



Communication

Subscriber access provided by UB + Fachbibliothek Chemie | (FU-Bibliothekssystem)

# **Rh(III)-Catalyzed Meta-C–H Olefination Directed by a Nitrile Template**

Hua-Jin Xu, Yi Lu, Marcus E. Farmer, Huai-Wei Wang, Dan Zhao, Yan-Shang Kang, Wei-Yin Sun, and Jin-Quan Yu

J. Am. Chem. Soc., Just Accepted Manuscript • DOI: 10.1021/jacs.6b13269 • Publication Date (Web): 27 Jan 2017

Downloaded from http://pubs.acs.org on January 27, 2017

## Just Accepted

"Just Accepted" manuscripts have been peer-reviewed and accepted for publication. They are posted online prior to technical editing, formatting for publication and author proofing. The American Chemical Society provides "Just Accepted" as a free service to the research community to expedite the dissemination of scientific material as soon as possible after acceptance. "Just Accepted" manuscripts appear in full in PDF format accompanied by an HTML abstract. "Just Accepted" manuscripts have been fully peer reviewed, but should not be considered the official version of record. They are accessible to all readers and citable by the Digital Object Identifier (DOI®). "Just Accepted" is an optional service offered to authors. Therefore, the "Just Accepted" Web site may not include all articles that will be published in the journal. After a manuscript is technically edited and formatted, it will be removed from the "Just Accepted" Web site and published as an ASAP article. Note that technical editing may introduce minor changes to the manuscript text and/or graphics which could affect content, and all legal disclaimers and ethical guidelines that apply to the journal pertain. ACS cannot be held responsible for errors or consequences arising from the use of information contained in these "Just Accepted" manuscripts.



Journal of the American Chemical Society is published by the American Chemical Society. 1155 Sixteenth Street N.W., Washington, DC 20036 Published by American Chemical Society. Copyright © American Chemical Society. However, no copyright claim is made to original U.S. Government works, or works produced by employees of any Commonwealth realm Crown government in the course of their duties.

8 9

10

11

12

13

14

15

16

17 18

19

20

21

22

23

24

25

26

27

28

29

30

31

32

33

34

35

36

37

38

39

40

41

42

43

44

45

46

47

48

49

50

51

52

53

54

55

56

57

58

59

60

### Rh(III)-Catalyzed Meta-C-H Olefination Directed by a Nitrile Template

Hua-Jin Xu,<sup>†</sup> Yi Lu,<sup>\*,†</sup> Marcus E. Farmer,<sup>‡</sup> Huai-Wei Wang,<sup>†</sup> Dan Zhao,<sup>†</sup> Yan-Shang Kang,<sup>†</sup> Wei-Yin Sun,<sup>\*,†</sup> Jin-Quan Yu<sup>\*,‡</sup>

<sup>†</sup> Coordination Chemistry Institute, State Key Laboratory of Coordination Chemistry, School of Chemistry and Chemical Engineering, Nanjing National Laboratory of Microstructures, Collaborative Innovation Center of Advanced Microstructures, Nanjing University, Nanjing 210023, China

<sup>‡</sup> Department of Chemistry, The Scripps Research Institute, 10550 N. Torrey Pines Road, La Jolla, California 92037,

USA

RECEIVED DATE (automatically inserted by publisher); luyi@nju.edu.cn, sunwy@nju.edu.cn, yu200@scripps.edu

catalyzed Abstract: Rh(III) ortho-C-H А range of functionalizations have been developed; however, extension of this reactivity to remote C-H functionalizations through large ring rhodacyclic intermediates has yet to be demonstrated. Herein, we report the first example of utilizing a U-shaped nitrile template to direct Rh(III)-catalyzed remote meta-C-H activation via a postulated 12-membered macrocyclic intermediate. Considering the ligands used for Rh(III) catalysts are significantly different from those of Pd(II) catalysts, this offers new opportunities for future development of ligand-promoted meta-C-H activation reactions.

