Chinese Chemical Letters 37 (2026) 111739

Contents lists available at ScienceDirect

Chinese Chemical Letters

journal homepage: www.elsevier.com/locate/cclet

Recent advanced in C–H borylation using BX_3 with different directing group auxiliary

Gaorong Wu[a], Tao Ma[b,*]

[a] Jiangxi Province Key Laboratory of Pharmacology of Traditional Chinese Medicine, School of Pharmacy, Gannan Medical University, Ganzhou 341000, China
[b] School of Chinese Materia Medica, Beijing University of Chinese Medicine, Liangxiang Campus, Beijing 102488, China

ARTICLE INFO

Article history:
Received 6 June 2025
Revised 4 August 2025
Accepted 17 August 2025
Available online 17 August 2025

Keywords:
Organoboron
C–H Borylation
BX_3
Directing group
Organic synthesis

ABSTRACT

Organoboron compounds have garnered significant attention in the fields of organic synthesis, materials science, medicinal chemistry and fine chemicals. In the past few decades, transition metal-catalyzed C–H borylation has been developed rapidly and efficiently. In recent years, in order to explore eco-friendly, economical and efficient method for constructing C–B bond, chemists are dedicated to developing metal-free BX_3-mediated borylation. In this review, we present a systematic and comprehensive overview of the borylation driven by BX_3 with different directing group auxiliary in the fields of organic synthesis and boron-containing organic materials since 2010, including (1) nitrogen directed C–H borylation, (2) oxygen directed C–H borylation, (3) sulfur directed C–H borylation and (4) phosphorus directed C–H borylation. The methods of borylation processes as well as the substance scopes, limits, and mechanisms of these routes are also discussed.

© 2025 Published by Elsevier B.V. on behalf of Chinese Chemical Society and Institute of Materia Medica, Chinese Academy of Medical Sciences.

1. Introduction

As a very important class of substances, organoboron compounds are widely used in organic synthesis, materials science, medicinal chemistry, fine chemicals, chemical sensing, and so on [1–4]. With the development of boron chemistry, more and more boron-containing drugs have been developed and benefited mankind, such as bortezomib, ixazomib, tavaborole, crisaborole and vaborbactam (Fig. 1) [5–9]. In addition, organoboron compounds, especially organoboronate esters, are indispensable synthetic reagents in the construction of carbon-carbon bond and carbon-heteroatom bond reactions due to their high stability, appropriate reactivity, low toxicity and easy processing [10,11].

In the past few decades, transition metal-catalyzed C–H borylation has been developed rapidly because of their unique selectivity and reactivity [12–15]. However, harsh reaction conditions, complex ligands, noble transition metals, especially the difficulty to remove toxic trace metals from pharmaceuticals limit the application of these methods. In sharp contrast, photoinduced borylation, electrocatalytic borylation, and metal-free borylation have therefore attracted considerable attention in recent years due to the mild, efficient and economical reaction conditions [16–18]. Recently, haloboranes (BX_3) have been attractive borylation agents in the field of metal-free C–H borylation, as they are commercially available in grams to kilograms and are cheaper than most common boron reagents [19]. In this review, we present a systematic and comprehensive overview of the literature on C–H borylation using BX_3 as boron source with different directing group auxiliary since 2010. The methods of borylation processes as well as the substance scopes, limits, and mechanisms of these routes are also discussed.

2. C–H borylation using BX_3 with different directing group auxiliary

2.1. Nitrogen directed C–H borylation

The pioneering work on N-directed electrophilic C–H borylation of arene was conducted by the Dewar's group. They synthesized a series of polycyclic aromatic hydrocarbons through N-directed C–H borylation using BCl_3 and $PhBCl_2$ with $AlCl_3$ as catalyst from 1958 [20–23]. However, these reactions usually need to be completed under forcing conditions. In 2009, Vedejs's group reported an important study on C–H borylation *via* $N{\rightarrow}BH_3$ intermediate using the trityl salt of the robust weakly coordinating anion $[B(C_6F_5)_4]^-$ to abstract hydride from *N*,*N*-dimethylbenzylamine borane [24]. However, this reaction still required high temperatures. After Vedejs' seminal work, N-directing groups, such as pyridine,

* Corresponding author.
E-mail address: 201701033@bucm.edu.cn (T. Ma).

https://doi.org/10.1016/j.cclet.2025.111739
1001-8417/© 2025 Published by Elsevier B.V. on behalf of Chinese Chemical Society and Institute of Materia Medica, Chinese Academy of Medical Sciences.

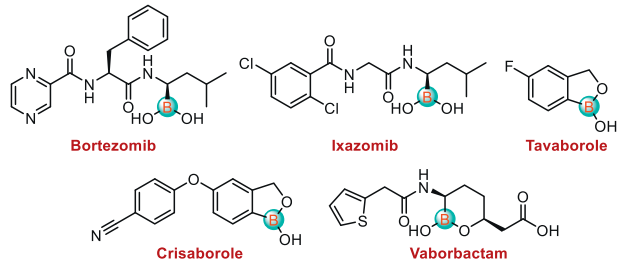
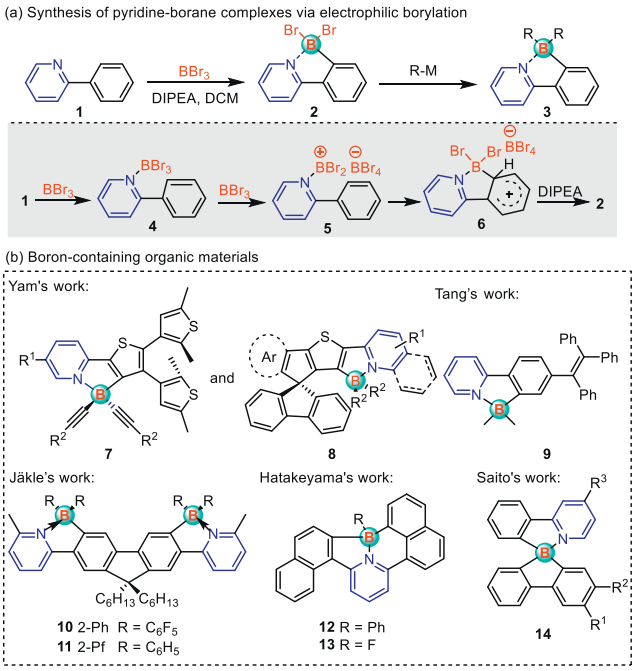


Fig. 1. Boron-containing drugs approved by the FDA.



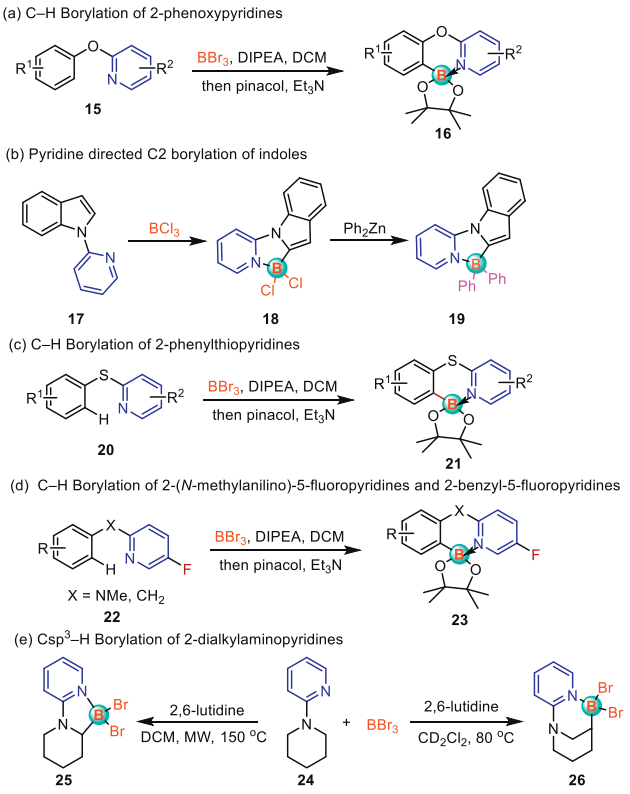
Scheme 1. Murakami's C–H borylation and its applications in organic materials.

pyrimidine, pyrazole, imidazole directed C–H borylation has been achieved using BX_3.

