ACS Catalysis

Subscriber access provided by Universiteit Utrecht

Letter

Ortho-Selective C–H Borylation of Aromatic Ethers with Pinacol-borane by Organo Rare-Earth Catalysts

Can Xue, Yong Luo, Huai-Long Teng, Yuanhong Ma, Masayoshi Nishiura, and Zhaomin Hou

ACS Catal., **Just Accepted Manuscript** • DOI: 10.1021/acscatal.8b01364 • Publication Date (Web): 30 Apr 2018

Downloaded from http://pubs.acs.org on May 1, 2018

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 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 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.

ACS Publications

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.

Ortho-Selective C-H Borylation of Aromatic Ethers with Pinacol-borane by Organo Rare-Earth Catalysts

Can Xue,[†] Yong Luo,[‡] Huailong Teng,[†] Yuanhong Ma,[‡] Masayoshi Nishiura[†,‡] and Zhaomin Hou*[,†,‡]

[†] Advanced Catalysis Research Group, RIKEN Center for Sustainable Resource Science, 2-1 Hirosawa, Wako, Saitama 351-0198, Japan

[‡] Organometallic Chemistry Laboratory, RIKEN Cluster for Pioneering Research, 2-1 Hirosawa, Wako, Saitama 351-0198, Japan

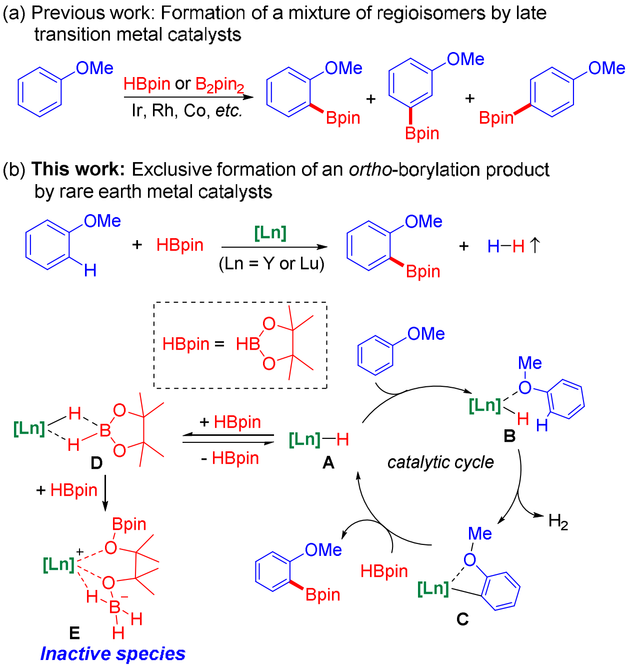
ABSTRACT: The regioselective C–H borylation of aromatic ethers such as anisoles is of much interest and importance, but has remained a challenge to date. We report herein the catalytic *ortho*-selective C–H borylation of a wide range of aromatic ethers with pinacolborane (HBpin) by rare-earth metallocene complexes. This protocol offers an efficient and straightforward route for the synthesis of a variety of borylated aromatic ether derivatives. A proper metal/ligand combination for the rare-earth metal catalysts was found to be critically important to promote this transformation.

KEYWORDS: Anisole, ortho-borylation, C-H activation, rare-earth metallocene, anisyl complex, metal hydride, metal-ligand combination

The direct C–H borylation of arenes with HBpin or B_2pin_2 by transition metal catalysts has attracted extensive attention in recent years, because this transformation offers an efficient and straightforward route for the synthesis of aryl boronates that can serve as useful precursors for diverse chemical transformations.[1,2] Aromatic ethers such as anisoles are important structural motifs in a large number of natural products, pharmaceuticals, and functional materials.[3] Therefore, the direct C–H borylation of aromatic ethers is of great interest and significance. However, a big challenge in the catalytic C–H borylation of aromatic ethers is the control of regioselectivity. The C–H borylation of anisoles with HBpin and B_2pin_2 by several late transition metal catalysts such as Ir, Rh and Co complexes has been sporadically reported in the literature, which usually gave a mixture of *para*-, *meta*-, and *ortho*-regioisomers of the borylation products (Scheme 1a).[4] The direct *ortho*-selective C–H borylation of anisoles has remained unknown to date. This is most likely due to steric influence and a lack of suitable catalysts that can effectively interact with an ether group to direct *ortho*-selective C–H activation and borylation without being deactivated by a borylation agent such as HBpin.

