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Carbon Dioxide-Driven Palladium-Catalyzed C–H Activation of Amines: A Unified Approach for the Arylation of Aliphatic and Aromatic Primary and Secondary Amines

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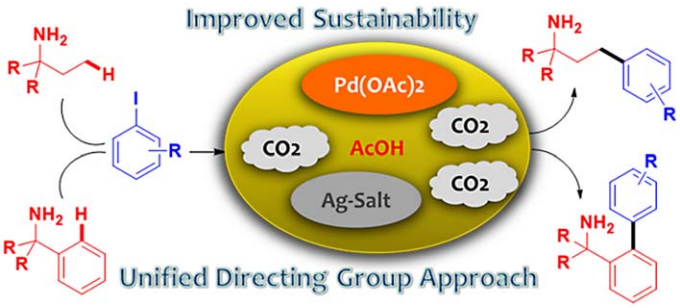

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Abstract Amines are an important class of compounds in organic chemistry and serve as an important motif in various industries, including pharmaceuticals, agrochemicals, and biotechnology. Several methods have been developed for the C–H functionalization of amines using various directing groups, but functionalization of free amines remains a challenge. Here, we discuss our recently developed carbon dioxide driven highly site-selective γ-arylation of alkyl- and benzylic amines via a palladium-catalyzed C–H bond-activation process. By using carbon dioxide as an inexpensive, sustainable, and transient directing group, a wide variety of amines were arylated at either γ-sp^3 or sp^2 carbon–hydrogen bonds with high selectivity based on substrate and conditions. This newly developed strategy provides straightforward access to important scaffolds in organic and medicinal chemistry without the need for any expensive directing groups.

Key words C–H activation, carbon dioxide, amines, sustainable chemistry, organometallics, synthetic methodology

Mohit Kapoor (Far Right) obtained his Ph.D. from National Tsing Hua University (Prof. Jih Ru Hwu) working on synthetic chemistry and medicinal chemistry. His current research at The University of Toledo involves developing more sustainable strategies for C–H activation.
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Daniel Liu (Left of Center) is a high school student participating in the Ohio College Credit Plus program, and has been enrolled in various undergraduate courses in Chemistry and Mathematics over the past three years at The University of Toledo, where he has also been working in the area of CO_2-directed C–H activation.
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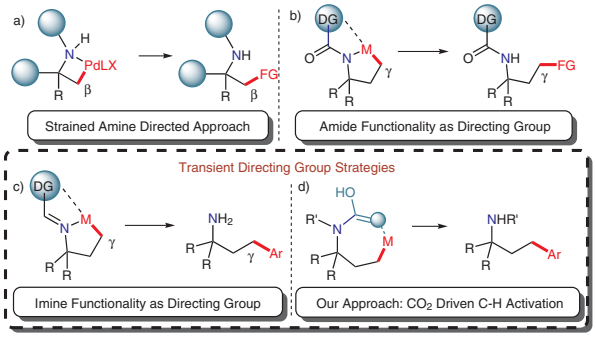
Michael C. Young (Right of Center) obtained his Ph.D. (Prof. Richard J. Hooley) at the University of California – Riverside studying molecular self-assembly. After a brief postdoctoral stint at the University of Texas – Austin (Prof. Guangbin Dong) investigating new directing group approaches for C–H alkylation of ketones, he began his independent career at The University of Toledo in 2016, where his group searches for more sustainable approaches to organometallic synthetic methodology.

1 Introduction

Amines are a pervasive functional group in a variety of molecules, and they are especially important in the pharmaceutical, agrochemical, and polymer industries.[1] While there are many classical approaches to synthesizing amines from other functional groups,[2] a growing trend is to approach the formation of complex molecules through Pd-catalyzed C–H activation.[3] In this way, more complex moieties can be added to a pre-existing amine, allowing molecular complexity to be doubled in a single synthetic step.[4] There are numerous challenges with performing C–H acti-

vation on amine substrates, however. First, amines are sensitive to oxidation in the presence of transition metals.[5] Second, free primary and secondary amines only serve as a viable directing group (DG) for transition-metal-catalyzed C–H activation in a few specific examples (many from the Gaunt group), such as for sterically congested secondary amines (Scheme 1a),[6] as well as benzylic[7] and homobenzylic[8] amines.



