JOURNAL OF THE AMERICAN CHEMICAL SOCIETY

Subscriber access provided by Uppsala universitetsbibliotek

Article

Chemoselective Cross-coupling of gem-Borazirconocene Alkanes with Aryl Halides

Chao Yang, Yadong Gao, Songlin Bai, Chao Jiang, and Xiangbing Qi

J. Am. Chem. Soc., **Just Accepted Manuscript** • DOI: 10.1021/jacs.0c03821 • Publication Date (Web): 04 Jun 2020

Downloaded from pubs.acs.org on June 4, 2020

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.

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.

Chemoselective Cross-coupling of *gem*-Borazirconocene Alkanes with Aryl Halides

Chao Yang,[†‡] Yadong Gao,[†‡] Songlin Bai,[‡] Chao Jiang,[*†] and Xiangbing Qi[*‡,§,¶]

[†]School of Chemical Engineering, Nanjing University of Science and Technology, Nanjing, Jiangsu 210094, China.

[‡]National Institute of Biological Sciences, 7 Science Park Road, Zhongguancun Life Science Park, Beijing 102206, China.

[§]Tsinghua Institute of Multidisciplinary Biomedical Research, Tsinghua University, Beijing 100084, China.

[¶]Lead Contact

ABSTRACT: The direct and chemoselective conversion of the carbon-metal bond of *gem*-dimetallic reagents enables rapid and sequential formation of multiple carbon-carbon and carbon-heteroatom bonds, thus representing a powerful method for efficiently increasing structural complexity. Herein, we report a visible-light-induced, nickel-catalyzed, chemoselective cross-coupling reaction between *gem*-borazirconocene alkanes and diverse aryl halides, affording a wide range of alkyl Bpin derivatives in high yields with excellent regioselectivity. This practical method features attractively simple reaction conditions and a broad substrate scope. Additionally, we systematically investigated a Bpin-directed chain walking process underlying the regioselectivity of alkylzirconocenes, thus uncovering the mechanism of the remote functionalization of internal olefins achieved with our method. Finally, DFT calculations indicate that the high regioselectivity of this reaction originates from the directing effect of the Bpin group.

■ INTRODUCTION

The selective cross-coupling of bimetallic nucleophiles is attracting increasing attention because it facilitates diverse transformations to rapidly elaborate structural complexity.[1] Among reported bimetallic reagents,[1b, 1g, 2] *gem*-borazirconocene alkanes are recognized as particularly valuable synthons that possess great synthetic potential (Figure 1A).[3] This stable reagent is easily generated from hydrozirconation of various alkenyl boronic esters with bis(cyclopentadienyl)zirconium chloride hydride (Schwartz reagent) in high yield and with excellent functional group tolerance. The difference in the polarity of the carbon-zirconium bond *vs* the carbon-boron bond allows for the sequential functionalization of *gem*-borazirconocene alkanes *via* a variety of reactions such as cross-coupling, nucleophilic substitution, or nucleophilic addition. Organozirconium compounds are much more reactive than organoboranes, which allows for the chemoselective conversion of organozirconium reagents to afford versatile organic boron intermediates.[3j] Despite the multiple advantages offered by these reagents, they have received substantially less attention for cross-couplings compared with alternative nucleophilic substitutions like halogenation,[3a-d] deuteration,[3e] amination,[3j, 3k] as well as Michael addition,[3f] or nucleophilic addition to acyl chlorides (Figure 1A).[3g] Indeed, the efficient utilization of organozirconium reagents for cross-coupling reaction would be of great value to rapidly increase structural complexity.[4] While cross-coupling reaction of primary alkylzirconocene reagents has been reported recently by our group,[5] to date, no general cross-coupling reaction has been developed for secondary alkylzirconocene including *gem*-borazirconocene alkanes,[3h] likely owing to the lack of available π-systems to stabilize the binding capability of zirconium to achieve suitable transmetalation.[6] Furthermore, the considerable steric hindrance caused by the zirconium complex decreases the nucleophilicity of the alkyl group with coupling partners. (Figure 1B).[3j]

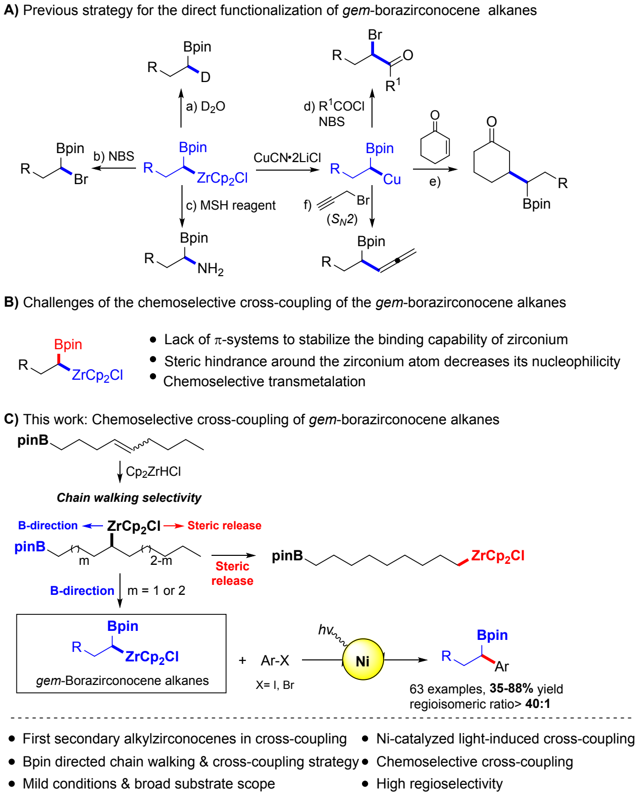


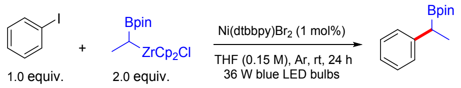
Figure 1. A) Previous strategy for the direct functionalization of *gem*-borazirconocene alkanes. B) Challenges with chemoselective

cross-coupling of *gem*-borazirconocene alkanes. C) Chemoselective cross-coupling of *gem*-borazirconocene alkanes.

The development of remote functionalization methods is receiving growing interest, probably because such methods allow for the activation of challenging C–H and C–C bonds distant from the initiation position *via* a fascinating "chain walking" process.[7] However, the manipulation of remote functional groups at different carbon centers represents a major challenge in synthetic chemistry.[8] Hydrozirconation of internal alkenes produces primary alkylzirconocene complexes wherein facile Zr–H eliminations and reinsertions enable the Cp_2ZrCl moiety to "chain walking" to the least sterically hindered terminal position of the alkyl chain.[6] To the best of our knowledge, there is no general method to selectively direct this chain walking process to afford stable secondary alkylzirconocenes with predictable regioselectivity.