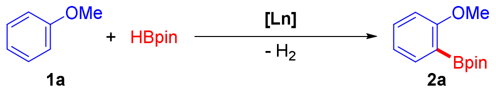
We have recently shown that some organo rare-earth (group 3 and lanthanide) metal complexes such as $Me_2Si(C_5Me_4)(N^tBu)Sc(CH_2C_6H_4NMe_2\text{-}o)$ and $(C_5Me_5)Sc(CH_2C_6H_4NMe_2\text{-}o)_2$ can serve as efficient catalysts for the *ortho*-selective C–H silylation[5] and alkylation[6] of anisoles. The exclusive *ortho*-selectivity was due to the affinity (oxophilicity) of rare-earth metal ions to an ether oxygen atom, which can effectively direct *ortho* C–H activation of an anisole unit. In principle, the *ortho*-selective C–H borylation of anisole could be achieved in a catalytic fashion, if a rare earth metal hydride species like **A** regioselectively activates (deprotonates) an *ortho* C–H bond of anisole followed by borylation of the resulting anisyl species like **C** through σ-bond metathesis with HBpin (see Scheme 1b). However, the rare-earth metal hydride species like **A** could also react with HBpin to irreversibly yield an inactive zwitterion compound like **E**[7] via ring-opening of the pinacolatoboron unit because of the strong oxophilicity of rare earth metal ions. Obviously, to make the catalytic C–H borylation operative, it is necessary to search for suitable catalysts that can show much higher activity toward anisole (to give **B** and **C**) than toward HBpin (to give **E**).

Scheme 1. Catalytic C–H Borylation of Anisole



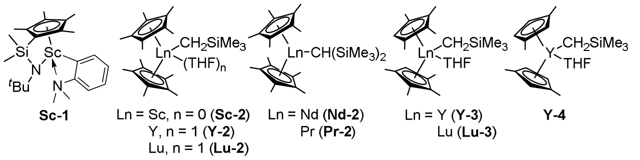
We report herein that the catalytic *ortho*-selective C–H borylation of a wide range of anisole compounds with HBpin can be achieved by using organo rare-earth metal complexes with an appropriate metal/ligand combination. This protocol constitutes the first example of *ortho*-selective C–H borylation of anisoles and offers an efficient route for the synthesis of a new family of *ortho*-borylated aromatic ether derivatives.

Table 1. C–H Borylation of Anisole with HBpin by Rare Earth Catalysts Bearing Different Ligands[a]



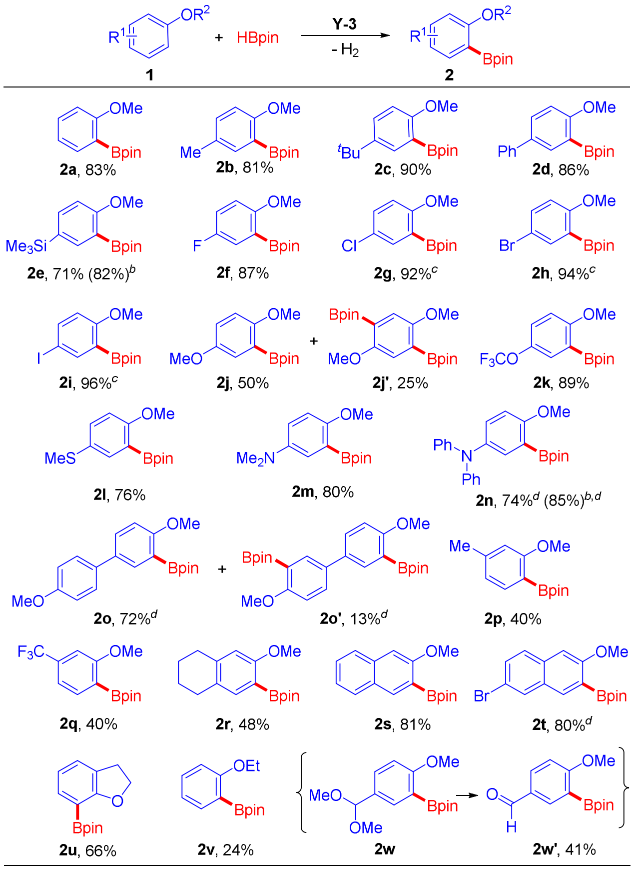
Entry	[Ln]	Solvent	Temp. (°C)	Yield of **2a** (%)[b]
1	**Sc-1**	Toluene	100	N.D.[c]
2	**Sc-2**	Toluene	100	7
3	**Y-2**	Toluene	100	36
4	**Lu-2**	Toluene	100	11
5	**Nd-2**	Toluene	100	2
6	**Pr-2**	Toluene	100	2
7	**Y-3**	Toluene	100	80
8	**Lu-3**	Toluene	100	80
9	**Y-4**	Toluene	100	Trace
10	**Y-3**	Hexane	100	85 (83)[d]
11	**Y-3**	Hexane	80	50

[a] Reaction conditions: **1a** (0.2 mmol), HBpin (0.22 mmol), [Ln] (10 mol%), solvent (2 mL). [b] Yield determined by ^{1}H NMR with CH_2Br_2 as an internal standard, unless otherwise noted. [c] Not detected. [d] Isolated yield.