Scheme 1 Schematic representation of C–H activation of amines using different approaches

While tertiary amines are well established for directing Pd-catalyzed C–H activation,[9] historically, the most prevalent method to achieve directed C–H activation of amine substrates entailed conversion of the amine into an amide, often with a chelating group to more tightly bind to the transition metal (Scheme 1b).[10] By using this approach, many groups, including Daugulis,[11] Yu,[12] Sanford,[13] Shi,[14] Chen,[15] and Zhao[16] among others have devised many elegant transformations involving the C–H activation of amine substrates to install new functional groups. However, these approaches are often undermined by the poor step and atom economy associated with installing and subsequently removing these functional groups,[17] assuming that they can be removed in the presence of more labile functional groups.[18]

To alleviate this challenge, a recent approach has been to use *transient* directing groups.[17] Pioneered by Jun for the C–H activation of aldehydes (also called olefin hydroacylation),[19] transient directing groups have grown in popularity for achieving C–H activation of numerous ketone,[20] aldehyde,[21] and even phenol[22] substrates. Initially used by Sames for anilines,[23] the first application of this approach to aliphatic amines did not come until 2016, when the groups of Dong[24] and Ge[25] simultaneously published two distinct transient directing groups for the γ-C(sp^3)–H arylation of aliphatic amines (Scheme 1c). The benefit of Ge's approach was that the directing group could be used catalytically in the reaction, thus decreasing the overall waste associated with an added directing group. Other reports followed from Yu[26] and Kamenecka[27] using a pyridine DG attached to an aldehyde, while Murakami[28] showed that sterically hindered salicylaldehydes were also a viable directing group. Very recently, the Bull group provided an alternative to using oxidatively sensitive aldehydes by instead introducing their aldehyde directing group as the more stable acetal.[29]

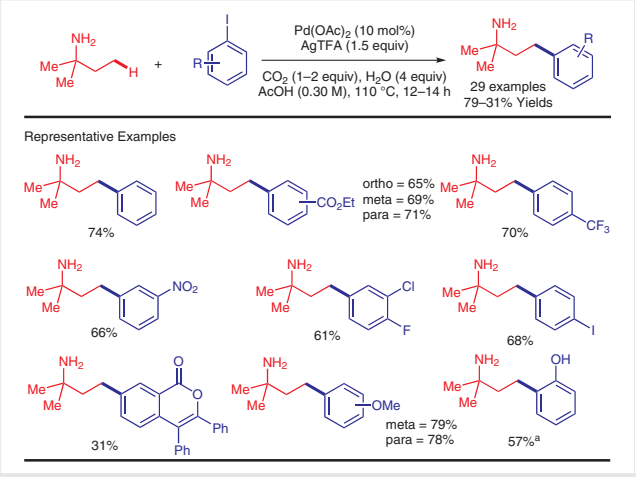
Despite these advances, we reasoned that there was still room for improvement: imines are sensitive to numerous side reactions, and although useful for relatively mild arylation reactions, they are not likely to be viable intermediates for reactions requiring more harsh or oxidizing conditions, such as C–H oxidation or acetoxylation. Additionally, the use of imines formed in situ as directing groups is only applicable to primary amines, leaving no viable strategy for performing C–H activation of oxidizable secondary amine substrates. Inspired by Larrosa's use of aryl and heteroaryl carboxylic acids as a *traceless* directing group for C–H activation,[30] we set out to develop the use of carbon dioxide as a *transient* directing group for the C–H activation of primary and secondary amine substrates (Scheme 1d). The hypothesis was that the carbamate formed *in situ* would be capable of binding to and thus direct the palladium catalyst to promote site-selective C–H activation, while simultaneously deactivating the amine for side reactions, especially oxidation.

2 C(sp^3)–H Arylation of Aliphatic Amines

The key to realizing carbon dioxide as a *transient* directing group involved an important mechanical quandary in addition to the standard mechanistic questions: how does one achieve satisfactory carbon dioxide pressure to promote the desired reactivity, while simultaneously allowing facile reaction screening? In principle reactions can be performed under one atmosphere of carbon dioxide pressure by using standard equipment and techniques (Schlenk lines or balloons), but if the desired reaction requires higher pressures, more expensive apparatus are required. Inspired by strategies for carbonylation chemistry that generate CO in situ through either liquid[31] or solid[32] precursors, we realized that carbon dioxide can also be introduced into a reaction as a solid – using dry ice.[33] By using this technique, we observed that simple reaction vials could be pressurized with between 2 – 20 atmospheres of carbon dioxide, thereby facilitating the desired C–H transformation in better yield than could be obtained at ambient pressures.[34] The use of inexpensive vials further led to increased screening efficiency, as the cost of a reaction vial with a PTFE (polytetrafluoroethylene) lined cap is approximately 1/3000th the cost of a comparably sized pressure reactor.

