Recent Advances in the Construction of Fluorinated Organoboron Compounds

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ABSTRACT: Fluorinated organoboron compounds are important synthetic building blocks that combine the unique characteristics of a fluorinated motif with the versatile synthetic applications of organoboron moiety. This review article guides the research on fluorinated organoboron compounds mainly from four aspects in recent years: selective monodefluor-oborylation of polyfluoroarenes and polyfluoroalkenes, selective borylation of fluorinated substrates, selective fluorination of organoboron compounds, and borofluorination of alkynes/olefins. In addition, this review will provide a necessary guidance and inspiration for the research on the valuable synthetic building block fluorinated organoboron compounds.
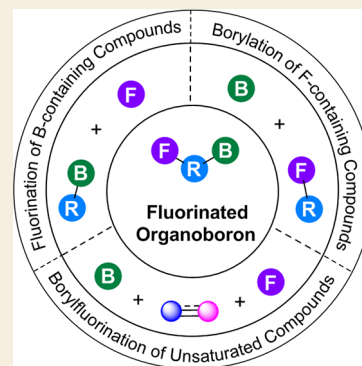
KEYWORDS: *organofluorine compounds, organoboron reagents, fluorinated organoboron compounds*

1. INTRODUCTION

Owing to their intriguing chemical and biological properties, organofluorine compounds are important to various fields such as pharmaceutical chemistry, agrochemistry, and materials science (Scheme 1A).[1−14] Usually, the fluorine atom can be regarded as a bioisostere of the hydrogen atom because of their similar atom radius, thus giving them potential for extensive applications in medicine. For example, it can effectively delay the oxidative metabolism of drugs in vivo. Moreover, the highly electronegative fluorine atom greatly increases the metabolic stability of the drugs, thus prolonging their curative effect. Moreover, the participation of fluorine atom or fluorine-containing groups also increases the lipophilicity of parent molecules, which can promote the absorption of the drugs. As a consequence, numerous fluorine-containing drugs such as antiepileptic, panomifene, 5-fluorouracil, halothane, and favipiravir, etc. have been approved by the FDA (Scheme 1A).

Organoboron reagents play an important role in assembly of pharmaceuticals, natural products, as well as organic materials (Scheme 1B).[15−25] Ever since the birth of organoboron compounds, the research enthusiasm for them has never been mitigated. For example, Suzuki−Miyaura cross-coupling, one of the most widely used name reactions, has been extensively employed in the construction of C−C bonds from C−B bonds (Scheme 1B).[15−25] Moreover, the C−B bonds can be easily and efficiently converted into various bonds[26−30] such as carbon−heteroatom bonds (C−O, C−S, C−N, C−P, C−H/ D, C−Si) and carbon−halogen bonds (C−F, C−Cl, C−Br, C−I) (Scheme 1B). In addition, a carbon−hydrogen bond can

be formed via protodeborylation, and carbon−metal bonds can also be generated in the presence of other organometallic reagents (Scheme 1B), by which a series of valuable and intriguing functional groups could be incorporated, making organoboron compounds very popular synthetic building blocks. Meanwhile, organoboron compounds are also an integral part of chemical sensors[31] (for example, ICT sensor), materials[32] (for example, aminoborane), and drug molecules,[33] such as Bortezomib[33] (treatment of multiple myeloma) and Ixazomib[33] (first oral medication, treatment of multiple myeloma) (Scheme 1B).
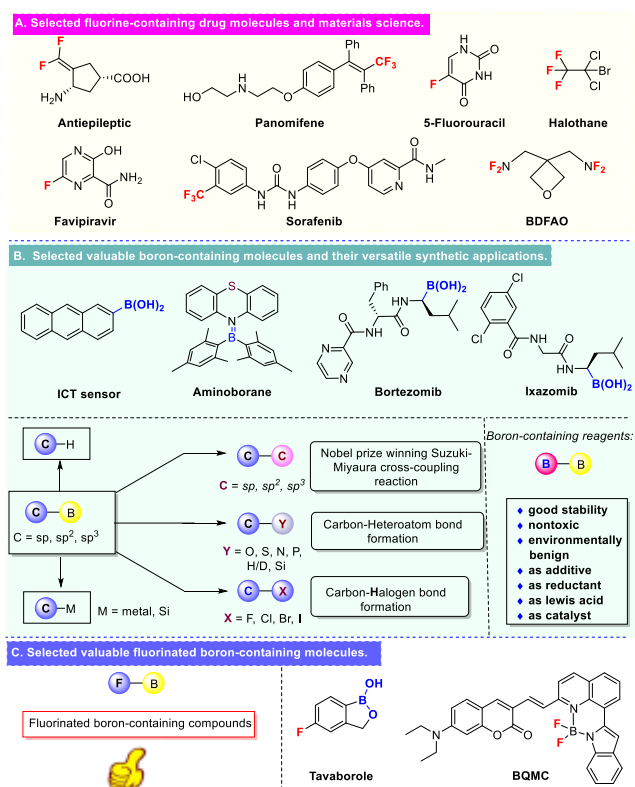
More intriguingly, fluorinated organoboron compounds are very useful building blocks as they combine the fluorine atom and the organoboron motifs into the same molecule. Although such compounds are very valuable in various fields, such as pharmaceuticals and materials science (Scheme 1C),[32,34] the types of fluorine-containing organoboron compounds are not abundant and their synthetic methods are also very limited. There are currently four means to prepare such compounds: (1) selective monodefluoroborylation of polyfluoroarenes and polyfluoroalkenes, (2) selective borylation of fluorinated

Scheme 1. (A) Selected Fluorine-Containing Drug Molecules and Materials Science, (B) Selected Valuable Boron-Containing Molecules and Their Versatile Synthetic Applications and (C) Selected Valuable Fluorinated Boron-Containing Molecules

fluorobenzene compounds.[35−37] In 2010, Braun and co-workers reported an elegant strategy in which a 16-electron rhodium(I)−boryl complex reacts with fluorinated substrates such as pentafluoropyridine and perfluoropropene to result in C−F activation and furnish fluorinated organoboron compounds (Scheme 2(I)),[35] although the substrate scope is

Scheme 2. Rh-Catalyzed Monodefluoroborylation of Polyfluoroarenes
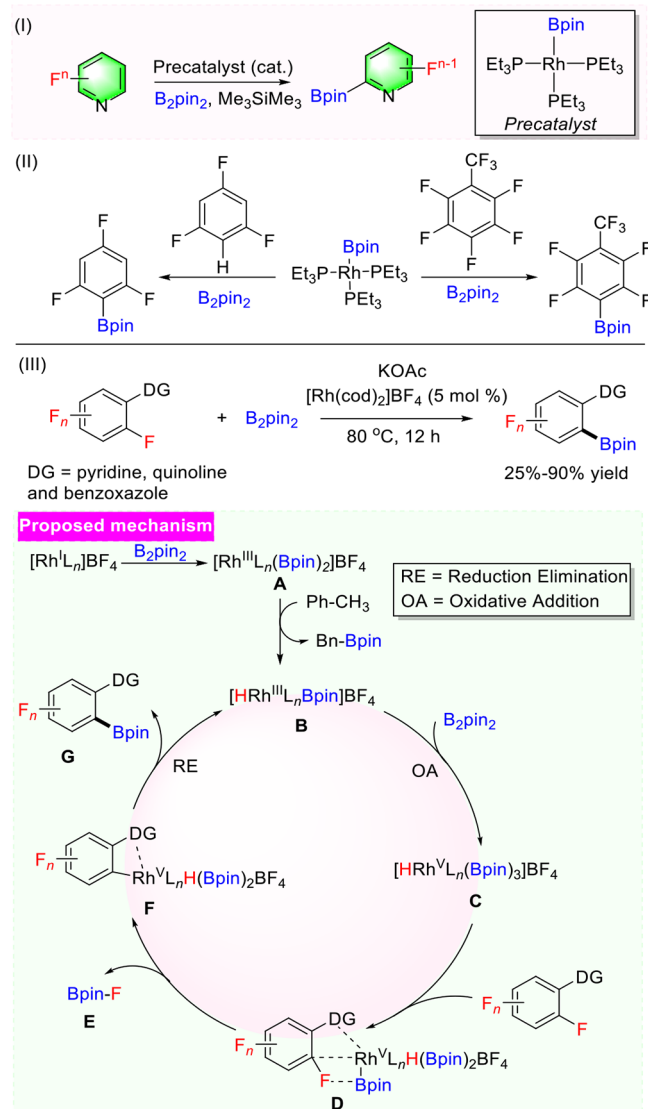
limited to the pyridine ring. In 2015, the same group developed a C−F bond activation by employing a rhodium-(I)−boryl complex to generate 2-Bpin-1,3,5-$C_6F_3H_2$, 2-Bpin-1,3-$C_6F_2H_3$, and 4-Bpin-$C_6F_4CF_3$ from 1,3,5-trifluorobenzene, 1,3-difluorobenzene, or perfluorotoluene (Scheme 2(II)).[36] Substrate scope was extended to common aromatic rings, and a C−H bond activation product could also be yielded in this reaction. In the same year, a rhodium-catalyzed *ortho*-selective monodefluoroborylation of N-heterocycle-substituted polyfluoroarenes was disclosed by Zhang's group (Scheme 2(III)).[37] This transformation is compatible with a wide range of substrates and provides a flexible method to prepare photoelectronic borylated fluoroarenes. In addition, preliminary mechanistic studies revealed the involvement of a Rh(III/

substrates, (3) selective fluorination of organoboron compounds, and (4) borylfluorination of olefins/alkynes. This review summarizes the elegant and intriguing progress on the synthesis of fluorine-containing organoboron compounds in recent decades from the synthetic point of view and then puts forward an outlook on the research direction of the fluoroboron chemistry.

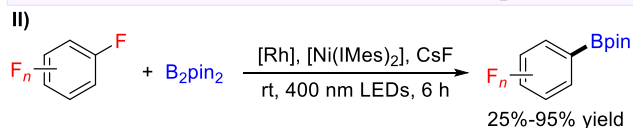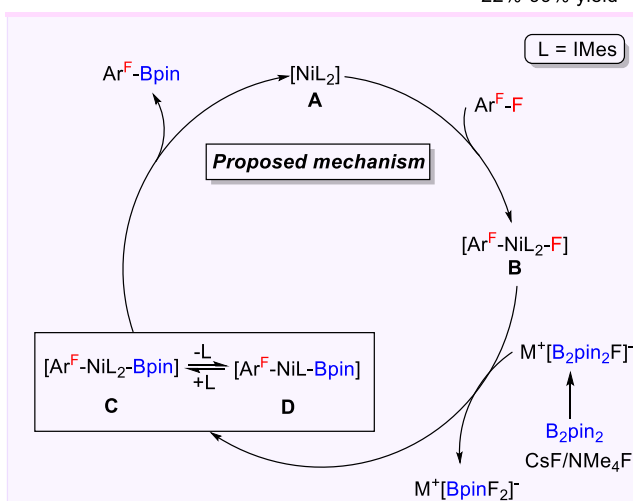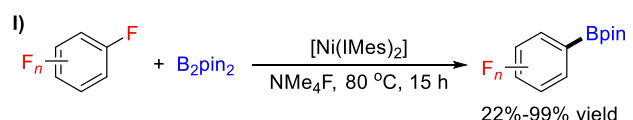## 2. SELECTIVE MONODEFLUOROBORYLATION OF POLYFLUOROARENES AND POLYFLUOROALKENES

The substrates for selective monodefluoroborylation of polyfluoroarenes and polyfluoroalkenes mainly include polyfluoroarenes, *gem*-difluoroalkenes, and α/β-trifluoromethyl alkenes and other polyfluoro compounds.

