# Markovnikov-Selective Hydroboration of Aryl Alkenes Catalyzed by Quaternary Ammonium Salts

Paweł Huninik, Hoyoung Im, Jakub Szyling, Mu-Hyun Baik,* and Jędrzej Walkowiak*

## Abstract

Despite recent advancements in the development of catalytic Markovnikov-selective hydroboration of alkenes, the metal-free procedure has long remained an unsolved challenge. Here, we report an organocatalytic Markovnikov-selective hydroboration of aryl alkenes using a commercially available quaternary ammonium catalyst. The method is operationally simple, scalable, and compatible with a wide variety of substrates and it can be successfully applied in the synthesis of active pharmaceutical ingredients (API) such as *Chlorphenoxamine*. Through in-depth experimental and DFT studies, we elucidate a nuanced understanding of the mechanism and regioselectivity of this reaction.

## Introduction

Organoboron compounds are highly attractive intermediates due to their ease of functionalization through various catalytic processes such as Suzuki coupling,[1] Chan-Lam coupling,[2] halodeborylation,[3] amination,[4] oxidation,[5] and many more.[6] Synthesis of organoboron compounds in a regio- and stereoselective manner by catalytic processes (including hydroboration, diboration and borylation reactions) is in high demand and the number of new protocols is constantly growing. Hydroboration reactions of alkenes typically favor the formation of linear, anti-Markovnikov products and are well documented.[7-9] Selectivity towards branched Markovnikov products is challenging and generally less frequently observed. Though progress has been made in recent years, transition metal (TM) complexes are exclusive in Markovnikov-selective hydroboration reactions (Figure 1a).[9, 10] Due to the limited availability of precious metals and environmental concerns, there has been

a focus on exploring alternatives involving earth-abundant metals (Mn,[11-13] Fe,[14-16] Co,[17-24] Ni,[25-27] Cu,[28-31]). However, the excessive use of borylating agent, the frequently low stability of the catalyst and base activators that are often required limit the applications of these systems. Challenges related to expensive pre-catalysts, multistep ligands synthesis, the use of toxic organic solvents as a reaction medium, and overall process sustainability are highly prominent in modern organoboron chemistry.

In the last few decades, organocatalysis has surfaced as a viable alternative to transition metal-based catalysis, primarily due to its cost-effectiveness and lower toxicity (absence of metal contamination), the ready availability of reagents, and its environmentally friendly nature. In recent years, quaternary ammonium salts (QASs) have been used as solvents and immobilization media for TM-catalysts but they have garnered significant attention as organocatalysts for the hydrofunctionalization of unsaturated C-C bonds.[32-37] We previously reported an ionic liquid-catalyzed anti-Markovnikov selective hydroboration of alkenes (Figure 1b).[38] In the current work, we investigated QASs as catalysts for hydroboration of alkenes leading to Markovnikov organoboranes (Figure 1c). We hypothesized that the high-energy alkene can be activated by the addition of hydrogen on the β-carbon *via* a dihydrideborate intermediate thereby determining the α-carbon nucleophilic towards pinacolborane. Herein, we report the hydroboration of aryl alkenes in a regioselective fashion. To our knowledge, this is the first method for the metal-free Markovnikov-selective hydroboration of alkenes. The simplicity of the catalyst and its high selectivity opens a new chapter in Markovnikov hydroboration reactions.

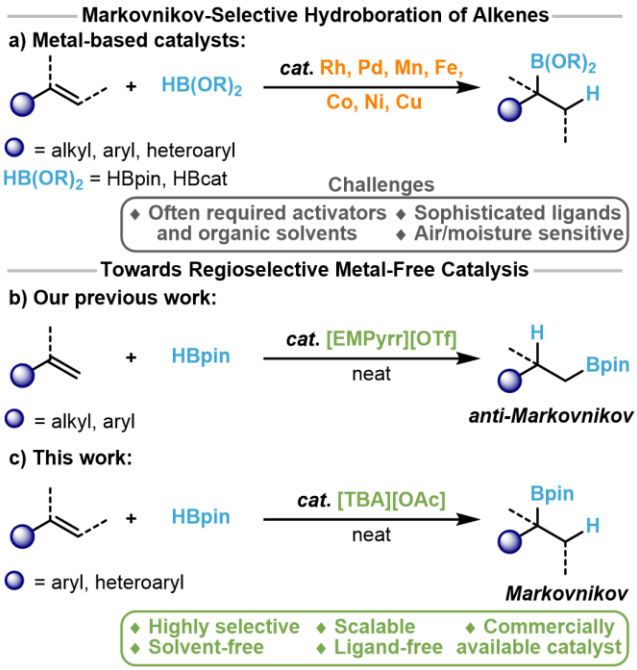


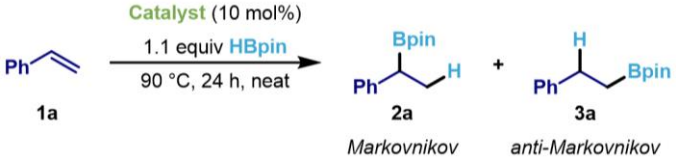

**Figure 1.** Markovnikov-selective hydroboration of alkenes.

## Results and Discussion

With this challenge in mind, we chose styrene (**1a**) and pinacolborane as the model substrates and screened a wide range of quaternary ammonium salts with simple carboxylate anions as catalysts. At the outset, the control reactions between **1a** and HBpin were conducted at 90 °C in the presence of commercially available or easy-to-prepare acetate-based QASs. The Markovnikov product **2a** was obtained with moderate selectivity and low yield after 24 h when [TMA][OAc] was used (Table 1, entry 1). Switching to [TBA][OAc] containing a cation with longer alkyl chains substituted to the nitrogen atom resulted in excellent regioselectivity, giving branched alkyl boronic ester **2a** with 97% yield. A nearly equal isomer ratio was noted with the use of hexadecyltrimethylammonium acetate [CTA][OAc] (Table 1, entry 3). Poor conversion of **1a** and moderate reaction selectivity were also observed for [BMIM][OAc] and [$NH_4$][OAc], indicating that the length of alkyl chains may play an important role in the catalysis (Table 1, entry 4-5). Lower yields of **2a** were observed when other carboxylate-based catalysts were used (Table 1, entries 6-7). An analog of [TBA][OAc] featuring a phosphonium cation was examined, revealing a significant decrease in selectivity (Table 1, entry 8). With [TBA][OH], no

product formation was detected (Table 1, entry 9). The use of potassium acetate or acetic acid as catalysts led to a notable decline in selectivities (Table 1, entries 10-11). As expected, the presence of the catalyst is crucial. Without a catalyst, no reaction was observed under applied process conditions (Table 1, entry 12). Based on the catalyst screening, tetrabutylammonium acetate [TBA][OAc] was chosen as the best catalyst for the B–H addition to styrene (**1a**) and used for further reaction conditions screening (see ESI). When the reaction temperature was lowered to 80 °C, the conversion of **1a** dropped to 79% (Table 1, entry 13). Reducing the quantity of HBpin from 1.1 equivalents to 1.0 equivalent gave **2a** in 87% yield (Table, entry 14). When 5 mol% of [TBA][OAc] was used, an evident drop in **1a** conversion was observed (Table, entry 15). However, it was found that 20 hours were sufficient for an excellent product yield (Table 1, entry 16).