With the technology in hand to quickly screen multiple reactions under moderate pressures of carbon dioxide, it was short work to find conditions for the desired C–H arylation reaction (Scheme 2).[35] For the C–H activation of primary amines, we found optimized conditions using 10 mol% of $Pd(OAc)_2$ as a precatalyst, 1.5 equiv of AgTFA as an additive

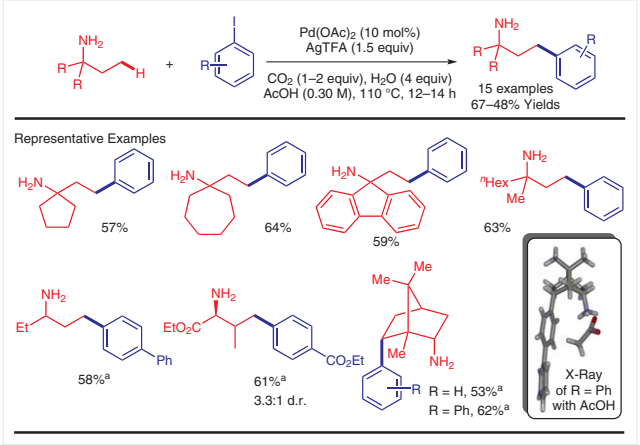
(important to activate the aryl halide electrophile), 2 equiv of aryl iodide, 4 equiv of water (to help facilitate carbamate formation), and between 1 and 2 equiv of CO_2 in the form of dry ice using acetic acid as the solvent. In the absence of CO_2, only trace product was observed.



Scheme 2 Aryl iodide substrate scope for γ-C(sp^3)–H arylation of 1° amines directed by CO_2. [a] AgOTf used in place of AgTFA.

Performing the reactions at 110 °C, conversion was usually complete after between 12 and 14 h. The substrate scope was broad with regard to aryl iodides, and F-, F_3C-, EtO_2C-, O_2N-, Me-, MeO-, BnO-, and Ph- substituents on the aryl iodide were all tolerated. Even some heterocycles, including N-tosylindole and a diphenylisocoumarin, could be incorporated in the reaction. Interestingly, while *ortho*-substituted aryl halides are generally unreactive in C–H arylation reactions, the use of a Ag salt with a weaker Lewis base (OTf instead of TFA) facilitated a number of these substrates in the reaction as well. While the exact reason for this is unknown, we do observe a lower reaction pH afterwards when AgOTf is used in place of AgTFA.

The reaction also worked with a variety of primary amines, bearing either carbocyclic or acyclic α-tertiary carbons (Scheme 3). It is noteworthy that when using an aminofluorene substrate, complete selectivity was observed for C(sp^3)–H arylation, despite the proximity of more reactive C(sp^2)–H bonds. By lowering the temperature by 20 °C, it was also possible to extend the chemistry to substrates with α-secondary carbons. Interestingly, lowering the temperature for the α-tertiary substrates was not effective, and led to decreased conversion, while performing the reactions at the higher temperature on α-secondary substrates led to increased decomposition. Under the milder reaction temperature, it was possible to achieve selective *monoarylation* using 3-aminopentane (similar selectivity could not be achieved using 3-amino-3-methylpentane). Notably, when this chemistry was applied to a chiral aminoester, no loss in *ee* was observed in the product. Moreover, the presence of the chiral amine led to a moderate level of diastereoselectivity in the arylation of one of two prochiral methyl groups. Even more noteworthy is that a rare example of transannular methylene C–H activation was possible using a rigid norbornylamine substrate.[36]

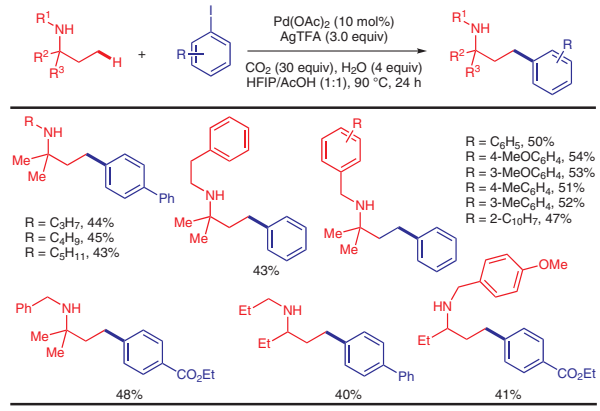


Scheme 3 Amine substrate scope for γ-C(sp^3)–H arylation directed by CO_2. [a] Temperature reduced from 110 to 90 °C.