The present study describes, for the first time, a Bpin group directed "chain walking" process for alkylzirconocenes, selectively generating diverse *gem*-borazirconocene alkanes. Inspired by our own recent findings[5], we speculated that the α-radical stabilizing effect of boron is likely to favor homolytic cleavage of the C–Zr bond, thus the *gem*-borazirconocene alkanes may serve as especially attractive secondary sp^3-hybridized alkylzirconocenes that undergo C-Zr activation in the presence of boron to enable chemoselective cross-coupling reactions (Figure 1C). Herein, we report a visible-light-induced nickel-catalyzed chemoselective cross-coupling reaction of *gem*-borazirconocene alkanes with aryl halides, affording a wide range of alkylborane derivatives. Such derivatives are well-established high-value building blocks, which can be employed for lithiation-borylation,[9] Zweifel olefinations,[10] Suzuki cross-couplings,[1h, 1j, 1l, 11] as well as the recently reported alkylborane cross-coupling reaction from the Fu group that enables rapid and efficient formation of sp^3 C-C bonds under mild conditions while offering both high regioselectivity and excellent substrate scope.[12]

Table 1. Variation of reaction parameters



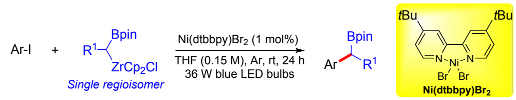
Entry	Change from standard conditions	Yield (%)[a]
1	none	96 (86)
2	w/o $Ni(dtbbpy)Br_2$	0
3	w/o light	0
4	$Ni(dtbbpy)Br_2$ (2 mol%)	91
5	15 W blue Light strip, instead of LED bulbs	84
6	15 W blue Light strip, instead of LED bulbs, + $Bu_4N^+OTs^-$ (1 equiv.)	82
7	15 W blue Light strip, instead of LED bulbs, + TBAB (1 equiv.)	94
8	$NiCl_2$, instead of $Ni(dtbbpy)Br_2$	trace
9	$Ni(COD)_2$, instead of $Ni(dtbbpy)Br_2$	trace
10	PhBr, instead of PhI	92

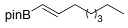
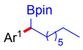
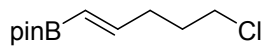
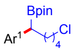
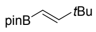
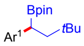
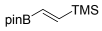
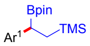
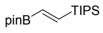
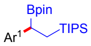
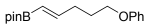
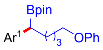
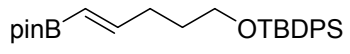
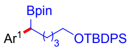
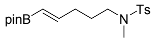
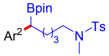
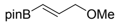
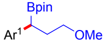
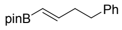
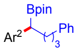
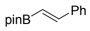
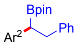
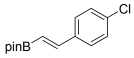
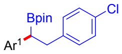
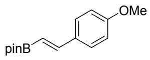
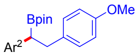
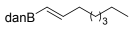
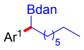
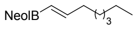
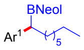
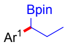
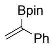
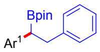
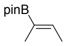
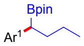
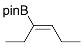
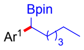
[a] All optimization reactions were carried out at a 0.1 mmol scale. The yields determined by ^1H NMR of crude samples using 1,3,5-trimethoxybenzene as an internal standard, in parenthesis is the isolated product yield (0.30 mmol scale). TBAB: Tetrabutylammonium bromide.

■ RESULTS AND DISCUSSION

Our initial efforts focused on examining ethyl *gem*-borazirconocene with iodobenzene under blue light excitation. After an extensive survey of catalysts, additives, solvents, and light sources (for detailed optimization studies, see Table S1-S7.), the desired cross-coupling product of aryl ethylboronate was achieved in 86% yield using a nickel precatalyst containing a 4,4'-*tert*-butyl-2,2'-bipyridine ligand in THF, with the aid of irradiation from blue-light-emitting bulbs at room temperature. Various control experiments including light–dark intervals revealed that the nickel catalyst and continuous irradiation with visible light are both essential for the reaction (Table 1, entries 2, 3, 8, 9, and the supplemental information, Figure S1). The reaction yield was increased upon addition of TBAB and by simply increasing the power of the light source from 15 W to 36 W (Table 1, entries 5 *vs* 7, entries 1 *vs* 5). We determined that the highly efficient nickel precatalyst could be reduced as low as 1 mol% (Table 1, entries 1 *vs* 4). Finally, we found that bromobenzene possesses comparable reactivity to iodobenzene under the optimized reaction conditions (Table 1, entry 10).

Table 2. The scope of *gem*-borazirconocene alkanes component[a]



Entry	Substrate	Product No.	Product	Yield (%)
1		**2a**		71 (72)[b]
2		**2b**		75
3		**2c**		74 (61)[b]
4		**2d**		83
5		**2e**		81
6		**2f**		68
7		**2g**		74
8		**2h**		66
9		**2i**		63
10		**2j**		75
11		**2k**		73
12		**2l**		68 (65)[b]
13		**2m**		81
14		**2n**		68
15		**2o**		75
16		**2p**		85
17		**2q**		53
18		**2r**		86
19		**2s**		0[c]

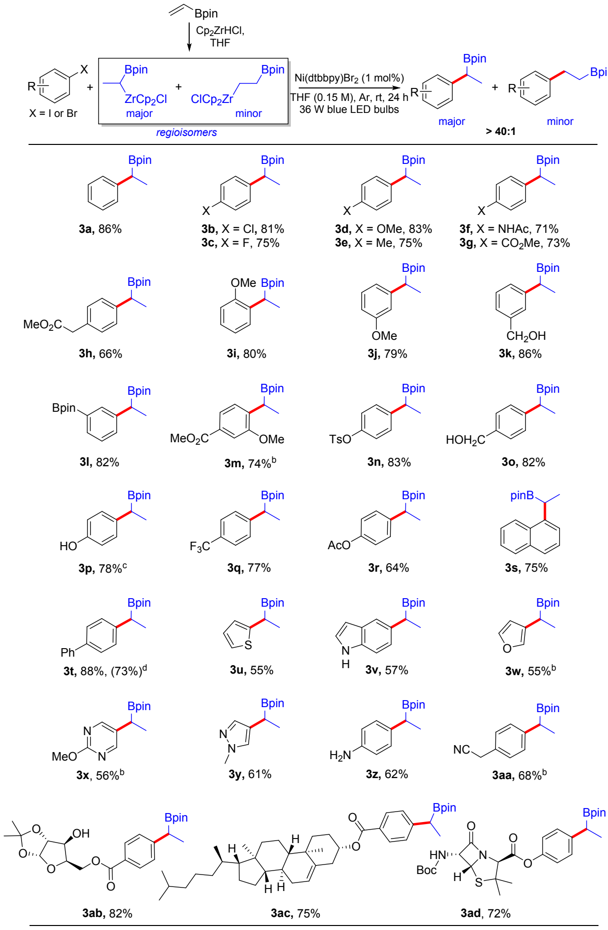
[a]Unless otherwise noted, yields of isolated products given at a 0.3 mmol scale; all reactions were performed with Ni(dtbbpy)Br_2 (1 mol%), *gem*-borazirconocene alkanes (0.6 mmol), aryl iodides (0.3 mmol), and THF (2 mL), at 25-30 °C with two 36 W blue LED bulbs for 24 hours. See the supplemental information for detailed reaction conditions, Ar^1 = 4-$HOCH_2(C_6H_4)$, Ar^2 = 4-$AcNH(C_6H_4)$. [b]The *gem*-borazirconocene alkanes were generated *in situ* from alkynes, HBpin, and the Cp_2ZrHCl reagents. [c]85% of starting material S3o was recovered.

With the optimal reaction conditions in hand, we next turned our attention to investigate the synthetic utility of this visible-light-induced nickel-catalyzed reaction. First, the substrate scope of *gem*-borazirconocene alkanes was examined, which were prepared *in situ* from hydrozirconation of corresponding alkenyl boronic esters. As illustrated in Table 2, a series of simple (**2a**, **2j**, **2n**, **2o**) and substituted borazirconocene alkanes containing chloro (**2b**), silane (**2d**, **2e**), ether (**2f**, **2g**, **2i**), or sulfonamide groups (**2h**), were viable coupling partners in our cross-coupling method. Substrates generated from hydrozirconation of electron-rich and electron-deficient aryl alkenyl boronic esters (**2k**-**2m**), as well as more sterically hindered alkenyl boronic esters (**2c**-**2e**) were also amenable to the cross-coupling reaction. The *gem*-borazirconocene alkanes generated simply *in situ* from alkynes, HBpin, and Cp_2ZrHCl reagents (**2a**, **2c**, **2l**) were also found to be productive coupling partners. (See the supplemental information for detailed reaction conditions). Notably, the alkenylboronate systems, such as entries 16-18, exhibit 1,2-boron migration during hydrozirconation until the stable *gem*-borazirconocene alkanes are generated, which also possess moderate to high reactivity in our cross-coupling reaction (**2p**-**2r**, 53-86 yield).[13] However, when the Bpin group is located further away from the terminal position (more than 2 carbons), neither boron migration nor cross-coupling product was observed. This indicated that long chain boron migration is likely more difficult than boron-directed zirconocene migration (entry 19, **2s**, 0% yield).

