Enhancing the nucleophilicity of benzylic boronates enables the divergent formation of C−C and C−X bonds

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Abstract: Tetracoordinated boron species generated from the complexation of organoboron compounds with bases are highly important intermediates in molecular fragments coupling. The type of base significantly impacts both the reaction activity and mechanism of organoboron compounds. Herein, our structural and mechanistic insights show that the full heterolytic cleavage of the C−B bond in benzylic boronates, leading to the formation of benzyl potassium species, can be achieved by increasing the amount of alkoxides. This, in turn, significantly enhances the nucleophilicity of both secondary and tertiary benzylic boronates. This mechanistic insight has proven valuable in the divergent construction of C(sp^3)−C(sp^3 or sp^2) and other C−X bonds (X = Si, Ge, Sn, S, Se), as demonstrated through the integration of base-catalyzed silylboration/diborylation reactions. Through machine-learning-assisted screening of approximately 10^4 substrate combinations, we have expanded the scope of electrophiles for this transformation to include challenging aromatic heterocycles. Moreover, the synthetic potential of this protocol was demonstrated through the construction of drug-relevant molecules that contain 1,1-diaryl pharmacophores.

Organoboronates are a valuable class of building blocks[1-2] in modern synthesis due to their divergent reactivity, ease of handling, and broad accessibility.[3-10] The activation of the C−B bond is one of the most critical steps in cross-coupling reactions of organoboronates, and it can be achieved through classical transmetalation reactions at the transition metal center.[11-14] Recently, the base-mediated strategy has also emerged as versatile tool for C−B bond activation, involving the thermodynamically favorable formation of base-boronate complex (**I**).[15-18] In some cases, the ate complex could undergo reversible cleavage of the C−B bond to form carbanion (**II**, Fig. 1a). The resulting ate complex or carbanion can ultimately react with electrophiles to form C−C or C−X bonds (X = Si, Ge, Sn, S, Se) (Fig. 1b). For example, Aggarwal et al. achieved impressive stereospecific coupling of organoboronates with different types of alkyl and heteroatom electrophiles using organolithium/boronate combinations.[19-21] Similarly, the groups of Morken, Chirik, and Meek demonstrated that alkoxides can promote the C−C coupling reaction of geminal boronates with alkyl halides and carbonyl derivatives.[22-24] Our particular interest lies in the base-mediated activation of benzylic organoboronates, as their coupling with aryl (pseudo)halides can produce highly valuable 1,1-diaryl alkanes, which are key pharmacophores in marketed drugs.[25-26] Note that Ohmiya recently reported an alkoxide-mediated cross-coupling of tertiary benzylic organoboronates with alkyl or aryl electrophiles, but attempts to extend this procedure to secondary benzylic organoboronates were unsuccessful.[27] Therefore, there is a continued need for approaches to expand the scope of base-promoted cross-coupling reactions involving benzylic organoboronates.

As we have discovered and reported herein, the reaction between benzylic organoboronates and alkoxide bases can be fine-tuned to achieve irreversible cleavage of the C−B bond and generate free carbanions by increasing the amount of base used (Fig. 1c). This results in enhanced nucleophilicity of both secondary and tertiary benzylic organoboronates. By integrating the alkoxide-mediated silaboration (or diborylation) reaction of aromatic alkenes with the nucleophilic-type reaction, we have developed a versatile platform for constructing C−C and C−X bonds under mild reaction conditions.[28-29] This bond-making approach is mechanistically unique from existing protocols achieved through transition-metal catalysis or radical processes.[30-33] It has a broad reaction scope, as demonstrated by successful reactions with up to 12 different classes of nucleophiles, including the challenging substitution of aromatic heterocycles and nucleophilic addition of carbon dioxide. The starting materials used in this approach are commercially available or readily synthesized, and

the reactions are generally rapid, ranging from less than one minute to several hours, making it a practical tool for constructing molecular diversity. Importantly, coupling this approach with aryl electrophiles provides a step-economic route to drug-relevant 1,1-diarylalkane derivatives.

