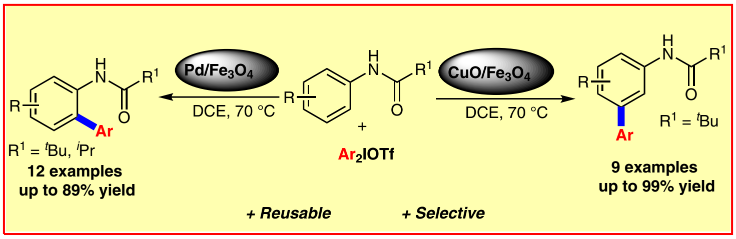
Reusable and Magnetic Palladium and Copper Oxide Catalysts in Direct *ortho* and *meta* Arylation of Anilide Derivatives

Suhelen Vásquez-Céspedes[a]
Michael Holtkamp[b]
Uwe Karst[b]
Frank Glorius*[a]

[a] Westfälische Wilhelms-Universität Münster, Organisch-Chemisches Institut, Corrensstrasse 40, 48149 Münster, Germany
glorius@uni-muenster.de
[b] Westfälische Wilhelms-Universität Münster, Instituts für Anorganische und Analytische Chemie, Corrensstraße 30, 48149 Münster, Germany

Dedicated to Prof. Victor Snieckus on the occasion of his 80th birthday



Received: 27.02.2017
Accepted after revision: 27.03.2017

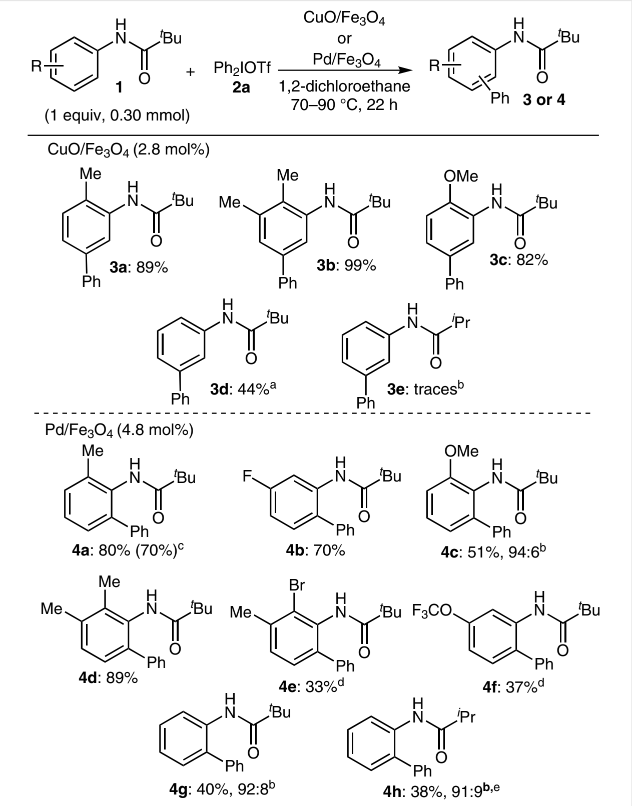
DOI: 10.1055/s-0036-1589007; Art ID: st-2017-r0147-l

Abstract We report a general, direct C–H arylation of anilide derivatives using reusable palladium or copper oxide on magnetite as heterogeneous precatalysts. Highly selective *ortho* and *meta* arylations are achieved using electronically and sterically diverse diaryliodonium salts. Catalytically active soluble species from the heterogeneous precursors were detected by experimental techniques. Preliminary mechanistic investigation suggests different reaction pathways for each of the catalysts.