To further assess the scope of this selective coupling reaction, a series of aryl iodides and bromides were investigated for this reaction. As shown in Table 3, this method displayed excellent functional group tolerance for the aryl iodides bearing chloro (**3b**), fluoro (**3c**), methoxy (**3d**, **3i**, **3j**, **3m**), methyl (**3e**), and trifluoromethyl (**3q**) groups, as well as more reactive functional groups such as amides (**3f**), esters (**3g**, **3h**, **3m**, **3r**, **3ab** -**3ad**), primary alcohols (**3k**, **3o**), phenols (**3p**), anilines (**3z**), and nitriles (**3aa**). Additionally, we observed that aryl tosylates and aryl boronic esters were also well tolerated under the mild conditions (**3l**, **3n**), illustrating a facile access to these compounds for further chemical modification. Notably, the electronic properties and substitution pattern had a negligible effect on the yield, and the corresponding cross-coupling products were all obtained in good to excellent yields with high regioselectivity (branch:linear >40:1, for detailed ^1H NMR of the crude samples, see supplemental information, Spectral data.). Compared with aryl iodides, aryl bromides were also feasible cross-coupling partners (**3m**, **3w**, **3x**, **3aa**). Furthermore, the potential application of this cross-coupling method in modern synthesis was demonstrated by carrying out at a gram scale process without compromising much efficiency (**3t**, 73% yield).

Regarding the scope of heteroaromatic halides, thiophene (**3u**), non-protected indole (**3v**), furan (**3w**), pyrimidine (**3x**), and pyrazole (**3y**), were all well tolerated, affording the corresponding products in moderate yields. Finally, aryl iodide derivatives from natural products, including xylofuranose (**3ab**), cholesterol (**3ac**), and aminopenicillanic acid (**3ad**), were compatible with the optimized cross-coupling conditions, showcasing the utility of this new process for the late-stage modification of complex natural products. Additional cross-coupling reactions of different electrophilic partners have been conducted to extend the scope of this method (discussed in detail in supplemental information, Table S8). Substrates, including primary alkyl and alkenyl halides were feasible cross-coupling partners although the yield of products were moderate (35-68%).[14]

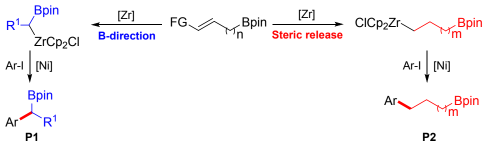
Table 3. The scope of aryl halide coupling partners[a]

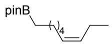
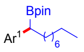
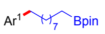
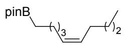
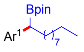
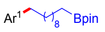
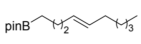
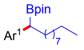
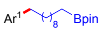
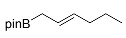
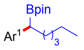
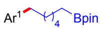
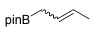
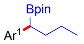
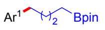
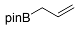
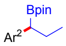
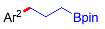
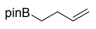
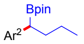
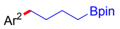
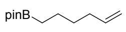
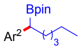
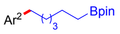
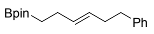
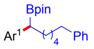
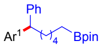
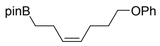
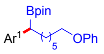
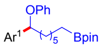
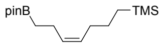
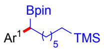
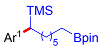
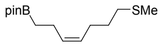
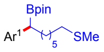
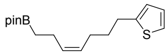
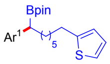
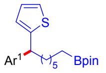


[a]Unless otherwise noted, yields of isolated products given at a 0.3 mmol scale; all reactions were performed with Ni(dtbbpy)Br_2 (1 mol%), ethyl *gem*-borazirconocene (0.6 mmol), aryl iodides (0.3 mmol), and THF (2 mL), at 25-30 °C with two 36 W blue LED bulbs for 24 hours. The regioisomeric ratio (branch/linear) in parentheses was determined by ^1H NMR of crude samples. See the supplemental information for detailed reaction conditions. [b]Bromoarene was used. [c]4 equiv. alkylzirconocene was used. [d]yields of isolated products given at a 3.6 mmol scale (1.008 g).

Under thermodynamic control, the general terminal or internal alkenes would all generate terminal linear alkylzirconocenes from hydrozirconation and subsequent rapid “chain walking” in the latter case that occurs to relieve the steric hindrance.[6] However, in the presence of terminal Bpin, we wondered whether this Bpin could be harnessed as a directing group to reverse the chain walking selectivity. To pursue this and gain insights about the regioselectivity of this type of chain walking and cross-coupling protocol, we designed a series of terminal Bpin substituted internal alkenes with different chain lengths and geometric isomers of the double bonds (Table 4). To our delight, when the double bonds are located in a reasonable range (half way or closer) to the Bpin group, the Bpin group directs the hydrozirconation and the “chain walking” process, generating the branched *gem*-borazirconocene alkanes exclusively, which further cross couples with aryl iodides to afford the benzylic secondary Bpin products in high regioselectivity (**4b-4e**, >40:1).

Table 4. The scope of chain walking strategy[a]



Entry	Substrate	Product	P1	P2	Ratio (P1:P2)	Yield (%)
1		**4a**			2:1	75^{b}
2		**4b**			>40:1	74
3		**4c**			>40:1	72
4		**2s (4d)**			only P1	72
5		**2r (4e)**			>40:1	72
6		**4f**			only P2	75^{c}
7		**4g**			only P2	74^{c}
8		**4h**			only P2	72^{c}
9		**4i**			only P1	54^{d}
10		**4j**			only P1	78^{e}
11		**4k**			only P1	81^{e}
12		**4l**			--	0^{e,f}
13		**4m**			--	0^{e,f}

[a]Unless otherwise noted, yields of isolated products given at a 0.3 mmol scale; the temperature of hydrozirconation is 50 ^{0}C. all reactions were performed with Ni(dtbbpy)Br$_2$ (1 mol%), *gem*-borazirconocene alkanes (0.6 mmol), aryl iodides (0.3 mmol), and THF (2 mL), at 25-30 °C with two 36 W blue LED bulbs for 24 hours, the regioisomeric ratio (branch/linear) in parentheses was determined by ^{1}H NMR of crude samples. See the supplemental information for detailed reaction conditions. Ar^1 = 4-HOCH$_2$(C$_6$H$_4$), Ar^2 = 4-AcNH(C$_6$H$_4$). [b]4 equiv. *gem*-borazirconocene alkanes was used. [c]1 equiv. of Bu$_4$N$^+$OTs$^-$ was added. [d]35% of starting material **S3o** was recovered. [e] yields of isolated products given at a 0.2 mmol scale. [f]More than 90% of starting material **S3o** was recovered.

Further exploration showed that, in a more regio-biased case, when the double bond is much far away (such as more than five carbons) from the Bpin group and closer to the unsubstituted terminal carbon (less than two carbons), *gem*-borazirconocene alkane is still the main product (**4a**, branch:linear = 2:1), although the terminal linear alkylzirconocenes can also be generated as minor products. Interestingly, allylic and homoallylic boronates exclusively generate the linear alkylzirconocenes and afford the corresponding products (**4f-4h**), findings in accordance with previous studies.[13]

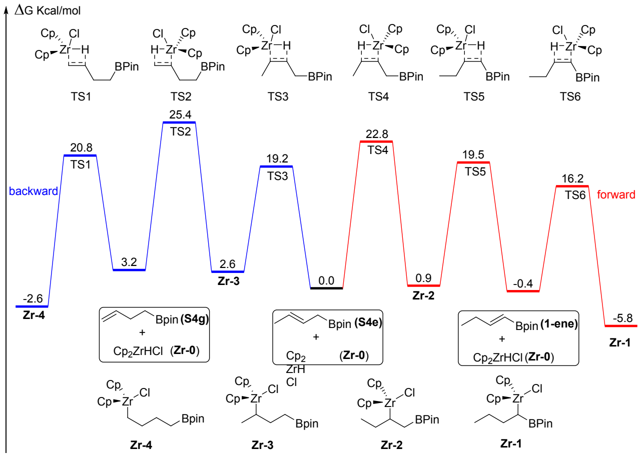


Figure 2. The DFT calculation result of the hydrozirconation process of 1-pinacolboron-2-butene (**S4e**). More details of the calculations are described in the supplementary information.