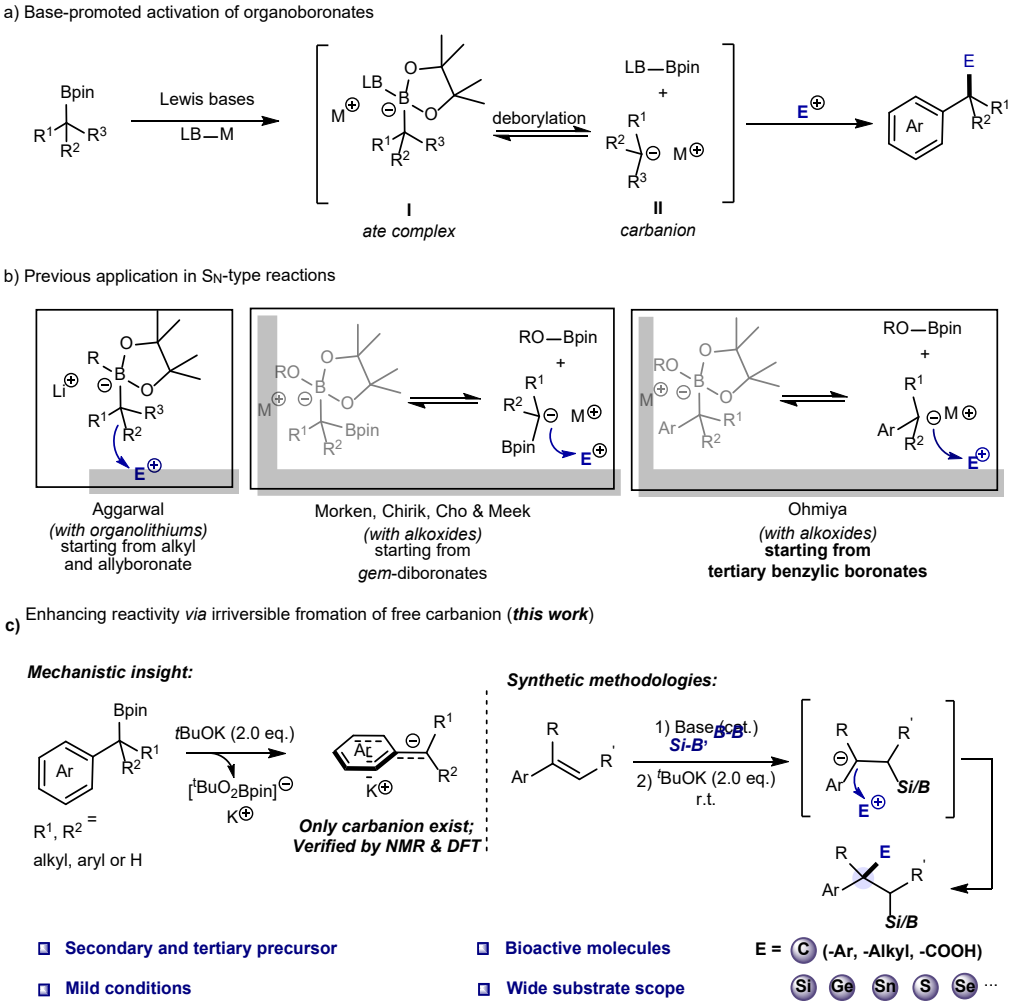


Fig. 1 | Base-promoted nucleophilic-type reactions of organoboronates. a, General figure of the application of organoboronates/base combinations in cross-coupling reaction. **b**, Previous studies: mediated by organolithium or alkoxides. **c**, This work: enhancing the reactivity for divergent bond formation.

Results and discussion

Mechanistic insight and reaction development. We began our studies with the reaction of ^{t}BuOK with *β*-silyl benzylic boronates **I′** (prepared *via* silylboration of styrene [28]) (Fig. 2a). Our density functional theory (DFT) calculations with M06-2X functional[34] show that the ate complex **II′**, resulting from the complexation of **I′** with ^{t}BuOK is thermodynamically stable ($\Delta G = -16.4$ kcal/mol). Its heterolysis into the *β*-sily benzylic anion and ^{t}BuOBpin complex **III′** is kinetically feasible ($\Delta G^{\ddagger} = 14.1$ kcal/mol), although this step is endergonic by 10.3 kcal/mol (Fig. 2a). If an

additional molecule of ^{t}BuOK reacts with the intermediate **III′**, the formation of carbanion species **V′** and [(^{t}BuO)$_2$Bpin]$^-$K$^+$ **IV′** is thermodynamically favorable (ΔG = −19.7 kcal/mol) through a barrierless process (see Supplementary Fig. 3 for calculated free energy profiles). These computational results suggest that the irreversible cleavage of C−B bond in benzylic organoboronates can be achieved by increasing the amount of alkoxide bases. To verify these mechanistic findings, we conducted some control experiments. According to the ^{11}B NMR analysis (in THF-d_8) presented in Fig. 2b, the signals of boron species depends on the amount of ^{t}BuOK. In the presence of 1.2 equivalent of ^{t}BuOK, two tetracoordinated boron resonances were detected at δ 6.9 and 4.3 ppm, which were assigned to the "ate" complex **II′** and [(^{t}BuO)$_2$Bpin]$^-$K$^+$ **IV′**, respectively, based on previous works[22] and our present DFT calculations (shown in red numbers). Upon increasing the base amount to 2.0 equivalent, the resonance at 6.9 ppm almost disappeared, but the peak at 4.3 ppm was retained. Further comparison of calculated and observed ^{1}H NMR analysis on the reaction mixture of **I′** and ^{t}BuOK (2.0 equivalents) confirm the definite formation of the carbanion intermediate **V′**. The negative charge of intermediate **V′** is calculated to be delocalized over the benzene ring, as supported by the upfield shifting of related hydrogen signals.

