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RESEARCH ARTICLE

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Cobalt-Catalyzed Asymmetric Remote Borylation of Alkyl Halides

Minghao Zhang,[a]# Zhiyang Ye,[a]# and Wanxiang Zhao[a]*

ABSTRACT: Enantioselective functionalization of racemic alkyl halides is an efficient strategy to assemble complex chiral molecules, but remains one of the biggest challenges in organic chemistry. The distant and selective activation of unreactive C−H bonds in alkyl halides has received growing interest as it enables rapid generation of molecular complexity from simple building blocks. Here, we reported a cobalt-catalyzed remote borylation of alkyl (pseudo)halides (alkyl−X, X = I, Br, Cl, OTs) with pinacolborane (HBpin) and presented a robust approach for the generation of valuable chiral secondary organoboronates from racemic alkyl halides. This migration borylation reaction is compatible with primary, secondary, and tertiary bromides, offering direct access to a broad range of alkylboronates. The extension of this catalytic system to the borylation of aryl halides was also demonstrated. Preliminary mechanistic studies revealed that this remote borylation involved a radical reaction pathway.

Introduction

Alkylboronates are recognized as one of the most versatile building blocks in chemical synthesis due to their diverse reactivity profile,[1] and have been extensively applied in pharmaceutical, material sciences, and agrochemicals.[2] The stereospecific transformations of chiral alkylboronates further enlarge their applications in synthetic chemistry.[3] Consequently, the alkylboronates have inspired remarkable synthetic endeavors toward the efficient construction of carbon−boron bonds, and significant advances have been achieved in the last decades.[4] Among the existing routes to alkylboronates, catalytic borylation of alkyl halides is one of the most convenient and straightforward strategies owing to the abundance of the starting materials and cost efficiency.[5] Specifically, transition metal-catalyzed borylation of alkyl halides pioneered by Marder, Fu, Ito, and Liu provides an efficient method to prepare alkylboronates under mild reaction conditions.[5a-c] In addition, photoinduced borylation of alkyl halides has recently proved to be an alternative synthetic tool for the construction of alkylboronates, and can be complemented with transition metal-catalyzed strategies in the synthesis of alkylboronates.[4g,6] Despite these outstanding advances, some significant challenges and limitations remain. For example, these protocols are limited to producing racemic alkylboronates, and the enantioselective borylation of alkyl halides is largely underdeveloped although it is highly desirable because it allows rapid access to value-added chiral alkylboronates. To date, only two asymmetric examples are available, which were disclosed by Fu[7] and Ito[8],

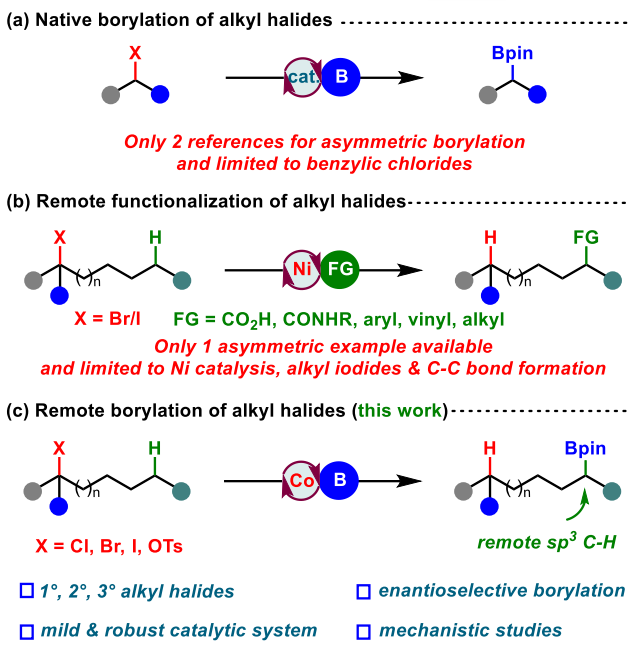

Figure 1. (a) Native borylation of alkyl halides. (b) Remote functionalization of alkyl halides (c) Remote borylation of alkyl halides.

respectively, delivering chiral benzylboronates from benzyl chlorides under nickel or copper catalysis. Moreover, diboron reagents such as bis(pinacolato)diboron (B_2pin_2) have been typically utilized in the known borylation of alkyl (pseudo)halides.[4] On consideration of atom economy, the catalytic borylation using borane is undoubtedly more attractive, but is much less developed.[5m,5n] Additionally, the existing approaches can only be used to convert C−X bonds to C−B bonds, i.e. native borylation of alkyl halides (Figure 1a), and the remote borylation of alkyl (pseudo)halides is yet to be reported to the best of our knowledge.

Direct elaboration of a distant aliphatic C−H bond has been shown to be a powerful platform in organic synthesis as it allows rapid generation of molecular complexity from easily available starting materials.[9] In this context, the fascinating chain-walking process of alkyl (pseudo)halides has attracted numerous attention,[10] enabling direct functionalization of C(sp^3)−H bonds without the need for prefunctionalization or installation of a directing group. For instance, Ni-catalyzed remote carboxylation and amidation of alkyl bromides with carbon dioxide and isocyanates as coupling partners were developed by Martin.[10b,10j] The remote migratory arylation, alkenylation and alkylation of alkyl bromides developed by Zhu,[10a] Rueping,[10h] Yin,[10c,10d] Feng,[10f,10i] Mei[10g] and Shu[10k] represent significant progress in distal functionalization of alkyl halides. However, the alkyl halides used in these disclosures are typically limited to alkyl bromides or iodides, and the challenging unactivated alkyl chlorides are barely utilized in chain-walking reactions. Furthermore, the known remote functionalization of alkyl halides is restricted to the use of nickel-based catalysts (Figure 1b). Given the low toxicity, environmentally benign nature, and various oxidation state of cobalt catalysts, the distant

