; Chen, C.-T.; You, J. *Chem. Commun.* **2010**, *46*, 3938−3940. (i) Takeda, D.; Yamashita, M.; Hirano, K.; Satoh, T.; Miura, M. *Chem. Lett.* **2011**, *40*, 1015−1017. (j) Jiao, L.; Bach, T. *J. Am. Chem. Soc.* **2011**, *133*, 12990−12993. (k) Lu, G.-P.; Cai, C. *Synlett* **2012**, *23*, 2992−2996. (l) Miao, T.; Li, P.; Wang, G.-W.; Wang, L. *Chem.—Asian J.* **2013**, *8*, 3185−3190. (m) Preciado, S.; Mendive-Tapia, L.; Albericio, F.; Lavilla, R. *J. Org. Chem.* **2013**, *78*, 8129−8135. (n) Zhang, L.; Li, P.; Liu, C.; Yang, J.; Wang, M.; Wang, L. *Catal. Sci. Technol.* **2014**, *4*, 1979−1988. (o) For a method related to *N*-methylazaindoles, see: Kannaboina, P.; Anilkumar, K.; Aravinda, S.; Vishwakarma, R. A.; Das, P. *Org. Lett.* **2013**, *15*, 5718−5721.
(11) (a) Pawar, G. G.; Singh, G.; Tiwari, V. K.; Kapur, M. *Adv. Synth. Catal.* **2013**, *355*, 2185−2190. (b) Tiwari, V. K.; Pawar, G. G.; Das, R.; Adhikary, A.; Kapur, M. *Org. Lett.* **2013**, *15*, 3310−3313. (c) Tiwari, V. K.; Pawar, G. G.; Jena, H. S.; Kapur, M. *Chem. Commun.* **2014**, *50*, 7322−7325.
(12) Crystal structures submitted to the Cambridge Cystallographic Data Centre, CCDC deposition nos. CCDC 1043459 (compound **2am**) and CCDC 1043486 (compound **2aq**), respectively.
(13) (a) Gorelsky, S. I.; Lapointe, D.; Fagnou, K. *J. Am. Chem. Soc.* **2008**, *130*, 10848−10849. (b) Lapointe, D.; Fagnou, K. *Chem. Lett.* **2010**, *39*, 1118−1126 and references cited therein.
(14) (a) Ackermann, L.; Vicente, R.; Potukuchi, H. K.; Pirovano, V. *Org. Lett.* **2010**, *12*, 5032−5035. (b) Ackermann, L. *Acc. Chem. Res.* **2014**, *47*, 281−295.
(15) Jana, C. K.; Grimme, S.; Studer, A. *Chem.—Eur. J.* **2009**, *15*, 9078−9084.

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