2.1.1. Pyridine directed C–H borylation

As a strongly coordinating group, pyridine is usually used as a directing group or ligand in C–H bond activation [25–27]. In 2010, Murakami's group reported the pioneering work on electrophilic aromatic borylation of 2-arylpyridines with BBr_3 to synthesize pyridine-borane complexes under metal-free conditions (Scheme 1a) [28]. This simple method was useful for the synthesis of aza-π-conjugated materials with boron-nitrogen coordination. The plausible reaction mechanism was presented as follows: the Lewis basic nitrogen atom in pyridine formed a coordination with the Lewis acidic boron center, thereby generating complex **4**. Another BBr_3 extracted bromide anion from complex **4** to deliver boron cations **5** [29]. Subsequently, the boron cation underwent an electrophilic attack on the adjacent aromatic group [30], and the following rearomatization process leaded to the formation of the pyridine-dibromoborane complex.

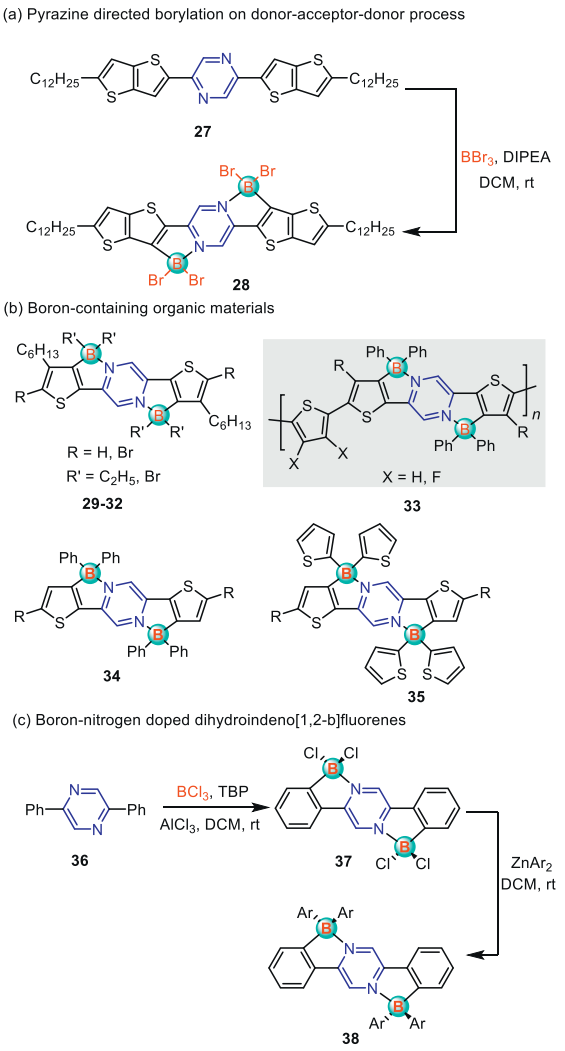
After that, many researches about BBr_3-mediated pyridine-directed borylation by similar method for preparing boron-containing organic materials had been reported (Scheme 1b). For example, Yam and co-workers designed and synthesized a series of diarylethene-containing N,C-chelate thienylpyridine-bis(alkynyl)borane complexes [31,32]. In 2013, Tang's team synthesized two novel N,C-chelate four-coordinate organoborons, which exhibited good thermal stability and could be used as efficient



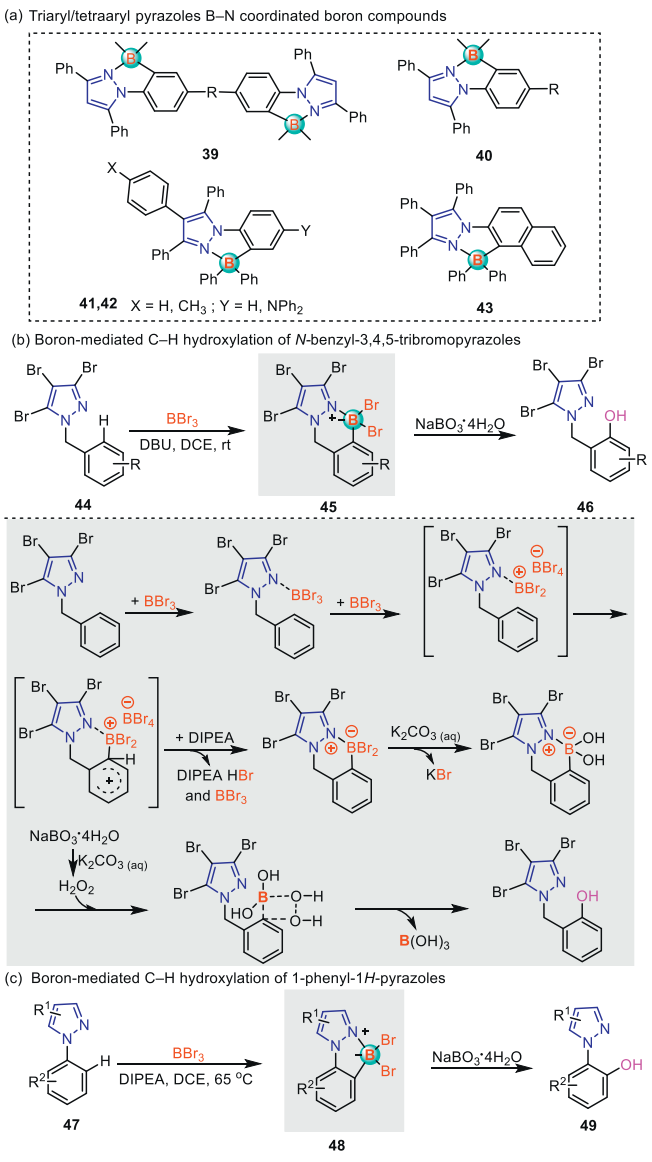
Scheme 2. Pyridine directed C–H borylation.

solid-state emitters [33]. In 2016, Jäkle's group obtained luminescent organoboron ladder compounds and Wang et al. generated a series of new N,C-chelate organoboron compounds with donor-functionalized aryl groups to investigate the effect of enhanced charge-transfer character [34,35]. In 2018, Hatakeyama and co-workers offered benzoaceanthrylene analogs with tetracoordinate boron at the ring junction through tandem electrophilic C–H borylation using BI_3 and the derivative was promised to be a viable n-type semiconducting material [36]. In 2022, Saito and co-workers obtained chiral aza-boraspirobifluorenes and evaluated their molecular structures as well as their photophysical properties, which provided important insights into the stereochemistry of chiral tetrahedral boranes [37]. Up to now, it is still an extremely hot topic to construct organic materials *via* Murakami's C–H borylation.

In the fields of organic synthesis, Murakami's C–H borylation has also been further developed and expanded. In 2012, Fu's group developed an efficient route to metal-free *ortho*-C–H borylation of 2-phenoxypyridines (Scheme 2a) [38]. The corresponding aryl boronates **16** were obtained in good yields and the pyridine group could be deprotected to offered 2-phenylphenol derivatives. However, the condition of removing the directing group was harsh (MeOTf/pyridine, then Na/MeOH). In 2021, Ingleson finished pyridine directed C2 borylation of indoles using BCl_3 (Scheme 2b) [39]. Subsequently, Ji's group reported a novel method for *ortho*-selective C–H borylation of 2-phenylthiopyridines using BBr_3 (Scheme 2c) [40]. The synthesized aryl boronates **21** were freely transformed into various useful products, which would be helpful to generate structurally diversified phenylthioethers. Then, they efficiently realized C–H borylation of 2-(*N*-methylanilino)-5-fluoropyridines and 2-benzyl-5-fluoropyridines (Scheme 2d) [41]. The corresponding compounds **23** contained both fluorine and boron elements, which could provide a practical tool for the discovery of new fluorine-containing compounds.



Scheme 3. Pyrazine directed C–H borylation.



Scheme 4. Pyrazole directed C–H borylation.