To gain insights into the relative propensity of Bpin directed effect of chain walking versus other potential directing group such as heteroatom, we designed several substrates containing different type of functional groups, which might affect the chain walking direction (entries 9-13). Substrates containing phenyl, ether, silane groups would not affect the migration selectivity of the Zr moiety and the corresponding cross-coupling products can be afforded in moderate to high yield (**4i-4k**, 54-81%). However, when thioether or thiophene groups were installed at the other terminal position, the Bpin directed chain walking process was almost completely inhibited (entries 12-13). The D$_2$O-quenching reaction showed the major products were the isomeric mixtures of the reduced substrates. And only trace amount of D-incorporation at the α-carbon of Bpin or thiophene group were observed, which indicated the chain walking selectivity in these substrates is not optimal due to the interruption by the thioether or thiophene groups.

To illustrate the chemical selectivity of the chain walking process, we carried out a DFT calculation of zirconocene “walking” forward (towards Bpin group) or backward on 1-pinacolboron-2-butene substrate (**S4e**). Analysis of the transition state of hydrozirconation revealed two clear types of TSs: *endo*-type and *exo*-type. For an *endo*-type TS, an alkylene inserts the Zr-H bond inside the H-Zr-Cl angle in 138 degrees (**TS1-TS6**); and for an *exo*-type TS, an alkylene inserts the Zr-H bond inside the H-Zr-Cl angle in 73 degrees (**TS7-TS12**). The DFT analysis indicated that the *endo*-type is more favorable than *exo*-type, and the Gibbs free energies are about 10 Kcal/mol lower for *endo*-type (discussed in detail in supplemental information, Table S10). The calculation results of *endo*-types are shown in Figure 2: terminal alkylzirconocene species are the most stable, and the branch *gem*-borazirconocene alkane **Zr-1** is more stable than the linear alkylzirconocene **Zr-4** (ΔG (**Zr-1**, **Zr-4**) = -3.2 kcal/mol). Considering that the walking processes of the non-terminal species are reversible at room temperature (ΔG_{TS}<23kcal/mol) (Table 4, entries 1-5), we speculate that the zirconocene should move from the middle position to Bpin side under thermodynamic control due to the stability of branch *gem*-borazirconocene alkane **Zr-1**. Kinetically, for the non-terminal species, the barrier of Zr walking forward is 22.8 kcal/mol, which is 2.6 kcal/mol lower than the barrier of walking backward. Using the Boltzmann distribution, we can calculate the ratio of **Zr-4** to **Zr-1** as 1.2%, which is close to the experimental ratio (<1:40). However, once the zirconocene has already isomerized to the terminal (Table 4, entries 6-8, **S4f-S4h**, and the more region-biased substrate, entry 1, **S4a**), the barrier to walk back to another side would be significantly high (>27kcal/mol) due to the stability of terminal-alkylzirconocene species. This calculation data was also confirmed by the experimental data of the chemoselectivity of substrate **4g**.

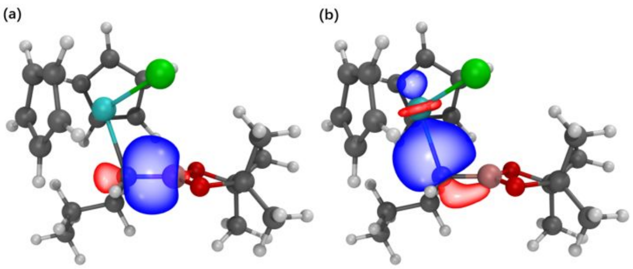


Figure 3. The localized molecular orbitals (LMO) of the **Zr-1**(gray: Carbon, white: Hydrogen, red: Oxygen, green: Chlorine, cyan: Zirconium, pink: Boron). (a) The bonding orbital of C-B bond. (b) The bonding orbital of C-Zr bond. LMOs were generated by Multiwfn 3.6 program[15] and drawn by VMD program[16].

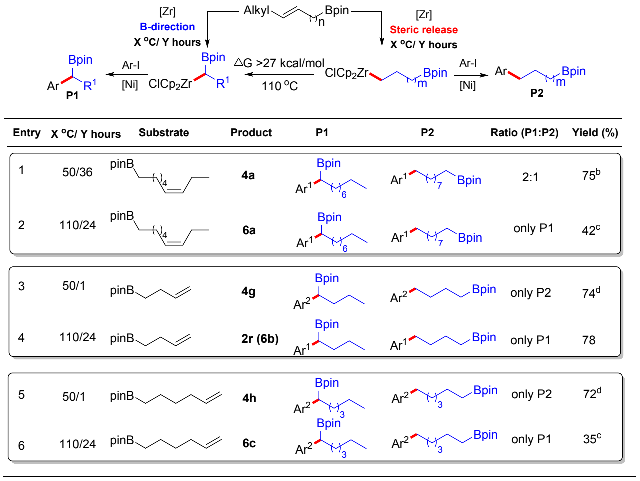
Table 5. Mayer Bond Orders of C-Zr bond and C-B bond. Generate by Multiwfn 3.6 program.

Mayer Bond Orders[17]		
	C-Zr	C-B
Zr-1	0.88	1.14
Zr-4	0.97	1.05

After localized the molecular orbital of **Zr-1**, as shown in Figure 3, the C-Zr bonding orbital delocalized to boron's p orbital. This σ-p hyperconjugation between C-Zr bond to boron's unoccupied p orbital enhances the C-B bond strength. Further evidence comes from the Mayer bond order, which indicates the electron pairs that are shared between two atoms. Table 5 shows that the Mayer bond order of C-Zr in **Zr-1**(*gem*-borazirconocene alkane) is decreased comparing with the **Zr-4**'s (terminal alkylzirconocene), while it's increased in C-B bond. This complementary variation also indicates the σ-p hyperconjugation. This unique effect in **Zr-1** might raise the activity of C-Zr bond and stabilized the *gem*-borazirconocene alkane species.

Inspired by the DFT calculation result mentioned above, we then investigate the possibility of reversing the chain walking selectivity of terminal-Zr motifs (Table 4, entries 1, 6, 8). As illustrated in Table 6, when the temperature of hydrozirconation of **S4a** and **S4g-h** were increased from 50 °C to 110 °C, which should be sufficient for the terminal-Zr motifs to cross the energy barrier (>27 kcal/mol), the terminal-Zr motifs could be gradually converted into the corresponding *gem*-borazirconocene *via* the Bpin directed chain walking process and further cross couples with aryl iodides to afford the benzylic secondary Bpin products in high regioselectivity (entries 1 *vs* 2, entries 3 *vs* 4, entries 5 *vs* 6). More interestingly, with these data in hand, we are able to design substrates (as entries 3-6) to synthesize a variety of broad branch (>110 °C) or linear (room temperature to 50 °C) alkylborane derivatives selectively. To the best of our knowledge, this is the first study demonstrating the conversion of primary zirconium alkane to secondary zirconium alkane with high regioselectivity *via* Bpin directed chain walking process.