2.1. Transition-Metal-Catalyzed Monodefluoroborylation of Polyfluoroarenes

Polyfluoroarenes are important building blocks for the construction of useful organofluorine compounds.[15,16] Highly fluorinated arenes such as hexafluorobenzene often act as electrophiles to undergo aromatic nucleophilic substitution (S_NAr reaction) with many nucleophiles because the aromatic ring becomes strongly electron-poor by the inductive effect of the electron-withdrawing fluorine atoms.[17] In addition, they also undergo C−F bond activation to form various bonds in the presence of transition metals. The transition-metal-catalyzed monodefluoroborylation of polyfluoroarenes is an efficient approach to assemble boron-containing (di-/tri-

V) catalytic process (Scheme 2(III)). First, $[Rh^I L_n]BF_4$ undergoes oxidative addition with B_2pin_2, generating a trivalent rhodium boryl complex **A**, which then reacts with toluene to form a Rh−H species **B**. Oxidative addition of **B** with another molecule of B_2pin_2 results in a pentavalent rhodium−boron species **C**. Subsequently, a boryl-assisted transition state **D** is involved in the process, which facilitates the generation of fluoroarylrhodium complex **F** along with the release of F-Bpin species **E**. Finally, with reductive elimination of **F**, the final product **G** is formed and the catalyst **B** is regenerated simultaneously. Compared to the above-mentioned meaningful works by Braun, Zhang's work presents a broader substrate scope.

Subsequently, a Ni-catalyzed defluoroborylation of monofluoroarenes was reported Hosoya's group[38] and Martin's group[39] in 2015. One year later, an efficient N-heterocyclic carbene (NHC)−nickel-catalyzed selective monodefluoroborylation of polyfluoroarenes was disclosed by Radius and co-workers,[40] as well (Scheme 3(I)). Various partially fluorinated arenes were converted into their corresponding boronate esters in this strategy. The reaction mechanism is proposed in

Scheme 3. Ni-Catalyzed Selective Monodefluoroborylation of Polyfluoroarenes
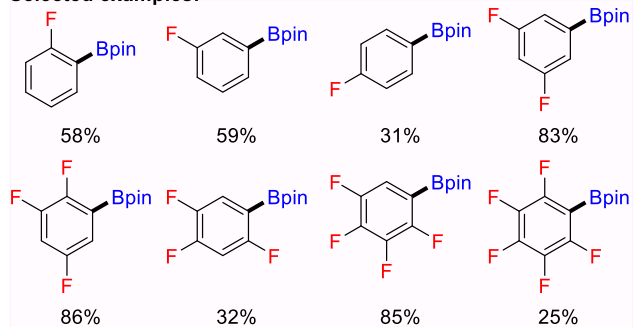
Scheme 3(I): $[Ni(IMes)_2]$ **A** and the fluoroarene undergo an oxidative addition of the C−F bond to form trans-$[Ni(IMes)_2(F)(Ar^F)]$ **B**. Subsequently, the complex **B** reacts with $[NMe_4]$-$[B_2pin_2F]$ through boryl transfer to provide trans-$[Ni(IMes)_2(Bpin)(Ar^F)]$ **C** and $[NMe_4]^+[F_2Bpin]^-$. A final reductive elimination step (e.g., after ligand elimination from a three coordinate species as indicated in Scheme 3(I) or after cis/trans isomerization of the boryl complex) provides the borylated fluoroaromatic Ar^F-Bpin and regenerates $[Ni(IMes)_2]$ **A** to complete the catalytic cycle.

In 2018, Marder and co-workers[41] reported a highly selective and general photocatalytic C−F borylation strategy that employs a rhodium biphenyl complex as a triplet sensitizer and a nickel catalyst for the C−F bond activation, leading to a defluoroborylation process. Various polyfluoroarenes are converted into corresponding borylation products in moderate to good yields (Scheme 3(II)). Mechanistic studies revealed that the exceptionally long-lived triplet excited state of the Rh−biphenyl complex as the photosensitizer allows for efficient triplet energy transfer to trans-$[NiF(ArF)(IMes)_2]$, which leads to the dissociation of one of the NHC ligands.[41]
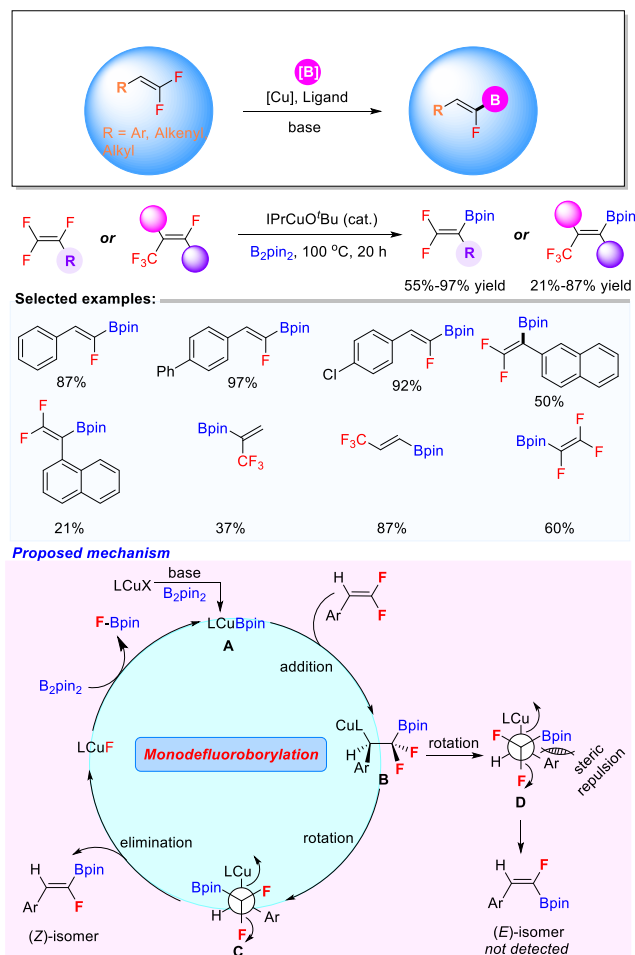
2.2. Transition-Metal-Catalyzed Monodefluoroborylation of Polyfluoroalkenes

For the assembly of fluorinated boron-containing compounds, selective monodefluoroborylation of gem-difluoroalkenes is an efficient and general approach. Cu-catalyzed regio- and stereoselective monodefluoroborylations of gem-difluoroalkenes with diboron reagents were achieved by Cao,[42] Ogoshi,[43] Wang,[44] Ito,[45,46] and others[47] (Scheme 4, top), rendering various α-fluoroalkenyl borates. More specifically, in 2017, Ogoshi and co-workers developed a practical synthetic method for borylated fluoroalkenes via copper-catalyzed monodefluoroborylation of polyfluoroalkenes.[43] This approach has been successfully applied to a wide range of substrates, such as (difluorovinyl)arenes, tetrafluoroethylene (TFE), (trifluorovinyl)arenes, and trifluoromethylated monofluoroalkenes (Scheme 4, middle). In addition, this strategy might facilitate the development of valuable functional molecules in various fields such as drug discovery and materials science.

The proposed mechanism for this selective monodefluoroborylation of gem-difluoroalkenes is described in Scheme 4 (bottom).[43] gem-Difluoroalkene first reacts with a catalytically active species CuL-Bpin **A**, which is formed in situ in the presence of base, ligand, and B_2pin_2, affording alkylcopper(I) species **B** via 1,2-addition. Rotation of the C−C single bond in alkylcopper(I) species **B** by ±60° results in the formation of two conformational isomers, **C** or **D**. The β-fluorine elimination of the conformational isomer **C** provides the specific (Z)-fluorinated alkenylborate and LCuF. Finally, LCuF reacts with B_2pin_2 and NaO^tBu to regenerate the active catalyst LCu-Bpin **A** to complete the catalytic cycle. On the other hand, the conformational isomer **D** is relatively unstable due to the steric repulsion of bulky Bpin and aromatics; therefore, the (E)-fluorinated alkenyl borate is not detected.

For selective monodefluoroborylation of α/β-trifluoromethyl alkenes, Hoveyda, Zhou, Shi, Ito, and Cao et al. have disclosed many elegant and intriguing works.[50−57] Specifically, in 2011, Hoveyda's group[50] discovered an example of the defluoroboration of α-trifluoromethylstyrene when they worked on the NHC-Cu-catalyzed hydroboration of 1,1-disubstituted aryl alkenes, leading to the gem-difluoroallylboronates in modest yields (Scheme 5a). In 2017, an FeCl₂-

Scheme 4. Selective Monodefluoroborylation of *gem*-Difluoroalkenes (Top), Copper-Catalyzed Regioselective Monodefluoroborylation of Polyfluoroalkenes En Route to Diverse Fluoroalkenes (Middle), and Proposed Mechanism (Bottom)

Scheme 5. Selective Asymmetric Monodefluoroborylation of *β*-Trifluoromethyl and Difluoromethyl Alkenes as Well as Rhodium-Catalyzed Formation of 2-Fluoroalkyl-1,3,2-dioxaborolanes by Catalytic Functionalization of Hexafluoropropene

catalyzed borylation/*β*-fluorine elimination of *α*-trifluoromethyl alkenes was developed by Liu and co-workers,[51] in which a series of substrates, including aryl olefins, alkyl olefins, 1,1-disubstituted olefins, 1,2-disubstituted olefins, and 1,1,2-trisubstituted olefins, all gave good results (Scheme 5b). In 2019, a copper-catalyzed monodefluoroborylation of *α*-trifluoromethyl alkenes was explored by Cao. The scope of substrates was further expanded to afford various boron-containing *gem*-difluoroalkenes in good to excellent yields under mild reaction conditions (Scheme 5c).[52,53] In addition, selective monodefluoroborylation of *α*-trifluoromethyl allenes was reported by Ito in 2020,[54] which provided an elegant method for the synthesis of boryl-substituted *gem*-difluorodienes (Scheme 5d). It is worth noting that, in 2018, Shi[55] and Ito[56] independently reported a copper-catalyzed enantioselective defluoroborylation of *α*-trifluoromethyl alkyl alkenes, leading to a series of enantioenriched *gem*-difluoroallylboronates (Scheme 5e) using ferrocene chiral phosphines as ligands. Moreover, in the latter one's work, trisubstituted alkyl olefins was compatible, whereas aryl olefins were all incompatible. In 2019, the Hoveyda group[57] used chiral NHC-Cu as a catalyst to achieve the asymmetric monodefluoroborylation of *β*-trifluoromethyl alkenes (Scheme 5f). This transformation features broad substrate scope, mild

reaction conditions, as well as high reaction efficiency. Based on the above-mentioned work, Ito and Hoveyda cooperated to develop an elegant protocol for the diastereo- and enantioselective assembly of allylic boronates bearing monofluoroolefin in good yields with excellent *Z/E* selectivity and enantiomeric ratio (Scheme 5g).[58]

The common reaction mechanism of monodefluoroborylation is summarized in Scheme 5h. The active Cu-Bpin complex **B** is generated from copper species **A** and B_2pin_2 via transmetalation under basic conditions. Subsequent addition of complex **B** to fluorine-containing alkenes leads to species **C** or **C′**; further *cis*-*β*-F elimination of **C** or **C′** delivers the final product **D** and **D′** along with CuL(F) **E**, which can undergo anion exchange with base to regenerate the active copper catalyst **A**. In addition, the product **D** may further be transmetallized with **A** to yield species **F** and its tautomer **G**,

which leads to the formation of protonated products **H** and **I**, respectively (Scheme 5h). The occurrence of these side reactions is particularly evident in the cases of aryl olefins bearing electron-withdrawing groups.