Transition metal catalyzed C-H functionalization has been an area of significant interest due to the enabling nature of these reactions to convert previously considered inert C-H bonds into a diverse range of carbon-carbon and carbon-heteroatom bonds. Directed C-H functionalization has been of particular interest as the pre-coordination of a given functional group to the transition metal catalyst enables highly selective C-H activation in a general and predictable manner.<sup>1</sup> This strategy has been demonstrated to be a useful tactic with a wide variety of metals and has been shown to be particularly versatile when using Pd(II), Ru(II), and Rh(III) as catalysts.<sup>1</sup> The use of other catalysts including Cu(II) and Ir(III) has also been demonstrated.1 Directed C-H activation typically proceeds via five or six-membered cyclometalation processes which precludes the functionalization of remote metaor para-C-H bonds. As one of several approaches towards meta-C-H functionalization of aromatics,<sup>2-5</sup> the development of a Ushaped directing template has successfully achieved a number of remote C-H activation reactions with several different classes of substrates.<sup>6</sup> Key to the success of this approach was the use of a nitrile embedded in the template which serves as a linear end-on directing group. The linearity of the nitrile group prevents the assembly of the classical cyclic pre-transition state required for ortho-C-H activation and instead, positions the palladium catalyst near the remote meta-C-H bond. This allows for a macrocyclic cyclophane-like transition state to be preferentially assembled which results in a meta-C-H functionalized product. Such precise recognition of distance and geometry has proven to be rather general in terms of substrate and reaction type.<sup>6-7</sup> Furthermore, this approach has been demonstrated to be compatible with both Pd(II)/(0) and Pd(II)/(IV) catalysis<sup>6</sup> and has been utilized to achieve *para*-C-H activation by modification of the template.<sup>7</sup>

Scheme 1. Directed Meta-C-H Functionalization



In light of the recent and rapid development of Rh(III)catalyzed *ortho*-C-H functionalizations,<sup>1g-j,8</sup> it is highly desirable to extend the templating approach to Rh(III)-catalyzed meta-C-H activation processes for a number of reasons. First, both substrate and reaction type can be complementary to that of Pd(II)catalyzed meta-C-H functionalizations. Second, the ligands used for Rh(III) and Pd(II) are often different which could offer new opportunities for developing ligand controlled, enantioselective remote C-H activation reactions. Third, the oxidation potentials for the reoxidation of low valent metal species are different which may lead to the use of more practical oxidants for closing the catalytic cycle. Herein, we report the first example of using a Rh(III) catalyst in the presence of a guiding template to provide a meta-selective C-H olefination of hydrocinnamic acids. The use of Cu(II) as the co-oxidant is an advantage compared to the Ag oxidant required for the related Pd chemistry. The generality of this approach is also demonstrated by accomplishing a meta-C-H olefination of aniline and indoline substrates bearing templates previously developed for Pd(II) catalysts.<sup>6b,c</sup>

Based on previous Pd(II)-catalyzed meta-selective C-H bond activation studies using a nitrile-containing template,<sup>6a</sup> we initiated efforts to develop a [RhCp\*Cl2]2-catalyzed meta-C-H olefination of hydrocinnamic acid (Scheme 1). We selected hydrocinnamic acid derived compound 1' (Table 1) as our initial substrate for optimization as this is a benchmark substrate for the analogous Pd(II) chemistry. Our studies began using Cu(OAc)<sub>2</sub> as a terminal oxidant for the reaction in dry toluene under an atmosphere of  $O_2$  at 100 °C. With these conditions, we were delighted to find our desired product in trace quantities. A thorough solvent screen was undertaken and DCE was found to be optimal, allowing formation of the desired product in 18% yield. A brief study of the temperature dependence of this reaction indicated that at 120 °C, 25% yield could be obtained. Though 140 °C provided a higher yield, the reaction profile was not as clean and we therefore decided to move forward with the