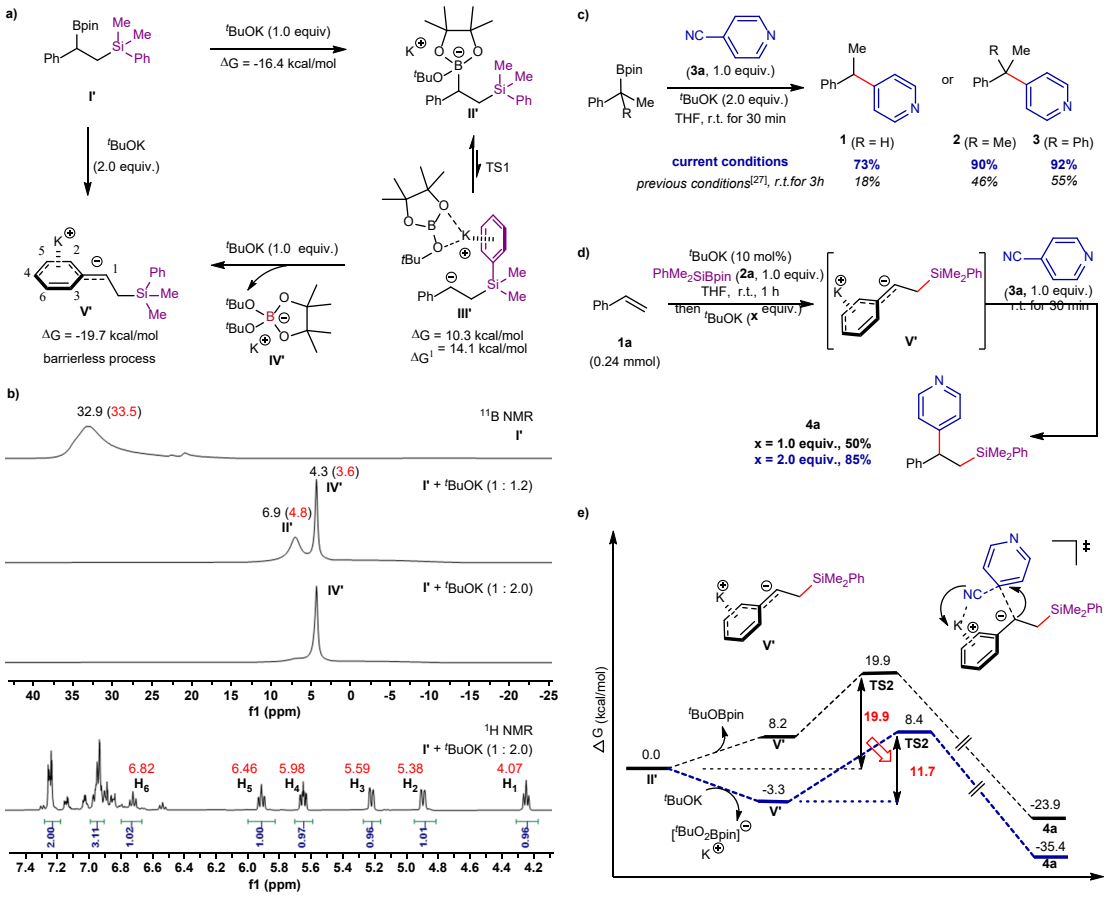


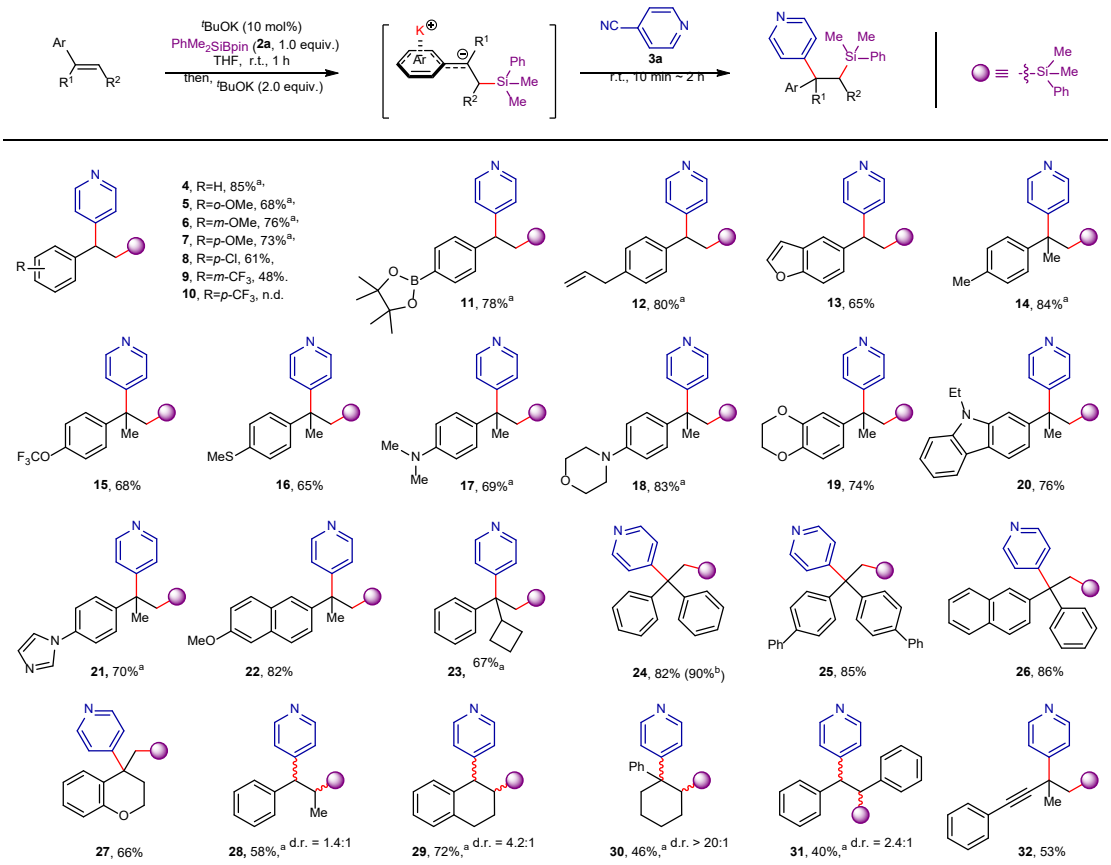
Fig. 2 | Mechanistic insight and reaction development. a, Computational studies on the reaction of benzylic boronate with ^{t}BuOK. **b**, NMR analysis on the reaction of benzylic boronate with different amounts of ^{t}BuOK. Chemical shifts shown in red were computed with the Gauge-independent atomic orbital (GIAO) method at B972/pcSseg-2 level of theory[35]. **c**, Enhanced reactivity of secondary and tertiary benzylic organoboronates for the cross-coupling with 4-cyanopyridine. **d**, Development of "one-pot" carbosilylation of aromatic alkenes with $PhMe_2SiBpin$ **2a** and 4-cyanopyridine **3a**, see Table S1 in SI for optimization details. **e**, Computational analysis on the enhancing effect of ^{t}BuOK (in black line: with 1.0 equiv; in blue line, 2.0 equiv.)

Previous studies by Ohmiya *et al* have demonstrated that the ^{t}BuOK-promoted cross-coupling of tertiary benzylic boronate with aryl halide requires high temperatures of 100~120 °C and is not applicable to secondary benzylic boronate.[27] However, based on our mechanistic findings, we predicted that the reactivity of both secondary and tertiary benzylic boronates can be enhanced by simply increasing the amount of ^{t}BuOK. This enhancement was demonstrated by performing the reaction with 4-cyanopyridine at room temperature, resulting in the corresponding products (**1**-**3**) in good to excellent yields within 30 minutes (Fig. 2c). Notably, the yields of reactions with secondary and tertiary benzylic boronates were lower (18% for **1**, 46% and 55% for **2** and **3**, respectively) in the presence of one equivalent of ^{t}BuOK as suggested by Ohmiya *et al*.[27] These results indicate

that expanding the scope of benzylic boronates through the current nucleophilicity enhancement strategy is feasible.

