Invited paper

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Direct deoxygenative borylation

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Abstract: Direct deoxygenative borylation is a highly enabling chemical transformation considering the attractive synthetic features of oxygenous feedstocks and organoboron compounds. Despite ranking among the synthetic ideality in different settings, such chemical space remained largely uncharted and underutilized until recent decades. This short review will summarize some key advances in the field of direct deoxyborylation of alcohols, ethers, aldehydes, ketones, and carboxylic acids and organize these contributions based on substrate classes. In each representative, the general features, including reaction conditions, product scopes and mechanistic insights, will be highlighted and discussed.

Keywords: borylation; C–O functionalizations; deoxygenation; IUPAC-SOLVAY International Award for Young Chemists; organoboron.

Introduction

Boron represents an ideal substituent, which played a central role in the functional group chemistries of modern synthesis [1–6]. As a highly diversifiable building block in both polar and radical regimes [7], organoboron often serves as the starting point for synthetic planning, and its modularity constitutes numerous downstream transformations like cross-couplings, metallate rearrangements and deborylative additions [5, 8–17]. Moreover, the unique reactivity and structural traits of boron compounds lead to their widespread application in material science and medicinal chemistry. Particularly in the latter, the boronic group could mimic the amide moiety during enzymatic hydrolysis and behave as the potent bioisostere of the carboxylic group during drug discovery [18, 19] (Scheme 1).

Despite its versatility and impact in various contexts, accessing organoboron heavily relies on manual synthesis owing to its scarcity in nature. Classic borylation reactions include hydroboration of unsaturated C–C bonds and transmetallation with organometallic reagents and boron electrophiles. The advent of transition metal-catalyzed Miyaura borylation marks a milestone, which reshapes the landscape of boron chemistry and considerably advances the modern borylation toolkit [20–30]. Encouragingly, recent advances in radical- [31–36] and carbene-mediated borylation [37–41] further enrich the synthetic route and scope of accessible organoboron. However, these precedent strategies mostly necessitate non-renewable or pre-functionalized substrates based on petroleum sources, which suffer limited availability, perceived instability and occasionally toxicity.

Oxygenous compounds are privileged chemical entities by virtue of their natural abundance, structural diversity and chemical stability [42]. These attractive features make the oxygenated feedstocks suitable surrogates for the non-renewable carbon electrophiles and forge C–B bonds directly from native functionalities. Nonetheless, such an ideal is often compromised by the thermodynamic stability of strong C–O bonds (bond dissociation energy, BDE = 90 kcal/mol for C–O in methanol and 175 kcal/mol for C=O in formaldehyde) [43]. In some cases, the kinetic inaccessibility of the C–O bond and the acidic O–H could also undermine deoxygenation. Although multistep C–O activation/borylation could be conceivable to impart the same

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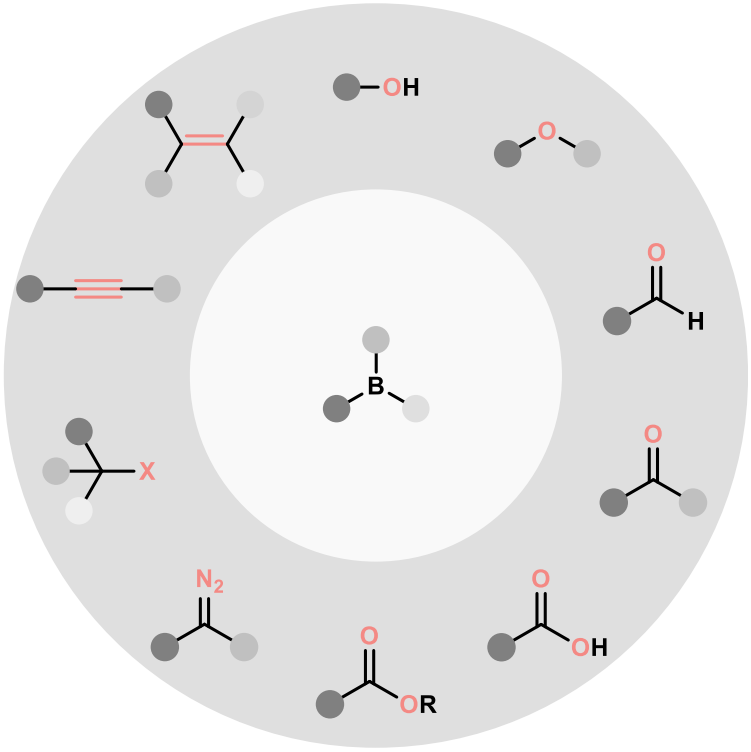

Scheme 1: Preparation of organoborons (Representative starting materials in the dark grey circle).

deoxy-borylation reactivity, direct deoxygenative borylation remains a long-sought-after goal, which reflects a general trend toward future sustainability in the synthetic community [44–46].

Clearly, stepping toward direct deoxygenative borylation mandates novel chemical means that could manipulate the inert C–O bonds with minimal step counts and waste production. Although challenging, such linchpin techniques might unlock the approach to previously elusive boron compounds and provide a great opportunity for editing complex molecules via orthogonal late-stage functionalization. Recent years have witnessed a growing number of direct deoxy-borylation manifolds in literature. This minireview aims to summarize these contributions per the C–O substrates and highlight some general borylation strategies that allow the valorization of oxygenated carbon electrophiles. Accordingly, direct C–O borylation of alcohols, ethers, and carbonyl compounds, including aldehydes, ketones, carboxylic acids and esters, will be presented.

Hopefully, this review could offer a timely update on the state-of-the-art boron compound synthesis via deoxygenation and some food for thought on the future direction of boron chemistry. To keep the text concise, only one-step deoxygenative borylation with complete removal of C–O bonds at the functionalized carbon will be included. Cascade reactions will not be covered unless closely related. Other oxides (e.g., nitro compounds and sulfoxides) are beyond the contents since the products obtained from the protodeoboronation of these boron intermediates would be more relevant to the synthetic practice.

Alcohol deoxygenative borylation

Alcohol is a straightforward surrogate of organohalide for boron compound synthesis. Advantageously, alcohol deoxygenative borylation could avoid the production of halide waste and only water or boron oxides will be generated as innocuous byproducts. In reality, such a direct O-to-B conversion via formal nucleophilic substitution was undermined by the reluctant –OH leaving group. Deoxygenation is even harsher after deprotonation under basic conditions. Clearly, new borylation catalysts or mechanisms are demanded to bridge the synthetic gap between alcohols and organoborons.

Metal-catalyzed deoxy-borylation of allylic, benzylic and propargylic alcohols

Considering the difficulty of alcohol direct borylation, the initial exploration in this field focused on some reactive alcohols like allylic alcohols. Pioneered by Szabó and his group, the direct deoxygenative borylation of free allylic alcohol was realized under mild palladium catalysis, among which ligand-free and ligand-enabled conditions were both feasible (Fig. 1A) [47–54]. For the latter, the PSP- and PSeP-type pincer-type ligands were crucial, managing the desired transformation under mild conditions and controlling linear product formation. In Szabó's proposed mechanism, the Lewis acidic B_2X_4 was dual-functional, serving as boron sources and activating the –OH in the allylic substrates. Counter anion BF_4^- of the palladium catalyst was also non-innocent, which would degrade into F^- and BF_3, assisting the transmetallation and activation of alcohols, respectively. The allylboron product could be directly subjected to carbonyl allylation in a one-pot manner.

