

Base Metal Catalysts for Photochemical C–H Borylation That Utilize Metal–Metal Cooperativity

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S Supporting Information

ABSTRACT: Heterobimetallic Cu–Fe and Zn–Fe complexes catalyze C–H borylation, a transformation that previously required noble metal catalysts. The optimal catalyst, (IPr)Cu–FeCp(CO)₂, exhibits efficient activity at 5 mol% loading under photochemical conditions, shows only minimal decrease in activity upon reuse, and is able to catalyze borylation of a variety of arene substrates. Stoichiometric reactivity studies are consistent with a proposed mechanism that exploits metal–metal cooperativity and showcases bimetallic versions of the classical organometallic processes, oxidative addition and reductive elimination.

One major goal toward attaining a sustainable and environmentally responsible paradigm for chemical synthesis is to replace catalyst materials based on noble metals (toxic, expensive, and scarce) with those based on base metals (nontoxic, inexpensive, and earth-abundant).^{1,2} However, because many catalytic transformations rely on two-electron redox processes (e.g., oxidative addition and reductive elimination) inherent to noble metal chemistry, the one-electron redox chemistry of base metals tends to lack the predictability, efficiency, and generality necessary for widespread use in homogeneous catalysis by direct replacement.³

Several strategies for achieving two-electron redox catalysis with earth-abundant elements have been advanced,⁴ including metal–ligand cooperativity^{3,5} and Lewis acid–base cooperativity,⁶ but their applications in catalysis have been limited to relatively simple transformations such as hydrogenation^{6,7} and dehydrogenation⁸ reactions. An alternate strategy involves exploiting metal–metal cooperativity⁹ between two different base metals that individually prefer one-electron redox processes in order to achieve net two-electron redox chemistry reminiscent of a single-site noble metal catalyst (Figure 1A).¹⁰ In this report, we show that this strategy can be used to develop heterobimetallic Cu–Fe and Zn–Fe complexes as efficient, robust, and versatile catalysts for C–H borylation, a sophisticated catalytic transformation of established¹¹ importance to organic synthesis that previously required use of noble metals such as Rh or Ir.

Prior to the development of noble metal catalysts for C–H borylation,¹¹ stoichiometric C–H borylation had been demonstrated under photochemical conditions with base metal systems including the boryliron complex, FpBcat (Fp = Fe(η^5 -C₅H₅)(CO)₂, cat = catecholates).¹² Catalytic turnover with this system was not achieved because conversion of the

