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1,4-氮硼杂芳环在有机和过渡金属催化中的应用

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摘要 总结了1,4-氮硼杂芳环在有机和过渡金属催化中的最新进展, 涵盖三部分内容: 一是简要介绍了1,4-氮硼杂芳环的发展历史; 二是重点介绍了 1,4-氮硼杂芳环作为有机小分子催化剂在光致氧化三芳基膦中的应用; 三是详细阐述了1,4-氮硼杂芳环作为配体在钯催化的烯炔的立体选择性硼化反应中的应用. 此外, 对这一领域的未来发展进行了展望.
关键词 1,4-氮硼杂芳环; 过渡金属; 光致氧化; 有机催化

Application of 1,4-Azaborines in Organic and Transition Metal Catalysis

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Abstract The recent progress of 1,4-azaborines in organic and transition metal catalysis is summarized, which consists of three parts. The first part briefly describes the history of 1,4-azaborines, the second part emphasizes on the application of 1,4-azaborines as an organocatalyst in the aerobic photooxidation of triaryl phosphines, and the last part discribes the use of 1,4-azaborines as the ligand in palladium-catalyzed stereoselective borylation of enynes. The future direction of this field is also proposed.
Keywords 1,4-azaborine; transition metals; photooxidation; organocatalysis

1 Introduction

Boron is an element of great importance in modern synthetic chemistry, as evidenced by three Nobel laureates William Lipscomb (1976),[1] Herbert C. Brown (1979),[2] and Akira Suzuki (2010)[3] with their contributions in boron chemistry. In most targeted synthetic applications, the boron atom is typically used as the activating partner in cross coupling reactions. Recently, the incorporation of a boron atom in the functional structures has become another important arsenal.[4] Due to the unique electronic properties and its ability to form covalent bonds with carbon, the inclusion of boron atom in organic flameworks has received increasing attention. In this regard, BN/CC isosterism, namely, replacement of a CC unit with an isoelectronic and isosteric BN unit, has emerged as a viable strategy to expand the chemical space of organic molecules. In this way, BN/CC isosterism of arenes or BN-heteroarene, has advanced research in the fields of biomedical research, materials sciences, and energy storage.[5-14] BN-heteroarenes that are isoelectronic with benzene and which contain only one BN unit are particularly interesting. This substitution pattern leads to three possible isomers, 1,2-azaborine,[15] 1,3-azaborine,[16-17] and 1,4- azaborine[18-20] (Scheme 1A). Thanks to modern synthetic methods, examples of each isomer have now been synthesized. Among these, 1,2-azaborine has been extensively studied since 1960s while people pay less attention to the other two presumably due to the shortage of available synthetic methods. Given that there are many reviews for 1,2-azaborines and only a few examples of 1,3-azaborines were reported, this review mainly focuses on 1,4-azaborines, with emphasis on its recent application in catalysis starting from the year of 2014.

2 Brief history of 1,4-azaborine

Compared to 1,2-azaborines, 1,4-azaborines received less attention although the first example of 1,4-azaborines and the representative structures were summarized in Scheme

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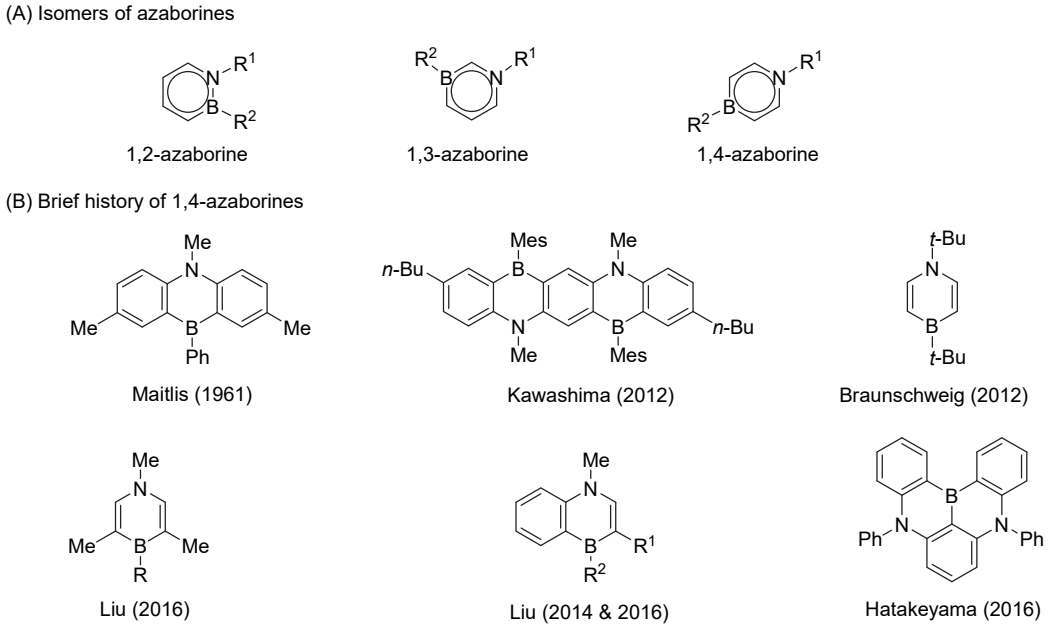


Scheme 1 Isomers of azaborines (A) and brief history of 1,4-azaborines (B)

1B, dibenzo-fused 1,4-azaborine (DBAB) could be traced back to 1961.[21] Almost 30 years later, the second molecule of DBAB was revealed by the group of Clark and its solid-state structure was unambiguously confirmed by X-ray diffraction analysis. In 2006, Kawashima and coworkers[22] reported a polycyclic ladder-type 1,4-azaborine which contains two units of 1,4-azaborine core. It was not until 2012 the group of Braunschweig[20] disclosed the first example of non-fused 1,4-azaborine enabled by an elegant transition metal-mediated [2+2+2] cycloaddition. Later, Liu and coworkers[18] revealed a solid route using dilithiation method to access non-fused 1,4-azaborine. The first example of monobenzo-fused 1,4-azaborine was also developed by the Liu group, using the key step of ring-closing metathesis (RCM).[23] In 2016, they developed a general and easy-to-scale-up route with the involvement of electrophilic cyclizative borylation, to afford monobenzo-fused 1,4-azaborine.[24] Since the concept term "multi-resonance HOMO (highest occupied molecular orbital)-LUMO (lowest unoccupied molecular orbital) separation" was demonstrated by the group of Hatakeyama for 1,4- azaborine,[25] its use in electroluminescent devices has emerged as a popular topic in academic and industrial research. Recently, its use in catalysis has also received considerable interest.