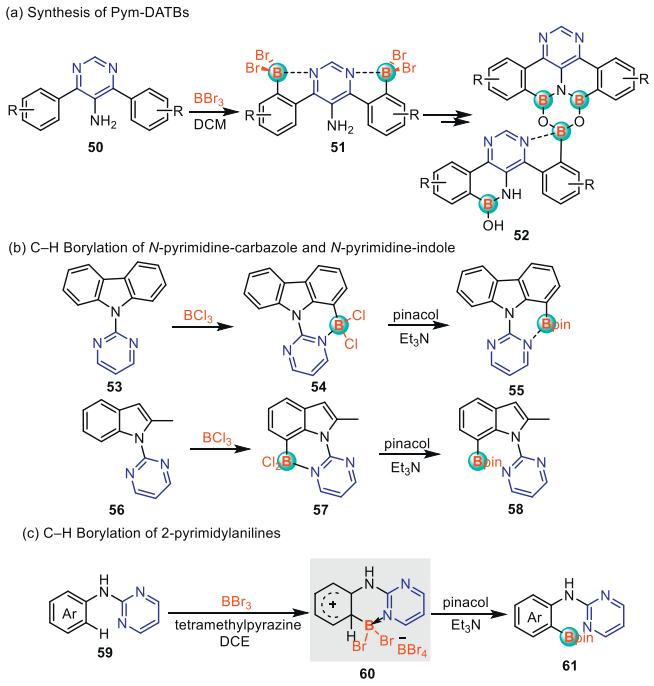
The catalytic borylation of Csp^3–H substrate presents unique challenges because of the sterically demanding geometry of Csp^3–H compared to planar Csp^2–H. In 2023, Fontaine's group developed site-selective Csp^3–H borylation of 2-dialkylaminopyridines (Scheme 2e) [42]. Interestingly, piperidine borate derivatives **25** and **26** at different positions were obtained when the reaction conditions were different. The mechanism studies suggested that an enamine intermediate was produced in the borylation followed by subsequent Csp^3–H insertion or electrophilic borylation.

2.1.2. *Pyrazine directed C–H borylation*

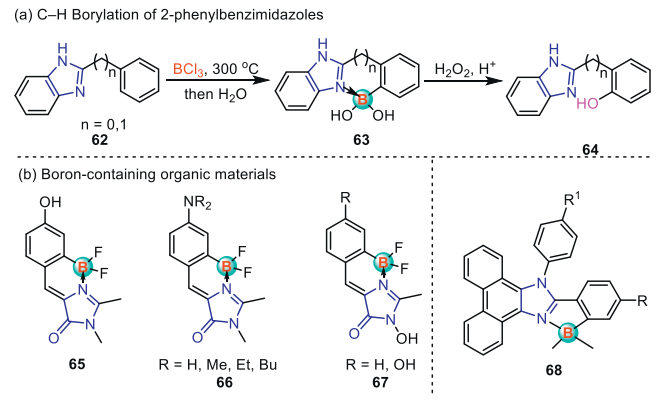
The studies of pyrazine directed C–H borylation using BX_3 was mainly focused on the preparation of boron-containing organic materials. In 2016, Feng and co-workers created low band gap coplanar organic materials **28** *via* pyrazine directed borylation on donor-acceptor-donor process (Scheme 3a) [43]. Then, Zhan's group synthesized four B–N embedded indacenodithiophene structures **29–32** and obtained a new electron-deficient moiety containing B–N bonds using BBr_3 **33** (Scheme 3b) [44]. Similarly, Huang's group disclosed two embedded units **34** and **35**, which exhibited good stability and strong electron-affinity in 2019 (Scheme 3b) [45]. Meanwhile, Gelfand and co-workers synthesized a series of boron-nitrogen doped dihydroindeno[1,2-*b*]fluorenes **38** which had a wide spectrum of visible to near-IR light absorption profiles (Scheme 3c) [46]. Pyrazine directed C–H borylation is worthy of further exploration in organic synthesis.

2.1.3. *Pyrazole directed C–H borylation*

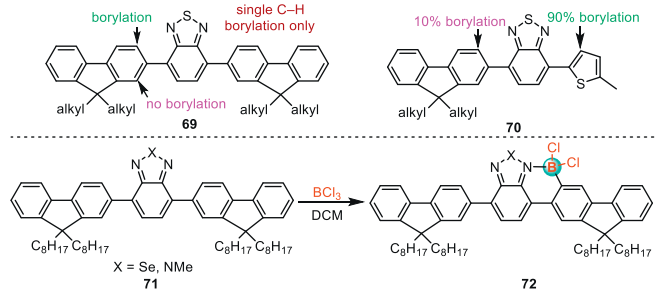
Pyrazole directed transition-metal catalyzed C–H borylation has been made significant progress in the past few decades [47,48]. However, as a common unit in organic compound, the studies of pyrazole directed C–H borylation under metal-free conditions were rarely reported, especially in the field of organic synthesis. In 2019–2022, Venkatasubbaiah's group synthesized a series of triaryl/tetraaryl pyrazoles B–N coordinated boron compounds **39–43** through electrophilic aromatic borylation strategy (Scheme 4a) [49–51]. All of these compounds exhibited good optical properties which were expected to be applied to luminescent materials. In 2022, Ji's group disclosed a novel method of boron-mediated C–H hydroxylation of *N*-benzyl-3,4,5-tribromopyrazoles (Scheme 4b) [52]. The corresponding phenols **46** could be obtained in moderate to excellent yields by borylation/oxidation using BBr_3 and $NaBO_3{\cdot}4H_2O$. Mechanism studies revealed that a six-membered B–N cyclic intermediate was formed in this reaction. Very recently, Huang and co-workers realized boron-mediated selective C–H hy-



Scheme 5. Pyrimidine directed C–H borylation.



Scheme 6. Imidazole/imidazolinone directed C–H borylation.



Scheme 7. Benzothiadiazole/benzoselenadiazole/benzotriazole directed C–H borylation.

droxylation of 1-phenyl-1*H*-pyrazoles (Scheme 4c) [53]. Compared to previous work of photo-induced C–H borylation/oxidation of 1-phenyl-1*H*-pyrazoles, this approach was more convenient, economical and practical. However, pyrazole directed C–H borylation using BX_3 should be further developed.

2.1.4. Pyrimidine directed C–H borylation

In 2019, Kumagai, Shibasaki and co-workers reported a reliable route to generate a series of Pym-DATBs (DATB = 1,3-dioxa-5-aza-2,4,6-triborinane) **52** from inexpensive materials through pyrimidine directed C–H borylation (Scheme 5a) [54]. And these obtained derivatives could be used as effective catalysts for dehydrative amidation. In 2021, Ingleson's group disclosed the site-selective C–H borylation of *N*-pyrimidine-carbazole **53** and *N*-pyrimidine-indole **56** by forming six membered boracycles using BCl_3 (Scheme 5b) [55]. The reason for site selectivity was due to blocking of the C2 position of indole. Then, Chatani's group presented an efficient directed *ortho*-C–H borylation of 2-pyrimidylanilines **59** under metal-free conditions (Scheme 5c) [56]. This protocol exhibited broad scope of substrates and high functional group tolerance. Various boronic esters and four-coordinated triarylborane derivatives **61** were obtained in good yields. In addition, the reaction could be conducted well even there were some external impurities. It might be due to the reaction proceeding rapidly. Mechanism studies suggested a Wheland intermediate was formed in this reaction.

2.1.5. Imidazole/imidazolinone directed C–H borylation

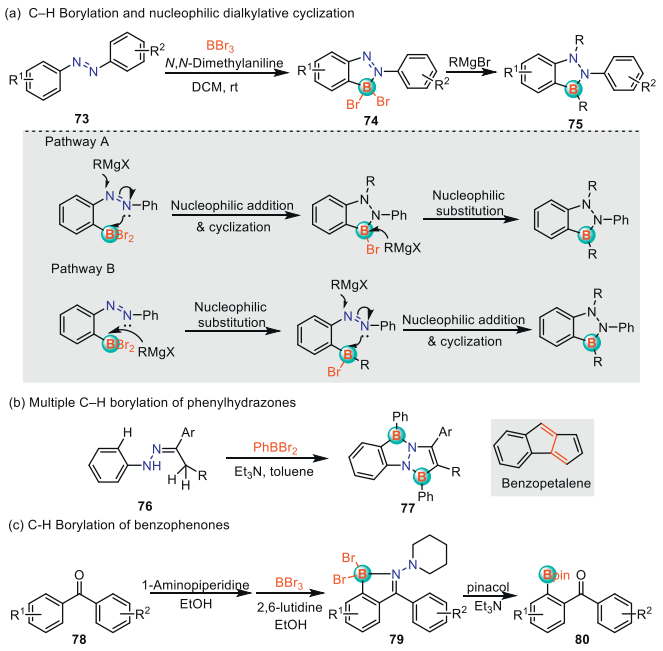
As early as 1963, MacLean's group achieved the borylation of 2-phenylbenzimidazoles using BCl_3 at 300 °C and subsequently obtained phenolic products (Scheme 6a) [57]. Until now, imidazole or imidazolinone directed metal-free C–H borylation in the field of organic synthesis had not made much progress, but there were certain applications in the field of organic materials. In 2012–2016, Solntsev and co-workers exploited a series of new fluorescent dyes **65–67** directed by imidazolinone using BBr_3 (Scheme 6b) [58,59]. Then, in 2018, Venkatasubbaiah's group obtained several phenanthroimidazole-based four coordinate organoboron compounds **68**, which possessed moderate to good solution state quantum yields (Scheme 6b) [60].