At first, we examined a series of rare-earth complexes bearing different Cp ligands for the reaction of anisole (**1a**) with HBpin at 100 ºC in toluene. Some representative results are shown in Table 1. The half-sandwich scandium complex **Sc-1** showed no catalytic activity for the C–H borylation of anisole (Table 1, entry 1), although it was highly active for the C–H silylation of anisole with $PhSiH_3$ under the similar conditions.[5] We presumed that the lack of activity of **Sc-1** for the C–H borylation reaction is probably due to the steric openness (constrained geometry) around the metal center, which may allow a hydride species (like **A**) to react with HBpin to give a zwitterion compound (like **E**) (see Scheme 1b and *vide infra*). To suppress this possible deactivation process, we then examined a series of rare-earth metallocene complexes bearing two sterically demanding C_5Me_5 ligands (Table 1, entries 2-6). Among these metallocene complexes, the yttrium complex **Y-2** showed the best performance, although it gave only a moderate yield (36%) of the target borylation product **2a** (Table 1, entry 3). When the C_5Me_5 ligands were replaced by two slightly less bulkier C_5Me_4 ligands (**Y-3** and **Lu-3**), the desired *ortho* C–H borylation product **2a** was obtained in a much higher yield (80%) (Table 1, entries 7 and 8). The use of a further smaller ligand C_5Me_2 (**Y-4**) completely deactivated the catalyst (Table 1, entry 9). These results demonstrate that the catalytic activity for the present C–H borylation reaction is significantly influenced by both the metal ion and the supporting ligands of the catalysts, and a proper metal/ligand combination is critically important to promote the C–H borylation reaction. The use of hexane instead of toluene as a solvent with **Y-3** as a catalyst gave a further higher yield of **2a** (85%) under the same conditions (Table 1, entry 10). The reaction at a lower temperature (80 ºC) gave a much lower yield (50%) (Table 1, entry 11).

Table 2. *Ortho*-Selective C–H Borylation of Aromatic Ethers by a Rare Earth Metallocene Catalyst[a]

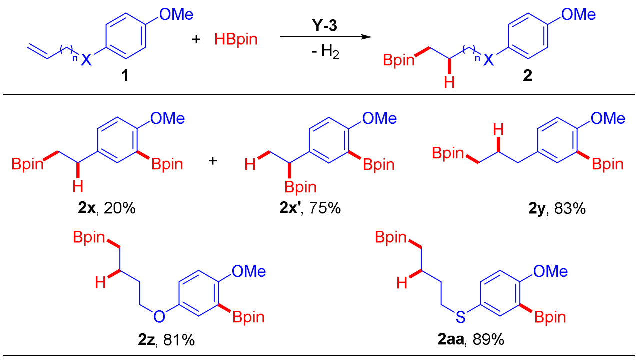


[a] Reaction conditions: **1** (0.2 mmol), HBpin (0.22 mmol), **Y-3** (10 mol%), hexane (4 mL), 100 °C, 24 h, isolated yield, unless otherwise noted. [b] **Lu-3** (10 mol%), NMR yield. [c] **Y-3** (5 mol%). [d] Toluene (4 mL).

With the optimized reaction conditions in hand, we next investigated the scope of aromatic ethers. Some representative results are summarized in Table 2. The *para*-methyl-, *tert*-butyl-, phenyl-, and trimethylsilyl-substituted anisoles were all selectively *ortho*-borylated by **Y-3** or **Lu-3** in hexane at 100 ºC, giving the desired products **2b-2e** in high yields (71–90%). Halide (F, Cl, Br, I) substituents were compatible with the catalyst, exclusively affording the corresponding halogenated anisyl boronate products **2f-2i** in excellent yields (87–96%). In the case of 1,4-dimethoxybenzene, the monoborylated product **2j** was obtained as a major product in 50% isolated yield together with the diborylated product **2j'** (25%). In the cases of 4-trifluoromethoxy-, 4-methylthio-, 4-dimethylamino-, and 4-

diphenylamino-substituted anisoles, the borylation reaction exclusively occurred at an ortho position of the MeO group, giving the corresponding functionalized anisyl boronate products **2k-2n** in 74–89% isolated yields.[8] The reaction of 4,4'-dimethoxybiphenyl with HBpin afforded the monoborylated product **2o** in 72% yield together with the diborylated product **2o'** as a minor product (13%). In the case of *meta*-substituted anisoles, the C–H borylation reaction took place exclusively at the less sterically demanding *ortho*-position albeit with lower conversion due to steric influence (see **2p–2r**). *β*-Methoxynaphthalenes could also be efficiently *ortho*-borylated (see **2s** and **2t**). The borylation of 2-methylanisole with HBpin did not take place under the same conditions, probably due to steric influence similar to the case of silylation.[5] However, 2,3-dihydrobenzofuran was efficiently borylated with HBpin to afford the desired product **2u** in 66% isolated yield, although its silylation reactivity was poor.[5] Ethoxybenzene (phenetole) was suitable for this reaction, but its conversion was much lower than that of anisole due to steric hindrance. Dimethyl acetal could survive the catalytic borylation conditions, affording the corresponding aldehyde-substituted anisyl boronate product **2w'** in moderate yield after silica gel chromatography.