In addition, there is a unique and smart approach to access fluorinated organoboron building blocks by C−F activation reactions. The majority of the reactions which are known to consist of hydrodefluorinations, although examples of C−F bond functionalization, in which the fluorine atom is replaced by a new group to provide higher-value fluorinated compounds, are very limited. For fluorinated olefins, such a transformation that involves a stoichiometric or even a catalytic cleavage of an olefinic C−F bond is very rarely reported. In 2009, Braun's group developed a unique catalytic process for the conversion of hexafluoropropene and 1,3,2-dioxaborolane into Bpin derivatives of trifluoropropane (Scheme 6). This

**Scheme 6. C−F Activation at Rhodium−Boryl Complexes**
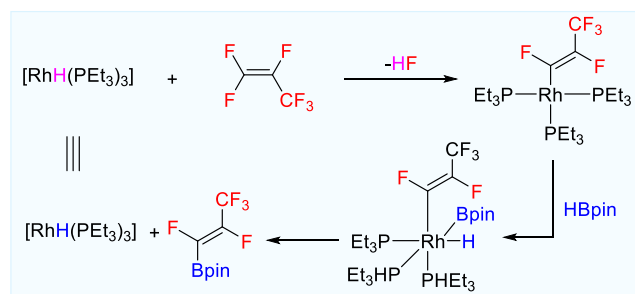
transformation proceeds at room temperature in quantitative NMR yields. The mechanistic studies indicated the involvement of a rhodium(I)−boryl species in most of the C−F bond activation steps. The resting state of the catalysts assumed the following composition of rhodium(III) complex *fac*-[Rh-(H)$_2$(Bpin)(PEt$_3$)$_3$]$_3$ by reductive elimination of HBpin.[59]

2.3. Radical-Promoted Monodefluoroborylation

Recently, reactions involving boryl radicals as important intermediates have been found to proceed through well-defined mechanisms, enabling pertinent molecular transformations.[60,61] Especially, NHC-boryl radicals have been widely investigated and were proven to be a class of powerful reactive species that allows various significant synthesis[62] and catalysis.[63] Originating from the robustness of the C−F bond and the lack of an efficient catalytic system, direct C−F bond borylation of polyfluoroarenes that generate fluorinated organoboron compounds remains challenging. However, some examples on the construction of fluorinated organoboron compounds via radical-promoted monodefluoroborylation have been reported in recent years (Scheme 7).[64−69] For instance, Wu[64] and co-workers reported a photocatalytic defluoroborylation strategy by direct B−H activation of N-heterocyclic carbeneboranes, which facilitated by the synergistic merger of a photoredox catalyst and a hydrogen atom transfer catalyst. This transformation features mild reaction conditions, high atom economy, and simple operation (Scheme 7a). Similarly, Yang's group also reported an elegant photoinduced single-electron transfer (SET) process for direct B−H bond activation to access fluorinated organoboron compounds (Scheme 7b).[65] This new method makes full use of the advantage of photoredox catalysis to provide the boryl radical via direct activation of a B−H bond. Good functional group tolerance and high regioselectivity offer this work

Scheme 7. Radical-Promoted Selective Monodefluoroborylation of Polyfluoroarenes
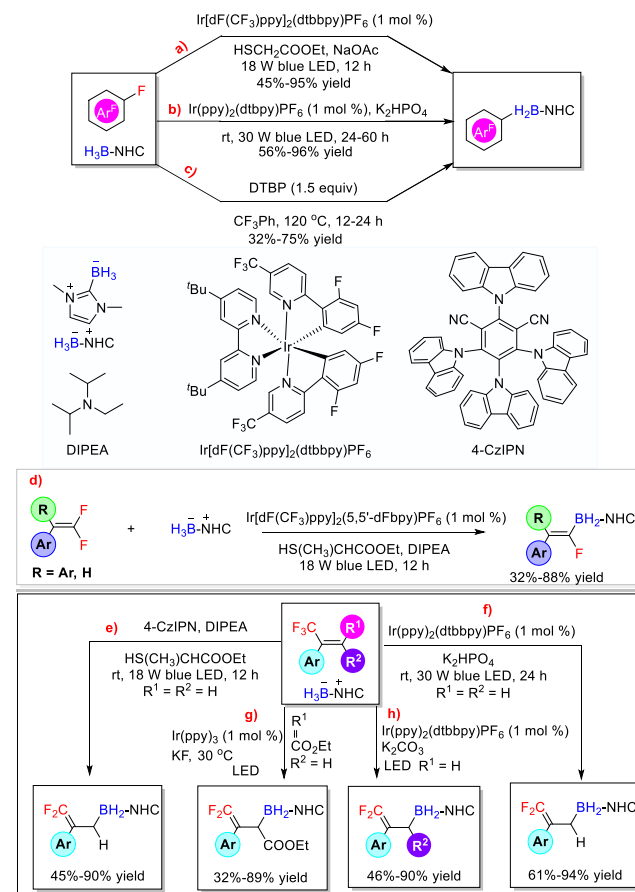
incomparable advantages in deriving a family of valuable polyfluoroarylboron compounds. Subsequently, in 2020, Taniguchi[66] and co-workers disclosed a radical-promoted selective monodefluoroborylation of polyfluoroarenes with the NHC-BH$_3$ in the presence of di-*tert*-butylperoxide (DTBP) (Scheme 7c). In this work, the C−F bond of polyfluoroarenes is substituted with an NHC-boryl group to provide β-aryl NHC-borane derivatives in the absence of transition metals. This developed synthetic strategy also was applied to the synthesis of novel borane-containing liquid-crystalline molecules that have highly thermal stability.[66]

In addition to radical-promoted monodefluoroborylation of polyfluoroarenes,[64−66] photocatalyst-mediated monodefluoroborylation of *gem*-difluoroalkenes and trifluoromethylalkenes is also reported as an alternative method. Wu and co-workers realized the defluorination of *gem*-difluoroalkenes and trifluoromethylalkenes (Scheme 7d,e).[64] At almost the same time, Yang and co-workers achieved the selective monodefluoroborylation of trifluoromethylalkenes when they studied the selective hydroboration of olefins under the efficient transformation conditions (Scheme 7f).[67] The above-mentioned two protocols feature broad substrate scope. Moreover, Wang's group has reported a monodefluoroborylation of trisubstituted trifluoromethylalkenes in the presence of visible light, resulting in fluorinated organoboron compounds with the boryl group at the α-position of the electron-withdrawing groups (Scheme 7g).[68] Mechanistic studies showed the oxidative formation of NHC-boryl radicals through a SET process in this reaction. In addition, this method is operationally simple and exhibits

broad substrate scope. In 2020, Liu and co-workers also disclosed similar conversion in the presence of visible light. Compared to Wang' work,[68] substrates with trisubstituted olefins and without the electron-assisted group assistance are compatible in Liu's reaction system (Scheme 7h).[69] This transformation features broad substrate scope, good functional group compatibility, as well as late-stage modifications of structurally complex compounds. Those photoredox catalytic modes of operation open up new avenues for the synthesis of densely functionalized organoborons.

## 3. SELECTIVE BORYLATION OF FLUORINATED SUBSTRATES

Selective borylation of fluorination substrates mainly includes the addition reaction of fluoroolefins, the C–H borylation of fluorinated arenes, the reactions of trifluorodiazoalkanes with organoborons, the ring-opening borylation of trifluoromethyl-conaining oxirane, the radical hydroboration of fluoroolefins, and other borylations of fluorinated substrates in this perspective.

3.1. Lewis-Acid-Induced or Transition-Metal-Catalyzed Boron Addition of Fluoroolefins

Commercially available halogenated boron and borane compounds (BX_3, HBX_2, H_2BX, H_3B) act not only as Lewis acid but also as a boron source in some reactions. Therefore, the construction of fluorinated organoboron compounds is popular using such reagents as the boron source. In 2001, Ramachandran[70] and co-workers reported a Markovnikov hydroboration of fluoroolefins using Lewis acid $HBCl_2$/$HBBr_2$ as the boron source for the construction of α-fluorinated alcohols via α-fluorinated boron-containing reaction inter-mediate generated in situ in this process (Scheme 8a). This hydroboration of substituted fluoroolefins presented a rare example of the formation of tertiary alcohols by stoichiometric hydroboration–oxidation. This transformation features ex-cellent regioselectivity. Moreover, it is presented that this regioselectivity does not entirely depend on the electronic effect of the fluoroolefins. The ligand-regulated rhodium-catalyzed regioselective hydroboration of fluoroolefins was also achieved by the same group,[71] in which both α- and β-fluorinated alcohols were obtained after oxidative treatment (Scheme 8b). This transformation also exhibited the controlling of the regioselectivity of the Markovnikov and anti-Markovnikov products via Rh-catalyzed hydroboration with catecholborane at low temperatures. Based on their previous work, they disclosed an asymmetric hydroboration of polyfluoroaryl olefins through the induction of chiral ligands for the preparation of fluorinated α-phenethanols[72] (Scheme 8c).

In 2017, a copper-catalyzed borylation of β-trifluoromethyl-α,β-unsaturated ketones with B_2pin_2 was developed by Yu's group.[73] The asymmetric studies were also achieved through the induction of chiral ligands, providing a series of chiral α-trifluoromethylated boronates in good yield with high enantioselectivities (Scheme 8d). However, substrates with large steric hindrance did not proceed smoothly under this reaction system. Subsequently, Zhang's group also reported a highly enantioselective Cu(II)-catalyzed borylation of β-trifluoromethyl β,β-disubstituted enones, providing a facile access to a broad of chiral alkylboronic esters with a quaternary stereocenter including both a trifluoromethyl group and a boron group.[74] Compared to the previous work, this process

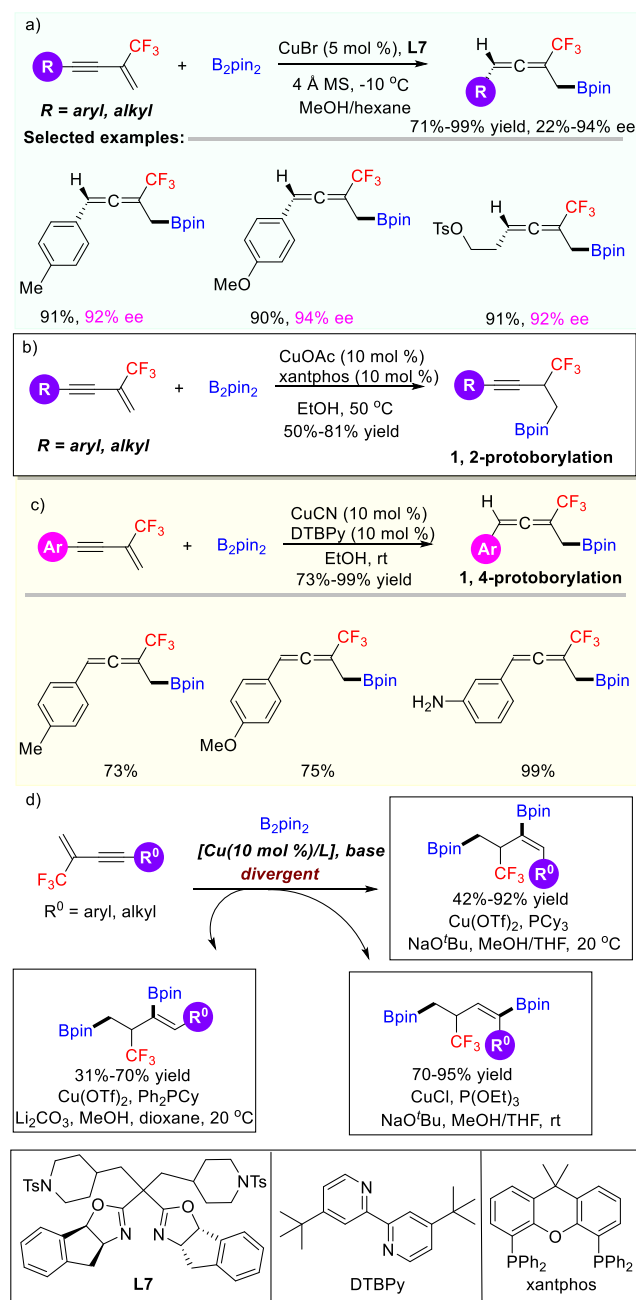## Scheme 8. Regioselective Hydroboration of Fluoroolefins
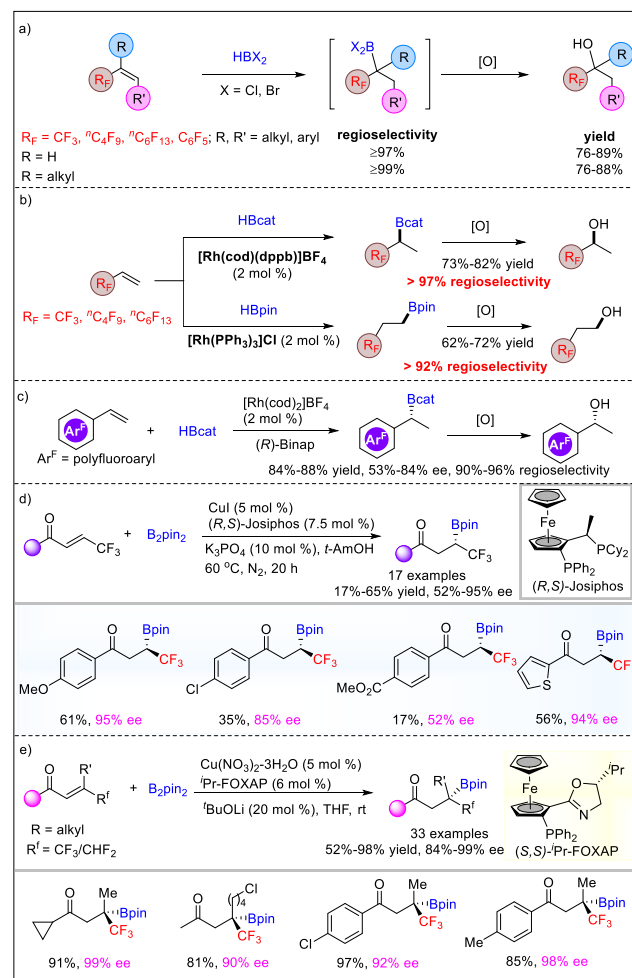
greatly broadened the substrate scope and improved the yields and enantiomeric excess (ee) values via carefully modifying the ligand (Scheme 8e). Meanwhile, CF_3-containing tertiary alcohol derivatives were obtained in high yield, with the ee value maintained via an one-pot methodology.