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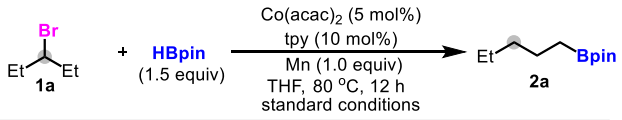
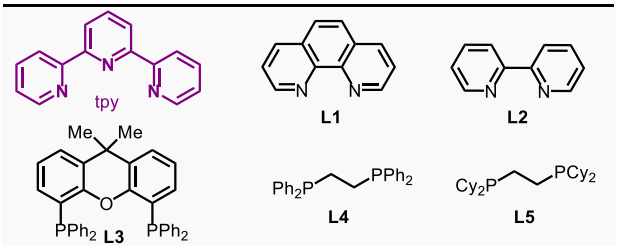
Table 1. Variation of reaction parameters.[a]



Entry	Variation from 'standard conditions'	Yield(%)[b]
1	none	85 (82)
2	**L1** instead of tpy	n.d.
3	**L2** instead of tpy	n.d.
4	**L3** instead of tpy	15
5	**L4** instead of tpy	trace
6	**L5** instead of tpy	25
7	DMF instead of THF	62
8	DME instead of THF	43
9	CyH instead of THF	n.d.
10	$CoBr_2$ instead of $Co(acac)_2$	79
11	$Co(acac)_3$ instead of $Co(acac)_2$	66
12	Zn instead of Mn	n.d.
13	w/o $Co(acac)_2$ or Mn or tpy	n.d.



[a] Reaction conditions: **1a** (0.2 mmol), $Co(acac)_2$ (5 mol%), ligand (10 mol%), HBpin (1.5 equiv), Mn (1.0 equiv), THF (1.0 mL), 80 °C, 12 h. [b] The yields were determined by GC using dodecane as the internal standard; isolated yield shown in parentheses; n.d. = no detected; w/o = without.

functionalization of alkyl halides catalyzed by cobalt is highly desirable, but remains to be explored. Of particular note is that only carbon–carbon bond formation is demonstrated in the reported remote functionalization of alkyl halides, and racemic products are usually provided in these reactions. The lone asymmetric example is a Ni-catalyzed asymmetric migratory acylation of alkyl iodides reported by Zhu very recently.[11] Catalytic enantioselective construction of carbon–heteroatom bonds is still a formidable challenge in this field. By virtue of diverse and stereospecific carbon−boron bond transformations, the enantioselective remote borylation of alkyl halides is enticing, but it still remains unknown.

In view of our long-standing interest in organoboron chemistry and our successes in the remote borylation of unactivated C(sp^3)−H bonds,[12] we sought to develop a catalytic strategy for the distant borylation of alkyl halides, especially for the asymmetric borylative coupling of racemic alkyl halides. Herein we report a cobalt-catalyzed asymmetric remote C(sp^3)−H borylation of alkyl bromides to afford a series of synthetically useful chiral benzylic organoboronates. The migratory borylation of alkyl (pseudo)halides (alkyl−X, X = I, Br, Cl, OTs) with terminal selectivity is also demonstrated (Figure 1c). Various primary, secondary, and tertiary bromides all successfully participated in this migratory borylation process, demonstrating the robustness of this protocol. Additionally, this strategy could also be applicable to the borylation of aryl (pseudo)halides (aryl−X, X = I, Br, Cl, OTf), providing aryl boronates in good to excellent yields. Notably, alkanes as raw materials obtained in bulk from petroleum processing could also be used as substrates to give value-added borylated products with excellent regio- and chemoselectivity, which is particularly appealing in the manipulation of alkanes.

Results and Discussion

To test the viability of cobalt-catalyzed remote C(sp^3)−H borylation of alkyl halides, the initial optimization studies involved a model reaction between secondary bromide **1a** and HBpin in the presence of cobalt catalyst, ligand, and reductant (Table 1). Upon screening a series of reaction parameters, the desired migratory borylative product **2a** was generated in 82% isolated yield when **1a** was treated with $Co(acac)_2$, terpyridine (tpy), HBpin, and Mn powder (Table 1, entry 1). The evaluation of ligands showed that the use of bidentate 1,10-phenanthroline (**L1**) and 2,2'-bipyridine ligand (**L2**) proved inefficient for this transformation (Table 1, entries 2-3). Moreover, the ligands **L3** and **L4** employed in our previous migratory hydroboration[12a,12b] gave significantly lower yields with the overwhelming majority of alkyl bromide **1a** recovered (Table 1, entries 4-5). It is worth noting that the ligand **L5** commonly used in cobalt-catalyzed migratory hydroboration of alkenes[12b,13] resulted in poor conversion (Table 1, entry 6). The survey of solvent effect revealed that the utilization of DMF, DME, and CyH all gave inferior outcomes (Table 1, entries 7-9). The cobalt catalysts were also evaluated. The borylative product **2a** was obtained in a slightly lower yield (79%) when $CoBr_2$ was used (Table 1, entry 10), although the utilization of $Co(acac)_3$ provided the desired product in an inferior yield (66%, Table 1, entry 11). Of note, this transformation was completely inhibited when Zn was employed instead of Mn powder (Table 1, entry 12). Finally, control experiments revealed that all of the reaction parameters were essential to ensure high reaction efficiency (Table 1, entry 13).