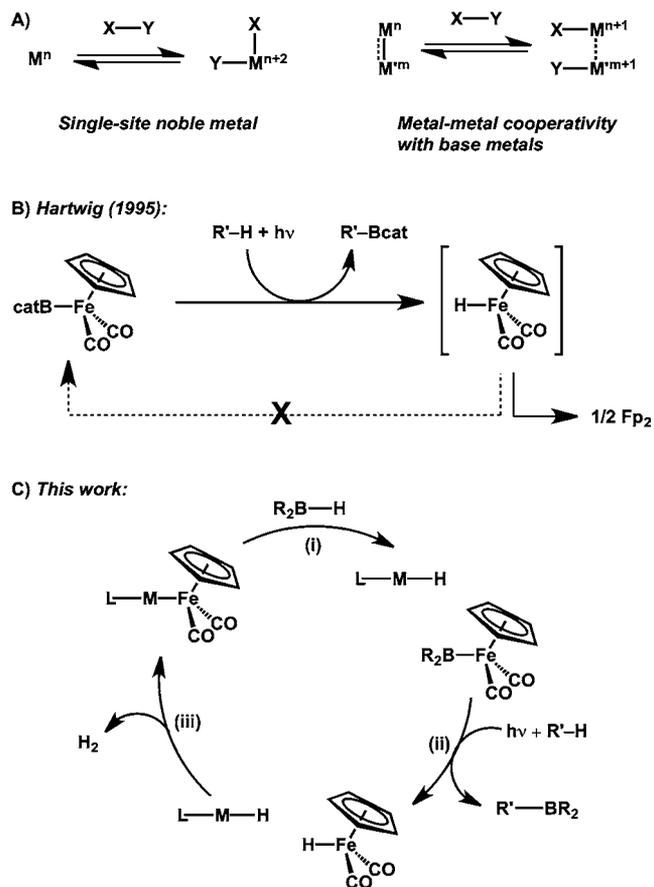


Figure 1. (A) Two-electron redox at single-site noble metal (left) and heterobimetallic base metal (right) cores. (B) Stoichiometric C–H borylation observed previously (see ref 12; Fp = Fe(η^5 -C₅H₅)(CO)₂; cat = catecholates). (C) Proposed mechanism for catalytic C–H borylation consisting of (i) bimetallic oxidative addition, (ii) C–H functionalization, and (iii) bimetallic reductive elimination.

immediate byproduct of C–H borylation, FpH, to a boryliron species likely would involve two-electron redox pathways unavailable to a single-site Fe system (Figure 1B). Instead, FpH rapidly converted to inactive Fp₂ by a one-electron (per Fe) redox process under the reaction conditions.¹² Although previously it was thought necessary to utilize single-site noble metal systems to achieve catalytic C–H borylation,¹³ our results show that catalysis can be achieved with the Fp-based

Received: August 27, 2013

Published: September 27, 2013

boryliron system by exploiting a mechanistic paradigm involving metal–metal cooperativity (Figure 1C).

Using pinacolborane, HBpin (pin = pinacolate), as a borylating reagent in neat C_6D_6 , several Cu–Fp and Zn–Fp complexes synthesized in our laboratory^{14,15} from readily available building blocks were successful in generating C_6D_5 Bpin catalytically (Figure 2 and Table S1).^{16,17} The optimal catalyst was (IPr)Cu–Fp (IPr = *N,N'*-bis(2,6-diisopropylphenyl)imidazol-2-ylidene), which at catalyst loadings as low as 5 mol% produced C_6D_5 Bpin in 71% yield after 24 h at room temperature under UV irradiation. Successful

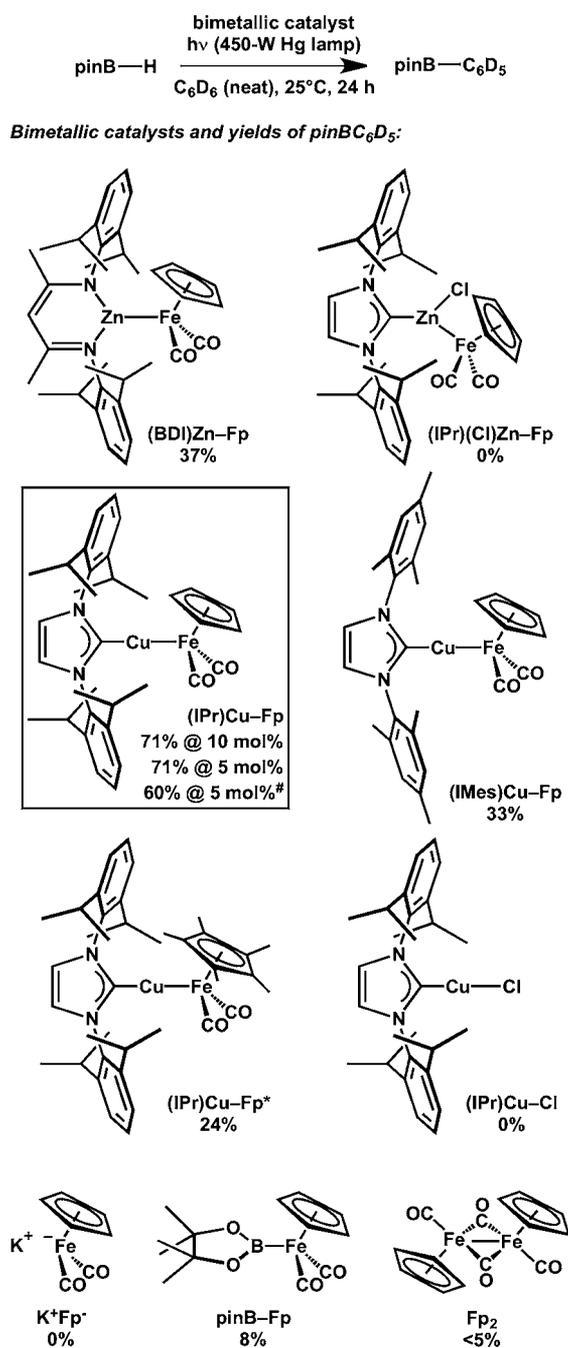


Figure 2. Selected catalyst optimization results for the photochemical C–D borylation of benzene- d_6 . Catalyst loadings were 10 mol% unless otherwise indicated. Full optimization results are presented in Table S1. # = yield for second consecutive use.