In collaboration with Aggarwal's group, they also unveiled a simple Pd-catalyzed protocol with a commercially available palladacyclic catalyst, giving a similar scope of allylboronates with high efficiency [49].

Encouraged by these prior efforts, the more economical iron catalysis was proved viable in the allylic alcohol borylation, as reported by Qu's and Liu's groups, respectively (Fig. 1B) [55, 56]. In both cases, primary allylboronates were the major products, while Liu's conditions were aligned with higher stereocontrol over the alkene geometry due to the Fe-embedded chair transition state. Interestingly, Qu's protocol required external Brønsted acid, H_3BO_3, for hydroxy group activation; however, a catalytic quantity of Lewis acidic iron was sufficient in the other case.

Recently, a heterogeneous deoxygenative borylation reaction of allylic and benzylic alcohol was accomplished by Shishido, Miura and their colleague by means of TiO_2-supported gold nanoparticles (AuNPs) (Fig. 1C) [57]. Since this AuNP catalyst was designated primarily for acetate borylation, only examples of cinnamyl alcohol and *p*-anisyl alcohol were shown, which might be converted *in situ* to the OBpin intermediates via hydrogen evolution to facilitate the C–O borylation.

Comparing the fruitful achievement of allylic alcohol borylation, the same transformation with benzyl alcohols was less investigated until Shi's 2015 discovery (Fig. 1D) [58]. In their work, a variety of naphthylmethanols were borylated using a simple palladium catalyst and bidentate phosphine. Similar conditions with the addition of Ti(IV) additive could include the less reactive benzyl alcohols in the scope, which constituted one of the rarely known catalytic systems that could manage the direct deoxygenative borylation of benzyl alcohols. Enlightened by Shi's work, the group of Marder and Szabó uncovered a copper version of benzyl alcohol deoxy-borylation using a chelating phosphine ligand with a large bite angle (Fig. 1E) [59]. Notably, allylic alcohols were also effective substrates with this copper catalyst at lower temperatures.

Similar Cu-catalyzed borylation manifold with the variation of additive, solvent and temperature could lead to a divergent synthesis of alkyl-, vinyl- and allenylboronic acid derivatives from propargyl alcohols, which was reported by the group of Marder and Szabó as well as the one of Ye independently (Fig. 1F) [59–61]. General mechanistic traits included the formation of a Cu–B complex and a Ti(IV)-coordinated propargyl alkoxide. The reaction outcomes were determined by the specific reaction conditions and partially by the structural properties of the substrates.

Metal-free deoxy-borylation of allylic alcohols

The prosperous development of metal-catalyzed direct deoxygenative borylation brings about the curiosity in metal-free deoxy-borylation [62]. Foreseeably, conditions used to break the alcohol C–O bonds without the assistance of metal catalysts could be harsh. Although the Lewis acidic trivalent boron reagent could alleviate the problem to some extent, substrate scope in this area was still restricted to allylic alcohols only.

In this context, Fernández and Szabó et al. co-developed a base-catalyzed direct deoxygenative borylation reaction of tertiary allylic alcohols, which was promoted by the "ate" complex made of B_2pin_2 and Cs_2CO_3 via

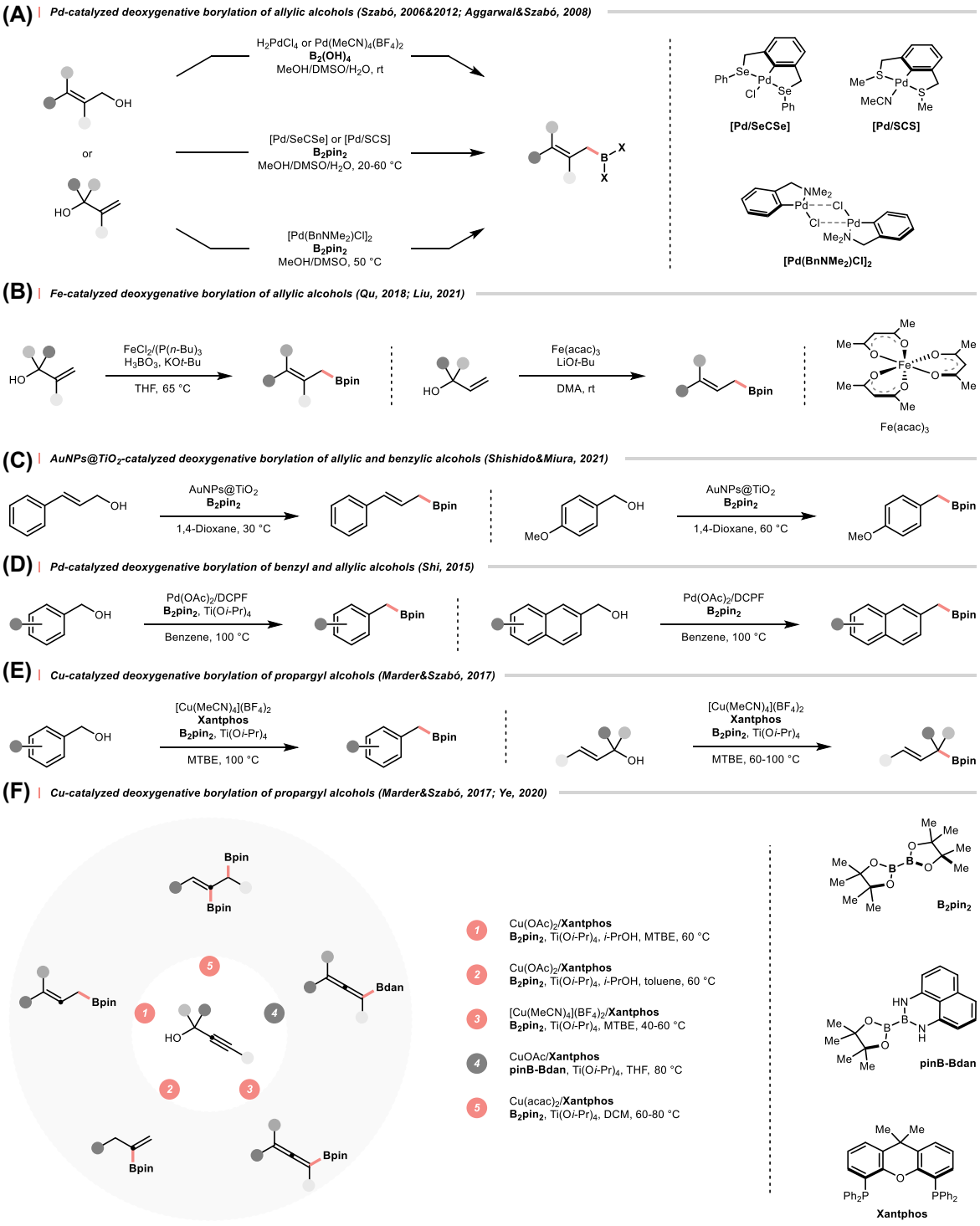

Fig. 1: Metal-catalyzed deoxygenative borylation of alcohols. DMSO, dimethylsulfoxide. B_2pin_2, bis(pinacolato)diboron; Bn, benzyl; THF, tetrahydrofuran; DMA, *N*,*N*-dimethylacetamide; Acac, acetylacetonate; OAc, acetate; DCPF, 1,1′-bis(dicyclohexylphosphino)ferrocene; MTBE, methyl *tert*-butyl ether; Xantphos, 4,5-bis(diphenylphosphino)-9,9-dimethylxanthene.