Key words regioselective direct C–H arylation, reusable palladium catalyst, reusable copper oxide catalyst, leaching–redeposition, anilide derivatives

Transition-metal-catalyzed C–H functionalization has greatly contributed to a plethora of new methods for the selective modification of hetero(arene) moieties.[1] Among them, the regioselective direct arylation (DA) of arenes has become a useful and commonly employed tool for the construction of aryl–aryl bonds.[2] In contrast to well-established cross-coupling methods, such as Stille,[3] Suzuki,[4] Kumada–Tamao–Corriu,[5] and Ullmann,[6] direct arylation has the advantage of avoiding the need to use prefunctionalized starting materials.[7] Most of the work on DA has been realized employing homogeneous catalyst precursors of rhodium, ruthenium, iridium, palladium, and copper.[2,8] These catalyst precursors, although easily tuneable with the help of ligands, are commonly used in high amounts and their recovery from the reaction medium becomes a very challenging task, preventing the reuse of the catalyst.[8]

Alternatively, heterogeneous catalysts have the potential advantage of easy separation of the metal from the reaction media, thus facilitating reuse.[9] Furthermore, supported catalysts are usually less sensitive to air and moisture. Recently, our group has contributed to the area of heterogeneous C–H functionalization employing simple and commercially available precatalysts. Using Pd/Al_2O_3 and Pd/C we have developed the direct C–H thiolation and arylation of electron-rich heteroarenes and polyaromatics.[10] However, we observed a series of differences in reaction yields depending on the commercial catalyst source and faced difficulties with recycling. Considering these limitations we recently explored the use of a magnetically recoverable and reusable heterogeneous copper catalyst. Prepared using a simple synthetic protocol, this CuO/Fe_3O_4 catalyst proved successful in the direct arylation of electron-rich heteroarenes with diaryliodonium salts. Furthermore, it could be reused five times with no decrease in reactivity.[11] These results prompted us to continue our investigation in this field and to further explore the reactivity and selectivity of CuO/Fe_3O_4 and of other magnetite-supported metals, such as palladium. Compared to its homogeneous counterparts, the use of heterogeneous copper and palladium catalysts, in direct arylation reactions of arenes, is considerably underdeveloped.[9] Limited research has presented insight into active catalyst species, reusability studies, and regioselectivity.[12] Supported and reusable catalysts for the DA of anilide derivatives, allowing for efficient and easy control of reaction regioselectivity, are still in high demand.[2,9] From the pioneering work of Gaunt[13] and Daugulis,[14a] the direct *meta* and *ortho* arylation of anilides was developed using homogeneous copper or palladium precursors.[14] However, studies regarding the comparable reactivity and regioselectivity of heterogeneous copper[15] and palladium precatalysts for the C–H functionalization of arenes are unprecedented to the best of our knowledge. Herein, we present the selective *ortho* and *meta* arylation of anilide derivatives with diaryliodonium salts employing easily recoverable and reusable Pd/Fe_3O_4 and CuO/Fe_3O_4 systems.



Scheme 1 Substrate scope of anilide derivatives. Isolated yields are given. General procedure unless specified otherwise: anilide (0.30 mmol, 1 equiv), diphenyliodonium triflate (2 equiv for CuO/Fe_3O_4, 1.5 equiv for Pd/Fe_3O_4), catalyst, in DCE (3 mL) at 70 °C, 22 h. [a] 2 equiv of **1** and 1 equiv of **2a** were employed. [b] Ratio *o*/*m* determined by GC–MS. [c] 5.0 mmol scale (4.2 mol% of catalyst used). [d] 90 °C. [e] Isolated as a mixture of regioisomers (*o*/*m*).

Following our previous results on the direct arylation of heteroarenes,[11] we explored the reaction of different anilide derivatives, such as **1**, with diaryliodonium salts **2** in the presence of CuO/Fe_3O_4 (Scheme 1). Inspired by the work from Gaunt and coworkers,[13] we used *N*-(*o*-tolyl)pivalamide (**1a**) as the standard reagent. Pleasingly, after optimization (Table S1, Supporting Information) the *meta*-arylated product **3a** was isolated in 89% yield (Scheme 1).

We considered whether a magnetic palladium precatalyst, such as Pd/Fe_3O_4,[16] could also promote this arylation. Using **1a** with diphenyliodonium triflate (**2a**), we were pleased to observe a change in regioselectivity to obtain the *ortho*-arylated product **4a** in 80% isolated yield (Scheme 1).