Inspired by previous studies on synthesizing benzylic boronates through base-catalyzed silaboration or 1,2-diboration of aromatic alkenes,[28-29] we therefore envisioned that combining these methods with the aforementioned C−B bond activation strategy and classical nucleophilic reactions would offer a valuable method for difunctionalization of alkenes, as well as for a divergent formation of both C−C and C−X bonds. Indeed, the addition of 2.0 equivalents of ^{t}BuOK and aryl electrophile 4-cyanopyridine **3a**, sequentially, to the resulting mixture of silaboration reaction of styrene **1a** under ambient temperature, produced the corresponding carbosilylation product **4** in 85% yield within 30 minutes (Fig. 2d). However, when 1.0 equivalent of ^{t}BuOK was used, the difuntionalization process only produced **4** in 50% yield. Our DFT calculations revealed that the deborylative cross-coupling reaction, involving two molecules of ^{t}BuOK, has a much lower activation barrier (11.7 kcal/mol) compared to the pathway with only one molecule of ^{t}BuOK (19.9 kcal/mol) for the nucleophilic substitution reaction between carbanion **V'** and 4-cyanopyridine (Fig. 2e, for the full free energy profile, see Supplementary Fig. 3 and 4). These computational findings are consistent with the observed difference in reactivity between performing the reaction in the presence of 1.0 and 2.0 equivalents of ^{t}BuOK. Additionally, the radical pathway for the C−C coupling can be ruled out because of the higher energy required for the corresponding SET process (see Supplementary Fig. 5 for detailed calculations).

Table 1. Scope of aromatic alkenes.

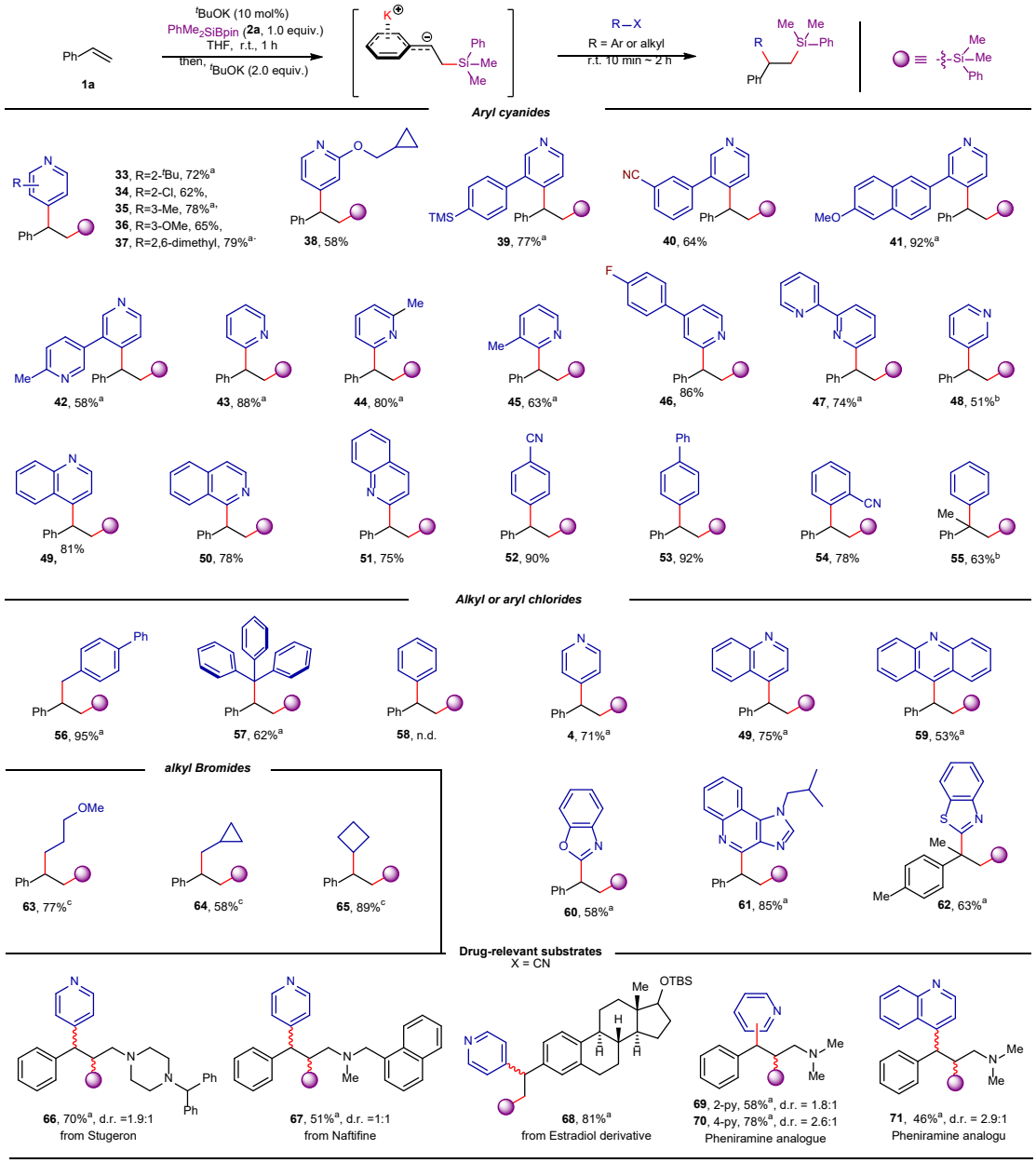


Reactions were conducted in a two-step procedure: **alkene** (0.20 mmol), **2a** (0.20 mmol), ^{t}BuOK (10 mol%) in 1.0 mL THF, r.t. for 1 h. Then, ^{t}BuOK (0.40 mmol) and 4-cyanopyridine (0.20 mmol) were sequentially added; the mixture was stirred at r.t. for 10 min to 2 h. Isolated yields. [a]1.2 equiv of alkenes and $PhMe_2Bpin$ were used. [b]In 5.0 mmol scale, 1.78g.