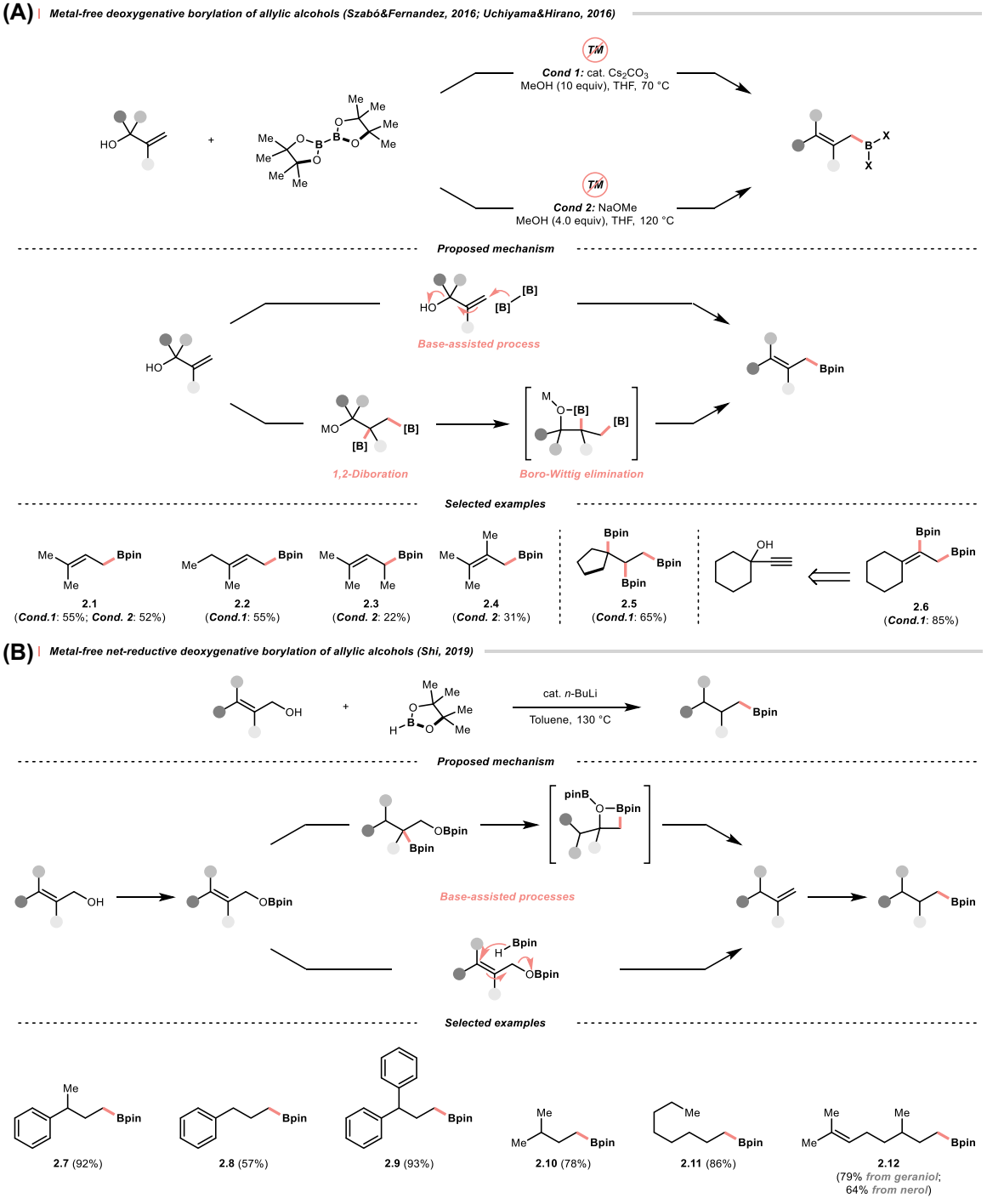

Fig. 2: Metal-free deoxygenative borylation of alcohols. THF, tetrahydrofuran.

S_N2' fashion (Fig. 2A) [63]. Concurrently, Uchiyama and Hirano et al. [64] found an identical transformation using a stoichiometric amount of NaOMe (Fig. 2A). Density functional theory (DFT) calculation compared the routes of S_N2' and diborylation followed by boron-Wittig elimination, indicating that the latter might experience a less energetic profile.

Impressively, Fernández's conditions could also give highly valuable 1,2,3-tris(boronates) products, which presumably originated from the follow-up alkene diborylation with the excessive B_2pin_2 after forming the nascent allylboronate. Moreover, propargyl alcohols could be diborylated with this protocol.

Using H-Bpin as the borylating reagent and catalytic *n*-BuLi, reductive relay hydroboration of allylic alcohol reaction was accomplished by Shi's group (Fig. 2B) [65]. The reaction started from the formation of the OBpin borate, which could undertake either a hydroboration/boron Wittig reaction sequence or an S_N2' hydride attack to give the terminal alkene intermediate. *Anti*-Markovnikov hydroboration will give the desired product. Such a reductive tandem reaction was complementary to previous approaches that gave allylboronates, resulting in an array of linear-chain aliphatic boronates in good yields.

Deoxy-borylation of phenols

Direct deoxygenative borylation of simple phenols remains hitherto unknown, while many indirect methods have been investigated successfully with some activated derivatives like triflates (Fig. 3) [66, 67]. Classic Miyaura-type aromatic borylation failed with free phenol owing to the strong C(sp^2)–O bond (BDE = 111 kcal/mol) and acidic phenolic hydrogen (p*K*a = 10). Despite these hurdles, Shi and his co-workers realized an unprecedented direct deoxygenative borylation of naphthol under nickel/*N*-heterocyclic carbene (Ni/NHC) catalysis [58]. Commercially available Ni(0) precursor was bound with a bulky NHC ligand, which borylated the 2-naphthol with B_2pin_2 in the absence of base. Unfortunately, the reaction efficiency was modest and other substrates, especially phenol, were unexplored.

Ether deoxygenative borylation

The abundance of naturally occurring ether makes it an equally important entity like alcohol in the regime of deoxygenative borylation. The close C–O bond strength in alcohol and ether indicates a similar extent of difficulty for deoxygenation. Although the C–O bonds in both compounds share some chemical similarities, the deoxygenative systems differ considerably. The lack of alcoholic hydrogen could minimize some related issues; however, regioselective C–O cleavage of ethers merits extra consideration.