2.1.6. Benzothiadiazole/benzoselenadiazole/benzotriazole directed C–H borylation

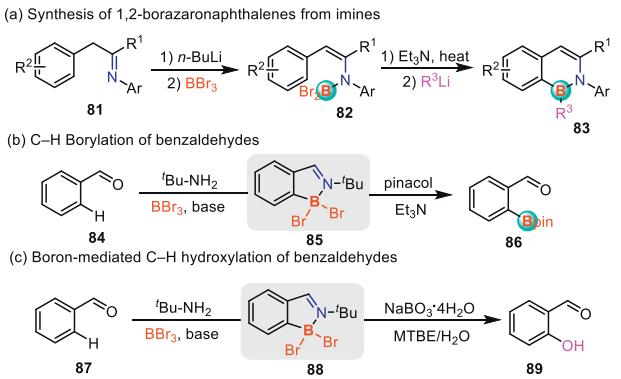
In 2015–2019, Ingleson, Turner and co-workers had been working on the construction of organic materials using benzothiadiazole/benzoselenadiazole/benzotriazole directed C–H electrophilic borylation (Scheme 7) [61–66]. As a conclusion, benzothiadiazole directed C–H borylations with BBr_3 or BCl_3 at room temperature were more rapidly than pyridyl, even in the absence of exogenous bases. This might be due to benzothiadiazole being more effective in promoting deprotonation. In addition, despite there were two nitrogen Lewis basic sites of benzothiadiazole, only a single electrophilic C–H borylation could be directed because of the lower Lewis basicity of benzothiadiazole. Furthermore, the steric hindrance effect was obvious in this type of electrophilic borylations, which usually only occurred at the less steric hindrance position (compound **69**). As expected, C–H borylation was more rapid with increasing arene nucleophilicity and the C–H borylation mainly occurred on the thiophene ring with a higher electron cloud density when using the unsymmetrically substituted derivatives (compound **70**).

2.1.7. Diazene/hydrazone directed C–H borylation

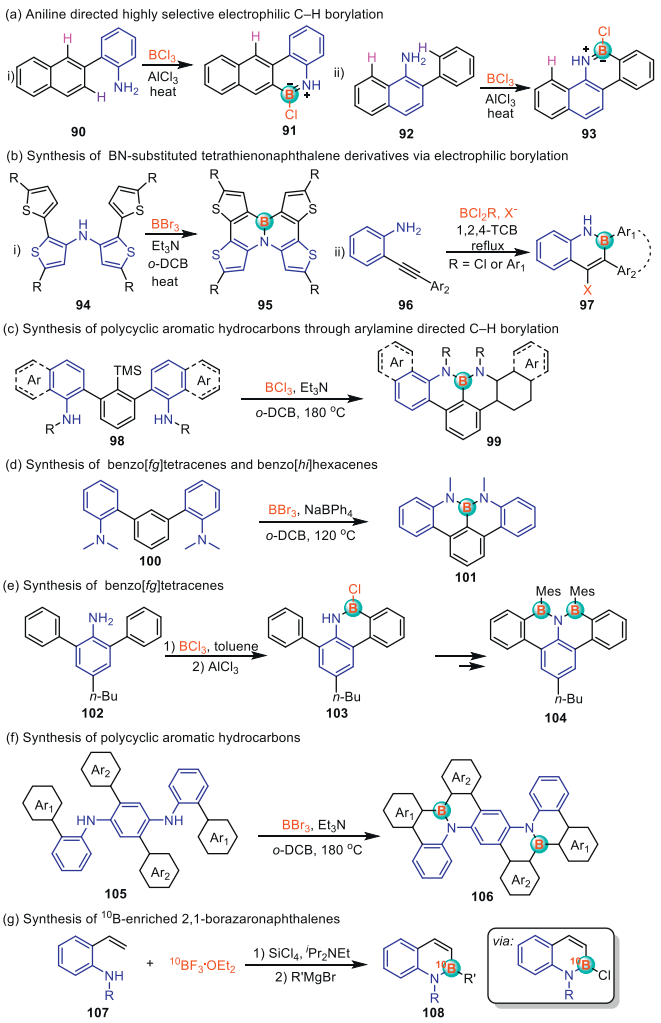
The studies of diazene directed C–H bond activation are not surprising on transition-metal-catalyzed. However, there are few reports on C–H borylation under metal-free conditions with diazene auxiliary. In 2021, Shigeno and co-workers disclosed a new route to construct 1,2,3-benzodiazaboroles **75** *via* C–H electrophilic borylation and additional nucleophilic dialkylative cyclization (Scheme 8a) [67]. The method exhibited good functional group tolerance with high yield, especially the yield of electrophilic borylation step could reach 100 %. Mechanistically, the reaction proceeded *via* nucleophilic addition of a Grignard reagent to the azo-unit, followed by intramolecular cyclization, and nucleophilic substitution of the B–Br bond.



Scheme 8. Diazene/hydrazone directed C–H borylation.



Scheme 9. Imine directed C–H borylation.



Scheme 10. Arylamine directed C–H borylation.

In 2015, Cui's group produced a series of novel B–N analogues of benzopentalene **77** by the one-pot multiple borylation through the C–H bond cleavage of $PhBBr_2$ mediated by triethylamine (Scheme 8b) [68]. In 2023, Ji's group achieved a metal-free C–H borylation of benzophenones using hydrazone as the traceless directing group (Scheme 8c) [69]. Similar to Shigeno's work, the dibromoboron intermediates could be generated in excellent yields and site selectivity. The arylboronic esters **80** could also be obtained in moderate to excellent yields and possessed a variety of transformations, which providing a practical tool to construct structurally diversified benzophenones.

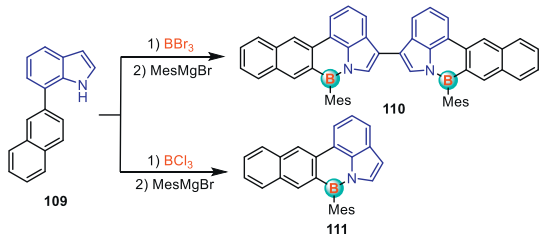
2.1.8. Imine directed C–H borylation

In 2015, Cui's group fabricated a series of 1,2-borazaronaphthalenes **83** from benzylic imines through base-facilitated borylation (Scheme 9a) [70]. In this reaction pathway, enamidyl dibromoborane was first formed, and then base-facilitated aromatic C–H bond borylation was performed to produce the polycyclic aromatic hydrocarbons with moderate yield.

In recent years, transient directing group assisted C–H bond functionalization has arisen. This strategy is step economical because the directing group does not need to be preinstalled and then removed after the activation. In 2021, Chatani and co-workers developed a metal-free *ortho*–C–H borylation of electron-deficient benzaldehydes using imine as a transient directing group (Scheme 9b) [71]. The method exhibited good functional group tolerance and site selectivity. Interestingly, the reaction could be gone well even in the presence of external impurities. Mechanism studies suggested a dibromo borane intermediate was formed in this reaction. Based on this, very recently, Chen, Feng and co-workers disclosed a boron-mediated *ortho*-C–H hydroxylation of benzaldehydes using imine as a transient directing group in a one-pot (Scheme 9c) [72]. The corresponding salicylaldehydes **89** could be obtained in moderate to good yields *via* borylation and oxidation using BBr_3 and $NaBO_3{\cdot}4H_2O$.