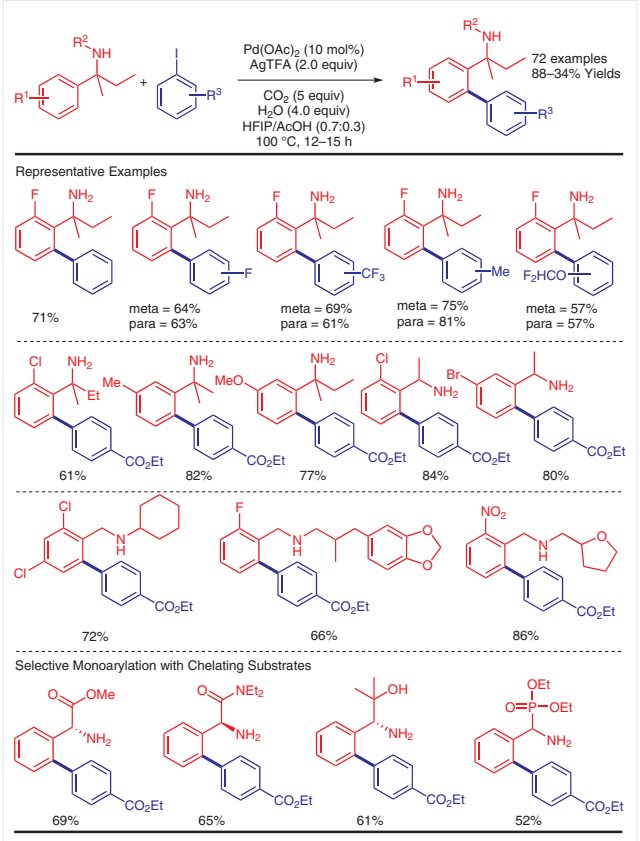
Gratifyingly, the transformation could also be performed on secondary amines containing oxidizable C–N bonds (Scheme 4). This represents a substrate class that is inaccessible with all of the direct or transient directing group approaches reported to date. To facilitate the reaction, it was necessary to use a lower temperature, as well as to dramatically increase the CO_2 loading from a mere 1–2 equiv up to approximately 30 equiv. When the CO_2 loading was not increased, low conversion into C–H arylation products was observed, with concomitant oxidation and hydrolysis of the more sensitive C–N linkages. Both aliphatic and benzylic/homobenzylic amines were viable for this transformation, even when both side chains contained oxidizable C–N bonds. This shows the utility of CO_2 not only as a directing group, but also as an in situ formed protecting group, as has been previously demonstrated by Leitner.[37] It is worth considering that, in many of these examples, selectivity is observed for C(sp^3)–H bonds even in the presence of what would normally be considered more reactive C(sp^2)–H bonds. Similar selectivity has recently been observed by Gaunt,[38] and the selectivity most likely derives from a more favorable conformation for C–H activation on the more sterically congested side of the amine.

3 C(sp^2)–H Arylation of Benzylic Amines

Generally C(sp^2)–H bonds are *more* reactive for C–H activation than their aliphatic analogues. It was surprising to us, therefore, that there were limited examples of the γ-C–H activation of benzylamines in the literature. To date, there



Scheme 4 2° Amine substrate scope for γ-C(sp^3)–H arylation directed by CO_2



Scheme 5 Scope of the γ-C(sp^2)–H arylation of primary and secondary benzylamines

are only two examples of successful C–H arylation on benzylamines, one using the amine directly,[7b] and one using a transient DG approach.[27] Notably, both approaches required harsh conditions (130 °C reaction temperature), and were incompatible with pre-existing stereocenters, as well as oxidizable secondary amine substrates. We considered that our strategy using CO_2 could facilitate a milder reaction that would obviate the challenges associated with the previous approaches.[39]

After re-optimization of the conditions for aliphatic amines,[35] we were delighted to find that we could achieve the selective γ-C(sp^2)–H arylation of benzylamines with a variety of aryl iodides (Scheme 5), including uncommon examples such as those containing F_3CO-, F_2HCO-, and even 2-iodostrychnine. Again, in the absence of CO_2, less than 10% yield of the *ortho*-arylated products was obtained. Furthermore, the reaction had a relatively broad substrate scope for both primary and secondary benzylamines, and numerous carbocyclic and heterocyclic-containing substrates were able to participate in the reaction without concomitant oxidation or other side decomposition-pathways impacting the synthetic utility.