With the optimal reaction conditions determined, we first investigated the scope of secondary bromides for this remote C(sp^3)−H borylation. As depicted in Table 2, a series of alkyl bromides with various substituents and functional groups all proceeded smoothly to deliver the migratory borylative products in good yields and excellent regioselectivities. The constitutional isomers of bromononane, 2-bromononane and 5-bromononane, were competent substrates to furnish exclusively product **2b** in comparable yields, showing the viability of implementing regioconvergent borylation processes. Moreover, the substrate with a cyclic alkyl group reacted efficiently to give the desired product **2c** in 78% yield. Although multiple primary C(sp^3)−H bonds in a substrate might lead to site-selectivity issues, the remote borylation exclusively occurred at the less-hindered primary C(sp^3)−H site (**2d**). In addition, a range of functional groups such as protected alcohol (**2e-2g**), NBn_2 (**2h**), ester (**2i**, **2l**), Cl (**2j**), acetal (**2k**), ether (**2m**), and sulfonamide (**2n**) were well tolerated. Intriguingly, a long-distance migration of eight carbon atoms could be accomplished to afford the product **2k** albeit in diminished yield with dehalogenation as the main side reaction. It is worth mentioning that the tolerance of susceptible functional groups, like esters (**2i**, **2l**, **2m**), Cl (**2j**), and acetal (**2k**) offered the possibilities for further downstream diversification. The efficiency of this reaction was not hampered when heteroaromatic substrates such as pyrrole (**2o**), indole (**2p**), and carbazole (**2q**) were employed. Noticeably, the mild reaction

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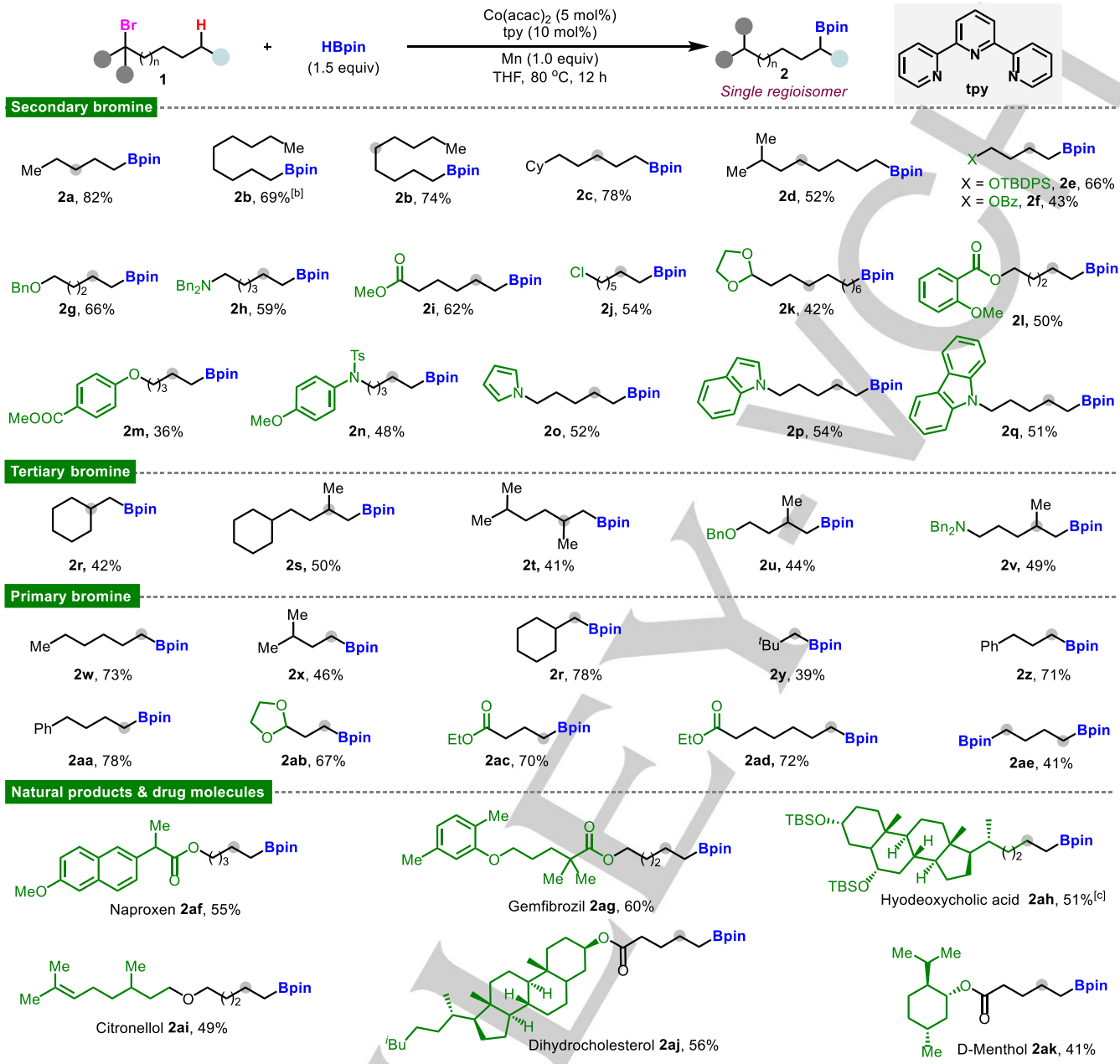
Table 2. Scope of alkyl bromides.[a]



[a] Reactions conditions: **1** (0.2 mmol), HBpin (1.5 equiv), $Co(acac)_2$ (5 mol%), tpy (10 mol%), Mn (1.0 equiv), THF (1.0 mL), 80 °C, 12 h; isolated yield. [b] 2-bromononane was used as substrate. [c] The reaction was conducted in 0.1 mmol scale.

conditions were compatible with sterically hindered tertiary alkyl bromides, leading to the formation of single regioisomers of migratory borylative products (**2r-2v**). Likewise, protected alcohol (**2u**) and NBn_2 (**2v**) in tertiary alkyl bromides were well tolerated. It is worth noting that primary bromides were also competent substrates, affording native borylation products (**2w-2ae**) in good efficiency. This method features mild reaction conditions and high functional-group tolerance and is suitable for the functionalization of drug molecules and natural products. To illustrate this point, an array of alkyl bromides bearing complex or bioactive fragments derived from drugs and natural products were subjected to standard conditions. As shown in Table 2, the alkyl bromides derived from naproxen (a non-steroidal anti-inflammatory drug) and gemfibrozil (a lipid-regulating drug) proceeded smoothly to give the corresponding products **2af** and **2ag** in 55% and 60% yields, respectively. Furthermore, the substrates bearing multiple primary C(sp^3)−H bonds prepared from hyodeoxycholic acid and citronellol were also amenable to this transformation to afford the corresponding linear borylative products **2ah-2ai** in moderate yields. Besides, the dihydrocholesterol and menthol skeletons were successfully introduced in the products **2aj-2ak** in acceptable yields.