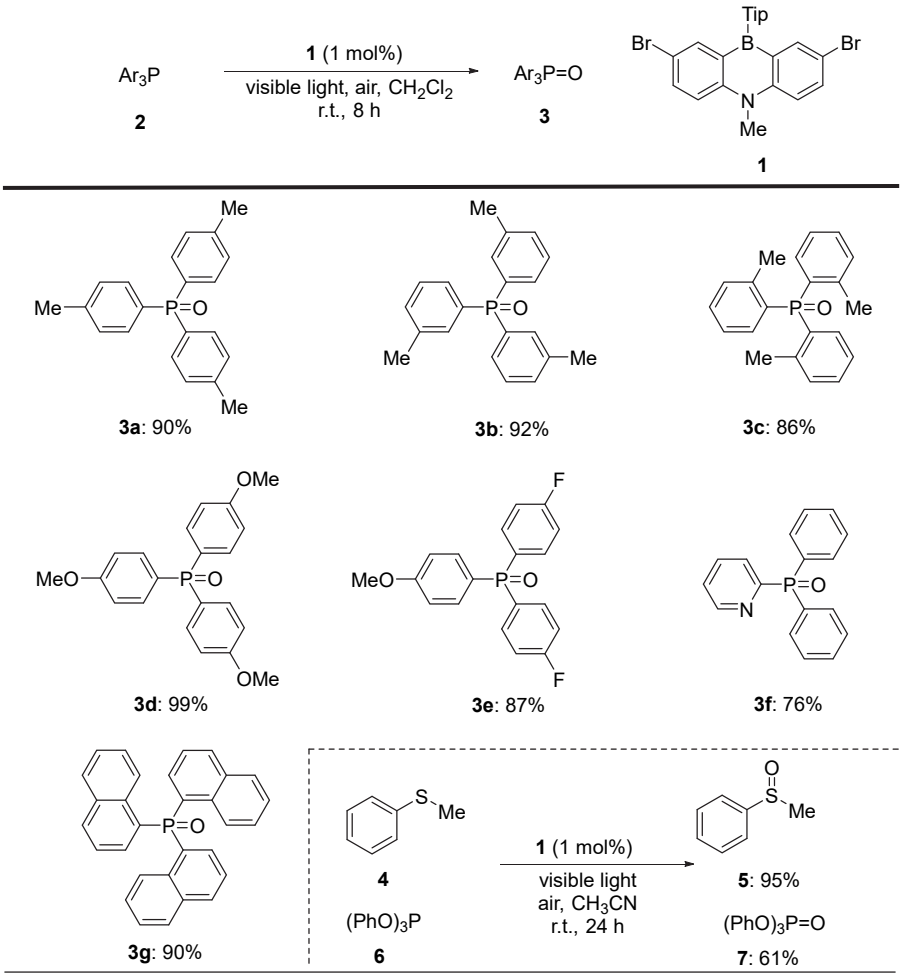
3 1,4-Azaborines as the organocatalyst

Recently, Kondo and Agou[26] found that DBAB could also be used as an organic photocatalyst in aerobic photooxidation of triarylphosphines in an aprotic solvent. Under the irradiation of visible light, the reaction proceeded smoothly in the presence of DABA **1** in air at room temperature using CH_2Cl_2 as the solvent (Scheme 2). A vast array of Ar_3P (**2**) was well-tolerated to furnish corresponding Ar_3P=O (**3**) in up to 99% yield. In addition to Ar_3P, thioanisole **4** and triphenyl phosphite **6** underwent aerobic oxidation smoothly with CH_3CN as the solvent, affording corresponding sulfoxides **5** and triphenyl phosphate **7** in 95% and 61% yields, respectively (Scheme 2). They proposed a plausible mechanism for the current aerobic oxidation of Ar_3P based on density functional theory (DFT) calculations and the literature (Scheme 3).[27] The DBAB (**1**) is excited by irradiation, converting $^3O_2$ to $^1O_2$ by an energy transfer (ET) process. $^1O_2$ is then trapped by Ar_3P (**2**) to furnish the corresponding phosphadioxrane intermediate **A**. Capture of **A** by DBAB results in the intermediate **B**, which could be subsequently attacked by another molecule of Ar_3P (**2**) to afford Ar_3P=O (**3**) with the current formation of the borate intermediate **C**. The release of Ar_3P=O (**3**) from **C** regenerates DABA (**1**) for the next catalytic cycle.