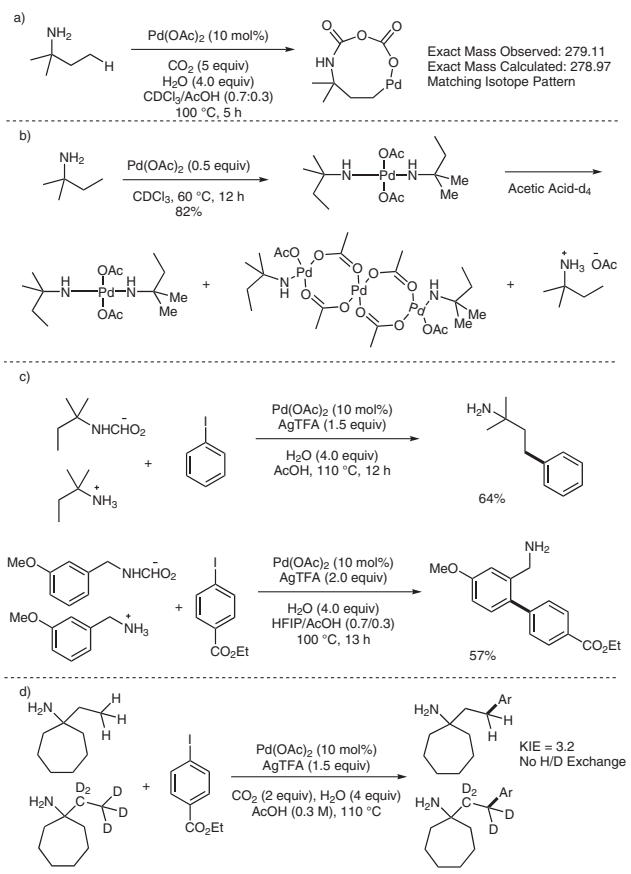
Notably, when the substrates possessed an α-chiral amine, complete retention of configuration was observed in the products, which can be a challenge for these phenylglycine derivatives.[29] Another interesting feature of this strategy was observed in the presence of chelating functional groups. While diarylation is typically challenging to shut down during C–H activation,[7b,29,40] by incorporating chelating groups such as alcohols, carbonyls, or even phosphonates β to the amine, complete selectivity for monoarylation was observed.

4 Mechanistic Questions

Despite our design element of using CO_2 as a directing group, we recognized that, under the reaction conditions, carbamate formation might not be favored. Although numerous Pd-carbamato complexes are known, they have typically been formed under basic conditions.[41] In our hands, the carbamate complexes were challenging to isolate. Attempted synthesis in situ during NMR experiments showed evidence of carbamate formation under acidic conditions, confirming that the carbamates could be accessed. Formation of these carbamate adducts in the presence of Pd gave different spectra, suggesting that Pd-carbamato complexes could be accessed even under acidic conditions.

Attempts to tease the intermediates out by mass spectrometry led to the observation of an interesting adduct involving two carbon dioxides, potentially implicating a unique nine-membered palladacycle (Scheme 6a) (a similar nine-membered metallacycle was recently supported computationally in another work).[42] Notably, under the optimized conditions, no α or β C–H activation of methyl groups (from a five-membered or six-membered palladacycle respectively) could be achieved, suggesting that if a *tran-*

sient carbamate is serving as a directing group, it is more likely to proceed through the larger ring intermediate. However, none of this confirmed the actual role of CO_2 in the reaction. An alternative role for CO_2 would be not as a directing group, but to disrupt catalytically inactive Pd-amine adducts.[43] In our hands, we found that dissolution of preformed Pd-amine adducts led to disproportionation, suggesting that CO_2 was not necessary to break up unreactive aggregates (Scheme 6b).



Scheme 6 Mechanistic experiments for the CO_2-mediated C–H activation of aliphatic and benzylamine substrates

To better assess the role of CO_2, we prepared the ammonium carbamate of both aliphatic amines and benzylamines, and found that better than substoichiometric arylation with regard to the CO_2 loading could be achieved (Scheme 6c), suggesting that it could be used substoichiometric in the reaction. Further studies demonstrated strong positive kinetic isotope effects for the aliphatic amine reaction (Scheme 6d), while a more moderate KIE of 1.5 was observed for the benzylamine reaction. It is noteworthy that running the reactions under deuterated solvent conditions led to no deuterium enrichment. Taken together, these experiments lend a great deal of credence that our initial design of carbamates as an in situ directing group as the cause for the observed reactivity.

5 Future Outlook

The use of CO_2 has the potential to revolutionize the directing groups that are used for C–H activation, as well as other transformations that require directing groups. This approach has the potential to be a viable directing group for installation of numerous new functional groups at otherwise inert C–H bonds. Additionally, while amines can react with CO_2, so too can other Lewis basic functional groups, including alcohols, thiols, and phosphines. This lays the foundation for carbon dioxide to serve as a *unified directing group* approach for C–H activation of multiple functional groups.