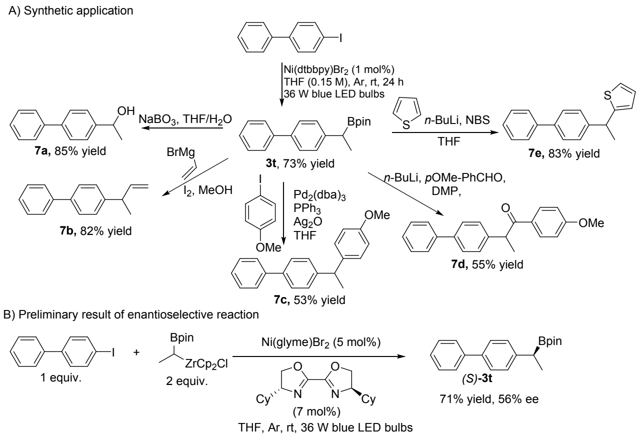
Table 6. The study of chain walking selectivity[a]



Entry	X °C/ Y hours	Substrate	Product	P1	P2	Ratio (P1:P2)	Yield (%)
1	50/36		**4a**			2:1	75[b]
2	110/24		**6a**			only P1	42[c]
3	50/1		**4g**			only P2	74[d]
4	110/24		**2r (6b)**			only P1	78
5	50/1		**4h**			only P2	72[d]
6	110/24		**6c**			only P1	35[c]

[a]Unless otherwise noted, yields of isolated products given at a 0.3 mmol scale; all reactions were performed with Ni(dtbbpy)Br_2 (1 mol%), *gem*-borazirconocene alkanes (0.6 mmol), aryl iodides (0.3 mmol), and THF (2 mL), at 25-30 °C with two 36 W blue LED bulbs for 24 hours, the regioisomeric ratio (branch/linear) in parentheses was determined by ^1H NMR of crude samples. See the supplemental information for detailed reaction conditions. Ar^1 = 4-$HOCH_2(C_6H_4)$, Ar^2 = 4-AcNH(C_6H_4). [b]4 equiv. *gem*-borazirconocene alkanes was used. [c] More than 40% of starting material **S3o** was recovered. [d]1 equiv. of $Bu_4N^+OTs^-$ was added.

Scheme 1. Synthetic application and preliminary result of enantioselective reaction.



The utility of our method is also summarized in Scheme 1. As illustrated, the Bpin group can act as a starting point, affording a series of different derivatizations of **3t** in moderate to high yield (**7a**-**7e**, 53%-85% yield), including the oxidation, lithiation-borylation, Zweifel olefinations, and Suzuki cross-couplings. Since enantiomerically enriched organoboron compounds are important and versatile intermediates in chemical synthesis[18] due to the wide applicability of the C-B bond and their stereospecific transformation, the development of enantioselective version of our method is of great significance. From our preliminary results, (*S*)-**3t** could be obtained with moderate enantioselectivity (56% ee) and yield (71%) using a chiral (*R*, *R*)-Cy-Biox ligand, which showed great potential to develop the enantioselective cross-coupling reaction between *gem*-borazirconocene alkanes and a variety of aryl halides.

■ CONCLUSION

In conclusion, we have disclosed a visible-light-induced nickel-catalyzed chemoselective cross-coupling reaction between the *gem*-borazirconocene alkanes and aryl halides, affording a range of secondary alkyl boronic esters in high regioselectivtity. Furthermore, by selectively harnessing the directing effect of the Bpin group, we have demonstrated that internal alkenes bearing a terminal Bpin can be converted into the desired coupled products with high regioselectivtity. Further ongoing work is focusing on the flow chemistry setting of hydrozirconation, chain walking and sequential cross-coupling of resulting *gem*-borazirconocene alkanes and R^{1}R^{2}B(pin). The catalytic asymmetric version is also under investigation.

ASSOCIATED CONTENT

Supporting Information.

Supporting information includes synthetic procedures, spectral data, compound characterization, and cartesian coordinates of computational structures. This material is available free of charge *via* the Internet at http://pubs.acs.org.

AUTHOR INFORMATION

Corresponding Author

***Chao Jiang** - School of Chemical Engineering, Nanjing University of Science and Technology, Nanjing, Jiangsu 210094, China.
Email: chaojiang@njust.edu.cn.

***Xiangbing Qi** - National Institute of Biological Sciences, 7 Science Park Road, Zhongguancun Life Science Park, Beijing 102206, China. Tsinghua Institute of Multidisciplinary Biomedical Research, Tsinghua University, Beijing 100084, China. Email: qixiangbing@nibs.ac.cn.

Notes

The authors declare no competing financial interests.

ACKNOWLEDGMENT

This work was supported by Chinese Ministry of Science and Technology 973 grant (2014CB849603), the National Natural Science Foundation of China (NSFC) (Grant No. 21772092) and the Priority Academic Program Development of Jiangsu Higher Education Institutions – China (PAPD). We thank Dr. Jianwei Bian for crucial comments and suggestions. The computational resources utilized in this research were provided by the Shanghai Supercomputer Center.

REFERENCES

(1) (a) Knochel, P.; Normant, J. F., Copper and zinc mixed *gem*-dimetallic organic compounds synthesis and reactivity. part 3. *Tetrahedron Lett.* **1986**, *27*, 4427-4430; (b) Marek, I.; Normant, J.-F., Synthesis and Reactivity of sp^3-Geminated Organodimetallics. *Chem. Rev.* **1996**, *96*, 3241-3268; (c) Marek, I.; Schreiner, P. R.; Normant, J. F., Allyl Zincation of Vinyl Metals: A Computational Study. *Org. Lett.* **1999**, *1*, 929-931; (d) Marek, I., Synthesis and Reactivity of sp^2 Geminated Organobismetallic Derivatives. *Chem. Rev.* **2000**, *100*, 2887-2900; (e) Shimizu, M.; Nakamaki, C.; Shimono, K.; Schelper, M.; Kurahashi, T.; Hiyama, T., Stereoselective Cross-Coupling Reaction of 1,1-Diboryl-1-alkenes with Electrophiles: A Highly Stereocontrolled Approach to 1,1,2-Triaryl-1-alkenes. *J. Am. Chem. Soc.* **2005**, *127*, 12506-12507; (f) Molander, G. A.; Sandrock, D. L., Orthogonal Reactivity in Boryl-Substituted Organotrifluoroborates. *J. Am. Chem. Soc.* **2008**, *130*, 15792-15793; (g) Klis, T.; Lulinski, S.; Serwatowski, J., Formation and Synthetic Applications of Metalated Organoboranes. *Curr. Org. Chem.* **2010**, *14*, 2549-2566; (h) Lee, J. C. H.; McDonald, R.; Hall, D. G., Enantioselective preparation and chemoselective cross-coupling of 1,1-diboron compounds. *Nat. Chem.* **2011**, *3*, 894-899; (i) Chen, M.; Roush, W. R., Enantioselective Synthesis of (E)-δ-Silyl-anti-homoallylic Alcohols *via* an Enantiodivergent Hydroboration-Crotylboration Reaction of a Racemic Allenylsilane. *Org. Lett.* **2013**, *15*, 1662-1665; (j) Mlynarski, S. N.; Schuster, C. H.; Morken, J. P., Asymmetric synthesis from terminal alkenes by cascades of diboration and cross-coupling. *Nature* **2014**, *505*, 386-390; (k) Xu, L.; Ding, S.; Li, P., Site-Differentiated Polyboron Arenes Prepared by Direct C–H Borylation and Their Highly Selective Suzuki-Miyaura Cross-Coupling Reactions. *Angew. Chem. Int. Ed.* **2014**, *53*, 1822-1826; (l) Crudden, C. M.; Ziebenhaus, C.; Rygus, J. P.; Ghozati, K.; Unsworth, P. J.; Nambo, M.; Voth, S.; Hutchinson, M.; Laberge, V. S.; Maekawa, Y.; Imao, D., Iterative protecting group-free cross-coupling leading to chiral multiply arylated structures. *Nat. Commun.* **2016**, *7*, 11065-11071; (m) Stephens, T. C.; Pattison, G., Transition-Metal-Free Homologative Cross-Coupling of Aldehydes and Ketones with Geminal Bis(boron) Compounds. *Org. Lett.* **2017**, *19*, 3498-3501; (n) Yamazaki, A.; Nagao, K.; Iwai, T.; Ohmiya, H.; Sawamura, M., Phosphine-Catalyzed anti-Carboboration of Alkynoates with 9-BBN-Based 1,1-Diborylalkanes: Synthesis and Use of Multisubstituted gamma-Borylallylboranes. *Angew. Chem. Int. Ed.* **2018**, *57*, 3196-3199.