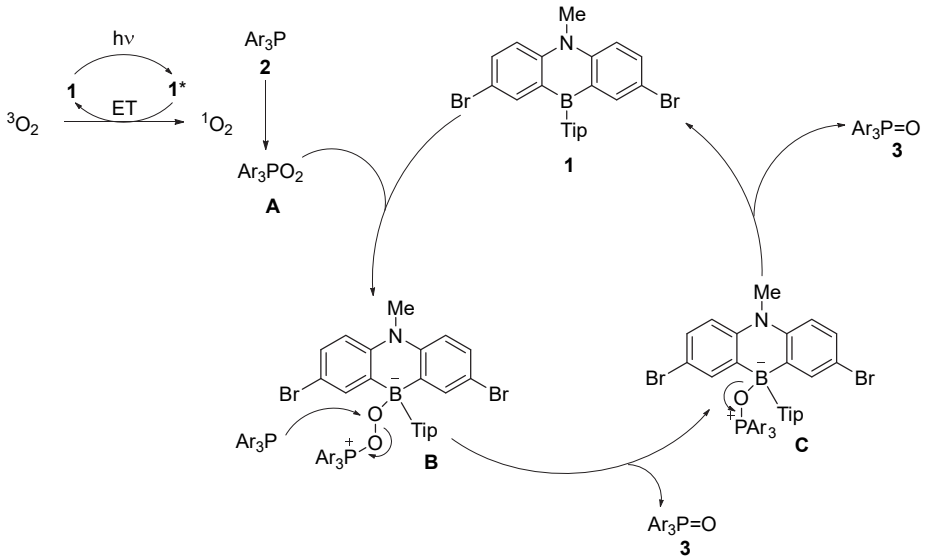
4 1,4-Azaborines as the ligand

4.1 *trans*-Hydroboration

In 2014, Liu and coworkers[23] disclosed the first example of monobenzo-fused 1,4-azaborine. As illustrated in Scheme 4, starting from commercially available 2-bromoaniline **8**, the diene intermediate **9** was synthesized within four steps. RCM reaction of **9** in the presence of 10 mol% Grubbs 2nd generation catalyst afforded 1,4-azaborine **10** in 52% isolated yield. The boron-diisopropylamino substituent in **10** could be quantitatively replaced by the methoxy group to afford **11** by treating **10** with 1.0 equiv. of MeOH. Subsequent nucleophilic attack of **11** by RLi (6-methyl-pyrid-2-lithium) followed by the treatment of trimethylsilylchloride (TMSCl) furnished **12** in 80% yield. Notably, **12** was found a dimer in the solid state, as evidenced by X-ray diffraction analysis. Interestingly, treatment of **12** with $[PtCl(\mu\text{-}Cl)(PEt_3)]_2$ followed by the addi-



Scheme 2 Selected examples for the DBAB **1**-catalzyed aerobic oxidation of Ar_3P



Scheme 3 Proposed mechanism for the **1**-catalyzed aerobic photooxidation of Ar_3P

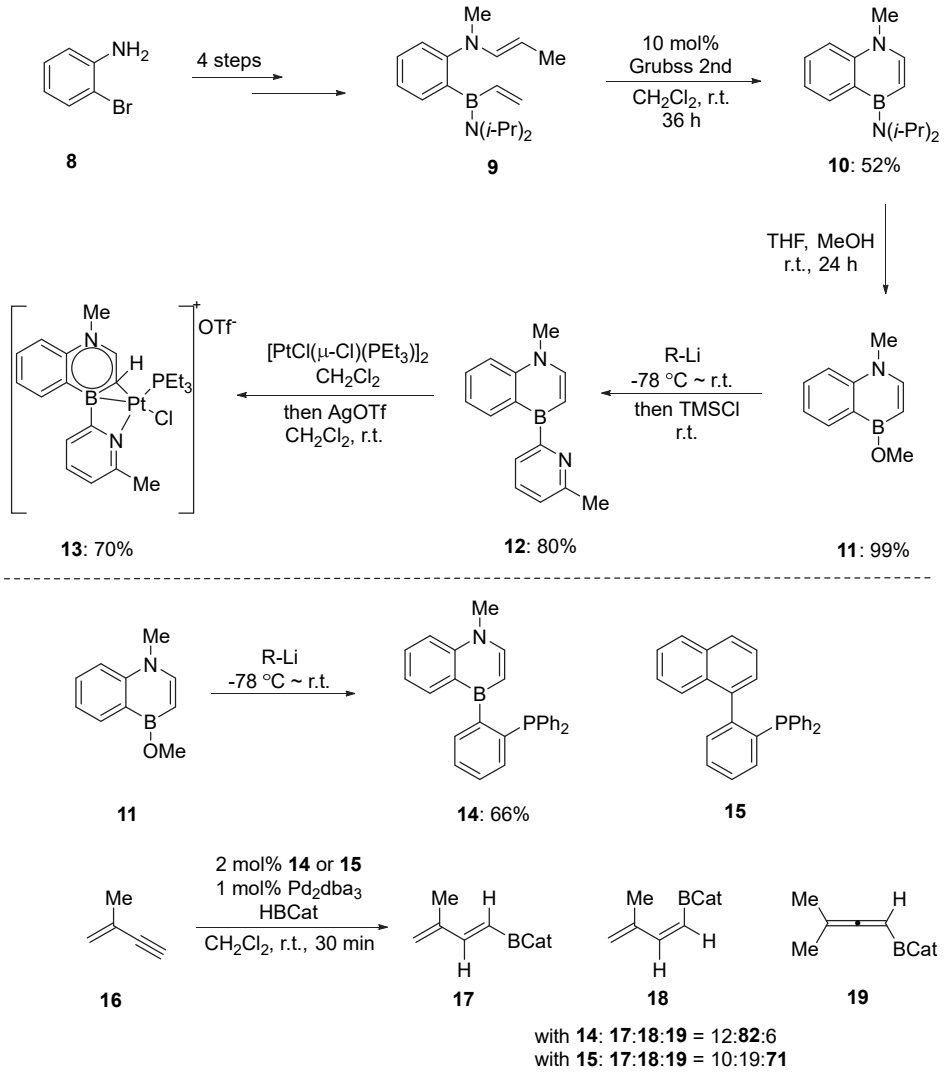
tion of AgOTf afforded κ^2-*N*-η^2-BC Pt complex **13** in 70% yield over two steps. To demonstrate the utility of the new ligand platform in organic synthesis, they synthesized a 1,4-azaborine-based phosphine ligand **14** and chose to investigate the palladium-catalyzed hydroboration of an enyne **15** as a model reaction (Scheme 4). Interestingly, the

regio- and stereoselectivities of this hydroboration largely depended on the nature of the phosphine ligand.[28] The use of **14** led to *trans*-hydroboration product **18** as the major product, while the reaction in the presence of a carbonaceous ligand **15** yielded predominantly allenylboronate **19**. Thus, 1.4-azaborine-based ligand provides a promise of offering unique selectivity that could not be achieved with other ligand architectures.