CF_3-containing 1,3-enynes are one type of simple and easily available synthetic blocks, and the borylation of 1,3-enynes has been explored well (Scheme 9). For example, Xu and co-workers[75] have developed the asymmetric protoborylation of 2-trifluoromethyl 1,3-enynes, giving chiral CF_3-containing homoallenylboronates in good yields with excellent regiose-lectivity and stereoselectivity (Scheme 9a). This work also provides a general approach to construct optically active homoallenylsilanes and homoallenylboronates in moderate to excellent yields with high enantiomeric excess using novel designed chiral bisoxazoline ligands. Meanwhile, the trans-formations of homoallenylsilanes and homoallenylboronates were also studied to synthesize valuable building blocks. Moreover, a ligand-controlled copper-catalyzed 1,2- or 1,4-protoborylation of 2-trifluoromethyl-1,3-enynes were realized by Cao[76] (Scheme 9b,c), in which the borylation of unsaturated C–C bonds (allenes and alkynes) was achieved. Moreover, this transformation features broad substrate scope and simple operations.

Differing from the common monoborylation of 1,3-enynes,[75,76] our group[77] has realized a Cu-catalyzed regio- and stereodivergent chemoselective diboration of CF_3-

Scheme 9. Copper-Catalyzed Borylation of CF$_3$-Containing 1,3-Enynes

3.2. C−H Borylation of Fluorinated Arenes

Recently, some protocols on C−H borylation of fluorinated arenes,[78] which are found widely in pharmaceuticals, agrochemicals, and organic materials arenes, have been reported (Scheme 10). Specifically, Tobisu and Chatani[79] utilized

Scheme 10. ortho-C−H Borylation of Arenes with Fluorine-Containing Compounds as Directing Groups
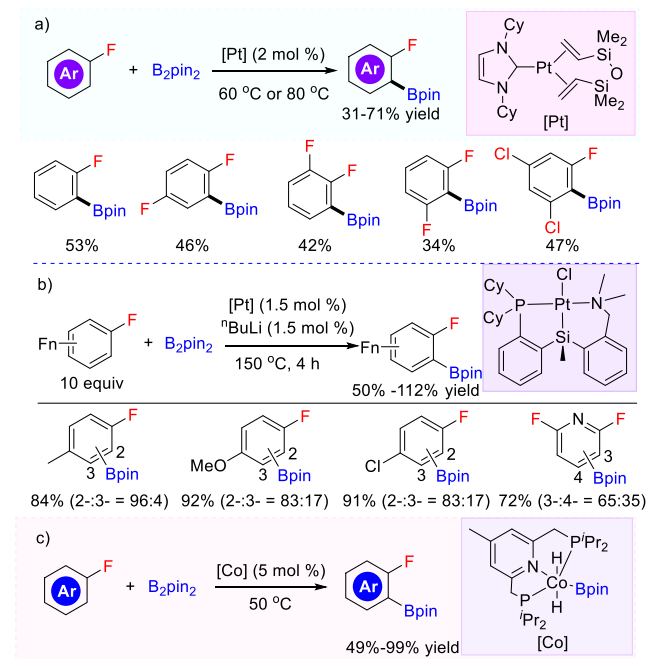
fluorinated arenes as substrates to achieve the ortho-C−H borylation of arenes and heteroarenes, giving fluorinated arylboronates in good to excellent yields in the presence of platinum (Scheme 10a). Notably, this strategy showcases good tolerance toward steric hindrance and provides rapid access to a series of polydisubstituted phenylboronic esters, valuable building blocks for further elaborations. Moreover, in 2015, Iwasawa's group realized the ortho-C−H borylation of fluorobenzene catalyzed by a PSiN−pincer platinum complex but failed to suppress meta-borylation (Scheme 10b).[80] This protocol clearly discloses the promising utility of the new PSiN−platinum catalyst in C−H borylation for the first time, which complements the well-developed Ir and Rh catalysis in reactivity and regioselectivity. In 2017, a cobalt-catalyzed ortho-C−H borylation of fluorinated arenes was developed by Chirik[81] (Scheme 10c), which suppressed meta-borylation very well. Moreover, Cui[82] developed a cobalt-catalyzed C−H borylation of fluorobenzene, although the regioselectivity could not be well-controlled and meta-borylation became the dominant path instead.

3.3. Reactions of Trifluorodiazoalkanes with Organoborons

The reaction between trifluorodiazoalkanes and organoborons is another approach to prepare fluorinated organoboron compounds. Molander's group[83] successively disclosed a metal-free-catalyzed route to α-trifluoromethylated alkylboron compounds and vicinal bis(trifluoromethylated) alkylboron compounds in 2013 (Scheme 11(i)). This strategy greatly enriches the reaction types and simplifies the synthesis of α-trifluoromethylated alkylboron compounds. Moreover, this is
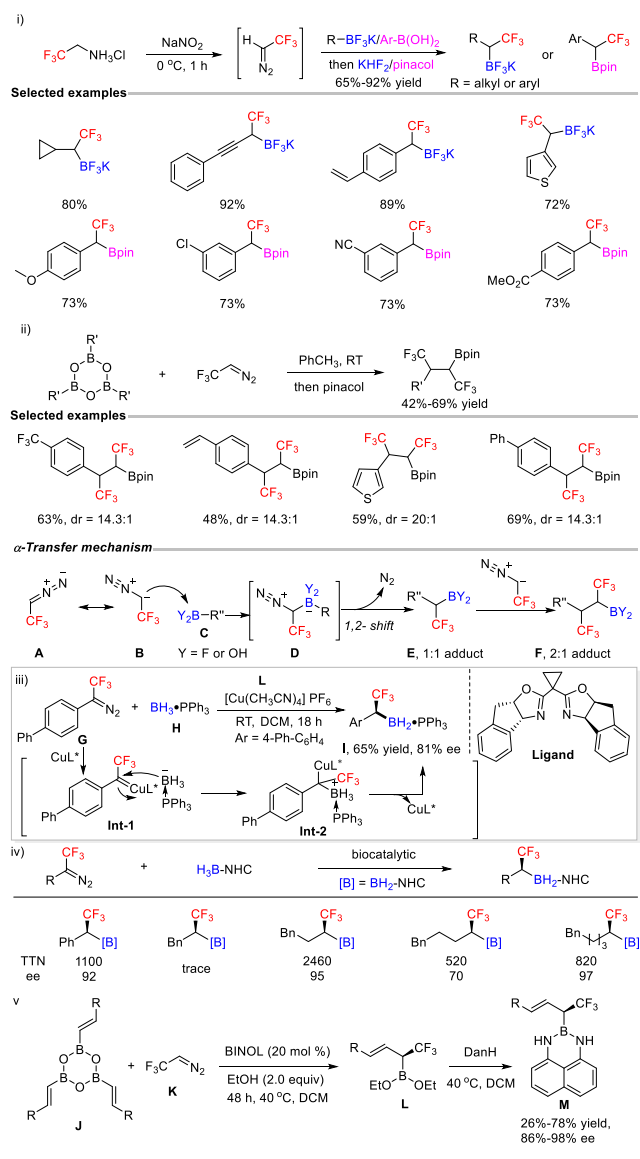
containing 1,3-enynes, giving a series of (E)-1,3-, (Z)-1,3-, and (Z)-1,4-diborylated olefins with the CF$_3$ group intact (Scheme 9d). The regulation of different bases afforded Z/E stereoselectivity for 1,3-diborylated olefins, and different P ligands determined the 1,3- and 1,4-regioselectivity. Mechanistic studies suggested that the CF$_3$ group on the alkene moiety plays a key role for the success of these transformations. In addition, homopropargylic boronates as important intermediates for (Z)-1,3- and (Z)-1,4-diborylated olefins and homoallenyl boronates for (E)-1,3-diborylated olefins were readily obtained by fine-tuning the reaction condition. The retention of CF$_3$ group might benefit from the rapid 1,3-copper migration of copper propargyl intermediate which is generated in situ by first Cu-Bpin addition to an alkene moiety via experimental and theoretical calculations (DFT calculation).[77]

Scheme 11. Reactions of 2,2,2-Trifluorodiazoethane with Organoboron Compounds and Proposed Mechanism

i)

Selected examples

80% 92% 89% 72%

73% 73% 73% 73%

ii)

42%–69% yield

Selected examples

63%, dr = 14.3:1 48%, dr = 14.3:1 59%, dr = 20:1 69%, dr = 14.3:1

α-Transfer mechanism

A B C D E, 1:1 adduct F, 2:1 adduct

Y = F or OH 1,2- shift

iii)

G H I, 65% yield, 81% ee Ligand

Int-1 Int-2

iv)

biocatalytic

[B] = BH₂-NHC

TTN 1100 trace 2460 520 820
ee 92 95 70 97

v)

J K L M
26%–78% yield, 86%–98% ee

the first time such compounds were prepared in the absence of transition metals. In the next year, the same group disclosed the construction of vicinal bis(trifluoromethylated) alkylboron compounds using a similar strategy, although only cyclic arylboroxines can promote successive insertions of 2,2,2-trifluorodiazoethane (Scheme 11(ii)).[84] From a perspective of yields, the second insertion is significantly more difficult than the first one.

A proposed mechanism is shown in Scheme 11(ii). 2,2,2-Trifluorodiazoethane **A** is generated in situ from 2,2,2-trifluoroethylamine and sodium nitrite, which gives its resonance structure **B**. The extremely electron-deficient organoboron compound **C** is attacked by **B**, resulting in an intermediate **D**. 1,2-Metalate shift of **D** leads to the product **E** (1:1 adduct) along with the release of nitrogen gas. The insertion of 2,2,2-trifluorodiazoethane (**A**) into product **E** will further give the product **F** (2:1 adduct).

