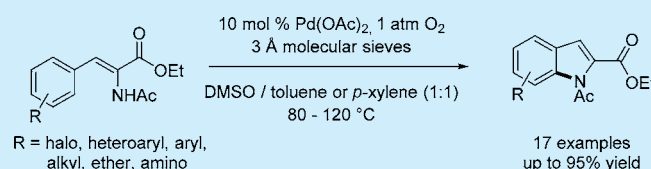


Synthesis of Indole-2-carboxylate Derivatives via Palladium-Catalyzed Aerobic Amination of Aryl C–H Bonds

Kyle Clagg,[†] Haiyun Hou,[†] Adam B. Weinstein,^{‡,||} David Russell,[§] Shannon S. Stahl,^{*,‡} and Stefan G. Koenig^{*,†}[†]Small Molecule Process Chemistry, Genentech, Inc., 1 DNA Way, South San Francisco, California 94080, United States[‡]Department of Chemistry, University of Wisconsin—Madison, 1101 University Avenue, Madison, Wisconsin 53706, United States[§]Small Molecule Analytical Chemistry and Quality Control, Genentech, Inc., 1 DNA Way, South San Francisco, California 94080, United States

S Supporting Information

ABSTRACT: A direct oxidative C–H amination affording 1-acetyl indolecarboxylates starting from 2-acetamido-3-arylacrylates has been achieved. Indole-2-carboxylates can be targeted with a straightforward deacetylation of the initial reaction products. The C–H amination reaction is carried out using a catalytic Pd(II) source with oxygen as the terminal oxidant. The scope and application of this chemistry is demonstrated with good to high yields for numerous electron-rich and electron-poor substrates. Further reaction of selected products via Suzuki arylation and deacetylation provides access to highly functionalized indole structures.

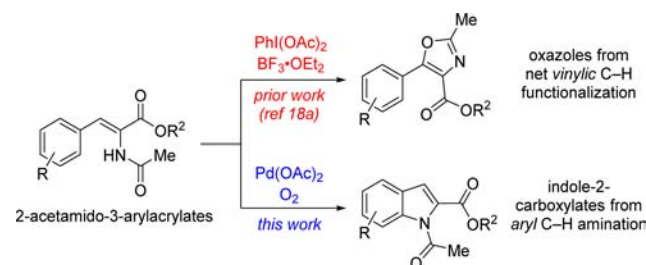


The construction of C–N bonds is of fundamental importance in the synthesis of biologically active organic molecules. Cross-coupling reactions between aryl halides and nitrogen nucleophiles in the presence of palladium catalysts (Buchwald–Hartwig coupling) provide an effective means of generating aryl C–N bonds.^{1,2} In the interest of streamlining the synthesis of complex molecules, significant effort has been devoted to the development of palladium-catalyzed methods for the generation of aryl C–N bonds by direct oxidative functionalization of aryl C–H bonds.^{3,4} A challenge with these reactions is the ability to couple the palladium-mediated oxidative transformation of the substrate with atom-economically attractive molecular oxygen (O₂) as the terminal oxidant.

Prior studies in the development of palladium-catalyzed intramolecular aryl C–H aminations⁵ have uncovered methods for the synthesis of indazoles from arylhydrazones,⁶ lactams from α -aryl-*N*-methoxyamides,⁷ benzimidazoles from *N*-arylbenzamides,⁸ indolines from β -arylethylamines,^{9,10} indoles from α -aryl oxime acetates,¹¹ carbazoles from 2-aminobiphenyls,^{12,13} and, most recently, indoles from (*Z*)-NTs-dehydroamino acid esters using Oxone as the oxidant.¹⁴ Notably, the only example in which O₂ was used as the terminal oxidant was the carbazole synthesis, and a limited substrate scope was demonstrated under the reported conditions.^{12,13d}

Here we report the discovery of a palladium-catalyzed aerobic amination of aryl C–H bonds for the synthesis of indole-2-carboxylate derivatives (Scheme 1). We envisioned that indole-2-carboxylates, which are useful building blocks in the synthesis of indole-containing bioactive molecules,¹⁵ could be derived from the intramolecular aryl C–H amination of 2-acetamido-3-arylacrylates. These substrates are particularly attractive because they are readily accessible from benzaldehyde derivatives and *N*-