**Table 1. Survey of catalysts and conditions in hydroboration of styrene with HBpin.**[a]




| entry | catalyst | conv. of 1a [%][b] | selectivity (2a:3a)[b] | yield of 2a [%][b] |
|---|---|---|---|---|
| 1 | [TMA][OAc] | 32 | 74:26 | 24 |
| 2 | [TBA][OAc] | >99 | 98:2 | 97 |
| 3 | [CTA][OAc] | 78 | 51:49 | 40 |
| 4 | [BMIM][OAc] | 68 | 10:90 | 7 |
| 5 | [$NH_4$][OAc] | 32 | 66:34 | 21 |
| 6 | [TBA][OBz] | 46 | 98:2 | 45 |
| 7 | [TBA][HCOO] | 90 | 93:7 | 84 |
| 8 | [TBP][OAc] | 88 | 75:25 | 66 |
| 9 | [TBA][OH] | n.r | - | - |
| 10 | KOAc | 71 | 34:66 | 24 |
| 11 | HOAc | 24 | 6:94 | 1 |
| 12 | none | n.r | - | - |
| 13[c] | [TBA][OAc] | 79 | 97:3 | 77 |
| 14[d] | [TBA][OAc] | 89 | 97:3 | 87 |
| 15[e] | [TBA][OAc] | 56 | 99:1 | 55 |
| 16[f] | [TBA][OAc] | 99 | 98:2 | 97 |

[a]Reaction conditions: **1a** (1.0 mmol), HBpin (1.1 mmol), catalyst (10 mol%), 90 °C, 24 h, argon atmosphere. [b]Determined by GC-MS and $^1$H NMR analyzes using mesitylene as an internal standard. [c]80 °C. [d]1mmol of HBpin was used. [e]5 mol% of the catalyst was used. [f]20 h reaction time.

With optimized reaction conditions in hand, we investigated the Markovnikov hydroboration of various alkenes with HBpin, including substituted styrenes, internal alkenes, and 1,1-disubstituted olefins (Figure 2). The reactions consumed only 10 mol% of [TBA][OAc] and

provided the targeted branched products with high isolated yields (>70%). Styrene derivatives bearing two methyl groups (**1b**) or phenyl ring at the *para* position (**1c**) had a marginal impact on the product yields. The reaction also worked efficiently for vinylnaphthalene (**1d**), giving a high yield (90%) and excellent regioselectivity (99:1). Styrenes possessing -Cl (**1e**) and -Br (**1f**) moieties in the *para* position were also tolerated. A doubly substituted phenyl ring with chlorine atoms adjacent to the vinyl group in 2,6-dichlorostyrene (**1g**) had no impact on the product selectivity (steric effect). High reactivities (88−90% yield) and regioselectivities (98:2−99:1) were obtained by using styrenes bearing trimethylsilyl (**1h**) and -Bpin (**1i**) groups in the *para* positions. It is noteworthy that the reaction extended beyond terminal styrenes, as geminal alkenes **1j**-**1s** were also successfully subjected to the procedure. The reaction of **1j** gave the tertiary boronic ester **2j** in 90% yield with great regioselectivity. The hydroboration of 1-phenylvinylboronic acid pinacol ester (**1k**) resulted in product **2k** containing two boryl groups on the same carbon atom with 89% isolated yield. Reaction with α-methylstyrene containing -F (**1l**) and -I (**1m**) groups in the *para* positions afforded alkylboronic esters **2l** and **2m** in 90 and 91% yields respectively, indicating that the catalyst is also tolerant to other halogens. Moreover, the protocol was applicable to alkene with a potentially reducible functional group, such as nitrile (**1n**). Only the double C–C bond underwent hydroboration affording product **2n** with an isolation yield of 88% with the nitryl group intact. The hydroboration of the alkene containing a thiophene heterocycle (**1o**) demonstrated remarkable regioselectivity, favoring the Markovnikov product **2o** (99:1). The catalyst showed the ability to tolerate significant steric hindrance, as demonstrated in the reactions of the highly sterically demanding 1,1-diphenylethylenes (**1p**-**1r**). These reactions proceeded without impediment, resulting in the formation of the corresponding Markovnikov hydroboration products (**2p**-**2r**) with excellent yields and selectivities. The reaction with an alkene containing both internal and geminal double bonds demonstrated the superior reactivity of the geminal C=C bond over the internal one, resulting in the formation of organoborane **2s** with an 86% isolation yield. Nevertheless, internal alkenes **1t** and **1u** were also successfully subjected to the procedure, providing the corresponding products in slightly lower yields (70−85%). Besides the aromatic alkenes, *trans*-

1-phenyl-1,3-butadiene (**1v**) could also be hydroborated, affording the 3,4-addition product **2v** in 91% isolated yield and with excellent selectivity. However, the application of allyl instead of vinyl groups exclusively yields anti-Markovnikov products (**3w-y**). This is caused due to the charge delocalization in the benzylic anion (see the Computational Mechanisms Study for details). Styrenes with strongly activating functional groups such as -OH, -$NH_2$, -$NMe_2$ were found to be incompatible with the catalyst (see the Supporting Information for more details).

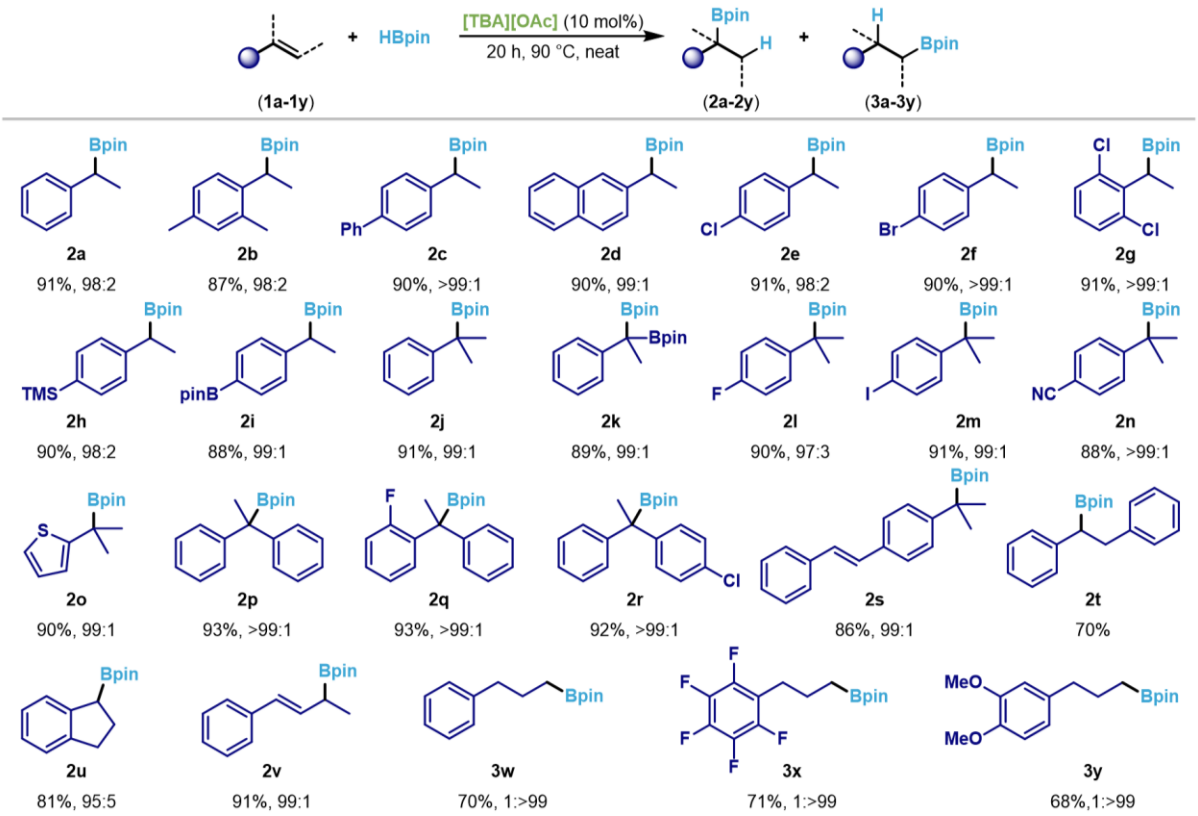



**Figure 2**. Hydroboration of various alkenes. Isolated yields are presented. Reaction conditions: **1a** (1.0 mmol), HBpin (1.1 mmol), [TBA][OAc] (10 mol%), 90 °C, 20 h, argon atmosphere. The process selectivity was determined by GC-MS and $^1$H NMR analyzes using mesitylene as an internal standard.