borylation also was achieved with catecholborane (HBcat) and bis(pinacolato)diboron ($B_2\text{pin}_2$) as boron sources, albeit with lower product yields (Table S1).¹⁸ (IPr)Cu–Fp is a highly robust catalyst under these conditions and can be reused by adding additional substrate to a reaction solution after a catalytic run without a significant decrease in efficiency (Figure 2 and Table S2). On the other hand, the homobimetallic species Fp_2 and the boryliron complex $Fp\text{Bpin}$ produced only trace amounts of borylated product under catalytic conditions, and no product was observed when the monometallic complexes (IPr)Cu–Cl or K^+Fp^- were used as catalysts. Metal–metal cooperativity inherent to heterobimetallic complexes such as (IPr)Cu–Fp apparently is necessary to achieve this catalytic C–H functionalization. Although metal–metal cooperativity has been used to develop catalytic transformations previously,^{9,10} it is rare to discover cases where the catalytic reaction cannot also be achieved with the individual monometallic components of the bimetallic system.^{15,19}

In addition to benzene, other aromatic substrates also were borylated using (IPr)Cu–Fp as a catalyst. The selectivity of $C(\text{sp}^2)\text{--H}$ borylation under these conditions is dictated by steric factors, akin to Ir-catalyzed borylation reactions.¹¹ For example, borylation of *meta*-xylene with HBpin proceeded selectively at the 5-position (Figure 3), which under standard

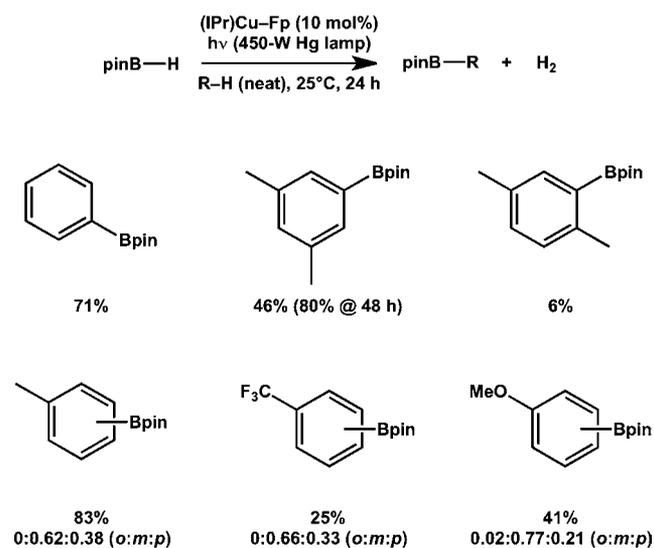


Figure 3. Substrate scope and regioselectivity of photochemical C–H borylation catalyzed by (IPr)Cu–Fp.

aromatic substitution conditions is the least reactive position. Attempted borylation of *para*-xylene produced only 6% conversion to borylated product due to the lack of sterically accessible $C(\text{sp}^2)\text{--H}$ bonds.²⁰ Borylation of toluene proceeded in high yield, with a ratio of *ortho:meta:para* functionalization of 0:0.62:0.38. Borylation of anisole and α,α,α -trifluorotoluene proceeded with lower product yields of 41% and 25%, respectively, and with regioselectivities closely mirroring that of toluene (Figure 3). Only in the case of anisole was *ortho*-borylation detected, likely due to the coordinating ability of the methoxy substituent to direct C–H activation.^{21,22}

A plausible mechanism for heterobimetallic C–H borylation, shown in Figure 1C, consists of three main stages: (i) B–H bimetallic oxidative addition with metal–metal bond cleavage; (ii) photochemical C–H borylation by the resulting boryliron intermediate; and (iii) H–H bimetallic reductive elimination

with metal–metal bond formation. Preliminary mechanistic studies with (IPr)Cu-Fp, detailed below and summarized in Figure 4, demonstrated the feasibility of each of these individual reaction stages.