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References

(1) (a) Guo, X.; Facchetti, A.; Marks, T. J. *Chem. Rev.* **2014**, *114*, 8943. (b) Froidevaux, V.; Negrell, C.; Caillol, S.; Pascault, J.-P.; Boutevin, B. *Chem. Rev.* **2016**, *116*, 14181. (c) Allred, T. K.; Manoni, F.; Harran, P. G. *Chem. Rev.* **2017**, *117*, 11994. (d) Manallack, D. T.; Prankerd, R. J.; Yuriev, E.; Oprea, T. I.; Chalmers, D. K. *Chem. Soc. Rev.* **2013**, *42*, 485.
(2) (a) Tafazolian, H.; Samblanet, D. C.; Schmidt, J. A. R. *Organometallics* **2015**, *34*, 1809. (b) Huang, H.; Zhao, Y.; Yang, Y.; Zhou, L.; Chang, M. *Org. Lett.* **2017**, *19*, 1942. (c) Ichikawa, S.; Zhu, S.; Buchwald, S. L. *Angew. Chem. Int. Ed.* **2018**, *57*, 8714. (d) White, D. R.; Wolfe, J. P. *Chem. Eur. J.* **2017**, *23*, 5419. (e) Ariyarathna, J. P.; Wu, F.; Colombo, S. K.; Hillary, C. M.; Li, W. *Org. Lett.* **2018**, *20*, 6462.
(3) (a) He, J.; Wasa, M.; Chan, K. S. L.; Shao, Q.; Yu, J.-Q. *Chem. Rev.* **2017**, *117*, 8754. (b) Lyons, T. W.; Sanford, M. S. *Chem. Rev.* **2010**, *110*, 1147.
(4) Chen, W.; Ma, L.; Paul, A.; Seidel, D. *Nature Chem.* **2018**, *10*, 165.
(5) (a) Mack, J. B. C.; Gipson, J. D.; Du Bois, J.; Sigman, M. S. *J. Am. Chem. Soc.* **2017**, *139*, 9503. (b) Zultanski, S. L.; Zhao, J.; Stahl, S. S. *J. Am. Chem. Soc.* **2016**, *138*, 6416. (c) Kolotilo, N. V.; Sinitsa, A. A.; Rassukana, Yu. V.; Onys'ko, P. P. *Zh. Obshch. Khim.* **2006**, *76*, 1260. (d) Chuentragool, P.; Parasram, M.; Shi, Y.; Gevorgyan, V. *J. Am. Chem. Soc.* **2018**, *140*, 2465. (e) Chen, K.; Wang, D.; Li, Z.-W.; Liu, Z.; Pan, F.; Zhang, Y.-F.; Shi, Z.-J. *Org. Chem. Front.* **2017**, *4*, 2097.