optimization using 120 °C. No distinct difference was observed when the reaction time was extended to 48 hours, indicating that the catalyst was no longer functional after 36 hours. A wide variety of oxidants were evaluated and Cu(O<sub>2</sub>CCF<sub>3</sub>)<sub>2</sub>·xH<sub>2</sub>O was found to be far superior to the others, enhancing the yield to 50% with 5% being di-substituted product. Interestingly, when we decreased the equivalence of Cu(O<sub>2</sub>CCF<sub>3</sub>)<sub>2</sub> xH<sub>2</sub>O to one equivalent, a significant increase of the total vield to 77% was obtained. Presumably, excess Cu(II) species could outcompete the Rh(III) for coordination with the nitrile template. We next examined the role of the oxidants in this transformation. First, since  $O_2$  can potentially turn over copper oxidation catalysts, we attempted the reaction under an atmosphere of oxygen with only 0.5 equivalents of  $Cu(O_2CCF_3)_2 \times H_2O$  and found that the yield decreased to 44%. This led us to evaluate the reaction under a nitrogen atmosphere in the presence of one equivalent of  $Cu(O_2CCF_3)_2 \cdot xH_2O$ ; however, the yield of the desired products under these conditions was a mere 13% indicating O2 is also necessary for this transformation (see supporting information). Further optimization of additives revealed that addition of one equivalent of CF<sub>3</sub>CO<sub>2</sub>H improved the yield to 89%. The use of a Cu(II) oxidant is a practical advantage over Pd(II) methods as Ag(I) salts are often needed in Pd(II)-catalyzed remote C-H functionalizations using nitrile templates.

Table 1. Optimization of reaction conditions.<sup>a</sup>

$ \begin{array}{c} \begin{array}{c} & & \\$							
Entry	Oxidant	Additive (1 equiv)	Yield (%) [mono:dí]	Entry	Oxidant	Additive (1 equiv)	Yield (%) [ <i>mono:di</i> ]
1	Cu(OAc) <sub>2</sub>	_	25 [25:0]	9	Cu(BF <sub>4</sub> ) <sub>2</sub>	_	NR
2	AgOAc	—	NR	10	Cu(CO <sub>2</sub> CF <sub>3</sub> ) <sub>2</sub> ·xH <sub>2</sub> O	—	50 [45:5]
3	Ag <sub>2</sub> CO <sub>3</sub>	—	NR	11 <sup>6</sup>	Cu(CO <sub>2</sub> CF <sub>3</sub> ) <sub>2</sub> .xH <sub>2</sub> O	—	77 [62:15]
4	AgPF <sub>6</sub>	—	NR	12 <sup>b, c</sup>	Cu(CO <sub>2</sub> CF <sub>3</sub> ) <sub>2</sub> ·xH <sub>2</sub> O	—	55 <b>[</b> 47:8]
5	Ag <sub>2</sub> O	—	NR	13 <sup>6</sup>	Cu(CO <sub>2</sub> CF <sub>3</sub> ) <sub>2'</sub> xH <sub>2</sub> O	HOAc	66 [54:12]
6	Phl(OAc) <sub>2</sub>	—	NR	14 <sup>6</sup>	Cu(CO <sub>2</sub> CF <sub>3</sub> ) <sub>2</sub> ·xH <sub>2</sub> O	PivOH	81 [55:26]
7	Cu(SO <sub>3</sub> CF <sub>3</sub> ) <sub>2</sub>	—	NR	15 <sup>6</sup>	Cu(CO <sub>2</sub> CF <sub>3</sub> ) <sub>2</sub> .xH <sub>2</sub> O	CF₃CO₂H	89 [63:26]
8	CuCl		NR	16 <sup>5</sup>	Cu(CO <sub>2</sub> CF <sub>3</sub> ) <sub>2</sub> ·xH <sub>2</sub> O	AcONa	23 [23:trace]

<sup>a</sup>Reaction conditions: 1' (0.1 mmol), 2a (0.6 mmol), [RhCp\*Cl<sub>2</sub>]<sub>2</sub> (5 mol %), oxidant (0.2 mmol), additive (0.1 mmol), dry DCE (2 mL),  $O_2$ , 36 h, 120 °C. Yield was determined by <sup>1</sup>H NMR analysis using CH<sub>2</sub>Br<sub>2</sub> as the internal standard. <sup>b</sup>Cu(CO<sub>2</sub>CF<sub>3</sub>)<sub>2</sub>·xH<sub>2</sub>O (0.1 mmol). <sup>c</sup>Air was used instead of O<sub>2</sub>.