Synthetic scope. With suitable conditions in hand, the scope of aromatic alkenes was firstly examined with $PhMe_2SiBpin$ as the boron source and 4-cyanopyridine as the other coupling partner (Table 2). The initially tested aryl alkenes represent an extensive sampling of both simple styrene and 1,1/1,2-disubstituted olefins with electron-rich or electron-deficient substituents. Substituted styrenes underwent silylarylation effectively with good to excellent yields (**5-9, 11**, and **12**), except for one instance in which a strong electron-withdrawing CF_3 group was installed at the *para* position of the C=C bond (**10**). Furthermore, we found that 1,1-disubstituted alkenes readily undergo addition reactions to give the difunctionalization products bearing quaternary carbon centers in good yields (**14-26**, 65%-94%), including three examples with highly crowded triaryl quaternary carbon centers (**24-26**). These results clearly illustrate the unique features of this method compared to

transition-metal-catalyzed difunctionalizations[36-39], in which the formation of the quaternary carbon center remains a great challenge[40-42]. Surprisingly, a series of substituents, such as boronic eater, allyl- groups, 4-trifluoromethoxyl-, 4-methylthio- or 4-dimethylamino- were well tolerated under the reaction conditions, affording the corresponding products **11-12, 15-17** in 65% to 84% yield. Notably, the heteroaromatic or aliphatic heterocycles substituted alkenes, such as 2,3-benzofuran, morpholine, 1,4-benzodioxan, *N*-ethyl-carbazole, imidazole, 2-methoxy-naphthalene, and chromane are all suitable for this base-mediated difunctionalization conditions well (**13**, **18-22**, **27**). Moreover, internal alkenes, such as *β*-methylstyrene, 1,2-dihydronaphthalene, 1,2-dihydronaphthalene, 1-phenyl-1-cyclohexene, and *trans*-1,2-diphenylethene are also suitable coupling partners under the current reaction conditions, providing the corresponding products in 40%-72% yields (**28-31**). 3-Methylbut-3-en-1-yn-1-yl)benzene, one of enynes, could be smoothly transformed to the corresponding product **32** in 53% yield. The scalability of the protocol was demonstrated by the gram-scale reaction conducted with 1,1-diphenylethylene in 90% yield (**24**, 5.0 mmol scale).

Table 2. Scope of nucleophiles.



Reactions were conducted in a two-step procedure: styrene (0.20 mmol), $PhMe_2SiBpin$ (0.20 mmol), ^{t}BuOK (10 mol%) in 1.0 mL THF, r.t. for 1 h. Then, ^{t}BuOK (0.40 mmol) and the related aryl nitriles or organohalides (0.20 mmol) were sequentially added; the mixture was stirred at r.t. for 10 min to 2 h. Isolated yields. [a]1.2 equiv of alkenes and $PhMe_2Bpin$ were used. [b]At 50 °C. [c]At 0 °C.

After establishing that a wide array of aromatic alkenes is applicable to this transformation, we turned our attention to the scope of electrophiles with different types of leaving groups. As exemplified in Table 2, the scope is striking because both C(sp^2)- and C(sp^3)-hybridized electrophiles, including aryl cyanide, aryl chloride, alkyl chloride, and alkyl bromides, could be employed. Using styrene as the model substrate, we found that most of the cyano-substituted

pyridines (**33**-**54**) are effective coupling partners, despite the electronic and substituent effects of the cyano group at the C-2, C-3, and C-4 positions. [43-46] These results clearly illustrate the true complementary nature of this method to Minisci-type reactions or radical-based *ipso*-substitution of pyridine nitriles[47-53] given that a challenging C-3 substituted pyridine is also accessible (**48**). More importantly, other aryl (or azines) cyanides, including 2 or 4-cyanoquinoline, 1-cyano-isoquinoline, 1,4- or 1,2-dicyanobenzene, 4-cyanobiphenyl, and even benzonitrile were also allowed in the reaction, providing the desired products **49**-**55** in moderate to good yields. Besides, this approach can facilitate access to the 1,2-difunctionalization of alkenes from the abundantly available aryl chloride, alkyl chloride, and alkyl bromides (**56**-**65**). For example, the bulky triphenylmethyl chloride was also a suitable coupling partner for the transformation, providing the desired product **57** in 62% yields. Although chlorobenzene (**58**) did not react under current conditions, chlorinated heterocycles, including 4-chloropyridine, 4-chloroquinoline, 9-chloroacridine and 2-chlorobenzothiazole provide the desired products in good yields (**4**, **49**, and **59**-**62**). The alkyl bromides were also suitable coupling partners in the reaction, providing the desired product **63**-**65** in 58%-89% yields. Given there are plenty of aromatic electrophiles commercially accessible, the reactivity of the different leaving groups was then examined with 2-substituted pyridines. We found that 2-chloro-, bromo-, iodo- and benzenesulfonyl-substituted pyridine are less effective, but 2-fluoropyridine, 2-cyanopyridine, 2-methoxylpyridine and 2-methylthiopyridine are viable 2-pyridinyl precursors (see Supplementary Table 2, and the observed reactivities are consistent with DFT calculations shown in Supplementary Table 3). Furthermore, this transformation is also applicable to the derivatization of drug-relevant molecules. Three alkenes derived from stugeron, naftifine, and estradiol derivatives could be readily converted to the corresponding products in 51-81% yields (**66**-**68**). In addition, this difunctionalization platform enables access to compound libraries of antihistamine pheniramine derivatives from abundantly available aryl cyanides. Using the readily accessible (*E*)-*N,N*-dimethyl-3-phenyl-2-propen-1-amine as the substrate, the desired pheniramine analogues **69**-**71** could be rapidly prepared in 46%-78% yields. It should be noted that both heterocycles and 1,1-diaryl motifs are privilege structures in medicinal chemistry[25, 54-55]; therefore, our one-pot, two-bond-forming transformation represents an attractive route to synthesize a wide range of compounds potentially relevant to medicinal applications from readily accessible precursors.