Deoxy-borylation of ethers for aromatic boron compound synthesis

Aryl ethers were challenging aromatic electrophiles in organometallic chemistry due to the strong C(sp^2)–O bonds and poor leaving ability of alkoxides. For diary ethers, differentiation of sites for metal borylation was proved difficult, which could entail decreased yields and purification problems. To address these issues, Chatani, Tobisu and their co-workers pioneered the field by developing an Rh-catalyzed deoxygenative borylation with aryl 2-pyridyl ethers, wherein the coordination of pyridine nitrogen was found essential for the

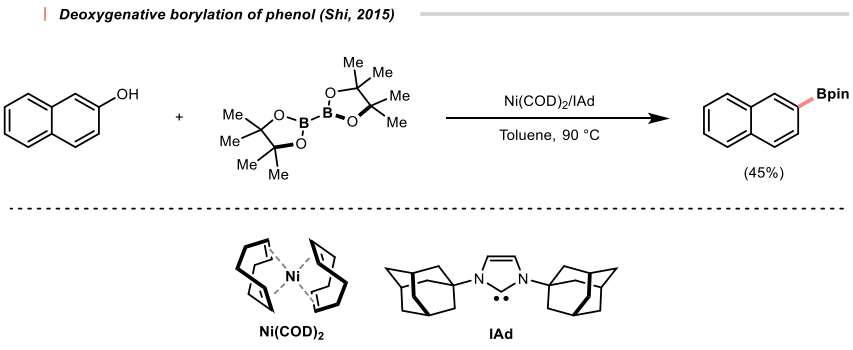

Fig. 3: Deoxygenative borylation of phenol. COD, 1,5-cyclootadiene; Ad, 1-adamantyl.

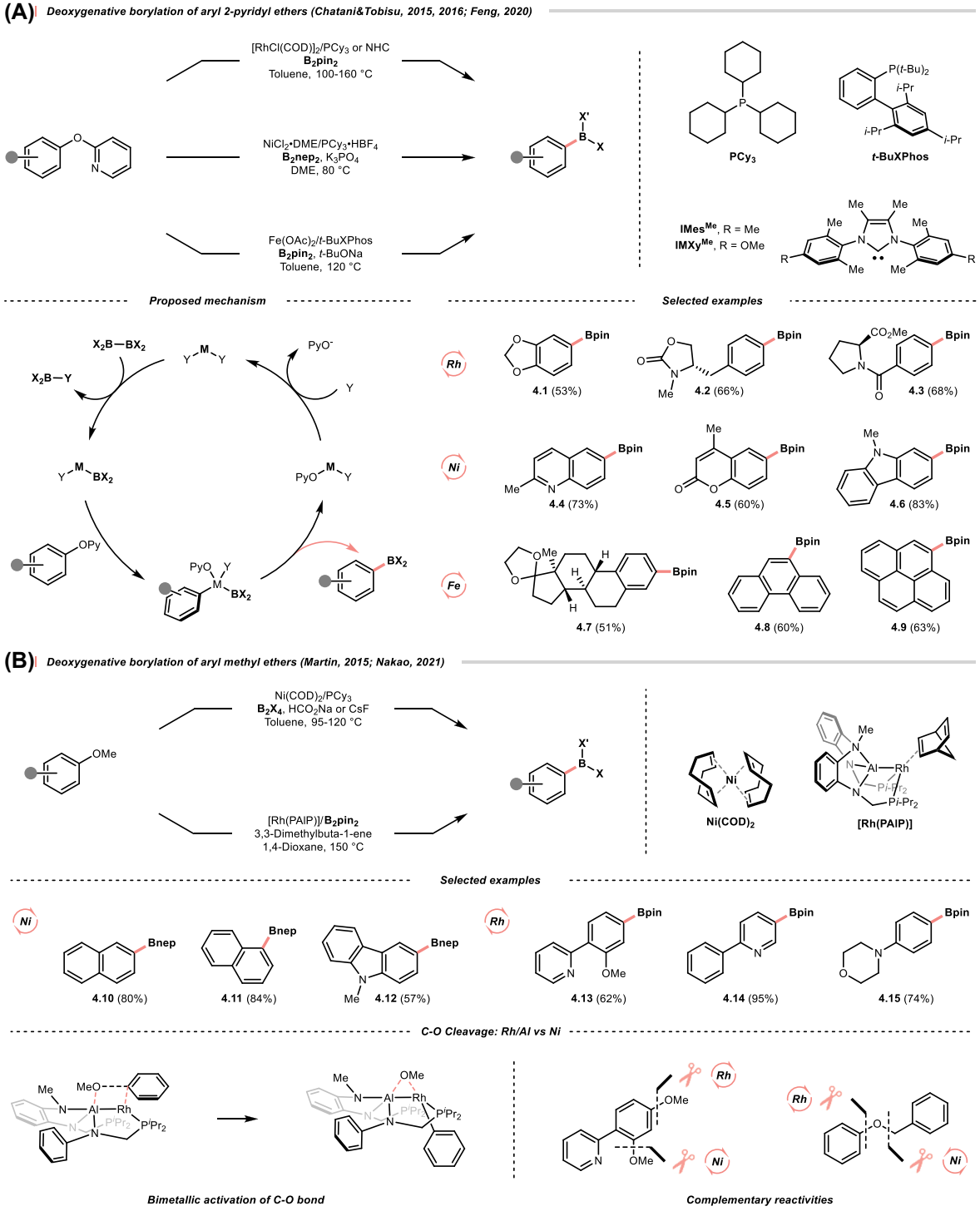

Fig. 4: Deoxygenative borylation of ethers for aromatic boron compound synthesis. COD, 1,5-cyclootadiene; NHC, *N*-heterocyclic carbene; DME, 1,2-dimethoxyethane; OAc, acetate; *t*-BuXPhos, 2-di-*tert*-butylphosphino-2′,4′,6′-triisopropylbiphenyl; B_2nep_2, bis(neopentylglycolato)diboron; Cy, cyclohexyl.

desired reactivities while minimizing the substrate decomposition (Fig. 4A, upper eq) [68]. Low-valent metal catalyst and electron-rich bulky ligand were the other two parameters that ensured the success of this transformation since they facilitated the C(sp^2)–O oxidative addition and enforced the product-forming

C(sp^2)–B reductive elimination. Such a novel approach provided not only an effective route for arylboronate synthesis but also repurposed the utility of the 2-pyridyloxy group, which was originally designed for metal directionality.

Guided by the same logic, Chatani and Tobisu et al. [69] presented another aromatic deoxy-borylation strategy by nickel catalysis (Fig. 4A, middle eq). Simple Ni(II) salt and trialkylphosphine ligand were combined, which afforded a similar scope of aromatic boronates but at a lower reaction temperature and chemical cost. It was worth mentioning that both catalytic methods developed were also applicable to the analogous benzyl ethers.

Inspired by these two elegant precedents, Feng's group contributed an Fe-catalyzed deoxygenative borylation reaction with the same pyridyl ethers (Fig. 4A, lower eq) [70]. Consistent with the Ni-catalyzed conditions, phosphine ligand and strong base were required. A broad range of ethers, which eventually derived from phenols, could be borylated in Feng's case, although applying the same conditions to aniline derivatives resulted in unsatisfactory yields of deaminative products.

Anisole and its derivatives could be obtained from lignin depolymerization; therefore, it is conceived as an ideal aromatic electrophile from renewable sources. Toward the direct deoxygenative borylation of aryl methyl ethers, nickel and rhodium stand out again as optimal catalyst options. In 2015, Martin and his colleagues disclosed a ground-breaking direct *ipso*-borylation reaction for naphthyl or aryl methyl ethers via deoxygenation (Fig. 4B) [71]. A unique promotive effect was observed with HCO_2Na as the base additive, and subtle sterics explained the higher reactivity with $B_2(nep)_2$ tentatively.