Moreover, transition-metal-catalyzed and biocatalytic reactions yielding fluorine-containing organoboron compounds have been reported recently. For example, a copper-catalyzed

insertion of 2,2,2-trifluorodiazoalkanes into B−H bonds has been reported by Gouverneur[85] and co-workers (Scheme 11(iii)), which rendered the α-trifluoromethylated boranes in moderate yields. Asymmetric insertion reactions of diazoesters were also furnished with BOX ligands in this reaction system. This transformation enables the synthesis of a large collection of novel and useful chiral CF₃-substituted molecules. However, the asymmetric reaction for this compound was not isolated in excellent enantioselectivity (81% ee, Scheme 11(iii)). Differing from the reaction mechanism in Molander's work, the deliverables of the copper−carbenoid **Int-1** originating from the substrates **G**, **H**, and Cu catalysis might be formed. Then, the attack of the boron complex to the carbenic carbon atom gives **Int-2**, from which the target product **I** was afforded along with CuL* (Scheme 11 (iii)).[86] Alternatively, Arnold's group[87,88] reported the assembly of chiral α-trifluoromethylated organoborons, an important class of organofluorine molecules that contains stereocenters and bears both CF₃ and boron groups, via a biocatalytic insertion into B−H bonds of H₃B-NHC with 2,2,2-trifluorodiazoalkanes (Scheme 11 (iv)).[88] The Fe element in the enzyme could form the Fe−carbene intermediate with the trifluoro-containing diazo compounds and NHC-BH₃ in this reaction system. Computational modeling suggests that the enzyme can provide stereo/enantioselectivity, thereby making diazo compounds with diverse structural features proceed in this transformation. This biocatalytic platform for construction of chiral α-CF₃ organoborons expanded the scope of carbene intermediates generated from heme proteins and provided new mechanistic insights into enzymatic carbene transfer reactions.[88]
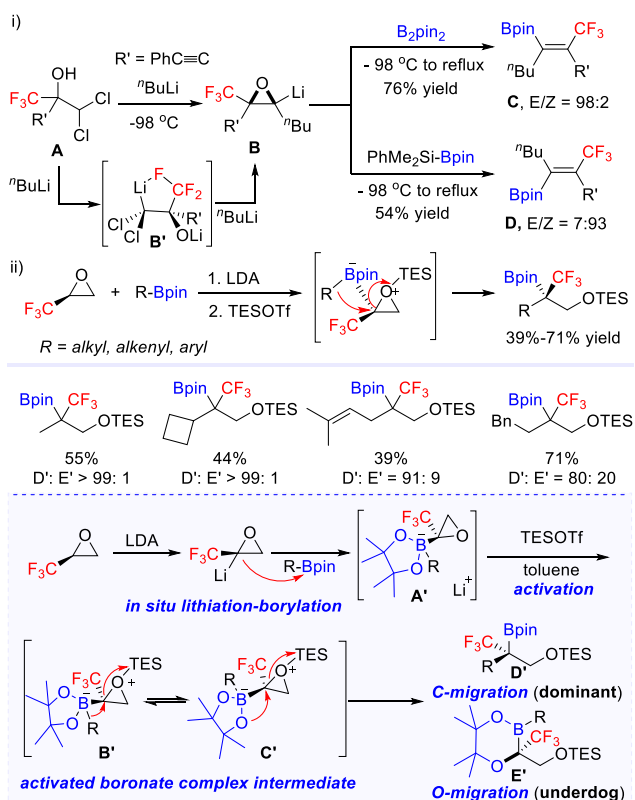
Chiral allylboronic acids are ideal reagents for asymmetric synthesis due to their high reactivity in self-catalyzed allylboration reactions.[25] However, the construction of those compounds has been an unmet challenge in organic synthesis. Recently, Szabó and co-workers developed a novel approach to afford chiral α-substituted CF₃-containing allylboronic acids by asymmetric homologation of alkenylboronic acids with CF₃-diazomethanes in the presence of BINOL catalyst and ethanol (Scheme 11(v)).[89] This process is realized using alkenylboroxine **J** and trifluoromethyl diazomethane **K** as reagents in the presence of a catalytic amounts of BINOL and stoichiometric amounts of EtOH to generate intermediate **L**. Subsequently, intermediate **L** reacted with DanH to from the target products **M** in moderate to good yields with high ee value. In this reaction, the enantioenriched α-CF₃ allylboronic acids obtained readily undergo in situ allylboration with aldehydes or can be converted to the corresponding allylic alcohols with high levels of chirality transfer. In addition, the purified chiral fluorinated boronic esters and diaminonaphthylboronamides are very reactive and highly stereoselective reagents in the allylation of ketones, imines, and indoles.

3.4. Ring-Opening Borylation of Trifluoromethyl Oxirane

In 2001, Shimizu's[90] group developed a novel and stereoselective route for the synthesis of CF₃-containing tetrasubstituted alkenylborates[91] by dechlorination of *gem*-dichloroalkanes in the presence of "BuLi and using B₂pin₂ or (dimethyphenysilyl)(pinacolato)borane (PhMe₂SiBpin) as the organoboron reagent (Scheme 12(i)). At first, intermediate **B** was generated from complex **B′**, which was derived from the transformation of dichloroalkane **A** and "BuLi. Subsequently, the **B** reacted with an organoborane (B₂pin₂ or PhMe₂SiBpin) stereospecifically to give CF₃-containing tetrasubstituted

Scheme 12. (i) Dechlorination−Carboboration of *gem*-Dichloroalkanes and (ii) Ring-Opening Lithiation−Borylation of 2-Trifluoromethyl Oxirane

Scheme 13. (a,b) Regioselective Radical Hydroboration of *gem*-Difluoroalkenes and (c) Regioselective Radical Hydroboration of Trifluoromethylalkenes


alkene **C** (E/Z = 98:2) or **D** (E/Z = 3:97) in moderate yields. The selectivity in the formation of **C** is determined during the elimination of one of the diastereotopic Bpin groups of the *gem*-diboron intermediate, whereas the selectivity in the formation of product **D** is due to the stereospecific reaction of diastereomerically enriched **B** to form a *gem*-silylboronate intermediate. Consequently, the stereoselectivity of this reaction is controlled well. Moreover, Aggarwal[92,93] and co-workers reported an elegant and intriguing route to versatile tertiary α-trifluoromethylated boronates in modest yields via a ring-opening lithiation−borylation of 2-trifluoromethyl oxirane in 2020 (Scheme 12(ii)).[92] For the reaction mechanism, first, lithiation−borylation of 2-trifluoromethyl oxirane with an organoboronic ester in the presence of LDA (lithium diisopropylamide) leads to a boronate complex **A′**, which is activated by TESOTf (triethylsilyl trifluoromethanesulfonate) to yield the boronate species **B′** or **C′** and then undergoes a 1,2-shift to render **D′** or **E′** via C-migration or O-migration, respectively.

3.5. Radical Hydroboration of Fluoroolefins

In addition to boron-radical-promoted monodefluoroborylation of polyfluoroarenes that provides fluorinated boron-containing compounds, the addition of a boron radical to fluoroolefins is an alternative and good approach. A regioselective radical hydroboration of *gem*-difluoroalkenes was successfully achieved to construct α-difluoroalkyl borons by Wang and Zhang's group[94] in 2019 (Scheme 13a), which can undergo hydrofluoro elimination under the activation of KO*t*Bu, leading to α-fluoroalkenyl borons (Scheme 13a). The transformation features broad substrate scope, excellent
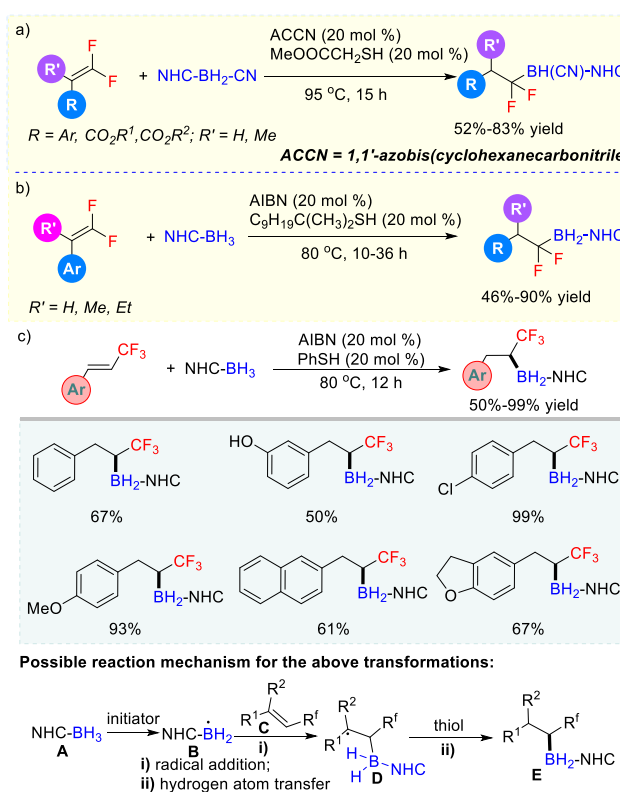
regioselectivity, and good functional group capability. Mechanistic investigation suggests that the α-selectivity was derived from the kinetically and thermodynamically more favorable α-addition step by DFT calculations.[94] Additionally, Wang and Liu's group[95] also reported a transformation with aryl *gem*-difluoroalkenes using AIBN (2,2′-azobis(2-methylpropionitrile)) as the radical initiator (Scheme 13b). This reaction features operational simplicity, high atom economy, and good functional group tolerance, enabling an efficient assembly of a wide range of α-difluorinated alkylborons and alkylsilanes in moderate to good yields under mild reaction conditions.

Moreover, in 2019, a regioselective radical hydroboration of various electron-deficient CF₃-containing alkenes was described by Wang's group by employing an NHC-boryl radical (Scheme 13c).[96] This transformation proceeds with exclusive α-regioselectivity, affording a broad range of α-borylated trifluoromethyl molecules in moderate to excellent yields from readily available starting materials. The above-mentioned three methods (Scheme 13a−c) are green and simple and without carbonyl positioning and metal involvement[97] to give rise to addition of boron radical. For the possible reaction mechanism, first, the boron radical **B** is generated from NHC-BH₃ (**A**) and an initiator (ACCN or AIBN), then radical addition occurs between fluoroolefins (**C**) and boron radical **B** to give intermediate radical **D**. Finally, the target product **E** is yielded via hydrogen atom transfer with thioalcohol (Scheme 13, bottom).

3.6. Other Borylations of Fluorinated Substrates

In addition to the above-mentioned strategies, a common and classic method for the construction of fluorinated organoboron compounds is the nucleophilic substitution reaction. For

example, Ramachandran[98−102] and Zhang[103] et al. reported a nucleophilic substitution reaction between fluorinated alkenyl lithium II (which was in situ generated from fluorinated alkene I and "BuLi) and halogenated alkylborates (III), leading to a series of *gem*-difluoroallylboronates IV in moderate yields (Scheme 14a).[98−102] The nucleophilic substitution of fluorinated alkenyl and aryl metal reagents with borates via transmetalation was also studied, which afforded the fluoro-

substituted alkenyl and aryl boronates or boron acid[104−107] (Scheme 14b,c).
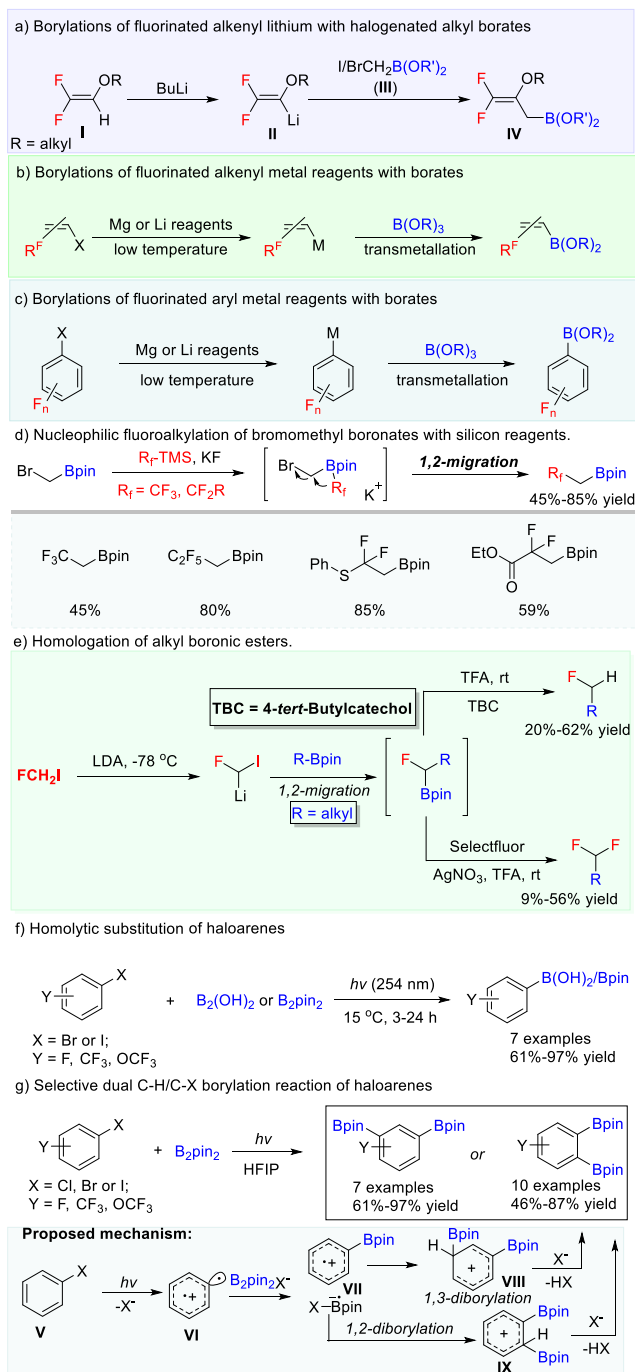
In 2013, Dilman and co-workers[108] disclosed a reaction in which the bromomethyl boronates reacted with fluorine-containing silicon reagents to construct pinacol boronic esters bearing a fluorinated group at the α-carbon atom (R_fCH_2Bpin) by the formation of tetracoordinated boronate salts followed by a 1,2-metalate shift in the presence of KF (Scheme 14d). This strategy employed stable and readily available fluorinated silicon reagents to replace sensitive fluorinated metal reagents, and a broad range of fluorine-containing organoboron compounds were procured in moderate yields under mild reaction conditions.