(2) (a) Tucker, C. E.; Knochel, P., A highly stereoselective olefination of aldehydes using new zinc and zirconium 1,1-bimetallic reagents. *J. Am. Chem. Soc.* **1991**, *113*, 9888-9890; (b) Tucker, C. E.; Greve, B.; Klein, W.; Knochel, P., Preparation of polyfunctional olefins and allenes using 1,1-bimetallics of zinc and zirconium. *Organometallics* **1994**, *13*, 94-101; (c) Normant, J. F., 1,1-Dimetallic Reagents for the Elaboration of Stereoselectively Di- or Trisubstituted Linear

Substrates. *Acc. Chem. Res.* **2001**, *34*, 640-644; (d) Marek, I., Synthesis and reactivity of geminated organobismetallic derivatives. *Actualite Chimique* **2003**, 17-24.

(3) (a) Zheng, B.; Srebnik, M., Preparation and selective cleavage reactions of boron-zirconium 1,1-bimetalloalkanes. *Tetrahedron Lett.* **1993**, *34*, 4133-4136; (b) Skrzypczak-Jankun, E.; Cheesman, B. V.; Zheng, B.; Lemert, R. M.; Asthana, S.; Srebnik, M., First example of a stable 1,1-bidentate Lewis acid based on boron and zirconium: synthesis, reactivity, X-ray analysis and NMR studies. *J. Chem. Soc. Chem. Commun.* **1994**, 127-128; (c) Zheng, B.; Srebnik, M., Synthesis of a new class of bidentate Lewis acids based on boronic esters and zirconocene. *J. Organomet. Chem.* **1994**, *474*, 49-53; (d) Zheng, B.; Srebnik, M., Reactions of N-halosuccinimides with 1,1-bimetallics based on zirconocene and boronic esters: A new synthesis of α-haloboronic esters. *Tetrahedron Lett.* **1994**, *35*, 1145-1148; (e) Zheng, B.; Srebnik, M., Diastereoselective hydrozirconation of optically active 1-alkenyl boryl derivatives: A conversion of 1-alkynes to optically active 1-deuterio primary alcohols. *Tetrahedron Lett.* **1994**, *35*, 6247-6250; (f) Pereira, S.; Srebnik, M., Conjugate addition of *gem*-borazirconocene alkanes to Michael acceptors. *Tetrahedron Lett.* **1995**, *36*, 1805-1808; (g) Zheng, B.; Srebnik, M., A new directed synthesis of enol borates from *gem*-borazirconocene alkanes, and their regioselective conversion to α-bromo ketones. *Tetrahedron Lett.* **1995**, *36*, 5665-5668; (h) Zheng, B.; Srebnik, M., Use of *gem*-Borazirconocene Alkanes in the Regioselective Synthesis of. alpha.-Allenic Boronic Esters and Conversion of the Latter to Dienes and Trienes. *J. Org. Chem.* **1995**, *60*, 486-487; (i) Wipf, P.; Jahn, H., Synthetic applications of organochlorozirconocene complexes. *Tetrahedron* **1996**, *52*, 12853-12910; (j) Zheng, B.; Deloux, L.; Pereira, S.; Skrzypczak-Jankun, E.; Cheesman, B. V.; Sabat, M.; Srebnik, M., Synthesis and Reactions of *gem*-Borazirconocenes. *Appl. Organomet. Chem.* **1996**, *10*, 267-278; (k) Touchet, S.; Carreaux, F.; Carboni, B.; Bouillon, A.; Boucher, J.-L., Aminoboronic acids and esters: from synthetic challenges to the discovery of unique classes of enzyme inhibitors. *Chem. Soc. Rev.* **2011**, *40*, 3895-3914.

(4) (a) Negishi, E.; Van Horn, D. E., Selective carbon-carbon bond formation *via* transition metal catalysis. 4. A novel approach to cross-coupling exemplified by the nickel-catalyzed reaction of alkenylzirconium derivatives with aryl halides. *J. Am. Chem. Soc.* **1977**, *99*, 3168-3170; (b) Negishi, E.; Okukado, N.; King, A. O.; Van Horn, D. E.; Spiegel, B. I., Selective carbon-carbon bond formation *via* transition metal catalysts. 9. Double metal catalysis in the cross-coupling reaction and its application to the stereo- and regioselective synthesis of trisubstituted olefins. *J. Am. Chem. Soc.* **1978**, *100*, 2254-2256; (c) Wiskur, S. L.; Korte, A.; Fu, G. C., Cross-Couplings of Alkyl Electrophiles under "Ligandless" Conditions: Negishi Reactions of Organozirconium Reagents. *J. Am. Chem. Soc.* **2004**, *126*, 82-83; (d) Lou, S.; Fu, G. C., Enantioselective Alkenylation *via* Nickel-Catalyzed Cross-Coupling with Organozirconium Reagents. *J. Am. Chem. Soc.* **2010**, *132*, 5010-5011; (e) You, H.; Rideau, E.; Sidera, M.; Fletcher, S. P., Non-stabilized nucleophiles in Cu-catalysed dynamic kinetic asymmetric allylic alkylation. *Nature* **2015**, *517*, 351-355; (f) Indukuri, K.; Riant, O., Transmetalation of Alkylzirconocenes in Copper-Catalyzed Alkyl–Alkynyl Cross-Coupling Reactions. *Adv. Synth. Cataly.* **2017**, *359*, 2425-2433; (g) Jacques, R.; Pullin, R. D. C.; Fletcher, S. P., Desymmetrization of meso-bisphosphates using copper catalysis and alkylzirconocene nucleophiles. *Nat. Commun.* **2019**, *10*, 21.

(5) Gao, Y.; Yang, C.; Wang, J.; Jiang, C.; Qi, X., Visible-Light-Induced Nickel-Catalyzed Cross-Coupling with Alkylzirconocenes from Unactivated Alkenes. *Chem* **2020**, *6*, 675-688.

(6) Song, Z.; Takahashi, T., Hydrozirconation of Alkenes and Alkynes. In Comprehensive Organic Synthesis. Elsevier, **2014**. 838–876. DOI: 10.1016/B978-0-08-097742-3.00825-9.