Scheme 1. Selective Oxidative Intramolecular C–H Functionalization Reactions with 2-Acetamido-3-arylacrylates

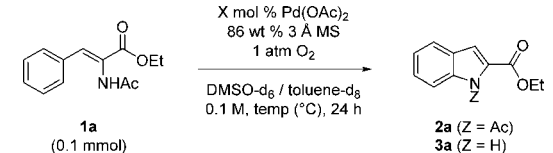


acetyl glycine via Erlenmeyer–Plöchl chemistry.¹⁶ This methodology has been used extensively in the synthesis of unnatural amino acids and is amenable to large-scale processes.¹⁷ Previous reports employing 2-acetamido-3-arylacrylate substrates under oxidative conditions have yielded oxazoles from alkene functionalization (Scheme 1, upper reaction pathway).^{18,19} In contrast, while 2-toluenesulfonamido-3-arylacrylates were shown to form indoles via palladium(II) catalysis with Oxone, the equivalent 2-acetamido substrates failed to do so.¹⁴ Here we show that aryl C–H amination with the latter substrates proceeds with Pd(II) catalysis and that these are capable of using O₂ as the stoichiometric oxidant.

We initiated our study by testing ethyl 2-acetamido-3-phenylacrylate (**1a**) under the aerobic oxidation conditions reported by Buchwald for carbazole synthesis (Table 1, entry

Received: June 1, 2016

Published: July 12, 2016

Table 1. Initial Investigation of Intramolecular Aerobic C–H Amination of Ethyl 2-Acetamido-3-phenylacrylate


entry	mol % Pd(OAc) ₂	DMSO: Tol	T (°C)	¹ H NMR yields (%) ^a		
				1a	2a	3a
1	10	1:0	120	45	23	22
2	10	1:0	80	16	61	23
3	10	3:1	80	10	69	21
4	10	1:1	80	2	77	15
5	10	1:3	80	2	80	12
6	10	1:9	80	31	50	13
7	10	0:1	80	80	1	0
8	7	1:1	80	5	85	10
9	5	1:1	80	35	60	5
10 ^b	7	1:1	80	49	36	12
11 ^c	7	1:1	80	0	0	0

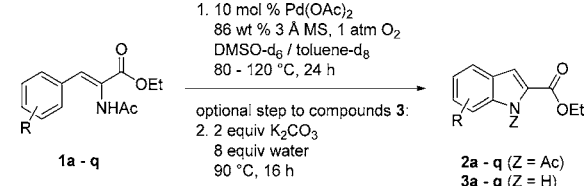
^a¹H NMR yields relative to PhTMS added at the end of the reaction.^bWithout 3 Å MS. ^cWith 2 equiv of PhI(OAc)₂.

1).¹² This catalyst system employed dimethyl sulfoxide as the solvent, allowing carbazole synthesis at high temperatures (120 °C) in reasonable yields for most substrates. Under these conditions, substrate **1a** reacted to give a mixture of acetylated indole product **2a** and indole product **3a** in 45% total yield. In contrast to Buchwald's findings, lowering the temperature facilitated the C–H amination but not the deacetylation (entry 2). Introduction of toluene as a cosolvent improved the yield of indole product **2a** to an extent (entries 3–6). Lowering the loading of the palladium catalyst from 10 to 7 mol % was tolerated, but the yield of indole began to drop at 5 mol % (entries 8 and 9). Introduction of diacetoxyiodobenzene, a strong oxidant commonly employed to access Pd(IV) species,²⁰ resulted in complete decomposition of the substrate without formation of the desired indole product (entry 11).

In a screen of various palladium(II) sources, Pd(OAc)₂ was revealed to be superior (see the [Supporting Information](#)). In the absence of any palladium, no detectable product was observed in the reaction mixture. Ligand additives that have been employed previously for C–H activation²¹ inhibited the conversion, while protic additives (AcOH, PivOH, and water) had little impact. With the optimized conditions for the unsubstituted arene, we analyzed the reaction conversion over the course of 24 h and identified the minimum reaction time to be 20 h.