Based on the previous work, Aggarwal's group[109] reported the homologation of alkyl boronic esters with fluoroiodo-methyl lithium generated in situ (Scheme 14e), which is a divergent, stereospecific reaction of fluoroiodomethyl lithium with boronic esters to give α-fluoroboronic esters. DFT calculations on a series of potential fluorinated carbenoids suggest that fluoroiodomethyl lithium was the optimal reagent for stereospecific homologation of boronic esters, which can be converted into CH_2F or CHF_2 groups. The strategy utilizes commercially available reagent and proceeds under mild reaction conditions with excellent stereocontrol.

Substitution reactions, such as homolytic substitution and aromatic nucleophilic substitution reaction (S_NAr), of fluorine-containing haloarenes with boron reagents are simple and common routes to prepare fluorinated organoboron compounds. In 2016, Larionov and co-workers developed a simple metal- and additive-free photoinduced borylation of haloarenes (Scheme 14f).[110] Reaction of haloarenes with tetrahydroxydiboron or B_2pin_2 processes in methanol/CH_3CN under ultraviolet irradiation ($\lambda = 254$ nm) produced phenylboronic acid in moderate to good yields after 3−24 h at 20 °C (Scheme 14f). Regrettably, the reaction mechanism was not confirmed in detail by experiments and other means. Next, the same group reported a similar photoinduced dual C−H/C−X borylation of chloro-, bromo-, and iodoarenes in the absence of transition metals.

The regioselectivity of the dual C−H/C−X borylation is determined by the solvent and the substituents in the parent haloarenes (Scheme 14g).[111] Compared to the previous work, a possible reaction mechanism was proposed (Scheme 14g). Photoinduced hemolysis is very efficient for haloarenes V in low and medium polarity solvents to form intermediate VI. The initial homolytic substitution at B_2pin_2 with the photo-generated aryl radical VI generated PhBpin radical. Then, the 1,3-diborylation or 1,2-diborylation process took place via the stabilization of the radical intermediate VIII or IX by conjugation with the boryl group.

Scheme 14. (a−c) Borylations of Fluorinated Alkenyl/Aryl Metal Reagents, (d) Nucleophilic Fluoroalkylation of Bromomethyl Boronates with Silicon Reagents, (e) Homologation of Alkyl Boronic Esters, (f) Homolytic Substitution of Haloarenes, and (g) Selective Dual C−H/C−B Borylation of Haloarenes

4. SELECTIVE FLUORINATION OF ORGANOBORON COMPOUNDS

Organoboron compounds, as a popular synthetic building block, have been widely explored by converting boryl moieties into fluorinated groups.[112−121] However, the use of a boryl moiety as a directing group to selectively introduce fluorinated functional groups into substrates is still underdeveloped. Selective fluorination of organoboron reagents to prepare the fluorinated organoboron compounds is a popular route for chemists. In 2016, the assembly of halorinated and trifluoromethylated α-boryl ketones via a one-pot oxidative difunctionalization of alkenyl MIDA boronates was disclosed

by Wang and co-workers (Scheme 15a,b).[122,123] This strategy combines the fluorine-containing groups, boryl group, and

### Scheme 15. Selective α-Fluorination and Trifluoromethylation of Alkenyl MIDA Boronates and Proposed Mechanism
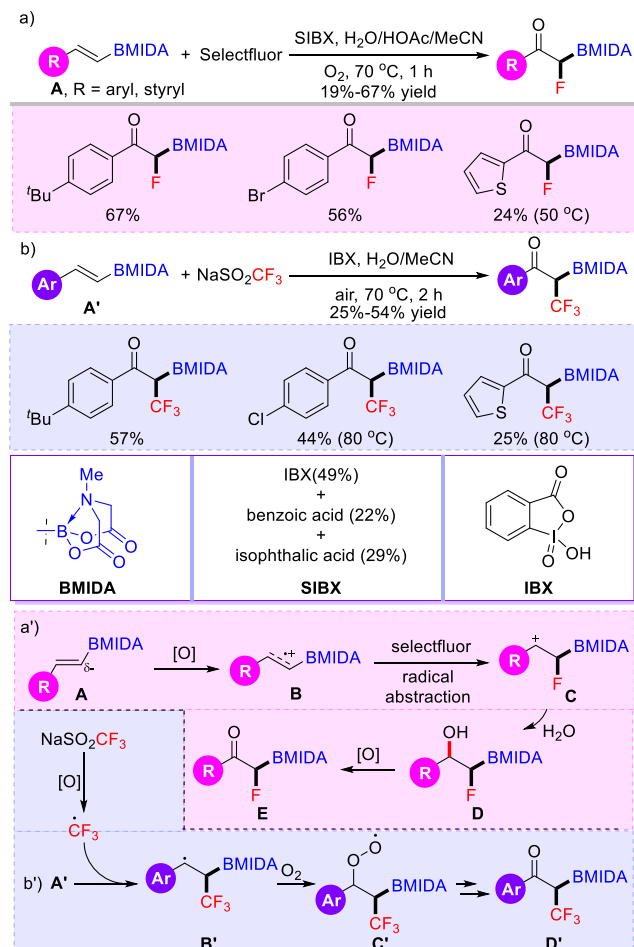
carbonyl group into the same one molecule, partially addressing the challenge of constructing densely functionalized organoborons. In addition, this approach can also achieve the selective 1,2-halohydroxidation of alkenyl *N*-methyliminodiacetyl (MIDA) boronates, such as iodination, bromination, and chlorination with corresponding halogenating reagents. The generality of this transformation was extensively investigated, and it is attractive due to readily accessible starting materials (Scheme 15a,b). The proposed mechanism of this transformation is depicted in Scheme 15. For α-monofluorinated α-boryl ketones (Scheme 15a′), alkenyl boronate **A** is oxidized to radical cation **B** by a single-electron transfer process, which can attract the fluorine atom from Selectfluor to carbon cation **C**. Carbon cation **C** is hydrolyzed to fluoroalcohol **D**, which is further oxidized to product **E**. For α-trifluoromethylated α-boryl ketones (Scheme 15b′), NaSO₂CF₃ is oxidized to •CF₃, which participates in the radical addition onto alkenyl boronate **A′**, resulting in benzyl radical **B′**. Radical **B′** is captured by O₂ to deliver the peroxy radical **C′**, which is further converted into the product **D′**.

In 2018, Wang's group developed an expedient strategy for the selective synthesis of α- and β-difluorinated alkylboronates via a migratory gem-difluorination of aryl-substituted alkenyl

N-methyliminodiacetyl (MIDA) boronates using commercially available Py·HF as the fluorine source and hypervalent iodine as the oxidant (Scheme 16A).[124] Various α- and β-

Scheme 16. gem-Difluorination of Alkenyl MIDA Boronates and Reaction Mechanism and an Iodofluorination of Alkynyl or Alkenyl MIDA Boronates
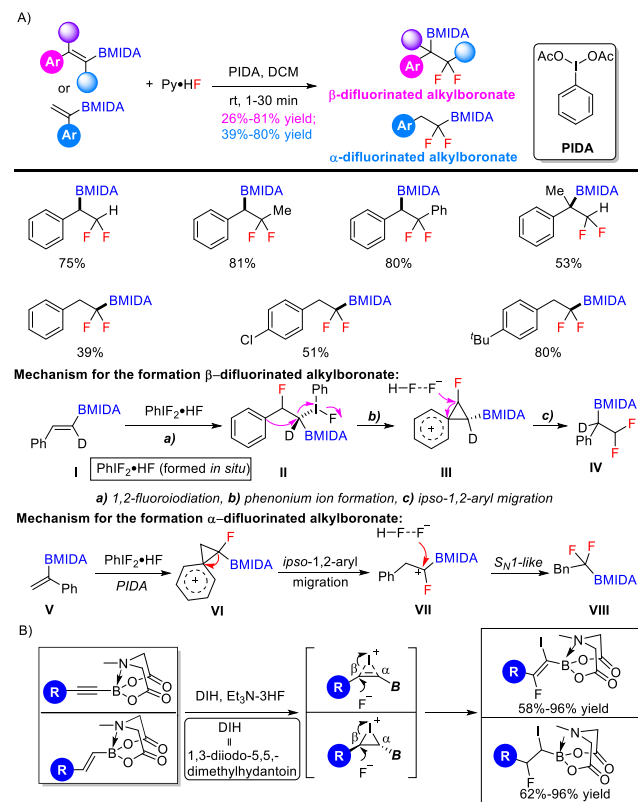
difluorinated alkylboronates were successfully prepared in moderate to good yields under mild reaction conditions within a short reaction time. Of note, these two types of fluorinated organoborons are very challenging to prepare, thus this strategy provides an efficient way to directly access the two valuable products.

The mechanism for the formation of both α- and β-difluorinated alkylboronates might involve the phenonium ion intermediate (Scheme 16A, middle and bottom). Initially, regioselective 1,2-iodofluorination of alkenyl MIDA boronate **I** with PhIF₂·HF generated in situ from PIDA and Py·HF yields the intermediate **II**. Subsequently, the intramolecular nucleophilic attack of the benzene ring results in the C–I bond cleavage to afford phenonium ion species **III**. The selective reattack of the fluoride anion leads to the ring opening of **III**, which is accompanied by the 1,2-aryl migration and finally affords β-difluorinated alkylboronates **IV** (Scheme 16A, middle). Similarly, the gem-difluorination of 1,1-disubstituted alkenyl MIDA boronate also undergoes ring opening of phenonium ion species **VI**, resulting in 1,2-aryl migration and the formation of carbocation species **VII**. Based on the stabilizing effects of boron and fluorine, fluoride reattacks the carbocation species **VII**, eventually leading to α-difluorinated alkylboronates **VIII** (Scheme 16a, bottom).

In 2020, a regioselective 1,2-iodofluorination of alkynyl and alkenyl MIDA boronates was developed by Wang and co-workers, delivering the fluorinated organoborons in good to

excellent yields (Scheme 16B).[125] Alkynyl or alkenyl MIDA boronate reacts with an electrophilic iodo source DIH (1,3-diiodo-5,5-dimethylhydantoin), giving the relatively stable three-membered halonium cation intermediates. Greater carbocation character at the β-position is expected due to the hemilabile nature of the MIDA B−N dative bond making the boron atom an electron acceptor to some extent, leading to a regioselective fluoride substitution. Also, the bulky nature of the B(MIDA) moiety may dictate the nucleophilic attack at the β-position. Therefore, the F anion selectively attacks the β-position, resulting in a nucleophilic S_N2 ring opening on the opposite side of the iodine (Scheme 16B). In addition, this strategy was amenable to gram-scale synthesis, as evidenced by the excellent yield obtained when multiple millimoles of the alkynyl or alkenyl substrates were employed in the system.