#### Table 2. Investigation of templates.<sup>*a,b*</sup>



<sup>*a*</sup>Reaction conditions: **1** (0.1 mmol), **2a** (0.6 mmol),  $[RhCp*Cl_2]_2$  (5 mol %),  $Cu(CO_2CF_3)_2 \cdot xH_2O$  (0.1 mmol),  $CF_3CO_2H$  (0.1 mmol), dry DCE (2 mL), O<sub>2</sub>, 36 h, 120 °C. <sup>*b*</sup>Yield was determined by <sup>1</sup>H NMR analysis using  $CH_2Br_2$  as the internal standard. <sup>c</sup>Isolated yield of reaction run at 100 °C, 48h.

Since the di-substituted product was non-negligible in the standard conditions, we endeavored to search for a suitable directing group which can inhibit the generation of di-substituted product. A brief evaluation of templates revealed that use of T3 containing a single nitrile group (Table 2) could slightly improve the mono:di ratio, enabling the mono-substituted product to be obtained in 68% yield and the di-substituted product in 22%. Based on these results, we selected template T3 as our final template. Importantly, the nitrile is key to achieving high selectivity as indicated by the mixture of products obtained when using T4. At this point, we attempted to lower the reaction temperature. As can be seen in Table 2, using the optimized conditions and template at 100 °C provided a comparable yield of the desired product. Under these milder conditions, the catalyst was active for over 36 hours and the optimal reaction time was extended to 48 hours.





<sup>a</sup>Reaction conditions: **1** (0.1 mmol), **2a** (0.6 mmol), [RhCp\*Cl<sub>2</sub>]<sub>2</sub> (5 mol %), Cu(CO<sub>2</sub>CF<sub>3</sub>)<sub>2</sub>·xH<sub>2</sub>O (0.1 mmol), CF<sub>3</sub>CO<sub>2</sub>H (0.1 mmol), dry DCE (2 mL), O<sub>2</sub>, 48 h, 100 °C. <sup>b</sup>Isolated yield

With the optimized conditions in hand, we examined the scope of hydrocinnamic acid derivatives using ethyl acrylate (2a) as the coupling partner (Table 3). Unsubstituted compounds 1a and 1b provided the highest total yields of 88% and 90% respectively. It is worth noting that there were no di-substituted products for the substrates with substituents at the ortho-, meta-, or para-positions. For ortho-substituted substrates, both electrondonating groups (3c, 3d) and halogens (3e-3g) were well tolerated, with the desired products being obtained in good yield. Substrate 1h containing an *ortho*-trifluoromethyl group could be coupled to provide the desired product in a modest, although synthetically useful yield of 55%. For meta-substituted substrates, those bearing electron-donating groups at the meta-position (1i, 1i) worked well in the reaction and the desired products were cleanly afforded in 85% (3i) and 81% (3j) yield with good metaselectivity. Substitution of the *meta*-position with halogens (entries 3k - 3m, Table 3) provided a slight depreciation of the yield, though the selectivity remained high. Meta-trifluoromethyl substituted substrate 1n gave the desired product 3n in a modest yield of 49%. Either methoxy or fluoride substitution at the para

1

2

3

4

5

6

7

8

9

10

11

12

13

14

15

16

17

18

19

20

21

22

23

24

25

26 27

28

1

2

3

4

5

6

7

8

9

10

11

12

13

14

15

16

17

18

19

20

21

22

23

24

25

26

27

28

29

30

31

32

33

34

35

36

37

38

39

40

41

42 43

44

45

46

47

48

49

50

51

52

53

54

55

56

57

58

59

60

position does not hamper this reaction (**3o**, **3p**). However, it is noteworthy that this reaction is somewhat sensitive to both sterics and electronics at the 4-position of the aromatic. We have attempted reactions using 4-*tert*-butyl- and 4-nitro-hydrocinnamic acid derived substrates, but neither provided significant quantities of olefination products.