With robust conditions for the aerobic intramolecular aryl C–H amination of substrate **1a** in hand (10 mol % Pd(OAc)₂, 24 h reaction time), we explored the scope of the reaction. In the absence of a nitrogen protecting group, 2-amino-3-phenylacrylate failed to undergo the C–H amination.²² *N*-Benzoyl and *N*-tosyl blocking groups were also tested. The *N*-benzoyl-substituted system gave no desired product, whereas the *N*-tosyl substrate resulted in decent conversion to the indole.²³ As we believed the *N*-acetyl group to be superior to *N*-tosyl in terms of ease of substrate preparation, yield, and cleavability, we decided to proceed with the former and vary the substitution on the arene.

We applied the conditions to a range of substrates, as illustrated in [Table 2](#). Initially, we observed that only methyl- and

Table 2. Evaluation of the Substrate Scope of the Intramolecular C–H Amination of Ethyl 2-Acetamido-3-arylacrylates


entry	substrate (R)	T (°C)	¹ H NMR yields (%) ^d		isolated yield (%)
			1	2	
1	1a (H)	80	0	100	95
2	1b (<i>p</i> -Me)	80	0	94	67 ^b
3	1c (<i>m</i> -Me)	100	0	89	77
4	1d (<i>o</i> -Me)	80	0	92	85
5 ^c	1e (2-Naph)	100	25	77 (2:1)	62 (5:3)
6	1f (<i>p</i> -Ph)	80	11	83	86
7	1g (<i>m</i> -Ph)	80	0	88	80 ^b
8	1h (<i>o</i> -Ph)	80	0	90	87
9	1i (<i>p</i> -F)	80	31	65	56
10 ^{c,d}	1j (<i>m</i> -F)	120	7	80 (3:2)	83 (4:3) ^b
11	1k (<i>p</i> -CF ₃)	100	39	45	45 ^b
12	1l (<i>m</i> -CF ₃)	80	48	38	36 ^b
13	1m (<i>p</i> -NMe ₂)	80	29	57	50
14	1n (<i>p</i> -OMe)	80	14	72	59 ^b
15	1o (<i>m</i> -OMe)	100	0	89	66 ^b
16	1p (<i>p</i> -5-Pyr) ^e	100	29	69	59
17	1q (<i>p</i> -Cl)	80	30	69	63 ^b

^a¹H NMR yields relative to PhTMS added at the end of the reaction time. Unless otherwise indicated, only 5-substituted indole products were observed from meta-substituted substrates. ^bProducts isolated as *N*-H indoles following optional deacetylation as indicated in the graphic. ^cThe ratio refers to a regioisomeric mixture of products, with the least sterically demanding product predominating in each case. ^dThe reaction was run in 1:1 DMSO-*d*₆/*p*-xylene-*d*₁₀. ^e*p*-5-Pyr refers to 5-pyrimidyl-substituted at the para position of the substrate.

phenyl-substituted arenes gave reasonable conversions (entries 2–4 and 6–8), while both electron-withdrawing and -donating groups were poorly tolerated. Resubjecting the challenging substrates to higher temperatures, however, led to a marked increase in yield (entries 5, 10, 11, and 15). The reason for this improvement is not presently understood, though it may be attributed to a higher energy barrier for palladium-mediated C–H activation. Most meta-substituted substrates led to the corresponding 5-substituted indole products on the basis of steric control (entries 3, 7, 12, and 15), while 2-naphthyl- and *m*-fluoro-substituted substrates led to mixtures of isomers (entries 5 and 10).

We then tested the reaction tolerance further by exploring more complex substrates, including ones with a distal heterocycle and a halogen substituent. While the initial result for the 5-pyrimidyl substrate was low (18% NMR yield), running the reaction at higher temperature gave an improved yield ([Table 2](#), entry 16). This successful result indicated that certain heterocycles should be tolerated in the C–H amination to support convergent approaches to indoles via this methodology. With ethyl 2-acetamido-3-(4-chlorophenyl)acrylate, the original temperature (80 °C) balanced C–H amination with subsequent deacetylation (entry 17). Interestingly, no dechlorination was

observed in the reaction, enabling subsequent functionalization to access diverse indole structures from a common intermediate.