2.1.9. Arylamine directed C–H borylation

In the past few years, the purpose of arylamine directed C–H borylation is mainly to construct B–N analogues of polycyclic aromatic hydrocarbons. As early as 1964, Dewar and Peosche developed aniline directed highly selective electrophilic C–H borylation using BCl_3 and $AlCl_3$ (Scheme 10a) [73]. Subsequently, Pei, Wang and co-workers performed a lot of in-depth researches in this filed. They synthesized a series of novel BN-substituted tetrathienonaphthalene derivatives **95** *via* electrophilic borylation in a one-pot (Scheme 10b) [74]. These works opened the door to the rapidly developing application of azaborine chemistry in electronic science. In 2016, they established an efficient route to generate BN-fused polycyclic aromatic hydrocarbons **97** with multiple function-



Scheme 11. Indole directed C–H borylation.

alized sites *via* electrophilic borylation and Suzuki cross-coupling (Scheme 10b) [75].

In 2016–2020, Zhang, Feng and co-workers obtained a range of structurally diverse polycyclic aromatic hydrocarbons **99** through arylamine directed C–H borylation (Scheme 10c) [76–78]. These works offered practical tools to fabricate tailor-made complex architectures such as dendrimers, conjugated polymers and organic framework materials. In addition, Hatakeyama's group synthesized several benzo[*fg*]tetracenes and benzo[*hi*]hexacenes **101** using the strategy of demethylative direct borylation (Scheme 10d) [79]. The results of the optimization of reaction conditions indicated that the key to successful synthesis was to select the appropriate boron source and Brønsted base. In 2017, Bettinger's group obtained a new compound benzo[*fg*]tetracene **104** which displayed blue fluorescence and had considerable antioxidant and reductive capabilities (Scheme 10e) [80]. Then, Zhou's group generated a range of polycyclic aromatic hydrocarbons **106** containing two pairs of BN units via electrophilic C–H borylation (Scheme 10f) [81]. In 2024, Song's group disclosed a practical method for producing ^{10}B-enriched 2,1-borazaronaphthalenes **108** from *o*-aminostyrenes and $^{10}BF_3$ in the presence of chlorosilane, which might provide new lead compounds for boron neutron capture therapy. The mechanistic studies indicated that this ^{10}B transformation might involve the formation of boron chloride species and subsequent cyclization with *o*-amino-styrene (Scheme 10g) [82].

2.1.10. Indole directed C–H borylation

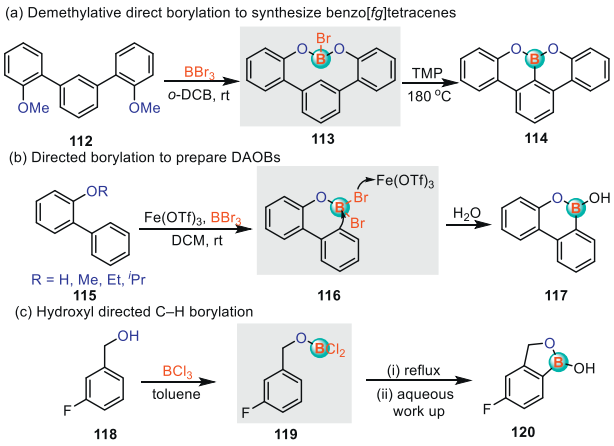
In 2024, Yu, Liu and co-workers developed an efficient method to generate BN-embedded polycyclic aromatic hydrocarbons via indole *N*-directed electrophilic borylation (Scheme 11) [83]. Notably, the types of products were dependent on the boron source. When using BBr_3 as the boron source, dimers of BN-polycyclic aromatic hydrocarbons **110** were obtained, while monomers of BN-PAHs **111** were generated when BCl_3 was used. Additionally, the dimers exhibited better photo-physical properties than monomers. This discovery opened new possibilities for expanding BN-doped polycyclic aromatic hydrocarbons by simply switching boron source.

2.2. Oxygen directed C–H borylation

Similar to N-directed electrophilic C–H borylation of arene, Dewar and co-workers also reported O-directed C–H borylation of 2-phenylphenol using BCl_3 and $AlCl_3$ in 1959 [84]. Unfortunately, the development of O-directed C–H borylation had been slow. In 1993, Nicholson's group developed the first example of a carbonyl directed electrophilic C–H borylation using BBr_3 [85]. Satisfactorily, in recent years, following the pioneering work of the Shi's and Ingleson's work, the acyl-directed borylation under metal-free conditions has developed rapidly.

2.2.1. Methoxyl/hydroxyl directed C–H borylation

Most of methoxyl directed C–H borylation undergoes the cleavage of ArylO-Me with BBr_3 to form Aryl$OBBr_2$ units that then effect intramolecular C–H borylation. In 2016, Hatakeyama and co-workers disclosed a demethylative direct borylation to synthesize



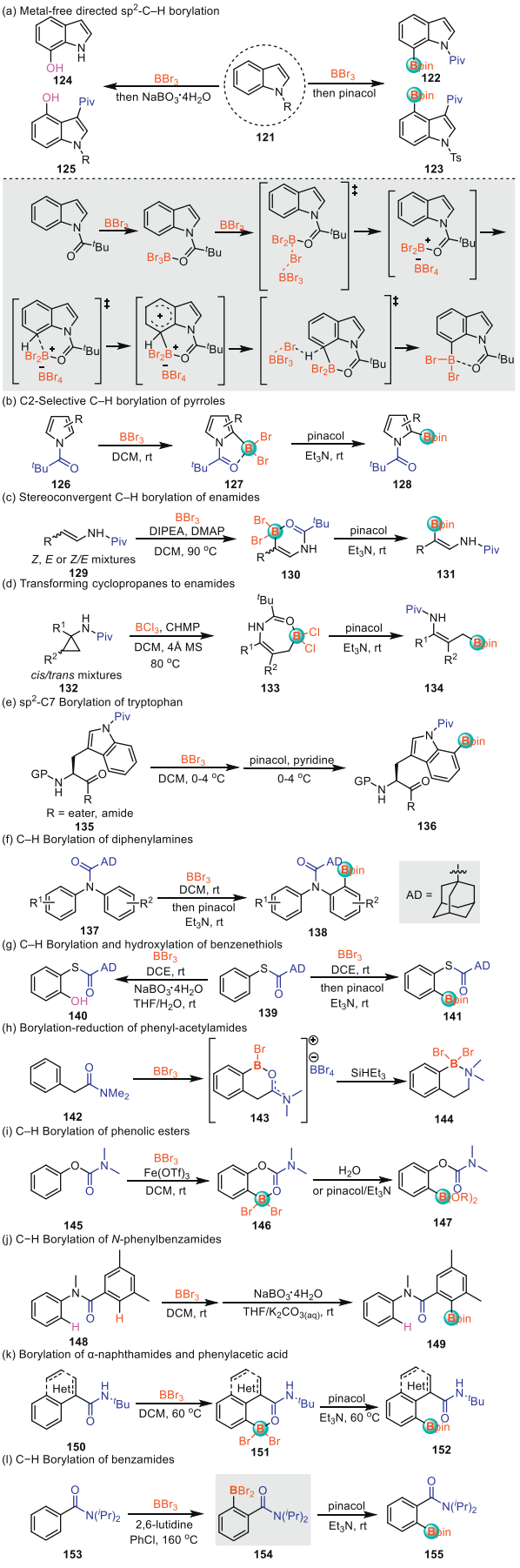
Scheme 12. Methoxyl/hydroxyl directed C–H borylation.

benzo[*fg*]tetracenes **114** using BBr_3 as a boron source and 2,6,6-tetra-methylpiperidine as a Brønsted base (Scheme 12a) [79]. Also, they successfully obtained the π-extended product 10,11-dioxa-10a-borabenzo[*hi*]hexacene in 76 % yield, which further verified the versatility of the direct borylation. In 2024, Chen's group reported a $Fe(OTf)_3$-promoted, directing group-controlled, regioselective C–H borylation of 2-arylphenolics **115** at room temperature using BBr_3 (Scheme 12b) [86]. In this reaction system, the anion ligand of Lewis acid played a crucial role and the diversity diaryloxaborin could be generated in moderate to excellent yields [87].

In the past few years, the reports of hydroxyl directed C–H borylation using BX_3 was rare. In recent patent literature, Liu's group developed a hydroxyl directed electrophilic C–H borylation to access benzoxaboroles **120** (Scheme 12c) [88]. Under low temperature conditions, benzyl alcohol was reacted with BCl_3 to form the RO-BCl_2 species, which underwent the C–H borylation after refluxing in toluene. Of note, the commercialized tavaborole could be obtained in moderate yield in this reaction system.