Encouraged by the successful implementation of this distal borylation of alkyl bromides, we sought to explore the remote C(sp^3)−H bond borylation of other alkyl electrophiles, especially the more inert and challenging unactivated alkyl chlorides. Especially noteworthy is that remote functionalization of alkyl chlorides through chain walking is yet to be reported to the best of our knowledge. Pleasingly, at the elevated reaction temperature, an array of alkyl chlorides proceeded smoothly to deliver the desired products as a single regioisomer in moderate to good yields, offering an important complement to the existing

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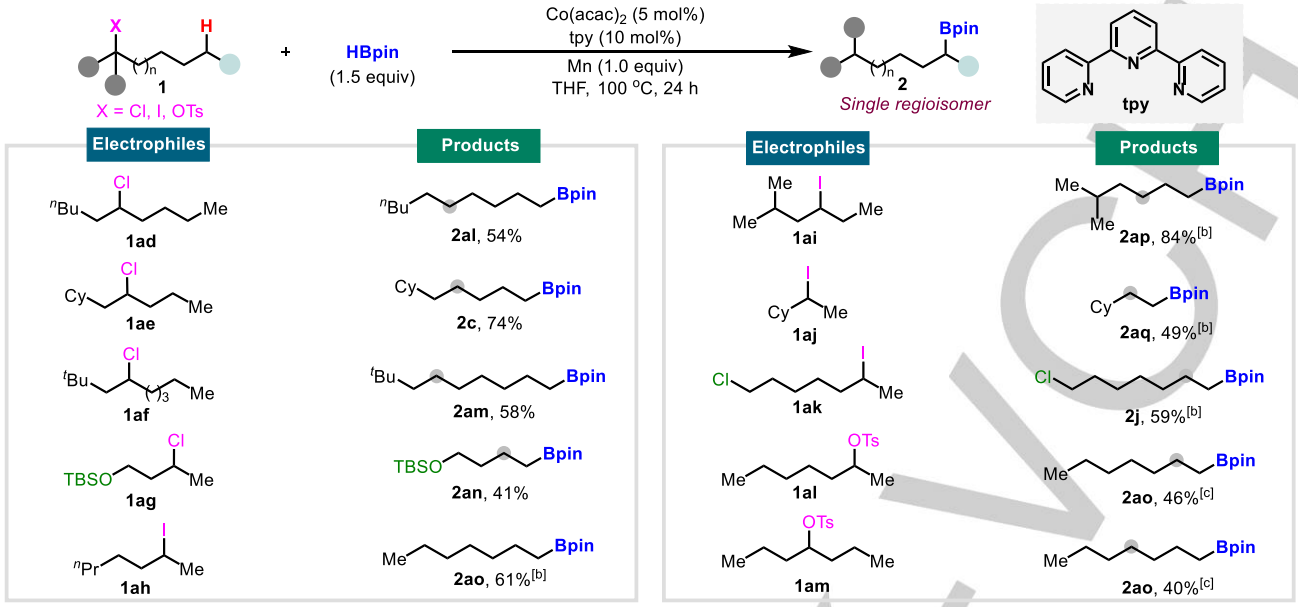
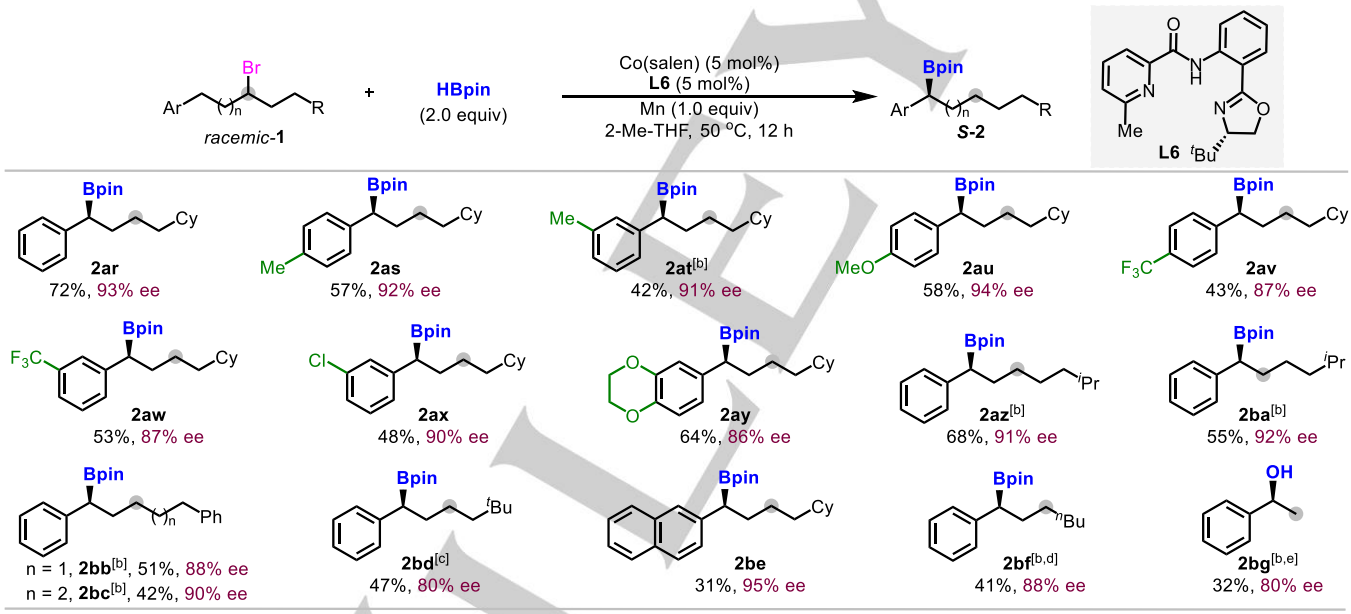
Table 3. Scope of other alkyl electrophiles.[a]



[a] Reactions conditions: **1** (0.2 mmol), HBpin (1.5 equiv), $Co(acac)_2$ (5 mol%), tpy (10 mol%), Mn (1.0 equiv), THF (1.0 mL), 100 °C, 24 h; isolated yield. [b] 50 °C, 12 h. [c] 120 °C, 36 h.