With the 1-acetyl-6-chloroindole-2-carboxylate **2q** in hand, we then tested the compatibility of the compound in various C–C cross-coupling reactions, as conditions that utilize indoles as the electrophilic coupling partner are uncommon.²⁴ The strongly basic conditions of Negishi and Kumada-type reactions cleaved the *N*-acetyl group and afforded none of the desired product above trace quantities (data not shown). In contrast, certain Suzuki cross-coupling conditions were effective and delivered the desired ethyl 6-phenyl-1*H*-indole-2-carboxylate (**3f**) from cross-coupling and deacetylation in a single pot (Table 3, entry 1).²⁵

Table 3. Evaluation of Suzuki Coupling with Ethyl 1-Acetyl-6-chloroindole-2-carboxylate

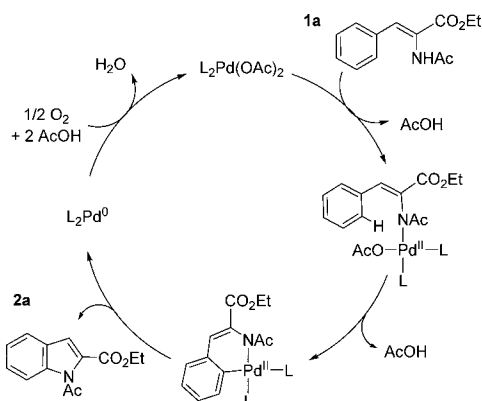
entry	boronic acid	solvent	HPLC area %			
			2q	3q	2X	3X
1	4f	5:1 dioxane/H ₂ O	2	0	0	76
2	4r	1:2 dioxane/H ₂ O	1	77	0	0
3	4s	1:2 dioxane/H ₂ O	0	73	3	17
4 ^a	4t	1:4 dioxane/H ₂ O	0	0	0	86 ^b

^aThe reaction was run with 4.2 equiv of K₃PO₄·H₂O. ^bThe isolated yield of **3t** was 80% following chromatography.

We tested three more boronic acid coupling partners (**4r–t**) to challenge what the acetyl protecting group could tolerate (entries 2–4). The phenolic partner **4r** was completely incompatible, and 5-aminopyrimidyl reagent **4s** gave a low yield of the desired product **3s**. On the other hand, fluoropyridylboronic acid **4t** was more effective in the one-pot Suzuki/deacetylation, giving access to important structures related to those under investigation for metabolic disorders.²⁶

Previous studies^{12,13} provide the basis for a plausible mechanism for the Pd-catalyzed oxidative cyclization reaction to afford indoles (Scheme 2). The substrate acetamide can undergo metathesis with an acetate ligand to afford a Pd(II)–

Scheme 2. Simplified Catalytic Mechanism for Pd-Catalyzed Oxidative Cyclization of 2-Acetamido-3-arylacrylates



amidate species that can metalate the arene to afford the chelated Pd(II)–(aryl)(amidate) species. Subsequent C–N reductive elimination can afford the indole product and a ligated Pd(0) species capable of undergoing oxidation by O₂ to regenerate catalytic Pd(OAc)₂. Previous studies of Pd-catalyzed aerobic oxidation reactions in DMSO provided evidence for the involvement of both molecular and nanoparticle catalysis.²⁷ Presently available data cannot distinguish between these two possibilities, but this issue warrants attention in future studies.

In summary, we have identified an aerobic palladium-catalyzed aryl C–H amination strategy for the synthesis of indole-2-carboxylates from 2-acetamido-3-arylacrylates with application to a diverse set of substrates. Notably, the mild and selective conditions tolerated electron-rich and electron-poor substrates, chlorinated arenes, and a heteroaromatic-substituted example. The chlorinated arenes also enable direct Suzuki cross-coupling following indole formation, allowing one to sidestep the N–H deprotection step prior to the coupling reaction. Moreover, the halogen substitution also holds promise as a handle for the introduction of boronic acid and boronate ester equivalents and rapid access to these types of indole building blocks. Our methodology complements existing approaches to indoles and should allow expedited installation of the heterocycle onto bioactive molecules.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.orglett.6b01592.