To investigate the generality of this reaction, the scope of olefin coupling partners was evaluated. As can be seen in Table 4, a wide range of olefin coupling partners can be employed in this transformation. Methyl acrylate, butyl acrylate, dimethyl acrylamide, ethyl vinyl ketone, acrolein, and diethylvinyl phosphonate could all be effectively coupled providing the desired products in good yield. A  $\beta$ -substituted enone and styrene derivatives were also compatible with this reaction, with electron withdrawing groups on the aromatic ring of styrene being favored. Phenyl vinyl sulfone also coupled well in this reaction.

Given the generality of this templating approach with Pd(II) catalysis, we sought to examine whether this Rh(III) system can be extended to other types of substrates. A brief examination of templates that have previously been utilized for Pd(II) catalysis<sup>6b,c</sup> indicated that indeed, Rh(III) catalyzed *meta*-C–H functionalization using this strategy will likely prove to be highly general. As can be seen in Scheme 2, both indoline and aniline were successfully olefinated at the meta-C-H bond using a template originally designed for Pd(II) catalyzed olefination of indolines.<sup>6e</sup> Interestingly, it was found that in these cases, the addition of TFA to the reaction hampered the reactivity of the catalyst. Further work on improving the scope and efficiency of this transformation using Rh(III), as well as other transition metal catalysts, is currently underway and will be reported in due course.

Table 4. Scope of olefin coupling partners.<sup>*a,b*</sup>



<sup>&</sup>lt;sup>a</sup>Reaction conditions: **1** (0.1 mmol), **2** (0.6 mmol),  $[RhCp*Cl_2]_2$  (5 mol %),  $Cu(CO_2CF_3)_2 \cdot xH_2O$  (0.1 mmol),  $CF_3CO_2H$  (0.1 mmol), dry DCE (2 mL), O<sub>2</sub>, 48 h, 100 °C. <sup>b</sup>Isolated yield. <sup>c</sup>The reaction was run in the absence of the TFA additive.

A plausible reaction mechanism for this reaction is proposed in Scheme 3. Coordination of the nitrile to the [Rh(III)] catalyst is followed by *meta*-C–H bond activation to give the corresponding 12-membered rhodacyclic intermediate **2**. Subsequent coordination to the olefin coupling partner followed by 1,2migratory insertion would yield intermediate **3**.  $\beta$ -Hydride elimination yields the desired product and a Rh(III) hydride 4. Reductive elimination, followed by reoxidation of [Rh(I)] to [Rh(II)] by Cu(O<sub>2</sub>CCF<sub>3</sub>·xH<sub>2</sub>O) and O<sub>2</sub> would restore the active catalyst, completing the catalytic cycle. In an attempt to probe whether C–H activation is rate determining in this catalytic cycle, we conducted experiments to determine the kinetic isotope effect (KIE) for parallel experiments. The KIE ( $k_{\rm H}/k_{\rm D} = 1.8$ ) revealed that the *meta*-C–H bond cleavage may be the rate determining step (see supporting information for details).

We next attempted to scale the reaction to gram scale. By refluxing the reaction mixture in toluene for 48 h under  $O_2$  (balloon), 75% yield (55% mono, 20% di, isolated) of the desired product could be obtained (see supporting information for details).