Table 4. Scope of asymmetric remote borylation.[a]



[a] Reactions conditions: *rac*-**1** (0.2 mmol), HBpin (2.0 equiv), Co(salen) (5 mol%), **L6** (5 mol%), Mn (1.0 equiv), 2-Me-THF (0.2 mL), 50 °C, 12 h; isolated yield. [b] $CoBr_2$. [c] 60 °C. [d] Benzylic/terminal = 4:1. [e] Isolated after oxidation with $NaOH/H_2O_2$, benzylic/terminal = 1.1:1.

methods towards transformations of unactivated alkyl chlorides. As shown in Table 3, the substrates bearing primary (**1ad**), secondary (**1ae**), and tertiary alkyl groups at *β*-position (**1af**) were competent to afford the corresponding products with good efficiency. Furthermore, heteroatom-containing alkyl chloride also successfully participated in this borylation reaction to furnish the valuable borylether product **2an** in synthetically useful yield. The reaction is also amenable to secondary alkyl iodides, affording primary alkylboronates **2ao-2aq** in good efficiency. Remarkably, the substrate **1ak** bearing Cl and I selectively afforded the product **2j** via the transformation of the C–I bond at the lower reaction temperature, and the C–Cl bond remained intact. In particular, the remote borylation of secondary alkyl tosylates proceeded well to furnish migratory borylation product **2ao** in a regioconvergent manner.

In light of the importance of chiral organoboronates in asymmetric synthesis[3] and inspired by the previous work from the Lu group involving asymmetric and remote borylation of alkenes,[9m] we next turned our attention to developing the asymmetric remote borylation of alkyl bromides. After exploring a series of reaction parameters (see SI for details), the desired chiral benzylic organoboronates **2ar** could be obtained in 72% yield and 93% ee when Co(salen) and **L6** were utilized as the precatalyst and the chiral ligand. It should be noted that the chiral *N*,*N*,*N*-tridentate ligand **L6** was first reported by Gossage,[14] and the use of **L6** and its analogues in asymmetric reactions was developed by Lu from 2018.[9m,15] We then examined the generality of alkyl bromides for this asymmetric

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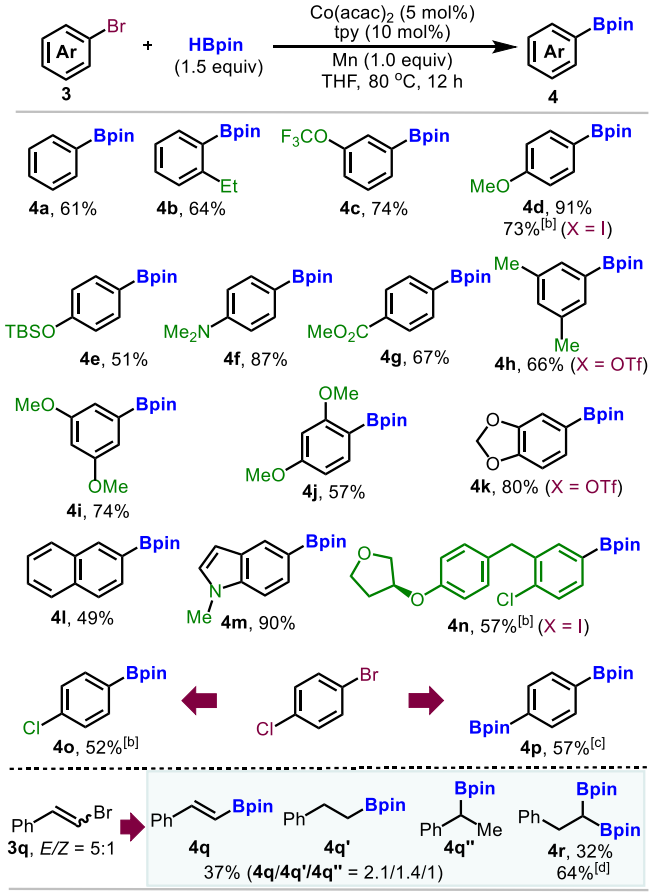
Table 5. Scope of aryl/vinyl (pseudo)halides.[a]



[a] Reactions conditions: aryl bromides (0.2 mmol), HBpin (1.5 equiv), $Co(acac)_2$ (5 mol%), tpy (10 mol%), Mn (1.0 equiv), THF (1.0 mL), 80 °C, 12 h; isolated yield. [b] 50 °C. [c] 2.5 equiv HBpin, 36 h. [d] 2.5 equiv HBpin.

migratory borylation reaction, and the results are summarized in Table 4. As shown, various functional groups such as Me, OMe, CF_3, and Cl were well tolerated, delivering the corresponding chiral alkylboronates **2as**-**2ax** in 87-94% ee. The disubstituted substrate was also applicable to afford the desired product **2ay** in good efficiency. Moreover, the reaction is amenable to the alkyl bromides with bromine located at different positions in alkyl chains (**2az**, **2ba**). The alkyl bromides bearing a phenyl and a tertiary alkyl were all applicable substrates, providing the corresponding products **2bb**-**2bd** in good enantioselectivities. In addition, the polyaromatic substrate was also competent to afford the product **2be** with 95% ee, albeit in diminished yield. Remarkably, the substrate with a linear alkyl chain also reacted to deliver **2bf** in 41% yield and 90% ee with a ratio of 4/1 (benzylic/terminal). It should be noted that a primary alkyl bromide is also suitable for this asymmetric migratory borylation to give chiral benzyl alcohol **2bg** after oxidation. Of note, the dehalogenation as a side reaction and the decomposition of alkyl boronates during the column chromatography separation, especially for benzylic organoboronates, were responsible for the moderate yields in most cases.