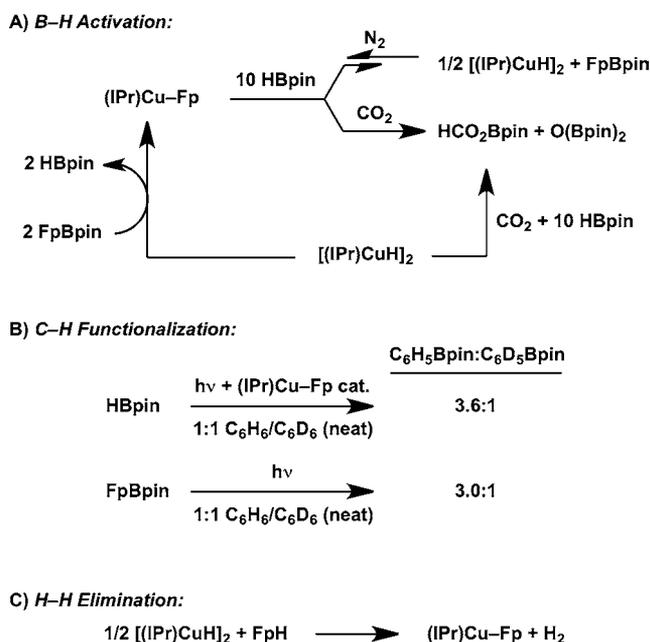


Figure 4. Mechanistic studies for the proposed elementary steps: (A) reversible B–H activation, (B) C–H functionalization, and (C) H_2 elimination.

Consistent with our previous reactivity studies,¹⁴ we expected that B–H activation of HBpin by (IPr)Cu-Fp would yield $[(IPr)CuH]_2$, a known copper hydride dimer,²³ along with FpBpin. To our surprise, mixing together (IPr)Cu-Fp and HBpin (10 equiv) in benzene- d_6 in the absence of UV irradiation produced no observable reaction, even at elevated temperatures. Furthermore, mixing together $[(IPr)CuH]_2$ and FpBpin rapidly generated (IPr)Cu-Fp and HBpin. However, a rapid reaction was observed when (IPr)Cu-Fp and HBpin were mixed under a CO_2 atmosphere. A roughly equimolar mixture of $O(Bpin)_2$ and HCO_2Bpin resulted, the latter of which is the known product of CO_2 hydroboration by $[(IPr)CuH]_2$.²⁴ We also note that when monitoring the photochemical borylation of C_6D_6 by ^{11}B NMR spectroscopy, rapid H/D scrambling was observed at the H_B -Bpin position (Figure S2). This process occurred much faster than C–D borylation and was likely the result of the FpBpin intermediate reacting with hydrogen- d_1 produced from initial C–D borylation.¹² Collectively (Figure 4A), these data indicate that bimetallic oxidative addition of HBpin by (IPr)Cu-Fp is an equilibrium process that lies to the Cu–Fe side, and that small concentrations of $[(IPr)CuH]_2$ and FpBpin account for the observed reactivity. Consistent with these observations, (IPr)Cu-Fp was observed as the sole catalytic resting state by 1H NMR spectroscopy when conducting catalytic reactions in C_6D_6 .