Full experimental details and characterization data for all isolated compounds (PDF)

■ AUTHOR INFORMATION

Corresponding Authors

*E-mail: stahl@chem.wisc.edu.

*E-mail: koenig.stefan@gene.com.

Present Address

^{||}A.B.W.: Department of Chemistry, Yale University, 225 Prospect Street, P.O. Box 208107, New Haven, CT 06520.

Author Contributions

All of the authors were employed at their respective institutions during completion of the work. K.C., H.H., and A.B.W. contributed equally to the experimental results.

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

The authors thank the NIH for financial support (R01 GM67173 for A.B.W. and S.S.S.) and the Genentech Summer Internship Program for supporting H.H. during the project. In addition, the authors thank Marie-France Morissette for analytical support and Francis Gosselin and Allen Hong (Genentech, Inc.) for helpful discussions on the manuscript.

■ REFERENCES

- (1) (a) Guram, A. S.; Buchwald, S. L. *J. Am. Chem. Soc.* **1994**, *116*, 7901–7902. (b) Paul, F.; Patt, J.; Hartwig, J. F. *J. Am. Chem. Soc.* **1994**, *116*, 5969–5970. (c) Hartwig, J. F. *Angew. Chem., Int. Ed.* **1998**, *37*, 2046–2067. (d) Hartwig, J. F. *Acc. Chem. Res.* **2008**, *41*, 1534–1544.

(e) Surry, D. S.; Buchwald, S. L. *Angew. Chem., Int. Ed.* **2008**, *47*, 6338–6361.

(2) Copper-catalyzed (Goldberg) cross-coupling reactions are also prominent. For reviews, see: (a) Kunz, K.; Scholz, U.; Ganzer, D. *Synlett* **2003**, 2428–2439. (b) Chemler, S. R.; Fuller, P. H. *Chem. Soc. Rev.* **2007**, *36*, 1153–1160. (c) Evano, G.; Blanchard, N.; Toumi, M. *Chem. Rev.* **2008**, *108*, 3054–3131. (d) Ma, D.; Cai, Q. *Acc. Chem. Res.* **2008**, *41*, 1450–1460.

(3) For examples of palladium-catalyzed intermolecular aryl C–H aminations, see: (a) Thu, H.-Y.; Yu, W.-Y.; Che, C.-M. *J. Am. Chem. Soc.* **2006**, *128*, 9048–9049. (b) Ng, K.-H.; Chan, A. S. C.; Yu, W.-Y. *J. Am. Chem. Soc.* **2010**, *132*, 12862–12864. (c) Sun, K.; Li, Y.; Xiong, T.; Zhang, J.; Zhang, Q. *J. Am. Chem. Soc.* **2011**, *133*, 1694–1697. (d) Xiao, B.; Gong, T.-J.; Xu, J.; Liu, Z.-J.; Liu, L. *J. Am. Chem. Soc.* **2011**, *133*, 1466–1474. (e) Yoo, E. J.; Ma, S.; Mei, T.-S.; Chan, K. S. L.; Yu, J.-Q. *J. Am. Chem. Soc.* **2011**, *133*, 7652–7655. (f) Shrestha, R.; Mukherjee, P.; Tan, Y.; Litman, Z. C.; Hartwig, J. F. *J. Am. Chem. Soc.* **2013**, *135*, 8480–8483. (g) Boursalian, G. B.; Ngai, M.-Y.; Hojczyk, K. N.; Ritter, T. *J. Am. Chem. Soc.* **2013**, *135*, 13278–13281.