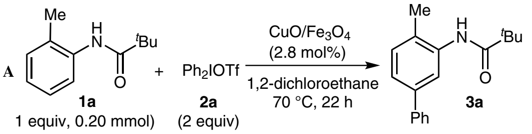
The scope of the transformations was explored. In the case of the CuO-catalyzed reaction, a perfect *meta* selectivity was observed (**3a**–**e**). However, functional-group tolerance was restricted to alkyl (**3a**, **b**) and methoxy groups (**3c**; see Supporting Information, Figure S6). A variation in the reaction stoichiometry allowed us to isolate the monoarylated product **3d** in acceptable yield. The transformation was restricted to the use of pivaloyl as amine protecting group, and a change to isobutyryl gave only traces of expected arylated product **3e**. The palladium-catalyzed transformation exhibited greater functional-group tolerance. Alkyl (**4a**, **d**), halide (**4b**, **e**), methoxy (**4c**), and trifluoromethoxy (**4f**) derivatives provided the corresponding *ortho*-arylated products with very high regioselectivity in moderate to good yields. The monoarylated product **4g** was obtained preferentially, although some bisarylation was also observed. Moreover, a small modification in the directing group could be realized to give the expected *ortho*-arylated product (**4h**), albeit in lower yield.

Next, we explored the scope of the diaryliodonium salt (Scheme 2). Electronically diverse iodonium salts were efficient coupling partners for the transformation, however, a preference for *para*-substituted diaryl reagents was observed in both catalytic systems. Diaryliodonium salts containing groups such as Br, F, Cl, and CO_2Me (**5a**–**e**, **6a**–**c**) were well tolerated and should allow for further functionalization of the products. The reaction also tolerated an electron-donating alkyl group (**6d**). Notably, the CuO-catalyzed reaction gave exclusively the *meta*-arylated products, while very high *ortho* selectivity was achieved in the palladium-catalyzed transformation, in preference to a mixture of *ortho*/*para* isomers that would be expected for an electrophilic aromatic substitution. Moreover, unsymmetrical iodonium salts containing a commonly nontransferable arene (mesitylene, Mes) were also employed. We also tested the developed reaction conditions with a series of different substrates and observed lack of reactivity or poor conversions (see Supporting Information, p. S25). The results indicated a restriction to aromatic pivalamides for both catalytic systems.

We were pleased to find that both catalysts could be easily recovered using a magnet and reused. In the case of CuO/Fe_3O_4, the *meta* arylation of **1a** proceeded successfully without loss of reactivity in five consecutive cycles (Table 1 A). However, Pd/Fe_3O_4 could be reused for only two cycles without loss of reactivity, with a marked decrease in product yield observed in the third and fourth cycles (Table 1 B).

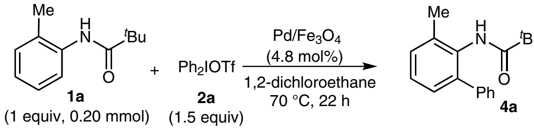
Table 1 Reusability Study of the Magnetic Catalysts[a,b]

A



Cycle	1	2	3	4	5
Yield (%)	89	88	89	87	90

B



Cycle	1	2	3	4[c]
Yield (%)	80	80	56	56

[a] Isolated yields are given.

[b] General procedure: See Scheme 1 and Supporting Information. The catalyst was washed with CH_2Cl_2 (3×) and dried at 75 °C for 45 min after every cycle.

[c] Reaction time: 48 h.

We became interested in understanding whether the catalysis was taking place on the surface of the catalysts or if the active species were in solution. To elucidate this, we initially analyzed the reaction kinetics (Figure 1) and observed an induction period of 15 minutes for both catalytic systems, possibly indicating in situ formation of a new catalytic species from the heterogeneous precursor.