Nakao's group reported an alternative approach to enable this tough transformation via ligand design (Fig. 4B) [72]. The rhodium was paired with an aluminyl ligand to form a heterobimetallic complex, which catalyzed the deoxy-borylation of different anisoles. A sacrificial trisubstituted alkene was added as the scavenger of HBpin, which was derived from an unidentified side reaction. Interestingly, this rhodium catalysis demonstrated complementary regioselectivity to nickel due to the metal-ligand cooperation in the former. Lewis acidic aluminum and the bulky ligand framework collectively favor the oxidative addition at the less hindered C(sp^2)–OR. In the same work, hydrodeoxygenation was also possible with silane as the hydrogen donor.

Deoxy-borylation of ethers for vinylic and aliphatic boron compound synthesis

Deoxygenative borylation of other types of ethers parallels the aromatic ones, which could foster vinylic and aliphatic C-B bonds accordingly.

Taking advantage of nickel catalysis, Ling, Qiu and their group realized the deoxy-borylation of methyl vinyl ethers, giving various vinylboronic acid esters with high *E*-selectivity (Fig. 5A, upper eq) [73]. Switching to Cu/NHC catalyst, (allenylmethyl) benzyl ethers became viable substrates for vinylboronate preparation, which underwent a formal S_N2'-type borylation via alkoxide elimination (Fig. 5A, middle eq) [74].

In 2016, Yorimitsu et al. [75] discovered an interesting borylative ring expansion with benzofuran (Fig. 5A, lower eq). Electron-rich NHC/Ni(0) was proposed to insert into the C2–O bond, which was transmetallated with B_2pin_2 and eliminated to form the spirocyclic vinylborates. After hydrolysis, benzoxaborins were produced. Moving such a single-atom editing strategy forward, Dong's group made another breakthrough in the boron-insertion chemistry with simple ether rings by using dibromoborane and zinc dust (Fig. 5B) [75]. Mechanistically, the initial stage of this novel transformation mimicked the classic dealkylation mechanism enabled by boron trihalides, during which the bromide displacement occurred selectively at the alkyl site with the bulky mesitylborane. Subsequently, nickel catalyzed the reductive borylation and closed the bimetallic cycles by forming oxaborinane. Noticeably, the bulky mesityl group reduced the propensity of dimerization and enhanced products' stability during purification. Under identical conditions, boron could also slip into C(sp^3)–N bond in the *N*-heterocycles.

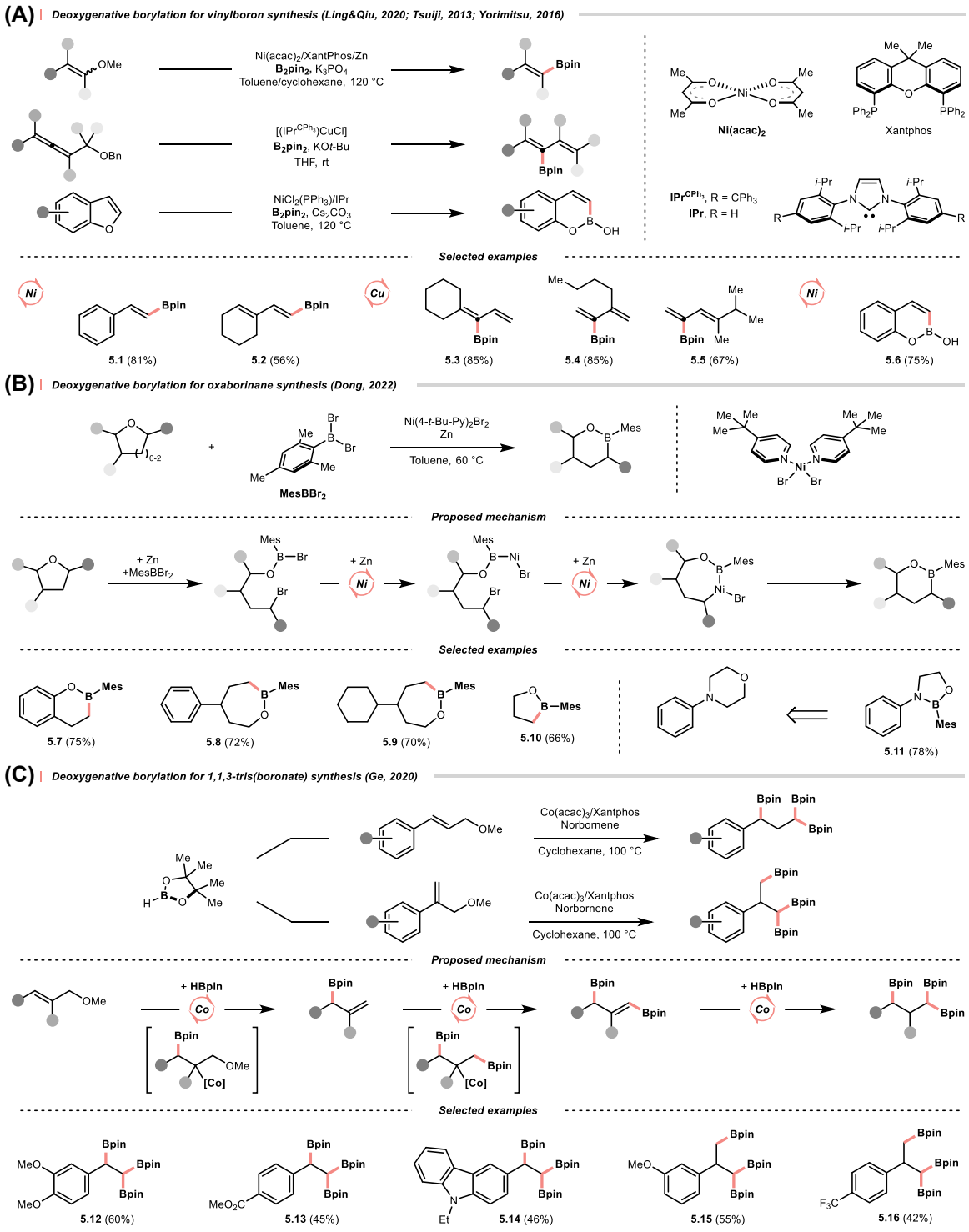

Fig. 5: Deoxygenative borylation of ethers for aliphatic and vinylic boron compound synthesis. Acac, acetylacetonate; Xantphos, 4,5-bis(diphenylphosphino)-9,9-dimethylxanthene; B_2pin_2, bis(pinacolato)diboron; 4-*t*-Bu-Py, 4-*tert*-butylpyridine; Mes, mesityl.

Multiboronates are important building blocks in synthetic planning due to the rich boron chemistry. Importantly, it could streamline deborylative transformations sequentially and selectively. Among them, 1,1,3-tris(boronates) remained elusive until the disclosure of Ge's Co-catalyzed deoxygenative triboration with

cinnamyl methyl ethers (Fig. 5C) [76]. The Bpin groups were installed stepwise, during which the allylboronate was believed to be a competent intermediate. Afterward, *gem*-diboration at the remote position was catalyzed by cobalt, and norbornene behaved as the terminal oxidant.