(7) For selected examples of chain walking. See: (a) Werner, E. W.; Mei, T.-S.; Burckle, A. J.; Sigman, M. S., Enantioselective Heck arylations of acyclic alkenyl alcohols using a redox-relay strategy. *Science* **2012**, *338*, 1455-1458; (b) Obligacion, J. V.; Chirik, P. J., Bis(imino)pyridine cobalt-catalyzed alkene isomerization-hydroboration: a strategy for remote hydrofunctionalization with terminal selectivity. *J. Am. Chem. Soc.* **2013**, *135*, 19107-19110; (c) Masarwa, A.; Didier, D.; Zabrodski, T.; Schinkel, M.; Ackermann, L.; Marek, I., Merging allylic carbon–hydrogen and selective carbon–carbon bond activation. *Nature* **2014**, *505*, 199-203; (d) Mei, T.-S.; Patel, H. H.; Sigman, M. S., Enantioselective construction of remote quaternary stereocentres. *Nature* **2014**, *508*, 340-344; (e) Vasseur, A.; Bruffaerts, J.; Marek, I., Remote functionalization through alkene isomerization. *Nat. Chem.* **2016**, *8*, 209-219; (f) Zhu, S.; Niljianskul, N.; Buchwald, S. L., A direct approach to amines with remote stereocentres by enantioselective CuH-catalysed reductive relay hydroamination. *Nat. Chem.* **2016**, *8*, 144-150; (g) Gaydou, M.; Moragas, T.; Juliá-Hernández, F.; Martin, R., Site-selective catalytic carboxylation of unsaturated hydrocarbons with CO_2 and water. *J. Am. Chem. Soc.* **2017**, *139*, 12161-12164; (h) He, Y.; Cai, Y.; Zhu, S., Mild and Regioselective Benzylic C-H Functionalization: Ni-Catalyzed Reductive Arylation of Remote and Proximal Olefins. *J. Am. Chem. Soc.* **2017**, *139*, 1061-1064; (i) Juliá-Hernández, F.; Moragas, T.; Cornella, J.; Martin, R., Remote carboxylation of halogenated aliphatic hydrocarbons with carbon dioxide. *Nature* **2017**, *545*, 84-88; (j) Singh, S.; Bruffaerts, J.; Vasseur, A.; Marek, I., A unique Pd-catalysed Heck arylation as a remote trigger for cyclopropane selective ring-opening. *Nat. Commun.* **2017**, *8*, 14200- 14209; (k) Bhunia, A.; Bergander, K.; Studer, A., Cooperative palladium/Lewis acid-catalyzed transfer hydrocyanation of alkenes and alkynes using 1-methylcyclohexa-2, 5-diene-1-carbonitrile. *J. Am. Chem. Soc.* **2018**, *140*, 16353-16359; (l) Bruffaerts, J.; Pierrot, D.; Marek, I., Efficient and stereodivergent synthesis of unsaturated acyclic fragments bearing contiguous stereogenic elements. *Nat. Chem.* **2018**, *10*, 1164-1170; (m) Chen, X.; Cheng, Z.; Guo, J.; Lu, Z., Asymmetric remote C-H borylation of internal alkenes *via* alkene isomerization. *Nat. Commun.* **2018**, *9*, 3939; (n) Kohler, D. G.; Gockel, S. N.; Kennemur, J. L.; Waller, P. J.; Hull, K. L., Palladium-catalysed anti-Markovnikov selective oxidative amination. *Nat. Chem.* **2018**, *10*, 333-340; (o) Obligacion, J. V.; Chirik, P. J., Earth-abundant transition metal catalysts for alkene hydrosilylation and hydroboration. *Nat. Rev. Chem.* **2018**, *2*, 15-34; (p) Peng, L.; Li, Y.; Li, Y.; Wang, W.; Pang, H.; Yin, G., Ligand-Controlled Nickel-Catalyzed Reductive Relay Cross-Coupling of Alkyl Bromides and Aryl Bromides. *ACS Cataly.* **2018**, *8*, 310-313; (q) Peng, L.; Li, Z.; Yin, G., Photochemical Nickel-Catalyzed Reductive Migratory Cross-Coupling of Alkyl Bromides with Aryl Bromides. *Org. Lett.* **2018**, *20*, 1880-1883; (r) Sommer, H.; Juliá-Hernández, F.; Martin, R.; Marek, I., Walking metals for remote functionalization. *ACS central sci.* **2018**, *4*, 153-165; (s) Sun, S.-Z.; Börjesson, M.; Martin-Montero, R.; Martin, R., Site-Selective Ni-Catalyzed Reductive Coupling of α-Haloboranes with Unactivated Olefins. *J. Am. Chem. Soc.* **2018**, *140*, 12765-12769; (t) Xiao, J.; He, Y.; Ye, F.; Zhu, S., Remote sp^3 C–H Amination of Alkenes with Nitroarenes. *Chem* **2018**, *4*, 1645-1657; (u) Kapat, A.; Sperger, T.; Guven, S.; Schoenebeck, F., E-Olefins through intramolecular radical relocation. *Science* **2019**, *363*, 391-396; (v) Kochi, T.; Ichinose, K.; Shigekane, M.; Hamasaki, T.; Kakiuchi, F., Metal-Catalyzed Sequential Formation of Distant Bonds in Organic Molecules: Palladium-Catalyzed Hydrosilylation/Cyclization of 1,n-Dienes by Chain Walking. *Angew. Chem. Int. Ed.* **2019**, *58*, 5261-5265; (w) Liu, J.; Yuan, Q.; Toste, F. D.; Sigman, M. S., Enantioselective construction of remote tertiary carbon–fluorine bonds. *Nat. Chem.* **2019**, *11*, 710-715; (x) Pang, H.; Wu, D.; Cong, H.; Yin, G., Stereoselective Palladium-Catalyzed 1,3-Arylboration of Unconjugated Dienes for Expedient Synthesis of 1,3-Disubstituted Cyclohexanes. *ACS Cataly.* **2019**, *9*, 8555-8560; (y) Romano, C.; Fiorito, D.; Mazet, C., Remote Functionalization of α,β-Unsaturated Carbonyls by Multimetallic Sequential Catalysis. *J. Am. Chem. Soc.* **2019**, *141*, 16983-16990; (z) Zhang, Y.; Xu, X.; Zhu, S., Nickel-catalysed selective migratory hydrothiolation of alkenes and alkynes with thiols. *Nat. Commun.* **2019**, *10*, 1752.

(8) Vasseur, A.; Perrin, L.; Eisenstein, O.; Marek, I., Remote

functionalization of hydrocarbons with reversibility enhanced stereocontrol. *Chem. Sci.* **2015**, *6*, 2770-2776.

(9) For selected examples of lithiation-borylationy reaction. See: (a) Thomas, S. P.; French, R. M.; Jheengut, V.; Aggarwal, V. K., Homologation and alkylation of boronic esters and boranes by 1,2-metallate rearrangement of boronate complexes. *Chem. Rec.* **2009**, *9*, 24-39; (b) Leonori, D.; Aggarwal, V. K., Lithiation-borylation methodology and its application in synthesis. *Acc. Chem. Res.* **2014**, *47*, 3174-3183; (c) Zhang, L.; Lovinger, G. J.; Edelstein, E. K.; Szymaniak, A. A.; Chierchia, M. P.; Morken, J. P., Catalytic conjunctive cross-coupling enabled by metal-induced metallate rearrangement. *Science* **2016**, *351*, 70-74; (d) Edelstein, E. K.; Namirembe, S.; Morken, J. P., Enantioselective Conjunctive Cross-Coupling of Bis(alkenyl)borates: A General Synthesis of Chiral Allylboron Reagents. *J. Am. Chem. Soc.* **2017**, *139*, 5027-5030; (e) Lovinger, G. J.; Morken, J. P., Ni-Catalyzed Enantioselective Conjunctive Coupling with C(sp^3) Electrophiles: A Radical-Ionic Mechanistic Dichotomy. *J. Am. Chem. Soc.* **2017**, *139*, 17293-17296; (f) Sandford, C.; Aggarwal, V. K., Stereospecific functionalizations and transformations of secondary and tertiary boronic esters. *Chem. Commun.* **2017**, *53*, 5481-5494; (g) Myhill, J. A.; Wilhelmsen, C. A.; Zhang, L.; Morken, J. P., Diastereoselective and Enantioselective Conjunctive Cross-Coupling Enabled by Boron Ligand Design. *J. Am. Chem. Soc.* **2018**, *140*, 15181-15185; (h) Namirembe, S.; Morken, J. P., Reactions of organoboron compounds enabled by catalyst-promoted metalate shifts. *Chem. Soc. Rev.* **2019**, *48*, 3464-3474.

(10) Armstrong, R.; Aggarwal, V., 50 Years of Zweifel Olefination: A Transition-Metal-Free Coupling. *Synthesis* **2017**, *49*, 3323-3336.