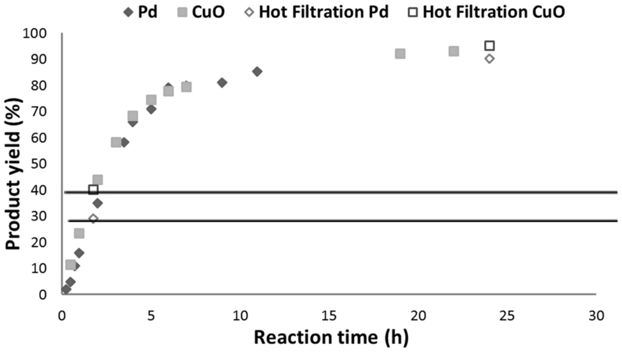
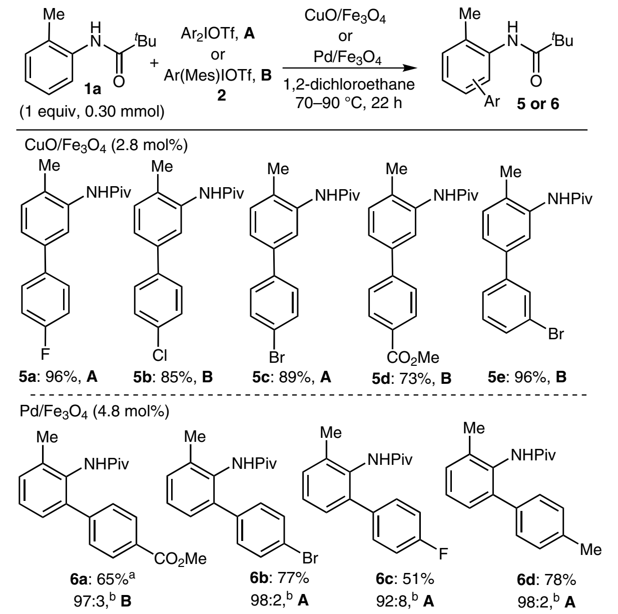


Figure 1 Kinetic profile for the reaction of *N*-(*o*-tolyl)pivalamide (**1a**) with diphenyliodonium triflate (**2a**) in the presence of the magnetic palladium and CuO catalysts. The lines represent the yield when the reactions were filtered.

Next, we applied a hot filtration test, one of the most indicative methods to differentiate between heterogeneous surface catalysis and solution-phase catalysis.[10,11] For the palladium system, filtration of the crude reaction through Celite at 29% conversion showed, after an additional 22 hours of reaction time, an increase to 90% yield. In the same fashion, filtration of the CuO system at 40% conversion showed an increase to 95% after additional 22 hours reaction time. These results clearly indicate the formation of soluble active species (Figure 1).



Scheme 2 Substrate scope of diaryliodonium salts. Isolated yields are given. General procedure unless specified otherwise: see Scheme 1.
[a] 90 °C. [b] Ratio *o*/*m* determined by GC–MS.

Intrigued by the results of reusability and hot filtration tests, a series of studies of metal content in solution were carried out using total X-ray fluorescence (TXRF; Table 2).[17] Results showed that after a conversion of more than 40% for both catalytic systems, the presence of copper and palladium metal is detected in solution. Arguably, this leached metal represents the active catalytic species. However, after 22 hours the metal content in solution showed a decrease to 6.6% in copper and 3.9% in palladium (Table 2). Surprisingly, the palladium abundance in solution after the reaction does not seem to correlate with the observed results of reusability. The diminished reactivity after two cycles is an indication of catalyst deactivation (Table 1 B). Apart from the small loss of metal, other factors including insufficient redeposition of the palladium on the support, the constant change in morphology due to aggregation of deposited metal particles and/or the coverage of the surface by byproducts from the reaction could lead to the pronounce decrease in reactivity of the palladium catalyst.[11,18] In the case of the CuO system, the abundance of metal in solution during the cycle and after catalysis possibly indicate that the amount of active catalytic species needed for the arylation is low and hence, the catalyst remained highly active (compare Tables 1 A and 2).

Table 2 Abundance of Metal in Solution According to TXRF Measurements

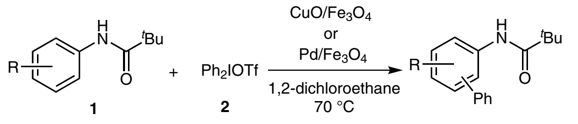
Conversion by GC-FID (%)	Cu (mg/L)	Cu in solution (%)[a]
40	46.0	26.3
96	11.6	6.6
Conversion by GC-FID (%)	Pd (mg/L)	Pd in solution (%)[b]
40	165.7	32.5
90	19.8	3.9

[a] With respect to the starting catalyst loading (2.8 mol%).
[b] With respect to the starting catalyst loading (4.8 mol%).