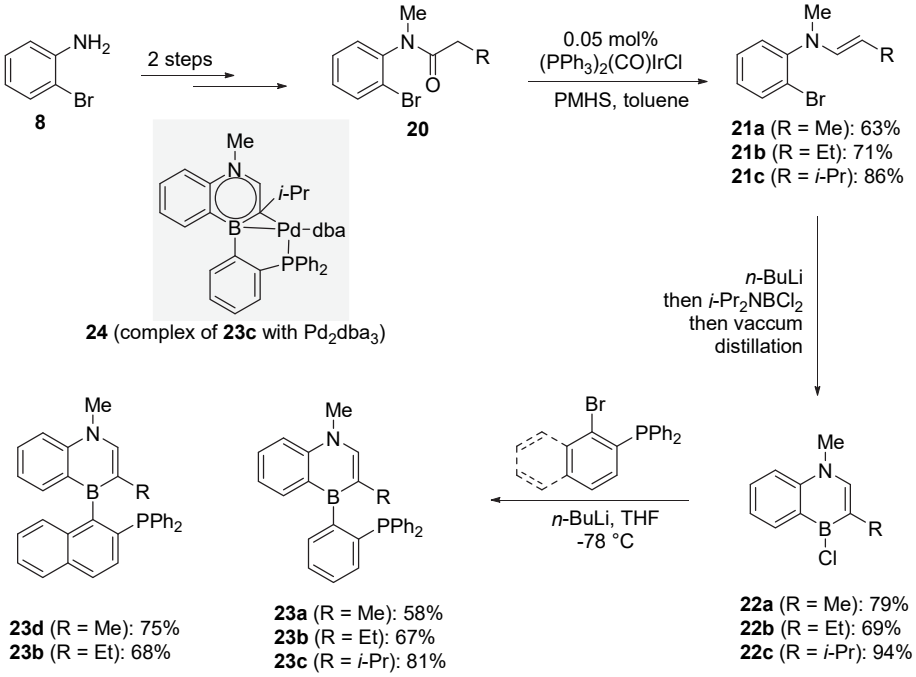
Due to the limitations of scale-up and the high cost of the relatively expensive Grubbs 2nd generation catalyst and alkene isomerization catalyst $(PPh_3)_3(CO)ClRuH$, the Liu group[24] revealed a solid pathway for monobenzo-fused 1,4-azaborine. As shown in Scheme 5, amides **20** could be derived from commercially available 2-bromoaniline **8** within two steps. In the presence of 0.05 mol% Vasaka's complex, $(PPh_3)_2(CO)IrCl$, amides **20** could be easily converted to the corresponding enamines **21** in 63%～86% yields. Boron-Cl substituted monobenzo-fused 1,4-azaborines **22** were obtained in 69%～94% yields after lithium-halogen exchange of **21** followed by the treatment of *i*-Pr_2NBCl_2. The structure of **22a** was firmly confirmed by X-ray diffraction analysis. Nucleophilic substitution of **22** with phosphine-containing lithium reagents afforded Senphos **23** in 58%～81% yields. In order to application of 1,4-azaborines in transition metal catalysis. Complexation of **23c** with Pd_2dba_3 resulted in the κ^2-*P*-η^2-BC Pd complex **24** (Scheme 5). The structure of complex **24** was unambiguously confirmed by X-ray diffraction analysis.

With a library of Senphos in hand, the Liu group achieved elegant *trans*-hydroboration of enynes. As summarized in Scheme 6, in the presence of 4 mol% sterically hindered Senphos **23c**, a vast array of terminal 1,3-enynes **25** underwent *trans*-hydroboration smoothly, affording 1,3-dienylboronates **26** with up to ＞98∶2 *trans*-selectivity.

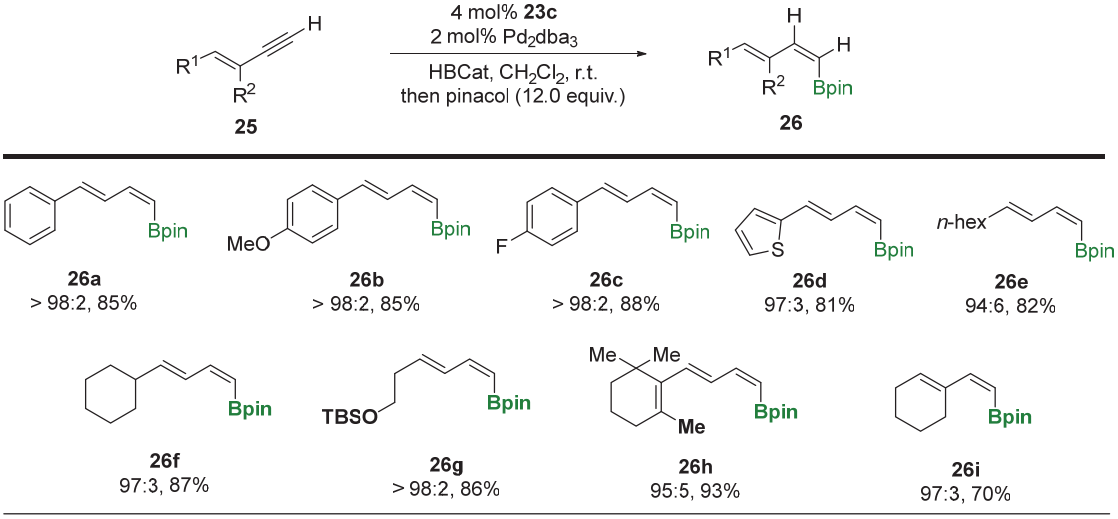
Compared with terminal 1,3-enynes, transition metal-catalyzed *trans*-hydroboration of internal 1,3-enynes is a more demanding problem and has no precedent in the literature. Internal 1,3-enynes are deemed less reactive toward hydroboration, and the control of both regio- and stereoselectivityies is a formidable challenge. Nevertheless, the Liu group was able to *trans*-hdyroborate internal enynes with a higher substrate concentration using 4 mol%