Machine-learning-assisted reaction space exploration. Recently, machine learning (ML) methodologies were demonstrated to be useful in the prediction of synthetic performance[56-59]. Here, several ML models were adopted to predict the reaction yield using 7~10 features (e.g., calculated NPA charges, molecular volume[60], and bond dissociation energies, etc. see Supplementary Tables 4 and 5). In the first round, eight features were chosen to build the ML model (ML-IV) after feature selection (Fig. 3a, and Supplementary Tables 6~9), 43 experimental data were collected to train the ML model (Supplementary Fig. 6, Tables 10~11). The XGBoost algorithm was found to provide better performance over other algorithms (such as DecisionTree, SVR, MLR, etc). The feature importance analysis showed that the NPA charge at the C-2 position of olefines has the greatest effect on reaction yield (Fig. 3b, Supplementary Table 12). The performance of ML models were then evaluated with 33 out-of-sample data (experimentally validated, See Supplementary Table 13 for details), revealing that prediction accuracy was 70%. Furthermore, 3 samples (≈10%) were randomly selected from the 28 'unseen' data to give feedback to the trained models in the second-round learning (Supplementary Table 8), demonstrating that the ML model (ML-IV) maintained stability.

The reaction yields were subsequently predicted on a much larger chemical space with the established prediction model, including 12642 pairs of combinations (86*147, 86 types of alkenes and 147 types of electrophiles, see Supplementary Fig. 7~9). Fig. 3c shows several recommended substrates (6 alkenes and 15 electrophiles), which might exhibit high reactivity. One can see that in addition to halogenated arenes, aromatic heterocycles might also be suitable electrophiles. Based on machine-learning-assisted predictions, we investigated the reactivity of aromatic heterocycles experimentally. We were delighted to find that even challenging aromatic heterocycles, such as pyridine, quinoline, and isoquinoline, 1,5-naphthyridine, pyrazine, and 5*H*-1-pyrindene are effective coupling partners (*via* direct C−H substitution), providing the desired products **4**, **29**, **49**-**50**, **73**-**76** in moderate to good yields and excellent *site*-selectivity under slightly different reaction conditions (as shown in Fig. 3d).