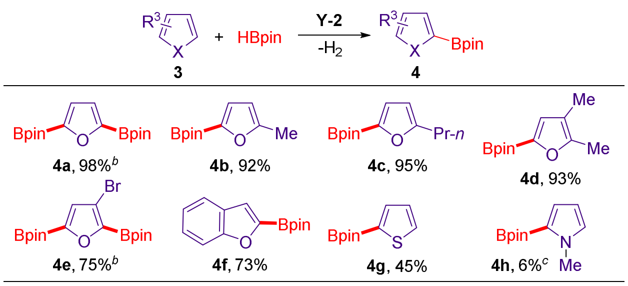
Table 3. Borylation of Aromatic Ethers Bearing Alkene Substituents[a]



[a]Reaction conditions: **1** (0.2 mmol), HBpin (0.44 mmol), **Y-3** (10 mol%), hexane (4 mL), 100 °C, 24 h, isolated yield.

In the case of anisole derivatives containing an alkene substituent, both the C=C double bond hydroboration and C–H borylation took place, affording the corresponding unique diborylation products (such as **2x–2aa**) in high yields (Table 3).[9,10]

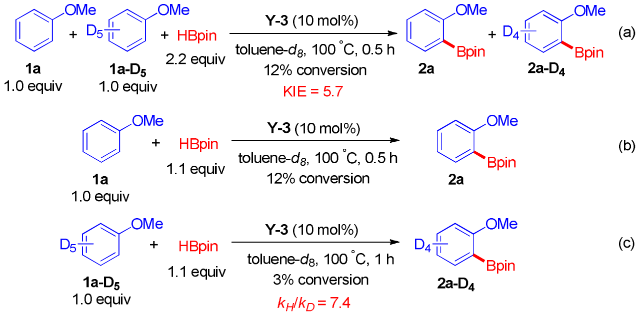
Table 4.C–H Borylation of Aromatic Heterocycles by Y-2[a]



[a]Reaction conditions: **3** (0.2 mmol), HBpin (0.22 mmol), **Y-2** (5 mol%), octane (2 mL), 80 °C, 24 h, isolated yield, unless otherwise noted. [b]HBpin (0.44 mmol). [c]NMR yield.

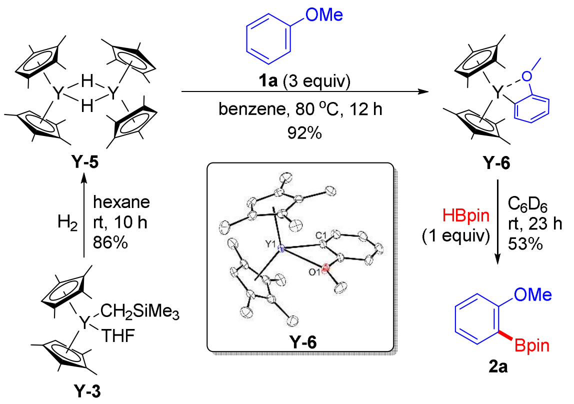
In the case of cyclic aromatic ethers such as furans, the C_5Me_4-ligated complex **Y-3** showed no catalytic activity for the C–H borylation with HBpin. In sharp contrast, the more sterically demanding C_5Me_5-ligated analogue **Y-2** showed high activity for the *ortho* C–H borylation of furans under the similar conditions (Table 4).[11] The reaction of furan with 2.2 equiv. of HBpin in the presence of 5 mol % of **Y-2** in octane at 80 ºC afforded the 2,5-diborylated furan product **4a** in 98% yield. In the case of 2-methyl-, 2-propyl-, and 2,3-dimethyl-substituted furans, the C–H borylation proceeded exclusively at the 5-position to give the monoborylation products **4b–4d** in excellent yields (92–95%). The reaction of 3-bromofuran with HBpin selectively afforded the 2,5-diborylation product **4e**, with the bromide substituent remaining intact. In the case of benzofuran, the reaction took place regioselectively at the 2-position, affording the 2-borylated benzofuran derivative **4f** in 73% isolated yield. Thiophene could also be borylated with HBpin by **Y-2**, which gave the corresponding monoborylation product **4g** in 45% yield. *N*-Methylpyrrole was less effective for the present borylation reaction probably due to steric hindrance.