Following our successful borylation of alkyl (pseudo)halides, we further extended the reaction scope to the aryl (pseudo)halides. To our delight, this catalytic system is also suitable for the borylation of aryl (pseudo)halides (aryl−X, X = I, Br, Cl, OTf). As demonstrated, a range of aryl halides with electronically and sterically varied substituents readily participated in this borylation to deliver the corresponding products with yields of up to 91% (Table 5). The substrates with substituents at *ortho*-, *meta*-, and *para*-positions all reacted efficiently to afford the desired products **4b-4d**. Of note, either electron-withdrawing or electron-donating functional groups were well tolerated, such as OCF_3 (**4c**), OMe (**4d**, **4i,** **4j**), NMe_2 (**4f**), ester (**4g**) and Cl (**4o**). Besides, polyaromatic and heteroaromatic substrates were also competent to afford the products **4l** and **4m** in 49% and 90% yields, respectively. Remarkably, the empagliflozin skeleton was successfully introduced in product **4n** with an acceptable yield. It is interesting to note that mono-borylation and diborylation products (**4o**, **4p**) could be selectively generated from 4-bromochlorobenzene in moderate yields via fine-tuning reaction conditions. In addition to aryl (pseudo)halides, the feasibility of borylation of vinyl bromide was also investigated. As shown in Table 5, a mixture of mono-borylation products **4q-4q"** and diborylation product **4r** were isolated when vinyl bromide **3q** was treated with the standard conditions. Notably, diborylation product **4r** possibly resulting from hydroboration of **4q** could be formed in 64% yield as the main product with an increased amount of borane.

To explore the scalability of this migratory borylation, the reaction was carried out on a gram-scale with an equimolecular mixture of regioisomeric bromooctane, providing isomerically

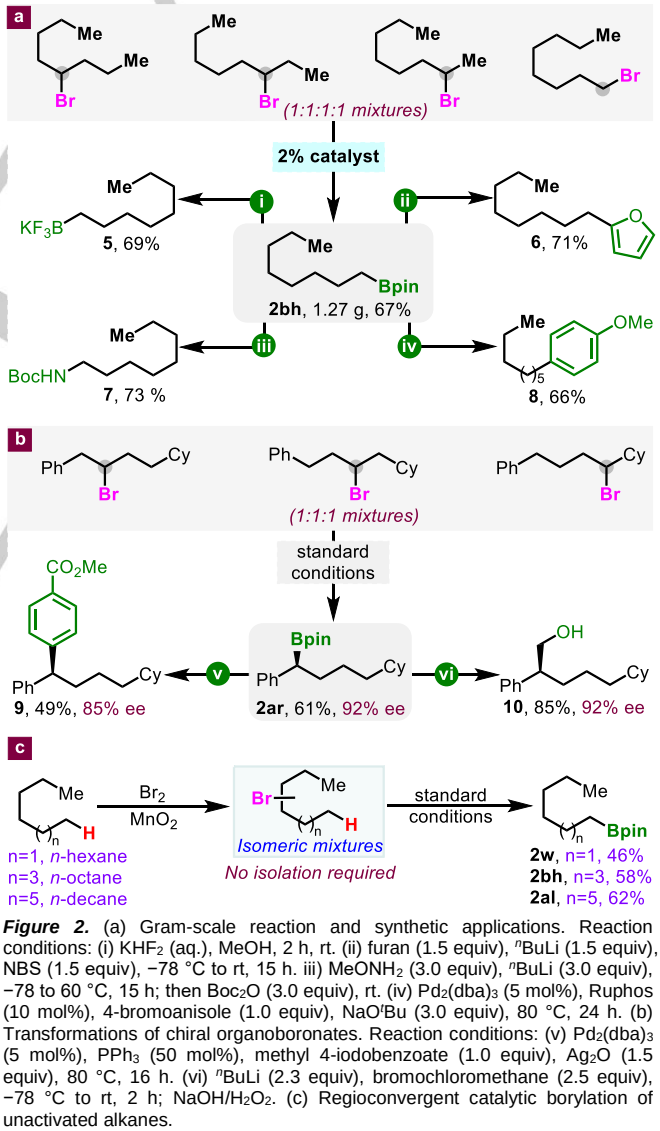


Figure 2. (a) Gram-scale reaction and synthetic applications. Reaction conditions: (i) KHF_2 (aq.), MeOH, 2 h, rt. (ii) furan (1.5 equiv), ^{n}BuLi (1.5 equiv), NBS (1.5 equiv), −78 °C to rt, 15 h. iii) $MeONH_2$ (3.0 equiv), ^{n}BuLi (3.0 equiv), −78 to 60 °C, 15 h; then Boc_2O (3.0 equiv), rt. (iv) $Pd_2(dba)_3$ (5 mol%), Ruphos (10 mol%), 4-bromoanisole (1.0 equiv), NaO^tBu (3.0 equiv), 80 °C, 24 h. (b) Transformations of chiral organoboronates. Reaction conditions: (v) $Pd_2(dba)_3$ (5 mol%), PPh_3 (50 mol%), methyl 4-iodobenzoate (1.0 equiv), Ag_2O (1.5 equiv), 80 °C, 16 h. (vi) ^{n}BuLi (2.3 equiv), bromochloromethane (2.5 equiv), −78 °C to rt, 2 h; $NaOH/H_2O_2$. (c) Regioconvergent catalytic borylation of unactivated alkanes.