To prove the utility of the established procedure, gram scale synthesis of **2a** and its further transformations were performed (Figure 3a). Product **2a** was isolated with high yield (89%) and retained regioselectivity (**2a**:**3a** = 98:2). Treatment of the hydroboration product **2a** with $BCl_3$ and benzyl azide, afforded product **5** in 92% yield. Suzuki-Miyaura coupling product (**6**) was obtained using the secondary alkyl boronate **2a** generated *in situ*, without encountering undesirable interferences from residual catalyst species. Based on the base-mediated dehydrogenative alkylation of secondary boronates,[39] the highly valuable α-boryl

functionalized alkane (**7**) was obtained in good yield (79%). The isolated **2a** was treated with lithiated methoxyamine delivering primary amine (**8**) with 67% yield.[40] Moreover, a multi-gram scale synthesis of tertiary boronic ester **2r** was conducted, and the practical feasibility of its synthesis was further demonstrated through one-pot transformations (Figure 3b). The as-synthesized **2r**, without isolation or purification, was used directly in a TBAF-catalyzed protodeboration reaction,[41] delivering product **9** in 82% isolated yield. Additionally, substituting $D_2O$ for $H_2O$ provided deuterium-labeled tertiary alkane **10** in 80% yield. Finally, regioselective hydroboration provided an efficient method for the synthesis of *Chlorphenoxamine* used as an antipruritic and antiparkinsonian agent. Treating the hydroboration reaction mixture of **2r** with $NaBO_3 \times 4H_2O$ resulted in the oxidation product **11** with a yield of 90%. This process further enabled the acquisition of product **12** through Williamson ether synthesis, achieving an excellent yield of 86%.

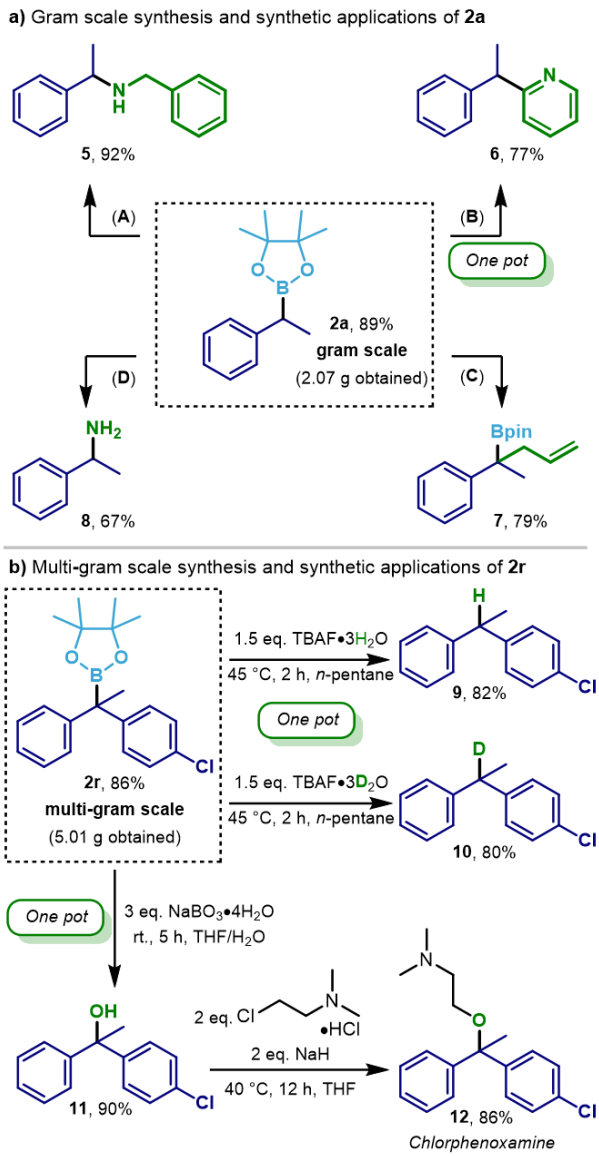



**Figure 3**. Gram scale synthesis and synthetic applications. Isolated yields are presented. Reaction conditions (A): **2a** (1.0 mmol), $BCl_3$ (1M in DCM, 5 eq.), rt., 4 h. Then $BnN_3$ (3 eq.), rt., 15 h. (B): **2a** (1.0 mmol), 2-bromopyridine (1.2 eq.), $[Pd(PPh_3)_4]$ (5 mol%), $Ag_2O$ (1.4 eq.), THF (5 mL), 75 °C, 24 h. (C): **2a** (1.1 mmol), LiTMP (1.1 mmol), 0 °C, 30 min. Then allyl bromide (1.0 mmol) in THF (2 mL), rt., 15 h. (D):$CH_3ONH_2$ (2M in THF, 3.0 mmol), *n*-BuLi (2.5M in hexanes, 3.0 mmol), THF (5 mL), -78 °C. Then **2a** (1.0 mmol), 60 °C, 12 h.

## Experimental Mechanism Study

To gain insight into the mechanism of the [TBA][OAc]-catalyzed alkene hydroboration, a deuterium-labeling experiment was performed (Figure 4a). The hydroboration of styrene-$d_8$ with HBpin resulted in the formation of the boronic ester **2a-*d*$_8$**, with the proton specifically

incorporated at the terminal methyl group (Fig. S14, ESI). This finding eliminated the possibility of styrene itself serving as the proton source. Dagorne *et al*. in their research on acetate-catalyzed hydroboration of carbon dioxide, proposed that the acetate anion from [TBA][OAc] salt combined with HBpin forms tetracoordinated borohydride Lewis adduct, which acts as a hydride source.[42] In accordance with other reports, tetracoordinated trialkoxyborohydride species have been found to be efficient catalysts in hydroboration reactions involving carbonyl compounds and *N*-heteroarenes.[43-45] To confirm the findings of Dagorne and better understand boronate catalyzed hydroboration reactions of alkenes, the NMR control experiments were conducted. A stoichiometric equivalent of pinacolborane was added to [TBA][OAc] and examined by $^{1}$H and $^{11}$B NMR spectroscopy (Figure 4b). In the $^{1}$H NMR spectrum acquired after 5 minutes, the signal attributed to the methyl hydrogen atoms of $^{-}$OAc (δ = 2.31 ppm) was completely replaced by new resonances at 2.20 and 2.13 ppm (Fig. S3, ESI). Additionally, the tetramethyl hydrogen signals originating from the pinacolborane (δ = 1.01 ppm) were entirely substituted by new resonances at 1.36 and 1.28 ppm, which were identified as **II** and **III**, respectively. $^{1}$H NMR analysis after 30 minutes and 1 hour revealed further relocation of these signals, along with an upfield shift of adjacent methylene groups to the nitrogen atom in the cation (Fig S4, ESI). Moreover, dihydrogen gas release was observed during the addition of pinacolborane, as verified by $^{1}$H NMR (δ = 4.47 ppm). In the $^{11}$B NMR spectrum, after 5 minutes the pinacolborane signal (δ = 28.5 ppm) disappeared and new broad resonance at 5.8 ppm (**II**) became apparent (Figure 4c). While Dagorne initially attributed the intermediate **II** to resonance at 11.4 ppm, this assignment is inconsistent with chemical shifts of trialkoxyborohydrides ($^{11}$B NMR: δ = 0 – 7 ppm).[44, 46] Following the 30-minute interval, we noted a broad peak at 8.15 ppm, identified as $^{-}$[$H_2$Bpin] anion (**III**).[45] Additionally, we observed a small signal at -36.5 ppm corresponding to $^{-}BH_4$, which can contribute to the formation of anti-Markovnikov side-products under the reaction conditions used.[44, 47] After 20 hours, the resonance assigned to intermediate **III** disappeared and the signal associated with AcOBpin (**I**, δ = 22.5 ppm) became evident.[48] Data obtained from $^{1}$H and $^{11}$B NMR recordings indicates the presence of various borohydride species that undergo coordination and decoordination of

$^{-}$OAc ion, aligning with the observations made by Dagorne. Since the addition of the HBpin to [TBA][OAc] in a 1:1 ratio does not reproduce the exact reaction conditions, we conducted additional control NMR experiments employing a stoichiometry that is consistent with the standard reaction conditions. Applying $^{11}$B NMR analysis of the reaction using an excess of HBpin relative to the catalyst (1.1:0.1 ratio), we observed only the formation of intermediate **II** and residual HBpin (Fig. S6, ESI). Furthermore, during the reactions of [TBA][OAc], styrene (**1a**) and HBpin in a 0.1:1:1.1 ratio (Fig. S7-13, ESI), we detected the formation of several minor borohydride signals, with resonances at -12 ppm and -14 ppm that were successfully assigned to $BH_3$ species.[44] Given the generation of a nucleophilic adduct (**I**) during the reaction, pinBOAc was assessed as a potential catalyst for the hydroboration of styrene under standard conditions (Figure 4d). Examination of the post-reaction mixture revealed the formation of an *anti*-Markovnikov product (**3a**) with high regioselectivity (2:98 ratio of isomers). This outcome rules out the possibility that pinBOAc (**I**) serves as the actual catalyst of the process (see Table S1 in ESI for more details).