The variation of the metal content in solution hints at the probable formation of soluble active catalytic species which are redeposited on the magnetite. This result, along with the reusability and hot filtration test, seems to indicate the presence of a leaching–redeposition (boomerang) mechanism.[18] Although the exact nature of the active species is unknown, the formation of stabilized active nanoparticles by interaction with the diphenyliodonium salt is one plausible explanation.[10,11]

Similarities have been observed between the two magnetic catalysts. However, the difference in regioselectivity seems to suggest different mechanistic pathways. Therefore, we decided to get more insight into the reaction mechanism. No H/D scrambling was observed when a deuterated pivalamide was treated separately with both catalytic systems in the presence of an excess of MeOH, suggesting that a metal-catalyzed C–H activation is unlikely or irreversible (see Supporting Information, Scheme S1). Moreover, absence of KIE was found for the Pd/Fe_3O_4 catalytic system (k_H/k_D = 1.0) and the same result was observed for CuO/Fe_3O_4 (k_H/k_D = 1.0), thus suggesting that C–H bond cleavage is not involved in the rate-determining step of the reaction (Table 3).[19]

Table 3 Comparative Results of Both Catalytic Systems



Study	CuO/Fe_3O_4	Pd/Fe_3O_4
Selectivity	*meta* arylation	*ortho* arylation
H/D scrambling	not observed	not observed
KIE	1.0	1.0
Radical inhibitors	no effect	inhibited
Reusability	5 times	2 times

We also found that the palladium-catalyzed reaction was suppressed by radical scavengers (Table 3), whereas the copper oxide system was not inhibited (see Supporting Information, Tables S9 and S10). Single-electron transfer (SET) to diaryliodonium salts with concomitant formation of a phenyl radical is known in the literature and could account for this result.[20] On the other hand, a free-radical pathway initiated by an SET from the palladium to the diaryliodonium salt would generate an aryl radical.[21] Its addition to the anilide seems unlikely due to potential byproducts from 1,6-HAT transfer to the *t*-Bu group[22] and the observed high product regioselectivity. Radical additions to *para*-substituted anilines have been reported to selectively give the *ortho* product,[23] however, mixtures of *ortho* and *para* products are observed when unsubstituted aniline is used.[23] In our case, using unsubstituted anilide derivatives (**4g**, **h**) led to mixtures of *ortho* and *meta* isomers. Furthermore, reports from Gaunt,[13] Wu and Li,[24] and Park,[15c] have shown an uncatalyzed reaction of pivaloylanilides with diaryliodonium to furnish the *meta*-arylated isomer; in our hands the *meta* selectivity was also observed albeit in low yield even when the reaction was conducted at 110 °C (see Supporting Information, Table S1). These results suggest a change in selectivity promoted by the palladium catalyst, whereas an acceleration of the *meta* selectivity is observed in the CuO-catalyzed system (see Supporting Information, p. S26).

As we are aware of the complexities surrounding heterogeneous-based catalytic processes,[10,11,25] the acquired evidence does not allow us to give a complete mechanistic overview of the reported transformations. However, for the CuO system, it can be suggested that a redox-neutral process promoting counterion dissociation could be involved in the reaction pathway, in-line with our previous report.[11] For the case of the palladium catalyst, an electrophilic palladation could be part of the reaction mechanism.[10]

In summary, the direct *ortho* and *meta* arylation of anilide derivatives was accomplished with reusable, magnetic palladium and CuO as heterogeneous precatalysts. Under operationally simple reaction conditions,[26,27] high *ortho* and *meta* regioselectivities were obtained using diaryliodonium salts as arylating reagents. The formation of catalytically active soluble species from the heterogeneous precursors was detected by hot filtration tests and TXRF analysis.

Acknowledgment

Generous financial support by the Deutsche Forschungsgemeinschaft (Leibniz award, SFB 858) is gratefully acknowledged. We thank Dr. Lisa Candish, Tobias Gensch, and Santanu Singha for helpful discussions and Lukas Schifferer for experimental support (all WWU Münster).

Supporting Information

Supporting information for this article is available online at https://doi.org/10.1055/s-0036-1589007.