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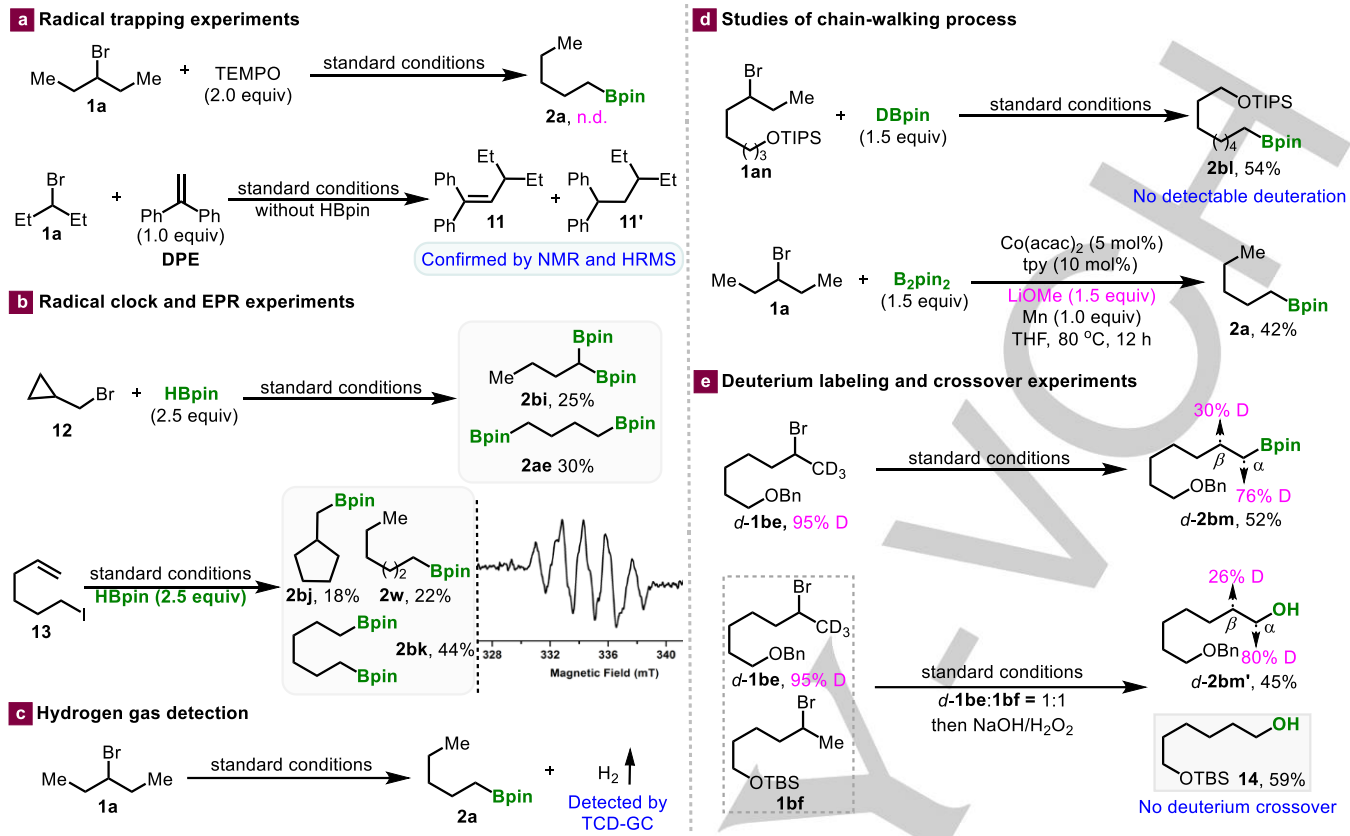

Figure 3. Mechanistic studies. (a) Radical trapping experiments. (b) Radical clock and EPR experiments. (c) Hydrogen gas detection. (d) Studies of chain-walking process. (e) Deuterium labeling and crossover experiments.

pure product **2bh** in 1.27 g and 67% yield (Figure 2a). The transformations of the borylation product were subsequently conducted to demonstrate the practicability of this protocol. First, product **2bh** was converted to synthetically valuable potassium organotrifluoroborate **5** in the presence of KHF_2.[16] Furthermore, the sp^2–sp^3 coupling of furan with **2bh** led to the formation of **6** in 71% yield.[17] The amination of alkylboronates developed by Morken proceeded efficiently to furnish product **7** in high efficiency.[18] Finally, Pd-catalyzed the Suzuki-Miyaura coupling of **2bh** with 1-bromo-4-methoxybenzene allowed for the synthesis of product **8** in 66% yield.[5c] Furthermore, the

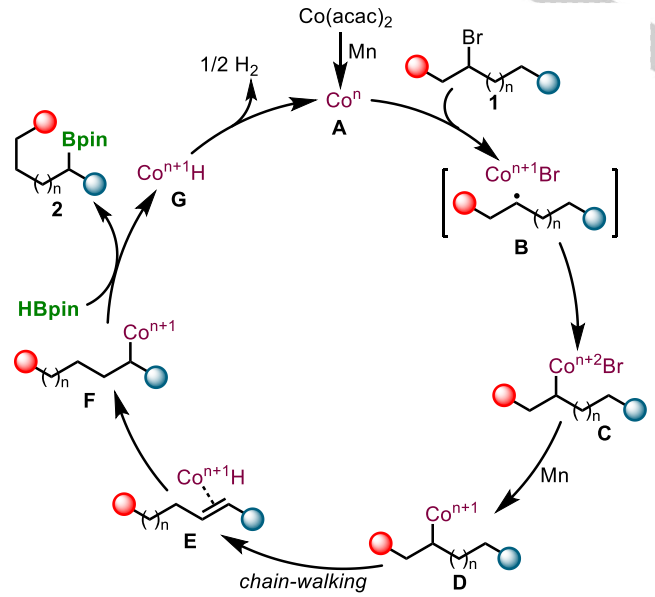

Figure 4. Proposed catalytic cycle.