2.2.2. Acyl directed C–H borylation

In 2019, Shi, Houk, and co-workers as well as the Ingleson group developed a pivaloyl group directed C4-, C7-borylation of indoles and *ortho*-borylation of anilines by just using BBr_3 (Scheme 13a) [89,90]. The method exhibited good functional group tolerance, offering the corresponding arylboronates **122**, **123** in moderate to excellent yields under simple, mild, and efficient conditions. Mechanistic studies indicated that the BBr_3 acting as both a catalyst and a reagent. Based on this, Shi's group reported a novel protocol for prepare diverse phenols **124**, **125** *via* BBr_3-mediated directed aromatic C–H hydroxylation (Scheme 13a) [91]. The practicability of this method has been confirmed by synthesizing some phenol intermediates of bioactive molecules. Subsequently, using the same directing group, they achieved the C2-selective C–H borylation of pyrroles under metal-free conditions (Scheme 13b) [92]. And they discovered that the site-selectivity hinged on chelation and electronic effects. In 2023, they disclosed a pivaloyl group directed stereoconvergent C–H borylation of enamides for constructing diastereomerically pure β-borylenamides **131** in the presence of 4-dimethylaminopyridine (DMAP) and *N*,*N*-diisopropylethylamine (DIPEA) (Scheme 13c) [93]. The mechanism studies revealed the key roles played by DMAP and DIPEA, the reactive boron species, and the phenomenon of stereoconvergence. In 2024, they realized the synthesis of stereochemically precise γ-borylenamides **134** *via* σ-C–C bond eliminative borylation using BCl_3 and 4-cyclohexylmorpholine (CHMP) under the directing of *N*-acyl group (Scheme 13d) [94]. This mild strategy exhibited excellent functional group compatibility and high efficiency. Mech-



Scheme 13. Acyl directed C–H borylation.

anism studies indicated that BCl_3 was unlikely to form a borenium species through proportionation as BBr_3 did. The practicability of this method has been further confirmed by Reddy's group (Scheme 13e) [95]. They described an efficient method for the C7-selective C–H borylation of tryptophan using BBr_3 and this strategy enabled peptide extension and late-stage borylation of peptides, natural product Brevianamide F and drug Oglufanide.

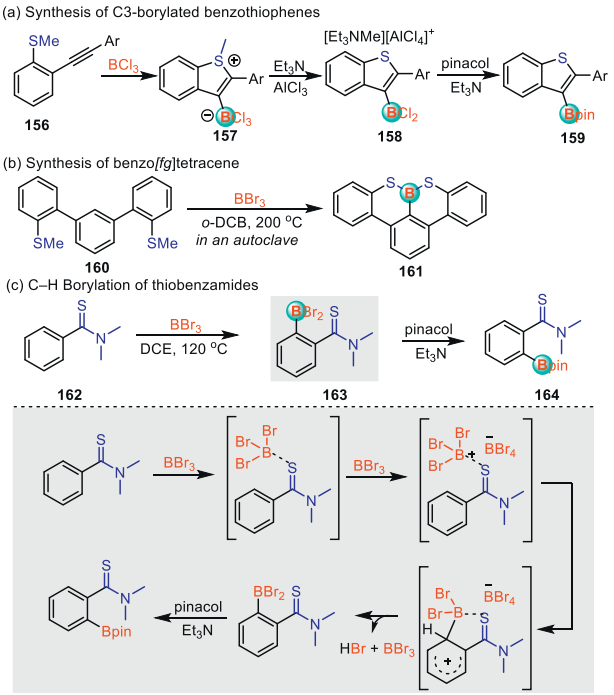
Inspired by Shi's work, Ji and co-workers developed a method for C–H borylation of diphenylamines **137** through adamantane-1-carbonyl auxiliary using BBr_3 under metal-free conditions in 2020 (Scheme 13f) [96]. This strategy exhibited excellent site exclusivity and most of the borylation occurred at the more electron-rich aromatic ring. Furthermore, the method showed good functional group compatibility and application prospect. Using the same directing group, they achieved the *ortho*-C–H borylation and hydroxylation of benzenethiols **139**, providing a useful tool for the construction of structurally diverse thiophenol (Scheme 13g) [97].

In 2023, Ingleson's group realized amide directed electrophilic borylation-reduction of phenyl-acetylamides, mono and diaminoarenes and carbazole using greater than or equal to 2 equiv. of BBr_3 and hydrosilanes (Scheme 13h) [98]. This approach was a useful addition to the metal-free borylation toolbox for obtaining valuable arylboron compounds and novel B,N-polycyclic aromatic hydrocarbons. Given the importance of (2-hydroxyaryl)boronic acid (2-HAB) in organic synthesis and medicinal chemistry, Chen's group conquered the competing Fries rearrangement and realized the *ortho*-C–H borylation of phenolic esters and carbamates, generating 2-HABs **147** in good yields (Scheme 13i) [86]. However, the substrate scope was relatively narrow, especially for the substrate with strong withdrawing group. It might due to the lower nucleophilicity of aryl ring. Besides, only two examples of substrates bearing fluorine or chlorine at *meta*-position were reported. The tolerance of substrates with electron-withdrawing groups at *ortho*- and *para*-positions need to be explored.

It is worth noting that the previously reported metal-free directed C–H borylation mainly focused on electron-rich arene systems, such as phenols, thiophenols, indoles and anilines. Achieving electrophilic borylation of electron-defect arenes is difficult because of the low electron cloud density in the aromatic ring. In 2024, Our group presented a regioselective C–H hydroxylation and borylation of *N*-phenylbenzamides **148** using BBr_3 (Scheme 13j) [99]. The method delivered the corresponding phenols and arylboronic esters **149** in moderate to excellent yields under metal-free conditions. Density functional theory calculations indicated that the preferred pathway for this C–H hydroxylation/borylation was to form a five-membered boracycle. Subsequently, Maiti's group achieved the BBr_3-mediated selective C–H borylation of α–naphthamides and phenylacetic acid **150** (Scheme 13k) [100]. This strategy appeared to be economical and cost-effective and the borylation of drug molecules such as ibuprofen and indoprofen could be performed efficiently. Compared to our work, this method was more likely to form a six-membered boracycle. Very recently, Zhang and co-workers reported a BBr_3-mediated *ortho*-C–H borylation of benzamides under metal-free conditions (Scheme 13l) [101]. Although this method could provide borylated benzamides **155** in moderate to good yields, it needed to be carried out at high temperature.

2.3. Sulfur directed C–H borylation

The first example of sulfur directed C–H borylation was also reported by Dewar's group in 1968 [102]. They found that the sulfur congener underwent C–H borylation most readily presumably as poorer π donation to the boron center (compared to O and N congeners) generates the most reactive boron electrophile of the series. However, sulfur directed metal-free C–H borylation

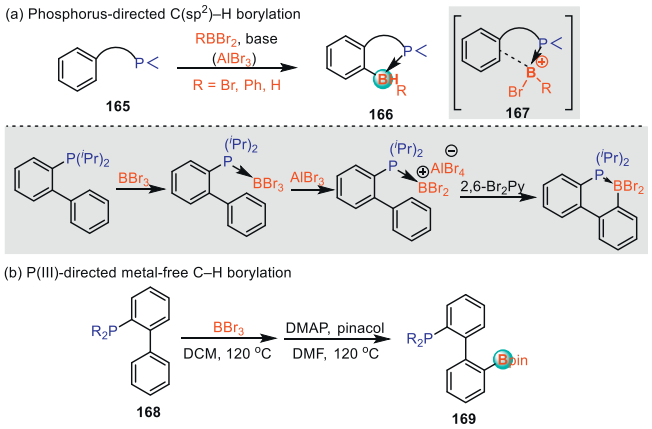


Scheme 14. Sulfur directed C–H borylation.

is a direction that urgently needs to be developed. In 2016, Ingleson's group established a novel strategy to form the C3-borylated benzothiophenes **159** *via* BCl_3-induced annulative thioboration and the activation process was revealed through ^{11}B NMR spectroscopy (Scheme 14a) [103]. Hatakeyama and co-workers reported a route to synthesize benzo[*fg*]tetracene **161** using thioester as the substrate *via* demethylative direct borylation (Scheme 14b) [79]. However, only 21 % yield of the desired compound could be obtained even at 200 °C. In addition, the target compound was air-stable, but immediately decomposed in protic solvents. In 2024, Zhang and co-workers disclosed a BBr_3-mediated *S*-directed *ortho* C–H borylation of thiobenzamides (Scheme 14c) [104]. The method exhibited wide functional group tolerance, affording the corresponding borylated thiobenzamides **164** in moderate to good yields. Nevertheless, when using *meta*-substituted thiobenzamide as the substrates, the site selectivity was poor and a mixture of regioisomers was delivered. The reaction mechanism was basically the same as that of the acyl-directed borylation, with the difference being that a strong S–B bond was not formed in the borylated product.