(4) Copper-catalyzed aryl C–H amination reactions are also prominent. For leading references, see: (a) Wendlandt, A. E.; Suess, A. M.; Stahl, S. S. *Angew. Chem., Int. Ed.* **2011**, *50*, 11062–11087. (b) Tran, L. D.; Roane, J.; Daugulis, O. *Angew. Chem., Int. Ed.* **2013**, *52*, 6043–6046. (c) Shang, M.; Sun, S.-Z.; Dai, H.-X.; Yu, J.-Q. *J. Am. Chem. Soc.* **2014**, *136*, 3354–3357.

(5) For a review, see: Mei, T.-S.; Kou, L.; Ma, S.; Engle, K. M.; Yu, J.-Q. *Synthesis* **2012**, *44*, 1778–1791.

(6) Inamoto, K.; Saito, T.; Katsuno, M.; Sakamoto, T.; Hiroya, K. *Org. Lett.* **2007**, *9*, 2931–2934.

(7) Wasa, M.; Yu, J.-Q. *J. Am. Chem. Soc.* **2008**, *130*, 14058–14059.

(8) Xiao, Q.; Wang, W.-H.; Liu, G.; Meng, F.-K.; Chen, J.-H.; Yang, Z.; Shi, Z.-J. *Chem. - Eur. J.* **2009**, *15*, 7292–7296.

(9) He, G.; Lu, C.; Zhao, Y.; Nack, W. A.; Chen, G. *Org. Lett.* **2012**, *14*, 2944–2947.

(10) (a) Mei, T.-S.; Wang, X.; Yu, J.-Q. *J. Am. Chem. Soc.* **2009**, *131*, 10806–10807. (b) Nadres, E. T.; Daugulis, O. *J. Am. Chem. Soc.* **2012**, *134*, 7–10. (c) Haffemayer, B.; Gulias, M.; Gaunt, M. J. *J. Chem. Sci.* **2011**, *2*, 312–315. (d) He, G.; Zhao, Y.; Zhang, S.; Lu, C.; Chen, G. *J. Am. Chem. Soc.* **2012**, *134*, 3–6. (e) Mei, T.-S.; Leow, D.; Xiao, H.; Laforteza, B. N.; Yu, J.-Q. *Org. Lett.* **2013**, *15*, 3058–3061.

(11) Tan, Y.; Hartwig, J. F. *J. Am. Chem. Soc.* **2010**, *132*, 3676–3677.

(12) Tsang, W. C. P.; Munday, R. H.; Brasche, G.; Zheng, N.; Buchwald, S. L. *J. Org. Chem.* **2008**, *73*, 7603–7610.

(13) (a) Tsang, W. C. P.; Zheng, N.; Buchwald, S. L. *J. Am. Chem. Soc.* **2005**, *127*, 14560–14561. (b) Jordan-Hore, J. A.; Johansson, C. C. C.; Gulias, M.; Beck, E. M.; Gaunt, M. J. *J. Am. Chem. Soc.* **2008**, *130*, 16184–16186. (c) Youn, S. W.; Bihn, J. H.; Kim, B. S. *Org. Lett.* **2011**, *13*, 3738–3741. (d) Weinstein, A. B.; Stahl, S. S. *Catal. Sci. Technol.* **2014**, *4*, 4301–4307.

(14) Jeong, E. J.; Youn, S. W. *Bull. Korean Chem. Soc.* **2014**, *35*, 2611–2612.

(15) For examples, see: (a) Perrault, W. R.; Shephard, K. P.; LaPean, L. A.; Krook, M. A.; Dobrowolski, P. J.; Lyster, M. A.; McMillan, M. W.; Knoechel, D. J.; Evenson, G. N.; Watt, W.; Pearlman, B. A. *Org. Process Res. Dev.* **1997**, *1*, 106–116. (b) Gan, T.; Liu, R.; Yu, P.; Zhao, S.; Cook, J. M. *J. Org. Chem.* **1997**, *62*, 9298–9304.

(16) Herbst, R. M.; Shemin, D. *Org. Synth.* **1939**, *19*, 1–3.