(6) (a) Ping, Z. M.; Cabrera-Pardo, J. R.; Cadahía, J. P.; Gaunt, M. J. *Chem. Sci.* **2018**, *9*, 7628. (b) Nappi, M.; He, C.; Whitehurst, W. G.; Chappell, B. G. N.; Gaunt, M. J. *Angew. Chem. Int. Ed.* **2018**, *57*, 3178. (c) Smalley, A. P.; Cuthbertson, J. D.; Gaunt, M. J. *J. Am. Chem. Soc.* **2017**, *139*, 1412. (d) Willcox, D.; Chappell, B. G. N.; Hogg, K. F.; Calleja, J.; Smalley, A. P.; Gaunt, M. J. *Science* **2016**, *354*, 851.
(7) (a) Albert, J.; Ariza, X.; Calvet, T.; Font-Bardia, M.; Garcia, J.; Granell, J.; Lamela, A.; López, B.; Martinez, M.; Ortega, L.; Rodriguez, A.; Santos, D. *Organometallics* **2013**, *32*, 649. (b) Lazareva, A.; Daugulis, O. *Org. Lett.* **2006**, *8*, 5211.
(8) Haffemayer, B.; Gulias, M.; Gaunt, M. J. *Chem. Sci.* **2011**, *2*, 312.
(9) (a) Tan, P. W.; Haughey, M.; Dixon, D. J. *Chem. Commun.* **2015**, 4406. (b) Cai, G.; Fu, Y.; Li, Y.; Wan, X.; Shi, Z. *J. Am. Chem. Soc.* **2007**, *129*, 7666. (c) Dong, Z.; Wang, J.; Dong, G. *J. Am. Chem. Soc.* **2015**, *137*, 5887. (d) Feng, R.; Yao, J.; Liang, Z.; Liu, Z.; Zhang, Y. *J. Org. Chem.* **2013**, *78*, 3688.
(10) Sambiagio, C.; Schönbauer, D.; Blieck, R.; Dao-Huy, T.; Pototschnig, G.; Schaaf, P.; Wiesinger, T.; Zia, M. F.; Wencel-Delord, J.; Besset, T.; Maes, B. U. W.; Schnürch, M. *Chem. Soc. Rev.* **2018**, *47*, 6603.
(11) Zaitsev, V. G.; Shabashov, D.; Daugulis, O. *J. Am. Chem. Soc.* **2005**, *127*, 13154.
(12) (a) Shi, H.; Herron, A. N.; Shao, Y.; Shao, Q.; Yu, J.-Q. *Nature* **2018**, *558*, 581. (b) Shao, Q.; Wu, Q.-F.; He, J.; Yu, J.-Q. *J. Am. Chem. Soc.* **2018**, *140*, 5322. (c) He, J.; Shao, Q.; Wu, Q.; Yu, J.-Q. *J. Am. Chem. Soc.* **2017**, *139*, 3344.
(13) (a) Aguilera, E. Y.; Sanford, M. S. *Organometallics* **2018**, 10.1021/acs.organomet.8b00533. (b) Cabrera, P. J.; Lee, M.; Sanford, M. S. *J. Am. Chem. Soc.* **2018**, *140*, 5599. (c) Topczewski, J. J.; Cabrera, P. J.; Saper, N. I.; Sanford, M. S. *Nature* **2016**, *531*, 220.
(14) (a) Yan, S.-Y.; Han, Y.-Q.; Yao, Q.-J.; Nie, X.-L.; Liu, L.; Shi, B.-F. *Angew. Chem. Int. Ed.* **2018**, *57*, 9093. (b) Zhang, Z.-Z.; Han, Y.-Q.; Zhan, B.-B.; Wang, S.; Shi, B.-F. *Angew. Chem. Int. Ed.* **2017**, *56*, 13145. (c) Zhan, B.-B.; Li, Y.; Xu, J.-W.; Nie, X.-L.; Fan, J.; Jin, L.; Shi, B.-F. *Angew. Chem. Int. Ed.* **2018**, *57*, 5858.
(15) (a) Zhang, S.-Y.; He, G.; Zhao, Y.; Wright, K.; Nack, W. A.; Chen, G. *J. Am. Chem. Soc.* **2012**, *134*, 7313. (b) Zhang, S.-Y.; He, G.; Nack, W. A.; Zhao, Y.; Li, Q.; Chen, G. *J. Am. Chem. Soc.* **2013**, *135*, 2124. (c) Li, Q.; Zhang, S.-Y.; He, G.; Nack, W. A.; Chen, G. *Adv. Synth. Catal.* **2014**, *356*, 1544.
(16) (a) Han, J.; Zheng, Y.; Wang, C.; Zhu, Y.; Shi, D.-Q.; Zeng, R.; Huang, Z.-B.; Zhao, Y. *J. Org. Chem.* **2015**, *80*, 9297. (b) Liu, P.; Han, J.; Chen, C. P.; Shi, D. Q.; Zhao, Y. S. *RSC Adv.* **2015**, *5*, 28430.
(17) (a) St. John-Campbell, S.; Bull, J. A. *Org. Biomol. Chem.* **2018**, *16*, 4582. (b) Gandeepan, P.; Ackermann, L. *Chemistry* **2018**, *4*, 199. (c) Bhattacharya, T.; Pimparkar, S.; Maiti, D. *RSC Adv.* **2018**, *8*, 19456.
(18) Zhang, Y.-F.; Zhao, H.-W.; Wang, H.; Wei, J.-B.; Shi, Z.-J. *Angew. Chem. Int. Ed.* **2015**, *54*, 13686.
(19) (a) Jun, C.-H.; Kang, J.-B.; Kim, J.-Y. J. *Organomet. Chem.* **1993**, *458*, 193. (b) Jun, C.-H.; Han, J.-S.; Kang, J.-B.; Kim, S.-I. *J. Organomet. Chem.* **1994**, *474*, 183.
(20) (a) Xing, D.; Dong, G. *J. Am. Chem. Soc.* **2017**, *139*, 13664. (b) Mo, F.; Dong, G. *Science* **2014**, *345*, 68. (c) Zhang, F.-L.; Hong, K.; Li, T.-J.; Park, H.; Yu, J.-Q. *Science* **2016**, *351*, 252. (d) Wang, J.; Dong, C.; Wu, L.; Xu, M.; Lin, J.; Wei, K. *Adv. Synth. Catal.* **2018**, *360*, 3709. (e) Hong, K.; Park, H.; Yu, J.-Q. *ACS Catal.* **2017**, *7*, 6938.