Scheme 2. Kinetic Isotope Effect (KIE) Experiments



The reaction of deuterated anisole **1a-D$_5$** with HBpin catalyzed by **Y-3** afforded the C–D borylation product **2a-D$_4$**, in which no D-H exchange was observed. The reaction of a 1:1 mixture of **1a** and **1a-D$_5$** with HBpin showed a significant kinetic isotope effect (KIE = 5.7) (Scheme 2a; see also Fig. S1). The relative ratio of the initial rates of the two side-by-side reactions using **1a** and **1a-D$_5$**, respectively, was determined to be $k_H/k_D = 7.4$ (Scheme 2b,c; see also Fig. S2). These results suggest that C–H activation is involved in the rate-determining step of this transformation.

Scheme 3. Stoichiometric Reactions of An Yttrium Hydride Complex Y-5 with Anisole and HBpin



To gain more information on the mechanistic aspects of the catalytic *ortho* C–H borylation, some stoichiometric reactions were carried out. The reaction of the alkyl complex **Y-3** with HBpin in C_6D_6 took place rapidly at room temperature, possibly yielding an yttrium hydride species.[9,12] However, attempts to isolate a pure product from this reaction were not successful, possibly due to further reactions with HBpin as shown in Scheme 1b.[7] To confirm if an yttrium hydride species is involved in the present catalytic C–H borylation reaction, we then synthesized a well-defined yttrium hydride complex **Y-5** by the reaction of **Y-3** with H_2[13] and examined its reactivity (Scheme 3). The reaction of **Y-5** with anisole at 80 °C afforded the *ortho*-metalated anisyl complex **Y-6** in 92% yield, which was structurally characterized by an X-ray crystallographic study.[14] The reaction of **Y-6** with HBpin at room temperature afforded the *ortho*-borylated anisole derivative **2a** in 53% yield. Both the hydride complex **Y-5** and the anisyl complex **Y-6** afforded **2a** in yields comparable to that with **Y-3** in the catalytic reaction of anisole with HBpin. These results strongly suggest that an yttrium hydride species such as **Y-5** (equivalent to **A** in Scheme 1b), which could be generated by the reaction of **Y-3** with HBpin,[9,12] should be a true catalyst species in the catalytic cycle of the C–H borylation of anisole with HBpin (see Scheme 1b).

In summary, we have achieved for the first time the catalytic *ortho*-selective C–H borylation of a wide range of aromatic ethers with HBpin by using rare-earth metallocene complexes bearing an appropriately tuned ligand environment (such as **Y-3**). This protocol features high atom efficiency, broad substrate scope, certain functional group tolerance, and no need for an H_2 acceptor, which constitutes a novel straightforward route for the synthesis of a new family of borylated aromatic ether derivatives. The success of this transformation is ascribed to the adequate oxophilicity of a rare-earth metal ion as well as a proper ligand environment provided by the Cp ligands for the rare-earth metal center, which can effectively suppress possible deactivation reactions and promote the *ortho* C–H activation and borylation of an aromatic ether. Further studies on the application of the unique features of organo rare-earth complexes to the C–H functionalization and other transformations of related organic substrates are currently in progress.

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acscatal.
Experimental details and characterization data (PDF).

AUTHOR INFORMATION

Corresponding Author

*E-mail: houz@riken.jp

Notes

The authors declare no competing financial interests.

ACKNOWLEDGMENT

This work was supported in part by a Grant-in-Aid for Scientific Research (S) (No. 26220802) and a Grant-in-Aid for Scientific Research on Innovative Areas (17H06451) from JSPS. We gratefully appreciate Mrs. Akiko Karube of Organometallic Chemistry Laboratory for the measurements of high-resolution mass spectra and elemental analyses.

REFERENCES

(1) Selected reviews on synthetic utility of organoboron compounds: (a) Miyaura, N.; Suzuki, A. Palladium-Catalyzed Cross-Coupling Reactions of Organoboron Compounds. *Chem. Rev.* **1995**, *95*, 2457-2483. (b) Miyaura, N. Metal-Catalyzed Cross-Coupling Reactions of Organoboron Compounds with Organic Halides. In *Metal-Catalyzed Cross-Coupling Reactions*; de Meijere, A., Diederich, F., Eds.; Wiley-VCH Verlag GmbH: Weinheim, **2008**, pp 41-123. (c) Hall, D. G. *Boronic Acids: Preparation and Applications in Organic Synthesis, Medicine and Materials, 2nd ed.*; Wiley-VCH: Weinheim, **2012**.