Scheme 4 Synthesis of monobenzo-fused 1,4-azaborine and its application



Scheme 5 Synthesis of monobenzo-fused 1,4-azaborine and its phosphine ligands (Senphos)



Scheme 6 Selected examples for the *trans*-hydroboration of terminal 1,3-enynes **25** with Senphos **23c**

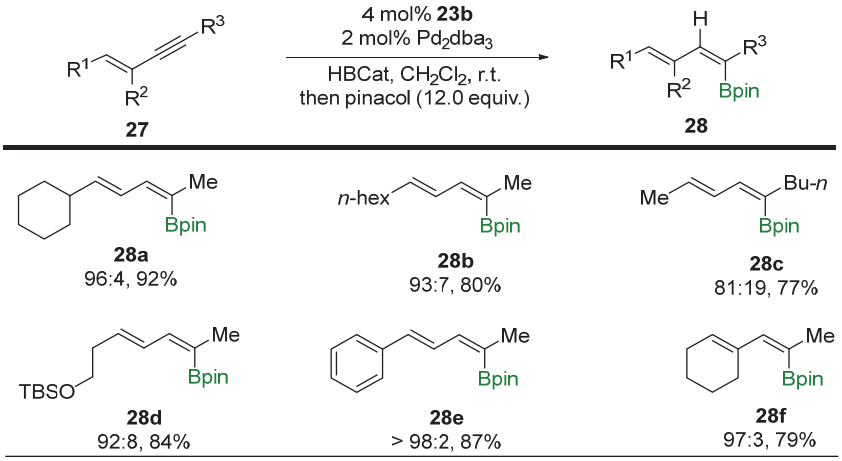
sterically less hindered Senphos **23b** (Scheme 7). A variety of functional groups could be well-tolerated, furnishing *trans*-hydroboration products **28** in good to excellent yields with up to ＞98∶2 *trans*-selectivity.

Shi and coworker[29] conducted DFT calculations and predicted the unusual reaction pathway that involved an outer-sphere oxidative addition of catecholborane (HB-Cat), followed by a hydride transfer and reductive elimination (Scheme 8).

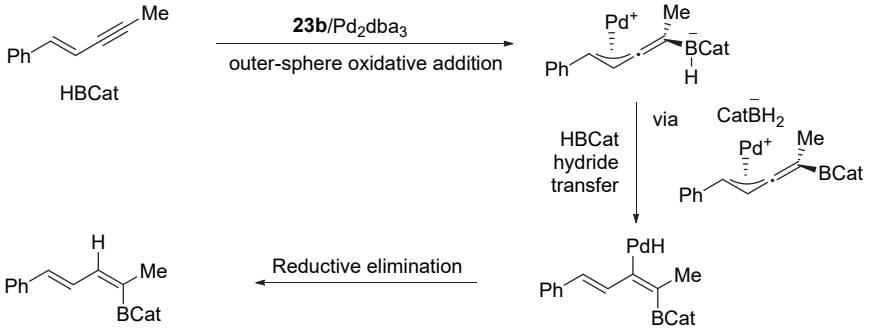
4.2 *trans*-Cyanoboration

Based on the proposed mechanism for *trans*-hydroboration of 1,3-enyenes, Liu and coworkers envisioned that chlorocatecholborane (CatB-Cl) could serve as a potential boron source capable of facilitating the outer-sphere oxidative addition step and an external cyanide anion would attack the resulting Pd complex to afford the cyanoboration product.[30] As shown in Scheme 9, in the presence of 5～7 mol% Senphos **29**, various alkyl/terminal 1,3-enynes (R^2＝alkyl, H) **30** were subjected to the Pd-catalyzed *trans*-selective cyanoboration in *o*-dichlorobenzene (*o*-DCB), followed by the addition of 1,8-diaminonaphthalene (dan), affording the corresponding *trans*-cyanoboration products **31** in good yields with up to 98% stereoselectivities.

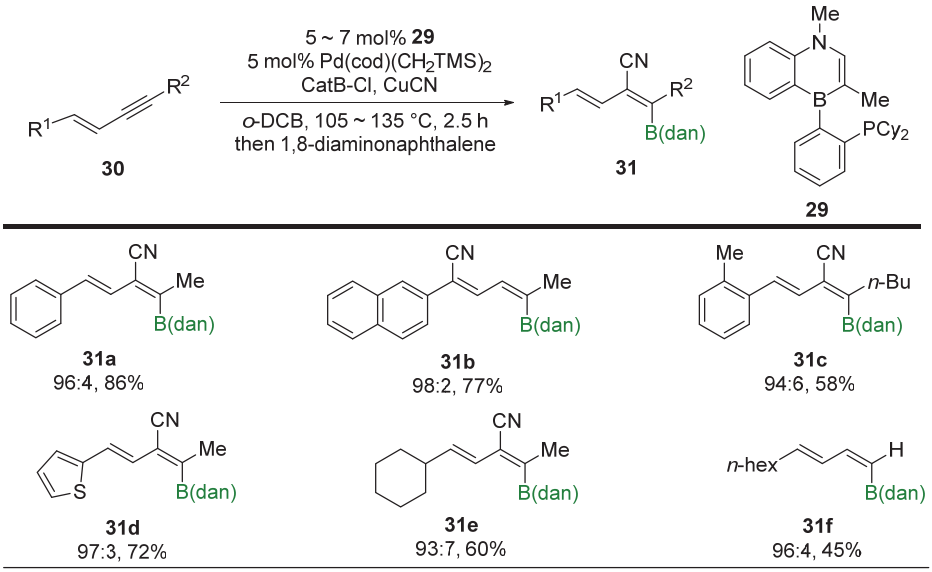
For aryl 1,3-enynes (R^2＝Ar) **32**, Senphos **23a** was found superior compared to **29** (Scheme 10). The diastereoselectivity of the reaction of diary 1,3-enynes (R^1＝Ar, R^2＝Ar) was highly dependent on the electronic nature of the R^2 group, while electron-deficient groups (**32c** and **32d**) resulted in higher *trans*-selectivity. For monoaryl 1,3-