(21) (a) Yang, K.; Li, Q.; Liu, Y.-B.; Ge, H.-B. *J. Am. Chem. Soc.* **2016**, *138*, 12775. (b) Chen, X.-Y.; Sorensen, E. J. *J. Am. Chem. Soc.* **2018**, *140*, 2789. (c) Chen, X.-Y.; Ozturk, S.; Sorensen, E. J. *Org. Lett.* **2017**, *19*, 1140.
(22) Bedford, R. B.; Limmert, M. E. *J. Org. Chem.* **2003**, *68*, 8669.
(23) (a) Dangel, B. D.; Godula, K.; Youn, S. W.; Sezen, B.; Sames, D. *J. Am. Chem. Soc.* **2002**, *124*, 11856. (b) Dangel, B. D.; Johnson, J. A.; Sames, D. *J. Am. Chem. Soc.* **2001**, *123*, 8149. (c) Johnson, J. A.; Sames, D. *J. Am. Chem. Soc.* **2000**, *122*, 6321.
(24) Xu, Y.; Young, M. C.; Wang, D.; Magness, D. M.; Dong, G. *Angew. Chem. Int. Ed.* **2016**, *55*, 9084.
(25) Liu, Y.; Ge, H. *Nature Chem.* **2017**, *9*, 26.
(26) Wu, Y.; Chen, Y.-Q.; Liu, T.; Eastgate, M. D.; Yu, J.-Q. *J. Am. Chem. Soc.* **2016**, *138*, 14554.
(27) Lin, H.; Wang, C.; Bannister, T. D.; Kamenecka, T. M. *Chem. Eur. J.* **2018**, *24*, 9535.
(28) Yada, A.; Liao, W.; Sato, Y.; Murakami, M. *Angew. Chem. Int. Ed.* **2017**, *56*, 1073.
(29) St. John-Campbell, S.; Ou, A. K.; Bull, J. A. *Chem. Eur. J.* **2018**, doi.org/10.1002/chem.201804515.
(30) (a) Luo, J.; Preciado, S.; Larrosa, I. *J. Am. Chem. Soc.* **2014**, *136*, 4109. (b) Font, M.; Quibell, J.; Perry, G. J. P.; Larrosa, I. *Chem. Commun.* **2017**, 3517. (c) Font, M.; Spencer, A. R. A.; Larrosa, I. *Chem. Sci.* **2018**, *9*, 7133.
(31) (a) Wang, H.; Dong, B.; Wang, Y.; Li, J.; Shi, Y. *Org. Lett.* **2014**, *16*, 186. (b) Gockel, S. N.; Hull, K. L. *Org. Lett.* **2015**, *17*, 3236. (c) Zhao, H.; Du, H.; Yuan, X.; Wang, T.; Han, W. *Green Chem.* **2016**, *18*, 5782.
(32) (a) Ren, W.; Yamane, M. *J. Org. Chem.* **2010**, *75*, 8410. (b) Iranpoor, N.; Firouzabadi, H.; Motevalli, S.; Talebi, M. *Tetrahedron* **2013**, *69*, 418.
(33) (a) Barcena, H.; Chen, P. *J. Chem. Educ.* **2016**, *93*, 202. (b) Hudson, R.; Ackerman, H. M.; Gallo, L. K.; Gwinner, A. S.; Krauss, A.; Sears, J. D.; Bishop, A.; Esdale, K. N.; Katz, J. L. *J. Chem. Educ.* **2017**, *94*, 480. (c) Baldwin, B. W.; Kuntzleman, T. S. *J. Chem. Educ.* **2018**, *95*, 620. (d) McKenzie, L. C.; Thompson, J. E.; Sullivan, R.; Hutchison, J. E. *Green Chem.* **2004**, *6*, 355.
(34) Kapoor, M.; Chand-Thakuri, P.; Maxwell, J. M.; Young, M. C. *J. Visualized Exp.* **2018**, *138*, e58281.
(35) Kapoor, M.; Liu, D.; Young, M. C. *J. Am. Chem. Soc.* **2018**, *140*, 6818.
(36) Coomber, C. E.; Benhamou, L.; Bučar, D.-K.; Smith, P. D.; Porter, M. J.; Sheppard, T. D. *J. Org. Chem.* **2018**, *83*, 2495.
(37) Leitner, W. *Acc. Chem. Res.* **2002**, *35*, 746.
(38) Hogg, K. F.; Trowbridge, A.; Alvarez-Pérez, A.; Gaunt, M. J. *Chem. Sci.* **2017**, *8*, 8198.
(39) Kapoor, M.; Chand-Thakuri, P.; Young, M. C. *ChemRxiv* **2018**, 7138088.
(40) Wang, J.; Li, R.; Dong, Z.; Liu, P.; Dong, G. *Nature Chem.* **2018**, *10*, 866.
(41) (a) Ozawa, F.; Ito, T.; Yamamoto, Y. *Chem. Lett.* **1979**, *8*, 735. (b) Anillo, A.; Dell'Amico, D. B.; Calderazzo, F.; Nardelli, M.; Pelizzi, G.; Rocchi, L. *J. Chem. Soc., Dalton Trans.* **1991**, 2845. (c) Srivastava, R. S.; Singh, G.; Nakano, M.; Osakada, K.; Ozawa, F.; Yamamoto, A. *J. Organomet. Chem.* **1993**, *451*, 221.
(42) Song, L.; Zhu, L.; Zhang, Z.; Ye, J.-H.; Yan, S.-S.; Han, J.-L.; Yin, Z.-B.; Lan, Y.; Yu, D.-G. *Org. Lett.* **2018**, *20*, 3776.
(43) Smalley, A. P.; Gaunt, M. J. *J. Am. Chem. Soc.* **2015**, *137*, 10632.