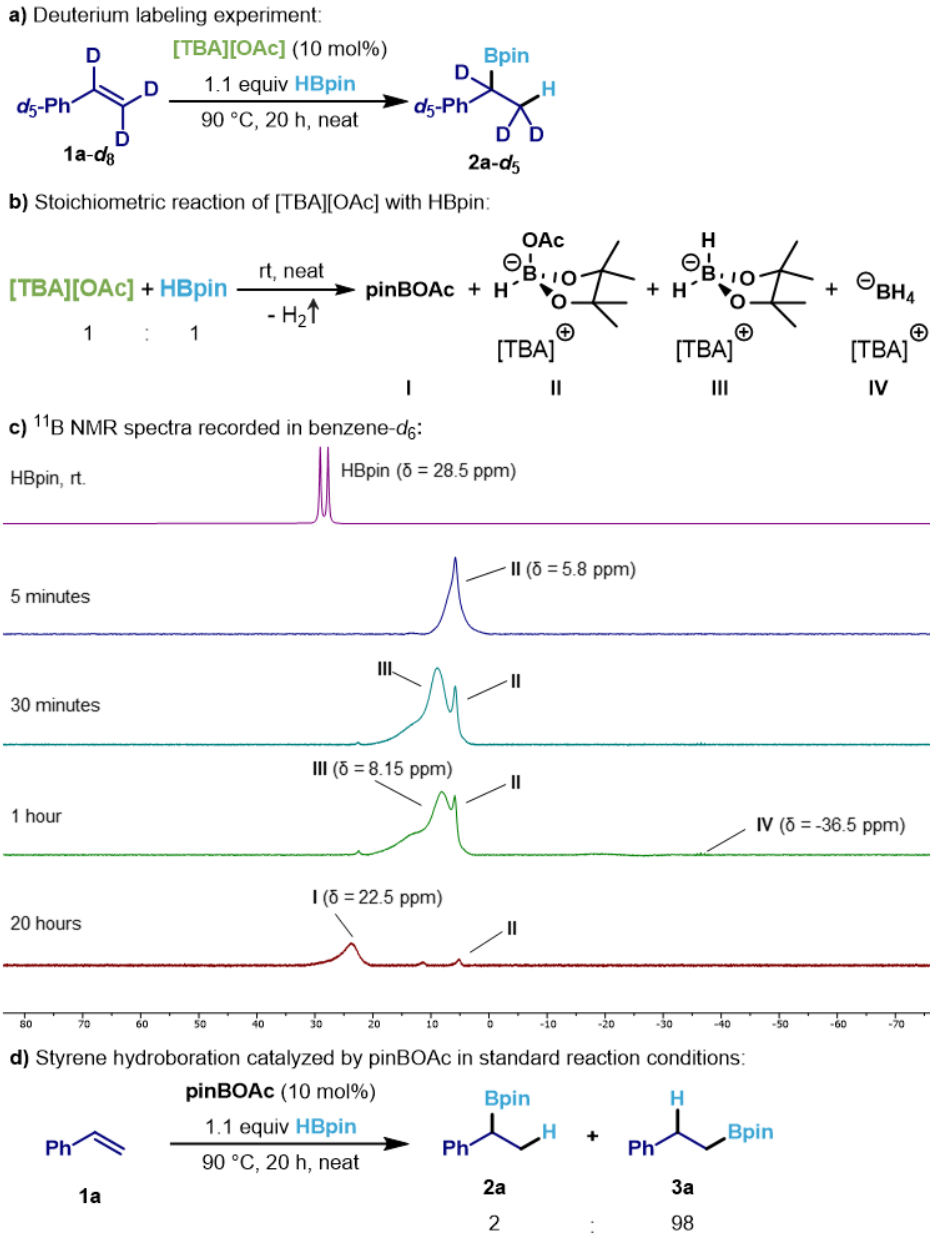


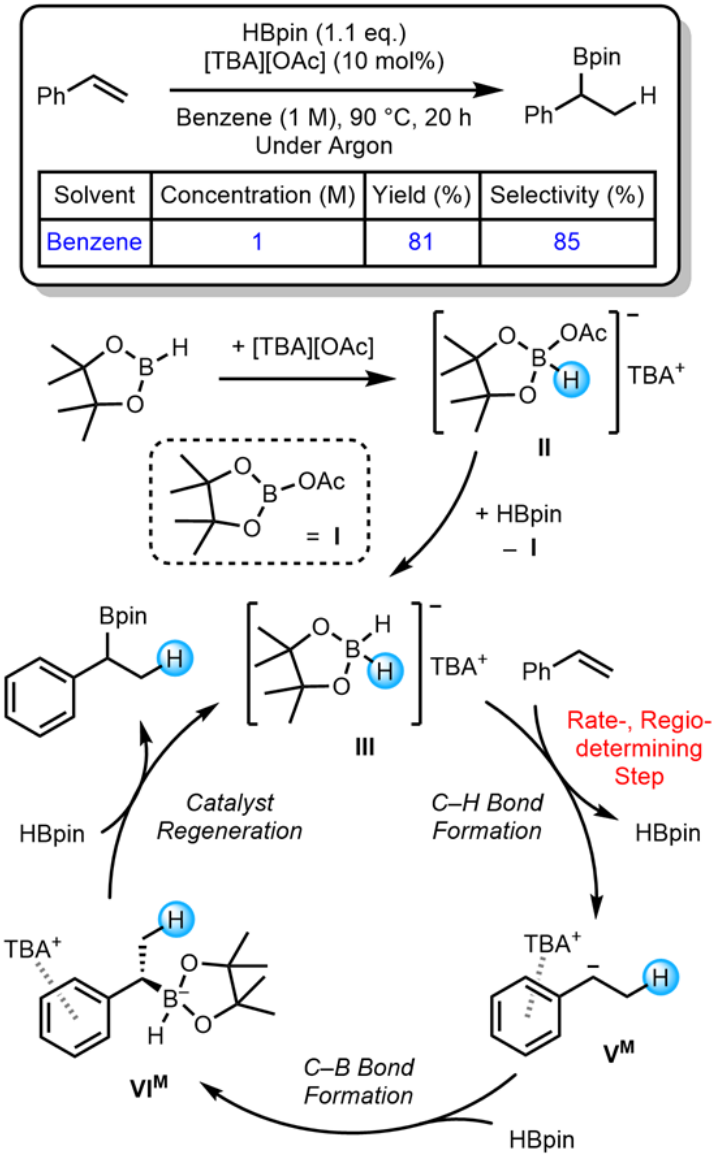

**Figure 4**. Experimental mechanistic studies on [TBA][OAc]-catalyzed hydroboration of alkenes.

## Computational Mechanism Study

In addition to the experimental investigation of the reaction mechanism, the density functional theory (DFT) calculations were carried out at the M06-2X/def2-TZVPPD// M06-2X/ma-def2-SVP level of theory.[49-58] To delve deeper, the reaction using [TBA][OAc] as a catalyst was chosen as a model reaction. Due to the challenges in modeling the neat reaction

mixture, we opted to investigate the control reaction using benzene as the solvent, as shown in Scheme 5 (see the Supporting Information for further details).