References and Notes

(1) (a) Gensch, T.; Hopkinson, M. N.; Glorius, F.; Wencel-Delord, J. *Chem. Soc. Rev.* **2016**, *45*, 2900. (b) Song, G.; Li, X. *Acc. Chem. Res.* **2015**, *48*, 1007. (c) Ye, B.; Cramer, N. *Acc. Chem. Res.* **2015**, *48*, 1308. (d) Ackermann, L. *Acc. Chem. Res.* **2014**, *47*, 281. (e) Kuhl, N.; Schroeder, N.; Glorius, F. *Adv. Synth. Catal.* **2014**, *356*, 1443. (f) Patureau, F. W.; Wencel-Delord, J.; Glorius, F. *Aldrichimica Acta* **2012**, *45*, 31. (g) Kuhl, N.; Hopkinson, M. N.; Wencel-Delord, J.; Glorius, F. *Angew. Chem. Int. Ed.* **2012**, *51*, 10236. (h) Arockiam, P. B.; Bruneau, C.; Dixneuf, P. H. *Chem. Rev.* **2012**, *112*, 5879. (i) Neufeldt, S. R.; Sanford, M. S. *Acc. Chem. Res.* **2012**, *45*, 936. (j) Yamaguchi, J.; Yamaguchi, A. D.; Itami, K. *Angew. Chem. Int. Ed.* **2012**, *51*, 8960. (k) Brückl, T.; Baxter, R. D.; Ishihara, Y.; Baran, P. S. *Acc. Chem. Res.* **2012**, *45*, 826. (l) Cho, S. H.; Kim, J. Y.; Kwak, J.; Chang, S. *Chem. Soc. Rev.* **2011**, *40*, 5068. (m) Engle, K. M.; Mei, T.-S.; Wasa, M.; Yu, J.-Q. *Acc. Chem. Res.* **2012**, *45*, 788.

(2) (a) Hassan, J.; Sévignon, M.; Gozzi, C.; Schulz, E.; Lemaire, M. *Chem. Rev.* **2002**, *102*, 1359. (b) Alberico, D.; Scott, M. E.; Lautens, M. *Chem. Rev.* **2007**, *107*, 174. (c) Ackermann, L.; Vicente, R.; Kapdi, A. R. *Angew. Chem. Int. Ed.* **2009**, *48*, 9792.

(3) Cordovilla, C.; Bartolomé, C.; Martínez-Ilarduya, J. M.; Espinet, P. *ACS Catal.* **2015**, *5*, 3040.

(4) Han, F.-S. *Chem. Soc. Rev.* **2013**, *42*, 5270.

(5) Li, W.-N.; Wang, Z.-L. *RSC Adv.* **2013**, *3*, 25565.

(6) Sambiagio, C.; Marsden, S. P.; Blacker, A. J.; McGowan, P. C. *Chem. Soc. Rev.* **2014**, *43*, 3525.

(7) Podgorsek, A.; Zupan, M.; Iskra, J. *Angew. Chem. Int. Ed.* **2009**, *48*, 8424.

(8) (a) Mousseau, J. J.; Charette, A. B. *Acc. Chem. Res.* **2013**, *46*, 412. (b) Daugulis, O.; Do, H.-Q.; Shabashov, D. *Acc. Chem. Res.* **2009**, *42*, 1074.

(9) (a) Vaccaro, L.; Santoro, S.; Ackermann, L.; Kozhushkov, S. *Green Chem.* **2016**, *18*, 3471. (b) Cano, R.; Schmidt, A. F.; McGlacken, G. P. *Chem. Sci.* **2015**, *6*, 5338. (c) Reay, A. J.; Fairlamb, I. J. S. *Chem. Commun.* **2015**, *51*, 16289. (d) Djakovitch, L.; Felpin, F.-X. *ChemCatChem* **2014**, *6*, 2175.

(10) (a) Vásquez-Céspedes, S.; Ferry, A.; Candish, L.; Glorius, F. *Angew. Chem. Int. Ed.* **2015**, *54*, 5772. (b) Collins, K. D.; Honeker, R.; Vásquez-Céspedes, S.; Tang, D.-T. D.; Glorius, F. *Chem. Sci.* **2015**, *6*, 1816. (c) Tang, D.-T. D.; Collins, K. D.; Ernst, J. B.; Glorius, F. *Angew. Chem. Int. Ed.* **2014**, *53*, 1809. (d) Tang, D.-T. D.; Collins, K. D.; Glorius, F. *J. Am. Chem. Soc.* **2013**, *135*, 7450.