Aldehyde and ketone deoxygenative borylation

Carbonyl groups (C=O) of aldehyde and ketone consist of one C–O σ bond and one C–O π bond; therefore, it poses an additional challenge for the deoxygenative hydroboration or diboration at the carbonyl carbon. Oftentimes, *α*-hydroxylboronates were the final products, emphasizing the challenge of complete deoxygenation [77–82]. Typically, deoxygenative borylation is achieved by activating the carbonyl substrate *in situ*, which could undergo borylation with relative ease.

General methods for deoxy-borylation of aldehydes and ketones

Vicinal diboration of alkenes by diboron is well-established for aliphatic boronate synthesis. In contrast, the analogous 1,2-diboration of carbonyl remained sluggish despite the structural similarity of C=C and C=O bonds. Presumably, this pivotal step could bring a highly activated *C*,*O*-diborylated intermediate, which not only reduces the C=O bond order but also facilitates the subsequent C–O cleavage due to the presence of two neighboring trivalent boron atoms.

Based on this assumption, Liu's and Li's groups presented two different strategies to achieve the deoxygenative borylation of aldehydes and ketones (Fig. 6). In 2019, Liu and his co-workers established a direct deoxygenative diboration for aldehydes and ketones with simple B_2pin_2 under Cu/NHC catalysis (Fig. 6A) [83]. This novel borylation reaction takes full advantage of the bis-electrophilicity of carbonyl compounds and could also be extended to an unprecedented silylborylation with pinB-$SiMe_2$Ph. Mechanistically, such a deoxygenative difunctionalization involved a Cu-catalyzed C=O 1,2-diborylation step followed by a borylative migratory substitution assisted by a base. The former step was initially studied by Sadighi et al. [78, 84] and later computed by Lin's and Marder's group collaboratively [85–87]. Harnessing Liu's conditions, a wide range of *gem*-diboronates and -silylboronates could be obtained from simple carbonyl starting materials. Impressively, small-molecule ketones (e.g., acetone) were also viable substrates, which remained unfeasible by conventional means.

Capitalizing on the same *C*,*O*-diboronate, slight condition modification could channel the original diborylation reactivity towards either deoxygenative hydroboration or carboborylation smoothly, further expanding the repertoire of deoxy-borylative transformations of aldehydes and ketones (Fig. 6B and C). However, the latter proceeded at the expense of separate steps of introducing carbon nucleophiles. Very recently, such deoxygenative logic was further enriched by Xu's group, who combined the Cu-catalyzed aldehyde diborylation and Ni reductive metallaphotoredox cross-couplings for the *α*,*α*-dialkyl boronates synthesis [88].

Encouraged by Liu's elegant studies, particularly the base-mediated migratory substitution of *C*,*O*-diboronates, Li and his colleague conceived a similar scenario wherein the first vicinal borylation was under reagent control, therefore, eliminating the metal catalysts from the overall deoxygenative borylation (Fig. 6D) [89]. The key finding in Li's case was a uniquely enabling diboron reagent, B_2cat_2, which unified the strong Lewis acidity and oxophilicity, promoting the formation of various benzylboronates from substituted benzaldehydes and aryl ketones via deoxygenation [17, 90]. Interestingly, a divergent reaction outcome was observed when subjecting the aliphatic substrates to similar reductive borylation in an anhydrous coordinating solvent, which exclusively gave 1,1,2-tris(boronates) as highly useful products.

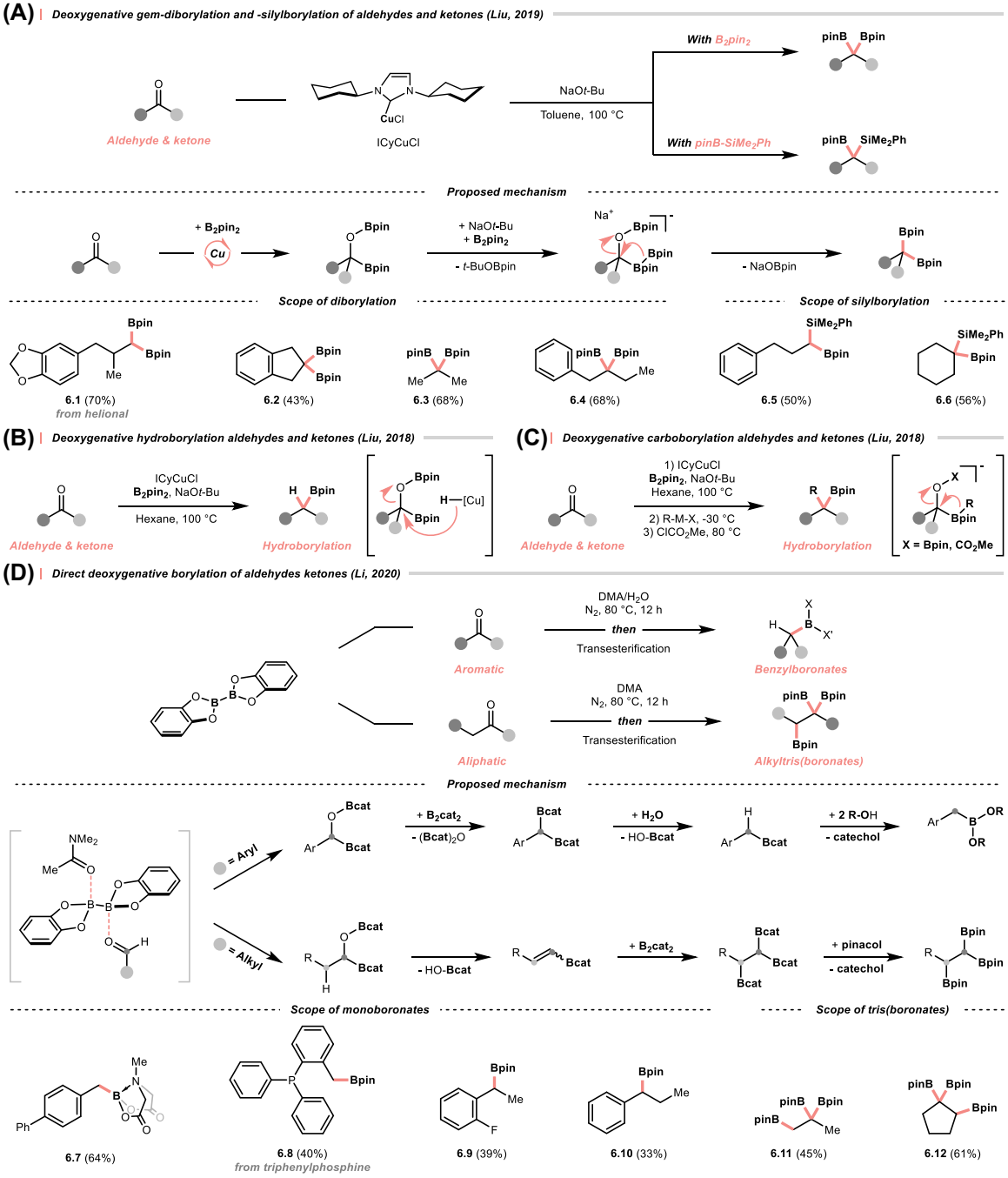

Fig. 6: General methods for direct deoxygenative borylation of aldehydes and ketones. B_2pin_2, bis(pinacolato)diboron; DMA, *N*,*N*-dimethylacetamide; B_2cat_2, bis(catecholato)diboron. Only key steps in the mechanism were shown. See the original papers for detailed description.