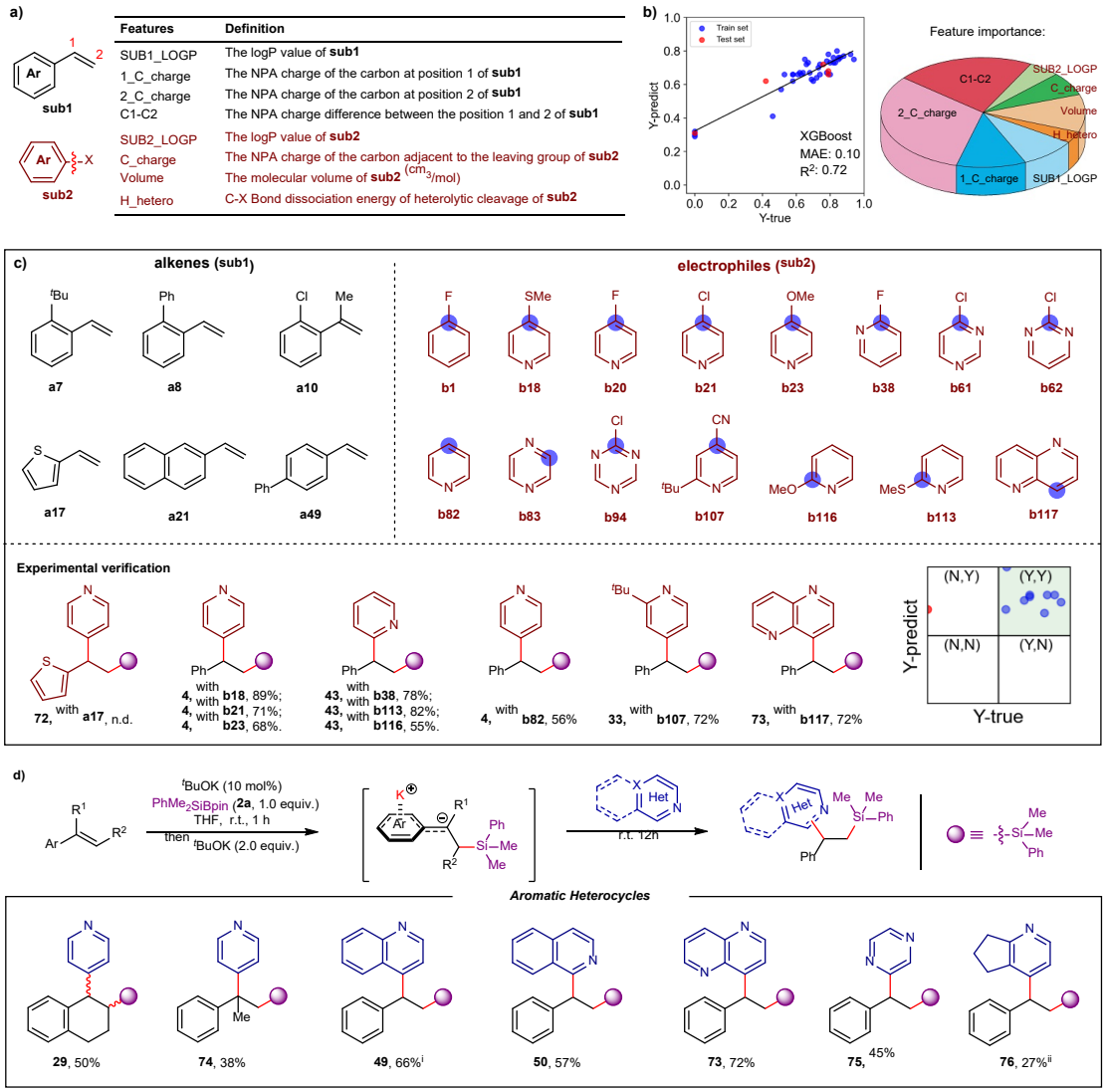


Fig. 3 | Machine Learning-assisted discovery and experimental validation. a, Features of aromatic alkenes **(sub1)** and aromatic electrophiles **(sub2)** molecules. **b**, The prediction performance evaluated by the XGBoost algorithm and the feature importance given by ML model. **c**, The recommended reactive substrates by the machine learning prediction. (Inset: The prediction performance of some recommended substrates and validated by experiments. Yields < 50% are marked with 'N', and yields > 50% are marked with 'Y'). **d**, Selected newly discovered reactions for the recommended substrates from the machine learning model prediction. Reactions were conducted in a two-step procedure: alkene (0.40 mmol), $PhMe_2SiBpin$ (0.40 mmol), ^{t}BuOK (10 mol%) in 1.5 mL THF, r.t. for 1h. Then, ^{t}BuOK (0.80 mmol) and the related aromatic heterocycles (0.20 mmol) were sequentially added; the mixture was stirred at r.t. for 12 h. Isolated yields. [i]Performed with N-oxide. [ii]NMR yield.

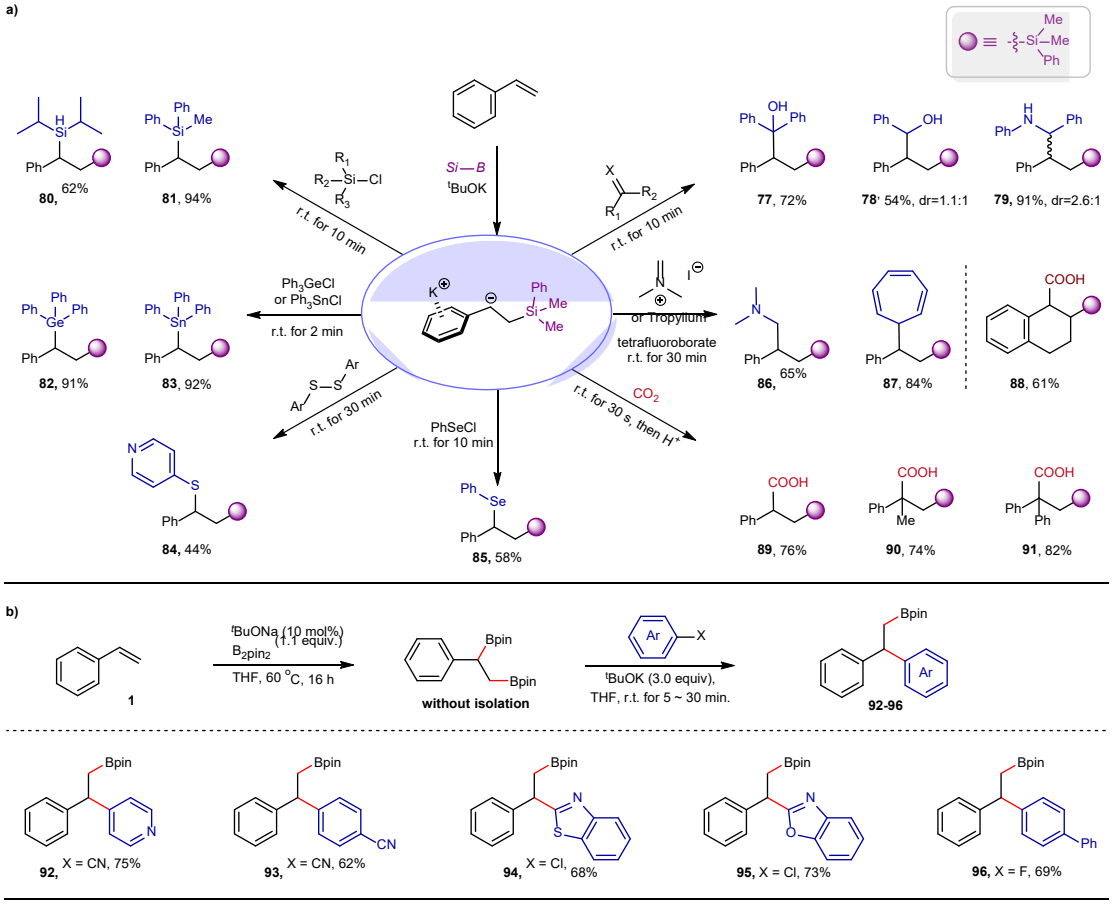


Fig. 4 | Scope extension. a, trapping the carbanion intermediate with other electrophiles. **b**, carboborylation of aromatic alkenes. Reactions were conducted in a two-step procedure, please see Supplementary Information for detailed conditions.

Further extension of substrate scope. The aforementioned studies demonstrate that the bench-stable benzylic boronate/^{t}BuOK combination (1:2 ratio) can function as a surrogate for benzyl potassium. Building on this finding, we conducted further experiments to explore its potential for reacting with other electrophiles, such as carbonyl derivatives (including benzophenone, benzaldehyde, and *N*-benzylideneaniline), chlorosilanes (such as iPr$_2$SiHCl and Ph$_2$MeSiCl), triphenylchlorogermane, triphenyltin chloride, disulfide, phenylselenenyl chloride, eschenmoser's salt, and others (Fig. 4a). Typically, these reactions proceed rapidly and align with the high reactivity of organometallic reagents. The resulting products (**77**-**87**), which contain a wide range of C−C and C−X bonds, were obtained in yields of 44-94%. It is worth highlighting that carbon dioxide (CO_2), an abundant but unreactive molecule, can also serve as a suitable C1 electrophile[61]. By directly bubbling dry CO_2 through a reaction mixture of alkene/PhMe$_2$SiBpin/^{t}BuOK, the corresponding

silacarboxylation products (**88-91**) were obtained in high yields within an exceptionally short reaction time of just 30 seconds. This single-flask difunctionalization approach was also extended to other combinations. For example, based on a base-catalyzed 1,2-diboration reaction[29] of aromatic alkenes with B_2pin_2, carboborylation reactions occur in moderate to good yields (**92-96**, 62-75% yields), as demonstrated by 5 examples collected in Fig. 4b. Given that there are thousands of readily accessible electrophiles and the silyl or boryl group in the resulting products can be easily modified, we reasoned that this base-mediated bond-forming strategy could offer a versatile platform for accessing a vast range of chemical and molecular diversity.