(11) Vásquez-Céspedes, S.; Chepiga, K. M.; Möller, N.; Schäfer, A. H.; Glorius, F. *ACS Catal.* **2016**, *6*, 5954.

(12) (a) Perumgani, P. C.; Parvathaneni, S. P.; Keesara, S.; Mandapati, M. R. *J. Organomet. Chem.* **2016**, *822*, 189. (b) Monguchi, Y.; Okami, H.; Ichikawa, T.; Nozaki, K.; Maejima, T.; Oumi, Y.; Sawama, Y.; Sajiki, H. *Adv. Synth. Catal.* **2016**, *358*, 3145.

(13) (a) Ciana, C.-L.; Phipps, R. J.; Brandt, J. R.; Meyer, F.-M.; Gaunt, M. J. *Angew. Chem. Int. Ed.* **2011**, *50*, 458. (b) Duong, H. A.; Gilligan, R. E.; Cooke, M. L.; Phipps, R. J.; Gaunt, M. J. *Angew. Chem. Int. Ed.* **2011**, *50*, 463. (c) Phipps, R. J.; Gaunt, M. J. *Science* **2009**, *323*, 1593.

(14) (a) Daugulis, O.; Zaitsev, V. G. *Angew. Chem. Int. Ed.* **2005**, *44*, 4046. For related palladium-based *ortho* arylation of anilides, see: (b) Bjorsvik, H.-R.; Elumalai, V. *Eur. J. Org. Chem.* **2016**, 5474. (c) Li, D.; Xu, N.; Zhang, Y.; Wang, L. *Chem. Commun.* **2014**, *50*, 14862. (d) Mousseau, J. J.; Vallee, F.; Lorion, M. M.; Charette, A. B. *J. Am. Chem. Soc.* **2010**, *132*, 14412. (e) Brasche, G.; García-Fortanet, J.; Buchwald, S. L. *Org. Lett.* **2008**, *10*, 2207. For examples of palladium-based heterogeneous precatalysts on direct arylation reactions, see: (f) Reay, A.; Neumann, L.; Fairlamb, I. J. S. *Synlett* **2016**, *27*, 1211. (g) Williams, T. J.; Reay, A. J.; Whitwood, A. C.; Fairlamb, I. J. S. *Chem. Commun.* **2014**, *50*, 3052. (h) Williams, T. J.; Fairlamb, I. J. S. *Tetrahedron Lett.* **2013**, *54*, 2906.

(15) For examples of copper-based heterogeneous precatalysts on direct arylation reactions, see: (a) Mathew, B. P.; Yang, H. J.; Jeon, H.; Lee, J. H.; Kim, J. C.; Shin, T. J.; Myung, K.; Kwak, S. K.; Kwak, J. H.; Hong, S. Y. *J. Mol. Catal. A: Chem.* **2016**, *417*, 64. (b) Székely, A.; Sinai, Á.; Tóth, E.; Novák, Z. *Synthesis* **2014**, *46*, 1871. (c) Lee, E.-Y.; Park, J.-W. *ChemCatChem* **2011**, *3*, 1127.

(16) Ranganath, K. V. S.; Kloesges, J.; Schäfer, A. H.; Glorius, F. *Angew. Chem. Int. Ed.* **2010**, *49*, 7786.

(17) Holtkamp, M.; Wehe, C. A.; Blaske, F.; Holtschulte, C.; Sperling, M.; Karst, U. *J. Anal. At. Spectrom.* **2012**, *27*, 1799.

(18) (a) Eremin, D. B.; Ananikov, V. P. *Coord. Chem. Rev.* **2017**, in press; DOI 10.1016/j.ccr.2016.12.021. (b) Genelot, M.; Dufaud, V.; Djakovitch, L. *Adv. Synth. Catal.* **2013**, *355*, 2604. (c) Gruttadauria, M.; Giacolone, F.; Noto, R. *Green Chem.* **2013**, *15*, 2608. (d) Zhao, F.; Shirai, M.; Ikushima, Y.; Arai, M. *J. Mol. Catal. A: Chem.* **2002**, *180*, 211.