**Scheme 1**. Proposed reaction mechanism




The mechanistic study began with a search for potential catalytic species, including **II**, **III**, and **IV** (Scheme 5). [TBA][OAc] and HBpin can form a Lewis acid-base adduct **II**, which is found to be endergonic for 1.0 kcal/mol. Upon hydride transfer from **II** to HBpin, the potential catalyst **III** can be formed while releasing **I**, exhibiting a free energy of 13.6 kcal/mol. These hydride species are expected to be in equilibrium, enabling each of them to undergo independent catalytic cycles. Furthermore, experimental observations suggest that $^{-}BH_4$ (**IV**)

exists in the reaction mixture, which is also capable of catalyzing the reaction. Based on these scenarios, we explored three catalytic cycles and found that the catalytic cycle involving **III** requires the least energy demand, as illustrated in Figure 5. Further details regarding the catalytic cycles involving **II** and **IV** can be found in the Supporting Information.

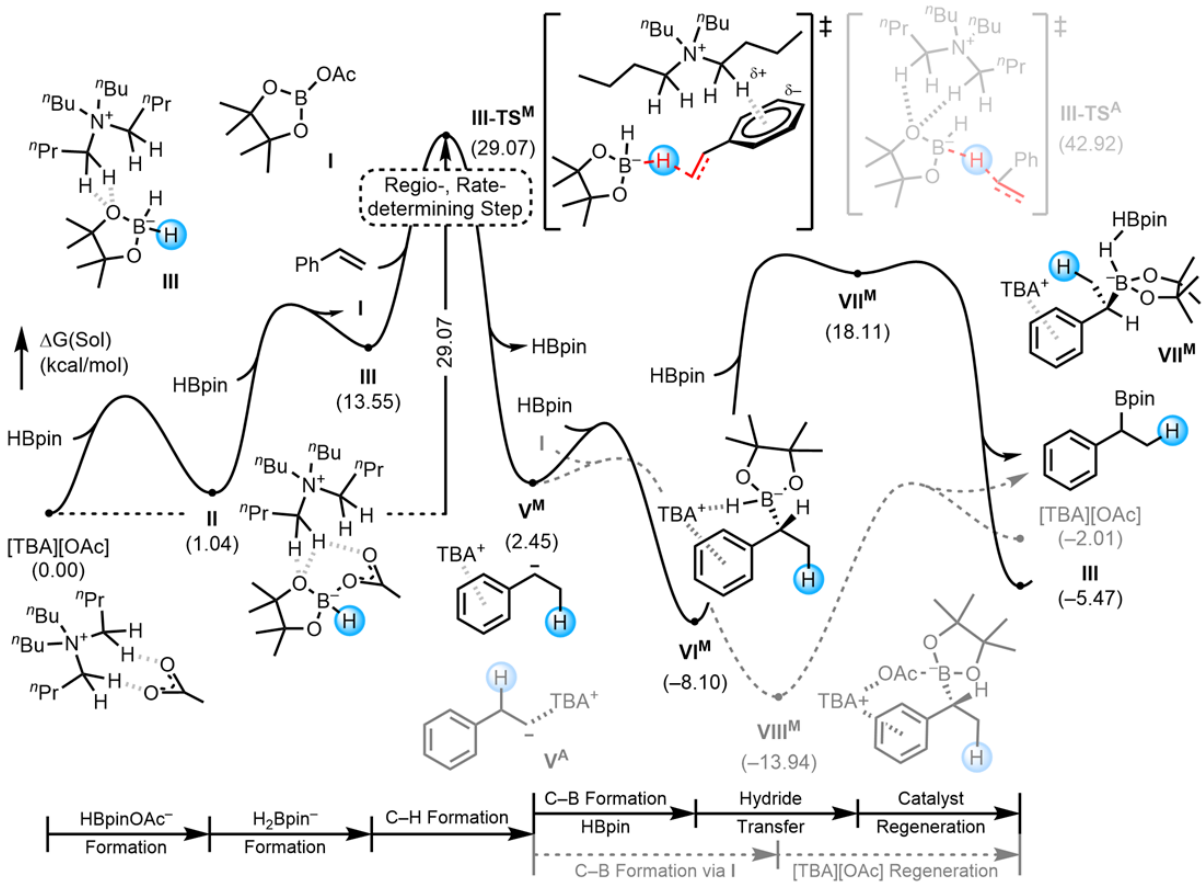



**Figure 5**. Proposed reaction mechanism. The hydrogen marked as blue represents the hydride involved in the C–H bond formation.

The catalytic cycle of **III** initiates with the formation of a C–H bond via hydride transfer to styrene, giving carbanion intermediate. Considering that the hydride can react with either the α- or β-carbon of the styrene and the process is likely to be irreversible, the C–H bond formation is anticipated to be the regiodetermining step.

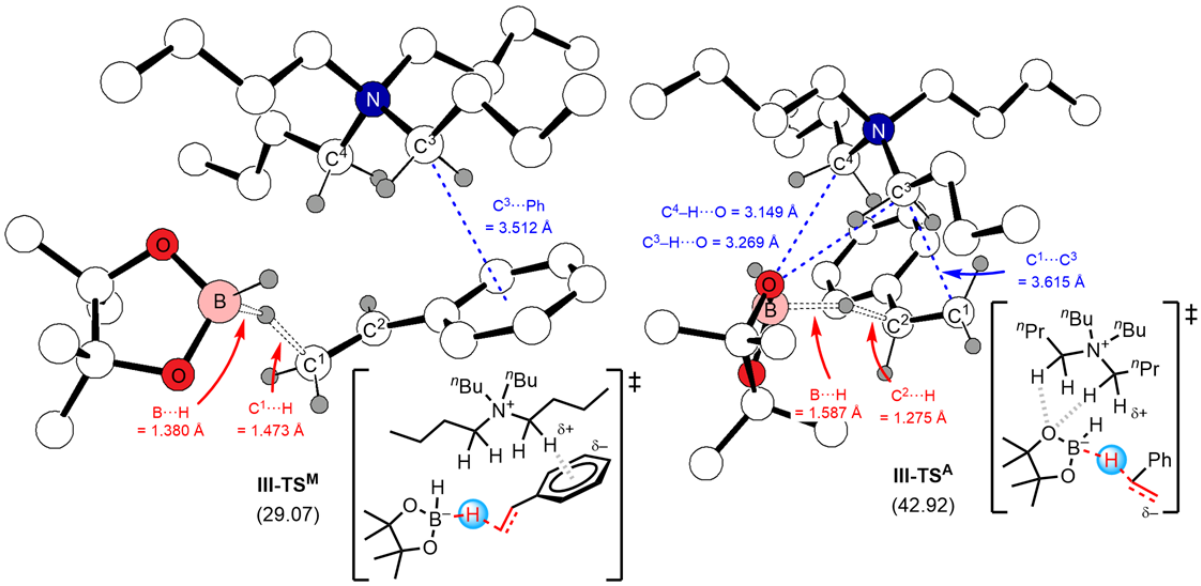



**Figure 6**. The structure of **III-TS$^{M}$** and **III-TS$^{A}$**. Some hydrogen atoms are omitted for clarity.

Calculations show that the barrier for the Markovnikov product is 29.1 kcal/mol, whereas the barrier for the anti-Markovnikov product is 42.9 kcal/mol. Furthermore, the C–H bond formation through **III-TS$^{M}$** is found to have the highest barrier, making the C–H bond formation a rate-determining step. The transition state structures shown in Figure 6 show that the positive α-carbon of $TBA^{+}$ stabilizes the negative charge formation via electrostatic interaction between the $TBA^{+}$ and the phenyl group of the substrate for **III-TS$^{M}$**. In the **III-TS$^{A}$**, the α-carbon of $TBA^{+}$ exhibits an electrostatic interaction with the β-carbon of the styrene and the oxygen of HBpin.