2.4. Phosphorus directed C–H borylation

Over the past years, boron hydride phosphide has been attracted considerable attention and significant progress has been made in the C–H borylation of phosphines catalyzed by transition metals [105]. However, the studies about metal-free phosphorus-directed C–H borylation are rare. In 2022, Bourissou's group developed a novel and straightforward method to obtain phosphine-borane **166** *via* phosphorus-directed C(sp^2)–H borylation under metal-free conditions (Scheme 15a) [106]. The method was applicable to various types of backbones and could conveniently realize the conversion of various substitution patterns at boron. The key intermediates P-stabilized borenium cations was verified by NMR and the existence and stabilizing effect of π-arene/boron interactions in the (biphenyl)(i-Pr)$_2$P→BBr_2^+ species was demonstrated *via* DFT. Subsequently, Shi and co-workers reported a protocol on P(III)-directed metal-free C–H borylation of phosphines **168** mediated by BBr_3 (Scheme 15b) [107]. Diverse phosphine boronate esters **169** could be obtained under the easily handleable, low cost, and environmental friendliness conditions.



Scheme 15. Phosphorus directed C–H borylation.

3. Conclusions and outlook

In conclusion, the recent advanced in C–H borylation using BX_3 with different directing group auxiliary was summarized. In terms of directing groups, these reactions mainly used functional groups containing elements such as nitrogen, oxygen, sulfur and phosphorus as directing groups, among which pyridine and acyl that have emerged in recent years were the most common. In terms of boron sources, BBr_3 with strong activity and low cost was the main choice. Although significant progress has been made in methods and applications for these reactions, the following challenges still exist: (1) these methods are electrophilic borylation, which have poor adaptability to electron-deficient compounds. The currently developed methods still have drawbacks such as harsh reaction conditions and narrow substrate applicability; (2) these methods are mainly suitable for Csp^2–H borylation but not to the Csp^3–H bond; (3) more efficient, concise, practical directing groups and traceless directing group or without directing group directed electrophilic borylation need be further developed; (4) in the field of organic boron materials, on the one hand, more types of directing groups other than nitrogen-containing groups should be further developed (such as double oxygen-containing functional groups [108]); on the other hand, more mild reaction conditions need to be explored. We believe that with the joint efforts of chemists, the above challenges will be overcome one by one, promoting the vigorous development of organoboron chemistry.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

CRediT authorship contribution statement

Gaorong Wu: Writing – original draft, Methodology, Funding acquisition. **Tao Ma:** Writing – review & editing, Funding acquisition.

Acknowledgments

We are grateful to Early-Career Young Scientists and Technologists Project of Jiangxi Province (No. 20244BCE52224), Jiangxi Provincial Natural Science Foundation (No. 20252BAC200240), the

Start-up Funds of Gannan Medical University (No. QD202406) and National Key R&D Program of China (No. 2023YFC3504100) for financial support.