(11) (a) Leonori, D.; Aggarwal, V. K., Stereospecific couplings of secondary and tertiary boronic esters. *Angew. Chem. Int. Ed.* **2015**, *54*, 1082-1096; (b) Chen, B.; Cao, P.; Yin, X.; Liao, Y.; Jiang, L.; Ye, J.; Wang, M.; Liao, J., Modular Synthesis of Enantioenriched 1,1,2-Triarylethanes by an Enantioselective Arylboration and Cross-Coupling Sequence. *ACS Catal.* **2017**, *7*, 2425-2429; (c) Choi, J.; Fu, G. C., Transition metal-catalyzed alkyl-alkyl bond formation: Another dimension in cross-coupling chemistry. *Science* **2017**, *356*, eaaf7230; (d) Zhang, Y.; Han, B.; Zhu, S., Rapid Access to Highly Functionalized Alkyl Boronates by NiH-Catalyzed Remote Hydroarylation of Boron-Containing Alkenes. *Angew. Chem. Int. Ed.* **2019**, *58*, 13860-13864; (e) Campbell, M. W.; Compton, J. S.; Kelly, C. B.; Molander, G. A., Three-Component Olefin Dicarbofunctionalization Enabled by Nickel/Photoredox Dual Catalysis. *J. Am. Chem. Soc.* **2019**. 141, 20069-20078.

(12) (a) Netherton, M. R.; Dai, C.; Neuschütz, K.; Fu, G. C., Room-Temperature Alkyl–Alkyl Suzuki Cross-Coupling of Alkyl Bromides that Possess β Hydrogens. *J. Am. Chem. Soc.* **2001**, *123*, 10099-10100; (b) Kirchhoff, J. H.; Dai, C.; Fu, G. C., A Method for Palladium-Catalyzed Cross-Couplings of Simple Alkyl Chlorides: Suzuki Reactions Catalyzed by [Pd2(dba)$_3$]/PCy$_3$. *Angew. Chem. Int. Ed.* **2002**, *41*, 1945-1947; (c) Saito, B.; Fu, G. C., Alkyl–Alkyl Suzuki Cross-Couplings of Unactivated Secondary Alkyl Halides at Room Temperature. *J. Am. Chem. Soc.* **2007**, *129*, 9602-9603; (d) Saito, B.; Fu, G. C., Enantioselective Alkyl–Alkyl Suzuki Cross-Couplings of Unactivated Homobenzylic Halides. *J. Am. Chem. Soc.* **2008**, *130*, 6694-6695; (e) Lu, Z.; Fu, G. C., Alkyl–Alkyl Suzuki Cross-Coupling of Unactivated Secondary Alkyl Chlorides. *Angew. Chem. Int. Ed.* **2010**, *49*, 6676-6678; (f) Owston, N. A.; Fu, G. C., Asymmetric Alkyl–Alkyl Cross-Couplings of Unactivated Secondary Alkyl Electrophiles: Stereoconvergent Suzuki Reactions of Racemic Acylated Halohydrins. *J. Am. Chem. Soc.* **2010**, *132*, 11908-11909; (g) Lu, Z.; Wilsily, A.; Fu, G. C., Stereoconvergent Amine-Directed Alkyl–Alkyl Suzuki Reactions of Unactivated Secondary Alkyl Chlorides. *J. Am. Chem. Soc.* **2011**, *133*, 8154-8157; (h) Zultanski, S. L.; Fu, G. C., Catalytic Asymmetric γ-Alkylation of Carbonyl Compounds *via* Stereoconvergent Suzuki Cross-Couplings. *J. Am. Chem. Soc.* **2011**, *133*, 15362-15364; (i) Wilsily, A.; Tramutola, F.; Owston, N. A.; Fu, G. C., New Directing Groups for Metal-Catalyzed Asymmetric Carbon–Carbon Bond-Forming Processes: Stereoconvergent Alkyl–Alkyl Suzuki Cross-Couplings of Unactivated Electrophiles. *J. Am. Chem. Soc.* **2012**, *134*, 5794-5797; (j) Fu, G. C., Transition-Metal Catalysis of Nucleophilic Substitution Reactions: A Radical Alternative to SN$_1$ and SN$_2$ Processes. *ACS Central Sci.* **2017**, *3*, 692-700.

(13) Pereira, S.; Srebnik, M., Facile boron migration during hydrozirconation of alkenylboronates. *J. Org.Chem.* **1995**, *60*, 4316-4317.

(14) The Ni-catalyzed cross-coupling reaction with different electrophilic partners such as primary alkyl and alkenyl halides had been studied in details and presented in the supplemental information (Table S8).

(15) Lu, T.; Chen, F., Multiwfn: A multifunctional wavefunction analyzer. *J. Comput. Chem.* **2012**, *33*, 580-592.

(16) Humphrey, W.; Dalke, A.; Schulten, K., VMD: Visual molecular dynamics. *J. Molec. Graphics* **1996**, *14*, 33-38.

(17) Mayer, I., Charge, bond order and valence in the AB initio SCF theory. *Chem. Phys. Lett.* **1983**, *97*, 270-274.

(18) (a) Noh, D.; Chea, H.; Ju, J.; Yun, J., Highly Regio- and Enantioselective Copper-Catalyzed Hydroboration of Styrenes. *Angew. Chem. Int. Ed.* **2009**, *48*, 6062-6064; (b) Sim, H.-S.; Feng, X.; Yun, J., Copper-Catalyzed Enantioselective β-Boration of Acyclic Enones. *Chem. Eur.* **2009**, *15*, 1939-1943; (c) Coombs, J. R.; Zhang, L.; Morken, J. P., Enantiomerically Enriched Tris(boronates): Readily Accessible Conjunctive Reagents for Asymmetric Synthesis. *J. Am. Chem. Soc.* **2014**, *136*, 16140-16143; (d) Mlynarski, S. N.; Schuster, C. H.; Morken, J. P., Asymmetric synthesis from terminal alkenes by cascades of diboration and cross-coupling. *Nature* **2014**, *505*, 386-390; (e) Potter, B.; Szymaniak, A. A.; Edelstein, E. K.; Morken, J. P., Nonracemic Allylic Boronates through Enantiotopic-Group-Selective Cross-Coupling of Geminal Bis(boronates) and Vinyl Halides. *J. Am. Chem. Soc.* **2014**, *136*, 17918-17921; (f) Schmidt, J.; Choi, J.; Liu, A. T.; Slusarczyk, M.; Fu, G. C., A general, modular method for the catalytic asymmetric synthesis of alkylboronate esters. *Science* **2016**, *354*, 1265-1269; (g) Jang, W. J.; Song, S. M.; Moon, J. H.; Lee, J. Y.; Yun, J., Copper-Catalyzed Enantioselective Hydroboration of Unactivated 1,1-Disubstituted Alkenes. *J. Am. Chem. Soc.* **2017**, *139*, 13660-13663; (h) Jang, W. J.; Yun, J., Copper-Catalyzed Tandem Hydrocupration and Diastereo- and Enantioselective Borylalkyl Addition to Aldehydes. *Angew. Chem. Int. Ed.* **2018**, *57*, 12116-12120; (i) Lee, H.; Yun, J., Copper(I)-Catalyzed Enantioselective 1,6-Borylation of α,β,γ,δ-Unsaturated Phosphonates. *Org. Lett.* **2018**, *20*, 7961-7964; (j) Wang, Z.; Bachman, S.; Dudnik, A. S.; Fu, G. C., Nickel-Catalyzed Enantioconvergent Borylation of Racemic Secondary Benzylic Electrophiles. *Angew. Chem. Int. Ed.* **2018**, *57*, 14529-14532. (k) Viereck, P.; Krautwald, S.; Pabst, T. P.; Chirik, P. J., A Boron Activating Effect Enables Cobalt-Catalyzed Asymmetric Hydrogenation of Sterically Hindered Alkenes. *J. Am. Chem. Soc.* **2020**, *142*, 3923-3930.

Insert Table of Contents artwork here