The regioselectivity of the C–H bond formation is expected to originate from charge stabilization by the phenyl group. When forming the C–H bond at the β-carbon of styrene, both the transition state **III-TS$^{M}$** and carbanion intermediate **V$^{M}$** can be stabilized by charge delocalization. On the contrary, C–H bond formation at α-carbon yields an alkyl carbanion, lacking the stabilization effect, thereby leading to a larger energy demand.

While the proposed mechanism can account for the formation of the Markovnikov product, the formation of the anti-Markovnikov product cannot be explained due to the unrealistic barrier concerning the reaction condition. The experimental observation of $BH_3$ and

their adducts with nucleophiles indicate the anti-Markovnikov hydroboration catalyzed by $BH_3$ potentially occurs in the reaction mixture.

Turning our attention back to the intermediate $\mathbf{V^M}$, the subsequent C–B bond formation can proceed with both HBpin and **I**, giving $\mathbf{VI^M}$ and $\mathbf{VIII^M}$, respectively. The C–B bond formation with HBpin releases 10.6 kcal/mol, while the C–B formation with **I** (shown as a dashed trace in Figure 5) is downhill for 16.4 kcal/mol. Despite the formation of $\mathbf{VIII^M}$ being thermodynamically favored, the formation of $\mathbf{VI^M}$ is expected to be dominant due to the concentration difference between HBpin and **I**. The concentration of **I** will depend on the concentration of **III**, which is in equilibrium with [TBA][OAc] and **II**. Given the significant energy difference between **II** and **III**, the active catalytic species **III** and side product **I** will be low in concentration. It is also worth noting that $\mathbf{VIII^M}$ is an off-cycle species based on the proposed mechanism. The intermediate $\mathbf{VIII^M}$ can regenerate [TBA][OAc] by releasing the product, giving a driving force of 2.0 kcal/mol for the first catalytic cycle. But considering that the intermediate $\mathbf{VIII^M}$ will play a role as a resting state for following catalytic cycles, the energy requirement to reach $\mathbf{III\text{-}TS^M}$ from $\mathbf{VIII^M}$ will exceed 40 kcal/mol. This makes the following catalytic cycles unlikely to occur under the reaction condition, leaving $\mathbf{VIII^M}$ incapable of undergoing further catalytic cycles.

After the C–B bond formation, the intermediate $\mathbf{VI^M}$ can form an adduct with HBpin to regenerate catalyst **III**. The $\mathbf{VI^M}$ undergoes an uphill process requiring 26.2 kcal/mol to give an HBpin adduct $\mathbf{VII^M}$ exhibiting 18.1 kcal/mol. Analogous to C–B bond formation, adduct formation with HBpin is expected to be dominant in the reaction mixture compared to that of AcOBpin. From $\mathbf{VII^M}$, catalyst **III** can be regenerated by product release, which is exergonic for 23.6 kcal/mol. In comparison with the catalytic cycle using **I** as a substrate for C–B bond formation, the resting state for the reaction is [TBA][OAc], which should be lower in energy compared to $\mathbf{VI^M}$. Thus the consecutive catalytic cycles would have the same barrier of 29.1 kcal/mol, with a driving force of –5.5 kcal/mol.

## Conclusions

In summary, we have disclosed a protocol for the synthesis of secondary and tertiary alkylboronic esters *via* Markovnikov-selective hydroboration of aryl alkenes with pinacolborane. The regioselective reaction was organocatalyzed by simple quaternary ammonium salt with good functional group tolerance. The utility of our method was further demonstrated by concise synthesis of *Chlorphenoxamine* and various useful products. Experimental and computational analyses delineated the reaction mechanism and its underlying regioselectivity. The new methodology fills a long-standing gap in the literature concerning Markovnikov-selective transition metal-free hydroboration of alkenes and utilizes diverse aspects of organocatalysis. We believe that the principles elucidated in this study will facilitate significant progress in the development of other challenging organocatalytic hydrofunctionalization reactions.

## Associated Content

### Supporting Information

The experimental procedures, characterization data, details for computational studies, and the structures for the key intermediates are available in the supporting information.

## Author Information

### Corresponding Authors

**Mu-Hyun Baik** − Center for Catalytic Hydrocarbon Functionalizations, Institute for Basic Science (IBS), Daejeon 34141, Republic of Korea; Department of Chemistry, Korea Advanced Institute of Science and Technology (KAIST), Daejeon 34141, Republic of Korea; 0000-0002-8832-8187; mbaik2805@kaist.ac.kr

**Jędrzej Walkowiak** − Center for Advanced Technology, Adam Mickiewicz University, Uniwersytetu Poznańskiego 10, 61-614 Poznań, Poland; 0000-0003-3683-8836; jedrzej.walkowiak@amu.edu.pl

### Authors

**Paweł Huninik** − Center for Advanced Technology, Adam Mickiewicz University, Uniwersytetu Poznańskiego 10, 61-614 Poznań, Poland; Faculty of Chemistry, Adam Mickiewicz University, Uniwersytetu Poznańskiego 8, 61-614 Poznań, Poland; 0000-0002-0305-1319.

**Hoyoung Im** − Department of Chemistry, Korea Advanced Institute of Science and Technology (KAIST), Daejeon 34141, Republic of Korea; Center for Catalytic Hydrocarbon Functionalizations, Institute for Basic Science (IBS), Daejeon 34141, Republic of Korea; 0000-0003-4133-9687.

**Jakub Szyling** − Center for Advanced Technology, Adam Mickiewicz University, Uniwersytetu Poznańskiego 10, 61-614 Poznań, Poland; 0000-0001-9680-5679.

### Author Contributions

The manuscript was written through the contributions of all authors. All authors have given approval to the final version of the manuscript.

### Notes

The authors declare no competing financial interest.

## Acknowledgment

We thank the Institute for Basic Science in Korea for financial support (IBS-R010-A1) and the National Science Centre in Poland, Grant No. UMO-2019/34/E/ST4/00068.