In addition to the above strategies mentioned, fluorinations/perfluoroalkylations of boronate complexes via 1,2-migration generating fluorinated organoboron compounds are intriguing and alternative methods. In 2017, Studer and co-workers developed radical polar crossover reactions of vinylboron ate complexes, in which radical anions underwent radical polar crossover: a 1,2-alkyl/aryl shift from boron to the α-carbon sp^2 center provided fluorine-containing secondary or tertiary alkyl boronic esters.[111] The intermediate **B** was formed in situ first via the reaction between boronic ester **A** and R^2Li at low temperature. Next, alcohol **C** was obtained by sequential radical addition and oxidation (Scheme 17(I)). Similarly, Aggarwal's group reported that vinyl boronates react with electron-deficient alkyl iodides in the presence of visible light to give fluorine-containing boronic esters in moderate yields (Scheme 17(II)).[115] For the reaction mechanism, the reaction proceeds via radical anion intermediate **E′** originating from addition of R radical to **E**, which undergoes single-electron oxidation to zwitterionic species **E″**, triggering a 1,2-metalate rearrangement to generate the target product **F** (Scheme 16(II)). In 2017, the same group utilized Selectfluor as fluorine source to obtain β-fluoroboronic esters in moderate to good yields and high diastereoselectivity (Scheme 17(III)).[116] The diastereoselectivity of the reaction is strongly dependent upon the nature of the electrophiles. Moreover, Morken and co-workers disclosed a Ni-catalyzed enantioselective conjunctive coupling with C(sp^3) electrophiles, which has only one example for fluorinated organoboron compounds. The vinylboron ate complexes **G** reacted with IC$_4$F$_9$ (**H**) to obtain the fluorinated alkyl halides **I** in 56% yield along with 50:50 er value (Scheme 17(IV)).[117] Using the same strategies, Renaud's group reported an alkyl (fluorine-containing) radical addition to alkenylboronates that spontaneously undergoes a [1,2]-metalate shift to achieve fluoroalkylations of boronate complexes (Scheme 17(V)).[118]

Cyclobutanes are very popular structural motifs that are finding increasing applications in medicinal chemistry due to their diverse bioactivities. Aggarwal and co-workers reported that electrophilic radicals stemmed from alkyl iodides under visible light irradiation added to the central strained bond of bicyclobutyl (BCB)−boronate complexes and provided 1,3-alkyl-disubstituted cyclobutyl boronic esters in good yields and with full stereospecificity and excellent stereoselectivity (Scheme 17(VI)).[119] There are a limited number of ring-contraction strategies which transform readily available five-membered rings into strained four-membered rings. Recently, the same group developed a photoinduced radical-mediated ring contraction of five-membered-ring alkenyl boronate

Scheme 17. Fluorinations/Perfluoroalkylations of Boronate Complexes
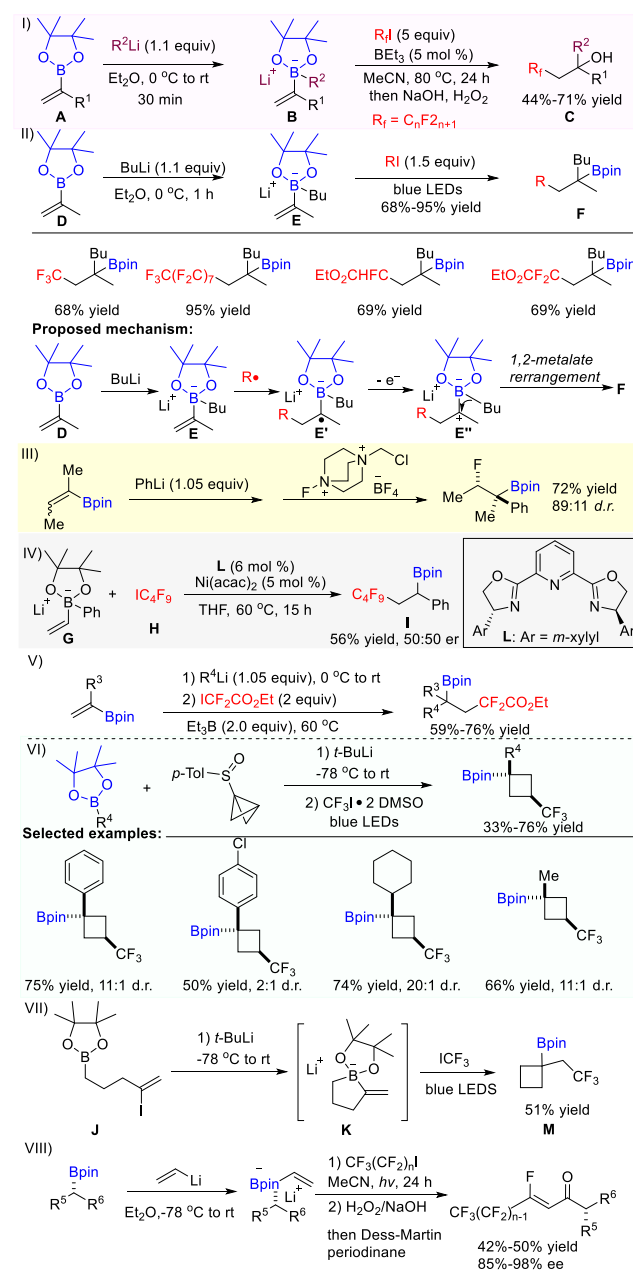
complexes into cyclobutanes. The transformation involved the addition of an electrophilic radical to the electron-rich alkenyl boronate complex, resulting in an α-boryl radical. Upon one-electron oxidation, ring-contractive 1,2-metalate rearrangement occurs to provide a cyclobutyl boronic ester (Scheme 17(VII)).[120]

In the above-mentioned methods for the construction of fluorine-containing organoboron compounds, the vinylboron compounds were always used as reactants. Of note, Studer and co-workers reported an interesting protocol with which vinyl boron ate complexes were generated in situ, derived from enantioenriched boronic esters and vinyllithium. Various fluorinated α-chiral ketones were constructed with high ee value in this transformation (Scheme 17(VIII)).[121]

5. BOROFLUORINATION OF ALKYNES/OLEFINS

Polyfunctionalization of unsaturated bonds is an important and practical means of constructing valuable molecules. Naturally, borofluorination of alkynes or olefins can effectively construct fluorinated organoboron compounds. However, in-depth research is highly desirable in this field. In 2018, a palladium-catalyzed *trans*-fluoroalkylation−borylation of alkynes was developed to fabricate fluoroalkylated alkenylboronates by Zhu's group[126] (Scheme 18(I)0). This transformation

Scheme 18. Palladium-Catalyzed Difluoroalkylation−Borylation of Alkynes and Proposed Mechanism
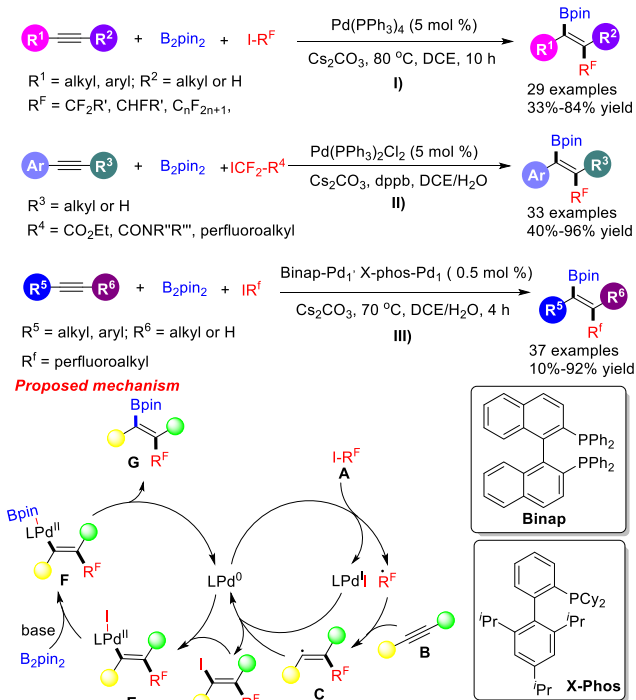

is effective for both internal and terminal alkynes and provides a straightforward and streamlined access to functionalized 1,2-fluoroalkylboronated alkenes in a highly regio- and stereo-controlled manner. Subsequently, Zhang and co-workers[127] reported a similar palladium-catalyzed *trans*-fluoroalkylation−borylation of alkynes with fluoroalkyl iodides and B₂pin₂ (Scheme 18(II)). This reaction tolerates a range of difluoroalkyl iodides and perfluoroalkyl iodides and enable coupling with a variety of alkynes, including internal and terminal alkynes, with high efficiency, high functional group compatibility, and high regio- and stereoselectivities. Moreover, Chaładaj' group[128] disclosed a resembled Pd-catalyzed three-component tandem *trans*-fluoroalkylation−borylation of terminal and internal alkynes (Scheme 18(III)), in which a regio- and stereoselective process is easily controlled by a temperature program. The various fluoroalkyl-substituted vinyl iodides, vinyl boronates, or olefins are obtained from the very same complex reaction mixture. The three elegant transformations greatly complement the synthetic methods of fluoroalkylated alkenylboronates which play an important role in modern organic synthesis.

The reaction mechanisms of the above-mentioned three transformations are described in the Scheme 18 (bottom).[126−128] Initially, the fluoroalkyl radical ●RF is initiated

by a Pd⁰L along with LPdᴵI species. Subsequently, the radical addition of ●RF and alkynes **B** affords vinyl radical **C**, providing a *trans*-fluoroalkylated alkenyl iodide **D** and the regeneration of Pd⁰. The oxidative addition of Pd⁰ to **D** provides the key intermediate palladium(II) species **E**, which undergoes transmetalation and reductive elimination to yield the fluoroalkylated alkenylboronates **G** and Pd⁰ to complete the second cycle (Scheme 18).

In 2018, a copper(I)-catalyzed borofluorination of alkynes was developed to deliver *cis*-(*β*-fluorovinyl) boronates by Sadighi's group[129] (Scheme 19(i)). The classic nucleophilic

Scheme 19. (i) Copper-Catalyzed Borofluorination of Alkynes and (ii) Dual-Catalysis-Promoted Boryldifluoroallylation of Alkynes
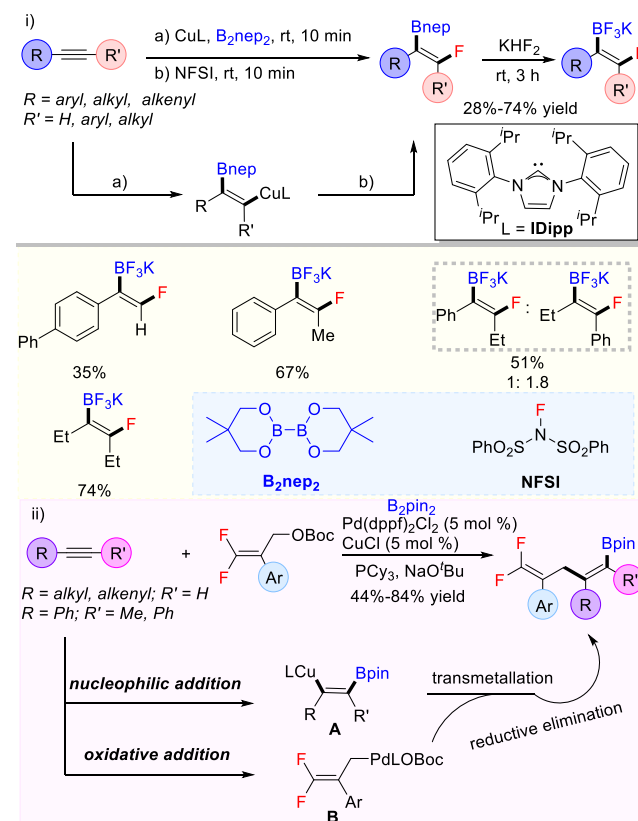
addition of alkynes with Cu-Bpin complex provides an alkenyl copper intermediate, which is captured by NFSI to furnish the *cis*-(*β*-fluorovinyl) boronates.

Moreover, in 2020, a dual-catalysis-promoted boryldifluoroallylation of alkynes was developed for the synthesis of boron-containing skipped *gem*-difluorodienes by Gong and Fu's group[130] with high regio- and stereoselectivity (Scheme 19(ii)). This transformation goes through nucleophilic addition of alkynes, leading to alkenyl copper species **A**. Meanwhile, the oxidative addition of palladium with nucleophiles leads to palladium species **B**. The transmetalation and elimination occur between **A** and **B** in succession, providing the final boryldifluoroallylation products.