Scheme 7 Selected examples for the *trans*-hydroboration of internal 1,3-enynes **27** with Senphos **23b**



Scheme 8 Mechanism of *trans*-hydroboration of **28e** based on DFT calculations

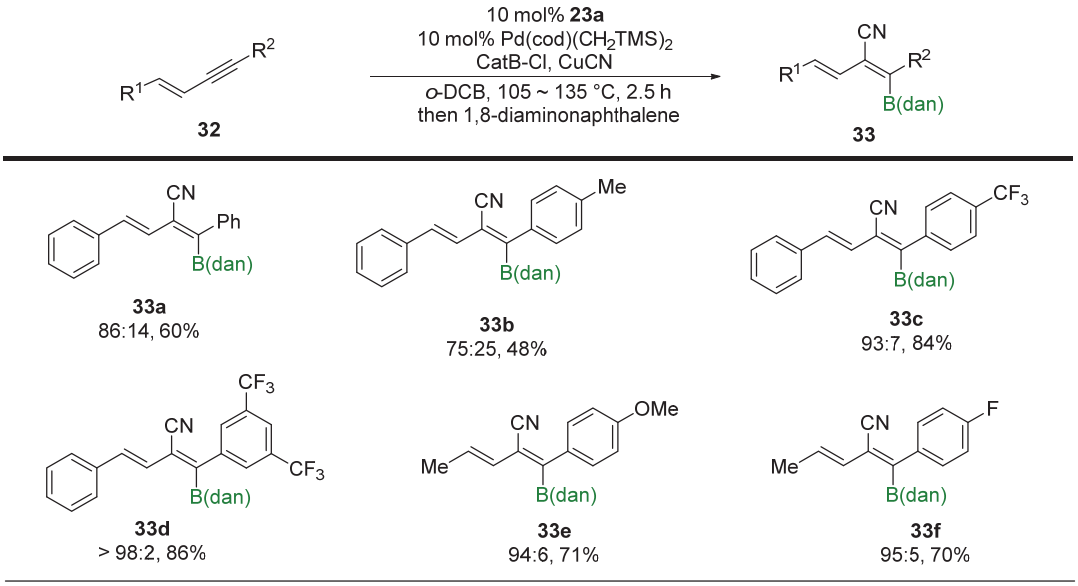


Scheme 9 Selected examples for the *trans*-cyanoboration of alkyl or terminal 1,3-enynes **30** with Senphos **29**

enynes (**32e** and **32f**), the observed *trans*-selectivity remains excellent regardless of the electronic nature of the R^2 group.

4.3 *cis*-Carboboration

In addition to cyanoboration of 1,3-enynes, the Senphos/Pd catalysis could also be used in the carboboration of internal 1,3-enynes. In this regard, Liu and coworkers developed a new family of carbon-bound boron enolates, generated by a kinetically controlled halogen exchange between CatB-Cl and silyl ketene acetals **34a** (Scheme 11A). They hypothesized that the outer-sphere oxidative addition, cooperative activation of the 1,3-enyne by Pd and Lewis acidic boron species **34a**, could result in a Pd-π-allyl intermediate that could undergo further transformation to deliver carboboration product (Scheme 11B).[31]



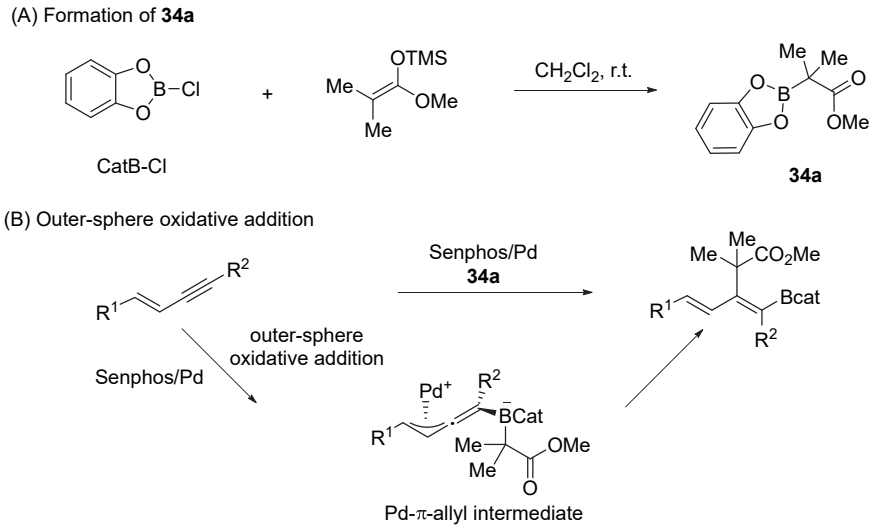
Scheme 10 Selected examples for the *trans*-cyanoboration of aryl 1,3-enynes **32** with Senphos **23a**

They found that Senphos **29** was optimal for the *cis*-carboboration of 1,3-enynes in terms of both reactivity and stereoselectivity. Carboboration of **27e** with different C-boron enolates **34** proceeded smoothly, affording the corresponding *cis*-carboboration products **35** with up to ＞98∶2 *cis*-selectivity (Scheme 12). The generality of this method with respect to the internal 1,3-enynes **27** was also reasonable (Scheme 13). Although the reaction became more sluggish using the substrates with steric demand at the R^2 group (R^2＞Me), high stereoselectivity was maintained (**36e** and **36f**).