In Li's tentative mechanism, the unique solvent effect led to the assembly of a putative ternary boron complex. Consistent with Liu's proposal, 1,2-diborylation, migratory bora-substitution and protodeboronation with H_2O will give the monoboration reactivity. Under an analogous mechanistic framework, vinylboronate could be derived via elimination, which was diborylated to deliver the tris(boronate).

Methods for deoxy-borylation of ketones

Ketone deoxygenative borylation could be operated via alkene or enolate by other means. For the former, Zhao's group launched a systematic study of Rh-catalyzed deoxygenative borylation of ketones, which could offer various mono-, di- and tris(boronates) selectively (Fig. 7A) [91, 92]. By fine-tuning the reaction conditions with ligand choice, borylating reagent and base additive, alkylboronates, vinylboronates,

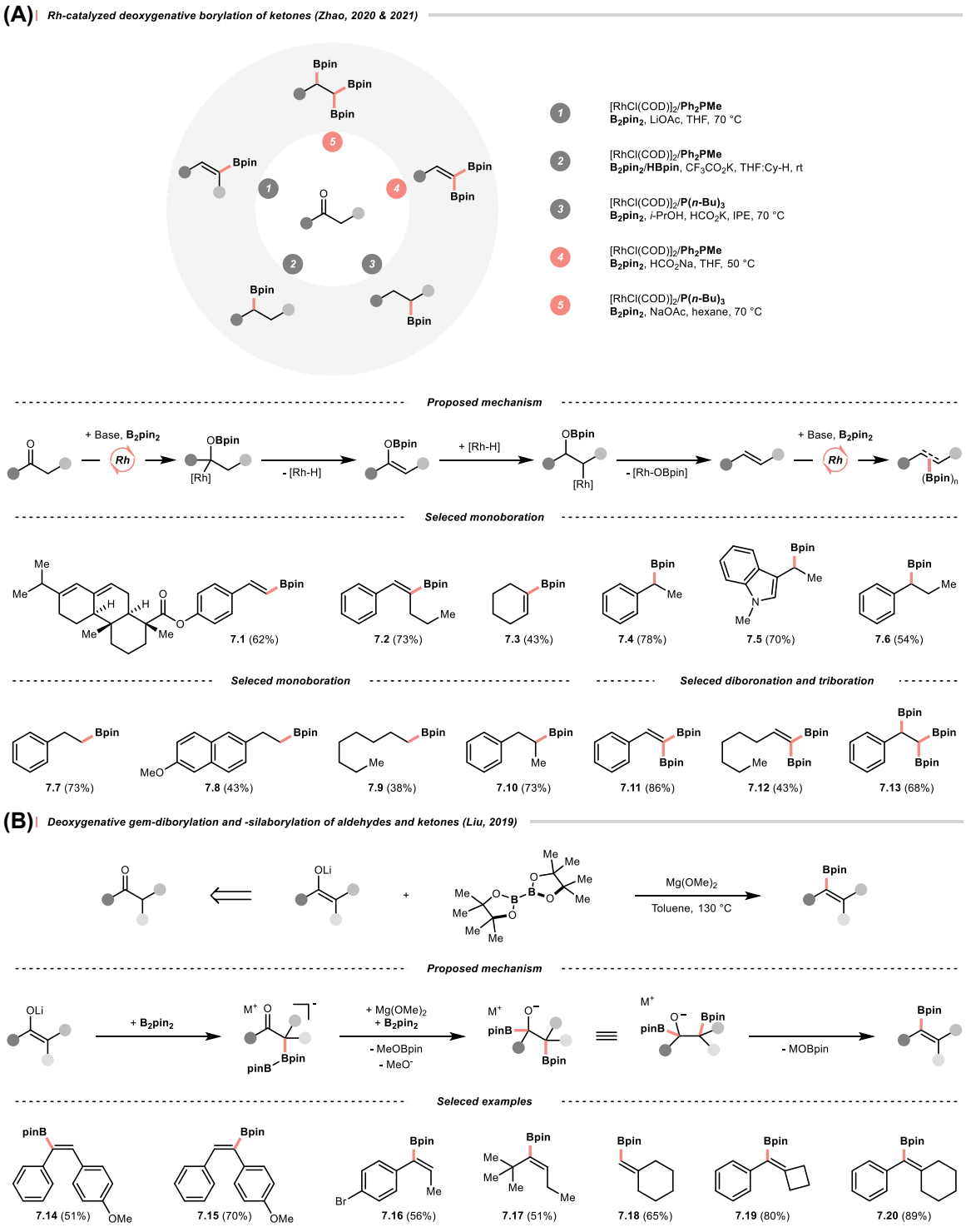

Fig. 7: Deoxygenative borylation of ketones. COD, 1,5-cyclootadiene; B_2pin_2, bis(pinacolato)diboron. IPE, 2-isoproproxypropane.

1,1-vinyldiboronates, and 1,1,2-tris(boronates) could be acquired from simple ketones with high chemo- and regioselectivity, which was governed by the ligated rhodium. In Zhao's case, the alkene intermediate was validated experimentally and computationally, which resulted from the deoxygenative desaturation under rhodium catalysis. Subsequently, the alkene was borylated under a similar catalytic manifold to provide the desired products.

Alternatively, the ketone deoxygenative borylation could be conducted without transition metals. In 2019, Liu's group contributed a stepwise deoxy-borylation protocol using the ketone-derived enolates (Fig. 7B). Assisted by the Lewis acidic $Mg(OMe)_2$, which might enhance the polarity of C=O, thereafter, the propensity of boron migration, the enolate was converted into an *α*,*β*-borylated alkoxide. This set the stage for a highly stereoselective boron-Wittig reaction and afforded the numerous trisubstituted and tetrasubstituted vinylboronates. Notably, a one-pot deoxygenative borylation reaction of free carboxylic acid was also described in the same work, wherein the acid was transformed into an *O*-borylated enolate (vinylborate) upon the cooperative action of *α*,*α*-diboroalkane and MeLi [93]. Later, the vinylborate was deoxygenated, giving the (*Z*)-vinylboronate as the major product.

Deoxygenative borylation of carboxylic acids and esters

Decarboxylative and decarbonylative borylation dominated the synthetic practice of organoboron from the derivatives of carboxylic acids and carboxylates. In contrast, direct deoxygenative borylation of this class of oxygenated compounds considerably lags behind due in part to the prohibitively high overall energy barrier of cleaving three C–O bonds for exhaustive deoxygenation. Besides, the carboxylic hydrogen is incompatible with most basic and reducing conditions, while they are common in borylation protocols. Although the highly oxidized carboxylic carbon provides opportunities for accessing intermediates in lower oxidation states and setting the stage for tandem borylation by the means mentioned above, strong reductants demanded for the initial reduction often lead to over deoxygenation and other off-target issues. To this end, a borylation system with robust and balanced reducing capability is required to confront this challenge, which could be resolved by either reagent or catalyst development.