References

[1] S. Tang, Z. Wang, M. Zhu, et al., Chin. Chem. Lett. 36 (2025) 110503.
[2] L.T. Pilarski, K.J. Szabo, Angew. Chem. Int. Ed. 50 (2011) 8230–8232.
[3] Q. Liu, M. Zhang, Y. Fu, et al., Chin. Chem. Lett. 34 (2023) 107612.
[4] C. Jin, K. Li, J. Zhang, et al., Chin. Chem. Lett. 35 (2024) 109532.
[5] Y. Yang, Y. Gao, J. Huang, et al., JCI Insight 7 (2022) e157081.
[6] S. Zanwar, J.P. Abeykoon, P. Kapoor, Expert Rev. Hematol. 11 (2018) 761–771.
[7] A.K. Gupta, S.G. Versteeg, Expert Rev. Clin. Pharmacol. 9 (2016) 1145–1152.
[8] A. Fantini, A. Demurtas, S. Nicoli, et al., Pharmaceutics 12 (2020) 491.
[9] D.C. Griffith, M. Sabet, Z. Tarazi, et al., Antimicrob. Agents Chemother. 63 (2019) e01659-18.
[10] F.L. Wang, L. Liu, C.J. Yang, et al., Angew. Chem. Int. Ed. 62 (2023) e202214709.
[11] J. Bouffard, K. Itami, Org. Lett. 11 (2009) 4410–4413.
[12] R. Bisht, C. Haldar, M.M.M. Hassan, et al., Chem. Soc. Rev. 51 (2022) 5042–5100.
[13] W. Miura, K. Hirano, M. Miura, Org. Lett. 18 (2016) 3742–3745.
[14] L. Xu, G. Wang, S. Zhang, et al., Tetrahedron 73 (2017) 7123–7157.
[15] L. Mao, R. Bertermann, S.G. Rachor, et al., Org. Lett. 19 (2017) 6590–6593.
[16] J. Wu, L. He, A. Noble, et al., J. Am. Chem. Soc. 140 (2018) 10700–10704.
[17] X. Kong, L. Lin, Q. Chen, et al., Org. Chem. Front. 8 (2021) 702–707.
[18] P. Nad, A. Mukherjee, ACS Omega 8 (2023) 37623–37640.
[19] Y. Qin, L. Qi, X. Zhen, et al., J. Org. Chem. 88 (2023) 4359–4371.
[20] M.J.S. Dewar, V.P. Kubba, R. Pettit, J. Chem. Soc. (1958) 3073–3076.
[21] E.L. Muetterties, J. Am. Chem. Soc. 82 (1960) 4163–4166.
[22] M.J.S. Dewar, R. Dietz, J. Chem. Soc. (1959) 2728–2730.
[23] M.J.S. Dewar, C. Kaneko, M.K. Bhattacharjee, J. Am. Chem. Soc. 84 (1962) 4884–4887.
[24] T.S. De Vries, A. Prokofjevs, J.N. Harvey, et al., J. Am. Chem. Soc. 131 (2009) 14679–14687.
[25] H. Yang, E. Wang, P. Yang, et al., Org. Lett. 19 (2017) 5062–5065.
[26] H. Zhao, X. Shao, T. Wang, et al., Chem. Commun. 54 (2018) 4927–4930.
[27] J.L. Han, Y. Qin, D. Zhao, ACS Catal. 9 (2019) 6020–6026.
[28] N. Ishida, T. Moriya, T. Goya, et al., J. Org. Chem. 75 (2010) 8709–8712.
[29] W.E. Piers, S.C. Bourke, K.D. Conroy, Angew. Chem. Int. Ed. 44 (2005) 5016–5036.
[30] T.S.D. Vries, A. Prokofjevs, J.N. Harvey, et al., J. Am. Chem. Soc. 131 (2009) 14679–14687.
[31] H.L. Wong, W.T. Wong, V.W. Yam, Org. Lett. 14 (2012) 1862–1865.
[32] B.Y. Wong, H.L. Wong, Y.C. Wong, et al., Chem. Eur. J. 222 (2016) 15095–15106.
[33] Z. Zhao, Z. Chang, B. He, et al., Chem. Eur. J. 19 (2013) 11512–11517.
[34] M. Yusuf, K. Liu, F. Guo, et al., Dalton Trans. 45 (2016) 4580–4587.
[35] S.K. Mellerup, K. Yuan, C. Nguyen, et al., Chem. Eur. J. 22 (2016) 12464–12472.
[36] S. Oda, H. Abe, N. Yasuda, et al., Chem. Asian J. 14 (2019) 1657–1661.
[37] Y. Yoshigoe, K. Hashizume, S. Saito, Dalton Trans. 51 (2022) 17035–17039.
[38] L.T. Niu, H.J. Yang, R.J. Wang, et al., Org. Lett. 14 (2012) 2618–2621.
[39] S.A. Iqbal, K. Yuan, J. Cid, et al., Org. Biomol. Chem. 19 (2021) 2949–2958.
[40] G. Wu, B. Pang, Y. Wang, et al., J. Org. Chem. 86 (2021) 5933–5942.
[41] G. Wu, X. Xu, S. Wang, et al., Chin. Chem. Lett. 33 (2022) 2005–2008.
[42] P.K.S. Ashwathappa, T. Higashi, V. Desrosiers, et al., Angew. Chem. Int. Ed. 62 (2023) e202309295.
[43] C. Zhu, Z.H. Guo, A.U. Mu, et al., Org. Chem. 81 (2016) 4347–4352.
[44] Y. Li, H. Meng, D. Yan, et al., Tetrahedron 74 (2018) 4308–4314.
[45] Y. Li, B. Pang, H. Meng, et al., Tetrahedron Lett. 60 (2019) 151286.
[46] M.M. Morgan, M. Nazari, T. Pickl, et al., Chem. Commun. 55 (2019) 11095–11098.
[47] T. Yamamoto, A. Ishibashi, M. Suginome, Org. Lett. 19 (2017) 886–889.
[48] T. Yamamoto, A. Ishibashi, M. Suginome, Org. Lett. 21 (2019) 6235–6240.
[49] V. Mukundam, S. Sa, A. Kumari, et al., J. Mater. Chem. C 7 (2019) 12725–12737.
[50] V. Mukundam, S. Sa, A. Kumari, et al., Chem. Asian J. 17 (2022) e202200291.
[51] S. Sa, A. Sahoo, S. Mukherjee, et al., Dyes Pigments 206 (2022) 110585.
[52] G. Wu, Z. Yang, X. Xu, et al., Org. Lett. 24 (2022) 3570–3575.
[53] G. Wu, Y. Liu, W. Chen, et al., J. Org. Chem. 89 (2024) 17453–17462.
[54] C.R. Opie, H. Noda, M. Shibasaki, et al., Chem. Eur. J. 25 (2019) 4648–4653.
[55] S.A. Iqbal, K. Yuan, J. Cid, et al., Org. Biomol. Chem. 19 (2021) 2949–2958.
[56] S. Rej, A. Das, N. Chatani, Chem. Sci. 12 (2021) 11447–11454.
[57] R.L. Letsinger, D.B. MacLean, J. Am. Chem. Soc. 85 (1963) 2230–2236.
[58] M.S. Baranov, K.A. Lukyanov, A.O. Borissova, et al., J. Am. Chem. Soc. 134 (2012) 6025–6032.
[59] S. Olsen, M.S. Baranov, N.S. Baleeva, et al., Phys. Chem. Chem. Phys. 18 (2016) 26703–26711.
[60] K. Dhanunjayarao, S. Sa, B.P.R. Aradhyula, et al., Tetrahedron 74 (2018) 5819–5825.
[61] D.L. Crossley, J. Cid, L.D. Curless, et al., Organometallics 34 (2015) 5767–5774.
[62] D.L. Crossley, I.A. Cade, E.R. Clark, et al., Chem. Sci. 6 (2015) 5144–5151.
[63] D.L. Crossley, R. Goh, J. Cid, et al., Organometallics 36 (2017) 2597–2604.
[64] D.L. Crossley, L. Urbano, R. Neumann, et al., ACS Appl. Mater. Interfaces 9 (2017) 28243–28249.
[65] D.L. Crossley, P. Kulapichitr, J.E. Radcliffe, et al., Chem. Eur. J. 24 (2018) 10521–10530.
[66] B.P. Dash, I. Hamilton, D.J. Tate, et al., J. Mater. Chem. C 7 (2019) 718–724.
[67] M. Shigeno, M. Imamatsu, Y. Kai, et al., Org. Lett. 23 (2021) 8023–8027.
[68] C. Ma, J. Zhang, J. Li, et al., Chem. Commun. 51 (2015) 5732–5734.
[69] Z. Yang, L. Hao, X. Xu, et al., Org. Lett. 25 (2023) 5875–5879.
[70] X. Liu, P. Wu, J. Li, et al., J. Org. Chem. 80 (2015) 3737–3744.
[71] S. Rej, N. Chatani, J. Am. Chem. Soc. 143 (2021) 2920–2929.
[72] R. Wang, X. Feng, B. Feng, et al., RSC Adv. 14 (2024) 19922–19925.
[73] M.J.S. Dewar, W.H. Poesche, J. Org. Chem. 29 (1964) 1757–1762.
[74] X.Y. Wang, H.R. Lin, T. Lei, et al., Angew. Chem. Int. Ed. 52 (2013) 3117–3120.
[75] F.D. Zhuang, J.M. Han, S. Tang, et al., Organometallics 36 (2016) 2479–2482.
[76] X. Wang, F. Zhang, K.S. Schellhammer, et al., J. Am. Chem. Soc. 138 (2016) 11606–11615.
[77] P. Qiang, Z. Sun, M. Wan, et al., Org. Lett. 21 (2019) 4575–4579.
[78] Z. Sun, C. Yi, Q. Liang, et al., Org. Lett. 22 (2020) 209–213.
[79] M. Numano, N. Nagami, S. Nakatsuka, et al., Chem. Eur. J. 22 (2016) 11574–11577.
[80] M. Fingerle, C. Maichle-Mossmer, S. Schundelmeier, et al., Org. Lett. 19 (2017) 4428–4431.
[81] Y. Chen, W. Chen, Y. Qiao, et al., Chem. Eur. J. 25 (2019) 9326–9338.
[82] W. Qiu, J. Zhu, R. Tao, et al., Org. Chem. Front. 11 (2024) 2733–2738.
[83] Y. Hao, Z. Yu, S. Zhou, et al., Inorg. Chem. Commun. 161 (2024) 112104.
[84] M.J.S. Dewar, R. Dietz, Tetrahedron Lett. 1 (1959) 21–23.
[85] V.L. Arcus, L. Main, B.K. Nicholson, J. Organomet. Chem. 460 (1993) 139–147.
[86] J. Kang, J. Liu, Z. Chen, Org. Chem. Front. 11 (2024) 4249–4257.
[87] C. Hansch, A. Leo, R.W. Taft, Chem. Rev. 2 (1991) 165.
[88] W. Di, C. Liu, Patent, CN106467557, 2017.
[89] J. Lv, X. Chen, X.S. Xue, et al., Nature 575 (2019) 336–340.
[90] S.A. Iqbal, J. Cid, R.J. Procter, et al., Angew. Chem. Int. Ed. 58 (2019) 15381–15385.
[91] J. Lv, B. Zhao, Y. Yuan, et al., Nat. Commun. 11 (2020) 1316.
[92] Z.J. Wang, X. Chen, L. Wu, et al., Angew. Chem. Int. Ed. 60 (2021) 8500–8504.
[93] T. Wang, Z.J. Wang, M. Wang, et al., Angew. Chem. Int. Ed. 62 (2023) e202313205.
[94] S. Kang, J. Lv, T. Wang, et al., Nat. Commun. 15 (2024) 7380.
[95] R. Meena, S. Shekhar, S.B. Ansari, et al., Chem. Asian J. 18 (2023) e202300638.
[96] G. Wu, X. Fu, Y. Wang, et al., Org. Lett. 22 (2020) 7003–7007.
[97] X. Xu, G. Wu, Z. Yang, et al., Org. Lett. 24 (2022) 7163–7167.
[98] S.A. Iqbal, M. Uzelac, I. Nawaz, et al., Chem. Sci. 14 (2023) 3865–3872.
[99] W. Chen, J. Xia, J. Huang, et al., Org. Lett. 26 (2024) 4631–4636.
[100] S. Maji, P. Rawal, A. Ghosh, et al., JACS Au 4 (2024) 3679–3689.
[101] Y. Liang, C. Du, C. Dong, et al., Org. Lett. 27 (2025) 4650–4655.
[102] F.A. Davis, M.J.S. Dewar, J. Am. Chem. Soc. 90 (1968) 3511–3515.
[103] A.J. Warner, A. Churn, J.S. McGough, et al., Angew. Chem. Int. Ed. 56 (2017) 354–358.
[104] J. Lv, Y. Liang, Y. Ouyang, et al., Org. Lett. 26 (2024) 3709–3714.
[105] J. Wen, D. Wang, J. Qian, et al., Angew. Chem. Int. Ed. 58 (2019) 2078–2082.
[106] O. Sadek, A. Le Gac, N. Hidalgo, et al., Angew. Chem. Int. Ed. 61 (2022) e202110102.
[107] J. Lv, X.J. Zhang, M. Wang, et al., Chem. Eur. J. 28 (2022) e202104100.
[108] L.Q. Wan, S.S. Ling, L. Yang, et al., Chem. Sci. 16 (2025) 12051–12057.