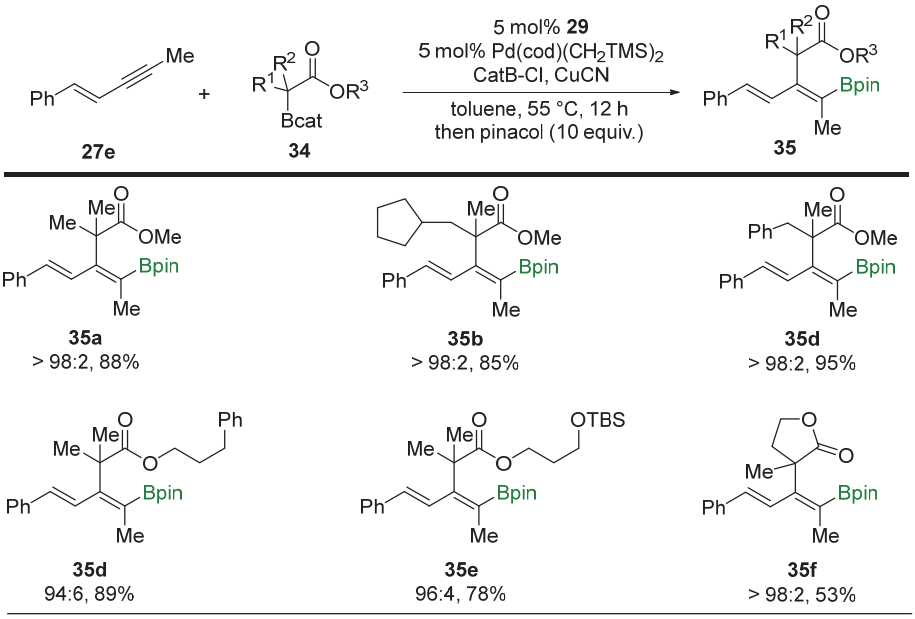
Very recently, the same group[32] reported a combined experimental and computational study of Senphos/Pd-catalyzed *cis*-carboboration of 1,3-enynes to gain more insights into mechanistic understanding. DFT calculations, ^{31}P NMR study, kinetic study, Hammett analysis, and Arrhenius/Eyring analysis revealed that a *syn* outer-sphere oxidative addition mechanism featuring a Pd-π-allyl intermediate followed by coordination-assisted rearrangements was consistent with all the experimental outcomes.

5 Summary and outlook

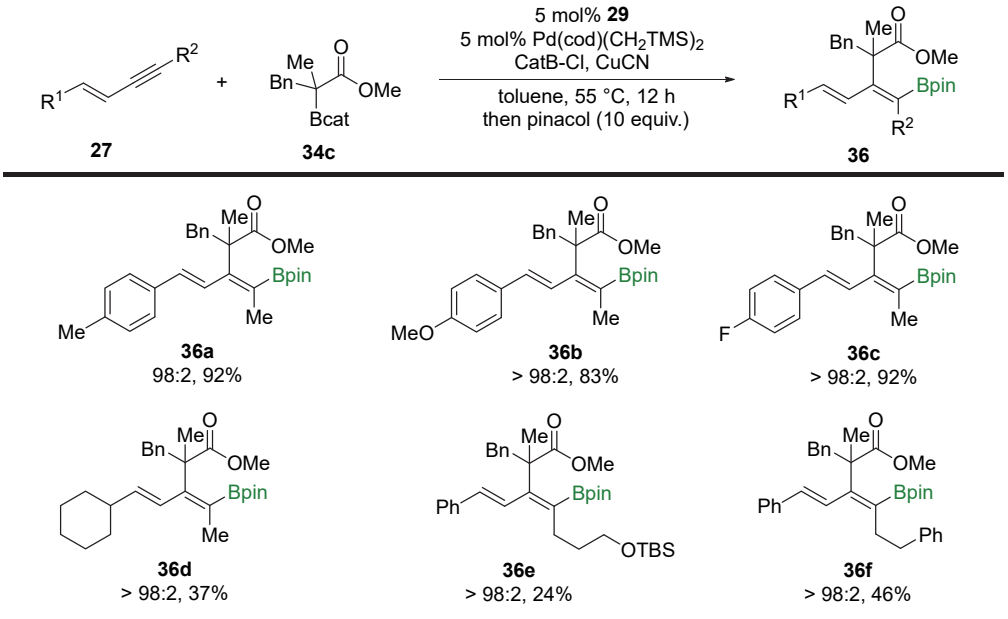
The recent progress on 1,4-azaborines in catalysis is summarized. The dibenzo-fused 1,4-azaborine could be used as the effective organocatalyst in the photooxidation of triaryl phosphines owing to its distinct photoelectronic properties. Monobenzo-fused 1,4-azaborine features a unique η^2-BC metal coordination mode. Its corresponding phosphine ligands (Senphos) were successfully applied in Pd-catalyzed *trans*-hydroboration, *trans*-cyanoboration, and *cis*-carboboration of 1,3-enynes with high stereoselectivity. 1,4-Azaborines in catalysis are still on the horizon.