Challenged by this perception, Li's group conceived a reagent-enabled stepwise deoxygenation scenario for free carboxylic acids, which were firstly degraded into a more reactive carbonyl intermediate via deoxygenation and further subjected to consecutive reductive borylation (Fig. 8A). For this purpose, a novel deoxyborylation protocol was established for free carboxylic acids or their sodium salts based on their prior efforts on carbonyl reductive borylation [94]. B_2cat_2 was identified as the only viable reagent in this case, which effected the acid C–O borylation in a more robust amide solvent (hexamethylphosphoramide, HMPA) and at a slightly higher temperature (100 °C). Consistent with their previous report, divergent reactivities were observed as benzoic acids or sodium benzoates gave benzyl monoboronates while aliphatic substrates (e.g., acetic acid) offer 1,1,2-(trisboronates). Mechanistically, B_2cat_2 served as both the oxygen transfer agent and boron source, and acylboron might be involved as a key intermediate, which underwent selective deoxy-borylation depending on its substitution patterns. Moreover, such a novel paradigm opened access to some unique boronates (e.g., structurally complex or isotope-labeled ones) that were of conceivable challenges under the conventional manifold.

Through advancing their Cu-catalyzed deoxy-borylation system for aldehydes and ketones, Liu's group realized the direct conversion of various carboxylic esters to *α*-diboronates under iron catalysis [95] (Fig. 8B). By fine-tuning the alkoxide additive and alcoholic source, the esters could be hydrogenated into aldehydes. By suppressing the formation of excessive Fe-H species, therefore, minimizing the overreduction, the subsequent *gem*-diborylation occurred smoothly. With the optimal combination of NaO*t*-Bu and EtOH, simple and complex esters could be diborylated easily, providing a library of *gem*-diborylated alkanes that were otherwise challenging to prepare based on the prior art. Interestingly, reductive hydroborylation biased the aliphatic esters over aromatic ones under Liu's conditions.

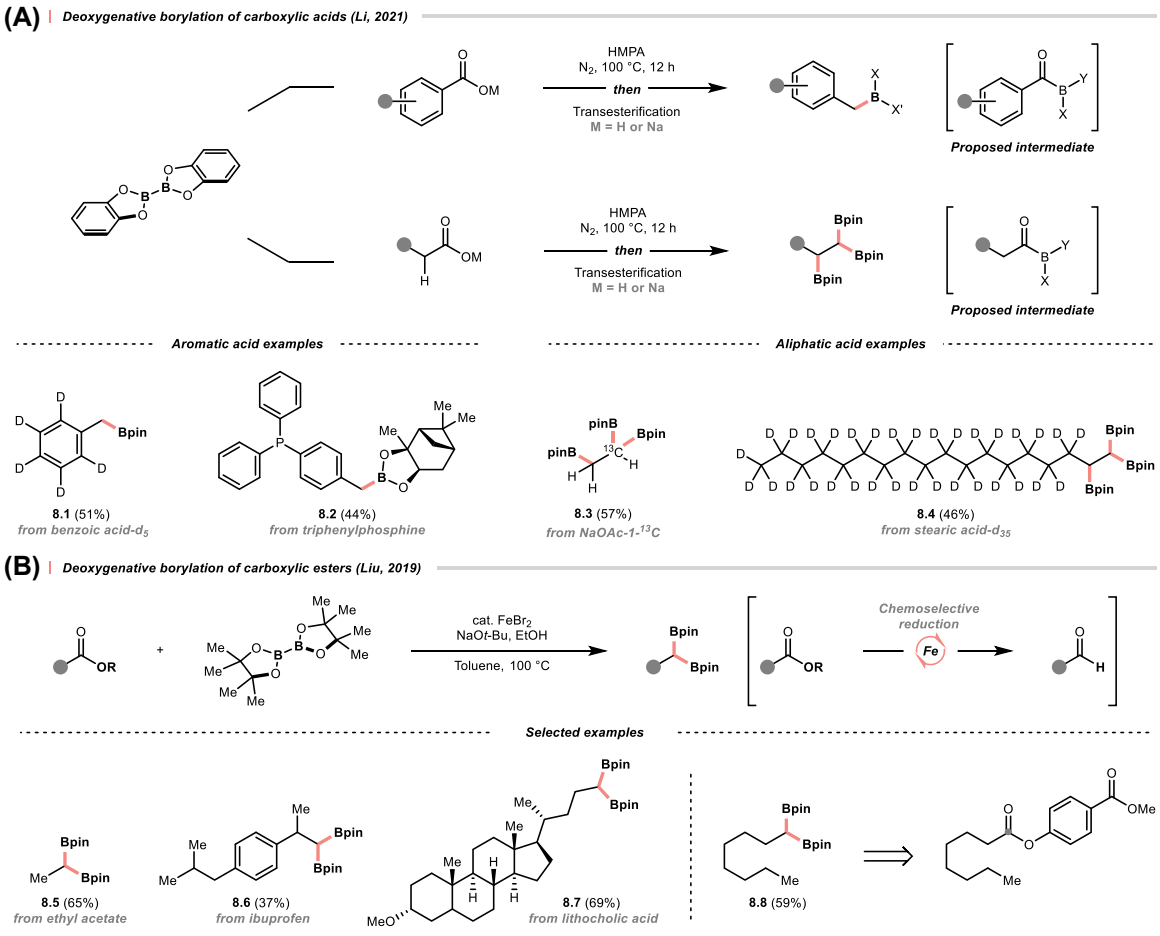

Fig. 8: Deoxygenative borylation of carboxylic acids and esters. HMPA, hexamethylphosphoramide; B_2cat_2, bis(catecholato) diboron.

Conclusion

Direct deoxygenative borylation is of high interest in academic and industrial settings, representing one of the stepping stones for the science community toward future sustainability. This review covers the direct deoxyborylation of earth-abundant oxygenated feedstocks in the recent 20 years and arranges them by alcohols, ethers, aldehydes/ketones, carboxylic acids/esters, which have progressively increased numbers of C–O bonds and, in principle, more difficulties for complete deoxygenation. In each category, substrate scope and mechanistic features were emphasized for some significant contributions and selected works. The similarities and differences of the key conditions and mechanistic traits between each class of collected examples were discussed.

En route to a more fruitful toolkit of direct deoxygenative borylation with higher reaction efficiency and broader substrate scope, some obstacles need to be surmounted in the next decades. In general, these paradigms still mandate high temperatures and strong bases. Simple and complex oxygenated molecules, especially alcohols and phenols, are beyond the reach of the current mainstay. Moreover, enantioselectivity is considerably underexplored in this field, although the asymmetric borylation of activated derivatives via deoxygenation, decarbonylation and decarboxylation has gained popularity in chiral organoboron synthesis. These limitations have compromised the wider uptake of direct deoxygenative borylation in various fields.

Toward this end, new thoughts on the catalyst and reagent design and modern technologies (photochemistry, electrochemistry and biocatalysis, among others) are worth of continuous research efforts. Since these oxygenous compounds are interchangeable through redox manipulation, systems featuring unified conditions could be envisioned, which could upgrade these promising yet underutilized feedstocks for the rapid buildup of the organoboron library. More importantly, during this exploration, the functionalization and defunctionalization logic might be applicable to other related interesting starting materials.

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