Conclusion

In summary, mechanistic insights into the reaction of alkoxide and benzylic boronate reveal that increasing the amount of alkoxide can convert benzylic boronate into a free carbanion, thereby significantly increasing the nucleophilicity of both secondary and tertiary benzylic boronates. This finding is demonstrated through the mild reaction conditions for the alkoxide-promoted cross-coupling reaction of benzylic boronate with 4-cyanopyridine. Based on these mechanistic findings, a highly efficient and operationally straightforward method has been developed for divergently constructing C−C and C−heteroatom bonds using benzylic boronate derived from the silaboration (or diborylation) reaction of aromatic alkenes. This method can tolerate a broad range of electrophiles, including aryl (pseudo)halides, aromatic heterocycles, carbon dioxide, carbonyl derivatives, etc. Of particular significance is its applicability to aryl electrophiles, allowing for the facile synthesis of valuable 1,1-diaryl frameworks. Moreover, the synthetic value of this strategy is evidenced by its potential for late-stage modification of drug-relevant molecules.

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Methods

General procedure for the difunctionalization of aromatic alkenes with $PhMe_2SiBpin$/^tBuOK combination. In an argon-filled glove box, an oven-dried 10 mL Schlenk-tube was charged with alkenes (0.2~0.24 mmol), $PhMe_2SiBpin$ **2a** (0.2~0.24 mmol, 1.0 equiv), ^tBuOK (10 mol%, 0.02~0.024 mmol), and tetrahydrofuran (1.0 mL) were successively added. The reaction mixture was stirred at room temperature for one hour. Then, ^tBuOK (0.4~0.48 mmol, 2.0 equiv.) and electrophile (0.2 mmol, 1.0 equiv.) were sequentially added into the reaction mixture and stirred for 30 seconds to 2 hours. After the reaction finished, saturated ammonium chloride solution (2 mL) was added to the reaction mixture, and the organic phase was separated. The aqueous layer was extracted with EtOAc (3×2 mL). Then, the organic layers were combined, dried over anhydrous sodium sulfate, and filtered. After removal of the solvent under reduced pressure, the crude material was purified by flash column chromatography on silica gel or preparative TLC to afford the corresponding products.

General procedure for the carboborylation of aromatic alkenes. In an argon-filled glove box, an oven-dried 10 mL Schlenk-tube was charged with styrene (0.24~0.3 mmol.), B_2pin_2 **2b** (1.1 equiv.), ^tBuONa (10 mol%), MeOH (5.0 equiv.) and tetrahydrofuran (1.0 mL). The reaction mixture was stirred at 60 ^oC for 16 h. After the reaction finished, the solvent was removed under vacuum, and the resulting residue was redissolved in 1.0 mL of tetrahydrofuran. Then, ^tBuOK (3.0 equiv.) and electrophiles (0.2 mmol) were successively added to the reaction mixture and stirred for 12 h. Purification by preparative TLC affords the corresponding carboborylation products.

Data availability

The data supporting the findings of this study, including material and methods, optimization details, synthetic procedures, mechanistic studies, DFT calculations, machine learning, and NMR spectra, are available in Supplementary Information.

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Author contributions

L.Z.G., G.Q.W. and S.H.L conceived the work and designed the experiments. L.Z.G. optimized the reaction conditions. L.Z.G., L.K.H. performed the experiments and analyzed the experimental data. X.Y.L and L.K.H. conducted machine-learning-assisted reaction discoveries. S.D.C. and J.C. reproduce the experiments for products **4**, **22**, **23**, and **31**. L.Z.G. and G.A.L. performed the DFT calculations and discussed the results with G.Q.W.. L.Z.G., X.Y.L. and G.Q.W. co-wrote the manuscript with the input from all the other authors. J.M., G.Q.W., and S.H.L. directed the project.

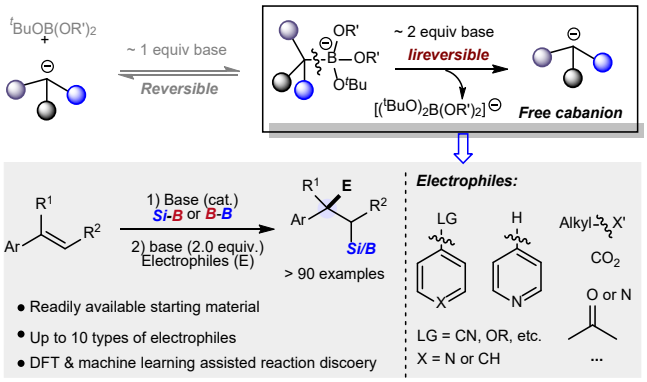
Competing interests

The authors declare no competing interests.

Additional information

Supplementary information The online version contains supplementary material available at Correspondence and requests for materials should be addressed to Shuhua Li, or Guoqiang Wang.

TOC


~ 1 equiv base
Reversible
~ 2 equiv base
lireversible
Free cabanion
1) Base (cat.)
Si-B or B-B
2) base (2.0 equiv.)
Electrophiles (E)
> 90 examples
Si/B
Electrophiles:
LG = CN, OR, etc.
X = N or CH
O or N
• Readily available starting material
• Up to 10 types of electrophiles
• DFT & machine learning assisted reaction discoery