(2) Selected reviews on C–H borylation: (a) Mkhalid, I. A. I.; Barnard, J. H.; Marder, T. B.; Murphy, J. M.; Hartwig, J. F. C–H Activation for the Construction of C-B Bonds. *Chem. Rev.* **2010**, *110*, 890-931. (b) Hartwig, J. F. Regioselectivity of the borylation of alkanes and arenes. *Chem. Soc. Rev.* **2011**, *40*, 1992-2002. (c) Hartwig, J. F. Borylation and Silylation of C–H Bonds: A Platform for Diverse C–H Bond Functionalizations. *Acc. Chem. Res.* **2012**, *45*, 864-873. (d) Ros, A.; Fernández, R.; Lassaletta, J. M. Functional group directed C–H borylation. *Chem. Soc. Rev.* **2014**, *43*, 3229-3243. (e) Hartwig, J. F. Evolution of C–H Bond Functionalization from Methane to Methodology. *J. Am. Chem. Soc.* **2016**, *138*, 2-24. (f) Xu, L.; Wang, G.; Zhang, S.; Wang, H.; Wang, L.; Liu, L.; Jiao, J.; Li, P. Recent advances in catalytic C–H borylation reactions. *Tetrahedron* **2017**, *73*, 7123-7157.

(3) (a) Lomovskaya, N.; Otten, S. L.; Doi-Katayama, Y.; Fonstein, L.; Liu, X.-C.; Takatsu, T.; Inventi-Solari, A.; Filippini, S.; Torti, F.; Colombo, A. L.; Hutchinson, C. R. Doxorubicin Overproduction in *Streptomyces peucetius*: Cloning and Characterization of the *dnrU* Ketoreductase and *dnrV* Genes and the *doxA* Cytochrome P-450 Hydroxylase Gene. *J. Bacteriol.* **1999**, *181*, 305-318. (b) Pacher, T.; Seger, C.; Engelmeier, D.; Vajrodaya, S.; Hofer, O.; Greger, H. Antifungal Stilbenoids from *Stemona collinsae*. *J. Nat. Prod.* **2002**, *65*, 820-827. (c) Umezawa, K.; Nakamura, Y.; Makino, H.; Citterio, D.; Suzuki, K. Bright, Color-Tunable Fluorescent Dyes in the Visible–Near-Infrared Region. *J. Am. Chem. Soc.* **2008**, *130*, 1550-1551. (d) Zhou, T.; Shi, Q.; Bastow, K. F.; Lee, K.-H. Antitumor Agents 286. Design, Synthesis, and Structure-Activity Relationships of *3'R,4'R*-Disubstituted-2',2'-dimethyldihydropyrano[2,3-*f*]chromone (DSP) Analogues as Potent Chemosensitizers to Overcome Multidrug Resistance. *J. Med. Chem.* **2010**, *53*, 8700-8708. (e) Wilken, R.; Veena, M. S.; Wang, M. B.; Srivatsan, E. S. Curcumin: A review of anti-cancer properties and therapeutic activity in head and neck squamous cell carcinoma. *Mol. Cancer* **2011**, 10:12. (f) Gaspari, R.; Prota, A.

E.; Bargsten, K.; Cavalli, A.; Steinmetz, M. O. Structural Basis of *cis*- and *trans*-Combretastatin Binding to Tubulin. *Chem* **2017**, *2*, 102-113.