Given the similarity of alkynes and alkenes, difunctionalizations of olefins have also been developed to construct fluorinated organoboron compounds. A copper-catalyzed regioselective borylfluoromethylation of alkenes was disclosed to afford valuable borylfluoromethylated alkanes in good yields

with excellent regioselectivity by Qing's group[131] (Scheme 20(I)). The mechanism is similar to that with alkynes, also via

Scheme 20. (I) Copper-Catalyzed Borylfluoromethylation of Alkenes and (II) Light-Induced Borofluoroalkylation of Unactivated Alkenes and Proposed Mechanism
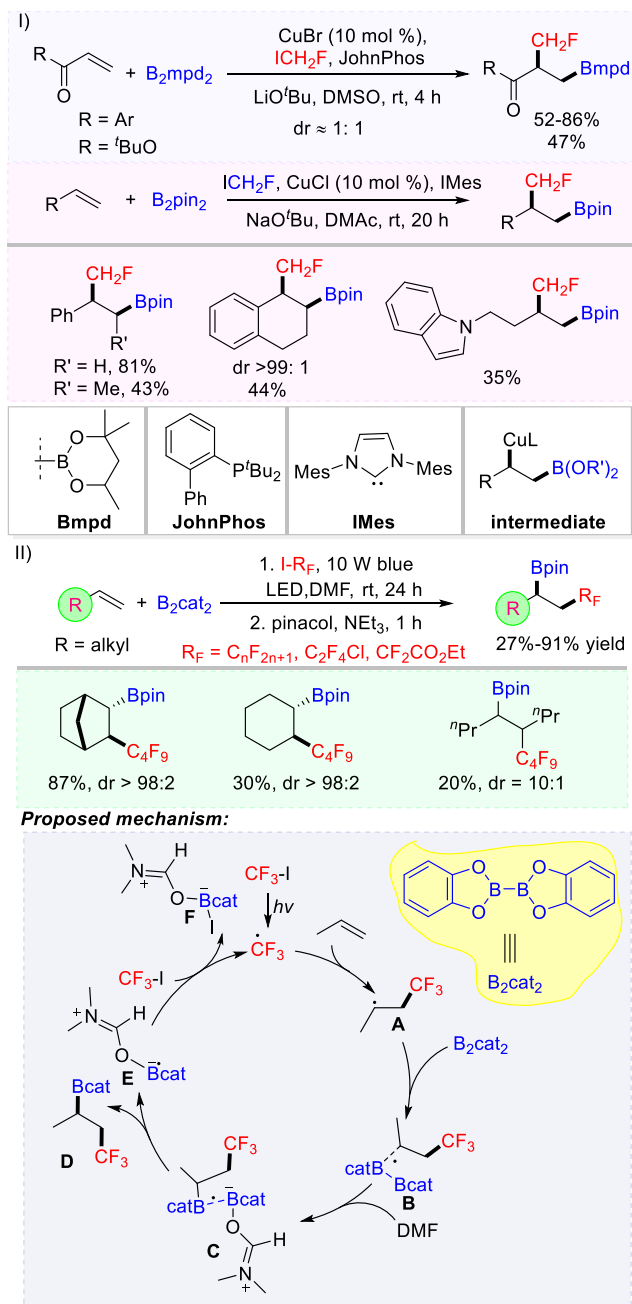
adducts of olefin−boryl−alkyl copper species. The synthetic application for this system is illustrated through the derivatization of organoboron products and preparation of monofluorinated ibuprofen. Based on the urgent requirements of green chemistry, Studer's group[132] reported a light-induced 1,2-borofluoroalkylation of unactivated olefins without transition metal in 2018 (Scheme 20(II)). This ground-breaking radical borylation transformation has greatly enriched the species and the synthetic methods of fluorinated organoboron compounds. Various borofluoroalkylation products were obtained in decent yields under the mild reaction conditions.

On the basis of control experiments and density functional theory calculations, the reaction mechanism for this transformation is proposed (Scheme 20 (bottom)). Initially, $\bullet CF_3$ is produced by the homolysis of the C−I bond in CF_3I under light induction, which adds to propene to give the secondary alkyl radical **A**. Subsequently, the alkyl radical **A** attacks the boron atom of B_2cat_2 to form an adduct **B**. Under the activation of DMF, **B** can be spontaneously converted into intermediate **C**. After cleavage of the B−B bond, borofluoroalkylated product **D** and DMF-complexed boryl radical **E** are provided. The single electron transfer between **E** and perfluoroalkyl iodide replenishes $\bullet CF_3$ and finishes the reaction cycle.

In addition, in 2020, Wang and co-workers designed a stable, cheap and highly active fluorinating reagent—IMDN-SO_2CF_3.[133] With these fluorinated reagents, photoinduced regio- and stereoselective 1,2-fluorocarboborylation of terminal alkynes and unactivated olefins was developed, which provided an alternative method for the synthesis of fluorine-containing organoboron compounds (Scheme 21(i)). Various fluorocarboborylation products were obtained in good yield with high regio- and stereoselectivity. Similarly, for the reactions of alkynes, the reactants and products are almost the same as those in the palladium-catalyzed reactions.[48,49]

As is well-known, allylboronates are widely used intermediates which contain both a boryl moiety and a carbon−carbon double bond.[134] Perfluoroalkyl radical-induced 1,2-boron shift of such compounds is a useful tool for the assembly of fluorinated boron-containing compounds. In 2019, Aggarwal and co-workers reported an example in which allylboronic ester undergoes photoinduced 1,2-boron shift with Langlois's reagent (CF_3-SO_2Na), leading to selective transformation of the more hindered fluorine-containing boronic esters (Scheme 21(ii)).[135] This transformation demonstrates, for the first time, a radical 1,2-boron shift under thermodynamic control. Subsequently, another perfluoroalkyl radical-induced 1,2-boron shift, enabling 1,2,3-trifunctionalization of allylboronates, was developed by Studer[136] and co-workers in 2020, which afforded synthetically valuable 1,2,3-trifunctionalized products with the trifluoromethyl group, boryl species, and the alkynyl (azidyl or alkyl) groups highly ordered assembly into one molecule (Scheme 21(iii)). The reaction starts with the radical addition of allylboronates with perfluoroalkyl radical to produce alkyl radical **A**. The intramolecular 1,2-boron shift then delivers a more stabilized alkyl radical **B**, which is captured by the radical receptor and eventually provides a 1,2,3-trifunctionalized products (Scheme 21(iii)).

Subsequently, the same group[137] developed a light-induced 1,3,4-trifunctionalization of homoallylmagnesium bromide via 1,4-boron migration, resulting in the fluorinated bisborylalkanes, as well as 1,4,5-trifunctionalization of corresponding substrates via 1,5-boron migration (Scheme 21(iv)). The corresponding products are obtained in modest to good yield under mild reaction conditions. The experimental results on the boron migration were supported by DFT calculations.

Very recently, Song[138] and co-workers reported a photoinduced weak base-catalyzed synthesis of fluorine-containing α-haloboronates (Scheme 21(v)). This strategy features mild conditions and good functional group compatibility. Moreover, a family of complex alkylboron compounds with fluorine groups, including α-aminoboron, gem-diboron, α-oxoboron, and α-thioboron compounds, were effectively prepared via further derivatization of the fluorine-containing iodoboronic

Scheme 21. (i) Integrated Redox-Active Reagents for Photoinduced Regio- and Stereoselective Fluorocarboborylation, (ii,iii) Perfluoroalkyl Radical-Induced 1,2,3-Trifunctionalization of Allylboronates, (iv) Fluorinated 1,*n*-Bisborylalkanes via Remote Radical Boron Migration, and (v) Photoinduced Weak Base-Catalyzed Synthesis of α-Haloboronates from Vinylboronates and Polyfluoroalkyl Halides
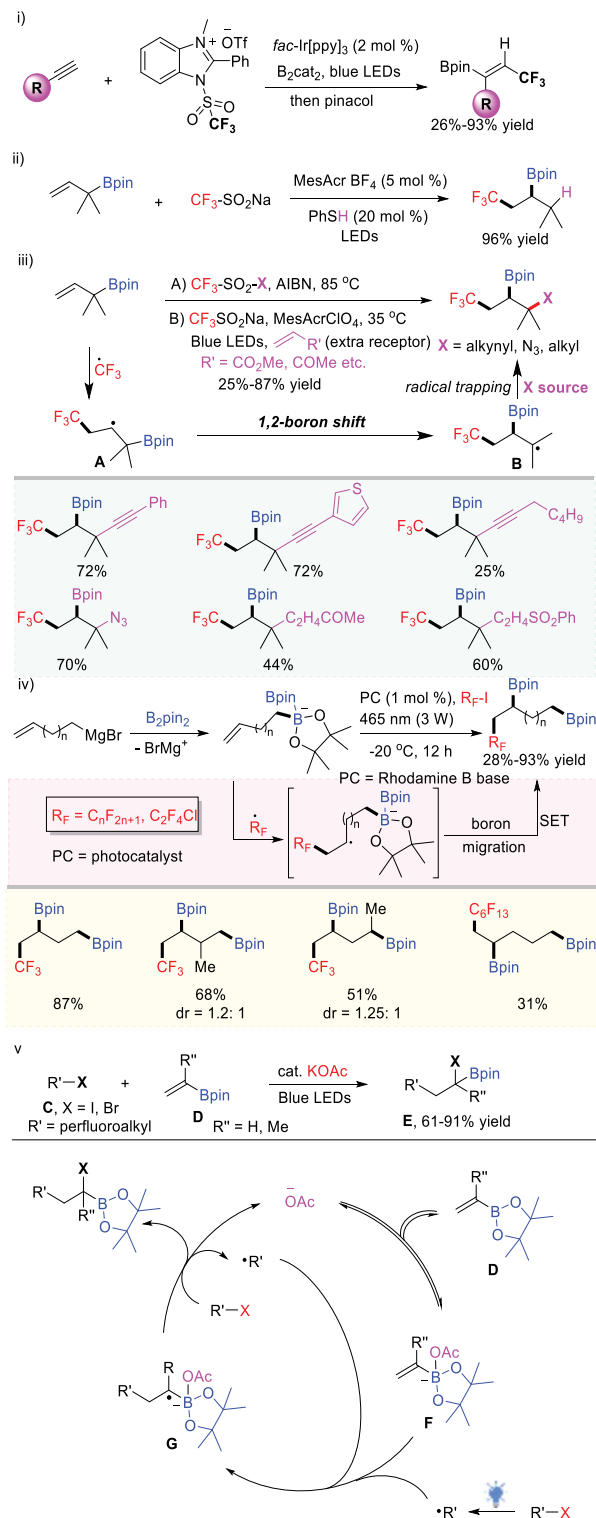
B species **F** in situ. Addition of radical to the C−C double bond of **F** occurs to afford a highly active α-sp³-boron radical **G**, which further reacts with the halogen atom of alkyl halide via SET reduction, followed by the release of an alkyl radical to produce fluorine-containing α-haloboronate. In addition, it is limited to R″ (R″ = H, Me) in substrate **D**.

6. SUMMARY AND OUTLOOK

Despite the predominant studies on the synthesis of organoboron compounds and organofluorine compounds, the combination of organoboron chemistry and organofluorine chemistry to access fluorine-containing organoboron compounds are relatively rare and have emerged as very attractive field. Fluorinated organoboron compounds are very valuable synthetic building blocks due to the unique properties of fluorinated groups and the versatile applications of boryl moieties. This review article will guide the research on fluorinated organoboron compounds in recent years mainly from four aspects: selective monodefluoroborylation of polyfluoroarenes and polyfluoroalkenes, selective borylation of fluorinated substrates, selective fluorination of organboron compounds, and borofluorination of alkynes/olefins. In addition, this review article will promote the fusion of organoboron chemistry and organofluorine chemistry to a certain extent.

However, most of the aforementioned strategies are transition-metal involved transformations, therefore, efficient and green methods without the aid of transition metals will be a welcome tactic in this field in the future. Meanwhile, the known strategies are mainly focused on the construction of fluorinated monoboronates, and it will be very fascinating if a more abundant molecular library of fluorinated multiple boronates could be built, which will greatly increase the feasibility for elaborations of those compounds as well as provide more opportunities for pharmaceutical candidates. Moreover, chemoselective cleavage of multiple C−F bonds to lead to C−B bonds is still a trouble-maker and will be an interesting point for this emerging field, in which either simultaneously cleaving multiple C−F bonds or selectively cleaving one of multiple C−F bonds will render polyborylated compounds.

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esters. For the reaction mechanism, a weak nucleophile could reversibly activate the B(sp²) of alkenyl boronate to form a sp³-

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Q.S., X.M., and Z.K. wrote and revised the paper and the reference format.

Notes

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