(17) (a) Humphrey, C. E.; Furegati, M.; Laumen, K.; La Vecchia, L.; Leutert, T.; Müller-Hartwig, J. C. D.; Vögtle, M. *Org. Process Res. Dev.* **2007**, *11*, 1069–1075. (b) Alimardanov, A.; Nikitenko, A.; Connolly, T. J.; Feigelson, G.; Chan, A. W.; Ding, Z.; Ghosh, M.; Shi, X.; Ren, J.; Hansen, E.; Farr, R.; MacEwan, M.; Tadayon, S.; Springer, D. M.; Kreft, A. F.; Ho, D. M.; Potoski, J. R. *Org. Process Res. Dev.* **2009**, *13*, 1161–1168. (c) Zhao, H.; Koenig, S. G.; Dankwardt, J. W.; Singh, S. P. *Org. Process Res. Dev.* **2014**, *18*, 198–204.

(18) (a) Zheng, Y.; Li, X.; Ren, C.; Zhang-Negretrie, D.; Du, Y.; Zhao, K. *J. Org. Chem.* **2012**, *77*, 10353–10361. (b) Wendlandt, A. E.; Stahl, S. S. *Org. Biomol. Chem.* **2012**, *10*, 3866–3870.

(19) Previous work by one of us (S.G.K.) had demonstrated that 2-acetamido-3-(2-haloaryl)acrylates can be transformed in a copper-catalyzed Goldberg reaction to give 1-acetyl indolecarboxylate products similar to those described herein. See: (a) Koenig, S. G.; Dankwardt, J. W.; Liu, Y.; Zhao, H.; Singh, S. P. *Tetrahedron Lett.* **2010**, *51*, 6549–6551. (b) Koenig, S. G.; Dankwardt, J. W.; Liu, Y.; Zhao, H.; Singh, S. P. *ACS Sustainable Chem. Eng.* **2014**, *2*, 1359–1363.

(20) For reviews, see: (a) Deprez, N. R.; Sanford, M. S. *Inorg. Chem.* **2007**, *46*, 1924–1935. (b) Muñoz, K. *Angew. Chem., Int. Ed.* **2009**, *48*, 9412–9423. (c) Hickman, A. J.; Sanford, M. S. *Nature* **2012**, *484*, 177–185.

(21) For a review of ligand-promoted Pd(II)-catalyzed C–H functionalization, see: Engle, K. M.; Yu, J.-Q. *J. Org. Chem.* **2013**, *78*, 8927–8955.

(22) For the formation of similar 2-amino-3-phenylacrylates, see: Zhu, Z.; Yuan, J.; Zhou, Y.; Qin, Y.; Xu, J.; Peng, Y. *Eur. J. Org. Chem.* **2014**, 511–514.

(23) Reference 14 was published during our investigation with molecular oxygen. With the *N*-tosyl substrate and O₂ as the terminal oxidant, we observed up to 83% NMR yield with 10 mol % catalyst in DMSO at 120 °C.

(24) Henderson, J. L.; Buchwald, S. L. *Org. Lett.* **2010**, *12*, 4442–4445 and references cited therein.

(25) Düfert, M. A.; Billingsley, K. L.; Buchwald, S. L. *J. Am. Chem. Soc.* **2013**, *135*, 12877–12885.

(26) (a) Deaton, D. N.; Navas, F., III; Spearing, P. K. Farnesoid X receptor agonists. WO2008157270 A1. (b) Fiorucci, S.; Cipriani, S.; Mencarelli, A.; Baldelli, F.; Bifulco, G.; Zampella, A. *Mini-Rev. Med. Chem.* **2011**, *11*, 753–762.

(27) For example, see: (a) van Benthem, R. A. T. M.; Hiemstra, H.; van Leeuwen, P. W. N. M.; Geus, J. W.; Speckamp, W. N. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 457–460. (b) Steinhoff, B. A.; Stahl, S. S. *J. Am. Chem. Soc.* **2006**, *128*, 4348–4355. (c) Steinhoff, B. A.; King, A. E.; Stahl, S. S. *J. Org. Chem.* **2006**, *71*, 1861–1868. (d) Pun, D.; Diao, T.; Stahl, S. S. *J. Am. Chem. Soc.* **2013**, *135*, 8213–8221.