Given these results regarding B–H activation, we propose that FpBpin is the active borylating reagent in solution. Indeed, C–H borylation by the related species, FpBcat, has been studied in detail by Hartwig and co-workers.¹² As support for FpBpin being the active borylating reagent present in our catalytic system, first we confirmed that FpBpin is indeed capable of stoichiometric benzene borylation (86% yield). We

also note (Figure 4B) that a competition experiment using a 1:1 mixture of C_6H_6 and C_6D_6 indicated a kinetic isotope effect (KIE) of 3.6 for catalytic C–H borylation by (IPr)Cu-Fp, which matches closely the KIEs of 3.3 and 3.0 observed for stoichiometric C–H borylation by FpBcat^{12b} and FpBpin, respectively, of the same mixture. Assuming C–H borylation by FpBpin produces FpH as the immediate byproduct, it is further reasonable to assume that protic²⁵ FpH would combine with hydridic^{23,24} $[(IPr)CuH]_2$ to release H_2 via bimetallic reductive elimination. To confirm the feasibility of this elementary step (Figure 4C), we mixed together *in situ*-generated FpH and $[(IPr)CuH]_2$ and observed rapid formation of (IPr)Cu-Fp by 1H NMR spectroscopy.

Together, our data indicate that catalytic C–H borylation, a transformation that previously required noble metal catalysts,¹¹ can be achieved with base metal catalysts by using a mechanistic paradigm that depends on intimate cooperativity between two closely associated yet distinct base metal sites. Because the proposed mechanism for this transformation involves bimetallic versions of classical organometallic reaction steps such as oxidative addition and reductive elimination, we are confident that this catalyst design strategy can be generalized to approach other important catalytic reactions that typically require noble metals to proceed.

■ ASSOCIATED CONTENT

📄 Supporting Information

Synthetic details, full catalytic results, stoichiometric studies, NMR spectra, and crystallographic data. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

Financial support was provided by start-up funds from the UIC Department of Chemistry and by a Pilot Research Grant from the UIC Campus Research Board. Dan McIlheny and Ben Ramirez assisted with NMR spectroscopy. John (Art) Anderson assisted with GC-MS measurements. Upul Jayarthne synthesized (IPr)CuFe(η^5 - C_3Me_5)(CO)₂ used for catalyst screening.

■ REFERENCES

- (1) Bullock, R. M., Ed. *Catalysis Without Precious Metals*; Wiley-VCH: Weinheim, 2010.
- (2) Friedman, D.; Masiangoli, T.; Olson, S. *The Role of the Chemical Sciences in Finding Alternatives to Critical Resources: A Workshop Summary*; National Academies Press: Washington, DC, 2012.
- (3) Chirik, P. J.; Wieghardt, K. *Science* **2010**, *327*, 794–795.
- (4) (a) Czaplík, W. M.; Mayer, M.; Cvengroš, J.; von Wangelin, A. J. *Chem. Sus. Chem.* **2009**, *2*, 396–417. (b) Bolm, C.; Legros, J.; Le Pailh, J.; Zani, L. *Chem. Rev.* **2004**, *104*, 6217–6254.
- (5) (a) Haneline, M. R.; Heyduk, A. F. *J. Am. Chem. Soc.* **2006**, *128*, 8410–8411. (b) Gunanathan, C.; Milstein, D. *Acc. Chem. Res.* **2011**, *44*, 588–602.
- (6) Stephan, D. W.; Erker, G. *Angew. Chem., Int. Ed.* **2009**, *49*, 46–76.
- (7) (a) Tondreau, A. M.; Atienza, C. C. H.; Weller, K. J.; Nye, S. A.; Lewis, K. M.; Delis, J. G. P.; Chirik, P. J. *Science* **2012**, *335*, 567–570. (b) Langer, R.; Diskin-Posner, Y.; Leitius, G.; Shimon, L. J. W.; Ben-David, Y.; Milstein, D. *Angew. Chem., Int. Ed.* **2011**, *50*, 9948–9952.

(8) (a) Boddien, A.; Mellmann, D.; Gartner, F.; Jackstell, R.; Junge, H.; Dyson, P. J.; Laurenczy, G.; Ludwig, R.; Beller, M. *Science* **2011**, *333*, 1733–1736. (b) Helm, M. L.; Stewart, M. P.; Bullock, R. M.; DuBois, M. R.; DuBois, D. L. *Science* **2011**, *333*, 863–866. (c) Myers, T. W.; Berben, L. A. *J. Am. Chem. Soc.* **2013**, *135*, 9988–9990. (d) Dunn, N. L.; Ha, M.; Radosevich, A. T. *J. Am. Chem. Soc.* **2012**, *134*, 11330–11333.