(19) Simmons, E. M.; Hartwig, J. F. *Angew. Chem. Int. Ed.* **2012**, *51*, 3066.

(20) (a) Yoshimura, A.; Zhdankin, V. V. *Chem. Rev.* **2016**, *116*, 3328. (b) Zhdankin, V. V.; Stang, P. J. *Chem. Rev.* **2008**, *108*, 5299.

(21) (a) Gu, J.-W.; Guo, W.-H.; Zhang, X. *Org. Chem. Front.* **2015**, *2*, 38. (b) Powers, D. C.; Ritter, T. *Top. Organomet. Chem.* **2011**, *503*, 129.

(22) Rey, V.; Pierini, A. B.; Peñéñory, A. B. *J. Org. Chem.* **2009**, *74*, 1223.

(23) (a) Hofmann, J.; Jasch, H.; Heinrich, M. R. *J. Org. Chem.* **2014**, *79*, 2314. (b) Hofmann, J.; Clark, T.; Heinrich, M. R. *J. Org. Chem.* **2016**, *81*, 9785. (c) Hofmann, J.; Heinrich, M. R. *Tetrahedron Lett.* **2016**, *57*, 4334.

(24) Chen, B.; Hou, X.-L.; Li, Y.-X.; Wu, Y.-D. *J. Am. Chem. Soc.* **2011**, *133*, 7668.

(25) Baumann, C. G.; De Ornellas, S.; Reeds, J. P.; Storr, T. E.; Williams, T. J.; Fairlamb, I. J. S. *Tetrahedron* **2014**, *70*, 6174.

(26) **General Procedure for *meta* Arylation**

To a 10 mL Schlenk tube with a magnetic stirring bar was added *N*-(*o*-tolyl)pivalamide (57.3 mg, 0.30 mmol), diphenyliodonium triflate (258 mg, 0.60 mmol), and CuO/Fe$_3$O$_4$ (75 mg, 0.0083 mmol). Then, DCE (3.0 mL) was added under air and the reaction stirred at 70 °C for 22 h. The reaction mixture was allowed to cool to r.t., the catalyst was separated using a magnet, and the crude reaction was concentrated in vacuo and purified by flash column chromatography.

Analytical Data for 3a

^{1}H NMR (300 MHz, CDCl$_3$): δ = 8.21 (d, *J* = 1.8, 1 H), 7.65–7.57 (m, 2 H), 7.45–7.36 (m, 2 H), 7.35–7.21 (m, 4 H), 2.30 (s, 3 H), 1.37 (s, 9 H). ^{13}C NMR (75 MHz, CDCl$_3$): δ = 176.67, 140.79, 140.12, 136.36, 130.86, 128.77, 127.50, 127.31, 127.24, 123.49, 121.44, 39.98, 27.89, 17.47.

(27) **General Procedure for *ortho* Arylation**

To a 10 mL Schlenk tube with a magnetic stirring bar was added *N*-(*o*-tolyl)pivalamide (57.3 mg, 0.30 mmol), diphenyliodonium triflate (193.5 mg, 0.45 mmol), and Pd/Fe$_3$O$_4$ (90 mg, 0.014 mmol). Then, DCE (3.0 mL) was added under air and the reaction stirred at 70 °C for 22 h. The reaction mixture was allowed to cool to r.t., the catalyst separated using a magnet, and the crude reaction was concentrated in vacuo and purified by flash column chromatography.

Analytical Data for 4a

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.46–7.36 (m, 3 H), 7.35–7.31 (m, 2 H), 7.31–7.27 (m, 2 H), 7.23–7.17 (m, 1 H), 6.84 (s, 1 H), 2.31 (s, 3 H), 1.15 (s, 9 H). ^{13}C NMR (101 MHz, $CDCl_3$): δ = 176.82, 139.73, 139.65, 136.72, 132.94, 130.20, 129.11, 128.37, 127.74, 127.49, 127.12, 39.22, 27.63, 18.64.