#### Scheme 2. Meta-C-H olefination of aniline and indoline



In summary, we have developed a Rh(III)-catalyzed *meta*-C–H olefination of hydrocinnamic acid derivatives using a modified mono-nitrile template. The identification of  $Cu(O_2CCF_3 \cdot xH_2O)$  as oxidant was crucial for this reaction. These results pave the way for further development of new ligands for Rh(III)-catalyzed remote C–H functionalizations

#### Scheme 3. Simplified mechanism for the olefination reaction.



Acknowledgements. We gratefully acknowledge the National Natural Science Foundation of China (grant no. 21201100, 21671097 and 21331002) and National Science Foundation (CHE-1465292) for financial support.

**Supporting Information Available:** Experimental procedures and spectral data for all new compounds (PDF). This material is available free of charge via the Internet at <u>http://pubs.acs.org</u>.

#### References

 For selected reviews on C-H activation, see: (a) Daugulis, O.; Do, H. Q.; Shabashov, D. Acc. Chem. Res. 2009, 42, 1074. (b) Lyons, T. W.; Sanford, M. S. Chem. Rev. 2010, 110, 1147. (c) Engle, K. M.; Yu, J.-Q. J. Org. Chem. 2013, 78, 8927. (d) Seregin, I. V.; Gevorgyan, V. Chem. Soc. Rev. 2007, 36, 1173. (e) Ackermann, L. Acc. Chem. Res. 2014, 47, 281.
(f) Mkhalid, I. A. I.; Barnard, J. H.; Marder, T. B.; Murphy, J. M.; Hartwig, J. F. Chem. Rev. 2010, 110, 890. For selected reviews that pertain to Rh(III) C-H activation, see: (g) G; Wang, F; Li, X. Chem. Soc. Rev. 2012, 41, 3651. (h) Colby, D. A.; Bergman, R. G; Ellman, J. A. Chem. Rev. 2010, 110, 624. (i) Colby, D. A.; Tsai, A. S.; Bergman, R. G; Ellman, J. A. Acc. Chem. Res. 2012, 45, 814. (j) Patureau, F. W.; Wencel-Delord, J.; Glorius, F. Aldrichim. Acta 2012, 45, 31.