regioconvergent and enantioselective borylation of an isomeric mixture of alkyl bromides was also carried out, affording the chiral organoboron **2ar** in 61% yield and 92% ee (Figure 2b). Moreover, the transformations of **2ar** were also performed. As shown, the Suzuki coupling of **2ar** with methyl 4-iodobenzoate gave product **9** in moderate yield and 85% ee with retention of configuration,[19] in which the slight erosion of the enantiomeric purity was in accordance with the reported results.[19] Additionally, homologation of **2ar** was conducted, delivering product **10** in 85% yield and 92% ee.[20] To extend the generality of our reaction, the employment of bulk raw material alkanes as substrates was also investigated. To our delight, isomerically pure products (**2w**, **2bh**, **2al**) were exclusively generated in moderate yields from the corresponding alkanes via a sequence of unselective bromination and regioconvergent migratory borylation, allowing the efficient synthesis of added-value compounds from alkanes and representing a powerful alternative to the existing methods towards chemical transformations of alkanes. Of note, neither purification nor isolation of the halogenated intermediates was required in this process, demonstrating the robustness of this synthetic streamlining.

Further investigations were performed to shed light on the mechanism. In the presence of a stoichiometric amount of radical inhibitor, TEMPO, the borylation reaction was significantly inhibited (Figure 3a). In addition, the radical-trapped products **11** and **11'** were detected by NMR and HRMS when 1,1-diphenylethylene (DPE) was utilized, implying that a radial mechanism is probably involved in this scenario. The radical clock experiments using (bromomethyl)cyclopropane **12** and 6-iodohex-1-ene **13** were also conducted. The diboronate products **2bi** and **2ae** were obtained in 25% and 30%, respectively, which

were generated via a ring-opening process. Furthermore, we found that cyclized product **2bj** can be formed in 18% yield along with **2w** (22%) and **2bk** (44%) when alkenyl iodide **13** was used (Figure 3b). These results also supported the radical mechanism. To further verify the radical process in this reaction, an electron paramagnetic resonance (EPR) experiment was performed with DMPO as the spin-trapping reagent (see SI for details), and EPR active signals were detected, which adequately suggested that the radical mechanism is likely to be involved in this remote borylation. Notably, the hydrogen gas generated from the model reaction was detected by TCD-GC, which indicates the hydrogen release pathway. To get more insights into the mechanism, control and deuterium experiments were also explored. As illustrated in Figure 3c, the reaction of **1an** with DBpin under the standard conditions proceeded smoothly to afford product **2bl** in 54% yield, but no deuterium incorporation was observed. Moreover, utilizing B_2pin_2 instead of HBpin, the migratory borylation product **2a** could also be obtained in the presence of a base. These results indicated that the HBpin might be uninvolved in the chain-walking process. Besides, the product *d*-**2bm** was obtained with 76% deuterium incorporation at the *α*-position and 30% deuterium incorporation at the *β*-position when deuterated alkyl bromide *d*-**1be** was subjected to the standard conditions. Finally, we performed a crossover experiment using a 1:1 mixture of *d*-**1be** and **1bf** (Figure 3d), and no deuterium crossover products were observed, suggesting that a free cobalt-hydride species that dissociates from the substrate is unlikely responsible for this migration borylation.

Based on the literature and aforementioned investigations, a tentative mechanistic proposal is illustrated in Figure 4. In the presence of Mn, the reduction of Co(II) occurs to form a low-valent Co(n) species,[21] which triggers bromide atom abstraction from **1** to afford radical pair **B**.[22] The resulting alkyl radical recombines with Co(n+1) to give intermediate **C**, which is subsequently reduced by Mn to provide the species **D**. The intermediate **D** undergoes a chain-walking process to form an alkene-coordinated cobalt intermediate **E**. The insertion of Co−H into the alkene delivers the intermediate **F**, which is the enantioselective step in the asymmetric borylation.[9m] The subsequent σ-bond metathesis or an oxidative addition/reductive elimination sequence with HBpin to afford the desired product **2** and Co−H species **G**.[23] Finally, Co(n) is regenerated from the Co−H species along with hydrogen release[24] to complete the catalytic cycle.

Conclusion

In conclusion, we have developed a cobalt-catalyzed enantioselective remote borylation of alkyl bromides to afford a series of synthetically useful chiral benzylic organoboronates, providing an efficient and robust strategy for enantioconvergent transformation of racemic alkyl halides. Notably, the migratory borylation of alkyl (pseudo)halides (alkyl−X, X = I, Br, Cl, OTs) with terminal selectivity was also demonstrated. In addition, the generality of this catalytic system could be extended to aryl halides, delivering aryl boronates with high efficiency. The utility of this method has been illustrated by various transformations of the alkylboronate products and catalytic regioconvergent borylation of chemical feedstock alkanes. Preliminary mechanistic studies suggested a radical reaction pathway was involved, and further efforts will be directed toward a detailed understanding of the reaction mechanism.

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Conflict of interest

The authors declare no competing financial interests.

Keywords: alkyl halides • asymmetric borylation • chain-walking • C−H activation • alkylboronates

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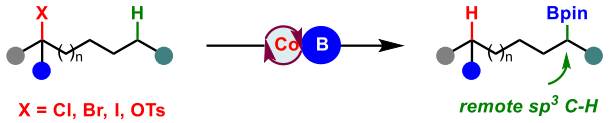

- *1°, 2°, 3° alkyl halides*
- *enantioselective borylation*
- *mild & robust catalytic system*
- *mechanistic studies*

A cobalt-catalyzed asymmetric remote borylation of alkyl bromides was reported. The generality of this migratory borylation system was extended to other alkyl electrophiles (alkyl-X, X=I, Br, Cl, OTs) and aryl halides. Additionally, the utility of this method was illustrated by a gram-scale reaction and the transformations of borylative products. Preliminary mechanistic studies indicated a radical reaction pathway may be involved.

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Cobalt-Catalyzed Asymmetric Remote Borylation of Alkyl Halides