(4) (a) Cho, J.-Y.; Iverson, C. N.; Smith, M. R. Steric and Chelate Directing Effects in Aromatic Borylation. *J. Am. Chem. Soc.* **2000**, *122*, 12868-12869. (b) Ishiyama, T.; Takagi, J.; Ishida, K.; Miyaura, N.; Anastasi, N. R.; Hartwig, J. F. Mild Iridium-Catalyzed Borylation of Arenes. High Turnover Numbers, Room Temperature Reactions, and Isolation of a Potential Intermediate. *J. Am. Chem. Soc*. **2002**, *124*, 390-391. (c) Chotana, G. A.; Rak, M. A.; Smith, M. R. Sterically Directed Functionalization of Aromatic C-H Bonds: Selective Borylation Ortho to Cyano Groups in Arenes and Heterocycles. *J. Am. Chem. Soc.* **2005**, *127*, 10539-10544. (d) Ishiyama, T.; Miyaura, N. Iridium-catalyzed borylation of arenes and heteroarenes via C–H activation. *Pure Appl. Chem.* **2006**, *78*, 1369-1375. (e) Boebel, T. A.; Hartwig, J. F. Silyl-Directed, Iridium-Catalyzed ortho-Borylation of Arenes. A One-Pot ortho-Borylation of Phenols, Arylamines, and Alkylarenes. *J. Am. Chem. Soc.* **2008**, *130*, 7534-7535. (f) Yamazaki, K.; Kawamorita, S.; Ohmiya, H.; Sawamura, M. Directed Ortho Borylation of Phenol Derivatives Catalyzed by a Silica-Supported Iridium Complex. *Org. Lett.* **2010**, *12*, 3978-3981. (g) Kawamorita, S.; Miyazaki, T.; Ohmiya, H.; Iwai, T.; Sawamura, M. Rh-Catalyzed *Ortho*-Selective C–H Borylation of *N*-Functionalized Arenes with Silica-Supported Bridgehead Monophosphine Ligands. *J. Am. Chem. Soc.* **2011**, *133*, 19310-19313. (h) Kuninobu, Y.; Iwanaga, T.; Omura, T.; Takai, K. Palladium-Catalyzed *ortho*-Selective C–H Borylation of 2-Phenylpyridine and Its Derivatives at Room Temperature. *Angew. Chem. Int. Ed.* **2013**, *52*, 4431-4434. (i) Mazzacano, T. J.; Mankad, N. P. Base Metal Catalysts for Photochemical C−H Borylation That Utilize Metal−Metal Cooperativity. *J. Am. Chem. Soc.* **2013**, *135*, 17258-17261. (j) Cheng, C.; Hartwig, J. F. Rhodium-Catalyzed Intermolecular C–H Silylation of Arenes with High Steric Regiocontrol. *Science* **2014**, *343*, 853-857. (k) Obligacion, J. V.; Semproni, S. P.; Chirik, P. J. Cobalt-Catalyzed C−H Borylation. *J. Am. Chem. Soc.* **2014**, *136*, 4133-4136. (l) Fernández-Salas, J.; Manzini, S.; Piola, L.; Slawin, A. M. Z.; Nolan, S. P. Ruthenium catalysed C–H bond borylation. *Chem. Commun.* **2014**, *50*, 6782-6784. (m) Kuninobu, Y.; Ida, H.; Nishi, M.; Kanai, M. A *meta*-selective C–H borylation directed by a secondary interaction between ligand and substrate. *Nat. Chem.*, **2015**, *7*, 712-717. (n) Dombray, T.; Werncke, C. G.; Jiang, S.; Grellier, M.; Vendier, L.; Bontemps, S.; Sortais, J.-B.; Sabo-Etienne, S.; Darcel, C. Iron-Catalyzed C−H Borylation of Arenes. *J. Am. Chem. Soc.* **2015**, *137*, 4062-4065. (o) Esteruelas, M. A.; Oliván, M.; Vélez, A. POP−Rhodium-Promoted C−H and B−H Bond Activation and C−B Bond Formation. *Organometallics* **2015**, *34*, 1911-1924. (p) Wang, G.; Xu, L.; Li, P. Double N,B-Type Bidentate Boryl Ligands Enabling a Highly Active Iridium Catalyst for C–H Borylation. *J. Am. Chem. Soc.* **2015**, *137*, 8058-8061. (q) Furukawa, T.; Tobisu, M.; Chatani, N. C−H Functionalization at Sterically Congested Positions by the Platinum-Catalyzed Borylation of Arenes. *J. Am. Chem. Soc.* **2015**, *137*, 12211-12214. (r) Furukawa, T.; Tobisu, M.; Chatani, N. Nickel-catalyzed borylation of arenes and indoles *via* C–H bond cleavage. *Chem. Commun.* **2015**, *51*, 6508-6511. (s) Bheeter, C. B.; Chowdhury, A. D.; Adam, R.; Jackstell, R.; Beller, M. Efficient Rh-catalyzed C–H borylation of arene derivatives under photochemical conditions. *Org. Biomol. Chem.* **2015**, *13*, 10336-10340. (t) Press, L. P.; Kosanovich, A. J.; McCulloch, B. J.; Ozerov, O. V. High-Turnover Aromatic C−H Borylation Catalyzed by POCOP-Type Pincer Complexes of Iridium. *J. Am. Chem. Soc.* **2016**, *138*, 9487-9497. (u) Sarkar, De S.; Kumar, N. Y. P.; Ackermann, L. Ruthenium(II) Biscarboxylate-Catalyzed Borylations of $C(sp^2)$–H and $C(sp^3)$–H Bonds. *Chem. Eur. J.* **2017**, *23*, 84-87. (v) Wang, G.; Liu, L.; Wang, H.; Ding, Y.; Zhou, J.; Mao, S.; Li, P. N,B-Bidentate Boryl Ligand-Supported Iridium Catalyst for Efficient Functional-Group-Directed C−H Borylation. *J. Am. Chem. Soc.* **2017**, *139*, 91-94. (w) Li, H.-L.; Kuninobu, Y.; Kanai, M. Lewis Acid–Base Interaction-Controlled *ortho*-Selective C–H Borylation of Aryl Sulfides. *Angew. Chem., Int. Ed.* **2017**, *56*, 1495-1499. (x) Chattopadhyay, B.; Dannatt, J. E.; Sanctis, I. L. A.-D.; Gore, K. A.; Maleczka, R. E.; Singleton, D. A.; Smith, M. R. Ir-Catalyzed ortho-Borylation of Phenols Directed by Substrate−Ligand Electrostatic Interactions: A Combined Experimental/in Silico Strategy for Optimizing Weak Interactions. *J. Am. Chem. Soc.* **2017**, *139*, 7864-7871. (y) Li, H.-L.; Kanai, M.; Kuninobu, Y. Iridium/Bipyridine-Catalyzed *ortho*-Selective C−H Borylation of Phenol and Aniline Derivatives. *Org. Lett.* **2017**, *19*, 5944-5947.