- Examples of non-directed meta-C-H borylation and silvlation: (a) Cho, J. (2)Y.; Tse, M. K.; Holmes, D.; Maleczka, R. E.; Smith, M. R. Science 2002, 295, 305. (b) Ishiyama, T.; Takagi, J.; Ishida, K.; Miyaura, N.; Anastasi, N. R.; Hartwig, J. F. J. Am. Chem. Soc. 2002, 124, 390. (c) Ishiyama, T.; Takagi, J.; Hartwig, J. F.; Miyaura, N. Angew. Chem., Int. Ed. 2002, 41, 3056. (d) Murphy, J. M.; Liao, X.; Hartwig, J. F. J. Am. Chem. Soc. 2007, 129, 15434. (e) Mkhalid, I. A. I.; Barnard, J. H.; Marder, T. B.; Murphy, J. M.; Hartwig, J. F. Chem. Rev. 2010, 110, 890. (f) Kuninobu, Y.; Ida, H.; Nishi, M.; Kanai, M. Nat. Chem. 2015, 7, 712. (g) Maleczka, R. E.; Shi, F.; Holmes, D.; Smith, M. R. J. Am. Chem. Soc. 2003, 125, 7792. (h) Holmes, D.; Chotana, G. A.; Maleczka, R. E.; Smith, M. R. Org. Lett. 2006, 8, 1407. (i) Hurst, T. E.; Macklin, T. K.; Becker, M.; Hartmann, E.; Kuegel, W.; Parisienne-La Salle, J.-C.; Batsanov, A. S.; Marder, T. B.; Snieckus, V. Chem.-Eur. J. 2010, 16, 8155. For examples of regioselective C-H metallation without the need for 1,3-disubstitution, see: (j) Cheng, C.; Hartwig, J. F. Science 2014, 343, 853. (k) Saito, Y.; Segawa, Y.; Itami, K. J. Am. Chem. Soc. 2015, 137, 5193. (1) Kuninobu, Y.; Ida, H.; Nishi, M.; Kanai, M. Nat. Chem. 2015, 7, 712.
- (3) (a) Saidi, O.; Marafie, J.; Ledger, A. E. W.; Liu, P. M.; Mahon, M. F.; Kociok-Koehn, G.; Whittlesey, M. K.; Frost, C. G. J. Am. Chen. Soc. 2011, 133, 19298. (b) Hofmann, N.; Ackermann, L. J. Am. Chem. Soc. 2013, 135, 5877. (c) Li, J.; Warratz, S.; Zell, D., De Sarkar, S.; Ishikawa, E. E.; Ackermann, L. J. Am. Chem. Soc. 2015, 137, 13894. (d) Teskey, C. J.; Lui, A. Y. W.; Greaney, M. F. Angew. Chem. Int. Ed. 2015, 54, 11677. (e) Paterson, A. J.; St. John-Campbell, S.; Mahon, M. F.; Press, N. J.; Frost, C. G. Chem. Comm. 2015, 51, 12807.
- (4) (a) Wang, X. C.; Gong, W.; Fang, L. Z.; Zhu, R. Y.; Li, S. H.; Engle, K. M.; Yu, J. Q. *Nature* 2015, *519*, 334. (b) Dong, Z.; Wang, J. C.; Dong, G. B. *J. Am. Chem. Soc.* 2015, *137*, 5887. (c) Shen, P.-X.; Wang, X.-C.; Wang, P.; Zhu, R.-Y.; Yu, J.-Q. *J. Am. Chem. Soc.* 2015, *137*, 11574. (d) Han, J.; Zhang, L.; Zhu, Y.; Zheng, Y.; Chen, X.; Huang, Z.-B.; Shi, D.-Q.; Zhao, Y. *Chem. Comm.* 2016, *52*, 6903. (e) Wang, P.; Farmer, M. E.; Huuo, X.; Jain, P.; Shen, P.-X.; Ishoey, M.; Bradner, J. E.; Wisniewski, S. R.; Eastgate, M. D.; Yu, J.-Q. *J. Am. Chem. Soc.* 2016, *138*, 9269.
- (5) For selected examples using copper and aryl iodoniums to achieve meta-C-H arylation, see: (a) Phipps, R. J.; Gaunt, M. J. Science 2009, 323, 1593. (b) Duong, H. A.; Gilligan, R. E.; Cooke, M. L.; Phipps, R. J.; Gaunt, M. J. Angew. Chem. Int. Ed. 2010, 50, 463. (c) Yang, Y; Li, R.; Zhao, Y.; Zhao, D.; Shi, Z.; J. Am. Chem. Soc. 2016, 138, 8734. For an example of using CO<sub>2</sub> as a traceless directing group, see: (d) Luo, J.; Preciado, S.; Larrosa, I. J. Am. Chem. Soc. 2013, 136, 4109. For an example using deprotonation to achieve meta-functionalization, see: (e) Martinez-Martinez, A. J.; Kennedy, A. R.; Mulvey, R. E.; O'Hara, C. T. Science 2014, 346, 834.