Scheme 11 Formation of carbon-bound boron enolate (A) and hypothesis for carboboration of 1,3-enynes (B)



Scheme 12 Selected examples for the reaction scope of C-boron enolates



Scheme 13 Selected examples for the reaction scope of internal 1,3-enynes

The unique photoelectronic feature makes it a promising photo sensitizer in numerous photo-induced organic transformations. The electron-deficient nature of the boron atom in 1,4-azaborines could be applied in Lewis acid catalysis. In addition, the unique coordinate mode of 1,4-azaborines with transition metals paves a new avenue for the discovery of new reactions with the distinct site- and stereoselectivity, including enantioselectivity.

References

[1] Lipscomb, W. N. *Angew. Chem.* **1977**, *89*, 685.
[2] Brown, H. C. *Angew. Chem.* **1980**, *92*, 675.
[3] Suzuki, A. *Angew. Chem., Int. Ed.* **2011**, *50*, 6722.
[4] Ji, L.; Griesbeck, S.; Marder, T. B. *Chem. Sci.* **2017**, *8*, 846.
[5] McConnell, C. R.; Liu, S.-Y. *Chem. Soc. Rev.* **2019**, *48*, 3436.
[6] Giustra, Z. X.; Liu, S.-Y. *J. Am. Chem. Soc.* **2018**, *140*, 1184.
[7] Chen, C.; Du, C.-Z.; Wang, X.-Y. *Adv. Sci.* **2022**, *9*, 2200707.
[8] Campbell, P. G.; Marwitz, A. J. V.; Liu, S.-Y. *Angew. Chem., Int. Ed.* **2012**, *51*, 6074.
[9] Abengózar, A.; García-García, P.; Fernández-Rodríguez, M. A.; Sucunza, D.; Vaquero, J. J. In *Advances in Heterocyclic Chemistry*, Eds.: Scriven, E. F. V.; Ramsden, C. A., Academic Press, **2021**, Vol. 135, p.197.
[10] Oda, S.; Hatakeyama, T. *Bull. Chem. Soc. Jpn.* **2021**, *94*, 950.
[11] Shin, I.; Lim, H. N.; Hong, W. P. *Synthesis* **2021**, *54*, 570.
[12] Morgan, M. M.; Piers, W. E. *Dalton Trans.* **2016**, *45*, 5920.
[13] Wang, X.-Y.; Wang, J.-Y.; Pei, J. *Chem.-Eur. J.* **2015**, *21*, 3528.
[14] Liu, Z.; Marder, T. B. *Angew. Chem., Int. Ed.* **2008**, *47*, 242.
[15] 14. Marwitz, A. J. V.; Matus, M. H.; Zakharov, L. N.; Dixon, D. A.; Liu, S.-Y. *Angew. Chem., Int. Ed.* **2009**, *48*, 973.

[16] Xu, S.; Zakharov, L. N.; Liu, S.-Y. *J. Am. Chem. Soc.* **2011**, *133*, 20152.
[17] Li, J.; Daniliuc, C. G.; Mück-Lichtenfeld, C.; Kehr, G.; Erker, G. *Angew. Chem.*, *Int. Ed.* **2019**, *58*, 15377.
[18] Liu, X.; Zhang, Y.; Li, B.; Zakharov, L. N.; Vasiliu, M.; Dixon, D. A.; Liu, S.-Y. *Angew. Chem.*, *Int. Ed.* **2016**, *55*, 8333.
[19] Schäfer, M.; Beattie, N. A.; Geetharani, K.; Schäfer, J.; Ewing, W. C.; Krahfuß, M.; Hörl, C.; Dewhurst, R. D.; Macgregor, S. A.; Lambert, C.; Braunschweig, H. *J. Am. Chem. Soc.* **2016**, *138*, 8212.
[20] Braunschweig, H.; Damme, A.; Jimenez-Halla, J. O. C.; Pfaffinger, B.; Radacki, K.; Wolf, J. *Angew. Chem.*, *Int. Ed.* **2012**, *51*, 10034.
[21] Maitlis, P. M. *J. Chem. Soc.* (*Resumed*) **1961**, 425.
[22] Agou, T.; Kobayashi, J.; Kawashima, T. *Org. Lett.* **2006**, *8*, 2241.
[23] Xu, S.; Haeffner, F.; Li, B.; Zakharov, L. N.; Liu, S.-Y. *Angew. Chem.*, *Int. Ed.* **2014**, *53*, 6795.
[24] Xu, S.; Zhang, Y.; Li, B.; Liu, S.-Y. *J. Am. Chem. Soc.* **2016**, *138*, 14566.
[25] Hatakeyama, T.; Shiren, K.; Nakajima, K.; Nomura, S.; Nakatsuka, S.; Kinoshita, K.; Ni, J.; Ono, Y.; Ikuta, T. *Adv. Mater.* **2016**, *28*, 2777.
[26] Kondo, M.; Agou, T. *Chem. Commun.* **2022**, *58*, 5001.
[27] Porcel, S.; Bouhadir, G.; Saffon, N.; Maron, L.; Bourissou, D. *Angew. Chem.*, *Int. Ed.* **2010**, *49*, 6186.
[28] Hayashi, T. *Acc. Chem. Res.* **2000**, *33*, 354.
[29] Yang, Y.; Jiang, J.; Yu, H.; Shi, J. *Chem.-Eur. J.* **2018**, *24*, 178.
[30] Zhang, Y.; Li, B.; Liu, S.-Y. *Angew. Chem.*, *Int. Ed.* **2020**, *59*, 15928.
[31] Wang, Z.; Wu, J.; Lamine, W.; Li, B.; Sotiropoulos, J.-M.; Chrostowska, A.; Miqueu, K.; Liu, S.-Y. *Angew. Chem.*, *Int. Ed.* **2021**, *60*, 21231.
[32] Wang, Z.; Lamine, W.; Miqueu, K.; Liu, S.-Y. *Chem. Sci.* **2023**, *14*, 2082.

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