(9) (a) Pérez-Temprano, M. H.; Casares, J. A.; Espinet, P. *Chem.—Eur. J.* **2012**, *18*, 1864–1884. (b) Powers, D. C.; Ritter, T. *Acc. Chem. Res.* **2012**, *45*, 840–850. (c) Radlauer, M. R.; Day, M. W.; Agapie, T. *J. Am. Chem. Soc.* **2012**, *134*, 1478–1481. (d) Reed, S. A.; White, M. C. *J. Am. Chem. Soc.* **2008**, *130*, 3316–3318.

(10) (a) Mulzer, M.; Whiting, B. T.; Coates, G. W. *J. Am. Chem. Soc.* **2013**, *135*, 10930–10933. (b) Uyeda, C.; Peters, J. C. *J. Am. Chem. Soc.* **2013**, *135*, 12023–12031. (c) Ogo, S.; Ichikawa, K.; Kishima, T.; Matsumoto, T.; Nakai, H.; Kusaka, K.; Ohhara, T. *Science* **2013**, *339*, 682–684.

(11) Mkhaliid, I. A. I.; Barnard, J. H.; Marder, T. B.; Murphy, J. M.; Hartwig, J. F. *Chem. Rev.* **2010**, *110*, 890–931.

(12) (a) Waltz, K. M.; He, W.; Muhoro, C.; Hartwig, J. F. *J. Am. Chem. Soc.* **1995**, *117*, 11357–11358. (b) Waltz, K. M.; Muhoro, C. N.; Hartwig, J. F. *Organometallics* **1999**, *18*, 3383–3393.

(13) (a) Hartwig, J. F. *Acc. Chem. Res.* **2012**, *45*, 864–873. (b) Cho, J.-Y.; Tse, M. K.; Holmes, D.; Maleczka, R. E.; Smith, M. R., III *Science* **2002**, *295*, 305–308.

(14) Jayarathne, U.; Mazzacano, T. J.; Bagherzadeh, S.; Mankad, N. P. *Organometallics* **2013**, *32*, 3986–3992.

(15) For a review of M-Fp complexes, see: Gade, L. H. *Angew. Chem., Int. Ed.* **2000**, *39*, 2658–2678.

(16) For a review of C–H functionalization using Fe catalysis, see: Sun, C.-L.; Li, B.-J.; Shi, Z.-J. *Chem. Rev.* **2011**, *111*, 1293–1314. See also ref 17.

(17) (a) Hennessy, E. T.; Betley, T. A. *Science* **2013**, *340*, 591–595. (b) Chen, M. S.; White, M. C. *Science* **2007**, *318*, 783–787. (c) Paradine, S. M.; White, M. C. *J. Am. Chem. Soc.* **2012**, *134*, 2036–2039.

(18) B₂pin₂ is converted to HBpin under the reaction conditions, likely by intermediate formation of (IPr)Cu-Bpin and subsequent reaction with FpH.

(19) Zhou, W.; Napoline, J. W.; Thomas, C. T. *Eur. J. Inorg. Chem.* **2011**, *13*, 2029–2033.

(20) Borylation of the benzylic position also was observed (<5%).

(21) A *o:m:p* ratio of 0.27:0.43:0.29 was observed for the stoichiometric borylation of anisole by FpBcat;¹² the difference in selectivity is likely dictated by the differing sizes of cat versus pin. The mass balance from anisole borylation consisted of pinBOBpin and an unknown product, possibly PhOCH₂Bpin.

(22) An attempt at using *p*-xylene as an inert solvent under these conditions for the borylation of benzene (10 equiv relative to HBpin) resulted in 24% conversion (roughly 1:1 borylation of benzene and *p*-xylene).

(23) Mankad, N. P.; Laitar, D. S.; Sadighi, J. P. *Organometallics* **2004**, *23*, 3369–3371.

(24) Shintani, R.; Nozaki, K. *Organometallics* **2013**, *32*, 2459.

(25) Estes, D. P.; Vannucci, A. K.; Hall, A. R.; Lichtenberger, D. L.; Norton, J. R. *Organometallics* **2011**, *30*, 3444–3447.