- (6) For selected examples of Pd-catalyzed *meta*-C–H functionalization using nitrile based templates, see: (a) Leow, D.; Li, G.; Mei, T.-S.; Yu, J.-Q. *Nature* 2012, 486, 518. (b) Tang, R.-Y.; Li, G.; Yu, J.-Q. *Nature* 2014, 507, 215. (c) Yang, G. Q.; Lindovska, P.; Zhu, D. J.; Kim, J.; Wang, P.; Tang, R. Y.; Movassaghi, M.; Yu, J. Q. J. Am. Chem. Soc. 2014, 136, 10807. (d) Lee, S.; Lee, H.; Tan, K. L. J. Am. Chem. Soc. 2013, 135, 18778. (e) Li, S. D.; Ji, H. F.; Cai, L.; Li, G. Chem. Sci. 2015, 6, 5595. (f) Bera, M.; Maji, A.; Sahoo, S. K.; Maiti, D. Angew. Chem., Int. Ed. 2015, 54, 8515. (g) Chu, L.; Shang, M.; Tanaka, K.; Chen, Q.; Pissarnitski, N.; Streckfuss, E.; Yu, J.-Q. ACS Cent. Sci. 2015, 1, 394.
- (7) (a) Bag, S.; Patra, T.; Modak, A.; Deb, A.; Maity, S.; Dutta, U.; Dey, A.; Kancherla, R.; Maji, A.; Hazra, A.; Bera, M.; Maiti, D. *J. Am. Chem. Soc.* 2015, *137*, 11888. (b) Patra, T.; Bag, S.; Kancherla, R.; Mondal, A.; Dey, A.; Pimparkar, S.; Agasti, S.; Modak, A.; Maiti, D. *Angew. Chem. Int. Ed.* 2016, *55*, 7751.
- (8) For examples of Rh(III) catalyzed ortho-C-H olefination, see: (a) Mishar, N. K.; Park, J.; Sharma, S.; Han, S.; Kim, M.; Shin, Y.; Jang, J.; Kwak, J. H.; Jung Y. H.; Kim, I. S. Chem. Commun. 2014, 50, 2350. (b) Wang, N.-J.; Mei, S.-T.; Shuai, L.; Yuan, Y.; Wei, Y. Org. Lett. 2014, 16, 3040. (c) Zhang, X.-S.; Zhu, Q.-L.; Zhang, Y.-F.; Li, Y.-B.; Shi, Z.-J. Chem. Eur. J. 2013, 19, 11898. (d) Li, B.; Ma, J.; Xie, W.; Song, H.; Xu, S.; Wang, B.; Chem. Eur. J. 2013, 19, 118803. (e) Liu, B.; Fu, Y.; Gao, Y.; Sun, C.; Xu C.; Zhu, J. J. Am. Chem. Soc. 2013, 135, 468. (f) Feng, C.; Feng D.; Loh, T.-P. Org. Lett. 2013, 15, 3670. (g) Zhou, J.; Li, B.; Hu F.; Shi, B.-F. Org. Lett. 2013, 15, 3460. (h) Presset, M.; Oehlrich, D.; Rombouts, F.; Molander, G. A. Org. Lett. 2013, 15, 1528. (i) Cui, S.; Zhang Y.; Wu, Q. Chem. Sci. 2013, 4, 3421. (j) Shen, Y.; Liu, G.; Zhou, Z.; Lu, X. Org. Lett. 2013, 15, 3366. (k) Ye, B.; Cramer, N. Science 2012, 338, 504. (l) Zhu, C.; Falck, J. R. Chem. Commun. 2012, 48, 1674. (m) Li, G.; Ding, Z.; Xu, B. Org. Lett. 2012, 14, 5338. (n) Kwon, K.-H.; Lee, D. W.; Yi, C. S.

*Organometallics* **2012**, *31*, 495. (o) Hyster, T. K.; Kn<sup>°</sup>orr, L.; Ward, T. R.; Rovis, T. *Science* **2012**, *338*, 500. (p) Tsai, A. S.; Brasse, M.;. Bergman, R. G; Ellman, J. A. *Org. Lett.* **2011**, *13*, 540. (q) Park, S.; Kim, J. Y.; Chang, S.; *Org. Lett.* **2011**, *13*, 2372. (r) Li, X.; Zhao, M. *J. Org. Chem.* **2011**, *76*, 8530. (s) Wang, F.; Song, G; Li, X. *Org. Lett.* **2010**, *12*, 5430. (t) Patureau, F. W.; Glorius, F.; *J. Am. Chem. Soc.* **2010**, *132*, 9982. (u) Ueura, K.; Satoh, T.; Miura, M. *Org. Lett.* **2007**, *9*, 1407.

59

60

### Journal of the American Chemical Society