## References


(1) Suzuki, A. Cross-Coupling Reactions Of Organoboranes: An Easy Way To Construct C-C Bonds (Nobel Lecture). *Angew. Chem. Int. Ed.* **2011**, *50*, 6722–6737, DOI: 10.1002/anie.201101379.
(2) Chen, J.-Q.; Li, J.-H.; Dong, Z.-B. A Review on the Latest Progress of Chan-Lam Coupling Reaction. *Adv. Synth. Catal.* **2020**, *362*, 3311–3331, DOI: 10.1002/adsc.202000495.
(3) Szyling, J.; Franczyk, A.; Pawluć, P.; Marciniec, B.; Walkowiak, J. A stereoselective synthesis of (E)- or (Z)-β-arylvinyl halides via a borylative coupling/halodeborylation protocol. *Org. Biomol. Chem.* **2017**, *15*, 3207–3215, DOI: 10.1039/C7OB00054E.
(4) Vantourout, J. C.; Law, R. P.; Isidro-Llobet, A.; Atkinson, S. J.; Watson, A. J. B. Chan–Evans–Lam Amination of Boronic Acid Pinacol (BPin) Esters: Overcoming the Aryl Amine Problem. *J. Org. Chem.* **2016**, *81*, 3942–3950, DOI: 10.1021/acs.joc.6b00466.
(5) Molloy, J. J.; Clohessy, T. A.; Irving, C.; Anderson, N. A.; Lloyd-Jones, G. C.; Watson, A. J. B. Chemoselective oxidation of aryl organoboron systems enabled by boronic acid-selective phase transfer. *Chem. Sci.* **2017**, *8*, 1551–1559, DOI: 10.1039/C6SC04014D.
(6) Magano, J.; Dunetz, J. R. Large-Scale Applications of Transition Metal-Catalyzed Couplings for the Synthesis of Pharmaceuticals. *Chem. Rev.* **2011**, *111*, 2177–2250, DOI: 10.1021/cr100346g.
(7) Obligacion, J. V.; Chirik, P. J. Earth-abundant transition metal catalysts for alkene hydrosilylation and hydroboration. *Nature Reviews Chemistry* **2018**, *2*, 15–34, DOI: 10.1038/s41570-018-0001-2.
(8) Das, A.; Panda, T. K. Metal-Free Catalytic Hydroboration of Unsaturated Compounds: A Greener Strategy for the Synthesis of Organoboranes. *ChemCatChem* **2023**, *15*, e202201011, DOI: 10.1002/cctc.202201011.
(9) Geier, S. J.; Vogels, C. M.; Melanson, J. A.; Westcott, S. A. The transition metal-catalysed hydroboration reaction. *Chem. Soc. Rev.* **2022**, *51*, 8877–8922, DOI: 10.1039/D2CS00344A.
(10) Fan, W.; Li, L.; Zhang, G. Branched-Selective Alkene Hydroboration Catalyzed by Earth-Abundant Metals. *J. Org. Chem.* **2019**, *84*, 5987–5996, DOI: 10.1021/acs.joc.9b00550.
(11) Weber, S.; Zobernig, D.; Stöger, B.; Veiros, L. F.; Kirchner, K. Hydroboration of Terminal Alkenes and trans-1,2-Diboration of Terminal Alkynes Catalyzed by a Manganese(I) Alkyl Complex. *Angew. Chem. Int. Ed.* **2021**, *60*, 24488–24492, DOI: 10.1002/anie.202110736.
(12) Zhang, G.; Zeng, H.; Wu, J.; Yin, Z.; Zheng, S.; Fettinger, J. C. Highly Selective Hydroboration of Alkenes, Ketones and Aldehydes Catalyzed by a Well-Defined Manganese Complex. *Angew. Chem. Int. Ed.* **2016**, *55*, 14369–14372, DOI: 10.1002/anie.201607579.
(13) Carney, J. R.; Dillon, B. R.; Campbell, L.; Thomas, S. P. Manganese-Catalyzed Hydrofunctionalization of Alkenes. *Angew. Chem. Int. Ed.* **2018**, *57*, 10620–10624, DOI: 10.1002/anie.201805483.
(14) Chen, X.; Cheng, Z.; Lu, Z. Iron-Catalyzed, Markovnikov-Selective Hydroboration of Styrenes. *Org. Lett.* **2017**, *19*, 969–971, DOI: 10.1021/acs.orglett.7b00227.
(15) Espinal-Viguri, M.; Woof, C. R.; Webster, R. L. Iron-Catalyzed Hydroboration: Unlocking Reactivity through Ligand Modulation. *Chem. – Eur. J.* **2016**, *22*, 11605–11608, DOI: 10.1002/chem.201602818.
(16) MacNair, A. J.; Millet, C. R. P.; Nichol, G. S.; Ironmonger, A.; Thomas, S. P. Markovnikov-Selective, Activator-Free Iron-Catalyzed Vinylarene Hydroboration. *ACS Catal.* **2016**, *6*, 7217–7221, DOI: 10.1021/acscatal.6b02281.
(17) Palmer, W. N.; Diao, T.; Pappas, I.; Chirik, P. J. High-Activity Cobalt Catalysts for Alkene Hydroboration with Electronically Responsive Terpyridine and α-Diimine Ligands. *ACS Catal.* **2015**, *5*, 622–626, DOI: 10.1021/cs501639r.

(18) Reilly, S. W.; Webster, C. E.; Hollis, T. K.; Valle, H. U. Transmetallation from CCC-NHC pincer Zr complexes in the synthesis of air-stable CCC-NHC pincer Co(iii) complexes and initial hydroboration trials. *Dalton Trans.* **2016**, *45*, 2823–2828, DOI: 10.1039/C5DT04752H.
(19) Peng, J.; Docherty, J. H.; Dominey, A. P.; Thomas, S. P. Cobalt-catalysed Markovnikov selective hydroboration of vinylarenes. *Chem. Commun.* **2017**, *53*, 4726–4729, DOI: 10.1039/C7CC01085K.
(20) Zhang, G.; Wu, J.; Wang, M.; Zeng, H.; Cheng, J.; Neary, M. C.; Zheng, S. Cobalt-Catalyzed Regioselective Hydroboration of Terminal Alkenes. *Eur. J. Org. Chem.* **2017**, *2017*, 5814–5818, DOI: 10.1002/ejoc.201701047.
(21) Tamang, S. R.; Bedi, D.; Shafiei-Haghighi, S.; Smith, C. R.; Crawford, C.; Findlater, M. Cobalt-Catalyzed Hydroboration of Alkenes, Aldehydes, and Ketones. *Org. Lett.* **2018**, *20* , 6695–6700, DOI: 10.1021/acs.orglett.8b02775.
(22) Verma, P. K.; A. S, S.; Geetharani, K. Markovnikov-Selective Co(I)-Catalyzed Hydroboration of Vinylarenes and Carbonyl Compounds. *Org. Lett.* **2018**, *20*, 7840–7845, DOI: 10.1021/acs.orglett.8b03356.
(23) Zhang, G.; Wu, J.; Li, S.; Cass, S.; Zheng, S. Markovnikov-Selective Hydroboration of Vinylarenes Catalyzed by a Cobalt(II) Coordination Polymer. *Org. Lett.* **2018**, *20*, 7893–7897, DOI: 10.1021/acs.orglett.8b03431.
(24) Li, C.; Song, S.; Li, Y.; Xu, C.; Luo, Q.; Guo, Y.; Wang, X. Selective hydroboration of unsaturated bonds by an easily accessible heterotopic cobalt catalyst. *Nat. Commun.* **2021**, *12*, 1–8, DOI: 10.1038/s41467-021-24117-5.
(25) Touney, E. E.; Van Hoveln, R.; Buttke, C. T.; Freidberg, M. D.; Guzei, I. A.; Schomaker, J. M. Heteroleptic Nickel Complexes for the Markovnikov-Selective Hydroboration of Styrenes. *Organometallics* **2016**, *35*, 3436–3439, DOI: 10.1021/acs.organomet.6b00652.
(26) Hashimoto, T.; Ishimaru, T.; Shiota, K.; Yamaguchi, Y. Bottleable NiCl2(dppe) as a catalyst for the Markovnikov-selective hydroboration of styrenes with bis(pinacolato)diboron. *Chem. Commun.* **2020**, *56*, 11701–11704, DOI: 10.1039/D0CC05246A.
(27) Liu, T.; Li, C.; Bai, J.; Zhang, P.; Guo, Y.; Wang, X. Markovnikov-Selective Hydroboration of Aryl Alkenes Enabled by a Simple Nickel Salt. *Chin. J. Chem .* **2022**, *40*, 2203–2211, DOI: 10.1002/cjoc.202200244.
(28) 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, DOI: 10.1002/anie.200902015.
(29) Grigg, R. D.; Rigoli, J. W.; Van Hoveln, R.; Neale, S.; Schomaker, J. M. Beyond Benzyl Grignards: Facile Generation of Benzyl Carbanions from Styrenes. *Chem. – Eur. J.* **2012**, *18* , 9391-9396, DOI: 10.1002/chem.201200642.
(30) Van Hoveln, R.; Hudson, B. M.; Wedler, H. B.; Bates, D. M.; Le Gros, G.; Tantillo, D. J.; Schomaker, J. M. Mechanistic Studies of Copper(I)-Catalyzed 1,3-Halogen Migration. *J. Am. Chem. Soc.* **2015**, *137*, 5346–5354, DOI: 10.1021/ja511236d.
(31) Feng, C.; Tang, L.; Yang, F.; Wu, Y. Copper-catalyzed Markovnikov hydroboration of aliphatic terminal alkenes using carbonyl as a weak directing group. *Org. Chem. Front.* **2023**, *10*, 4692–4697, DOI: 10.1039/D3QO00988B.
(32) Andoh, H.; Nakamura, K.; Nakazawa, Y.; Ikeda-Fukazawa, T.; Okabayashi, S.; Tsuchimoto, T. Quaternary Ammonium Salts: Catalysts for Hydrosilylation of Alkynes with Hydrosilanes. *Adv. Synth. Catal.* **2023**, *365*, 4583–4594, DOI: 10.1002/adsc.202300423.
(33) Du, Y.-D.; Chen, B.-H.; Shu, W. Direct Access to Primary Amines from Alkenes by Selective Metal-Free Hydroamination. *Angew. Chem. Int. Ed.* **2021**, *60*, 9875–9880, DOI: 10.1002/anie.202016679.
(34) Guo, Q.; Shen, G.; Lu, G.; Qian, J.; Que, Q.; Li, J.; Guo, Y.; Fan, B. Hydrogenation of Alkynes and Olefins Catalyzed by Quaternary Ammonium Salts. *Adv. Sci.* **2023**, *11*, 2305271, DOI: 10.1002/advs.202305271.
(35) Kumar, R.; Saima; Shard, A.; Andhare, N. H.; Richa; Sinha, A. K. Thiol–Ene “Click” Reaction Triggered by Neutral Ionic Liquid: The “Ambiphilic” Character of [hmim]Br in the Regioselective Nucleophilic Hydrothiolation. *Angew. Chem. Int. Ed.* **2015**, *54*, 828–832, DOI: 10.1002/anie.201408721.