(5) Oyamada, J.; Nishiura, M.; Hou, Z. Scandium-Catalyzed Silylation of Aromatic C–H Bonds. *Angew. Chem., Int. Ed.* **2011**, *50*, 10720-10723.

(6) (a) Oyamada, J.; Hou, Z. Regioselective C–H Alkylation of Anisoles with Olefins Catalyzed by Cationic Half-Sandwich Rare Earth Alkyl Complexes. *Angew. Chem., Int. Ed.* **2012**, *51*, 12828-12832. (b) Shi, X.; Nishiura, M.; Hou, Z. C−H Polyaddition of Dimethoxyarenes to Unconjugated Dienes by Rare Earth Catalysts. *J. Am. Chem. Soc.* **2016**, *138*, 6147-6150. (c) Shi, X.; Nishiura, M.; Hou, Z. Simultaneous Chain-Growth and Step-Growth Polymerization of Methoxystyrenes by Rare-Earth Catalysts. *Angew. Chem., Int. Ed.* **2016**, *55*, 14812-14817.

(7) For formation of a zwitterion compound in the reaction of a lanthanum metallocene hydride complex with HBpin, see: Dudnik, A. S.; Weidner, V. L.; Motta, A.; Delferro, M.; Marks, T. J. Atom-efficient regioselective 1,2-dearomatization of functionalized pyridines by an earth-abundant organolanthanide catalyst. *Nat. Chem.* **2014**, *6*, 1100-1107.

(8) The C–H borylation of thioanisole and *N,N*-dimethylaniline (without a methoxy group) was not observed under the same conditions.

(9) For alkene hydroboration with HBpin by lanthanide metallocene complexes, see: Harrison, K. N.; Marks, T. J. Organolanthanide-catalyzed hydroboration of olefins. *J. Am. Chem. Soc.* **1992**, *114*, 9220-9221.

(10) When 1.0 equiv. of HBpin was used, only the C=C hydroboration was observed.

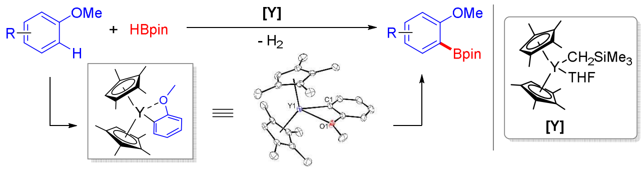
(11) The lack of activity of the C_5Me_4-ligated complex **Y-3** for the borylation of furan is probably due to the relative steric unsaturation around the metal center, which could allow coordination of more than one molecule of furan (which is less sterically demanding than anisole) and thus hamper the reaction of a metal furyl species with HBpin. In the case of **Y-2**, the two sterically demanding C_5Me_5 ligands may prevent the coordination of excess furan molecules to the metal center and thus allow the Y−furyl species to react with HBpin and give the borylation product efficiently. The lower efficiency of the sterically demanding complex **Y-2** for the borylation of anisole (see Table 1, entry 3) is probably due to the larger steric hindrance of anisole than that of furan.

(12) Bijpost, E. A.; Duchateau, R.; Teuben, J. H. Early transition metal catalyzed-hydroboration of alkenes. *J. Mol. Catal. A: Chemical* **1995**, *95*, 121-128.

(13) Jeske, G.; Lauke, H.; Mauermann, H.; Swepston, P. N.; Schumann, H.; Marks, T. J. *J. Am. Chem. Soc.* **1985**, *107*, 8091-8103.

(14) (a) Arndt, S.; Trifonov, A.; Spaniol, T. P.; Okuda, J.; Kitamura, M.; Takahashi, T. Metalation of aromatic heterocycles by yttrium alkyl complexes that contain a linked amido-cyclopentadienyl ligand: synthesis, structure and Lewis base adduct formation. *J. Organomet. Chem.* **2002**, 158-166. (b) Spaniol, T. P.; Okuda, J.; Kitamura, M.; Takahashi, T. *ortho*-Metalation of aromatic ethers by yttrium alkyl complexes that contain a linked amido-cyclopentadienyl ligand. *J. Organomet. Chem.* **2003**, 194-199.

Insert Table of Contents artwork here



- ♣ *Exclusive ortho-selectivity*
- ♣ *Simple reaction conditions*
- ♣ *Broad substrate scope*
- ♣ *No need for H_2 acceptor*