(36) Onuska, N. P. R.; Schutzbach-Horton, M. E.; Rosario Collazo, J. L.; Nicewicz, D. A. Anti-Markovnikov Hydroazidation of Activated Olefins via Organic Photoredox Catalysis. *Synlett* **2020**, *31*, 55–59, DOI: 10.1055/s-0039-1690691.
(37) Margrey, K. A.; Nicewicz, D. A. A General Approach to Catalytic Alkene Anti-Markovnikov Hydrofunctionalization Reactions via Acridinium Photoredox Catalysis. *Acc. Chem. Res.* **2016**, *49*, 1997–2006, DOI: 10.1021/acs.accounts.6b00304.
(38) Huninik, P.; Szyling, J.; Czapik, A.; Walkowiak, J. Organocatalytic hydroboration of olefins in pyrrolidinium ionic liquids. *Green Chem.* **2023**, *25*, 3715–3722, DOI: 10.1039/D2GC04163D.
(39) Jin, H.; Han, J.; Liu, X.; Feng, C.; Zhan, M. Access to Diverse Organoborons by α-Deprotonation and Functionalization of Benzylboronates. *Org. Lett.* **2023**, *25*, 4168–4172, DOI: 10.1021/acs.orglett.3c01465.
(40) Mlynarski, S. N.; Karns, A. S.; Morken, J. P. Direct Stereospecific Amination of Alkyl and Aryl Pinacol Boronates. *J. Am. Chem. Soc.* **2012**, *134*, 16449–16451, DOI: 10.1021/ja305448w.
(41) Nave, S.; Sonawane, R. P.; Elford, T. G.; Aggarwal, V. K. Protodeboronation of Tertiary Boronic Esters: Asymmetric Synthesis of Tertiary Alkyl Stereogenic Centers. *J. Am. Chem. Soc.* **2010**, *132*, 17096–17098, DOI: 10.1021/ja1084207.
(42) Sokolovicz, Y. C. A.; Nieto Faza, O.; Specklin, D.; Jacques, B.; López, C. S.; dos Santos, J. H. Z.; Schrekker, H. S.; Dagorne, S. Acetate-catalyzed hydroboration of CO2 for the selective formation of methanol-equivalent products. *Catal. Sci. Technol.* **2020**, *10*, 2407–2414, DOI: 10.1039/D0CY00118J.
(43) Query, I. P.; Squier, P. A.; Larson, E. M.; Isley, N. A.; Clark, T. B. Alkoxide-Catalyzed Reduction of Ketones with Pinacolborane. *J. Org. Chem.* **2011**, *76*, 6452–6456, DOI: 10.1021/jo201142g.
(44) Bage, A. D.; Hunt, T. A.; Thomas, S. P. Hidden Boron Catalysis: Nucleophile-Promoted Decomposition of HBpin. *Org. Lett.* **2020**, *22*, 4107-4112, DOI: 10.1021/acs.orglett.0c01168.
(45) Jeong, E.; Heo, J.; Park, S.; Chang, S. Alkoxide-Promoted Selective Hydroboration of N-Heteroarenes: Pivotal Roles of in situ Generated BH3 in the Dearomatization Process. *Chem. – Eur. J.* **2019**, *25*, 6320–6325, DOI: 10.1002/chem.201901214.
(46) Brown, H. C.; Cha, J. S.; Nazer, B. Addition compounds of alkali-metal hydrides. 24. A general method for preparation of potassium trialkoxyborohydrides. A new class of reducing agents. *Inorg. Chem.* **1984**, *23*, 2929–2931, DOI: 10.1021/ic00187a006.
(47) Bage, A. D.; Nicholson, K.; Hunt, T. A.; Langer, T.; Thomas, S. P. The Hidden Role of Boranes and Borohydrides in Hydroboration Catalysis. *ACS Catal.* **2020**, *10*, 13479–13486, DOI: 10.1021/acscatal.0c04051.
(48) Wang, W.; Luo, M.; Zhu, D.; Yao, W.; Xu, L.; Ma, M. Green hydroboration of carboxylic acids and mechanism investigation. *Org. Biomol. Chem.* **2019**, *17*, 3604–3608, DOI: 10.1039/C9OB00485H.
(49) Lee, C.; Yang, W.; Parr, R. G. Development of the Colle-Salvetti correlation-energy formula into a functional of the electron density. *Phys. Rev. B* **1988**, *3*, 785-789, DOI: 10.1103/PhysRevB.37.785.
(50) Becke, A. D. Density-functional thermochemistry. III. The role of exact exchange. The *J. Chem. Phys.* **1993**, *98*, 5648-5652, DOI: 10.1063/1.464913.
(51) Zhao, Y.; Truhlar, D. G. The M06 suite of density functionals for main group thermochemistry, thermochemical kinetics, noncovalent interactions, excited states, and transition elements: two new functionals and systematic testing of four M06-class functionals and 12 other functionals. *Theor. Chem. Acc*. **2008**, *120*, 215-241, DOI: 10.1007/s00214-007-0310-x.
(52) Rappoport, D.; Furche, F. Property-optimized Gaussian basis sets for molecular response calculations. *J. Chem. Phys.* **2010**, *133*, 134105, DOI: 10.1063/1.3484283.
(53) Zheng, J.; Xu, X.; Truhlar, D. G. Minimally augmented Karlsruhe basis sets. *Theor. Chem. Acc.* **2011**, *128*, 295-305, DOI: 10.1007/s00214-010-0846-z.
(54) Weigend, F. Accurate Coulomb-fitting basis sets for H to Rn. *Phys. Chem. Chem. Phys.* **2006**, *8*, 1057-1065, DOI: 10.1039/B515623H.

(55) Neese, F. Software update: The ORCA program system—Version 5.0. *Wiley Interdiscip. Rev. Comput. Mol. Sci.* **2022**, *12*, e1606, DOI: https://doi.org/10.1002/wcms.1606.
(56) Helmich-Paris, B.; de Souza, B.; Neese, F.; Izsák, R. An improved chain of spheres for exchange algorithm. *J. Chem. Phys.* **2021**, *155*, 104109, DOI: 10.1063/5.0058766.
(57) Barone, V.; Cossi, M. Quantum Calculation of Molecular Energies and Energy Gradients in Solution by a Conductor Solvent Model. *J. Phys. Chem. A* **1998**, *102*, 1995-2001, DOI: 10.1021/jp9716997.
(58) Lange, A. W.; Herbert, J. M. A smooth, nonsingular, and faithful discretization scheme for polarizable continuum models: The switching/Gaussian approach. *J. Chem. Phys.* **2010**, *133*, 244111, DOI: 10.1063/1.3511297.